Detriment Index based Ranking Technique for painkiller drugs in Noncommunicable Diseases (NCD's)

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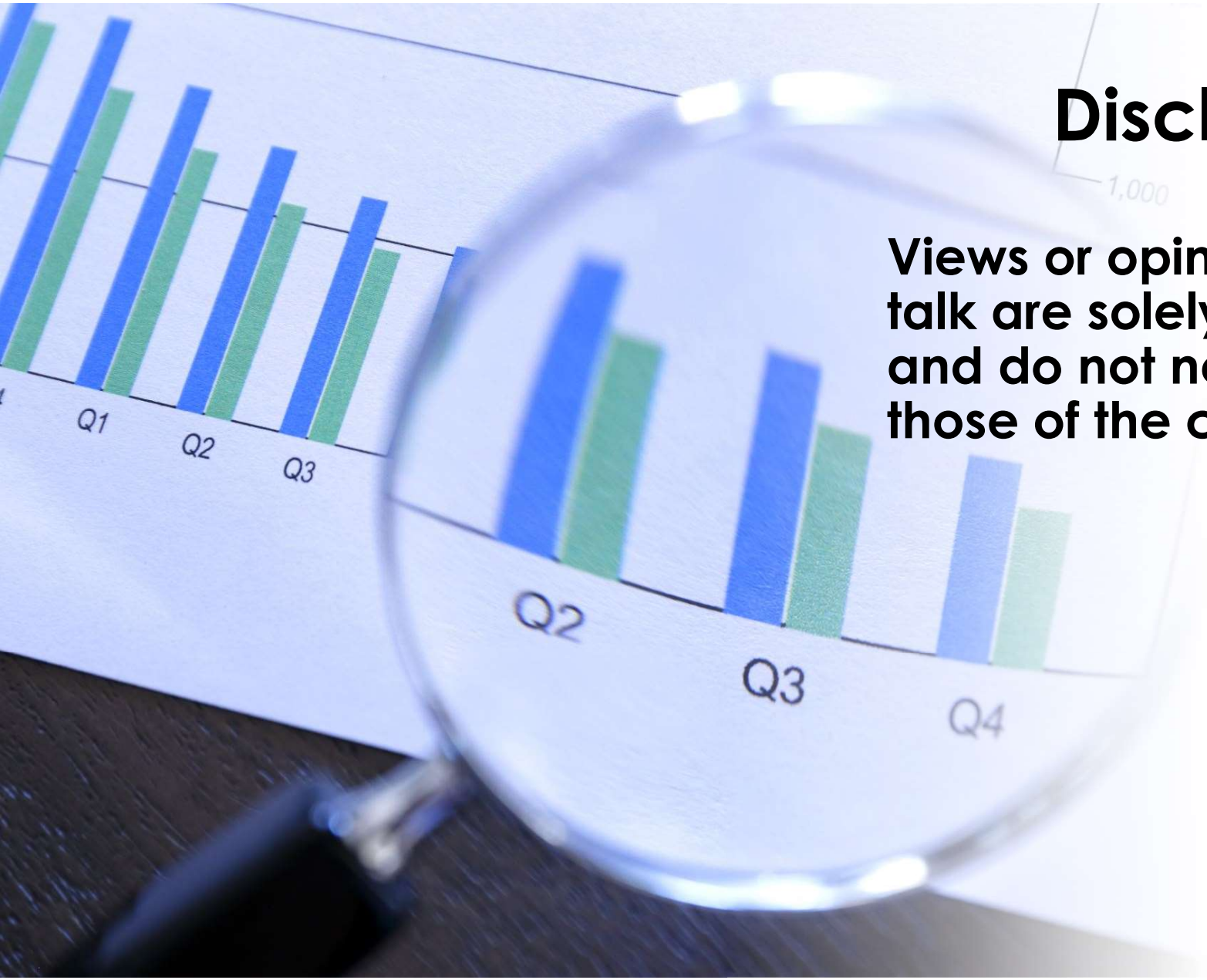

