Scientific fraud – Philosophy & Science and History & Culture

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Abstract

This study examines the developments of SSRIs and the presence of them in the market. Dr. Peter Gøtszche's book *"Deadly Medicines and Organized Crime"*, claims that scientific fraud is a big part of the pharmaceutical industry and the whole healthcare system in general. Through analyzing Peter Gøtszche's book and several of his sources, the study aims to create a roadmap in the project, that resembles the process of the antidepressant drugs have to go through, to go from an idea to a patient. In the study we examine one of the most important case of Peter Gøtszche's book; the case of the SSRI called Prozac. This examination of the case of Prozac shows, that illegitimate factors have made it possible for Prozac and SSRIs to emerge and stay on the market as drug to treat depression. This study indicates that these illegitimate factors are seen and substantiated by valid scientific evidence in every step of the roadmap.

The results of the study has shown a trail of scientific misconduct, or at the very least; a lack of knowledge about good scientific ethics. The study has indicated, that more than a few different kinds of scientific frauds are used to make an antidepressant pill the most prominent, and used treatment to treat depression worldwide, even if this antidepressant has been shown to be dangerous.

Motivations

In the beginning we did not have the exact same motivations for writing this project. What unified us was our curiosity as to how scientific fraud was conducted, and in such a way that it could end up affecting so many people negatively on a large scale. So we chose the title 'Scientific Fraud' and after a number of intense discussions, we decided to focus on 'Selective Serotonin Uptake Inhibitors' (SSRIs), also known as antidepressants, or (a variant drug) 'Prozac'. We chose this because of our fascination with the cases, and because of the relevance to society. As we will see, a huge percentage of the population is, or has been on antidepressants, despite the questionable history of the drugs, their efficacy and the many reported cases of negative side effects.
As we started looking into the cases involving SSRIs, we realized that there were indeed cases of scientific fraud involved with them, but that scientific fraud wasn't the only issue. We found that dishonesty and fraud was present in several, if not most, of the links of the chain of events leading to the final distribution of these drugs. We found each link relevant to the next, and in order to understand the full picture of how such widespread fraud has happened at the expense of ordinary unknowing citizens, we investigated the most significant factors. One of our main sources of motivation became the indignation we all felt when we started learning more about the state of affairs.
One of our primary go-to sources, and portal to other relevant material in this field, has been 'Deadly medicine and organized crime' written by the Danish author Peter Gøtzsche. Gøtzsche is the leader of the Nordic Cochrane Center, a part of the respected, non-profit, 'Cochrane collaboration' known especially for its impartial reviews of trials. So we have drawn extensively on his work- and that of Cochrane, since they have provided a compass in a sector so filled with conflicting information. At the same time, though admittedly hard with the described cases - we have tried to stay as detached and objective as possible.

The human mind is delicate, complicated and should be handled with care. Yet, knowing this we see more and more people being medicated with antidepressants for sleep disorders, stress and even back problems etc. Why does this happen with medication that has side effects, which can be harmful, especially given to the "wrong" people? Are these pharmaceutical companies, who are expected to support public health, actually neglecting the very same thing and acting as just another corporation in pursuit of profit? What is the actual root problem? Is it merely a problem of overprescribing? Or is it a core problem in which even the effectiveness of the drug is nonexistent? Has oversight of the pharmaceutical industry been pervasive enough, and if not then who is to blame? These are all questions we have asked ourselves before, during and even after the completion of the project.

As we will see, the definition and use of the word 'depression' can be a controversial endeavor. In the current DSM and ICD diagnosis systems, the term is subdivided into

several subcategories. For this reason we rely on this definition of depression by The World Health Organization throughout our whole project (unless mentioned otherwise):
"*Depression is a common mental disorder, characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness and poor concentration. It can be long lasting or recurrent, substantially impairing a person's ability to function at work or school, or cope with daily life. At its most severe, depression can lead to suicide. When mild, depression can be treated without medicines but, when moderate or severe, people may need medication and professional talking treatments. Non-specialists can reliably diagnose and treat depression as part of primary health care. Specialist care is needed for a small proportion of people with complicated depression or those who do not respond to first-line treatments. Depression often starts at a young age. It affects women more often than men, and unemployed people are also at high risk.*"[1]

Introduction

In this project we want to give the reader an understanding of the most significant factors in the pharmaceutical industry, society and scientific conduct that leads to the approval of antidepressants.
To do so, we will be going through a 'roadmap' we developed throughout the writing process. This roadmap consists of: demand and idea; research and development; approval; marketing and patients. It represents the "path" a drug goes throughout it's "life", from the 'idea' to the effects from consumption of the finished product.
The ***Demand and Idea*** gives us knowledge about how pharmaceutical companies produce medicine. Some of the questions we will work on are; is it possible to cure something without knowing the cause? Depression is a term casually used, but what does it mean to suffer from depression?

In the next chapter, ***Research and Development***, we go more in depth actually explaining how trials are conducted, getting volunteers and how data is interpreted - how inconvenient data is concealed. In this chapter we will refer to a Prozac case trial were data and results were fraudulent. In view of philosophy of science we discuss the biases and bad science, biomedical ethics and what SSRIs consist of.

The falsifications and deceiving done in the research and development have a purpose in approval. In this chapter of ***Approval*** we explain how medicine is approved, what influences pharmaceutical companies have on regulation agencies and medical journals, and how ghostwriting is misused. We address some of the problems and loopholes there are in the regulatory authorities. From lies to bribery through expensive gifts and vacations, it is as if there exist no moral or ethical 'rules'.

[1] http://www.euro.who.int/en/health-topics/noncommunicable-

While approval is important - marketing is a huge factor, and the factors described in this chapter are intimately related to all the other points. In this chapter we focus on the CSR (Corporate Social Responsibility) and how pharmaceutical companies are acting in a socially irresponsible manner that is destructive to society, and how mechanisms in society in fact lead to- or facilitate this. 'Marketing' and 'Approval' overlap quite a bit, since some of the same mechanisms are used in both areas by industry, to promote both, as we will see in our Prozac example. In relation to marketing we will comment on me-too drugs and off-label marketing, where we refer to study 329.
After this, we naturally found it relevant to see the cases from the side of the ***Patients***, who the ones dealing with the consequences of consuming the drugs. In this chapter we will look at possible side effects, withdrawal symptoms and whether there are effective alternatives for treating depression.
Throughout the project we have experienced difficulties with this division into categories - as all of them are closely related. However we see this roadmap as the most effective way of explaining the process behind the release-, and the problems that exist in relation to SSRIs.

Problem definition:

- Which illegitimate factors have made it possible for SSRIs to emerge on and stay on the market?

Working questions:

- What kinds of bad science do we find in relation to SSRIs?
- How is depression defined within the diagnosis systems and are there problems within the diagnosis systems?
- How is fraud conducted in the development and approval of SSRIs?
- Is the treatment with SSRIs as beneficial as promised?
- How do some pharmaceutical companies and doctors break the principles of Biomedical Ethics?
- How are the codes of scientific conduct broken with the actions of multinational pharmaceutical companies?
- Are the pharmaceutical companies acting in a socially responsible manner, and if not, why?
- For what reasons do many doctors indiscriminately follow the advice of pharmaceutical companies?
- What mechanisms in society and in the market have helped in the widespread distribution of SSRIs?

Dimensions

This project will cover the dimensions “Philosophy and Science” and “History & Culture”. In order to do so, it will explore the ethical dilemmas concerning the use of antidepressants (psychopharmacology) to treat people suffering from depression. The project will analyse and discuss, taking both a utilitarian and deontological perspective, arguments for and against using antidepressants to cure depression, as well as looking into how antidepressants go from idea in someone’s head to the hands of millions of people affected by mental diseases. We will analyse this through a roadmap of the antidepressants pills road from idea to patient. We will use Dr. Peter Gøtszche’s Book *“Deadly Medicine and organized Crime”* as well as looking into the ethics of doctors and pharmaceutical companies through “*Principles of biomedical ethics”* by Beauchamp and Childress. To get a historical perspective on what made this development in medicine and psychiatry possible, we are intertwining the procedure of making lobotomy* a common medical treatment within our historical introduction to what made it possible for the science of medicine to believe, that by changing factors of the human brain, you could cure the illness of the human mind. To look into lobotomy as the history of psychopharmacology, we’re using Valenstein's book *“Great and Desperate cures.”* The most prominent and important case of our project, the case of Prozac, is presented through the eyes of a former marketing official of Prozac itself in the book *“Side Effects”* by John Virapen. To get an understanding of what science is we will use Herbert Feigl’s *“Criteria of science”*. This is a way for us to distinguish between common sense knowledge and scientific knowledge, and to know what makes a scientific theory reliable. Furthermore we will use books such as *“Corporate Social Responsibility – readings and cases in a global context”* by Andrew Crane, Dirk Matten & co to understand the marketing ethics and strategies of the pharmaceutical industry to get a drug marketed as the new miracle cure for depression. These books, and many more will take us through the roadmap and the developments of antidepressants from idea to patient.

Run through of theories and methods

To get an understanding of what science is we will use Herbert Feigl’s **criteria of science**. This is a way for us to distinguish between common sense knowledge and scientific knowledge, and to know what makes a scientific theory reliable.
In the philosophy of science will use the scientific theory of **causation and correlation** to distinguish between random correlations and causes behind certain outcomes.
A method of collecting and interpreting data is through **empiricism**. We refer to researchers, doctors and journalists who have collected empirical data, and we will be critical of how the data is collected, and whether it is based on strong or weak evidence. For interpretation of data we are using the information we have learned from the researchers who we refer to. We will be looking at the possible **biases** that

may occur when forming theories or conducting research. To understand the art of medicine on a philosophical level, we will look through the scope of **biomedical ethics.** We will be using **utilitarianism** that promotes the greater good for the largest amount of people and **deontology** that defines the rightness and the wrongness in terms of a duty or an obligation respecting the right and values of the individual person. The last mentioned establishes constraints on what we can or what we cannot do to others.
In relation to marketing we will utilize the **stakeholder** theory to analyze the approach and actions of the pharmaceutical companies in relation to their different stakeholder groups, which are affected by the actions of the corporations. Furthermore we will go through Corporate Social Responsibility, especially to understand whether the current level of supervision and regulation (leaving more 'responsibility' to the corporations themselves) is actually sufficient and healthy for Society. We are using the method of **case studies**, more specifically we are looking at the cases of Prozac, Paxil, Cipralex among others. In every source we are looking into, we are using source criticism as a method.

Introduction to the Prozac case

When researching which examples we should use to analyze the different frauds conducted in antidepressants, we decided on Prozac. This example is talked about in the book we first found in relation to our project, Deadly Medicine And Organized Crime by Peter Gøtzsche. We find this case to be a good case to analyze for different reasons that will be presented throughout the project.
Prozac is one of the first SSRIs* sold on the market and was developed and marketed by Eli Lilly. Eli Lilly were in deep financial debt when they launched the Prozac pill, and their survival were relying on the pills success. The problem was that this drug was actually not showing the results the company needed when doing the to be a "*totally unsuitable treatment for depression, considering the benefits as much as the risks*."[2]
But this did not stop the company which after changing data in trials, bribing physicians and even regulatory authorities, managed to make a blockbuster* out of Prozac. A 'Blockbuster' is a concept used in the pharmaceutical industry to denote a drug that generates "*...more than $1 billion of revenue for its owner each year. It is a drug which you are able to sell to even the people that are not sick! And so make such enormous incomes*."[3]
Through the eyes of John Virapen, who worked as a salesman and later became a general manager at Eli Lilly, we follow the development of Prozac. He tells us, from an insider's perspective, all the tricks and frauds that were done to change a drug from "totally unsuitable for treating depression" to becoming a 'suitable' blockbuster.

[2] Gøtzsche, 2013, p. 202
[3] Ibid, p. 73

We will be elaborating on the Prozac case throughout our roadmap. What is described in the Prozac case is shocking and not what we were expecting from a company being as influential and high profile as Eli Lilly with "*approximately 38,000 employees worldwide, Clinical research conducted in more than 55 countries and Products marketed in 125 countries*."[4]
One of the end results of Eli Lilly's actions is seen in the statistics. From 1988 to 2001 the drug made an income of $21 billion for Eli Lilly. However we see that an estimated 250.000 people tried to commit suicide on Prozac, and 25.000 actually managed. As we will see, that is well beyond the statistical occurrence in depressed people.

Lobotomy

Motivation for choosing lobotomy

The motivation for choosing the psychosurgical procedure, lobotomy, was due to various reasons. First of all the procedure was performed in the years leading up to the invention of the antipsychotic medication in the 1950s, which in its early years was referred to as "a medical lobotomy". From that perspective it seemed natural to investigate the frontrunner of psychopharmaca, the psychosurgery. When the expression psychosurgery is used it is the overall term for brain surgeries where the goal is to get a psychological reaction. This term includes both leucotomy° and lobotomy.

This gave of the idea to investigate today's most popular medical psychotreatment – the antidepressant. We quickly got an understanding for how much antidepressants are part of the postmodern society. In Denmark more than 458.300 people were diagnosed with depression in 2012. More than 13% of the population is diagnosed with a mental illness and more than 8% are diagnosed with depression [5,6]. So much for the happiest country on earth.

Researching this subject we realized some similarities in the "road map" for the lobotomy, and the one for psychopharmaca. We found it interesting to make some kind of historical perspective to the antidepressants that are over consumed today, therefore we came back to the idea of including lobotomy as a case to look for the same patterns as we were interested in in the pharmaceutical industry. We will try to give an understanding of the situation the doctors were in at the time of the rise and decline of the lobotomy to get a better understanding of the tendency to believe in what your doctor tells you.

[4] http://www.lilly.com/about/key-facts/Pages/key-facts.aspx
[5] Statens Serum Institut (www.medstat.dk)
[6] Dansk Statistik

A brief historical resume

The history of lobotomy starts in Portugal where the Portuguese neurologist Egas Moniz is performing the prefrontal leucotomy in 1935.[7] The procedure shows some good results and the young American physician Walter Freeman takes a lot of the interest in this new treatment for depression. Freeman, with his partner James Watts, fast masters the technique and especially Freeman dedicates his life to modifying and market this procedure, but with his name, lobotomy[8]

Freeman would over the next three decades operationalize the lobotomy procedure and travel around the world teaching the technique to other doctors, and performing them on more than 3400 patients before he retired at the age of 57 in 1968.

The story of lobotomy does not end with the retiring of W. Freeman. The procedure suffers a decline after the invention of psychopharmaca, and it comes to a stop in Denmark in 1983 when the last patient is lobotomized. But the story of lobotomy might not be completely over. The lobotomy epoch is now over and it is a closed part of the medical history that humanity hopes never have to relive. But are we living with a new lobotomy just with a modern labeling? And if so, is psychopharmaca the new lobotomy, and will psychopharmaca suffer the same fate as lobotomy eventually did? These questions are relevant to ask oneself if one wants to investigate the pharmaceutical industry with our angle.

An act of desperation

The invention of lobotomy was at a time where any treatment that had a potentially positive outcome should be tried.[5] In Elliot S. Valenstein's book "*Great and Desperate Cures"* he devotes a full chapter named: "*Anything That Holds Out Hope Should Be Tried*"[9]. In this chapter paints a picture of the state psychiatry in the first four decades of the twentieth century was in.[10] Having people suffering from severe and chronic mental illness was a social problem that had been at a stand still for very long. Desperate times call for desperate measures, and when Dr. Freeman's lobotomy results showed an improvement in some patients. The psychiatrist working in the insane asylums quickly welcomed the new "miracle treatment". Freeman's operationalized transorbital lobotomy was a fast and easier procedure that could easily be taught and mastered. Freeman himself could perform these in a matter of minutes and the results looked like the ones the doctors had wished for. The problem was that the results Freeman presented was not remotely close to the reality. 63% improved, 23% unchanged and 14% worse: these were the results Freeman presented after he had conducted his first 200 prefrontal lobotomies. But as the years went by and the long-term results started to show. The patients' families started to see a change in the

[7] Valenstein, 1989, p. 3
[8] Ibid, p. 3
[9] Ibid, p. 45
[10] Ibid, p. 23

patients' personality. Because of the nature of the procedure, the cutting of neuron in the frontal lobes, it caused a change in the patients' character, which frightened people's relatives, which lead to a decline in the practice of the procedure. Along with the invention of the less radical antipsychotic medication lobotomy suffered a strong decline, which lead to its full stop in Denmark in 1983. We will return to the lobotomy case in the discussion part.

Demand / Idea

So how did the demand for antidepressants emerge? Let us start by looking at how society may have changed to accommodate the use of antidepressants. The post-modern society has among many things created a disconnection or change in structure of social life, which has had a major impact on the social relations among individuals. It reflects itself in temporary, short, unstable social communities. The focus in life is centered around the staging of the individuals self and their image. This appears to be a result of an increased focus on materialism and self-realization. The importance of traditions diminishes and are seldomly replaced by new ones. This is replaced with an increased focus on individuality and the terms of life this leads to in the post-modern society. The constant reflexion upon the self and the life you're living as well as the constant and very dynamic social and technological development of the society. This increases the pressure upon the individual to create the perfect self and the perfect life according to the ideals of society, as well as keeping up with the pace of the developments in the society on a regular basis. This constantly accelerating development of the self and Society might cause stress and depression due to the large amount of pressure that comes with keeping track and participating in the Post-modern Society. This pressure from the constant changes of social demands and the need for quick actions could be one of the many reason why we see an increased number of people taking antidepressants.

Today the ideal of a good and happy life has become more of a demand from Society, than a personal ambition. The constant strive for happiness, success and fortune and the multiple options and possibilities in society have increased the demand for treatment of mental illnesses in the Western world *(write source below as footnote)*. In spite of centuries of evolutionary scientific and technological achievements that have improved our lives in so many ways, there are an increasing number of people supposedly in need of antidepressive care.[11]

An indication of the extent of the problem was published by The U.S. Substance Abuse and Mental Health Services Administration which reported that one in five Americans experienced some sort of mental disorder in January this year.[12] Comparatively in 2012 there were 13,8% diagnosed depressed people in Denmark. That is approximately 441.500 people.[13+14]

[11] Sørensen, A.D. & Thomsen, H.J, 2005
[12] http://www.businessweek.com/news/2012-12-02/psychiatrists-redefine-disorders-including-autism)
[13] http://wee.laegemiddelstyrelsen.dk/ShowElement.aspx?ElementId=5&FilterExpression=%5bIndikator%5d%3d'Psykiske+lidelser'
[14] Statens Serum Institut (www.medstat.dk)

This means, that the increased numbers of people with depression is comparable to an epidemic in society. The increased number of people getting depressed, will need treatment and in that a need for antidepressants comes.[15]

The first SSRI marketed for depression was launched in 1988. It was called Prozac (which was based on the active ingredient Fluoxetine) created by the German company Eli Lilly.

Today the sales of SSRIs in Denmark have reached a level that could provide 71% of the entire population with treatment of adult doses everyday for their entire lives or all Danes could be in treatment for 6 years.[16] The result of that is more than 400.000 anti-depressant pills being sold every year. Of the 400.000 antidepressants 100.000 are SSRIs.

The increase in depression also concerns children and young adults. In 2007 more than 500.000 children in the US diagnosed with depression. In 1987 (before SSRIs were on the market) very few children were diagnosed with a mental disorder. This means that in 20 years there has been a 35-fold increase in depression amongst children.[17]

The amount of mental disorders has increased and the definitions have been loosened through the development of the health care system. We might even be able to talk about normal reactions to the loss of a loved one (like mourning and normal temporary unhappiness) being made pathological and therefore being something that needs medical attention instead of time and compassion.[18]

In the postmodern society of today it is the constant evolution which demands the ability to adapt to quick changes. Today's society created the idea of a 'quick fix' and since then quick solutions have been requested everywhere. Especially in the medical sector dealing with issues concerning the human psyche. When people suffer from depression, it might seem like a more practical solution to use medicine instead of spending time with a therapists. There seems to be a need for escapism due to the higher demands on individuals from our present day society, as well as matters of the subconscious. A demand of a belief of persisting feelings of sadness and depression might lead people to taking actions, they would not usually do. Like taking pills to feel better. Then antidepressants is the perfect product to provide humans with a mood lifting wonder.[19]

The quick fix does not only concern the patients, it also concerns the doctors. The financial crisis have put governments all over the world under strict financial rules, that left only a small amount of money to invest in the health industry. This affected how the doctors interact with their patients because they would have less time to treat and talk to them due to lack of funding[20+21] - (Impact of economic crises on mental

[15] Wiley-Blackwell, 2010, p. 19
[16] Gøtzsche, 2013, p. 202
[17] Ibid, p. 119
[18] http://www.psychologytoday.com/blog/dsm5-in-distress/201212/dsm-5-is-guide-not-bible-ignore-its-ten-worst-changes
[19] *Trine Hjorth Sindberg, Cand. Psych. " Hjælp til et quick fix." Tidsskriftet Psykolog Nyt. Nr. 20, S. 6. 2011*
[20] http://www.reuters.com/article/2008/10/09/us-financial-health-mental-idUSTRE49839M20081009
[21] http://www.euro.who.int/__data/assets/pdf_file/0008/134999/e94837.pdf

health by WHO, Regional Office For Europe.[22+23] The solution to depression is in many cases the quick-fix, for both the doctor and the patient. Doctors, are often having time constraints, and a prescription makes room for more patients who are waiting. The solution to the treatment of a depression will not necessarily be the best, but the quickest and easiest which is anti-depressant medicine. The quick fix is a result of the postmodern society and has therefore created a demand for medicalization of mental illnesses. As the number of people with mental disorders, have been increasing steadily over the past 20 years, so have the health care costs of medical insurances all over. A large amount of Americans get their prescription medicine paid ether through their medical insurance or directly from the states. This is seen in the North American Mental Health-care costs which increased 63 % from 1996 to 2006, which meant the total cost was now $57.5 billion. As well as the total grossings of antidepressive medicine, who has increased from 17 billion dollars annually to more than 80 billion dollars a year in the united states in the last 25 years.[24+25]

Peter Gøtszche claims that psychiatry is in a deep crisis. Acute conditions have been made chronic, and normality has been mediatized.[26] A medicalization of what used to be a normal state of mind creates a diagnosis system within the health industry, that increases the number of people on antidepressants. Inappropriate medicalization might lead to both disease mongering, as well as massive amounts of people experiencing negative side effects that could lead to an actual illness or worsen the condition they had before taking the drug.

