The Evolving World of Natural Language Processing in Healthcare and Life Sciences

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Presenters

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Agenda

+ Introduction to Information Extraction in Healthcare
+ Blending Methods
+ IQVIA NLP Information Extraction Pipeline
+ Demo: Applied ML in Life Sciences
  • GSK
  • Northshore
  • Using ML for Extraction of Adverse Events
+ Summary
+ QA
Information Extraction in Healthcare
Disruption in Healthcare has been accelerated by a combination of the digital revolution and COVID responses

**Explosion in Data**
The volume and pace of research, breadth and depth of digital and other interactions in diverse formats, all contribute to the explosion in data and information overload.

**Real-World & Patient Centricity**
Unlocking unstructured medical records, the ever-increasing role of real-world data, and focus on patient voice is disrupting development, access and commercialization.

**Accelerating Digital**
Digital interactions have taken a leap as a result of the pandemic, with acceptance of digitalization and new technologies to handle and analyze data.

**AI & Expert Augmentation**
Evolution and revolution in ML methods, accelerating pace of change, and need for human in the loop for impactful data and deep insights.
Unlock medical, business and scientific context

Input: Raw Health Records
- Increased Tumour Size
- Tumour margins negative
- EGFR T790 positive
- Ejection Fraction 40%
- Failed treatment with cisplatin
- PDL1 negative

Input: Patient Questions
- Can I get a flu shot while taking Drug A?
- Can I take Drug A while pregnant?
- Should I try for a baby while taking Drug A?

Result: Business Context

Input: Research Activity

Result: Scientific Context

Medical Context

Human Centric Content

Input: Social Determinants
- Former smoker
- Quit 10 years ago
- Problems walking
- Lot of stress
- He lives alone
- Missed 3 month appointment

Normalized Value
- Ex smoker
- Ambulatory Status: walking difficulty
- High levels of stress/Stress
- Social Isolation
- Did not attend
Healthcare Data is Complicated

Different word, same meaning
- cyclosporine
- ciclosporin
- Neoral
- Sandimmune

Different grammar, same meaning
- 5mg/kg of cyclosporine per day
- 5mg/kg per diem of cyclosporine
- cyclosporine 5mg/kg per day

Different expression, same meaning
- Non-smoker
- Does not smoke
- Does not drink or smoke
- Denies tobacco use

Same word, different context
**Dermatome**
- An area of the skin supplied by a specific nerve root
- A surgical instrument used to cut the skin
Blending Methods
Two main types of Natural Language Processing

NLP for data transformation and better value from your unstructured text

There are many different natural language processing system, which fall into the two main categories:

**Rules-based systems:**
- Linguistic rules which are transparent, deterministic and repeatable
- Rules instruct the system to use semantically relevant elements of text to identify relevant entities, relations, categories based on its content
- Rules can be developed relatively rapidly, without large sets of training data
- If the rule doesn’t exist, the system will be unable to ‘understand’ the human language and thus will fail

**Machine learning-based systems:**
- Use statistical methods to create a “black box”
- ML systems learn to perform tasks based on training data they are fed, and adjust their methods as more data is processed
- Can use deep learning, neural networks, transformer models (e.g. BERT), large language models (e.g GPT)
- Generally need large volumes of annotated training data

Newer Tools are Bigger. And Better?

• Cost, Convenience, Accuracy

• The latest tools require massive amounts of compute to create the models and then to run them at production scale, risking large bills and vendor lock-in

• Simple problems should not require complex solutions.
IQVIA NLP
Information Extraction Pipeline
IQVIA NLP Ontologies

Over **6.5 million** synonyms from a wide range of ontologies in many categories

- **Diseases & Phenotypes**: COVID-19, Diseases & Symptoms, HPO, MeSH, NCI
- **Biological Entities**: Orphanet, ICD-9-CM, ICD-10-CM, LOINC, SNOMED, TNM Stages
- **MeSH**: NCI
- **SNOMED**: TNM Stages
- **UNII**: Orphanet, ICD-9-CM, ICD-10-CM, LOINC, SNOMED, TNM Stages
- **RxCUI**: MeSH, NCI
- **LOCN**: Date, Duration & Frequency
- **Reactions**: Context Terms, Relations
- **Dates**: Date, Duration & Frequency
- **Organizations**: MeSH, NCI

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Very Accurate Biomedical NER across a Range of Entities

Identical NER benchmark run with IQVIA NLP tools plus four other systems
Our Core Pipeline

