Title: *A data-driven analysis of right-to-try and its comparison to the FDA’s expanded access program*

Abstract:

*Patients with terminal illnesses face limited options when existing medication and treatment options are exhausted. The expanded access program predecessors have been in place since 1987, allowing terminally-ill patients who have exhausted all prior options access to investigational drugs not yet approved by the FDA. Recently, however, some patient advocates have argued that expanded access does not go far enough, since patients seeking access to pre-market drugs must still gain approval of the FDA and a IRB to use them. This has led to recent legislation, known as right-to-try, that would grant terminally-ill patients the right to use experimental medications on a doctor’s order, bypassing the FDA entirely. Here we investigate the potential impact of right-to-try legislation on the patient population of a large New York hospital system. This is done by examining the current amount of terminal patients using unapproved drugs or drugs in off-label manners. Then predicating the amount of patients who are both terminal and have exhausted all drug treatment options who could reasonably want to use right to try policies. Through showing the amount of people eligible for both right to try and expanded access policies we can try to predict the potential growth in the use of non-fda approved drugs as easier pathways to unapproved drugs appear. This work is crucial because there is no research quantifying how many people can be taking advantage in alternate drug pathways. Thus the potential impact of these new access programs are very unclear.*

Where I get 1987 Investigational new drug, antibiotic, and biologic drug product regulations: treatment use and sale. Fed Regist 1987;52:19466-19466

Introduction:

When comparing expanded access and right to try the main focus is often on weather right to try makes drugs more accessible to patients. One of the main complaints about expanded access is how it requires FDA approval for access to investigational drugs. This complaint can be summed up to two main sub-complaints. Frist FDA might not approve your drug usage and second the additional time required. It turns out in over 99% of cases the FDA approves access [1]. Additionally, for non-emergency requests the median approval time is 4 days and less than a day for emergency requests [2]. As far as industry approval rates it’s hard to know across the board due to some companies fear of how adverse events will affect the approval process. It turns out there has only been two incidences in which adverse events caused a drug to be placed on clinical hold in the past ten years both however ended up being removed from hold[3] .Additionally the expanded access approval rate from Pfizer one of if not the biggest pharmaceutical companies was 98% [4]. With FDA approval times being small and the necessity of drug company approval being required my both expanded access and right to try the main differentiating factors in practice for patients seem to be expanded access’s IRB approval requirement and right to try’s liability protection. Institutional review boards have in the past been shown to charge between $2000 and $3500 for them to review a request [5]. This makes sense since if an medical center does not have an IRB they must use an independent one it still provides a barrier. additionally, there were concerns when full IRB approval was required about how often IRB’s might meet [6]. This perhaps might be mitigated in part now that expanded access merely requires approval by one member of the IRB [7]. However, as with all steps this places another potential cost and delay on treatment. These factors might be part of the reason only \_\_\_\_\_ out \_\_\_ studies on clinicaltrails.gov were available for expanded access [8].

Methods:

Using the Drugs@FDA database I opened the products.txt file through pandas to create a dataframe. Using that generated dataframe I created a list of all unique DrugNames. This gave me a collection of 7088 drugs that the FDA has approved.

Then through the clinical trials database I downloaded all drugs listed in interventions for both trails listed as phase 3 that have statuses of either: not yet recruiting, recruiting, enroll by invitation, active not recruiting or suspended (but not including completed) and trails listed as available and/or approved for marketing in their expanded access program. From both these lists I found all unique drug entries and removed all those in the approved drugs@FDA database and those with the text phrase placebo. Because these databases are not linked it’s possible that this does not remove all the approved drugs to contain just the experimental drugs. However, this still provides value as an estimate of what is available.

Using PharmaGKB I downloaded a comprehensive drugs database. From this I created a python program that allowed for me to easily parse their database and query all drugs from Id’s, all Id’s from each drug and all the different terms used for each drug. This was done to create a more compressive list of all terms used for each drug such that one can quickly determine if a drug listed in the warehouse is novel or simply not the main name.

Using DrugBank I parsed the database to find all drugs that were deemed in the approved group and found their indication field. This field was then parsed to determine what the drug is approved to treat. From this I hope to find out the related icd10/9 codes from the drug.

Results:

Discussion:

[1]<https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/INDActivityReports/UCM597781.pdf>

[2] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5443564/> references the form <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM504572.pdf> which they say states the median approval time but I can’t find it.

[3] <https://www.ncbi.nlm.nih.gov/pubmed/27917324>

[4] <https://www.pfizer.com/purpose/medicine-access/compassionate-use>.