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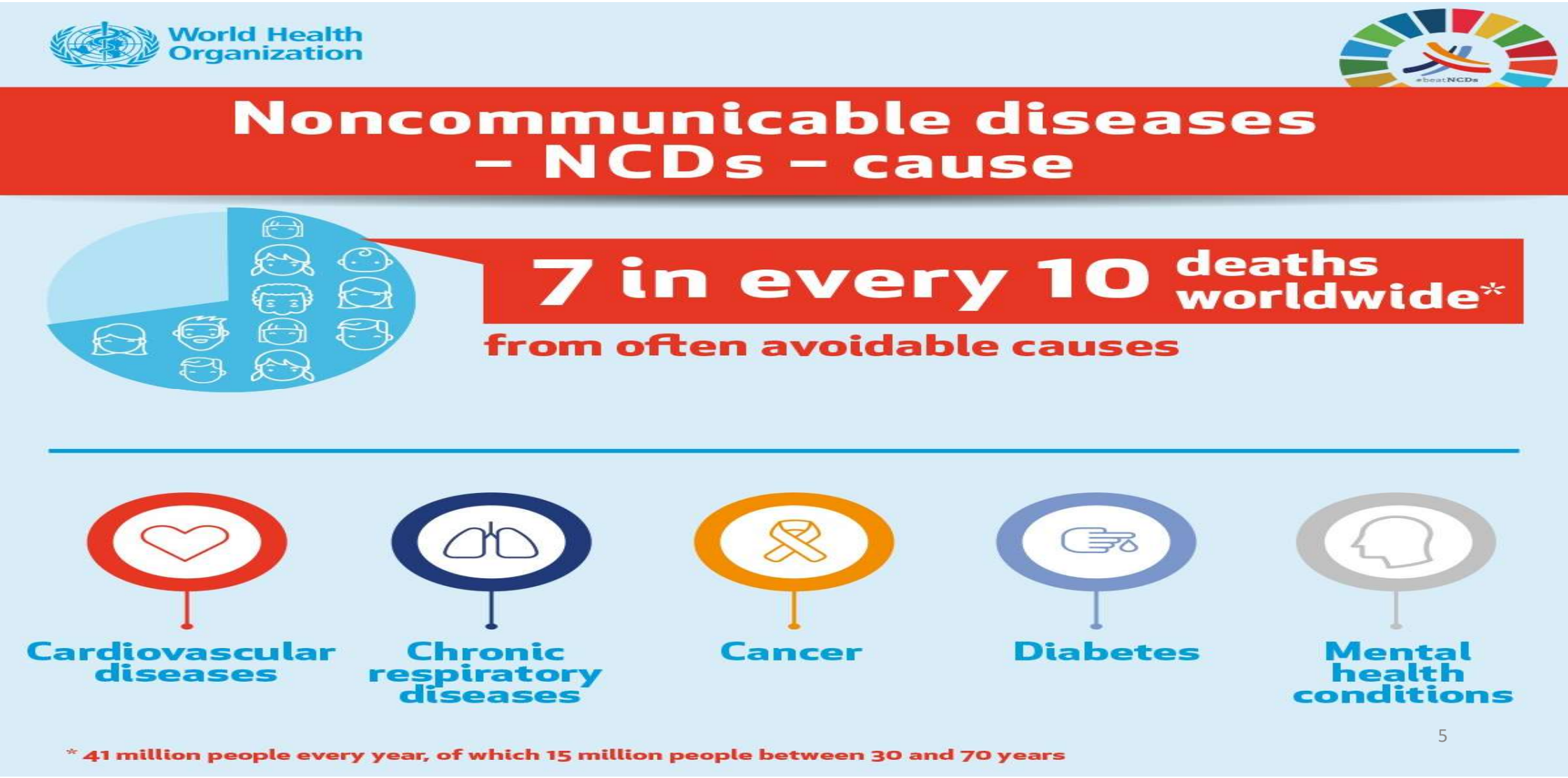
Outline

- Non-Communicable diseases (NCD's)
- Opioid crisis
- Problem & Proposal
- Data
- Fitting exponential growth model
- Computations
- Results
- Conclusions
- Benefits
- Further research


Opiod Crisis
Deaths
Tamoxifen
Docetaxel
Lenalidomide
Methotrexate
Imatinib
Methadone
Avastin
Vicodin
Morphine
Pain
Demerol
Amitriptyline
Trastuzumab
NCD
Emergency
Bleomycin
Percocet
Ranking
Serious
Rituxima
Hydrocodone
Detriment Index
Fentanyl
Vincristine
Painkillers
Oxycontin
Codeine
Cisplatin
Drug Reactions
Revlimid
Cancer
Paclitaxel
Doxorubicin
Pembrolizumab
Tramadol
Hydromorphone

Non-Communicable diseases (NCD's)