APIs within the NLP pipeline allow integration of existing components, prototyping and extensibility
Combine NLP techniques using GUI or SDK

- **Run interactively or programmatically**
  - Integration with pre- and post-processors
  - YAML-based rich query language
  - Configuration GUI

- **Built-in Sentence Detection**
  - Configurable distance constraints
  - Linguistic wildcards
  - Transformer-based NER
  - Dictionary-based entity normalization
  - Output schema definition

- **Medical Transcription Samples with BERT**
  - Output mode:
    - HTML
  - Ordering:
    - Frequent first
  - Produce:
    - Docs/annotation
  - Hits/doc/annotation
  - Matches/column/Hit words displayed
  - Global Settings (Within Query)
    - Disambiguation
    - Boundaries
    - Language
  - Column Options
    - Default
Applied ML in Life Sciences
NLP-enhanced Social Media & News analysis for brand teams

Situation

• Global, regional and country brand teams needed social media derived analysis and insight to inform marketing and stakeholder engagement for multiple products across key therapy areas
• For indications with high volumes of posts and mentions there is a high % of noisy or irrelevant posts that make usable insights challenging to derive

Outputs and User Impact

• By categorising posts with sentiment, written perspective, medical terms, treatment and many more dimensions the analysis allows brand teams to get a better understanding of the key needs, concerns and experiences of patients and other stakeholders
• Topic analysis of news articles helps understand the media content that patients and others are seeing and reading
• Beyond core topics of interest, the analyses identified adjacent topics and profiles that might inform targeted marketing and communication activities
• Thanks to noise reduction it was easier to quickly understand the content and move from insight to action

Solution

• IQVIA used a combination of social listening tools, machine translation and natural language processing to create an enhanced data feed
• This data feed was then ingested into a data warehouse and then fed into interactive visuals developed to surface trends, highlight key topics
• The algorithms make use of a combination of comprehensive biomedical ontologies, linguistics, pre-trained models and supervised machine learning to create powerful tags and remove noise

Methods:
• Fine-tuned BERT
• Ontologies & Linguistics
• Pre-trained classifiers

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Methods used to combine i2e, ML and GPT

Relationships (i2e)
- Linguistic relationships used to identify key content

Ontologies (i2e)
- Broad use of ontologies to classify and explore the data

Topic Analysis (i2e)
- Known topics are defined within i2e queries

ML BERT Classifier (Perspectives)
- Classify which tweets are written from the perspective of patients, HCPs or caregivers

Unsupervised Topic Modeling
- Top2Vec used to generate unsupervised topic clusters based on the data

Topic Cluster Naming and Simple Summaries
- GPT3.5 used to create topic cluster names
## Ontology-Based Extraction

### Ontology (8/8)

<table>
<thead>
<tr>
<th>Ontology</th>
<th>Terms</th>
<th>Text Snippet</th>
<th>Doc</th>
<th>#Hits</th>
<th>Hit</th>
<th>Export?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs &amp; Symptoms</td>
<td>Pruritus</td>
<td>itches</td>
<td>999</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Feel Tired</td>
<td>tired</td>
<td>999</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
<td>tired</td>
<td>999</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cough</td>
<td>cough*</td>
<td>998</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Obsessive thoughts</td>
<td>self-obSESSION</td>
<td>999</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Obsessive Behavior</td>
<td>self-obSESSION</td>
<td>999</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pyrexia</td>
<td>fever</td>
<td>1000</td>
<td>1</td>
<td>@MissFrancaise nono, fever &amp; tickly cough.</td>
<td>✔️</td>
</tr>
<tr>
<td></td>
<td>Cough</td>
<td>cough</td>
<td>1000</td>
<td>1</td>
<td>@MissFrancaise nono, fever &amp; tickly cough.</td>
<td>✔️</td>
</tr>
<tr>
<td></td>
<td>Cough</td>
<td>a cough attack</td>
<td>1000</td>
<td>1</td>
<td>jus had a cough attack.</td>
<td>✔️</td>
</tr>
</tbody>
</table>

### Term (8/139)

- Cough
- Fatigue
- Feel Tired
- Fever
- Obsessive Behavior
- Obsessive thoughts
- Pruritus
- Pyrexia
# Relationships