When television advertising laws no longer demanded that all side effects must be mentioned in a 30-seconds commercial, it became a lot easier to marked antidepressant and pharmaceutical drugs in general. This resulted in an enormous increase in pharmaceutical ads, that created an average of 16 hours of pharmaceutical ads for an average american tv-viewer. This amount of advertising for pharmaceutical drugs have increased the idea of needing medication. The viewers see the ad, they think they're depressed and they think medicine is the best solution for their problem. They see the colorful pill and the smiling, good-looking faces in the ad and they directly run to their local GP who in 95% of the cases will prescribe the drug. An FDA Associate Director for Science of Drug Safety, David J. Graham MD MPH explains:

> *"The Visual Image has one message, then there's the voice over and in the end there's a 30 sec voice over. The Direct-To-Consumer Advertising has created this wave of demand. Fostered this demand. And then the doctors are*

[22] http://www.euro.who.int/__data/assets/pdf_file/0011/186932/Health-and-economic-crisis-in-Europe4.pdf
[23] http://www.europarl.europa.eu/document/activities/cont/201208/20120827ATT49942/20120827ATT49942EN.pdf
[24] http://www.businessweek.com/news/2012-12-02/psychiatrists-redefine-disorders-including-autism)
[25] http://www.washingtonpost.com/business/economy/antidepressants-to-treat-grief-psychiatry-panelists-with-ties-to-drug-industry-say-yes/20%2012/12/26/ca09cde6-3d60-11e2-ae43-cf491b837f7b_story.html
[26] Gøtzsche, 2013, p. 198

just saying OK. You want this drug, you want the purple pill, here's your prescription."[27]

When the increase in pharmaceutical ads on television became a reality in Western Society, so did the increase of depressed diagnosed people and so did the increase of people with a prescription for an antidepressant. Since 1997 the sales of antidepressants and the number of depressive people have escalated. More than 1 in 4 women in the U.S. is on an antidepressant, and more than a 100 million people worldwide are using some sort of psychotropic drug.[28]

This is a dangerous tendency since, as we will see, there can be numerous adverse side-effects from ingesting SSRIs. This is not just limited to SSRIs. According to studies by Cochrane and Gøtzsche, around 100 000 people in the United States die each year due to drugs they take, even though they are taken correctly. Another 100 000 die from a dose that is too high or contradictory use of drugs. In the EU the European Commission has estimated that about 200 000 EU citizens die annually due to adverse reactions from drugs.[29] If these are the amounts of deaths, what about the less dramatic adverse side-effects?

"*Drugs are the third leading cause of death after heart disease and cancer*"[30]

A critique against the medicalization in society brought by the scientific industries themselves were published in an editorial in 2002 in the British Medical Journal. The dangers of medicalization were pointed out such as unsubstantiated decisions leading to poor treatment decisions, unnecessary labelling, economic waste and iatrogenic illness. At the same time resources will be diverted away from the prevention and treatment of more serious disease. Instead of choosing a quick fix solution (focusing on undue attention on individualised, privatised and pharmacological solutions).

These societal trends of depression, medicalization and malpractice of the pharmaceutical companies are not local phenomena, but global. As the world (especially, but not limited to the Western one) has grown more globalized (including culture, paradigms, norms and the market) the pharmaceutical companies have established themselves on these markets and brought their unique issues with them. Beyond the globalization and harmonizing of the markets that we have already seen, at the time of writing the United States and the EU are working on what could well be the biggest free trade agreement in history called Transatlantic Trade and Investment Partnership agreement, or TTIP. One of the main aims of this agreement is to remove differences in regulation between the US and European nations, removing trade barriers and harmonizing markets. One of the implications are that if the US or an EU country wants to block a product from the market, even on grounds of consumer protection, the country will open itself up to massive lawsuits from multinational corporations for 'lost profit'. This has already happened to South American nations, and even to Canada which is liable to the NAFTA agreement. In the case of Canada, the courts revoked two patents owned by (American) Eli Lilly, on the grounds that not

[27] http://www.huffingtonpost.com/2011/11/16/women-and-prescription-drug-use_n_1098023.htmlhttp://www.health.harvard.edu/blog/astounding-increase-in-antidepressant-use-by-americans-20111020362.
[28] Ibid.
[29] Gøtzsche, 2013, p. 269
[30] Gøtzsche, 2013, p. 1

enough evidence was produced on the claims of its beneficial effects. Eli Lilly's response? A lawsuit against the Canadian government for 500 million dollars and the demand that the Canadian patent laws be changed.[31]
Therefore we cannot look at these corporations from the perspective of just one country or local market. Looking at these corporations from a global perspective, we will get the full picture and we understand the fundamental mechanisms behind their actions. That is what we are doing in this project. Therefore we will be including cases from around the world mostly the EU and the US (since the numbers and cases are more readily attainable).

A culture of interventionism

According to N.N Taleb, the legal system in USA (for an example) generally favors interventionism in opposition to letting the body or psyche heal itself. And therefore doctors have incentives to prescribe SSRIs because if a patient for example commits suicide without treatment, the doctor might be sued for not intervening; From another perspective, the consequences of overmedicating have little or no legal consequences.[32]
Might there be economic and social incentives to intervene rather than doing nothing, even when it is more harmful? As already mentioned, doctors would find themselves in trouble, if they did not intervene and their patient died. They would probably be accused of not doing their job, and might face a lawsuit. From the doctors perspective it is a smaller risk to overtreat than to not treat, even if not treating was possibly healthier[33]. The whole culture of intervention and "via positiva" (adding something to a system such as antidepressants in the human body) could hypothetically be exploited by companies with interests in economic gains. As Taleb puts it:
..."*looking for disease among healthier and healthier people, lobbying for reclassifications of conditions, and fine-tuning sales tricks to get doctors to overprescribe. Now, if your blood pressure is in the upper part of the range that used to be called "normal," you are no longer* **"***normotensive" but "pre-hypertensive," even if there are no symptoms in view*" [34]

DSM

The Diagnostic and Statistical Manual of Mental Disorders (DSM) is a manual providing a common language and classification criteria for mental disorders in the United States. It is a framework developed by the APA (American Psychiatric Association) that is used in almost every area related to mental disorders, including the legal system, companies, researchers etc. Most importantly it is the system used by psychiatrists to diagnose patients with mental illness. DSM was first published in 1952 and the most recent edition, DSM-5 (published May 18. 2013), has now grown

[31] http://www.theguardian.com/commentisfree/2013/nov/04/us-trade-deal-full-frontal-assault-on-democracy
[32] Taleb, 2012, p. 363
[33] Ibid, p. 356
[34] Ibid, p. 360

to become a vast system categorizing a wide array of mental illnesses, with anything from 'psychosis risk syndrome' to 'ego-dystonic sexual orientation'.

Despite having been praised for standardizing psychiatric diagnostic criteria, it has come under a lot of criticism for lacking precision and being a too vague. Recently the National Institute of Mental Health "NIMH" (the largest agency in the world in research of mental health) withdrew its support of DSM on these grounds, saying "*There was very little systematic research, and much of the research that existed was really hodgepodge—scattered, inconsistent, ambiguous*.", also casting doubt on whether the sickness in question ever really existed.[35]

One of the questionable and very controversial recent developments in the DSM system is that it no longer distinguishes between reactions to situational contexts and actual disorders. Situational context can be life crises like disease, loss of job or divorce, episodes caused by external factors that usually subside after resolution or a certain amount of time. This has a host of negative implications, apart from the ethical and philosophical discussion about avoiding-dealing with life through pills. There are countless cases of healthy individuals having temporarily turned to pills after being suffering common life-events and subsequently getting worse or even becoming suicidal. [36]

Besides being vague, the system is also too easy to manipulate with, partly due to "revolving doors" in the APA. 'Revolving doors' refers to a phenomenon seen throughout industry, where individuals having worked at influential posts (such as the DSM board in the APA) are afterwards conveniently offered high-ranking and/or well-paid jobs in the industry. This appears to have biased the DSM system, and left psychiatrists more exposed to corruption and influences from pharmaceutical companies.[37] Furthermore, psychiatrists are not immune to corruption and 'kickbacks' since, as it turns out, they receive more money from pharmaceutical companies than any other medical specialist.[38]

What seems to be the source of many of the faults and loose diagnostic criteria in the DSM system are the ties to the pharmaceutical industry. Of the panel members responsible for 'mood disorders' in the DSM system, *all of them* had financial ties to the pharmaceutical industry.[39] Furthermore pharmaceutical companies supply one third of the APA's budget, necessarily raising the question of their neutrality.[40]

There seems to be a dangerous tendency for over-prescribing pills, and psychiatrists themselves are aware of it too. In a survey conducted in 2007; out of 108 danish psychiatrists 51% said that they prescribed too much medicine whereas only 4% said that they prescribed too little. This is widening the gap between psychiatrists. This is especially seen in the APA, at the launch of DSM-5 as well as its new diagnoses has created a lot of discussion about the ethics of labelling patients with unsubstantiated diagnoses. Many psychiatrists within the APA believe that the DSM-5 Board Committee has gone to far. Labelling people in a bereavement period for longer than

[35] http://www.psychologytoday.com/blog/side-effects/201305/the-nimh-withdraws-support-dsm-5
[36] Pillens mørke skygge. http://www.dr.dk/tv/se/pillens-moerke-skygge/. Vist: DR1, 15. APR. 2013
[37] Gøtzsche, 2013, p. 191
[38] Ibid, p. 191
[39] Ibid, p. 194
[40] Ibid, p. 80

2 weeks with depression symptoms, and labelling children, who have emotional outbursts more than 3 times a week with disruptive mood dysregulation disorder (DMDD) is going too far.

The chairman behind DSM-5 Dr. David Kupfer says: "*The aim is not to expand the number of people diagnosed with mental illness, but to ensure that affected children and adults are more accurately diagnosed so they can get the most appropriate treatment*".[41] However many psychiatrists do not agree, many believe that DSM-5 is one step closer to disease mongering as well as a more open market for the pharmaceutical industry to invent more drugs. Dr. David Fassler, the group's treasurer and a University of Vermont psychiatry professor, does not believe that DSM-5 can be misused in any way and-stated that DSM-5 "*represents a significant step forward for the field. It will improve our ability to accurately diagnose psychiatric disorders*"[42]

In the United States diagnosis and 'treatments' have skyrocketed. 12% of the US population from 18 to 54 years received treatment in 1990-92. This was up to 20% in 2001-2003, according to a study in New England medical journal. The study found that (despite there being hundreds of diagnoses in DSM-4) only about half of the people who were in treatment met the diagnostic criteria! Taking these studies into consideration, it should be of concern that in 2012 25% of Americans were reported to have a mental illness according to a study from the US Centers for Disease Control.[43]

The APA trustees of DSM's board decide what a mental disorder consists of a decision, that is made by 10-12 people casting a vote on whether or not a set of symptoms put together, can define a mental disorder. If there is a superior vote, for example 6 to 10, then the set of symptoms becomes a disorder in DSM as well as in the psychiatric system. These decisions affect millions of individuals across the USA (and influence psychiatry in the rest of the world). It extends also to mental illnesses and treatments, that a health insurance company will cover as well as which conditions schools establish for giving special care for children and young adults with mental disorders.[44]
Critics of DSM-5 claim that it pathologies totally normal behaviors. Chairman Dr. David Kupfer of the DSM-5 Task Force claims that DSM-5 has not increased in number of mental disorders and conditions, when compared to previous ones. Psychologist Frank Farley of Temple University in Philadelphia, who is among those leading an effort for an International Summit on Diagnostic Alternatives next year says as a response to the DSM-5, says that DSM-5 " *overmedicalizes human distress*,". Allen Frances (Psychiatry Professor, Emeritus at Duke, Chaired the DSM-4 Task Force) of Coronado, Calif., who chaired the task force for the 1994 revision of the manual, is worried about such repercussions: "*The issue isn't how many diagnoses you have,*" he says. "*The issue is how many new people will be diagnosed*." Chairman

[41] http://news.yahoo.com/aspergers-dropped-revised-diagnosis-manual-233900974.html;_ylt=A2KJ3CaahbtQFggA8cvQtDMD
[42] Ibid
[43] Gøtzsche, 2013, p. 193
[44] http://www.usatoday.com/story/news/nation/2012/12/01/psychiatrists-changes-diagnosis-manual/1739301/

Kupfer of DSM-5 responds: "*I don't believe we will have radically changed the prevalence*." He says it is a "*myth that we are pathologizing normal behavior*."[45]

The DSM system and the APA have been criticized for years for their wide definition of depression. Despite what Kupfer says, the definition has now gotten even broader with the DMS-5, which was only released in May 2013. We have yet to see the outcomes of the new release.[46]

"When you loose someone you love, you will often feel grief. If you feel grief for more than 2 weeks, you have major depressive disorder."[47] Dr. Allen Frances calls this medicalizing and trivializing our most normal and common emotional reactions as a human being. When you lose a loved one, its necessary and expectable to have emotional reactions concerning the loss of a loved one. Dr. Allen Frances believes that *"APA and DSM-5 now substitute pills and superficial medical rituals for the consolations of family, friends, religion and the resiliency that comes with time and the acceptance of the limitations of life"* Dr. Allen Frances believed that when APA approved the DSM-5 it marked *" a sad day for psychiatry."*[48]

Financial ties

Marsha Linehan is a university of Washington professor and a leading expert on personality disorders. *"In short the approval this weekend of DSM-5 ends years of editing but begins years of debate."* She also claims that *"This is a huge money-maker for the American Psychiatric Association"*[49]. DSM-5 opens up for a new market of drugs for the new diagnoses it presents. (http://www.healthnewsreview.org/2012/12/critic-calls-american-psychiatric-assoc-approval-of-dsm-v-a-sad-day-for-psychiatry/) A panel of experts from 90 universities worldwide revised the manual at a cost expected to be about $25 million. Mental health-care costs rose 63% to $57.5 billion in 2006 from a decade earlier, according to the National Institutes of Mental Health.[50]

An article in the Washington Post shows that eight out of eleven members of the APA committee that lead the change reported financial connections to pharmaceutical companies — either receiving speaking fees, consultant pay, research grants or holding stock as seen in secret documents, containing information about the APA committee and their financial ties to the industry as seen by the Washington Post's journalists. Six of the eleven DSM Board panelists appointed by APA reported financial ties during the time that the committee met, and two more reported financial ties in the five years leading up to the committee assignment, according to APA records. A key adviser to the committee — who wrote the scientific justification for the change — was the lead author of the 2001 study on Wellbutrin, sponsored by GlaxoWellcome, showing that its antidepressant Wellbutrin could be used to treat bereavement.

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[45] Ibid.
[46] http://healthland.time.com/2012/12/03/redefining-crazy-the-bible-of-psychiatry-changes/#ixzz2mESA6SLw
[47] http://www.healthnewsreview.org/2012/12/critic-calls-american-psychiatric-assoc-approval-of-dsm-v-a-sad-day-for-psychiatry/
[48] Ibid.
[49] http://www.businessweek.com/news/2012-12-02/psychiatrists-redefine-disorders-including-autism
[50] Ibid.

In 2010, another APA panel developed guidelines on how to treat patients once they have been diagnosed with major depression, including advice on medication. Six of the seven panelists had received consultant pay, lecture fees or research support from pharmaceutical companies, according to their disclosures. The association also appointed an oversight panel that declared that the recommendations had been free of bias, but most of the members of the "independent review panel" had previous financial ties to the industry.[51]

Research and Demand

Correlation does not imply causation.

In the philosophy of science "correlation does not imply causation" is a commonly used phrase of scientific reasoning. A common mistake is that "correlation proves causation". There are 4 statements that are possible. (1.) ***A*** causes ***B***. (2.) ***B*** causes ***A***. (3.) ***B*** and ***A*** has the same cause, but do not cause each other (4.) There is no connection between **A** and **B**; the correlation is coincidental.[52]
When you are doing a study with different types of data and control groups, it is important to recognize that even though **A** can cause **B**, and **B** can cause **A**, then **A** and **B** can also just be consequences of the same cause. But even though **B** and **A** are the consequences of a common cause in the study, **A** and **B** might not cause each other. This tells us, that the correlation could be coincidental, and that there is no proven connection between **A** and **B**.
The documentary *"Panorama - The Secrets of Seroxat from 2004*-helps us understand how two groups on the antidepressant medicine called Paxil (Seroxat) might feel better after taking the drug, compared to the control group on the placebo drug, even though it could be caused by unknown random factors. It would be assumed that Paxil was effective in treating their depression, but we could also see it as coincidental that these groups felt better being on Paxil. It is also not scientifically proven that the drug is the cause of both treatment groups feeling better. This could be caused by an effect of a milieu change or maybe even a change in treatment outside the study, for example other medications, diet changes, increased work out or a completely different factor, creating the same outcome in both groups.
In many studies done by pharmaceutical companies, Randomized Clinical Trials are done as part of the process of getting a drug approved. Randomized Controlled Trials are designed to improve our lack of knowledge about what other unknown causes might be responsible for a certain outcome. This is also known as the warranting causes.[53]

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[51] http://www.washingtonpost.com/business/economy/antidepressants-to-treat-grief-psychiatry-panelists-with-ties-to-drug-industry-say-yes/2012/12/26/ca09cde6-3d60-11e2-ae43-cf491b837f7b_story_1.html
[52] http://www.princeton.edu/~achaney/tmve/wiki100k/docs/Correlation_does_not_imply_causation.html
[53] Cartwright, 2007, p. 31

Often the hypotheses and arguments behind the trials are very simple. The hypotheses, in almost all the cases, claim that the drug is superior compared to placebo.
In addition to these claims, in many cases we see that random probabilities are mistaken as causes. In most studies, you would need every possible source of variation of data, so the conclusion will be significant and not just a result of randomness. In some summaries of data - where variables are left out, these are used to draw supposedly valid conclusions. But such conclusions are not valid, since all variables of data were not presented in these data summaries. In fact you could get the wanted result by not measuring all the variables. The lack of control of variables of any kind is seen in study 329 on the drug Paxil (Seroxat)[54] This lack of control is just another source of uncertainty about the hypotheses, as well as the conclusions made in the last phase of the clinical trial. In some cases scientists might mistake random probabilities with no causal source for statistically significant causes. The pharmaceutical industry uses randomization in its clinical trials to supposedly ensure that all causal factors for a drug's benefit or lack there of, are distributed in an equal manner in both the control groups and the treatment groups. Instead of looking at the other causal factors for an outcome, most studies aim to eliminate other sources of dependency, which is a form of selection bias. As well as controlling for factors and certain positive or negative data, that randomization misses. This means that a drug that tests well in a perfectly conducted randomized controlled trial will indeed be curing some group of the test by giving them the drugs, but it could simultaneously be fatal for a larger amount of people in a smaller or a different group. This can show us, that with any deductive method, the conclusion can only be as certain and valid as the premises of the study and the clinical trials themselves. The important point, which we can learn from these types of studies, is that by randomizing, controlling and blinding in various ways, we will automatically eliminate other sources of probabilistic randomness, or at least have calculated the effects of other sources of probabilistic randomness. When doing a study on a drug's effect and benefits or lack of benefits, it is always crucial to watch out for the placebo effect, experimenters bias, selection bias and other similar types of biased outcomes of clinical trials. Many clinical trials are biased in their outcome. Among these trials could be the study 329 of Paxil.[55] Some scientists call these continuously apparent occurrences *problems* and others call it *natural effects* of conducting clinical trials. To have a valid and honest conclusion in the last phase of a clinical trial, you need to have confidence in the results of the study. To conduct these clinical trials automatically requires someone who has a broad knowledge about the specific populations used in the trials as well as a lot of knowledge about all the procedures that are used throughout all phases of the trials. Scientists and people in the field of research and medicine, generally talk as if there already is a formula for how a study should be conducted. As all trials are different, so will the way of conducting them be. We can only make a general

[54] BBC, 2004
[55] Ibid.

point about studies, clinical trials and their methods: When there is a lack of good judgement, a lack of sound detailed prior knowledge or plain good sense in conducting a study, then it will be difficult to remain unbiased.[56]

Conducting trials

The starting point of any drug is (supposedly) in the *research and development* stage, where extensive laboratory research and testing on animals and human cells are done. Dividing the two; the research part is where the disease is understood in details on molecular levels. The development part begins after that, with the preclinical and clinical stages. Preclinical stage has to do with finding proper drug candidates and studying their properties in animals and human cells. This stage is crucial for the future of any drug as this leads to further testing on actual test subjects and therefore closer to the final approval. Hence, the clinical stage, that consists of four different phases:
Phase I *studies assess the safety of a drug or device. This initial phase of testing, which can take several months to complete, usually includes a small number of healthy volunteers (20 to 100), who are generally paid for participating in the study. The study is designed to determine the effects of the drug or device on humans including how it is absorbed, metabolized, and excreted. This phase also investigates the side effects that occur as dosage levels are increased. About 70% of experimental drugs pass this phase of testing.*

Phase II *studies test the efficacy of a drug or device. This second phase of testing can last from several months to two years, and involves up to several hundred patients. Most phase II studies are randomized trials where one group of patients receives the experimental drug, while a second "control" group receives a standard treatment or placebo. Often these studies are "blinded" which means that neither the patients nor the researchers know who has received the experimental drug. This allows investigators to provide the pharmaceutical company and the FDA with comparative information about the relative safety and effectiveness of the new drug. About one-third of experimental drugs successfully complete both Phase I and Phase II studies.*

Phase III *studies involve randomized and blind testing in several hundred to several thousand patients. This large-scale testing, which can last several years, provides the pharmaceutical company and the FDA with a more thorough understanding of the effectiveness of the drug or device, the benefits and the range of possible adverse reactions. 70% to 90% of drugs that enter Phase III studies successfully complete this phase of testing. Once Phase III is complete, a pharmaceutical company can request FDA approval for marketing the drug.*

Phase IV *studies, often called Post Marketing Surveillance Trials, are conducted after a drug or device has been approved for consumer sale. Pharmaceutical companies have several objectives at this stage: (1) to compare a drug with other drugs already in the market; (2) to monitor a drug's long-term effectiveness and impact on a patient's quality of life; and (3) to determine the cost-effectiveness of a drug therapy relative to other*

[56] Cartwright, 2007, p. 25-42

traditional and new therapies. Phase IV studies can result in a drug or device being taken off the market or restrictions of use could be placed on the product depending on the findings in the study.