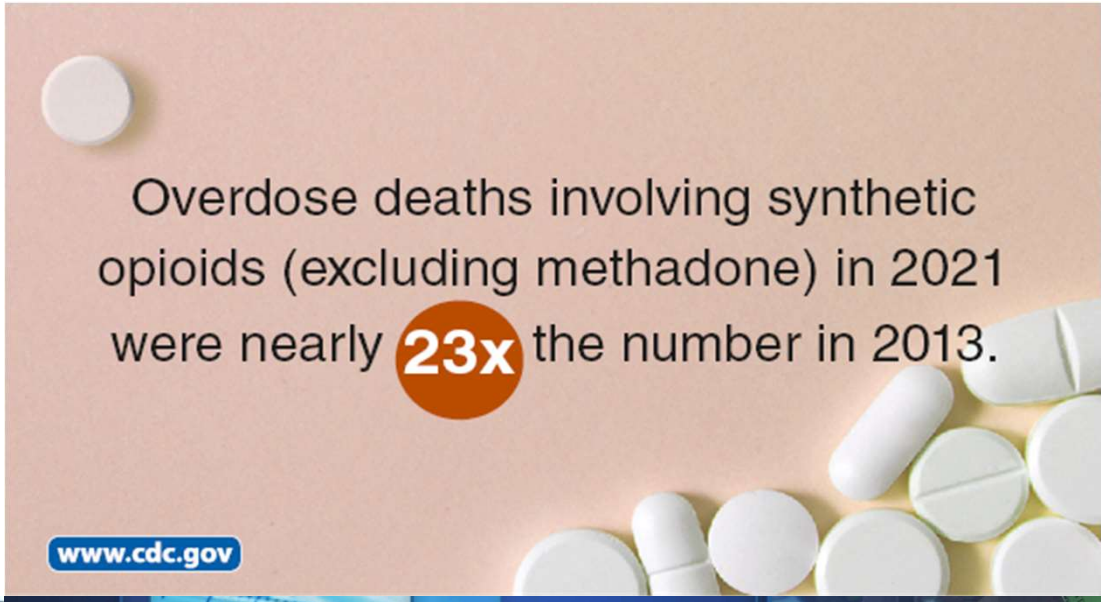


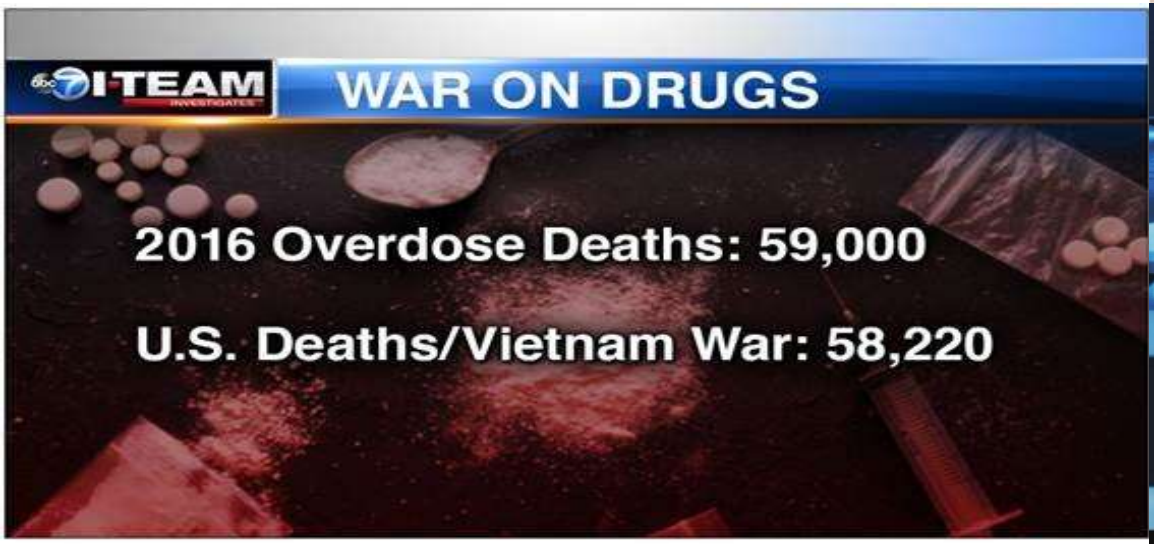
Opioid crisis

Opioid overdose deaths to 'grow exponentially' without action.

1.2M opioid overdose deaths forecasted in US and Canada.