<table>
<thead>
<tr>
<th>Class1</th>
<th>Relation</th>
<th>Class2</th>
<th>Doc</th>
<th>#Hits</th>
<th>Hit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>due</td>
<td>Exposure</td>
<td>4729</td>
<td>1</td>
<td>My research went from asthma due to aerosol exposure to mf pesticide exposure because of frequent use of baygon ahrngldh</td>
</tr>
<tr>
<td>Asthma</td>
<td>due</td>
<td>Pollen</td>
<td>1804</td>
<td>1</td>
<td>I’ll remember that next time I have a severe asthma attack due to pollen, dust, perfumes, or smoke from prescribed burning.</td>
</tr>
<tr>
<td>Asthma</td>
<td>due</td>
<td>Air Filters</td>
<td>57</td>
<td>1</td>
<td>RT @ankitaup 41% reduction in acute asthma events due to air purifier use: AIIMS-IIT Delhi study Indianexpress.com/article/cities... via @IndianExpress</td>
</tr>
<tr>
<td>Asthma</td>
<td>due</td>
<td>Air Pollution</td>
<td>3584</td>
<td>1</td>
<td>The traditional Kujirabune Festival made a comeback to revitalize the Isuzu area of Yokkaichi, Mie Prefecture, where many people suffered from asthma due to the air pollution in the city.</td>
</tr>
<tr>
<td>Asthma</td>
<td>due</td>
<td>Weather</td>
<td>7329</td>
<td>1</td>
<td>I thought it was her asthma playing up due to Spring weather and high humidity.</td>
</tr>
<tr>
<td>Asthma</td>
<td>due</td>
<td>Humidity</td>
<td>7329</td>
<td>1</td>
<td>I thought it was her asthma playing up due to Spring weather and high humidity.</td>
</tr>
</tbody>
</table>

## Class1 (1/3)

<table>
<thead>
<tr>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

## Relation (47/82)

<table>
<thead>
<tr>
<th>reduce</th>
<th>manage</th>
<th>generate</th>
<th>due</th>
<th>role</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

## Class2 (6/99)

- Air Filters
- Air Pollution
- Exposure
- Humidity
- Pollen
- Weather
<table>
<thead>
<tr>
<th>Sentiment</th>
<th>Text Snippet</th>
<th>Doc</th>
<th>#Hits</th>
<th>Hit</th>
<th>Export?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>I was given an inhaler but I was warned that if I healed that means covid worsened my asthma.</td>
<td>9305</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>It's 2am and my asthma has flared up so I can't sleep ☹️ literally coughing non stop.</td>
<td>3354</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>new car smell triggers my asthma lmao</td>
<td>3871</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>I cannot wear the Disposable masks as they trigger my Asthma I wear australiasfacemasks.com.au WHO approved</td>
<td>9678</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>not me feeling extremely guilty that I got sick on tuesday (I'm the one that usually and mostly gets sick if anything cause my asthma and allergies suck) and now my parents and brother are sick when they haven't gotten sick in months 😢😭</td>
<td>9686</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>RT @stu_dowling @ProfGlantz ANTZ: Vaping causes asthma Us: My asthma's better now ANTZ: Vaping causes COPD Us: My COPD symptoms are gone ANTZ: Vaping causes lung damage Us: I no longer have to use oxygen ANTZ: Vaping causes lung Infections Us: I haven't been sick in years ANTZ: YOU'RE WRONG!</td>
<td>1213</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>Because I can't go to the shed (my asthma is very bad... and the shed triggers the asthma) partner photographed some of the bookshelves.</td>
<td>9137</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>I forgot how bad my asthma hit me from sprints yEESH</td>
<td>1468</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>I think something just triggered my asthma hehe just making sure it's not covid again so im wearing mask na 😊 have a nice day!</td>
<td>2072</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# NLP-Topic classification & extraction (known Topics)

