The Bioethical Implications of the Orphan Drug Act on Healthcare in the United States

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Motivations

According to the Rare Diseases Clinical Research Network:

There are approximately 7,000 orphan diseases that affect "more than 25 million Americans and their families". These diseases often go underrepresented and unresearched due to the lack of profit motive for pharmaceutical companies.

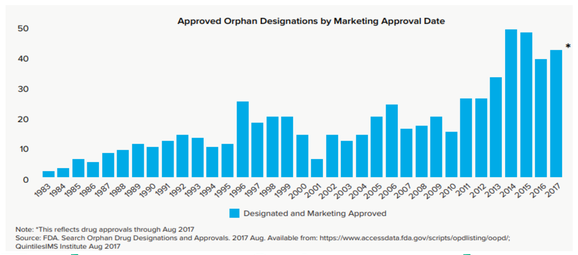
The *intent* of the Orphan Drug Act of 1983 (ODA) was to create incentives for research into these ailments. The ODA resulted in a handful of corporations beginning research, but, the drugs produced still remained costly, inaccessible, and difficult for physicians to prescribe. I examined the intent behind the creation of the ODA and how that intent has manifested the negative patient-physician relationship to orphan diseases present in modern healthcare.

Background

In the United States, an orphan disease is defined as a rare illness that affects fewer than 200,000 patients. Many of theses illnesses are hereditary or caused by genetic mutations and have an extreme negative effect on an individual's quality of life. **The effects of the diseases** I have listed here **range from internal organ failure**, **mental degradation, infertility, muscular atrophy, and** (if untreated) **death. The primary reason the ODA was written and passed was due to the lobbying efforts of patient groups frustrated by** lack of treatment options, medication, and **overall exclusion from the healthcare system**. As a result, the Orphan Drug Act was passed in 1983 to spur the creation of treatment for individuals who previously had no options. In order to do this, the ODA established two primary changes to orphan pharmaceutical development: **the company undergoing trials would receive an income tax credit that is equal to 50% the cost of clinical trials & the drug produced would have a 7-year market exclusivity provision. As indicated by the figure below**, the results of the ODA have been considered – on balance – successful.

A few "common" orphan diseases are:

- Phenylketonuria
- Lysosmal Acid Lipase
- Lymphangioleimyomatosis
- Cystic Fibrosis
- Gaucher Disease
- Ovarian Cancer: BRCA mutation
- Chronic Myeloid Leukemia
- Acute Lymphoblastic Leukemia
- Gastrointestinal Stromal Tumors
- Still's Disease
- Uveitis
- Hidradenitis Supppurativa



Prior to the ODA less than 10 drugs for orphan diseases existed; as of 2017 around 177 drugs have been developed and approved to treat orphan diseases. Although the ODA spurred the existence of these medications, **overtime the changes in the legislation and the cost of the market incentives has fallen onto physicians and patients** who manage orphan diseases.

Techniques & Approaches

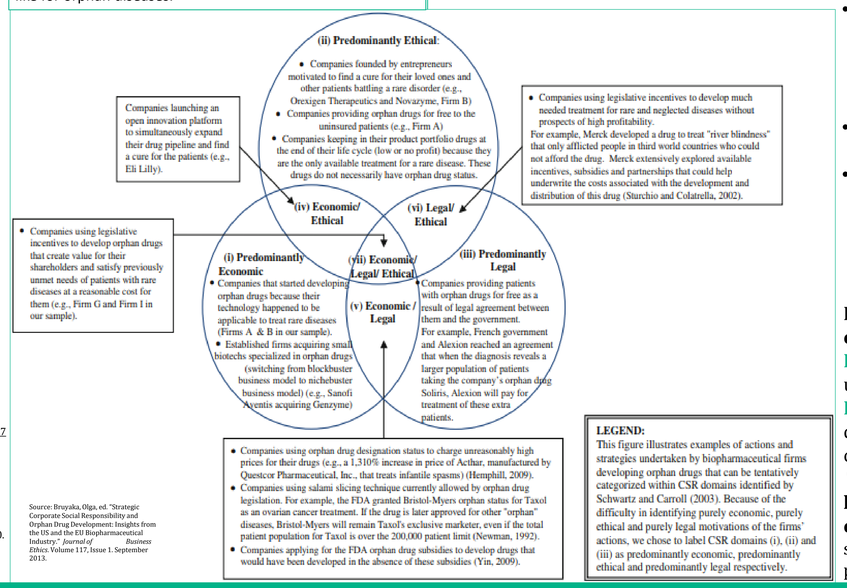
The overall lack of literature on orphan diseases made the beginnings of my research difficult. The Orphan Drug Act is the only piece of legislation specifically directed to address rare disease drug production. I carefully examined a timeline of legislation from the 97th Congressional session – in which the ODA was passed – to the 115th Congressional session of 2017-2018. **In that time 23 pieces of legislation have been proposed to combat the resulting inaccessibility of orphan drugs. The only legislation that passed were 2 amendments that further expanded market incentives.** I then read the original transcripts of these notable congressional sessions and committee meetings in order to parse out the ethical reasoning of legislators. It was extremely difficult to discern the motivations of certain legislators. But, I had gathered relevant information on the *intended* effect of the original legislation and amendments.

