Biggest Differences between Right to Try and expanded acess

* Right to try doesn’t need an IRB
* Right to try blocks liability of all parties involved.
  + Medical Negligence Determinations, the Right to Try, and Expanded Access to Innovative Treatments Denise Meyerson

Paper Ideas in rank of easiest to hardest

1. Follow a single patient using expanded acess and note how long it takes for irb approval by physician and drug company approval.

Pro’s

-would be an interesting case study

-almost no info out on how long irb takes or drug approval would take. This is especially true now that irb only needs single irb member approval.

Con’s

-Only looking at one patient is kinda lame

2. Try to find two similar patients one using right to try the other using expanded access and talk about the timeline both took to get the drugs they need

Pro’s

-Can’t find anything like this in literature and would provide a quasi-direct comparison

Of two programs in practice.

Con’s

-I would suspect that the right to try system hasn’t really been put in practice at mount Sinai whereas the expanded access has. To look into right to try might have to compare it to other papers published or even worse cases listed on the right to try site.

3. Find a legal database and see if there have been / how many cases of medical malpractice have been brought into suit due to adverse events resulting from the use of investigational drugs.

Pro’s

-If we could show that their have been almost no suits brought up and that those that have been brought up were won by the doctor we can help show that the effects of blocking liability from right to try is reliable.

-for ny would have to use <https://www.health.ny.gov/regulations/foil/howto.htm> to request the database <https://www.nydoctorprofile.com/> this would allow me to get all malpractice suits against ny doctors or mount Sinai one’s

-if worth exploring could probably find better database

Con’s

-not really mount Sinai focused and doesn’t use the warehouse

4. Explore mount Sinai’s IRb policy. I would bet money if it mentions expanded access it requires a full committee approval when that’s no longer required. Could explore it’s policy and things like how often it meets. One really cool paper did a review of 100 irb’s it would be cool to do something similar but on a smaller scale.

5.Explore mount sinai’s expanded access irb approval rates and average length of time. This number doesn’t exist and would be very valuable.

Pro’s

-again no real numbers on this exist so would be valuable to see if we could get logs of irb meeting or make predictions from the warehouse

6. Explore health disparities in expanded access thought patient insurance policy and location.

Pro’s

-if 100% of people using expanded access aren’t on medicare or Medicaid in a database where 80% of patients are that shows that there is unequal levels of access.

-Can also use location as a rough proxy for wealth. If you live in a project your more likely to be less well off.

Con’s

-don’t know if insurance info is in the warehouse and using location as proxy alone would be week. This might be overcome if there is racial information included because that could also be used to show disparity.

7.Generate Cost information for experimental treatments based off patient’s billings.

Pro’s cost is unknown so it comes up a lot in articles would be interesting to try to quantify it.

Con’s I don’t think the datawarehouse would have this info so it would be tricky to link patients with billing info which I also don’t think is available.

8. IRB APPROVAL TIME PRE AND POST ONE COMMITTEE MEMBER ONLY REQUIREMENT

DON’T NEED IRB IN RIGHT TO TRY NEED ONE PERSON IN IRB TO APPROVE AT MINAMUM SOME IRB PROCESSES MAY BE DIFFERENT. IF NOT IRB NEED TO PAY FOR OUTSIDE IRB.

-average time irb took

-amount of time drug company response took

-both factors in total time of right to try vs expanded acess not really covered

-Look at rate of irb approvals in mount Sinai system that is the paper. If we can use warehouse data or irb logs we can provide an element not really analyzed.

Title: Comparative analysis of treatment options available through the right to try legislation and the expanded access program. (I don’t think this title is valid anymore)

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.

-RXNorm might do something similar

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>

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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)]

<https://jech.bmj.com/content/jech/72/7/557.full.pdf> - high level impact on expanded acess

<http://journals.sagepub.com/doi/abs/10.1177/2168479018759661> - talks about IRB’s very valuable (analyzed data set of 100 irb’s to see what policies common)

Could be intressting to explore impact of one IRB member review policy

Could be cool to search through 100 irb’s with nlp

OOOO could hit up mount Sinai irb to see if we could review their records of drug access and from there acess the acceptance rate. This is novel because no estimates of this number exists.

Possible we could bypass this through looking at patient info in data warehouse

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2684626> - shows a lot of drugs in expanded acess program get approved soon after

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2684626> - very similar to what we were doing originally looking at the approved drugs in drugs@fda and those in expanded acess in clincialtrials. They simply used this info to provide a timeframe about how long it took from expanded access to approval. Coolest thing is they used the expanded access flag as if it had value which we stated didn’t.

[**https://www.nature.com/articles/nbt0418-294**](https://www.nature.com/articles/nbt0418-294) **- nothing really intressting**

[**https://www.tandfonline.com/doi/pdf/10.1080/13543784.2018.1430137?needAccess=true**](https://www.tandfonline.com/doi/pdf/10.1080/13543784.2018.1430137?needAccess=true)

**-good sources descriptions**

Federal Right-to-Try Legislation — Threatening the FDA’s Public Health Mission Steven Joffe, M.D., M.P.H., and Holly Fernandez Lynch, J.D., M.B.E

-most famous paper on topic probs

[**https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5821240/**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5821240/)

**-right to try v v bad**

[**https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2669909**](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2669909)

**-righ try bad**

Exploring length of time irb takes

<https://www.ncbi.nlm.nih.gov/pubmed/29902956>

<https://www.ncbi.nlm.nih.gov/pubmed/27429877>

<https://ascpt.onlinelibrary.wiley.com/doi/pdf/10.1111/cts.12255>

-comparison chart of right to try and expanded access best I’ve found so far in contrasting the two programs.

-best paper I found