Evaluating the Risks of Drugs and Surgery

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ABSTRACT
The pharmaceutical industry spends $3.2 billion on Direct-to-Consumer medications that lead to over prescribing of unnecessary, expensive, and potentially harmful medications. Adverse Drug Reactions (noxious, unintended and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis, or therapy) are the fourth leading cause of death in American killing 106,000 patients [(11)]. Patients need to evaluate the risks and benefits when deciding to use pharmaceutical drugs or undergo surgery. In order for pharmaceutical companies to be accountable for their product, the Food and Drug Administration (FDA) is likely to be more effective if it requires that companies conduct post-marketing tests. The FDA needs to regulate that non-profit and non-affiliated groups also conduct research that is considered to support drug licensing.

INTRODUCTION
The current system of monitoring the safety of a drug consists of one preclinical testing followed by three phases of clinical studies. Post-marketing studies are optional [(14)]. This strategy is not regulated enough and therefore 51% of drugs have label changes because of major safety issues discovered after marketing. Pharmaceutical companies do not have an incentive to do post-marketing safety studies because they are expensive and often result in either no useful finding or bad news[(14)]. Other limitations of the current system show that carefully selected individuals for pre-marketing studies may not reflect real-life patients, these selected individuals might receive better care, and studies will limit the length of time so that long term effects cannot be found. Companies may compare new treatments against a placebo rather than against a drug that is known to be effective. Conflict of interest is also another problem with the current system. In 92% of all FDA Drug Advisory Committee meetings between January 1, 1998 and June 30, 2000 at least one voting member had a conflict of interest. At one meeting considering the cardiovascular toxicity of the diabetes drug Muraglitazar, the panel failed to include a cardiologist due in part to conflict of interest[(13)] .

New models are being developed to change the current system. One new model would still include a preclinical study followed by three phases of clinical studies, but it would require post-marketing studies conducting trials on 30,000 to 300,000 patients [(14)].

When evaluating whether or not to consume a drug or have surgery, many factors need to be considered. In one year, from September 1997 to September 1998, nearly 20 million patients in the United States took at least one drug that had been withdrawn from the market. It is possible that more drugs caused adverse reactions in people but only 10% of Adverse Drug Reactions are reported to the FDA. Why are so many Adverse Drug Reactions brought to knowledge only after drug approval? Pharmaceutical companies spend $30 Billion on research and development alone, however this does not include the 3.2 billion pharmaceutical companies send on Direct-to-Consumer advertising. To earn quicker returns on investment, companies may rush new drugs to market because of concerns about patent life, a desire to mold prescribing habits prior to the market entry of competitors, and with hopes for a fast "ramp up" in sales that will encourage investors and increase stock prices [(10)]. Direct-to-Consumer advertising can add to the number of adverse drug reactions because advertising may lead to inappropriate prescription. Advertising by the company may increase use because a physician will prescribe it in response to the patient's stated expectation.

METHODOLOGY:
For this research poster, I gathered information from different peer-reviewed journals including the *Journal of the American Medical Association* (JAMA), *New England Journal of Medicine* (NEJM), and from the online electronic journal of *Expanded Academic ASAP*.

RESULTS
In 1994: 2,216,000 hospitalized patients had serious Adverse Drug Reactions and 106, 000 had fatal adverse drug reactions. Adverse Drug Reactions are the fourth leading cause of death after heart disease, cancer, and strokes.

In one example, a pharmaceutical company delayed the publication of a study for seven years, concluding that a widely prescribed drug, Levothyroxine, was no more effective than the less expensive generic form [(12)].

In a study of 298 Standardized Patients (SP) going to their doctors:
In instances of major depression: 53% of doctors prescribed medication on the patient's first visit, 31% was brand specific.
In instances of adjustment disorder: 55% of doctors prescribed medication on the patient's first visit, 39% was brand specific.
Any combination of anti-depressant referral, mental health referral, or follow up within two weeks was offered to 98% of the Standardized Patients. When the doctors referred them to medication, 90% of it was brand name. Pharmaceutical companies have the power to influence doctors as well as patients[(7)].