Opioid Crisis

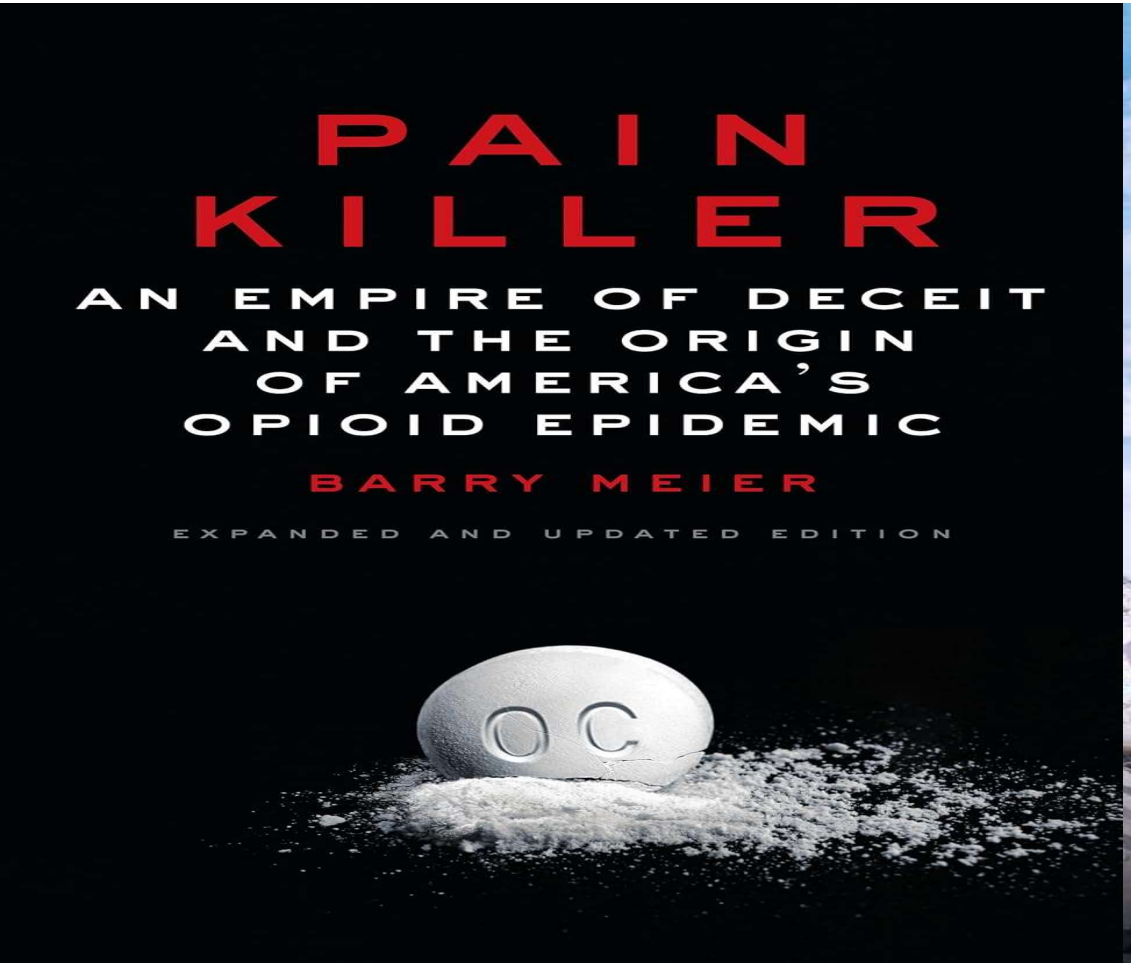




Opioid crisis

4 US firms to pay $26B for fueling opioid crisis

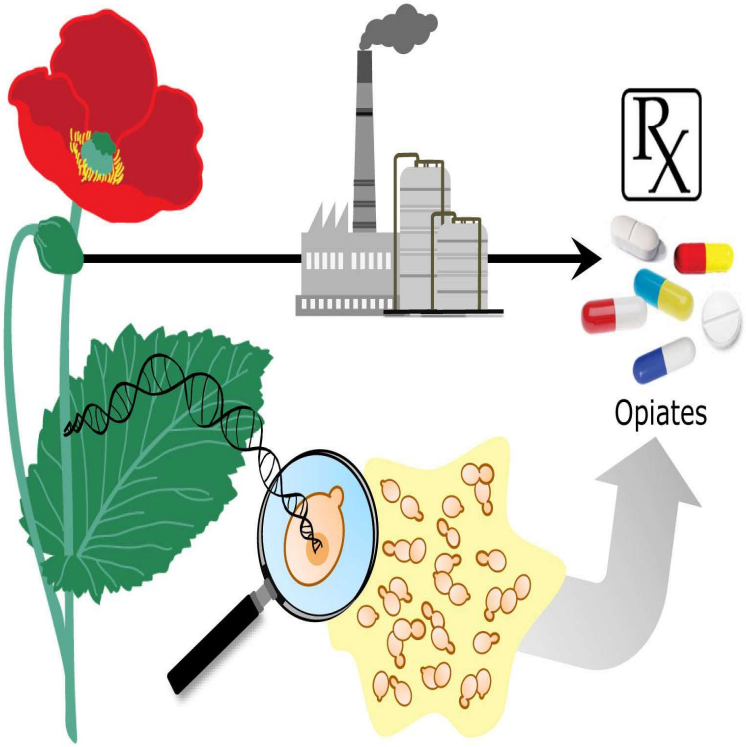
Is your pain big pharma's gain?



Oxycontin - Purdue pleaded guilty, paid $600 million for misbranding

Opioids

- Drugs can be made from the poppy plant
- Made in the lab
- Relieve pain



Problem and Proposal

- **Problem**
  - **Not feasible to stop prescribing**
  - **Very useful as painkillers but highly addictive**
  - **Which opioids are less dangerous?**
  - **Can we rank opioids in terms of safety?**
  - **Choose the best drug based on their safety reports or ADR**
- **Proposal**
  - **Use voluntary adverse drug reaction (ADR) counts**
  - **Lower the count safer the drug**

Data

VigiAccess™ Uppsala Monitoring Centre | WHO Collaborating Centre for International Drug Monitoring | FAQ

covid-19 vaccine Search

covid-19 vaccine contains the active ingredient(s): **Covid-19 vaccine**.
Result is presented for the active ingredient(s).
Total number of records retrieved: **2555971**.