Advanced technology and getting volunteers

Because of the advances in technology over the past decade the process of research and development has accelerated and made it possible for chemists to produce ten times as many compounds a year as in the past.[57]

This naturally increases the need for more test subjects, and that in itself has created new "markets" for the industry. In 1998 almost half of all patients involved in clinical trials were referred by their physician. In 2003 nearly two out of three test subjects referred themselves - going outside their care network.[58] Nowadays anyone can volunteer for clinical trials, if they fulfill the criterias given by the researcher.

Another beneficiary of the "new market" are the CRO's - contract research organization, which were, according to M.D. Marcia Angell, created out of need or rather out of the possibility for faster drug production. The CRO work's as a service where they provide *high-quality conduct of clinical studies primarily on behalf of pharmaceutical.*[59]

Trials - interpretation of data

If a company gets results in clinical trials that are inconvenient for them, the data can be hidden with no consequences. Further it can bias a trail if actions of patients are placed in the wrong category.
It is also possible to conceal suicide attempts by not measuring patients in risk of suicide and thereby biasing the trial. Underreporting suicides is also common by drug companies. Peter Gøtzsche shows that the US food and drug administration (FDA) are missing a lot of suicides in their analyses compared to data from meta analyses showing the real rate of suicides.
And then there are all the events happening after the treatments. Suicides or suicide attempts go unregistered when the treatment has stopped. The aftereffects are not measured and that means again that a lot of suicides and suicidal behaviors, among

[57] http://www.citizen.org/documents/rdmyths.pdf
[58] http://www.amazon.com/An-Industry-Evolution-CenterWatch-Staff/dp/1930624417
[59] http://web.archive.org/web/20100311082536/http://www.acrohealth.org/cro-market.php

other negative aftereffects, will be blamed on the "disease" rather than the drug. Last but not least we often see outright buried data in archives, especially the negative data.[60] The reality of the SSRIs will not be visible if documents are buried. If companies design their own trials, naturally objectivity is lost.

Concealing data and changing categories

When dealing with statistical evidence, one should be aware of randomness in amplitude and varieties in sample sizes. As an example, extremes are more likely to be found in small sample sizes. Daniel Kahneman says, there is "t*he law of small numbers*" and the illusion of patterns.[61] He argues that there is a great risk of finding extreme results, the smaller the sample size. E.g. a town of 200 inhabitants could have an extremely high occurrence of any cancer compared to the rest of the country. In another small town of 200 one could find no cases at all. Does that mean there is a certain cause of those data in the environment? It is just a common fallacy when measuring small samples. The smaller the sample size, the more prone it is to randomness.

N.N. Taleb talks about the problem of variables in sampling: "*it seems that medicine has a hard time grasping normal variability in samples—it is hard sometimes to translate the difference between "statistically significant" and "significant" in effect*"[62]

Could it be that random extremes in amplitude would heighten the average, even though it would not be significant in effect.

As explained in Peter Gøtzche's book (2013) we see very small variances between drugs, which could be due to statistical variables, that inevitably would be found in comparison between two samples: "*After 8 weeks, the difference between the two drugs was 1, on a scale that goes from 0 to 60, and the difference between active drugs and placebo was 3*" (the two drugs being cipramil and cipralex).[63]

In this case, (cipralex being 19 times more expensive than cipramil), Lundbeck had a drug that was more expensive, but that would only vary 1 point on a scale of 1 to 60. The new and more expensive drug was then marketed as more effective, and was recommended by doctors.

The difference between Cipramil and Cipralex is not necessarily significant in effect, as the difference might as well be the result of a common error in sampling. But the difference in price is totally out of proportion to the different in effect, to the cost of Danish taxpayers, as Gøtsczhe points out.

[60] Gøtzsche, 2013, p. 222-223
[61] Kahneman, 2011, p. 112
[62] Taleb, 2012, p. 371
[63] Gøtzsche, 2013, p. 224-225

Biases and bad science in opposite to intentional scientific fraud

It is important to note, that there is a distinction between badly conducted science and intentional scientific fraud. Science is prone to error when measuring. The body and especially the brain is a very complex system. When trying to measure illness or psychiatric disease, one should be aware of biases and fallacies in measuring. There is a tendency to focus on the things that get reported naturally, for example; post traumatic stress is much easier to show evidence of, as it gets reported when the patient talks to his physician, whereas post traumatic growth (psyche gaining from a trauma) is harder to measure if measured at all. What is not measured, we can call "non evidence". "*Absence of evidence is not evidence of absence."*[64] Are the depressed people who never go to the doctor then counted in the statistics if they improve by themselves? probably not.
It is possible that measuring the effects of psychopharmaca is prone to this fallacy. It is also possible that readers of scientific papers will not be able to be critical of the data if papers have not measured the absent evidence.
Peter Gøtzsche is referring to a 2005 meta analysis of trials, suggests that suicide attempts purposely were not reported in a lot of trails, or reported as something else he suggests that some reports did not even look for suicide attempts.[65] Here we have a problem, is it intentional fraud, or are the trails just prone to common fallacies? There is also a problem when you only do subgroup analysis. If you do not measure the risk groups of suicides, then you might not find results that are significant to the whole population of patients.
"A 2005 meta- analysis of published trials including 87650 patients conducted by independent researchers included all ages and found double as many suicide attempts on drug than on placebo. Even so, they found that many suicide attempts must have been missing, e.g. by asking the investigators, some of whom responded that there were suicide attempts they had not reported, while others replied that they didn't even look for them in their trials. There were other issues related to trial design that likely led to underestimation of suicide attempts, e.g. events occurring shortly after active treatment is stopped might very well be caused by the drug but were not counted."[66]

The above quote is a clear example of not measuring the data that is not there. The example of not measuring after treatments have ended could possibly give favorable results to the SSRI drugs. Not necessarily outright fraud, but at least an example of turning the blind eye to the possibility of suicide after ended treatment.

[64] Taleb, 2012, p. 250
[65] Gøtzsche, 2013, p. 223
[66] Gøtzsche, 2013, p. 223

Challenging the generally accepted view that serotonin imbalance causes depression

Despite being a widespread belief, and the official standpoint of numerous medical boards/governments, there is in fact little sound scientific evidence that lack of serotonin is the cause of depression.

Go to webmd.com and you will find a common theory on the cause of depression. It refers to "glitches" in the brain where there is a lack of serotonin receptors, an inability for serotonin to reach the receptors or an inability to produce tryptophan which is later made into serotonin.[67]
Many patients are told that they have a chemical imbalance in their brain, compared to a hormone imbalance causing diabetes. Just like a diabetic needs insulin, a person who has anxiety, depression, OCD or premature ejaculation needs an increased amount of serotonin in for the receptors in the nervous system. That is the hypothesis that Gøtzsche refuses: "*It has never been documented that any of the large psychiatric diseases is caused by a biochemical defect and there is no biological test that can tell us whether someone has a particular mental disorder. As an example, the idea that depressed patients lack serotonin has been convincingly rejected*"[68]
This seems like bad science or at least there is lack of compelling evidence to support the hypothesis of the chemical imbalance. He goes further and writes: "*Psychotropic drugs don't fix a chemical imbalance, they cause it, which is why it is so difficult to come of the drugs again. If taken for more than a few weeks, these drugs create the disease they were intended to cure*".[69] Effect might be confused for cause according to Gøtszche.
According to Alan Frazer[70], Professor of pharmacology and psychiatry, there is a cultural reason for this brain defect theory. He says in an interview on npr.org(2) that people feel more comfortable taking pills when they feel that it is a biological imbalance that needs to return to normal, compared to if they had to admit that it was a function of character.
Frazer says that there is a good side effect to the wrong belief that serotonin imbalance is the cause of depression. If people believe it is a biochemical imbalance, then it makes it more socially acceptable to admit that you are depressed and thereby more people do something about their depression. The negative thing according to Frazer is that people and psychiatrists are in this wrong belief and overlook the fact that depression has other methods of treatments than SSRIs. Talk therapy can work just as well, and unfortunately that is often overlooked according to Frazer.

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[67] http://www.webmd.com/depression/features/serotonin
[68] Gøtzsche, 2013, p. 199
[69] Ibid, p. 199
[70] http://www.npr.org/blogs/health/2012/01/23/145525853/when-it-comes-to-depression-serotonin-isnt-the-whole-story

We could potentially be looking at a false premise in the case of lack of serotonin being the cause of depressions. There might be a correlation, but the exact cause does not seem to have been isolated, if there is such an exact cause in such a complex system as the human psyche.
From observations a hypothesis about serotonin imbalance has been induced, and from that hypothesis it has been deduced that increasing the serotonin uptake must be the way to treat depression.
The hypothesis is made from inductive reasoning, both from blood tests and observations of patients on the drugs. Blood test: "In 1975, pathologists performed autopsies on depressed patients to measure serotonin levels. The initial findings were suggestive: depressed patients typically tended to have lower levels of brain serotonin compared with controls." [71]
Patient data with different drugs made way for the chemical imbalance theory. Raudixin lowered the mood: *"In 1954, a 28-year-old woman was prescribed Raudixin to control her blood pressure. A few months later, she returned to the hospital, complaining of crying spells, dullness and lethargy. She felt futile, guilty and hopeless, she told her doctors."* [72]
Iproniazid heightened the mood.- "In the autumn of 1951, doctors treating tuberculous patients at Sea View Hospital on Staten Island with a new drug — iproniazid — observed sudden transformations in their patients' moods and behaviors. The wards — typically glum and silent, with moribund, lethargic patients — were "*bright last week with the happy faces of men and women,"* a journalist wrote. "*Patients laughed and joked in the dining hall, as if a dark veil of grief had lifted*"[73]
These two observations helped make way for the chemical imbalance theory of depression. A new paradigm had risen, from observations and inductive reasoning. But the criteria for science that was suggested by Herbert Feigl were not abided by. Contradictory observations were made in 1987, with finer measure devices, but apparently the science did not regulate itself.
"*But in 1987, when researchers in Scandinavia performed a similar experiment with newer tools to measure serotonin more accurately, serotonin levels were found to be higher in depressed patients. Further experiments only deepened these contradictions. In some trials, depressed patients were found to have decreased serotonin levels; in others, serotonin was increased; in yet others, there was no difference at all.*"[74]
The scientific method was not abided by. The results were not reproduced indepently, but still the paradigm and belief of serotonin deficiency were dominating. The theory should have been revised. Feigl's criteria for example "Reliability, or a sufficient degree of confirmation" was not abided by when this theory took form, because of the contradictory data. Theories in the realm of medicine also have problems by

[71] http://www.nytimes.com/2012/04/22/magazine/the-science-and-history-of-treating-depression.html?pagewanted=1&_r=0
[72] http://www.nytimes.com/2012/04/22/magazine/the-science-and-history-of-treating-depression.html?pagewanted=3&_r=0
[73] Ibid.
[74] http://www.nytimes.com/2012/04/22/magazine/the-science-and-history-of-treating-depression.html?pagewanted=3&_r=0

abiding by the "Intersubjective testability", as there is often some cultural or economic biases as we shall see later in the chapter about marketing.

Double blind tests

Double blind tests are an essential part of medical trials, where groups trying the drug are compared to control groups. In double blind tests neither the subject nor the prescribing doctor should be aware of whether the subject is receiving the actual drug or a placebo. There are numerous examples of this not being carried out properly, for instance the doctor (who's in contact with the subject) knowing which is which, or the use of 'non-active placebos' vs. 'active placebos' - all of which can affect the trials for a better-than-placebo outcome for the tested drug.

Double blind placebo studies are used to sort out biases from expectations of the study. Expectations or time gone by can also affect the process, and that is where placebo comes into the picture. Neither the subjects participating in the study, nor the doctors giving the drugs are aware of the drugs used. An independent researcher conducts the study and prepares an active drug and a placebo. To make an effective placebo, the placebo drug should mimic the real drug in side-effects but without containing the active substance from the real drug. Two similar groups of subjects are chosen, and they must have the same conditions and characteristics (sex, disease, age). One group is given the real drug, and the other group is given the placebo. The doctors giving the two different drugs should now be able to do their own reflections and they should not know what drug is the real and what is the placebo. Neither patients nor doctors can favor one drug when they don't know what drug is the placebo. When the results are found, it is reported back to the researcher who can now judge whether the real drug is better than the placebo.[75]
According to Peter Gøtszche double blind control studies are not conducted well enough. "*As an example, researchers that performed six double blind studies of antidepressants or tranquilisers noted that in all cases, the placebo was different from the active drug in physical properties such as texture, colour and thickness. Second, even when drug and placebo are indistinguishable in their physical properties, it is usually difficult to maintain the blind during trial conduct because drugs have side effects, e.g. antidepressant drugs cause dryness of the mouth.*"[76]

He further argues that if just a few of the blinds are broken, it may be the that the result of the trail tips from insignificant to significant. Just a few patients can be the difference in whether the drug comes out as better than the placebo. he says that if the p-value, which is an indicator of the statistical significance, is below 0,05, then there is a common belief in the scientific community that the difference is statistically

[75] http://www.scientificpsychic.com/workbook/scientific-method.htm.

[76] Gøtzsche, 2012, p. 44

significant. This value is easily disturbed by just a few failed blinds, and those few failed blinds can make a drug go from ineffective to effective.[77]

Prozac trials

The Prozac trials are interesting to look at because they proclaim how trials are being carried out in a fraudulent way. John Virapen gives us a good understanding of it in his book. Here he uses a letter that Eli Lilly wrote to american doctors on August, 31th in 1990, because of fear that Prozac could increase suicidal tendencies in patients. In the letter the company wrote, it said:

"More than 11,000 individuals took part in clinical studies for Prozac, in which more than 6,000 were treated with Prozac."[78]

So according to this letter there were 6000 patients taking the actual drug. From these 6000, 400 were imaginary. From the 5600 patients that remain, not all of them took part in the clinical studies under scientific conditions. Elsewhere in this letter it is stated that only 4000 patients took part in the trials, and that many of the trials were not double-blind, comparative trials.

Only 1730 patients took part in the double blind tests. Also, on these double-blinded tests, the doctors could easily recognize the test subjects that had been taken Prozac as opposed to another non-SSRI antidepressant and placebo, as the side effects were very clearly dependent on what the patient had been taken.[79]

When looking at the patients and how they were chosen for the trials and reacted to the drug throughout the trials it showed how they are not very significant in proving how save the drug is; Some of the test subjects on Prozac had been given other drugs at the same time, and others had to stop testing due to intolerance to the treatment. Children and older people were excluded from the trials, even though once this drug was approved they would be used on them. So were also subjects with suicidal tendencies and those in psychiatric wards.

In these double blind tests, subjects that reacted too well on the placebo were excluded too. This is a measurement they took, as not to let the actual drug (Prozac) look too bad. If the placebo had been working to good compared to the actual drug, it would not have been approved.[80]

After excluding all these patients, we are left with 286 patients, taking part in a 4-6 weeks study. At the end, only 63 patients took the drug for more than 2 years. Only half of the patients that had been taking Prozac finished the minimum time required of 6 weeks.[81]

[77] Ibid, p. 45
[78] Virapen, 2010, p. 113
[79] Ibid, p. 113
[80] Virapen, 2010, p. 114
[81] Virapen, 2010, p. 115

Finally, the tests showed that out of 1000 of the subjects taking Prozac 12,5 percent of them committed suicide. Compared to this, 3.8 of the ones taking non-SSRI antidepressants and 2,5% of the test subjects taking placebo committed suicide.[82]

Biomedical ethics

History of biomedical ethics

The ethical dimension of providing care to sick people have very ancient roots. With the Hippocratic Oath, the most famous medical oath, the physicians recognized to have duties and responsibilities towards patients, colleagues and society. Redacted between the fourth and fifth centuries BC, it included, the prohibition of abortions, the use of knifes and the practice of euthanasia*.

The first real code of medical ethics, *Formula Comitis Archiatrorum* was published under Theodoric the Great in the 5th century which demanded from the physicians that they confronted themselves with others and deepened their knowledge.

In the 18th and 19th century medical ethics became more and more self-conscious thanks to Thomas Percival author of the first modern code of medical ethics.

In 1815, the Apothecaries Act was passed by the Parlement of the United Kingdom This was the beginning of regulation of the medical profession in the UK while it was first in 1847 that the American Medical Association adopted its first code of ethics, based in large part upon Percival's work.

It was after the revelation of Nazi-experiments on humans during world war II that the second biggest scientific revolution from medical ethics to bioethics happened. Bioethics* is generally defined as the study of the moral dimensions of medicine and biomedical sciences. Since the early seventies, it gradually took over from the older tradition of medical ethics, lead only by physicians. One of the most significant features of the new bioethics discipline is represented by the entry of other figures (jurists, theologians, philosophers, social workers, economists) in decision-making areas that were once solely within the purview of doctors and their patients and the interdisciplinarity of the subject including philosophy, philosophy of science, medicine, biology, genetics, epigenetics, embryology, jusnaturalism, politics and law.

In consequence to the Nuremberg trials*(1947), the foundation of WMA* and the declaration of Geneva* (1948) the renewed principles within biomedical ethics were summarized in june 1964 in the declaration of Helsinki*. The latter has since then been subject to six revisions and two clarification, and remains until today the most important set of ethical principles regarding human experimentation developed by the World Medical Association.

[82] Virapen, 2010, p. 108

Respect for Autonomy

The word autonomy comes from the Greek *autos* ("self") and *nomos* ("law"). Originally it was referred to the political situation of the ancient Greek *poleis* but acquired after that different meanings as self-governance, liberty rights, privacy, freedom of choice and will. Clearly autonomy can not be considered a univocal concept.

What establishes the autonomy of a person? When is a person autonomous?

An autonomous individual acts freely within an established plan of rules, laws, morality etc., whereas, for example, we ignore prisoners or mentally ill peoples autonomy by institutionalization or mental incapacitation limits.

Virtually, autonomy is based on two conditions: *liberty* as independence from controlling influences and *agency* as capacity of intentional action.

Some theories feature these two conditions with other capacities as understanding, reasoning, deliberating and independent choosing. (The latter is highly interesting as it often happens that even people with self-governing capacities, considered autonomous on the paper, fail. The cause can be anything as temporary constraints caused by illness, depression, ignorance, coercion, etc.)