[5] Darrow, J.J., A. Sarpatwari, J.Avorn, and A.S. Kesselheim. 2015. Practical, legal, and ethical issues in expanded access to investigational drugs. The New England Journal of Medicine 372(3): 279–286. Which is refrenced in the really really good paper on the medical neglicance side

<https://link.springer.com/content/pdf/10.1007%2Fs11673-017-9791-z.pdf>

[6] <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.110>

This is the interpretation of its impact on expanded access which states what I said <http://journals.sagepub.com/doi/abs/10.1177/2168479018759661>

[7] <https://blogs.fda.gov/fdavoice/index.php/2017/10/expanded-access-fda-describes-efforts-to-ease-application-process/> might be better source for number [6] as well

[8] clinicaltrails.gov this format though was done by [5] as there citation number [19]

[99] <http://www.solutionsirb.com/faqs/> Says how independent irb takes up to 48 hours and lists some associated costs might be useful info.

[99] <http://www.consortiumofirb.org/membership-info/> a consortium of independent irb

[99] Electronic Code of Federal Regulations, Part 314.510. US Food and Drug administration silver spring. MD US Food and Drug Administration; 2008.  Can charge for direct cost through expanded access

[99] Expanded access to investigational drugs for treatment use: final rule. Fed Regist2009;74:40900-40945 Can take up to 120 man hours to prepare a protocol for intermediate size population

<https://www.ajmc.com/journals/evidence-based-oncology/2018/patient-centered-oncology-care-2017/weighing-the-merits-of-righttotry-laws-and-fdas-expanded-access-program>

1. Pennsylvania becomes the 38th state to pass right to try. Goldwater Institute website. goldwaterinstitute.org/article/pennsylvania-becomes-38th-state-to-pass-right-to-try/. Published October 13, 2017. Accessed January 16, 2018.  
  
2. Karlin-Smith S, Kim SM. Senate approves ‘right-to-try’ drug bill. Politico. politico.com/story/2017/08/03/senate-right-to-try-drug-bill-241293. Published August 3, 2017. Accessed January 16, 2018.  
  
3. FDA Expanded Access (Compassionate Use). FDA website. fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5534121/>

6. Falit BP, Gross CP. Access to experimental drugs for terminally ill patients. JAMA. 2008;300:2793–2795. doi: 10.1001/jama.2008.828.[[PubMed](https://www.ncbi.nlm.nih.gov/pubmed/19088356)] [[Cross Ref](https://dx.doi.org/10.1001%2Fjama.2008.828)]

9. Welch MJ, Lally R, Miller JE, et al. The ethics and regulatory landscape of including vulnerable populations in pragmatic clinical trials. Clin Trials. 2015;12(5):503–510. doi: 10.1177/1740774515597701. [[PMC free article](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4662375/)] [[PubMed](https://www.ncbi.nlm.nih.gov/pubmed/26374681)] [[Cross Ref](https://dx.doi.org/10.1177%2F1740774515597701)]

13. Mackey TK, Schoenfeld VJ. Going “social” to access experimental and potentially life-saving treatment: an assessment of the policy and online patient advocacy environment for expanded access. BMC Med. 2016;14:17. doi: 10.1186/s12916-016-0568-8. [[PMC free article](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4739083/)][[PubMed](https://www.ncbi.nlm.nih.gov/pubmed/26843367)] [[Cross Ref](https://dx.doi.org/10.1186%2Fs12916-016-0568-8)]

17. Downing NS, Shah ND, Neiman JH, Aminawung JA, Krumholz HM, Ross JS. Participation of the elderly, women, and minorities in pivotal trials supporting 2011–2013 U.S. Food and Drug Administration approvals. Trials. 2016;17(1):1. doi: 10.1186/s13063-016-1322-4. [[PMC free article](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4832528/)] [[PubMed](https://www.ncbi.nlm.nih.gov/pubmed/27079511)] [[Cross Ref](https://dx.doi.org/10.1186%2Fs13063-016-1322-4)]

20. Heiat A, Gross CP, Krumholz HM. Representation of the elderly, women, and minorities in heart failure clinical trials. Arch Intern Med. 2002;162(15):1682–1688. doi: 10.1001/archinte.162.15.1682.[[PubMed](https://www.ncbi.nlm.nih.gov/pubmed/12153370)] [[Cross Ref](https://dx.doi.org/10.1001%2Farchinte.162.15.1682)]