Distribution

- Adverse drug reactions (ADRs)
- Geographical distribution
- Age group distribution
- Patient sex distribution
- ADR reports per year

Year	Count	Percentage
2021	2553539	100
2020	2299	0
2019	94	0
2018	33	0
2017	3	0

FDA Adverse Events Reporting System (FAERS) Public Dashboard — U.S. FOOD & DRUG ADMINISTRATION

Home | Search | Disclaimer | Report a Problem | FAQ | Site Feedback

Total Reports 28,655,483 | Serious Reports (excluding death) 15,867,446 | Death Reports 2,615,699

Reports by Report Type

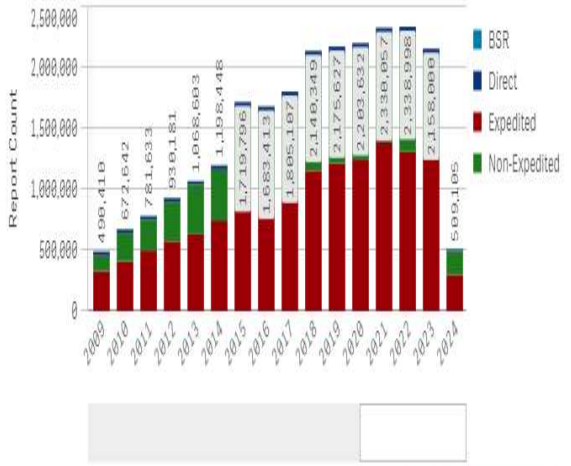
All Years | Last 10 Years

Reports received by Report Type

Year | Report Type

	Total Reports	Expedited	Non-Expedited	Direct	BSR
Total Reports	28,655,483	15,664,587	11,720,616	1,269,417	863
2024	509,105	299,367	194,147	15,591	-
2023	2,158,000	1,250,834	838,536	68,630	-
2022	2,338,998	1,389,915	951,004	78,079	-
2021	2,330,057	1,389,243	868,265	72,549	-
2020	2,203,632	1,242,822	882,250	78,560	-
2019	2,175,627	1,215,347	854,892	105,388	-