An autonomous person is characterized by capacities of self-governance as being able to make choices, to hold views and to take action based on personal beliefs and values and in order to respect this, *respectful actions* are required.[83] Respectful action in fact not merely consists in respectful attitude or noninterference in others' personal affairs. It includes the obligation to build up the capacities for autonomous choice, to allay fears, considerable the worst enemy of autonomous and conscious choices, to acknowledge decision-making rights and to enable people to autonomous action. Although cases of conscious disinformation are frequent. Within the medical world there is a culture that allows the acceptance of easy money. In the hole world there are cases of drug companies offering to transfer money in the strangest ways to physicians in order to keep it unseen.[84]

Why do we owe people all this respect? Two philosophers principally influence nowadays conception of autonomy: Immanuel Kant (1724-1804) and John Stuart Mill (1806-1873). Kant sets a moral imperative of respectful treatment arguing that, as all person have unconditional worth, being able to determine his or her own moral destiny, it would be as using the means that is without regard to that person's own goals. John Stuart Mill, on the other hand, requires not interfering and actively strengthening autonomous expression. For Mill autonomy was almost synonymous of

[83] Beauchamp, 2001, p. 63
[84] Gøtszche, 2013, p. 71

individuality, in that sense that society should give individuals the possibility to develop according to their beliefs, convictions until they don't interfere with the freedom of others.

Respect for autonomy obligates professionals in health care to disclose information, to probe for an ensure understanding and voluntariness, and to foster adequate decision making.[85] Although, even if physicians often act in bona fide, they are subjected to too much noise, meaning too much conflicting information, oftentimes provided by the industry and not backed up by proper science. "*Doctors only have access to selected and manipulated information and therefore believe drugs are far more effective and safe than they really are*".[86]
The opinion of the co-editor of the British Medical Journal is that the pharmaceutical industries are not always to be considered the villains and doctors the victims. For doctors to do the best for their patients, they will have to prescribe the products the pharmaceutical industry develops, and furthermore:
"*[...]and it's reasonable that the industry should be able to promote its products. But surely doctors should be looking also to independent sources of information, and how did we reach a point where so many doctors won't attend an educational meeting unless it's accompanied by free food and a bag of "goodies"? Something's wrong, and medical journals are part of what's wrong*."[87]

In general we can say that autonomy within health means respecting the patient values, choices, beliefs and personal views before taking action. This is for example also why physicians are requested by the law to declare officially if they collaborate and are paid by pharmaceutical industries.[88]

As a starting point every individual has control over one's own body. Respect for autonomy is exercised by obtaining an informed consent before starting any kind of treatment. It is the physician's duty to inform, explain and make sure the patient has understood everything about the proposed treatment before signing a consent form and then taking action. Because of the way in which respect for autonomy functions in the moral life, it is capable of supporting other moral rules as telling the truth, respecting privacy, protecting confidential information, obtaining consent and, when asked, giving good advice.

Respect for autonomy has only prima facie standing and can sometimes be overridden by competing moral considerations.[89] If our choices imply potential harm to others, others can legitimately restrict our autonomy. Furthermore, the obligation to respect autonomy can't be extended to people who are unable to act in an autonomous way such as children, irrationally suicides or drug-dependents. Nevertheless the choice of

[85] Beauchamp, 2001, p. 64
[86] Gøtzsche, 2013, p. 37
[87] http://www.bmj.com/content/326/7400/1202?maxtoshow=
[88] Gøtzsche, 2013, p. 72
[89] Beauchamp, 2001, p. 65

deeming a patient incompetent of autonomy isn't left in the hands of each individual physician. Standards of incompetence express the range of inabilities required to be deemed incompetent of autonomy, which are: inability of stating a preference, inability of understanding information and appreciating one's situation and inability of reasoning through a consequential life decision.

Nonmaleficence

Primum non nocere

"Above all do not harm". The principle of nonmaleficence sets the obligation of not bringing harm to others. The maxim, not appearing in the Hippocratic oath, is although contained in the latter: "*I will use the treatment to help the sick according to my ability and judgment, but I will never use it to injure or wrong them*"[90]

The principle of nonmaleficence is although backed up by more specific and moral rules such as:

- Do not kill.
- Do not cause pain or suffering.
- Do not incapacitate.
- Do not cause offense.
- Do not deprive others of the goods of life.[91]

The principle of nonmaleficence not only consists in an obligation of not inflicting harms but includes also the duty of not imposing risk of harm. Undoubtedly it can happen that a persona can harm or put someone in risk without any malicious or harmful intent and the juridical/moral border in these cases is very subtile. In case of risk imposition a set of moral and juridical rules fixing the standard of due care determines if the responsible agent is morally and juridically guilty. Due care is taking sufficient and appropriate care to avoid causing harm, the the circumstances demand of a reasonable and prudent person.[92] This standard implies that the goal justifies the risk. Goal and risk have to be proportional.

Negligence is the absence of due care and it covers two types of situations: (1) intentionally imposing risk of harm that brings to a knowingly unwarranted risk and (2) unintentionally imposing risk of harm that brings to an unknowingly performance of harm that should have been known and avoided. Of cause both types of negligence are reprehensible, though circumstances can sometimes mitigate the blameworthiness.

[90] Beauchamp, 2001, p. 113
[91] Ibid, p. 117
[92] Ibid, p. 118

In any case it is duty of the Courts to determine who is responsible, in which grade, and which actions are blameworthy. Professional malpractice is, for instance, an example of negligence. A physician not following the prearranged standards doesn't do his or her job correctly, as the standards require proper training, diligence and skills.

The precise task of nonmaleficence in health care has been subjected to religious tradition, to philosophical thinking and not the less to the law with particular attention to treatment and nontreatment decisions. Some of the established guidelines are up to date and helpful while some of them are to be revised or replaced. One of the mostly debated guidelines is about the omission/commission distinction, more precisely the distinction between withholding (not starting) and withdrawing (stopping) treatments. Especially family members, more sentimentally involved, but also physicians themselves feel allowed an justified to withhold a treatment but not in withdrawing a treatment already started. The human perception of stopping a treatment is more directly linked to killing someone than not giving a treatment at all. So what is the right thing to do? If we have a patient shortly to die, should we or should we not start a treatment? What about those people confined to a vegetative state with no hope of recovering? Should their treatments be suspended? Tom Beauchamp and James Childress conclude that the distinction between withholding and withdrawing is morally extremely complex and dangerous. "*Decisions about beginning or ending a treatment should be based on considerations of the patient's rights and welfare, and therefore on the benefits and burdens of the treatment, as judged by a patient or authorized surrogate*". [93]

Beneficence

We can consider beneficence as the moral requests of contributing in a person's welfare. Differently from the principle of nonmaleficence, beneficence consists in an agent taking an active positive step to help others. There are two types of beneficence: positive beneficence and utility. The first one requires agents to provide benefits while the second one is based on the balance between benefits and drawbacks to assure the best outcome.

The term beneficence connotes acts of mercy, kindness, and charity. Forms of beneficence also typically include altruism, love and humanity. Beneficence refers to an action done to benefit others; benevolence refers to the character trait or virtue of being disposed to act in benefice of others (Beauchamp, Childress 166:2001).

As *Nonmaleficence,* also beneficence is supported by many moral rules as:

- Protect and defend the rights of others.
- Prevent harm from occurring to others.

[93] Beauchamp, 2001, p. 122

- Remove conditions that will cause harm to others.
- Help persons with disabilities.
- Rescue persons in danger.[94]

We can see that there are clear differences between the rules and principles of beneficence and nonmaleficence. Nonmaleficence is based on (1)negative prohibitions, that need to be (2)followed impartially, and provides (3)moral reasons for legal prohibition. On the other hand beneficence is based on (1)positive requirements of action that (2)not always need to be followed impartially and it (3)rarely provides reasons for legal punishments. The second condition, impartial adherence, is interesting and worth to deepen. It is morally incorrect to harm anyone while it is morally permitted to behave partially regarding beneficence. We are allowed to help and benefit those with whom we have a special relationship (family, friends, lovers, acquaintances, etc.) before helping people with whom we have no special bond.

Sometimes the "relation" between beneficences and the rules of nonmaleficence can be turned over: the requirement to benefit may be overridden if we can produce a major benefit by causing a minor harm, or a major benefit for more people while causing a minor harm for only a few.[95]

Since ever it seems that the primary obligation in health care is beneficence. However, in recent years medicine has increased patients rights to judge independently about their own medical fate leaving apart all professional opinion. In result to this we can say that the problem of paternalism looms and increases proportionally with autonomy rights.

Treating a patient, the physician not only has to consider the rules of beneficence but also the costs and the risks of the treatments. Costs are "*the resources required to bring about a benefit*". Risk "*refers to a possible future harm*" while harm "*should be perceived as a setback to interests, especially in life, health and welfare*". The term *benefit* "*refers to something of positive value, such as life or health*"[96]. The job of the physician will be to find the best balance between the beneficence, the cost and the risk in order to assure the best overall benefits of the patients.

Justice

Conscious of the fact that many principles of justice proposed by various philosopher through the years are not distinct and independent of other biomedical principles as beneficence and nonmaleficence, justice is considered as "*fair, equitable and appropriate treatment in light of what is due or owed to a person*". Standards of

[94] Ibid, p. 167
[95] Beauchamp, 2001, p. 168
[96] Ibid, p. 194

justice take over whenever a person is harmed by someone else, so in fact in need of his/her due benefits or burdens. On the other side distributive justice refers to "*fair, equitable and appropriate distribution determined by justified norms structuring the terms of social cooperation*".[97] Problems about distributive justice arise when you have conditions of scarcity and competition.

Issues about the fairness of distribution bring to the formulation of principles of justice such as:

- To each person an equal share.
- To each person according to need.
- To each person according to effort.
- To each person according to contribution.
- To each person according to merit.
- To each person according to free-market exchange.[98]

Several theories have been proposed in order to distribute and redistribute in the best way social burdens, goods and services as health care. Within them, one of the most quoted is Utilitarianism. According to this theory the standards of justice should depend on seeking the maximized overall good.

The principle of justice, which requires from healthcare professionals that they treat their patients with just and fairly, puts in question the other principles of biomedical ethics and sets limits to them. Re-calling into question the universality of the three previous principles, justice adds further moral dilemmas to the many ones already existing. Although justice is necessarily to be considered whenever a physician is asked to make a moral decision about a patient's treatment.

Utilitarianism

Utilitarianism is a consequence-based theory that aims to establish rightness or wrongness according to the balance between good and bad consequences. The right act is that act bringing the best overall result. Utilitarianism presents one and only central basic principle: the principle of utility. This principle asserts that we always ought to produce the maximal balance of positive value over disvalue.[99] The classical origins of utilitarianism are found in Jeremy Benthams and John Stuart Mills words. Their idea about utilitarianism was mainly referred to everyday life, showing that we all engage in utilitarianism in very simple and practical ways. As hedonistic utilitarians they conceive utility as happiness and pleasure.

[97] Ibid, p. 226
[98] Beauchamp, 2001, p. 228
[99] Ibid, p. 341

However many utilitarians question which are the right values to be maximized. Often agent-neutral and intrinsic goods such as happiness, freedom, health seem to be the best answer. Nowadays , many philosophers argue that different values as friendship, knowledge, health, beauty, autonomy, achievement, success, understanding, enjoyment and relationships also are intrinsic values to be maximized. The list of values may differ through time but what remains unchanged is the main principle that we should pursue the "*greatest good in terms of the total intrinsic value produced by an action*"[100]

There are two types of utilitarianism: (1) rule utilitarianism and (2) act utilitarianism. The first one considers the consequences of behaving according to rules while the second one skips any kind of rule and justifies actions referring directly to the principle of utility. The act utilitarians question "which consequences will result from this action and circumstances?". Rules are totally in second instance. For the rule utilitarians the rightness of an act is set by following or not following justified rules. Act utilitarians do believe that telling a lie is allowed if the lie protects the individual, whereas rule utilitarians absolutely prohibit deception in health care. To clarify, act utilitarians allow physicians to lie to a patient if this will help the latter, keeping him or her from getting worse, jeopardizing their treatments or give them hope. Rule utilitarians, on the other hand, totally dismiss deception, sustaining that doctors should always be truth-telling. Utilitarianisms affirms that the only absolute principle is utility. "*The rule utilitarian argues that we should support rules permitting killing if, and only if, those rules would produce the most favorable consequences. Likewise, there should be rules against killing if and only if those rules would maximize good consequences*."[101] Utilitarians also say; "*we do not presently permit physicians to kill patients because of the adverse social consequences that we believe would follow from those directly and indirectly affected*."[102] Undoubtedly there are different critical evaluations of utilitarianism. One of the biggest issues is that we can't know what are good and what are bad consequences and which consequences are the most important ones. (Opinions are subjective, so rightness and wrongness changes from person to person.) These insecurities make utilitarianism a not so applicable theory as it originally seemed. For this, the theory shouldn't be dismissed totally but one must observe that we can use utilitarianism for some cases, but not for all of them. In conclusion we can say that utilitarianism is a consequence-based theory but also a beneficence-based theory so "*a theory with a principle of beneficence that is balanced by other principles should eliminate all the problems with an unqualified use of the principle of utility*."[103]

[100] Ibid, p. 341
[101] Beauchamp, 2001, p. 345
[102] Ibid, p. 345
[103] Ibid, p. 348

Deontology

Deontology or Kantianism, can be understood as the set of ethical rules that are opposed to consequentialism. While consequentialism, consequence-based, determines the goodness of actions by their results, deontology, duty-based, states that ends and means are closely dependent on each other, which means that rightness will be the end result of using just means.

The name *deontology* comes from the Greek "Δέω"-deo- which means "duty" and "λόγος"-logos- which means "discourse". The objective in the formulation of Kant's theory was to establish an ethical system that did not depend on subjective experience, but on irrefutable logic. Importance isn't given to the consequences of actions but to actions themselves. Deontologists look at the world through fixed rules (categorical imperatives), establishing if actions are prohibited or made obligatory. Kant assigns to logic, through the categorical imperative, the duty to determine the reasonableness of an action. Categorical imperatives are usually of a negative nature, as for example "do not lie" or "do not kill" but can also be expressed positively such as "tell the truth" or "respect every ones life". According to deontology one must follow attentively the rules, and as long as one does so, he or she can't be denounced as all consequences are unpredictable.

In deontology we find some actions that are universally bad and prohibited, considered wrong in themselves, such as killing or lying.

This theory introduces the word *universality*. What is right or wrong for one person should be right or wrong for all.

According to deontology, very self-focused theory, the most important thing is ones own "goodness". It is morally accepted to favour at first you own benefit before helping others. Although one of the major loopholes of deontology is that it does not take in consideration the consequences that actions may have. Even if one may in theory have acted according to morality, the outcome of this might be highly negative.

The Prozac case through biomedical ethics

The main aim of this chapter will be to analyze the very multifaceted case of Prozac through the established and ingrained basic rules and theories of biomedical ethics.

In itself, respect for autonomy within psychopharmaca is a very delicate subject. People who are affected, pretend to be affected or are diagnosed to be affected by depression often happen to be, in some way, mentally instable. The reasons can be different from case to case: it could be physical/chemical, psychological causes or even a social situation inclined to disorders of any kind. So that a patient can be considered responsible of his/her own choices, he/she must fulfill the criteria

establishing the ability or inability of judgment, of rational and logical thinking and of conscious decision-making. However, even if a person can be deemed as incapable of deciding his/her medical best, physicians are required to respect personal principles (unless they severely interfere with the health of patient himself). The situation is different from for example someone refusing blood transfusion for religious belief, and is on a more ideological level. (Suicide tendencies)

In nowadays society antidepressant are not anymore a simple pill, taken by who is in need of them, but a phenomenon that is taking over. Not any more menaced by open field wars, by atomic bombs or by epidemics, humanity finds the time to think about more intimate, personal, sentimental things. The result is a huge wave of "new" fears, more mental and irrational in opposition to the former ones, more instinctive. People are depressed, anxious or scared and the pharmaceutical industry work intensely to find some kind of cure for it. But a cure for what? A cure for normality, for everyday life? We need to get used to which way the world is going and this may eventually take years.

(law about informed consent) Within the respect for autonomy doctors and the pharmaceutical industries have precise duties established by deontology such as disclosing the right information, in the right amount and in a way that is clear and comprehensible to the patient. Deontology is there to protect the patient. This set of negative principles state maxims that establish the relation between doctors and patients. For example, physicians are not allowed to lie to autonomous patients or harm them in any way. If the patient is incapable of autonomy, then the doctor would be requested to act paternalistically. Deontology, furthermore, has been summarized in the law about informed consent. Prozac in itself arises as a drug running against these principles. Presented as a totally new product with revolutionary effects, Prozac is the marketing name of fluoxetine edited in 1988. Eli Lilly found itself in huge economical problems and decided that they were in need of a "blockbuster" able to revive their situation. Fluoxetine had been judged "*totally unsuitable for the treatment of depression*", but it was brought on the marked, simply changing it's name and organizing false approvals in Sweden to make it's efficiency more reliable and truthful.[104] Prozac appeared from the start on the international horizon as a lie. Doctors were introduced to this new, revolutionary, helpful antidepressant, presented to them during long, 100% paid, vacations to the Carribbean.[105] The information dynamics started out in the wrong way. Eli Lilly "attacks" the physicians by relating to feelings of friendship, pleasure, enjoyment and sense of duty securing, in this way, the selling of their pill. From the total start of the chain the autonomy principle is broken. The opinion of the physicians is conditioned and deviated through inputs absolutely not regarding an academic interest. Physicians are informed incorrectly or only partly about the necessary details such as side effects, applicability, approval circumstances etc., and are therefore incapable of giving an objective and correct

[104] Gøtzsche, 2013, p. 202
[105] Ibid, p. 202

report about the drug to their future patients. If asked so, a physician should be able to help with a reasonable, true, objective decision-making, but what about this case? One could probably support that a very high percentage of the marketing of Prozac worldwide takes place under conditions of "conscious" disinformation.

The basic principle of a doctor's job is to help people. By going to the doctor you would expect help to get better. The problem nowadays is the tendency to the quick fix. We want to be cured as fast as possible so we can return to our everyday life. The problem is that many times, the best cure for an illness is time. When a patient with depression goes to his doctor and wants to get a "solution" to his problem the fastest way of getting it will be in form of pills. In different tests it has been proven that alternative treatments, such as sports, can be very effective. Their only disadvantage is that they are not as suitable for all patients as a pill, because of matters of time, money, etc. A further obstacle arises when a patient's time requests are incompatible with the doctors time schedule. This leads in some cases to prescribing not the exact drug, matching for the symptoms, but the one that pops up on the computer, as explained in the chapter of approval.[106]

A point we thought to be very interesting for this case was the idea of withholding vs. withdrawing medicines. This refers to not giving a patient a treatment instead of giving them something that may even harm them. As seen in other chapters of this project interventionism is very spread in our society. Doctors would find themselves in trouble, if they did not intervene and their patient died. They would probably be accused of not doing their job, and might even face a trial. These are some of the reasons why the main tendency to prescribe drugs very fast, often without it being necessary. In the worst cases physicians, threatened by the interventionistic "trend", prescribe medicine for the wrong reason. Peter Gøtzsche talks about many different examples in which people suffering from headache, dizziness, stress, tiredness were recommended to take antidepressant even if their prognosis wouldn't at all declare them so.

"*I'm scared that my son will also be turned into the type of person that the pharmaceutical industry loves the most – a willing pill-popper, who takes medicines for made-up illnesses and those you are talked into having, with deadly side effects included in the price. The pharmaceutical industry is changing the reasoning of the coming generation.*"[107]

The medical profession is based on the principle of beneficence. As a doctor your main interest should be the well-being of your patients. You should be aiming to do the best for ill people trying to find out what is the most fitting solution for each

[106] Virapen, 2010, p. 31-32
[107] Virapen, 2010, p. 12

single case. The Hippocratic Oath forbids the doctors to "do harm to anyone". This is a fixed ethical rule, which insures that a doctor would not misuse their knowledge to harm their patients. But is misleading not a form of harming of the patients? Misleading can cause harm to a patient if the patient is misinformed or in any other way does not know the full information of the treatment the doctor is giving or performing. The Hippocratic Oath is more of a moral codex today than a binding contract. Today a doctor who performs malpractice will be judge after the laws of the country, but most of the elements of the oath are also a part of the laws concerning the medical practice.

The oath origins from ancient Greece, and even though we in live in a society where illegal actions are punished by laws, the oath still laid out some ground principals for a doctor to follow.

Psychopharmaca is an excellent example of an enterprise that is unethical. Pills are produced for illnesses that are made-up by companies themselves in order to make more money. One is not interested in finding out what the real problem is, but in selling most samples to the largest range of people with the most different symptoms possible.[108]

Doctors seem, contrarily to what one would expect, to be totally disinterested in what the drug in fact implies. They appear detached, almost unaware of the consequences of their acts.[109]

Beneficence is a totally subjective principle. One can be more or less benevolent depending on ones own character traits. Impartiality is allowed because natural and human; one tends to be more compassionate with people nearly attached. The absurdity about a case as Prozac is that pharma-insiders such as John Virapen don't pass from being not beneficent to some and beneficent to others but from seriously harming thousands of people to realizing, through, for instance, the birth of a baby son what they actually are doing and reacting in the total opposite way, maybe rejecting their former work. In the pharmaceutical pharmacy it is more difficult to establish when something is wrong or right as it deals with human minds, with the psyche, unpredictable, and very different from person to person.