From that point, I shifted my research from a political focus to a bioethical focus.

I was able to find a handful of detailed articles that critiqued the affect the Orphan Drug Act has on physicians and patients. After having information on the *results* of the ODA versus the original *intent* I now had an area to examine the ethical connection between the legislature and individual's lives. I then sought to answer a few questions:

- **Do current profit incentives prioritize patients' lives?**
- **Do private pharmaceutical companies have an ethical burden to make their drugs accessible?**
- **Can our profit-centered healthcare system provide ethical care for patients with orphan diseases?**

The **figure below** examines the current multifaceted relationship pharmaceutical companies have towards the development of rare disease medication. Pharmaceutical companies obligations fall into three categories: Ethical, Legal, and Economic. The Corporate Social Responsibility (CSR) matrix is used to visualize the varying degrees of overlap and motivations between these three categories and what the results of prioritizing each responsibility would look like for orphan diseases.

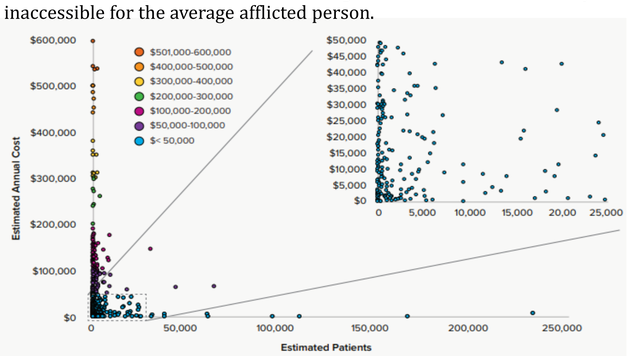


Results & Analysis

The chart on the right displays the way each of the four universal guiding principles of bioethics and three basic principles of need would prioritize patient care. Despite the ODA's success in spurring pharmaceutical development the **implications of the Orphan Drug Act and it's amendments are:**

Ethical Principle	Mode of Operation for Healthcare Providers
Beneficence	Healthcare providers have a primary obligation to prevent and remove harm from the patient.
Non-maleficence	Healthcare providers should not intentionally cause injury or harm towards a patient and must provide adequate care that minimizes potential harms.
Autonomy	The patient must be treated as a rational agent and is capable of informed consent and voluntary decisions. The patient should also be free of controlling influences that would impede voluntary decisions.
Distributive Justice	Healthcare providers should fairly distribute resources according to each person's need. When resources are scarce, providers may defer to factors according to each person's: need, effort, contribution, merit, or free-market exchanges.
Egalitarianism	Healthcare providers should prioritize those most in need of care – even at the risk of a net-loss of goods.
Sufficientarianism	There should be a common standard of care that healthcare providers ensure everyone can reach.
Prioritarianism	Healthcare providers should prioritize the worse off and improvements for patients should be weighted to the treatment's advantage. Unless the needs of the better off exceed in greater advantage or number.

- **Inaccessibly expensive medications –** The graph below demonstrates the annual cost per patient (y) and total number of patients receiving the treatment (x). Each point represents a different treatment. The average co-pay for orphan drug patients is 48% with a 39% deductible; the median annual cost of treatment is $32,000. The high cost of treatment coupled with lack of coverage makes medication virtually inaccessible for the average afflicted person.