Table 1: Drugs withdrawn from the market for safety reasons, 1975-2000

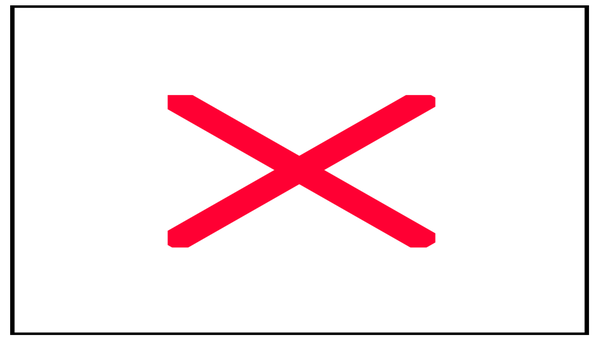
Drug Name	***Date Approved***	Warning- Withdrawn for safety reasons	Time, before withdrawn (years)
Ticrynafen	2-May-1979	Hepatic Toxicity	0.7
Benoxaprofen	19-Apr-1982	Jaundice	0.3
Terfenadine	8-May-1985	Reacts with other drugs	12.8
Floswquinan	30-Dec-1992	Cardiotoxicity increased	0.5
Cisapride	29-July-1993	Mortality	0.5
Bromfenas	15-July-1997	Hepatic Failure	3.1

Table 2. Risk -Benefit Analysis

Type of Diagnosis:	Benefit	Risk
Aspirin	•500,000 women, and 40,000 men indicated that low-dose aspirin therapy is associated with significant reduction in cardiovascular events in both men and women [(2)] •Aspirin therapy for an average of 6.4 years results in an average absolute benefit of approximately 3 cardiovascular events prevented per 1000 women and 4 cardiovascular events prevented per 1000 men [(2)].	•Women: Increase risk for strokes Women: total of 625 Men: total of 597 •Men: risk of Myocardial Infarction MI for women: 469/51342 (0.91%) MI for men: 1023/44144 (2.32%) •Women and Men: Major bleeding[(2)] Women: 301 major cases of bleeding Men:288 major cases of bleeding "Aspirin use is associated with a significant risk of major bleeding irrespective of sex"
Bariatric Surgery	•Effective weight-loss was achieved in morbidly obese patients after undergoing bariatric surgery •Diabetes: decreased 76.8% •Hyperlipidemia: decreased 70% •Hypertension: decreased 61.7% •Obstructive sleep apnea: decreased 85.7% [(3)]	•Out of 16,155 Medicare patients, with a mean age of 47.7: 7.5% mortality for men within a year 3.7% mortality for women within a year •Risk increases in older patients: Ages 65-74: 13% mortality for men within a year 6% mortality for women within a year [(1)]
Antidepressants-Used During Pregnancy	• (PPHN) Persistent Pulmonary Hypertension, 99% of newborns will be unaffected •Stopping medications may result in relapse of depression during pregnancy that endangers the health of the mother and child • Risk of stopping medication: 68% relapse • More research is being done to help women know which drugs are harmful and which are helpful[(4)]	•Increased risk of neonatal abstinence syndrome (condition that includes jitteriness and restlessness in newborns exposed to Selective Serotonin Reuptake Inhibitors. • 30% of newborns are affected with neonatal abstinence syndrome [(5)] • PPHN in women taking fluoxetine cause 10% of deaths to the child[(6)]
Estrogen plus Progestin- in healthy postmenopausual women	•Mortality does not occur •Placebo group fared better •6% fewer cases of colorectal cancer •5% fewer cases of hip fractures[(8)]	•Overall health risks exceeded benefits from use of combined estrogen plus progestin for an average 5.2 year follow up • Over one year: 10,000 women taking Estrogen plus Progestin experienced: •7 more cases of Coronary heart disease • 8 more strokes within a year •8 more invasive breast cancers[(8)]
Direct-to-consumer (DTC)advertising	• DTC advantages can serve a useful educational function and help avert under use of effective treatments for conditions that may be poorly recognized or highly stigmatized [(9)]	DTC advertising leads to over prescribing of unnecessary, expensive, and potentially harmful medications [(9)]

DISCUSSION
Consumers need to evaluate whether or not their risk-benefit analysis of using certain medication or undergoing surgery helps them lead a healthier life. Maintaining a healthy life starts with how you live, by exercising daily and eating a healthy diet, but when those measures seem not enough to live comfortably taking pharmaceutical drugs and undergoing surgery may be the only answer. However, changing the pharmaceutical system is one way that we can enhance our ability to benefit from the dangerous possibilities of drugs and surgery.
•The FDA needs to regulate so that post-marketing occurs when a new drug goes to market.
•Independent, non-governmental organizations are needed for non-regulatory tasks that are independent from the FDA
• Marketing should be reduced to those who truly need it, for whom the risk-benefit balance is in favor of using pharmaceutical drugs and surgery.
•The FDA should provide incentives for companies that do post-marketing studies, and have consumers realize that Adverse Drug Reactions are not a failure of the pharmaceutical companies, so there is not a stigma when drugs are taken off the market, but rather acknowledges the concern for the health of the consumer.
• The FDA should be able to detect important Adverse Drug Reactions that occur more frequently than once per thousand uses of a drug.
•An integral function of the post-marketing surveillance system should be used to report the uses and effects of new and old prescription drugs[(14)].

Table 3. Total number of new drugs approved in the United States from 1987-2001



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