Reports received by Report Type



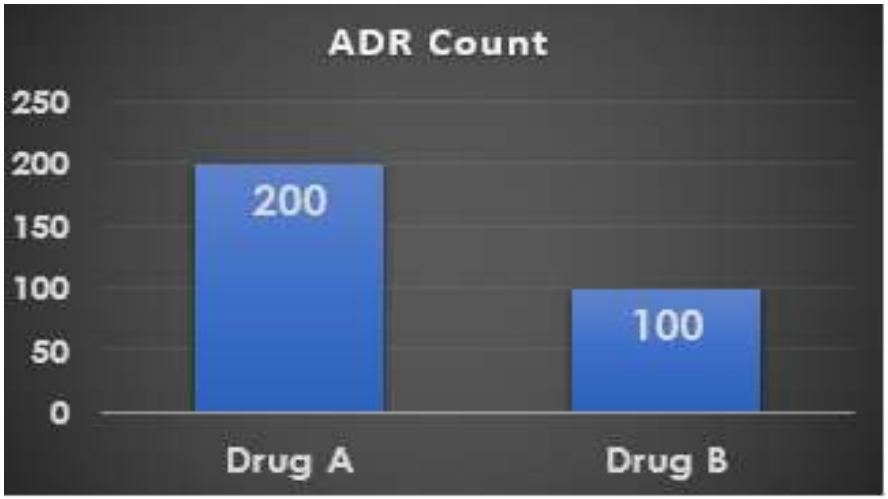
Data as of March 31, 2024

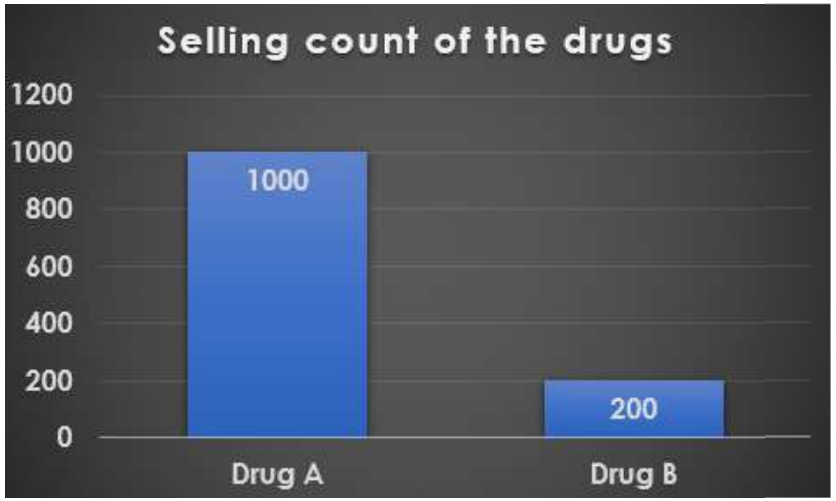
Vulnerability Disclosure Policy

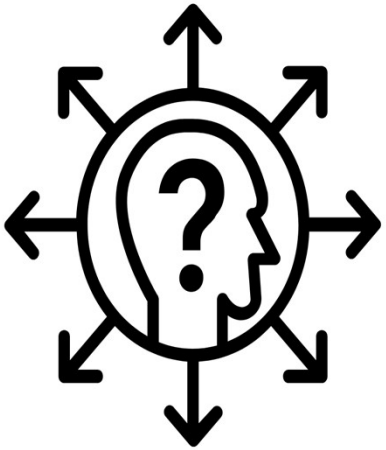
This page displays the number of adverse event reports received by FDA for drugs and therapeutic biologic products by the following Report Types.

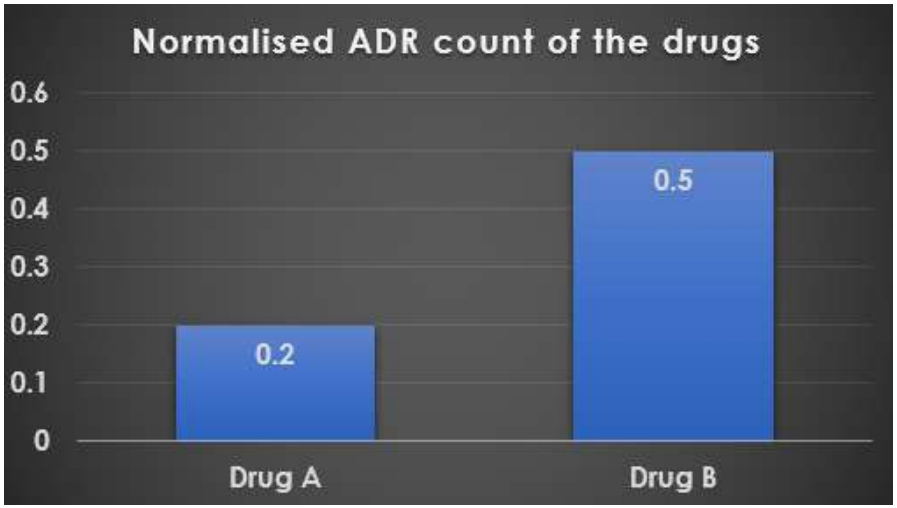
- Direct Reports are voluntarily submitted directly to FDA through the MedWatch program by consumers and healthcare professionals.

Problem with the proposal









- **Unique choice is not possible**
- **Solution: Take cumulative count & fit exponential growth model**

Exponential growth model

- Equation

$$Y_t = \alpha * \exp(\beta t)$$

- Where slope (β)= detriment index (growth rate) decides shape, t = time
- Higher value of β, faster the explosion of ADR count, lower value of β slow rise, β=0 flat graph
- Higher the value of β, worse the drug
- Exponential model has been fitted well and it has a special property

Exponential growth model

- Satisfy is independence of total exposure/total use/total sale etc.
- If model depends on total exposure, total use it's a failure
- Growth rate parameter shouldn't correlate with usage volume
- Large use drug can become more unsafe
- Attempt other models, but due to this difficulty hence used exponential