- **Legislative barriers that hinder future development and access to medication:** In 2015 the President of the National Association for Rare Disorders (NORD) wrote a letter to (at the time) Chairman Paul Ryan asking he support H.R. 3678: Preserving Access to Orphan Drugs. The resolution sought to exclude medications that had one or more orphan designation from the *Patient Protection and Affordable Care Act* (PL 111-148) annual fee. The multi-million dollar cost "unintentionally created an imbalance for rare disease therapies" and "the annual fee will have an adverse impact on innovation and eventual access to life-saving orphan drugs" by lowering market incentive and increasing existing cost for patients. H.R. 3678 did not pass.
- **Health insurance provider's obstructing physician care:** Due to annual orphan disease budgeting, private and public health insurance companies will often first deny a physician's prescribed treatment of an orphan drug because of the high cost. Instead, health insurance providers will first prompt physicians and patients to attempt a cheaper treatment and prove that treatment failed before approving the originally prescribed medication.
- **Pharmaceutical corporations exploiting the tax credit and market exclusivity:** The majority of pharmaceutical companies providing orphan drugs will charge extremely high prices for the medication due to lack of cost regulation, they companies will 'salami-slice' drugs by "re-defining drug indications to increase the population treated by the same orphan drug", and also applying for government tax credits and subsidies even when the medication would have been developed for a non-orphan disease regardless of subsidies.

- **The consequences of the Orphan Drug Act indicate that a for-profit pharmaceutical development healthcare system is ultimately incapable of prioritizing the principles of bioethics over potential revenue.**
- **There is no obligation to operate a patient-first.**
- **The burden of for-profit pharmaceutical development interferes with a physician's ability to act beneficently.**
- **Health insurance provider's have no incentive to adhere to the non-maleficence principle.**
- **The burden of cost often impedes a patient's autonomy by hindering their ability to clearly and voluntarily make decisions about their care.**
- **Access to medication is controlled by affordability; there is currently no provision for distributive justice of orphan drugs for those who cannot afford access.**

Next Steps

Profit-incentive spurs the development of medication, but does nothing for accessibility and care. A major shift in incentive for development is necessary.

In the short-term legislation like H.R. 3678 would create more accessibility to orphan drugs by ultimately lowering the cost assumed by the patient.

In the long-term, there needs to be a severe paradigm shift in the motivations behind research, development, and administration of rare disease medication. Under each principle of need, a health-care system should (ideally) have the capability of providing care for all patients.

The primary barrier for accessibility is cost. A long-term shift from a profit-centered healthcare industry to a patient-centered one is necessary to the overall sustainability of ethical patient care. The most resource-efficient and ethical way to achieve this is through a form of socialized healthcare, where developmental resources are pooled to eliminate the need for profit-incentive provisions, lower the overall cost of development, increase distribution, and emphasize patient accessibility.

References

Aitken, Murray. "Orphan Drugs in the United States". QuintilesIMS Institute (2017). Web. 19 Aug. 2018

Asbury, Carolyn. "Collaborative efforts on behalf of orphan diseases." *Orphan Diseases and Orphan Drugs*, edited by Scheinberg, Herbert, and J. M. Walshe, Manchester University Press, 1986, 106-118.

Bruyaka, Olga, ed. "Strategic Corporate Social Responsibility and Orphan Drug Development: Insights from the US and the EU Biopharmaceutical Industry." *Journal of Business Ethics.* Volume 117, Issue 1. September 2013. https://link.springer.com/article/10.1007/s10551-012-1496-y

Cohen, Merrill. "The Bioethical Principle of Distributive Justice and the State." *Medical Sentinel.* Volume 7, Issue 2. Summer 2002.

Juth, Niklas. "Challenges for Principles of Need in Health Care." *Health Care Analysis.* Volume 23, Issue 1. March 2015. https://link.springer.com/article/10.1007%2Fs10728-013-0242-7

"NIH Fact Sheets - Rare Diseases Clinical Research Network." National Institutes of Health, U.S. Department of Health and Human Services, Oct. 2010, report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=126.

Saltonstall, Peter. "RE: Preserving Access to Orphan Drugs Act (H.R.3678)." 12 October 2015.

Tambuyzer, Erik. "Rare diseases, orphan drugs and their regulation: questions and misconceptions." *Nature Reviews Drug Discovery.* Volume 9. 2010. https://www.nature.com/articles/nrd3275

Trouiller, Patrice, ed. "Drug development for neglected diseases: a deficient market and a public-health policy failure." *The Lancet.* Volume 360, Issue 9337. 21 September 2002. https://doi.org/10.1016/S0140-6736(02)09096-7

Wellman-Labadie, Olivier, and Youwen Zhou. "The US Orphan Drug Act: Rare disease research stimulator or commercial opportunity?" *Health Policy.* Volume 95, Issues 2-3. May 2010. https://doi.org/10.1016/j.healthpol.2009.12.001

Yin, Wesley. "Market incentives and pharmaceutical innovation." *Journal of Health Economics.* Volume 27. 2008. DOI: 10.1016/j.jhealeco.2008.01.002

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