As it has been explained before, utilitarianism is based on the idea of pursuing "the greater good". The goal in utilitarianism is to have as many people happy as possible. In this special case the utilitarian approach is interesting as it can give us an idea why Prozac is being marketed even though it is known to be harmful. When the people responsible for these products talk about it they usually have an utilitarian approach: The drug may not work for everybody, but it saves many others peoples lives![110] This is a very common point of view. In this case though the problem is that Prozac has

[108] Ibid, p. 80
[109] Ibid, p. 83
[110] http://www.veoh.com/watch/v251729w7zYxt2H-Documentary

been proven to not help their patients. In most of the cases patients get very severe side effects sometimes developing suicidal tendencies. If we look at how many get injured from Prozac compared to the ones getting better we see it is not "the greater good" that is being done in this case. In numbers, the tests show that out of 1000 persons taking Prozac 12,5 persons of them committed suicide. Only 3.8 of the ones taking non-SSRI antidepressants and only 2,5 of the ones taking placebo committed suicide.[111] Looking at this numbers we see that even through an utilitarian approach, applied by big companies who try to excuse themselves, it does not work.

[111]Virapen, 2010, p. 105-108

Approval and Regulation

The FDA (Food and Drug Administration), is a regulation agency located in the United States where they administrate the market of food and drugs. According to themselves they are:

"..responsible for protecting the public health by assuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.

FDA is also responsible for advancing the public health by helping to speed innovations that make medicines more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medicines and foods to maintain and improve their health.."[112]

FDA being the biggest regulatory agency in the world they do work together with other agencies outside the USA. In Europe or rather in the EU there is the EMA (European Medicines Agency) which is located in London. They are responsible as well as the FDA, to evaluate the development of medical drugs produced by pharmaceutical companies in the EU. The two agencies work closely together when reviewing medical products.[113]

What it takes for a drug to be approved

The research and development part of a drug consists of two main stages - preclinical and clinical. The relevance it has in the approval part is in the clinical stage which is regulated by the FDA. Before any drug can be approved it has to provide evidence to the regulator that the drug is safe and effective. The evidence requires a series of clinical trials that again are divided into three different stages. Stage one is where to establish safe dosage levels, it's metabolism and side effects. Stage two is when the drug is given to patients with relevant disease which then is compared to patients not on the specific drugs. Finally at stage three clinical trials are undertaken. If the trials are successful the drug gets approved.

However, to get to these stages, the first thing any pharmaceutical company has to do, before trials can begin, is to fill out an application with the FDA, where they present their new drug. Once the FDA has approved the application the preclinical and clinical stages can begin. After conducting trials, which normally take a few years, companies have to fill out another application, so they can sell the drug. Once again, the FDA has reviewed the application with the help of eighteen advisory committees from outside of the FDA, the drug is ready to go on the market.[114]

The process is long, it can go on for decades even, and there is an enormous amount of money at stake for the pharmaceutical companies. Because of these factors it is

[112] http://www.fda.gov/AboutFDA/WhatWeDo/default.htm

[113] http://www.fda.gov/internationalprograms/fdabeyondourbordersforeignoffices/europeanunion/default.htm

[114] Angell, 2004. p. 31

highly crucial for a companies drug to get approved. It could decide the life or death of a company.

This could very much support the claims of bribery, improper trials, changing of numbers in official documents and overall corruption in the business, that among many others, Peter Gøtzsche and Marcia Angell talk about.

Influence of drug companies on approval agencies

In 2004-05 the health committee of the British house of commons published a report examining the pharmaceutical industry. The report found that the industry's influence was "enormous and out of control". Regulation was found to often be ambiguous and weak. Also reporting that influence was 'bought' over doctors, patient groups, journalists, charities and politicians. Despite this damning report, government officials decided that there was no evidence that there was negative industry influence on public health.[115] Unfortunately this is not a rare response to see from governments, and one could wonder if this very influence bought over politicians has something to do with it.

Because of the enormous amount of money at stake in the industry, pharmaceutical companies tend to have an influence on approval agencies even though there is a conflict of interest.

As Peter Gøtzsche mentions, it is difficult to understand and explain some of the things that go on in the industry unless money is involved. Believing that this is how it works one can see how pharmaceutical companies make their influence by paying off reviewers, scientists, entire regulatory agencies and even politicians; to change laws, falsify papers, keep secrets or overlooking factors that would eliminate a drug.

In 2012 a former scientist at FDA, Ronald Kavanagh, who worked as a drug reviewer, uncovered some crime and gangster like methods that went on while he has working for FDA. In an interview done by the website; Truth Out, he talks about how he was repeatedly told not to ask questions that could delay or prevent the approval of a drug, how he and his co-workers sometimes were told to accept applications without checking the actual data and safety issues. He even experienced on one occasion a company saying that they "paid for an approval".[116]

Another criticism of the medical industry is from British physician Ben Goldacre whose book called Bad Pharma, published in 2012, talks about how the pharmaceutical companies control the approval agencies and the "revolving door" concept, where people go back and forth in the industry, working for regulators and pharmaceutical agencies.

[115] Angell, 2004. p. 37
[116] Gøtzsche, 2013, p. 111-112

Medical journals

Medical journals like *the New England journal of medicine, British medical journal, Lancet* are all dedicated to bring the best information about medical findings, research and other relevant features in the medical industry.

A big part of what journals do is publishing trials. Trials performed by pharmaceutical companies, that presents their current work and how it works on test subjects. Having trials published means a lot to the company behind the trials. There is a lot at stake in relation to the reputation of the company and also because how time consuming and expensive conducting trials are. This has created conflict of interests in the industry and medical journals often have no other choice than to follow the wishes (demands) from pharmaceutical companies.

Richard Smith, former editor of the high-impact journal 'BMJ' wrote a paper called *'Medical journals are an extension of the pharmaceutical companies'*. This title summarizes a current crisis that the medical journals face, stemming from financial influence from pharmaceutical companies. The objectivity of medical journals is compromised when they are dependent on advertisement revenue (coming from pharmaceutical companies themselves), and reprints, which are ordered in the thousands, if the journals print favourable reviews of their drugs. Richard Smith explains how companies sometimes would call in and offer to buy reprints if their paper was accepted.

A concrete example of the influence from advertisement was when the BMJ back in 2004 dedicated a whole issue to the theme of conflicts of interest in the industry. Subsequently the industry threatened to withdraw 75 000 pounds in advertising. 'Annals of Internal Medicine' lost in revenue and estimated 1-1.5 million US dollars in advertising after publishing a study critical of industry advertisements.[117]

This is where the industry starts to crumble and focus is shifted from actual providing good articles to the reader, to a matter of money - where pharmaceutical companies "buy" out the journals and therefore have control over what is being published and how it is being published. It turns into another marketing scheme and a way for the pharmaceutical companies to promote themselves.

Ghostwriting

Ghostwriter: to write a book or article, etc. for another person, so that they can pretend it is their own or use it themselves – Cambridge online dictionary

Ghostwriting is the practice of biased entities such as pharmaceutical companies or PR-agencies writing part of-, or the whole research paper or review - instead of the seemingly independent, objective doctor whose name is on the paper (which the doctor often agrees to for some kind of payment). The intention of this practice is to intentionally deceive doctors, who believe that the paper is objective and written by disinterested, credible academics and not corporate interests. Therefore it can also be seen as a type of deception or even fraud, as doctors are deliberately deceived about the source, credibility, and their judgments are manipulated in a covert manner.

[117] Gøtzsche, 2013, p. 64

Though it's difficult to determine the scope of the use of ghostwriting due to its shadowy nature, legally this whole area is in a grey zone. Companies work hard on getting academics to put their names on papers that they have often not read, or only read brief summaries about. Often getting tens of thousands of dollars in exchange.

According to Gøtzsche, because of social desirability bias ghostwriting is underestimated, and so are the estimates of the extent of this practice. Nonetheless a study found no less than 13% of all papers published in six major medical journals where ghost authored, and 21% had guest authorship.[118]

Unofficially ghostwriting is used to deliberately deceive and withhold information from doctors and everyone else that reads the reviews, and persuades them into buying their product. The ghostwritten documents deceive and manipulate when they are presented as if they are written to give doctors a reliable verification of an effective and safe drug, namely because they are ghost-written.

As we have read and learned by now; many medical reports have been fraudulent in some way or another and by using ghostwriters they can cover up the reality and make it appear to the public as if the paper came from some disinterested, prominent academic and not from a corporate sponsor. To get the academies to sign off on a paper they have never even seen, they get paid thousands of dollars. Ghostwriting corrupts the trust that is so essential for the medical industry.

Marketing and CSR

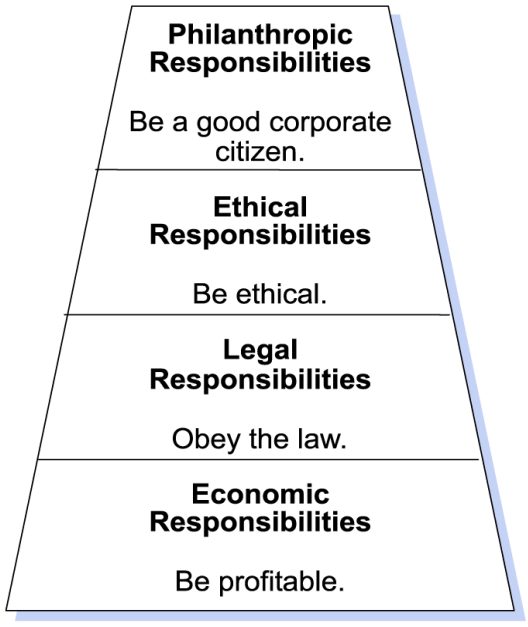
What is CSR and why is it relevant?

Corporate social responsibility (CSR) is a type of self-regulation built into an existing business model of the corporation. CSR represents an approach corporations can take to comply with certain ethical stands, rules of law and societal norms.
Some of the reasoning behind applying the CSR perspective is that the corporations, specifically in this sector, seem to have a disproportionate amount of regulatory power in their own hands. According to Gøtzsche they basically 'regulate themselves' making the fine analogy that to allow the industry to conduct its own trials, is like allowing yourself to be your own judge in a court case:[119]
Imagine being accused of a crime, turning up in court with boxes containing 200 000 pages of evidence for your innocence that you had produced yourself (which is apparently the standard volume of clinical documentation for a new drug) and telling the judge that this was the only material there was which he had to base a verdict on. That obviously wouldn't be accepted in a court of law, but is comparable to what's happening with the approval process of industry trials. The corporations have confidential partnerships and non-disclosure agreements, severely limiting the leakage of any information getting out about research & development and trials. The trials themselves are run, interpreted and promoted by the companies themselves (see 'Trials - trials interpretation of data'). Due to influence of the industry on regulatory agencies, doctors, marketing etc. bought from lobbyism and kickbacks - the industry itself appears to be in a much better position of power than the public and regulators when it comes to the release of pharmaceuticals. The 'judgement' is largely left to the company, while it has many means to cover up any

[118] Gøtzsche, 2013, p. 91
[119] Gøtzsche, 2013, p 107

negative evidence.[120] If it is indeed sensible to leave so much power and responsibility to the industry as many radical free market advocates believe, then we must expect these corporations to assume the social responsibility to all 'stakeholders' (patients, researchers, society etc. as explained further down) that public has relinquished.
Acting according to CSR the corporation takes responsibility to comply to these standards itself, independent of external regulation, hence the use of the word 'responsibility'. A broad argument summarizing the need for CSR is that the whole business community benefits from socially responsible behaviour. As Ralph Nader stated: "If we are not good, they will move in", 'they' meaning 'big government' and regulators. So it is assumed that it is in the corporations own interest to act according to generally accepted ethics, norms and of course the law. It is also assumed that this is beneficial for PR reasons, thus ultimately also turnover.[121]
We will approach the actions of Eli Lilly from a stakeholder analytical viewpoint, and the perspective of CSR to understand what went wrong. In the end we will discuss if CSR, an approach widely used (or boasted by) corporations, and used for justification of lower regulation of markets, in itself is actual a viable approach to have corporations abide by ethical standards, social norms and the law.

CSR Theory and its application on cases



Source: Carroll (1996)

For our analysis we also apply 'The CSR pyramid' constructed by Archie Caroll, who is seen to provide the most widely accepted understanding of CSR.[122]
For CSR to attain its legitimacy, it had to address the entire range of obligations that the corporation has, including most essentially the economic. Afterwards come legal, ethical and philantropic responsibilities - each part dependant on the levels below them to be able

[120] Gøtzsche, 2013, p. 53
[121] Crane, 2008, p. 33-35
[122] Ibid, p. 55

to exist and together they comprise complete CSR theory as seen in the pyramid above. Bear in mind that philanthropy is not considered an essential responsibility and is considered "icing on the cake".Economic responsibilities are the most essential since, the corporation cannot exist if these are not met.[123] From society's perspective businesses are expected to operate according to a profit motive, and pr definition can't function otherwise.

Explaining Stakeholder approach and its relation to CSR

As mentioned earlier, a corporation will have responsibilities to the society it is part of, according to CSR. To determine and make a systematic overview of relevant social groups we use the 'Stakeholder approach' which was first mentioned under this name by R. Edward Freeman.

A stakeholder is essentially a group or an individual who has a stake (or interest) in the company. When using a stakeholder approach, you take these groups into account and prioritize them according to the size of their stake in order to analyze the possibilities/challenges the company will have when making decisions, especially when it comes to marketing.

The stakeholder approach is important when it comes to CSR in the sense that it enables the company to 'map' their stakeholder groups and make sure they are not breaking their responsibilities towards these. So not only is this considered a strategically rational way of marketing but also a morally right approach towards the society in which the company is.

Basically, what one does when managing stakeholder, is categorizing the groups which have influence on or are influenced by the outcome of the decision: The company will have to know what stake the groups have in the company, how important they are to the company, and how to care for the relationship to the chosen stakeholder groups (transaction). This in itself does not seem ethical in any way, but it is a tool for analyzing and understanding the reasoning behind marketing choices made by these companies, and by doing that you will be able to investigate whether it is a case of ethical marketing or not.

Having gone through the basic features of the stakeholder approach, it is important to point out the difference between the four categories:

- *Instrumental* : Explaining the role different groups have in reaching the company's goal.
- *Managerial* : A tool for the manager to handle the stakeholder groups successfully.
- *Normative* : All stakeholders' interests in the company are legitimate and should be paid attention to.
- *Descriptive* : What managers actually do and which groups are taken into account.

Of these we will mostly be using Normative and Descriptive Stakeholder approach in order to explain the concept behind the tactic of the company and to shed light on the issue of handling shareholders (stockholders) as well as stakeholders in an ethically correct manner.

So simply spoken, stakeholder approach is a tool for the manager to steer the balance between the interest of shareholders and other stakeholders. Shareholders will, naturally, be interested in the company making profit, whereas other stakeholder groups, such as customers for example, would like a fair-prized quality product. This is where one of the most significant problems with CSR and the stakeholder approach shows, which we will return to later in this chapter.

[123] Crane, 2008, p. 62

Case: the approval/marketing of Prozac explained by stakeholder approach

We are using this approach based on Freeman's earlier view from 1984 of stakeholder approach (seeing stakeholders as means to a financial end). His newer theory from 1993 has a more normative perspective, as it views stakeholders as ends in themselves *(Stakeholders, Friedman&Miles, oxford university press, 2006, p. 47)*. Still, we find his original view (which is more company-centric) a more honest reflection of reality considering the circumstances we have seen with the Prozac case and the pharmaceutical industry through our readings. Therefore we will use his older questionnaire-model as a starting point to understand the view the company's management has on its stakeholders. Afterwards we will analyse the decision made by the company with utilitarianism. When we have analysed the case, we will be able to get a clearer picture of the reasons for the different decisions made in the Prozac case, and we will determine whether it is a case of ethical marketing or not.
We analyse the Prozac case using Freeman's original stakeholder approach, leading us to understand the company's perception of their stakeholders:

1. Who are the current and potential stakeholders?
2. How does each stakeholder affect the company with their interests/rights, and vice versa?
3. What assumption does the company's current strategy make about each important stakeholder?
4. What are the current 'environmental variables' that affect the company and it's stakeholders and how do we measure the impact of these?
5. How does the company keep score with its stakeholders? [124]

The reason for using this simplified version of the 'stakeholder-map-model'[125] is to gain an overview in a complex case and help us narrow down our focus to the most involved stakeholder groups.

Looking at the model we have the stakeholders within the company, more specifically shareholders. This group has an interest in the company staying competitive on the market and having stable or increasing profit because the shareholders' stake in the company is money. Looking at Eli Lilly, they were in financial crisis after the withdrawal of Vioxx from the market.[126] Unless there is good reason to invest money in the company (or in other words if the company is not profitable) shareholders will not invest and Eli Lilly's mere existence would have been threatened, due to lack of funding. This meant that in order to keep Eli Lilly on the marketplace as well as

[124] Friedman, 2006, p. 85-86
[125] Crane, 2008, p. 114
[126] Virapen, 2010, p. 79-80

keeping his job, John Virapen (manager at the time) was left with little choice. As he explains in his book, there was no time to draw up new elaborate studies for the Prozac, so the company was relying on getting it approved now without further testing.[127]

He refers to Eli Lilly not having time for better tests of their drug because they would have to close down if they were to wait the 7 years it might take to get a drug approved.[128] When in financially critical situations like this, Eli Lilly would have to please their shareholders as much as possible in order to secure a future in the market. In other words, the management of Eli Lilly is pressured to do more or less whatever it takes to secure profit and returns for the shareholders.

Going back to the model, we see on the one side there are the stakeholders that are 'outside' of the company, but nevertheless affected by its decisions (and vice versa, which is to a certain extent only in this case). In this category we include doctors (assuming that they have no financial ties to the company), customers plus their relatives and society. Here, the stakeholders do not have the same united stake, but they do connect clearly:

Doctors: Their job, and assumed role in society, is to treat patients and do what they can to ease or cure whatever health problem there might be. An integral part of the doctors' practice is to treat through medicine, thus for successful treatment they need safe and effective drugs. So the interest of doctors in any pharmaceutical company like Eli Lilly ought to be neutral, and that their product is tested, developed and distributed under the proper conditions.
Sadly, this is not the case, and more specifically neither in the case of Prozac:

> *"I produced a list of 40 doctors to win over for seeding trials. I invited them to the Caribbean for a week. (...)None of the doctors who were invited refused my invitation. On the first day I held a small presentation in our five star hotel in Puerto Rico and introduced our project. I explained that our new active ingredient, Fluoxetine, had been developed enough that it could now enter so-called Phase IV clinical trials. The doctors present had been chosen to take part in this test phase, due to their outstanding work. We would carefully evaluate the results, which they had obtained with their patients and, of course, the names of the participating doctors would be mentioned in a prominent place in the study. That was enough motivation for a lot of the doctors to take part. (...) My doctors saw to it, that as many of their patients as possible enjoyed them"*[129]

This case (among many others) disputes the notion of the financially unbiased doctor' in relation to industry. With the doctors' new found stake in the company being fame and money, Virapen knew that if he influenced the doctors the right way, through promise of status and even through bribery he would get a foot in the door towards getting the actual approval and hereby saving Eli Lilly from bankruptcy.

[127] Virapen, 2010, p. 79-80
[128] Virapen, 2010, p. 92
[129] Virapen, 2010, p. 83-85

Consumers & their relatives: The interest of this group is that the product is effective and safe. Both consumers and their relatives are interested in a better life for the one affected. Changing this stake would be an already lost battle, but making the consumers believe they get what they want is not as difficult. John Virapen had to make sure the drug would be attractive for potential buyers which he did by changing the name:

> *"First, we had to find a suitable name, with which we could successfully market the active ingredient. "Flu-o-xe-tine" is difficult to pronounce, even more difficult to remember, (...). No, it had to be something trendy. The name was to be on everyone's lips, within the shortest possible time. After all, that's where all the pills were going to go, too. Eli Lilly paid a company, specialized in branding, hundreds of thousands of dollars to crack this hard nut*"[130]

The drug was heavily marketed and ended up getting huge exposure. Marketing and promotion is crucial in the pharmaceutical industry, and as we will see later in this chapter it takes up a, disproportionately, huge part of the budget of the bigger pharmaceutical companies.

Society: In theory, the most general rights and interests society has, are defended through the law of the country, assuming the law is accepted through a democratic process (like in the USA and western European countries). Beyond making profit which benefits the shareholder group, the pharmaceutical companies are assumed to have the role of contributing positively to society through development and manufacture of medicine that can heal the 'sick' in society. Eli Lilly broke the law, and navigated in grey areas through clever marketing (the 'illness' of depression was marketed before the drug was approved and doctors were bribed to use it in seeding trials in Sweden and through this malpractice they were able to have the numbers changed in the medical trials in order to get the drug approved (see 'approval' chapter).[131] The drug got approved through what from the outside looked like legitimate procedures, but beneath the surface it was actually tainted by corruption and targeted marketing.

Using utilitarianism to analyze the ethics of the decision made and the decisions available, we will attempt to determine whether the actions of Eli Lilly were ethical correct or not.