Exponential growth model

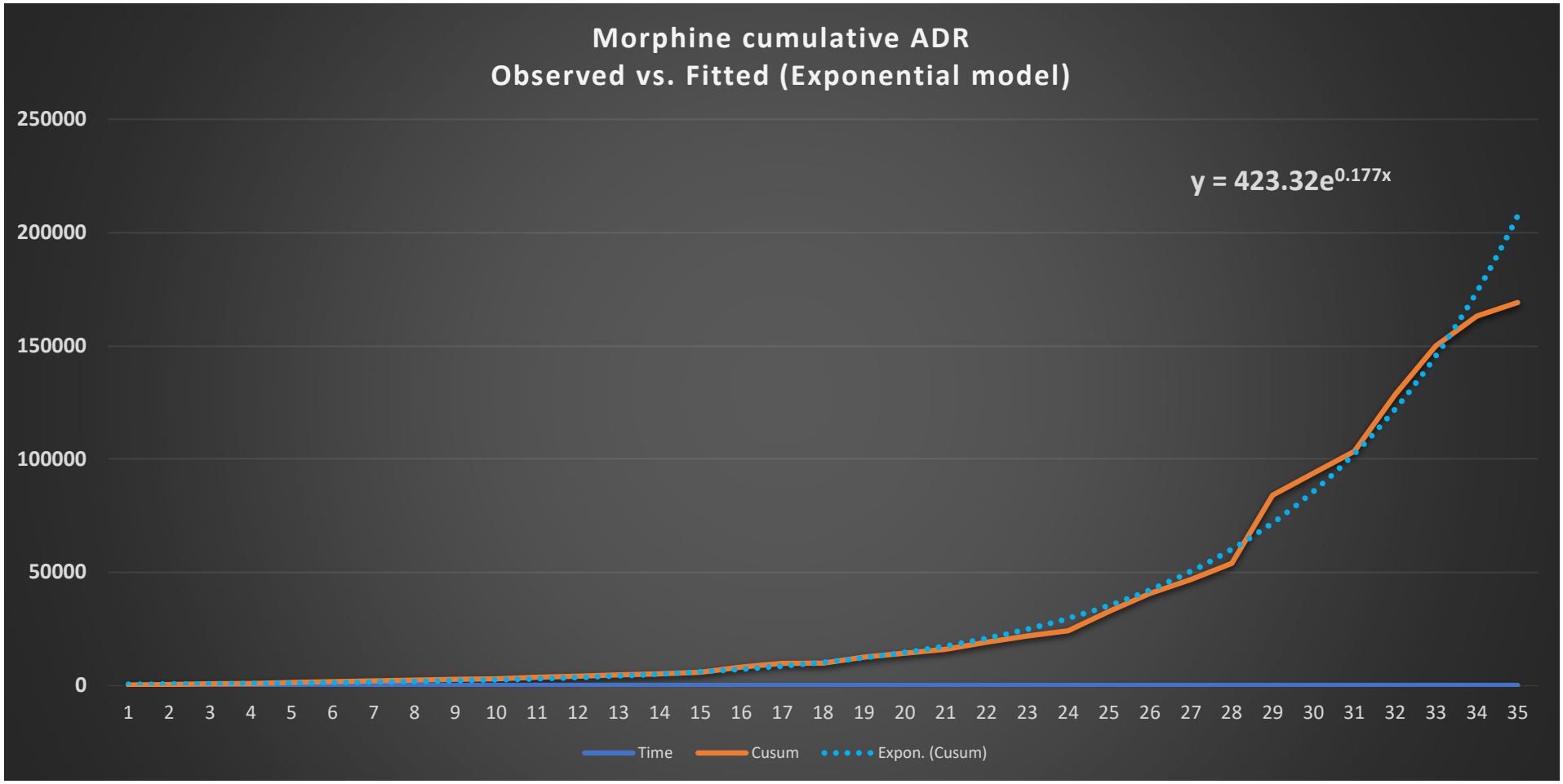
- Linear, Cubic or quadratic or non-linear models etc. can't be used
- Linear model - slope (β) that changes with total exposure ($2y=2a+2\beta$)
- Useful if all drugs in question follow the same pattern
- Forecast future trends in opioid-related adverse events

Difficulty

- Question: Does depend on popularity or volume of use?
- Answer: No $$Y_t = \alpha * \exp(\beta t)$$
- Multiply both $$2Y_t = 2\alpha * \exp(\beta t)$$

- Growth rate slope (β) is unaffected by volume of drug use
- If all y values double, then value of intercept (a) doubles but value of β remains unchanged
- We call 'β' the **Detriment Index** of the drug

Question: Does exponential model fit well?



Results based on growth rate (all ADR)

Ranking based on growth rate			
#	Drug Name	Detriment Index (β)	Rank
1	DEMEROL- Pethidine	0.1236	1
2	AMITRIPTYLINE	0.1253	2
3	CODEINE	0.1659	3
4	MORPHINE	0.177	4
5	FENTANYL	0.2101	5
6	PERCOCET	0.2143	6
7	TRAMADOL	0.2252	7
8	METHADONE	0.2284	8
9	VICODIN	0.2337	9
10	HYDROMORPHONE	0.2372	10
11	HYDROCODONE	0.2913	11
12	OXYCONTIN	0.3096	12

Objection on choice of data

1. Objection on use of all ADR count together
2. Highest concern is with opioid deaths
3. Combining counts of deaths with all other ADR such as minor overdose reactions - Not acceptable
4. Solution?
5. Use the counts of deaths only. Exclude other ADR.
6. Data?

Results based on growth rate (Death)

Ranking based on growth rate (ADR to Death Count)			
#	Drug Name	Detriment Index (β)	Rank
1	DEMEROL-Pethidine	0.1755	1
2	VICODIN	0.1789	2
3	MORPHINE	0.2025	3
4	PERCOCET	0.2073	4
5	AMITRIPTYLINE	0.2096	5
6	CODEINE	0.2183	6
7	OXYCONTIN	0.2303	7
8	HYDROCODONE	0.2304	8
9	METHADONE	0.2341	9
10	FENTANYL	0.2583	10
11	TRAMADOL	0.2736	11
12	HYDROMORPHONE	0.2857	12

Change in ranking (ADR to death count)

#	Drug Name	ADR Rank	Death Rank	Diff
1	DEMEROL- Pethidine	1	1	0
2	AMITRIPTYLINE	2	5	-3
3	CODEINE	3	6	-3
4	MORPHINE	4	3	1
5	FENTANYL	5	10	-5
6	PERCOCET	6	4	2
7	TRAMADOL	7	11	-4
8	METHADONE	8	9	-1
9	VICODIN	9	2	7
10	HYDROMORPHONE	10	12	-2
11	HYDROCODONE	11	8	3
12	OXYCONTIN	12	7	5

Another Problem

- Excluding life threatening ADR?
- Not reasonable

- Solution?