<table>
<thead>
<tr>
<th>Topic Category</th>
<th>Text Snippet</th>
<th>Doc</th>
<th>#Hits</th>
<th>Hit</th>
<th>Export?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Branded</td>
<td>I have ventolin, after awhile I'm ok.</td>
<td>7332</td>
<td>1</td>
<td>I have ventolin, after awhile I'm ok.</td>
<td>✔️</td>
</tr>
<tr>
<td>Branded</td>
<td>RT @Dayveeb17 I used to apply those two but now only seretide ease my pain.</td>
<td>6935</td>
<td>1</td>
<td>RT @Dayveeb17 I used to apply those two but now only seretide ease my pain.</td>
<td>✔️</td>
</tr>
<tr>
<td>Branded</td>
<td>Massive thanks to our ambulance service, my colleagues in emergency department and Ventolin.</td>
<td>6554</td>
<td>1</td>
<td>Massive thanks to our ambulance service, my colleagues in emergency department and Ventolin.</td>
<td>✔️</td>
</tr>
<tr>
<td>Branded</td>
<td>I've given in, I'm taking ventolin.</td>
<td>5425</td>
<td>1</td>
<td>I've given in, I'm taking ventolin.</td>
<td>✔️</td>
</tr>
<tr>
<td>Branded</td>
<td>The ventolin isn't great for my arrhythmia.</td>
<td>7337</td>
<td>1</td>
<td>The ventolin isn't great for my arrhythmia.</td>
<td>✔️</td>
</tr>
<tr>
<td>Branded</td>
<td>I have ventolin, after awhile I'm ok.</td>
<td>7337</td>
<td>1</td>
<td>I have ventolin, after awhile I'm ok.</td>
<td>✔️</td>
</tr>
<tr>
<td>Branded</td>
<td>Best to carry Ventolin or other reliever medication.</td>
<td>2761</td>
<td>1</td>
<td>Best to carry Ventolin or other reliever medication.</td>
<td>✔️</td>
</tr>
<tr>
<td>Branded</td>
<td>@Kidcowboy2 @AlboMP Not me, my Seretide I take for my asthma isn't getting cheaper, the pharmacist actually said it will go up.</td>
<td>5605</td>
<td>1</td>
<td>@Kidcowboy2 @AlboMP Not me, my Seretide I take for my asthma isn't getting cheaper, the pharmacist actually said it will go up.</td>
<td>✔️</td>
</tr>
<tr>
<td>Branded</td>
<td>The ventolin isn't great for my arrhythmia.</td>
<td>7332</td>
<td>1</td>
<td>The ventolin isn't great for my arrhythmia.</td>
<td>✔️</td>
</tr>
<tr>
<td>Causes</td>
<td>&quot;I started training and I learned that I actually was much stronger than I realized and my allergies were what was causing my asthma.</td>
<td>7814</td>
<td>1/2</td>
<td>&quot;I started training and I learned that I actually was much stronger than I realized and my allergies were what was causing my asthma.</td>
<td>✔️</td>
</tr>
<tr>
<td>Causes</td>
<td>RT @CaptMarvelNews &quot;I started training and I learned that I actually was much stronger than I realized and my allergies were what was causing my asthma.</td>
<td>7487</td>
<td>1</td>
<td>RT @CaptMarvelNews &quot;I started training and I learned that I actually was much stronger than I realized and my allergies were what was causing my asthma.</td>
<td>✔️</td>
</tr>
<tr>
<td>Causes</td>
<td>@GovKathyHochul Do you know what triggers my asthma, RATS.</td>
<td>2694</td>
<td>1</td>
<td>@GovKathyHochul Do you know what triggers my asthma, RATS.</td>
<td>✔️</td>
</tr>
<tr>
<td>Causes</td>
<td>Not my asthma being triggered by cold air 🤢нет today huhu</td>
<td>2410</td>
<td>1</td>
<td>Not my asthma being triggered by cold air 🤢нет today huhu</td>
<td>✔️</td>
</tr>
</tbody>
</table>
In the ongoing saga of my health I snuck in a drâ€™s visit today: bronchitis (caught it before COVID pneumonia) Knocking it out nor before surgery. /r4de1l

I'm gonna see how i go tmr anyway and see if my lungs decide to relapse with my asthma hahaha hahahah buuuuul will see how i go. Cant wait to rock up all

Today is my last day as a 32-year-old ðŸ¥‡ I wanted to take this time to thank my body for keeping me alive, for carrying me through the darkest time of my life, for living through getting COVID despite my asthma, and for reminding me that rest is a part of the process â™¥ï¸œ
t/we mentioning topic of suicide I think it's been almost two months since I started taking anti- depressants and I haven't had an episode of self harm or intense suicidal ideation since. Think these meds might be saving my life and like... Wow.

hey so I caught COVID and it didn't help my transition but my depression just became way worse? do i get my money back?

Friday night: yay! I can breathe again and seem fully recovered from my chest infection. Sunday afternoon: *tests positive for covid* ðŸ©œðŸ¥‡ Ah well, at least I didn't get covid on top of the chest infection. With my asthma, that would have been BAD.

I haven't put myself out there because I'm still healing and trying to stabilize my epilepsy.

16 wks after testing positive to covidâ€¦ Cough, breathlessness, and fatigue remain. My respiratory system is broken. lâ€™m now on regular asthma medication (I didnâ€™t have asthma before). CT scan last week. Next step, lung function test and referral to a lung specialist. #LongCovid

Fuck sore throat, man, I feel like I'm going to rip my skin open and scratch it inside, just to treat this itchy irritating shit.