"Acting solely in favour of the shareholders".
According to the writings of Peter Gøtzche and John Virapen this is the decision made by the manager of Eli Lilly. The stakeholder group known as 'shareholders' is prioritized first. When the company favored their shareholders it had a negative impact on the rest of the stakeholders.
Consumers were kept in the dark of the full effects of the drug (questionable benefits and dangerous side effects) and were given the pills despite evidence pointing to the non-efficacy and harmful side effects of the drug.[132]

[130] Virapen, 2010, p. 80-81
[131] Virapen, 2010, p. 80-85
[132] Virapen, 2010, p. 73-74

According to some economists it would still be valuable to maximize share-value of the corporation, even with collateral. Society would earn money off taxation of the increased profit of the company, and the increased wealth of the company would go back to society through taxes and more jobs.

"Acting in favor of as many stakeholders as possible"

This option is based on the essence of utilitarianism; striving to create the maximum amount of happiness while creating the lowest amount of suffering. In this approach you want as high a portion as possible of the stakeholders helped, with as few negative outcomes as possible. So contrary to the first option, that is focused more on maximizing the benefits of a limited group of shareholders, using this approach on drug companies and the hypothetical outcome ought to be something like: more focus on releasing thoroughly tested, safe medicine to the market at competitive prices. This would mean that the consumer stakeholder group was spending less of its money on drugs, especially 'me-too drugs', which as we saw with Cipralex was 19 times more expensive than the generics that later appeared on the market when the patent expired (as we see later, the majority of the profit of bigger pharmaceutical companies comes from me-too drugs). A utilitarian approach would also, ideally, lead to less side effects in consumers which is obviously of huge benefit to them and their relatives. Less side effects in the vast patient/consumer stakeholder group will also benefit society a great deal, since this would lead to less stress on the medical sector, less paid sick days etc.

What seems to be happening with SSRIs and in parts of the pharmaceutical industry in general is what is referred to in socio-economics as "cost-externalization", meaning that corporations do not even take *financial responsibility* for the full 'costs' of the sales of their product and the concurrent expenses related to its release on the market. As mentioned with the first option, describing a shareholder-centric approach, when people suffer side effects from the unsafe drugs, it is usually not the companies whom the expenses fall on, but the patients, their families and the healthcare system.
A parallel example from a different sector could be from the mining industry where immoderate, but *cheaper* methods of extracting minerals are used (with the outcome being e.g. toxic chemicals being released into nature or mountainsides being blown up) at the long-term expense of environment and the local population. The method for extraction is cheaper for the mining company, and gives the company and its shareholders higher returns on investment, but the 'bill' falls in the lap of the local population stakeholder group, who end up with a polluted environment and a lower standard of living. In the same way, these costs are being 'externalized' to the patient & relatives and society stakeholder groups in the marketing and distribution of unsuitable drugs by pharmaceutical companies.

In the Eli Lilly case we can easily assume that, in the hunt for profit, they are not using a utilitarian approach. Is it only Eli Lilly though? A BMJ report has shown that the pharmaceutical industry spends 19 times more money on advertisement and self-promotion than on basic research. A provocative finding, considering the widespread

idea that the industry needs to charge high rates on drugs, in order to support 'further research'.
What the industry is making most of it's money off are the me-too drugs,[133] hence why it makes sense to invest in advertising rather than innovative research from the company's point of view.
As it turns out, most of the basic science that takes place enabling medicine to progress comes from universities, institutes and the non-profit sectors. (Gøtzsche, Peter, p. 253) This makes sense considering the much ignored truth (in the marketplace at least) that what is behind motivation and innovation, is not actually profit but curiosity and a '*drive to create*', be creative and (in this case) make a difference.[134] Very much contrary to popular belief, but nonetheless proven time and again. A US Congress report from 2000 found that *"Of the 21 most important drugs introduced between 1965 and 1992, 15 were developed using knowledge and techniques from federally funded research"*(Gøtzsche, Peter. 2013 p. 253). The point is that financial reward does not drive innovation, and that we cannot expect industry to innovate, for this very reason, and because of this historical evidence.

Overview of factors within a corporation that impede ethical behavior and CSR

As we have seen with the Prozac case, but as happens with many other corporations dealing with pharmaceuticals (and many others that do not), the companies do not always act in an ethically, lawfully or socially responsible manner. In fact judging by many of these cases you could be compelled to conclude that they will not hesitate to break these rules whenever there is financial benefit involved and - get away with it. Specifically in the United States, the pharmaceutical industry has a very poor track record, around three times as many serious, or moderately serious law violations than other companies. As for international bribery, corruption, and 'criminal negligence in the unsafe manufacture of drugs' it's not looking much better for the industry either.[135]
Let us look at some of the factors present in organizations and the larger system of society and the economy that impede adherence to CSR. Does and can CSR really work in practice? Many critics of CSR dismiss advocates of CSR as naive, pointing to the nature of corporation and that these inherently create problems, and cannot solve them. According to sociologist Melvin Tumin, socially responsible behavior is not possible in our economic system. Tumin talks about "the principle of least morality", that competition and greed causes companies to depart from the rules, and thus 'standardize' unlawful or unethical behavior in the whole industry as the different companies try to stay competitive. There is a great deal of evidence to back up this view.[136]
Eli Lilly practically going bankrupt with Prozac, before bending the rules is a prime example of this.
Theorists including Nobel prize-winning Milton Friedman (not to be confused with 'Freeman') would say that corporations cannot act ethically, just as a building or other human constructs cannot have ethical values,[137] so it is up to the individuals within the corporation to keep checks on ethical behavior. However structural hindrances within and without the corporation may make this approach unfeasible.

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[133] http://www.huffingtonpost.com/2012/08/09/pharmaceutical-companies-marketing_n_1760380.html
[134] http://www.youtube.com/watch?v=rrkrvAUbU9Y
[135] Gøtzsche, 2013, p. 39
[136] Crane, 2008, p. 36
[137] Ibid, p. 24

Structure of corporations

A survey conducted by J.S. Bowman (1976) found that 64 percent agreed with the statement "*private managers feel under pressure to compromise personal standards to achieve organizational goals*", a belief especially found in lower and middle management levels.
Furthermore another 78% agree with the statement: "*I can conceive of a situation where you have good ethics running from top to bottom but because of pressures from the top to achieve results, persons down the line compromise their beliefs*". These numbers speak for themselves, but let us put them alongside an internal survey of Pfizer employees from 2001; showing that around 30% did not agree with the statement, '*Senior management demonstrates honest, ethical behaviour*'. A staggering high percentage coming from employees about their own firm.
According to Ackerman most business leaders would like to avoid doing what is irresponsible, however the divisionalized structure of corporations gets in the way. In this type of structure, the divisions are responsible for running their individual business and are mostly controlled by 'the top' through financial performance measurement systems. This means that the managers of the divisions are judged by their bottom lines, and not by their social, environmental, CSR performance. As we will see, the benefits of implementing CSR are very intangible. The division managers have to reach their financial targets, given by headquarters, and this gives them limited maneuvering capability, even when they would like to do good.[138] The system is often quite simply too tight to introduce CSR from the bottom, and implementing it from the top is also difficult due to, as we will see, external market pressures.
James Waters having studied various testimonies of congressional investigation committees of corporate malpractice, interviewed some of the managers who had been involved. Based on these studies, the tendencies he found and what he learned, he developed the term "organisational blocks" which are "aspects of organisations that may get in the way of the natural tendency of people to react against illegal and unethical practices". These include:

- Strong role models, involving the socialization of new employees into existing unethical practices and their identification with those responsible for them [139]
- Strict lines of command that discourage questioning such practices (responsible social-)
- Task group cohesiveness (thus having employees let go of own morals in return of cooperating with team)
- Ambiguity about priorities, phenomenon that pitted vague social guidelines against specific financial targets
- Separation of decisions, forcing employees to work in terms of given strategies in contacts where unethical practices are the norm.
- Division of work, so that employees do not know about unethical practices, ignore them if they do, or are bypassed if they try to resist them;
- The tendency for firms to avoid investigating their own wrongdoing for fear of public exposure.[140]

And these factors seem to be very much at work in the industry. Previous global vice president of marketing for Pfizer (turned whistle-blower) said this *"(...) The mob bribes politicians and others, and so does the drug industry… well, I'd say 99% anyway look upon themselves as law-abiding citizens, not as citizens who could ever rob a bank … However, when they got together as a group and manage these corporations, something*

[138] Crane, 2008, p. 43
[139] Ibid, p. 136-138
[140] Ibid, p. 45

seems to happen … to otherwise good citizens when they are part of a corporation. It's almost like when you have war atrocities; people do things they don't think they're capable of(...)"[141] It's not that managers themselves are evil, but it is the mechanisms fostered in these group environments that lead to what could be called evil acts.

Internal competition, pressures and influences

According to Michael MacCody who wrote a book about internal competition, which is another factor. The corporate hierarchy favors the "games men", people who value winning, and "climbing" above all else, as opposed to so called "qualities of the heart"(such as friendliness, loyalty, compassion). Again, a reason for this being results measured in bottom-line numbers and raw performance, not social activity. Gøtzsche writes:[142]

> *The profit per unit sold has always been much higher in the drug industry than in other industries, e.g. 11% in 1960 compared to 6% in all the Fortune 500 companies, big pharma included (source). But in 1980s, when marketers took over, the drug industry's profit skyrocketed and was 19% in 2011 (figure 5.1) In 2002 the combined profits for the 10 drug companies in Fortune 500 exceeded the profits for all the other 490 businesses put together"*[143]

The people inside the corporation, and the corporate environment in general has a lot to do with what decisions are made by the company. Some companies seem to have a more competitive internal corporate structure, which can sometimes be attributed to their actions in the marketplace.

"...to encounter someone whose position you strive for is very motivating. You compare yourself with him. You ask yourself what he might have that helped get him there. Can you keep up with him? ."[144]

External competition, pressures and influences

Some examples of the benefits of CSR are high employee morale, positive impact on society and good reputation. But how much do these things actually mean on the market? The main argument for big corporations to implement CSR are the economic gains they can get from the PR, and as described, the positive relationship with governments and less limited access to markets. Unfortunately there is no proof that CSR makes firms more profitable, nor is there much proof that it makes them less profitable. It is quite simply too difficult to determine the effects.[145] Depending on the sector, dimension and scale that CSR is implemented, it will be an extra expense, rendering the company less competitive. This leads to companies often using it in a limited, explicit way as publicity that can later be 'cashed in'.

An example of factors the marketplace that can lead to socially irresponsible behavior, and fraud is the bonus system in the US. Gøtzsche points it out saying that it

[141] Crane, 2008, p. 38
[142] Gøtzsche, 2013, p. 42
[143] Ibid, p. 59
[144] Virapen, 2010, p. 86
[145] Crane, 2008, p. 182

"creates a minimal incentive for innovation and huge incentive for fraud". In large pharmaceutical companies, top executives can hold unexercised stock options that are often larger than 50 million creating the incentive to increase the prices of the stock (in a dishonest way) and subsequently leaving the firm.[146]

Loosely regulated free market factors

Melvin Tumin talks about the "principle of least morality", basically that competition or greed causes some businesses to not follow the rules (the rules of business responsibility already being vague and not officially enforced), forcing others to follow suit. Thus creating a 'race to the bottom' so to speak. Tumin concludes that business "*tends to bring out, standardize, and reward the most unsocialized impulses of man*".[147]
All these cases from industry that are mentioned (and many more) are not 'just' malpractice, fraud and actions leading to inhumane treatment of fellow human beings. It is also stifling innovation because of the way funds are channeled into profit-focused imperatives such as me-too drugs, advertisement, off-label marketing, lobbying and so on. This also serves to create a lot of counterproductive 'noise' in this, essential, life-saving industry, misleading doctors, decision makers and patients.[148] Industry that took the needs and rights of all its stakeholders (especially patients) into account would doubtfully create this same end-result. Gøtzsche himself believes that this disproportionate influence over the medical practice by market economics is highly deteriorative for this very reason, and as a solution Gøtzsche seems to suggest overall tougher regulation of the market, and a lot more public research, regulatory and treatment facilities - rather than private, since the former ultimately serve patients better. He refers to research consistently finding higher costs, higher rates of medical complications and death, and lower quality of care in for-profit facilities than in public facilities in the United States. Even billing fraud is more common than in public facilities.[149]
We can conclude that it is not really in the core, financial interest of the bigger pharmaceutical corporations to act in a socially responsible way. They can get away with not doing so - and in many cases by not abiding by the law either. With the insufficient regulation, and the large amount of patients suffering side-effects and financial losses due to these marketing tactics and fraud, we are faced with an issue that appears to have a structural origin. Structural meaning that the problem does not lie "with a few bad apples", but in the way the market and society is shaped to allow such cases to happen. In the discussion we will look at potential solutions, but first we will elaborate some of the consequences of this loose regulation within psychopharmaca, more specifically 'me-too drugs' and 'off-label marketing'.

Me-too drugs

Marcia Angell calls it 'leftover food' and Peter Gøtzsche describes it as 'buying new bumpers for an old Volvo and calling it a different car'. What they both point out is that me-too drugs are only slightly different versions of former drugs and there is nothing innovative about them. Still, this is what pharmaceutical companies are

[146] Gøtszche, 2013, p. 264
[147] Crane, 2008, p. 36
[148] Gøtzsche, 2013, p. 12
[149] Ibid, p. 264

promoting as new and better drugs.[150] Why they do this, we are not a liberty to say, we can only point to the fact that it is easy money.

How come these drugs get approved when there are evidences showing that they are not innovative and not better than drugs already on the market? To some extent it has to do with a "flaw" or a "weak spot" in the FDA's regulation, so that pharmaceutical companies only have to show the FDA that their new drugs are effective. The drug does not even have to be more effective than the previous or already existing drugs.

When testing drugs, the proper way is considered to be when new drugs are compared with drugs already on the market. However when testing new (me too) drugs, the drugs are usually compared with placebo pills[151] and not with the best treatment ~~drugs~~ on the market. By doing these improper comparisons, companies can get their drug approved without the risk of denial of approval. One of the biggest reasons for companies producing these "me too" drugs is to stay ahead in the industry and keep producing blockbuster drugs. When a drug is running out of patent, the company stands to lose millions of dollars and can potentially go bankrupt. To avoid competition from other generic manufacturers getting ahead in the market of a particular drug, companies behind the existing blockbuster have strategically planned for a new (me too) drug to be approved just in time for the patent expiration.

An example of where this might be practiced is with the new drug by Danish Lundbeck and the it's Japanese partner Takeda. They announced only few months ago the FDA approval of their new antidepressant Brintellix™ (vortioxetine). According to Lundbeck and Takeda this new drug for treating major depressive disorder (MDD) supposedly is *the first and only compound with this combination of pharmacodynamic activity*. Lundbeck's current blockbuster antidepressant Escitalopram will soon run out of patent and the company stands to lose millions.[152] Though we cannot verify it, it is hard not to assume that the new antidepressant Brintellix is a me too drug. Looking into what our primary resource (Peter Gøtzsche) writes about this matter; Lundbeck stands to receive $43 million payment from Takeda now that the drug has been approved.[153]

Making an assumption like this might be risky but after learning about how pharmaceutical companies create 'new' drugs it becomes more and more difficult to stay non critical to new drugs. Although we might not be able to officially say that this is what Lundbeck and Takeda are doing, the industry is not very credible to people in the know.

[150] Angell, 2004, p. 75
[151] Ibid, p. 75-76
[152] Gøtzsche, 2013, p. 111
[153] Ibid, p. 111

To make it more credible, there is an example showing that even before Brintellix, there have been other times when Lundbeck supposedly created a me too drug with the same components.
In 1989 Lundbeck launched Citalopram also known as Cipramil and Celexa which became the company's blockbuster drug. As the patent was running out some years later, in 2002, Lundbeck introduced a me too drug called Escitalopram (also known as Cipralex and Lexapro).
When the patent for citalopram expired, generics of Cipramil were sold to much lower prices. In 2009 Cipralex costed 19 times more than Cipramil. This should have stopped the sales of Cipralex, but it didn't.
If patients (both in hospitals and primary care) would have gotten the cheap pill, taxpayers would have saved 30 million €(225 million kr.) a year in Denmark, it would have been 87% of the total amount spent on SSRIs.

How pharmaceuticals promote their new (me too) drugs

The marketing behind promoting a new (me too) drug is well thought through and there is nothing coincidental about it, if we were to agree with Marcia Angell. According to her given information, the way the marketing works is so well that people do not even notice that there has been a change in product.
Pharmaceutical companies launch massive advertising campaigns where they promote the new drug as if it is better than their previous or existing one. They stop all references to their *older* drug and soon it no longer exists in people's minds. They might even lower the price of the new drug for a period of time, offer discounts to hospitals and hand out free examples to physicians. In one known example the pharmaceutical company AstraZeneca offered coupons in newspapers when promoting their new drug Nexium (a me too drug of Prilosec). All this to convince consumers and doctors to choose differently.

Off Label marketing

Off label marketing is explained as when a drug is being used and marketed for something it has not been approved for.

One of the biggest reasons for the creation of the FDA (around 1930's) was because of off label marketing; to prevent incorrect use of drugs and to secure the safety of patients in need of them.
However, off label use is still relevant. Today, off label marketing is illegal and the concept is known and understood by people in two very different ways. For people working in the medical industry, off label is not referred to but the "method" is frequently used by physicians when treating patients. Marketing of off label use is illegal but physicians are allowed to prescribe whatever drug they want to anyone if found reasonable. There seems to be no skepticism around it, looking at how many off label prescriptions are prescribed.
As for patients, off label use of medicine is seen as a necessity if prescribed. Patients might feel nervous about taking a drug not intended/approved for their illness (if they

are told about it) but they accept it because patients usually believe that their health and wellbeing is in the best interest of their doctors.

Over the years there have been opposing examples where off label use has had damaging results in Prozac and other pharmaceuticals. Since Prozac is our prime case it would be natural to refer to it again in this section but for this part the example we have chosen to use, is with Paxil. It has been one of the largest healthcare fraud settlements in History. In 2012 GlaxoSmithKline (GSK) pleaded guilty in having marketed Paxil and other drugs illegally for off-label use. The company was also found guilty in bribing physicians with large amounts of money and expensive vacations. They got a 3 Billion dollar fine. GlaxoSmithKline has previously (in 2004) been faced with criminal charges for illegally marketing Paxil to children. The prosecutor, however, ended up in favor of Paxil because Paxil was well prepared and was able to defend their doings.
In all this the part that interests us the most is the off-label prescription of antidepressants to children, because it is relevant to our project.[154]

Study 329
The fraud with off label use of Paxil started around 1999. GlaxoSmithKline had at that point 1 million prescriptions worldwide on their antidepressant Paxil earning them 2 billion dollars per year. To broaden their market and extend their patent on Paxil, they started a research trial on children, which gave them an extra six months on their patent.
Study 329, which were one out of three studies, would later turn out to be one big case of fraud containing manipulated data and withholden results of trials showing negative outcomes. All three trials were conducted in the years 1994 to 2001, to show Paxil's safety and efficacy in treating children and adolescents for depression. It turned out that Paxil "*was not only not effective in treating minors but that it increased the risk that they would attempt suicide*".[155] GSK however marketed as if it was.

When the internal unpublished trials were exposed they revealed that *"at least eight children became suicidal on Paxil versus one on placebo"* and *"there were 11 serious adverse effects in total among 93 children treated with Paxil and 2 among 87 children treated with placebo"*[156] There are numerous examples in books, magazines and documentaries where people tell their stories, and the stories of others. An example is 18-year-old Jamie who was prescribed Paxil to treat his depression. His mother explained how he gradually starting getting worse because of sleep loss and began self-harming which eventually lead to him committing suicide. Or the story of an 11-year-old boy who hanged himself in the closet with the leach of his new pet puppy.

[154] http://truthaboutpaxil.com/approved-uses/
[155] Ibid
[156] Gøtzsche, 2013, p. 217

Patients

Drug dependency

Withdrawal symptoms are seen in SSRIs and the latter may have severe effects on patients. These symptoms mimic the disease that the medicine was supposed to treat. Patients have become dependent on the drug, just like people become dependent on narcotics or alcohol. It seems that antipsychotics and other forms of psychotropics such as cocaine, amphetamines, opiates and heroin can damage and change the brain chemistry. But long-term use of SSRIs can also damage the brain permanently. When serotonin levels increase in the synaptic cleft between the presynapse and the post synapse, the serotonergic system does not ignore the increase, but adjusts and compensates for it, down regulating the number of 5-HT1A receptors that are responsible for the serotonin uptake. When the increased flow of serotonin is removed from absence of SSRIs, because a patient gets of the drug, the receptors will have decreased in number and thereby giving a patient the serotonin deficiency, which was believed to be the cause of the depression from the beginning. Now with decreased serotonin levels in the post synapses, the withdrawal symptoms gets to the surface. These 5-HT1A receptors are slow at growing back on the postsynapse, which confirms that it can be dangerous to stop abruptly with SSRIs. It is important to gradually step down on the doses throughout time. Research, according to www.psychologytoday.com[157] has shown that some patient's 5-HT1A receptors do not grow back, and thereby keeping patients in the need of SSRIs. This is where the psychological dependency rises - as it is much more comfortable to continue medicating than to stop.