- Combine count of deaths with life threatening events

Results based on growth rate (LT + Death)

Ranking based on growth rate (ADR to LT and Death Count)			
#	Drug Name	Detriment Index (β)	Rank
1	DEMEROL- Pethidine	0.0681	1
2	CODEINE	0.0938	2
3	MORPHINE	0.101	3
4	AMITRIPTYLINE	0.1313	4
5	FENTANYL	0.1521	5
6	VICODIN	0.187	6
7	PERCOCET	0.1945	7
8	HYDROMORPHONE	0.1954	8
9	HYDROCODONE	0.2366	9
10	OXYCONTIN	0.2585	10
11	METHADONE	0.3059	11
12	TRAMADOL	0.3441	12

Change in ranking (ADR to LT + death count)

#	Drug Name	Rand (Death)	Rank (LT + Death)	Diff
1	DEMEROL- Pethidine	1	1	0
2	AMITRIPTYLINE	2	6	-4
3	CODEINE	3	3	0
4	MORPHINE	4	7	-3
5	FENTANYL	5	4	1
6	PERCOCET	6	2	4
7	TRAMADOL	7	10	-3
8	METHADONE	8	9	-1
9	VICODIN	9	11	-2
10	HYDROMORPHONE	10	6	4
11	HYDROCODONE	11	12	-1
12	OXYCONTIN	12	8	4

Results based on growth rate (all ADR)

Ranking based on growth cancer drugs			
#	Drug Name	Detriment Index (β)	Rank
1	Tamoxifen	0.0972	1
2	Avastin	0.1211	2
3	Bleomycin	0.139	3
4	Paclitaxel	0.1673	4
5	Vincristine	0.1706	5
6	Methotrexate	0.1853	6
7	Cisplatin	0.1859	7
8	Doxorubicin	0.208	8
9	Docetaxel	0.267	9
10	Rituxima	0.2771	10
11	Trastuzumab	0.3025	11
12	Revlimid	0.5431	12
13	Lenalidomide	0.5432	13
14	Pembrolizumab	0.8277	14

Results based on growth rate (ADR to LT + Deaths)

Ranking based on growth cancer drugs			
#	Drug Name	Detriment Index (β)	Rank
1	Bleomycin	0.1412	1
2	Methotrexate	0.1436	2
3	Cisplatin	0.1833	3
4	Paclitaxel	0.1844	4
5	Doxorubicin	0.2187	5
6	Tamoxifen	0.2391	6
7	Revlimid	0.2391	7
8	Rituxima	0.2455	8
9	Trastuzumab	0.2459	9
10	Docetaxel	0.2478	10
11	Avastin	0.3288	11
12	Lenalidomide	0.4581	12
13	Vincristine	0.607	13
14	Pembrolizumab	0.6851	14

Change in ranking (ADR to LT + death count)

#	Drug Name	Rank (ADR)	Rank (LT + Death)	Diff
1	Tamoxifen	1	6	-5
2	Avastin	2	11	-9
3	Bleomycin	3	1	2
4	Paclitaxel	4	4	0
5	Vincristine	5	13	-8
6	Methotrexate	6	2	4
7	Cisplatin	7	3	4
8	Doxorubicin	8	5	3
9	Docetaxel	9	10	-1
10	Rituxima	10	8	2
11	Trastuzumab	11	9	2
12	Revlimid	12	7	5
13	Lenalidomide	13	12	1
14	Pembrolizumab	14	14	0

- **Rank opioid or painkillers drugs by fitting exponential models to deaths**
- **Ranking remains consistent when including life-threatening events with deaths**
- **The method used does not depend upon popularity or total exposure of an opioid**

Benefits

- Rank drugs for safer cancer treatment, reducing side effects
- Prioritize low-risk drugs to lower treatment burden
- Optimize resource allocation in healthcare systems
- Collaborate using Detriment Index to fight against opioid crisis
- Innovative approach contributes to the safe and effective management of pain in patients, ultimately improving their quality of life and well-being

Further research

Beyond the Basics: Statistical Innovations for Deeper Understanding of Opioid Addiction and trends

Further research

- Identify socioeconomic backgrounds linked to higher addiction rates
- Explore machine learning for predicting high-risk opioid misuse
- Explore trends in opioid prescribing, hospital admissions & overdose deaths over time
- Time-series forecasting models to predict future opioid-related trends
- Branching process models provide a stochastic framework for ranking drug safety

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Thank you for your time!

Any Questions?

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