Negative side effects

In the long run, the effects of SSRIs seem to cause permanent personality changes, such as emotional flatness and a decline of cognitive abilities. Gøtzsche goes so far as saying that SSRIs are narcotics on prescription.[158]

Commonly accepted side effects include physical symptoms such as sweating, loss of appetite, insomnia, dry mouth, dizziness, blurred vision, diarrhea and feeling sick affect around 1 in 10 people using SSRIs. Bruising or bleeding, weight gain and hallucinations are side effects affecting 1 in 100 people using SSRIs. Erectile dysfunction, lower libido, lack of orgasm and lack of ejaculation are the side effects on the sexual organs.[159] Suicide risk and suicide ideation are side effects that have been observed especially in children and adolescents. The Food and Drug Administration, as an example, requires that SSRIs have a black box warning, which is the highest level of warning that can be labeled on medicine. Considering it has a black box warning, it makes sense that the risk is really there, and it is backed up by

[157] http://www.psychologytoday.com/blog/side-effects/201107/antidepressant-withdrawal-syndrome
[158] Gøtzsche, 2013, p. 200-202
[159] http://www.nhs.uk/Conditions/SSRIs-(selective-serotonin-reuptake-inhibitors)/Pages/Side-effects.aspx

Gøtszche who mentions this: "*A 2005 meta- analysis of published trials including 87650 patients conducted by independent researchers included all ages and found twice as many suicide attempts on drug than on placebo*".[160]

How antidepressants compare to other treatments

Viable alternatives to antidepressants

There were not many peer reviewed trials we could find comparing SSRIs to natural, non-industry, alternatives. One could speculate that this has to do with the lack of financial and professional incentive there would be in performing such trials. Hence why the size of the trials are smaller in comparison to the larger scale trials that are performed with SSRIs. Nevertheless, we will include some trials pointing to the efficacy of cheaper, more natural alternatives which do not have the side effects of SSRIs, can not be patented (yet!) and do not have the funded PR either.
One study funded by the NIH, with GSK providing the pharmaceuticals found cognitive therapy on average being as effective as pills, yet having more permanent results. This kind of study does of course have many more variables than otherwise, as results depend on the therapist, interpersonal factors in patient to therapist relationship.[161]

A four month trial was performed with individuals suffering from major depression, comparing a group following an exercise program, another taking sertraline (Zoloft) and a third combining the two. The trial found similar effect in the group that took sertraline as with the group that exercised, however 6 months later only 30% of the people in the exercise group were depressed, as opposed to 52% in the sertraline group and 56% in the group that was randomized to exercise and take sertraline. A Cochrane review of exercise found similar results.[162]

There is a lot of evidence pointing to nutrition being a major factor in depression, with the average western diet having moved, in the last decades, more and more into the realm of processed, salty, sugary foods, with additives containing less of the essential 'ingredients' than you would find in a natural diet. Diets of depressed people have been found, by average, to be less balanced and more lacking of essentialities. More specifically diets in American and Asian countries have been found to often be deficient in minerals, essential vitamins and omega-3 acids - deficiencies which are prevalent in people suffering mental disorders such as bipolarism, schizophrenia or depression. Studies have found that daily intake of essential nutrient supplements such as amino-acids (that can be converted to neurotransmitters) tryptophan, tyrosine and most notably; omega 3 acids, alleviated the symptoms of depression and other mental health problems.[163+164]

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[160] Gøtzche, 2013, p.223
[161] http://www.medicalnewstoday.com/releases/22319.php
[162] Gøtzsche 2013, p.208
[163] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2738337/
[164] http://psychcentral.com/lib/can-nutrition-help-fight-or-ward-off-depression/0003150

Adding more of these essential nutrients to your diet is not difficult, and does not have to be at the cost of changing your diet altogether. Among other foods that have been found to alleviate symptoms of depression, and increase mental health are: cocoa,[165] maca,[166] bacopa monnieri extract[167]

Why, then, should we ask ourselves, is there not more awareness about the importance of diet in relation to depression and mental health in general? Most people are well aware by now (albeit by varying degrees) that diet is an important consideration when wanting to be healthy, lose weight and have more energy. However even in these fields there is a lot of confusion, disagreements and contradictory information. One of the explanations, apart from the lacking presence of industry money in research on nutrition, is probably the low amount of education doctors get in this field at medical schools. A study found that the vast majority of medical schools in the United States failed to meet the minimum recommended 25 hour instruction on nutrition,[168] 25 hours in itself being a low amount of hours, considering the importance of nutrition for maintaining our bodies and staying balanced.

Testosterone replacement treatment.

In some males, testosterone can be an effective antidepressant[169] if the patient has low levels of testosterone or if antidepressants are ineffective. Harvard psychiatrist Harrison Pope conducted a blinded placebo study[170] on males with severe depression and low levels of testosterone, with the FDA approved AndroGel, a testosterone gel. In his study, 12 were on active gel, and 10 were on placebo. With Androgel, 3 subjects showed almost no improvement, 4 showed moderate relief, and had "striking, dramatic gains". The placebo group showed little or no improvement. This is definitely a call for a larger study, and maybe it is an effective treatment in the subgroup of males, who are depressed and have low levels of testosterone. There is an awareness here that it is out of the reach of the project to say whether there is a causal link or not, from low testosterone levels to low serotonin levels. It might just be correlational, or it might be depression causing low testosterone levels in some patients, or low testosterone making some patients more prone to depression.

[165] http://science.naturalnews.com/2010/2195464_Consumption_of_cocoa_flavanols_results_in_acute_improvements_in_mood.html
[166] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1534053/
[167] http://science.naturalnews.com/2008/1613304_Effects_of_a_standardized_Bacopa_monnieri_extract_on_cognitive_performance.html
[168] http://www.nytimes.com/2010/09/16/health/16chen.html?_r=0
[169] http://www.ncbi.nlm.nih.gov/pubmed/19625884
[170] http://news.harvard.edu/gazette/2003/01.09/01-testosterone.html

Hypothyroidism - inadequate amounts of thyroid hormones such as T3, T4 and TSH.

Hypothyroidism is more prevalent in the depressive disorders, and depression is more prevalent in people with hypothyroidism "A 2004 study[171] found that 38 percent of older patients with hypothyroidism also reported symptoms of depression." writes Margarita Tartakovsky on psychcentral.com.[172] In some patients, there might be a link and it is difficult to say if hypothyroidism is the dominant cause in some patients, but we can probably say that there is a causal link among other causes. At least it can be said that people with hypothyroidism are more prone to depression. Hypothyroidism also might be an effect of depression, but either way, it seems that in some patients and subgroups of depression, thyroid hormone replacement treatment is very effective. Unfortunately hypothyroidism is rarely in the scope of the doctor diagnosing the patient, and therefore this hormonal treatment is not taken into consideration.[173]

In defense of SSRIs

Pedro Delgado, M.D. agrees with Alan Frazer, Ph.D. that uncertainty about the symptoms of depression can be harmful for patients. They say that people need an explanation for their negative emotions and moods, and that the chemical imbalance theory provides such an answer for them. They say that stress hormones and the unknown can worsen the depression, or at least keep it stagnant. Explanations of the cause seems important in the eyes of the two. It gives patients peace of mind.[174] We are aware that some people believe in SSRIs more than others, such as Gøtszche who, according to us, is very critical towards SSRIs.

Peter D. Kramer, in a New York Times interview[175] defends the use of SSRIs. He is a psychiatrist and has written books such as "*Listening to Prozac*" and "*Against Depression*".

Along with Peter Gøtzsche and Marcia Angell, who we have used as sources, he is listed as one of the independent medical experts on bmj.com[176]

According to the source, Kramer is an independent medical researcher, not on pharmaceutical company payroll, and therefore his argument should be viewed upon with seriousness.

In the interview he first refers to a trial with stroke patients, where stroke patients on

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[171] http://www.ncbi.nlm.nih.gov/pubmed/15388067

[172] http://psychcentral.com/blog/archives/2012/04/26/is-thyroid-dysfunction-driving-your-depression/

[173] http://www.nytimes.com/2011/11/22/health/for-some-psychiatric-troubles-may-begin-with-the-thyroid.html

[174] http://www.npr.org/blogs/health/2012/01/23/145525853/when-it-comes-to-depression-serotonin-isnt-the-whole-story

[175] http://www.nytimes.com/2011/07/10/opinion/sunday/10antidepressants.html?pagewanted=all&_r=0

[176] http://www.bmj.com/content/337/bmj.a930?ijkey=51VaCZNnRtCQvUz&keytype=ref.

Prozac recovered faster, and better than a control group. He says that Prozac helped protect the memory and regain mobility much faster along with treating post-stroke depression as originally intended. Kramer further argues that studies that say that SSRIs are as effective as placebos have gained more space and ink in the news than they deserve.
Kramer claims that often times in trials, subjects who are not really sick and exaggerate their symptoms attend the trial because they get gifts, payments or free medicine for attending the trial. If a patient who is not depressed is on antidepressants for three weeks, then after three weeks, that patient is still not depressed, and it may therefore seem like there was no improvement on the SSRI. But this is due to the bias that it is not really a sick subject. He points to a recruitment problem rather than placebo drugs being just as effective. He points out that specific disease groups get a larger benefit compared to a randomized group of people who are depressed and even not depressed. With depression in specific groups, such as multiple sclerosis, interferon induced depression (a medicine used to treat hepatitis), epilepsy and children with anxiety, SSRIs seem to be significantly more effective than placebo.
He turns the table, and puts blame on the media in defense of pharmaceutical industry. He says that the media love stories on "debunking" studies, and love to "reveal" things. Criticizing the pharmaceutical companies will make headlines and thereby sell more newspapers. We interpret that he makes pharmaceutical companies look like victims. Arguing that SSRIs are essential for treating severe anxiety and depression, he calls for better-designed research in the future, to see in which categories of mood disorders SSRIs cease to have a function.

Discussion

After learning about the pharmaceutical industry and having more insight into the actual market and the aspects around it, it leaves us with this ambivalent emotion of frustration and new understanding, filled with questions.
It is frustrating to see that so many people are diagnosed with depression on an unsound basis. Is it because of today's society where the pressure of expectations strain the body and mind so that we seek medical help. Or might it be the criteria for depression that has been vaguely characterized so that it is almost impossible not to relate to it in some way?

We have determined that the most influential factors in terms of misconduct came from marketing, which we covered in the 'marketing' section of the project. We see that the medical industry acts like any other industry where money is involved - there is a constant striving to get ahead and increase profit. This is contrary to our initial assumption; that the interests of the developers of pharmaceuticals was first and foremost to help people. The actions of the pharmaceutical companies we have looked at, that are the largest manufacturers of SSRIs in the world all seem geared towards maximizing profit at the expense of consumers and society. This might seem cynical

but learning about how corrupted the industry is, it is difficult not to be. We have also learned that research of the pharmaceutical companies is, by and large, not innovative. Trials have been falsified, research papers have been tampered with, the pills have been marketed incorrectly and it all ends up harming people.

We (and most people, it seems) may have been naive to think that the situation with pharmaceuticals was any different than it actually is. It is difficult to comprehend how medical doctors and physicians who devote their life to helping people may actually be contributing to our harm. Regulatory agencies who are responsible for our protection through only approving safe and effective medicines, have been compromised, and as we have seen this can be traced back to corruption and lobbyism.
The profit motive is a big factor. Pharmaceutical companies earn handsome profits on people being diagnosed as mentally ill and being prescribed whichever pill the company is selling. Roughly put; The greater amount of people being sick (or at least thinking they are), and being prescribed the drug in question, the greater the profit for the pharmaceutical company. It is not difficult to see where this is going, especially not when remembering how widespread corruption is when looking at the financial ties between DSM-board members and the pharmaceutical industry. A clear example that the diagnosis concept has gone out of hand is the newest edition of the diagnosis manual, DSM-5.
The former Chair, Allen Frances, is concerned with the direction this has taken:

> "*Except for autism, all the DSM 5 changes loosen diagnosis and threaten to turn our current diagnostic inflation into diagnostic hyperinflation. Painful experience with previous DSM's teaches that if anything in the diagnostic system can be misused and turned into a fad, it will be. Many millions of people with normal grief, gluttony, distractibility, worries, reactions to stress, the temper tantrums of childhood, the forgetting of old age, and 'behavioral addictions' will soon be mislabeled as psychiatrically sick and given inappropriate treatment.*"[177]

Furthermore, he points out that when this happens, the people who *are* sick and need treatment will lose important resources because of all the healthy people (who due to DSM 5 will believe they are sick) will use those resources.[178]

Depression has come to be a very board concept in the later DSM relatable to many kinds of symptoms. Much of the time, being or not being sick is somehow verifiable by external factors while when it comes to illnesses concerning the psyche it is very difficult to establish when someone is ill and what it even means to be ill. Our mind has huge power, as seen with the potency of the placebo effect.[179] We can convince ourselves that we are deadly ill, causing a much faster worsening of our health or be optimistic about our potentially serious disease helping our body to cope with it in the best way. It can often come down to a matter of belief but what do we believe in? Today we seem to exaggerate the importance of any indication that we might be sick. We seem to raise concerns, emphasizing them until they actually become a problem.

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[177] http://psychcentral.com/blog/archives/2011/07/02/how-the-dsm-developed-what-you-might-not-know/
[178] http://www.psychologytoday.com/blog/dsm5-in-distress/201212/dsm-5-is-guide-not-bible-ignore-its-ten-worst-changes
[179] Gøtzsche, 2013, p. 43

In day to day life, a tendency in society is to gravitate towards the quick fix, trying to find the fastest solution to our "problems" instead of dealing with them, or preventing them by other means.

There are different views on what the causes of depression are. These different views can be divided into two main groups which are called the mechanical/organic perspective (where we view the body as a machine where the pieces may break and need to be replaced or repaired) and the functional perspective (where we take the mind-body relation more into consideration).
As we pointed out earlier we see that the widely accepted reason among psychiatrists for using SSRIs is to reestablish balance in the serotonin system (Mechanical/organic perspective). The roots of the illness are in the patient's physical body. From this perspective the focus of the treatment is on correcting the physical abnormality that causes the mental illness. This is the perspective used to justify the development of psychoactive drugs meant to re-balance a patient's chemical imbalance. According to the current paradigm, the theory is that a deficiency of the neurotransmitter causes depression. But we have discovered through our reading of Gøtszche and Angell, among others, that it is more complex than that, and that it might not even be the cause of depression, but a side effect and correlation. We have seen that there is no method of measuring serotonin directly in the brain, only indirect evidence from serotonin- and serotonin down-breaking enzymes present in the bloodstream. As discussed in 'research and development' reveals that SSRIs have the effect of down regulating the serotonin uptake receptors, and in some patients, the natural number of receptors are not recovered after the treatment ended and thereby creating the serotonin deficiency that was first hypothesised to be there. Long term use of SSRIs might result in depletion of the serotonin receiving receptors. Even if serotonin deficiency causes depression, one should ask oneself what causes serotonin imbalances in the first place. In the complex chain of causes for depression and anxiety, there must be a more primary cause that is treatable. We found that generally in patients, the causal links to depression are more complex than serotonin deficiency. It simply makes more sense to talk about multi causality, and to us it has come to seem rather naive to believe that depression is mono causal. In males, testosterone deficiency seems to be an overlooked cause, and yet in other patients it has connections to deficiency in the thyroid hormones. But then again we can ask ourselves what the causes are for these deficiencies. It seems to be very likely due to 'external factors' such as unmet psychological needs, tough life-experiences or environmental factors such as lack of sunlight. For other patients it might have some deeper psychological causes, calling for a therapeutic treatment. This latter perspective shares standpoints with the functional perspective, which arose with psychology and Freudian psychoanalysis.
The functional standpoint takes psychological experiences as possible causes of a mental illness. Where the mechanical perspective focuses on mono causality, the functional allows multi causality not only from one science but from multiple: biology and psychology.
Indeed these deeper psychological 'causes' may be the psychosomatic reasons for the various chemical imbalances even happening in the first place. A rapidly growing area of neuroscience is 'neuroplasticity', meaning that the brain changes continually through life and is more dynamic, self regulating- and healing than imagined. Findings point in the direction that we as humans have a lot more control than previously thought-through changing our psychology and also changing the

physiological makeup of our brains. It is also revealed that our current neurological makeup is very much affected by our past thoughts and habits. This lends credence to the point that our brains and minds are much more fluid and dynamic than commonly known, due to the findings being relatively new, and the implications paradigm-shifting from the old 'mechanistic' viewpoint of our bodies and brains. Understand this, ~~and~~ all of a sudden, humanities emerge in a new light in relation to depression treatment – or could we perhaps turn it around and say the pursuit of 'happiness' (which is arguably and opposite of depression)?
There are lots of treasures in philosophy and from traditions all over the world that can aid us in this quest. Yet as we have mentioned, in our society we have become cut off from our traditions and some of the rich sources of wisdom inherent in it. Besides that; lots of research in psychology, the humanities and social sciences have found tools and fundamental formulae we can follow to become well-integrated, functioning and, especially, happy human beings. These fields may go under "soft sciences" and have less credibility in the biomedical domain than hard sciences for solving depression but as we have seen, the science behind SSRIs and the answers supplied have not proven to be based on sound evidence. These 'soft tools' and resources, plus the other alternatives we suggested under 'alternatives to SSRIs' in the report, can be mobilized at an individual level -_however solutions at a social level are called for as well, and we want to learn from our mistakes and go for the root cause instead of the symptoms.
What social factors play a role in the high levels of depression, discontentment and demand for antidepressants? There appears to be a paradigm as discussed in the introduction, which promotes the ideology of having to be perfect, performing and well adjusted all the time. This coupled with the factors of: an increasingly tradition-less society, increased levels of isolation; less intimacy; new social factors that undermine fundamental sources of happiness; financial pressures on all actors in society, and a perhaps too mechanistic view of the brain may compose the larger part of the factors that brought us the current situation with anti-depressants.

When drug sales are so high, not just for an individual, nor communities but countries and even globally – then we ought to know that we have a problem on our hands that demands we take a step back and consider which faulty structural mechanisms are at play here.

We have cultural norms pushing for unnatural behaviors and expectations of individuals in society, which of course are not to be underestimated. There are the environmental factors such as pollution, what we ingest, and the nutrition (or lack there of) that we have in our diets that can be influential factors. Interconnected to all these issues, and the motivator behind many of the preposterous cases we have seen in this paper are the economic pressures. As we have seen these pressures influence all actors including corporations pushing for profit, approval agencies, medical journals, decision makers bought or otherwise influenced by industry money, doctors being under time constraints, ordinary people having little money for treatment, being influenced by advertisement or targeted advertising and disinformation.

Some would say: "it's the free market system - told you", and call for a revolution. We won't necessarily go that far, but propose some fundamental overhauls in the

power and free reign that these corporations are given, since, as we have seen and history shows, they do not act responsibly.
First of all the fact that the industry gets away with such wide reaching cases of fraud, corruption and misconduct, and so often, suggests that there is a lot of room for improvement. Criminal psychology has found that what is one of the larger deciding factors in whether a crime is perpetrated is not how big the fine is, or even the ethical implications, but how big the risk is of being caught. Obviously the corporations feel that they can get away with their actions, and looking at the different cases, it seems like they actually do get away with them without suffering significant legal and financial losses (perhaps excluding cases like GlaxoSmithKline having to pay a 3 billion dollar settlement in 2011 for off label marketing of its antidepressants).[180]

Solid oversight of trials and regulation of drugs is needed. This is a problem both in the United States and in Europe. As mentioned, the industry itself should not be responsible for handling trials of its own drugs, even though regulatory agencies get to see the data. The data of the trials can be too easily distorted or hidden, and (as we have seen) there are plenty of cases of this happening. Since the introduction of "Prescription Drug User Fee Act" the FDA has had a fee system for approving drugs which increases the risk of what is technically bribery, and also increasing the the probability of approval of expensive, ineffective drugs according to Gøtzsche. With this and also considering the costs to society due to side effects of 'bad drugs' (as mentioned in marketing, with 'externalization of costs') leads to greater financial strain on the public than if trials were run by government or non-profit entities. Gøtzsche suggests that a mere 0.5% tax on prescriptions could actually cover all these costs. [181]
He also suggests (citing a study) that universities can perform these trials for down to a tenth of the current average cost of drug trials.[182]

The problem isn't just in industry, but also in regulatory agencies. In the United States FDA scientists and whistle blowers have been complaining about managerial and political pressures to do such things as ignoring important details from trials and self-censorship. This is, again, due to financial pressures like the fact that the FDA is dependent on fees payed by the industry to conduct trials, and political pressure from politicians that are influenced by lobbyism and campaign donations from pharmaceutical companies. This is, as we have seen, also a problem in the APA and DSM system where there is a huge representation of the industry on the DSM board. It is a problem in the EU and danish parliaments as well, where politicians are being pushed with donations, lobbying and sometimes even bribery. Many politicians in Brussels report: *"constantly being hunted by representatives from big pharma"*. This is an issue that calls for increased transparency across the board, because shedding the 'light' of public scrutiny is the surest measure against fraud and corruption, and that the needs of the public are met.[183]
Transparency can be increased in different ways. Regulation from public and/or non-profit entities should be part of the solution. An example would be laws that support

[180] Gøtzsche, 2013, p. 27
[181] Ibid, p. 116
[182] Ibid, p. 266
[183] Ibid, p. 110-114

and protect whistle blowers, e.g. through them receiving a share of settlement fees, which is one of the strengths in the US legal system, as opposed to the EU and Danish systems where the fines are negligible in comparison. Clear guidelines about donations and kickbacks to doctors, politicians and decisions makers are essential. Transparency on from whom to whom money flows, and which entities are involved in giving financial support to decision makers and public regulatory bodies is of the utmost importance. Disclosure of this has been found to be very beneficial for ethical and lawful conduct. The potential for transparency in the western world has increased in the recent years with the dawn of the information age. We have vast untapped resources for potentially analyzing data and sifting through medical trials, with the possibility of conducting meta analysis in seconds - if only the data is made available. There is lots of potential for improvement, yet things seem to be going the wrong way. Many of these problems are political in nature, but not only so. Public awareness of the issues of: questionable financial ties, loopholes, and so on, are needed, hence the need for 'transparency' across the board - along with proper dissemination of information and media coverage on these issues.

As for SSRIs do the benefits outweigh the risks? In heavily depressed patients that have suicidal tendencies or have been depressed for a long time, then you could say that a risky treatment would have the possibility for the patient to get more positive effects than negative. However, when a "patient" is mildly depressed or anxious, there would be more to lose by going through a risky treatment. Other methods would be more appropriate if there is more to lose by risking SSRI treatment. All this calls for more loyalty to the philosophy of science. When conducting science and forming a theory, it should respect all the criteria of science. Experiments should be reproducible, and falsified hypotheses should not have ad hoc solutions where speculative explanations are added just to maintaining the same paradigm.
Doctors should have a set of ethical codes that are more up to date, and they should have unbiased education and knowledge available.

Lobotomy was one of the biggest mistakes in history of medicine. But we learn from our mistakes, don't we?

Lobotomy was a treatment that could potentially help a small group of hopeless patients as a last solution. It had some good results for some patients, and was a treatment that could be considered if other alternative treatments had failed. The problem was that it got out of hand - it almost got mainstreamed. The very radical procedure was often given to people who actually did not need any kind of medical treatment.
Lobotomy is a very radical and irreversible procedure so it seemed natural to turn to less radical treatments when they became available – hereby referring to antidepressant medicines. It would seem to make sense if the doctors in question had started treating patients with the least radical, invasive methods - but this was not what the doctors who performed the lobotomies were doing. They started with a very radical procedure - at the peril of many patients' long term mental health.
Are doctors still making the same mistakes today, when medicating people that have mild or moderate symptoms of mental illness?
Lobotomy started as a treatment for the chronically mentally ill, and it ended up being given to average teenagers.

Antidepressants were developed to help patients suffering from major depression, and now every 12th Dane is medicated with them.
It took 50 years from the invention of lobotomy before it was stopped entirely. Half a decade seems like a long time to realize that this procedure only resulted in very few positive outcomes in comparisons to the thousands of negative.
Psychoactive drugs have now been available for more than 60 years, and from our research it we are led to believe that the negative effects far outweigh the positive ones, contrary to what the pharmaceutical companies tell us.

Conclusion

The definition of depression within the diagnoses system has been changing with time. It was once a more specific diagnosis, but we see that the criteria have become more loose with the passing years, allowing for a huge amount and variety of people to be diagnosed. The problem is that the line between normal behaviour and what is defined as disease has become blurred with the current diagnosing systems.
We have come to the belief that SSRIs are so wide-spread, because of an interplay between a cultural belief in medical intervention and an economic need for creating economic surplus in companies, leading to unethical choices.
We see that there are problems with biased trials not living up to the codes of scientific conduct, such as Feigl's criteria for science. Placebo double blind tests are often conducted improperly, with the groups measured not being large enough, the lacking use of 'active' placebos or 'selective measuring'. This badly conducted science makes way for SSRIs seeming favorable compared to placebos and alternative treatments. However we have found evidence of several other alternatives being just as beneficial as SSRIs, and often more.
We believe that SSRIs emerged as a result of the serotonin deficiency theory. When discussing depression however, serotonin deficiency is not the "whole story". Depression is the complex result of biochemical and functional factors. A chemical imbalance might be one cause among many others, or an effect.
SSRIs have side effects that can create a serotonin deficiency by reducing the uptake receptors and thereby creating dependency. However judging whether SSRIs are as beneficial as promised, makes for a complicated discussion, because it may be very beneficial to some subgroups of patients, and very harmful to other groups of patients.

It happens that doctors seem to neglect the ethical principles that are at the very foundation of their profession. We are lead to question their real vocation to the very delicate and important occupation they have chosen. Our conclusion is that their tendency to evade the basic principles of biomedical ethics is caused by different factors. Doctors act within a terribly "noisy" field. The industry intentionally creates confusion in order to market their products, even if they are harmful. Often it is nearly impossible to find or access the correct information about the products on the market. Doctors are also in many cases placed in a battle against pecuniary temptations offered to them, such as kickbacks and other forms of 'rewards' from the industry. The ethical principles they are expected to follow are not up-to-date to current challenges, and appear sometimes to be incompatible and radical.
Marketing and the drive for profit seems to be the main source and motivation for most of these problems. The enormous financial power that the big pharmaceutical

corporations acquire is being used for marketing and more illegitimate forms of self-promotion such as lobbyism and even corruption. The big pharmaceutical companies that we describe in our cases are, by and large, not acting in a socially responsible manner. In fact there is a ton of evidence to suggest that their drugs are causing great harm to consumers.

Arguably, companies that supplied drugs that there is a real demand for, wouldn't need to promote themselves in such ways. This has to do with unrestrained, unregulated market factors decided by our politicians and ultimately allowed by the population. We believe that more transparency in trials, in companies, financial records and public entities (such as approval agencies, decision-makers) and more knowledge about this are essential ingredients in solving the troubling state of affairs that we are now faced with.

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Commented Bibliography of our two main Sources

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This book was our main inspiration for the project. It contains a lot of different examples of fraud within the medical realm. The book is very informative and it has a good reference system which makes it a very reliable source. Peter C. Gøtzsche himself is very critical in most of the cases and this makes it sometimes difficult to maintain a *super partes* approach in order to pay attention to all the relevant facts. The book provided us good information regarding SSRIs in general, about the marketing dynamics within the pharmaceutical industries, etc.

Virapen, John. 2010. Side Effects: Death - Confessions of a pharma insider.
This source was very helpful when we had to start with our analysis. It gives a very good insight of the pharmaceutical companies, and how it is to be an insider. John Virapen explains in details how he worked for different industries , including Eli Lilly (The producer of Prozac), and how he helped them to cover up lies and frauds. We tried to remain as objective as possible towards all the information he gave us, as we know that his opinion about this company might be very biased.

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Project technique

The forming of the group was quick. We had similar goals and ideas for how a group should work. The only problem that appeared was later on, when the main idea of the project had to be formed.
When we started working, we momentarily split up into two groups; one being interested in fraud within lobotomy and the other in psychopharmaca. However, as the storming began we were slowly drawn together again. It became clear that we wanted a project that was more relevant for today's society so we chose psychopharmaca, with some comparison to lobotomy in order to create a deeper reflection upon the historical aspect of the project. Hereby we also covered both our main problem formulation and some very important sub-questions which helped us do further brainstorming.

The actual storming process was somewhat chaotic. There was a lot of information on our topic and the amount of directions we could take the project were almost unmanageable. We had to keep on reading, discussing, 'cutting down', agreeing and then reading some more to elaborate on what the group had agreed on. It helped, when dividing tasks into smaller assignments but we were still swimming in an ocean of knowledge. We had agreed on using Peter Gøtzsche's book "Deadly medicine and organized crime" as a red thread and added more sources to both backup and criticizes the direction the project would be taking.

The most difficult process of our project work was norming. When being 8 people in a group it will always take skills to plan meetings where everyone can attend. The communication and personal initiative must be close to flawless for all 8 people in order to work together smoothly as well as making sure everyone follows the same rules set for the project. The recursion of this process was exhausting and kept stirring up problems but because we all knew from the start that this would happen, we were able to solve and find compromises to make sure everyone was satisfied with the rules for our work.

The performance of the group was rather diverse. Some found it most comfortable to start writing early on and some waited till the last 3 weeks, having spent the rest of the semester reading and building a structure on which to base their part. We pulled through quite smoothly with the actual writing but the correcting period was too short in order for us to reach our original goal. Turning a project with 8 authors into a coherent text has a lot of challenges (especially with one member being very ill), which are usually dealt with when correcting the text, so we did not succeed as much in this as we would have liked. We did, however, manage to discover and edit serious mistakes made by misunderstandings.

The project technique helped us understand that even though serious problems can occur, there is alway a possible solution. When having 8 people dealing with such a huge topic, the book and lectures gave us guidelines to help us out of 'tricky' situations, and it helped us understand just how important communication is. The 'tool' we have used the most is the knowledge of group dynamics and how to use it to the group's advantage. Especially in the last process (performing) we had to draw on our knowledge because of the time pressure. Here, it is very important to know who can transform a text into a nice and

easily readable product, who can check the grammar, and who has the overview of the entire story being told and knows whether it is coherent and covers all aspects.

Even though the overall experience of this project has been positive, a few things must be said about ideas for change. We all agree that a group of 8 people is not a good foundation for project work. It is simply too many people.
The second thing is the beginning of the performing process. We started too late and it ended up costing us valuable time to correct the project as one text. The stress of being 8 people and the pressure of the deadline definitely made it a difficult time for us. Even when bearing in mind that we knew we would have problems and we knew we would be stressed.

Overall, this experience of writing our first project with the help of project technique has prepared us for future projects.

Word list

-**Apothecaries Act**
The Apothecaries Act 1815 was an Act of the Parliament of the United Kingdom.he Act introduced compulsory apprenticeship and formal qualifications for apothecaries, in modern terms general practitioners, under the license of the Society of Apothecaries. It was the beginning of regulation of the medical profession in the UK.

-BGA - The German Federal Health Office

The German Federal Health Office (BGA) was founded in 1952 as the successor to the Reich Health Office and was the central state research institute in the Federal Republic of Germany in the area of public health. It was based in Berlin. Its task was to recognize the risks to human and animal health at an early stage, to evaluate these and contain them, within the framework of its legal competence. In 1994, it was abolished, during a restructuring process. Six independent organizations arose out of it. Today the Federal Institute for Drugs and Medical Devices (BfArM) is responsible for the approval of drugs.

-Bias(ed)
A particular tendency or inclination, especially one that prevents unprejudiced consideration of a question; prejudice.

-Bioethics

From ancient greek ἔθος - ethics, behavior and βίος - bio, life, bioethics cope with ethical questions that arise in the relationships among life sciences, biotechnology, medicine, politics, law, and philosophy.

-Blockbuster (in relation to drugs)
Blockbuster: *is much more than a drug generating more than $1 billion of revenue for its owner each year. It is a drug which you are able to sell to even the people that are not sick! And so make such enormous incomes.* – Deadly Medicine and Organized Crime, P. Gøtzsche, P.73

-Clinical Trial
Clinical research is research that directly involves a particular person or group of people, or that uses materials from humans, such as their behavior or samples of their tissue.
A clinical trial is one type of clinical research that follows a pre-defined plan or protocol. By taking part in clinical trials, participants can not only play a more active role in their own health care, but they can also access new treatments and help others by contributing to medical research.

-Cochrane Collaboration

A non profit organisation, started in 1993 (oxford, united kingdom). The collaboration is built on a frustration among researchers and others, that most medical research is of poor quality and biased. The need of systematic reviews of the randomized trials that tell clearly what the costs and benefits of the interventions are.

-CSR
Stands for "Corperate Social Responsibilities". CSR referes to the corporation having several responsibilities to the community it is in. Of these, the most significant are economic (being profitable), legal (obeying the law), ethical (don't lie, cheat or utilize others for your own good) and philanthropic (contribute voulentarily to community with resources).

-Declaration of Geneva

It is a declaration of physicians' dedication to the humanitarian goals of medicine, a declaration that was especially important in view of the medical crimes which had just been committed in Nazi Germany

-Declaration of Helsinki

The declaration of Helsinki is a set of rules regarding medical experimentation on humans.

-DSM
The Diagnostic and Statistical Manual of Mental Disorders (DSM) published by the American Psychiatric Association (APA) provides a common language and standard criteria for the classification of mental disorders. It is used or relied upon by clinicians, researchers, psychiatric drug regulation agencies, health insurance companies, pharmaceutical companies, the legal system, and policy makers. It is also a tool for collecting and communicating public health statistics. The DSM consists of three major components: the diagnostic classification, the diagnostic criteria sets, and the descriptive text.

-**Euthanasia**

The painless assisted death of a suffering patient, incurably ill or in an irreversible coma.

-FDA

Food and Drug Administration. See: Regulatory Authority

-Ghostwriting

- ""**Ghost** authoring" refers to making substantial contributions without being identified as an author.

- "**Guest** authoring" refers to being named as an author without having made substantial contributions.
- "**Ghostwriting**" refers to assisting in presenting the author's work without being acknowledged. The term "ghostwriting" is often used to encompass all three of these practices."
  –The American Medical Writers Association [1]

Ghostwriting can be seen as fraud as the intention of this practice is to intentionally deceive doctors, who believe that the paper is objective and written by disinterested, credible academics and not corporate interests. Examples of where you find ghostwriters are with: scientific papers, review (of papers), educational materials or other material important for marketing (or even approval). These are then circulated to patients, conferences, doctors, and medical journals and used as marketing instruments.

Iatrogenesis (Iatrogenics)
"*Iatrogenesis is an inadvertent adverse effect or complication resulting from medical treatment or advice, including that of psychologists, therapists, pharmacists, nurses, physicians, and dentists.*
Causes of iatrogenesis include negative effects of drugs, chance, medical error, negligence, unexamined instrument design, anxiety or annoyance related to medical procedures, and the adverse effects or interactions of medications. The term iatrogenic can also be used without negative connotation to describe the results of treatment; for example, scars created by surgery are said to be iatrogenic even though they do not represent improper care and may not be problematic." -
Wikipedia: Iatrogenesis

-The International Statistical Classification of Diseases and Related Health Problems (ICD)
Produced by the World Health Organization (WHO), is another commonly used manual which includes criteria for mental disorders. This is in fact the official diagnostic system for mental disorders in the US, but is used more widely in Europe and other parts of the world. The coding system used in the DSM is designed to correspond with the codes used in the ICD, although not all codes may match at all times because the two publications are not revised synchronously.

-**Leucotomy**

Referring to *prefrontal leucotomy*. A surgical brain procedures invented by the Portuguese neurologist Egas Moniz in 1935. Prefrontal leucotomy is a surgical cutting of white nerve fibres within the frontal lobes of the brain. The procedure was formerly

used to treat mental illness. In 1949 Egas Moniz won the Nobel Prize for *Physiology or Medicine*. (Greek λευκός – *leukos*: "clear/white" and τομή – *tome*: "cut/slice")

-Lobotomy

Lobotomy is the general expression for modified version of Moniz's leucotomy. Operationalized by neurosurgeon Walter Jackson Freeman. (Greek: λοβός – lobos: "lobe (of brain)" and τομή – tomē: "cut/slice")

-Nuremberg trials

The Nuremberg Trials consist in a series of military tribunals, held after World War II.

-Physician

A person who practices general medicine as distinct from surgery.

-Regulatory Authority

The approval of drugs is a sovereign, national task of protecting the general interests of the public, because the health of the population is dependent on the quality, efficacy and safety of (approved) drugs. In the United States, the FDA (Food and Drug Administration) is the regulatory authority. In Germany, it was the Federal Health Office (BGA) up until 1994, and now it's the Federal Institute for Drugs and Medical Devices (BfArM).

Scientific fraud

"*The term "scientific fraud" is used to describe intentional misrepresentation of the methods, procedures, or results of scientific research. Behavior characterized as scientific fraud includes fabrication, falsification, or plagiarism in proposing, performing, or reviewing scientific research, or in reporting research results. Scientific fraud is unethical and often illegal. When discovered and proven, fraud can end the scientific careers of researchers who engage in it. Nonetheless, the substantial financial and reputational rewards that can accrue to scientists who produce novel and important re-search or who obtain certain desired results have induced some scientists to engage in scientific fraud.*" - http://www.encyclopedia.com/doc/1G2-3401803766.html

-Seeding Trial

A possibility to get a medicine onto the market before it has been approved by inviting doctors to partake in studies with their patients. The aim is to distribute the drug and familiarize doctors and patients with a drug, which has not yet been approved in order to generate turnover (short-term aim) and to put pressure on the

authorities by creating awareness of and demand for this drug (long-term aim).

-Serotonin

A neurotransmitter in the brain. According to the serotonin theory: There is a certain balance of serotonin, which is good and imbalance can lead to depression, hyperactivity and all kinds of possible evils. The list is added to daily by the pharmaceutical industry. But, the serotonin theory is scientifically untenable and incorrect. Nevertheless, the idea sells itself splendidly. It reduces complex connections to just one single chemical.

- Shareholder

An individual, group, or organization that owns one or more shares in a company, and in whose name the share certificate is issued.
It is legal for a company to have only one shareholder. Also called (in the US) stockholder. - http://www.businessdictionary.com/definition/shareholder.html

-Side Effects

Every substance, which enters the human body, affects more than just one thing. The manufacturer defines what counts as the effect and what counts as the side effect of a drug. They check to find out, which effect they are most likely to get approval for, where they can trick in the simplest way. Once it has been approved, it is easier to get the active ingredient approved for other indications

-SSRI

Abbreviation for selective serotonin re-uptake inhibitor. An active ingredient, which stops the reuptake of serotonin in the brain. For more information see: Serotonin.

-**Whistle blowers**

A person who tells someone in authority about something illegal that is happening, especially in a government department or a company.

-WMA

The World Medical Association (WMA) is an international and independent confederation of free professional Medical Associations, therefore representing physicians worldwide.

Limitations

The biggest challenge before us, as it seems to often be the case with big projects, was the challenge of focusing our research and project and narrowing the scope of our inquiry.

Our problem formulation reads: “Which illegitimate factors have made it possible for SSRIs to emerge - and stay on the market?” A very general question indeed, however the reasoning behind us choosing this formulation was that we wanted to understand how a drug/compound (SSRI) with such questionable background, safety and efficacy was developed, approved and still exists on the market to this day. Our inquiry started with what we initially thought was the primary reason for this, namely "scientific fraud”. Scientific fraud being an umbrella term for deliberate scientific misconduct, such as rigging trials and deliberately conducting what would be considered bad science to achieve certain end results. However we quickly found that there were many factors behind the release and continued existence of this drug besides just *scientific* fraud. These factors include, but are not limited to; corruption, financial interests, adherence to seemingly flawed science and demands from society. All these topics cover areas that could be projects, or even books in themselves and that we had to restrain ourselves from going too much into, due to space and time constraints. We have endeavored to bring out all the more relevant factors into chronological steps; from ‘idea and demand’ to consumption by the ‘patient’. We do this since we believe that these steps are all interrelated and relevant to understanding the full picture and answering our project formulation.

Another challenge that emerged frequently while writing our project was not going too much into the causes of depression, since this is an interesting, complex and controversial topic. None the less, the aim of this project is to determine what kind of fraud has been behind the release of SSRIs onto the market, so it has been unavoidable to look into the origin of depression, mostly seeking to evaluate the validity of the theory of depression supporting the use of SSRIs. Other talk about the origin of depression is covered briefly in the discussion.

Summary (Danish)

Vi har i dette projekt prøvet at belyse de forskellige former for videnskabelig bedrageri, der er tegn på i psykofarmaka industrien, med fokus på subgruppen af antidepressivaet SSRI. Ud fra Peter Gøtzsches bog *"Dødelig Medicin og Organiseret Kriminalitet"* har vi taget nogle forskellige industri sager som vi har belyst med forskellige teorier for at kunne få et bedre indblik i denne industri. Vi har bygge vores projekt på et selvkonstrueret "roadmap", som tager læseren igennem et medikaments udvikling fra idé gennem godkendelse, videre til markedsføring og til sidst ud til forbrugeren.
Vi har i projekt redegjort for de forskellige etiske problematikker som man som industri står overfor, når man producerer et produkt, der er skabt til at hjælpe folk, der lider af psykiske lidelser. Endvidere redegør vi også for den etik som gælder for doktorer og læger, der udskriver denne form for medicin.
Endvidere diskuterer vi nogle af de spørgsmål, der naturligt viser sig gennem arbejdet med dette emne. Diskussionsdelen sætter vi spørgsmålstegn ved hvorfor så mange bliver diagnoseret med depression, og hvorfor farmaceut-industrien har valgt at holde så meget information skjult. Resultaterne af denne rapport har vist et spor af videnskabeligt embedsmisbrug, og en mangel på viden om god videnskabelig etik, som er observeret i alle trin i "roadmap'et". Undersøgelsen har indikeret flere forskellige former for videnskabelige bedrageri bliver brugt for at opretholde SSRIs som den mest fremtrædende og anvendte behandling af depression på verdensplan.