The CDC says 5 days â€¦ I didnâ€™t develop a fever til Day 5, I did not lose my taste and smell til Day 6 â€¦ My Covid case turned into pneumonia and A lung infection â€¦ I spent the night in the hospital on my 11th day â€¦ and my fever did not break til my 13th day.

I was supposed to go back to work on Wednesday, not looking likely though. I'm very fortunate my asthma wasn't playing up before this horridness hit me and I'm lucky to have some asthma medication that I hope is helping before it becomes a problem.

Same happened to me last week and i am still suffering from congestion in chest with thick flu. But i did not opt for STEROIDS due to side effects which people usually undergone with during Pneumonia medication during Covid. Luckily i am recovering with Antibiotic/Anti-Allergicâ™™.

I started taking magnesium for my asthma years ago and my mind has been much quieter since then

Update: I went to the doctor and he told me that my heart and lungs are ok and that it doesn't seem like my heavy breathing episodes are caused by asthma, covid or allergies either. That means that this is all probably caused by anxiety and that I need therapy

Fun fact, I have been put under meds for bipolar disorder even before any doctor told be the word "bipolar". It was "to regulate my depression and my anxiety". Even today I say I've been diagnosed but my psychiatrist just said the word many times talking about my experience... 1/2

Its been a year since i started my depression/PTSD meds and 6 months since i started my anxiety meds can i get a W in chat

Between a bad allergy attack and resulting headache and congestion limiting my ability to breathe properly, and then dizziness and drowsiness from the antihistamines mixed with the painkillers and decongestant I took, i've had a rough morning.

I started my anxiety meds can I get a W in chat. I'm lucky to have some asthma medication that I hope is helping before it becomes a problem.

Update: I went to the doctor and he told me that my heart and lungs are ok and that it doesn't seem like my heavy breathing episodes are caused by asthma, covid or allergies either. That means that this is all probably caused by anxiety and that I need therapy

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Examples of GPT Generated Topic Naming

<table>
<thead>
<tr>
<th>Therapeutic Area</th>
<th>Cluster ID</th>
<th>Number of posts per cluster</th>
<th>Topic</th>
<th>Short Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Infectives</td>
<td>6</td>
<td>3050</td>
<td>Common Bacterial and Viral Infections Treatments</td>
<td>This topic is about different types of antibiotics, antivirals, and medicines that are commonly used to treat bacterial and viral infections.</td>
</tr>
<tr>
<td>Anti-Infectives</td>
<td>13</td>
<td>2590</td>
<td>Antibiotic Prescriptions</td>
<td>A topic related to prescribing antibiotics, including the names of various antibiotics, physicians, pharmacists, and prescription medications.</td>
</tr>
<tr>
<td>Anti-Infectives</td>
<td>67</td>
<td>1704</td>
<td>Antibiotic Prescriptions</td>
<td>Social media discussions related to the prescription, dosage, and side effects of antibiotics such as amoxicillin, cephalaxin, and azithromycin.</td>
</tr>
<tr>
<td>Anti-Infectives</td>
<td>12</td>
<td>1101</td>
<td>Patient Experiences and Feedback</td>
<td>Social media posts about experiences and opinions on medical treatments and healthcare providers.</td>
</tr>
<tr>
<td>Anti-Infectives</td>
<td>138</td>
<td>865</td>
<td>Prescription Medication</td>
<td>Social media users discussing various prescription medications, including antibiotics and psychiatric drugs, as well as healthcare professionals who prescribe them.</td>
</tr>
<tr>
<td>Anti-Infectives</td>
<td>97</td>
<td>724</td>
<td>Alternative medicine in India</td>
<td>This topic pertains to discussions on alternative medicine practices and products in India.</td>
</tr>
</tbody>
</table>

‘antibiotics’ ‘antibiotic’ ‘augmentin’ ‘azithromycin’ ‘amoxicillin’ ‘flu’
14 SDOH models with over 60 subcategories

- Ambulatory Issue
- Transportation Issue
- Food Insecurity
- Victim of Crime and Violence
- Living Condition
- Weight Range Category
- Limited English
- Physical Activity
- Social Isolation
- Depression
- Stress
- Employment Status
- Substance Abuse
- Financial Issue

IQVIA NLP SDOH Models
Case Study: Clinical Risk for Social Determinants of Health

Real World Impact of applied AI with Northshore University Health System

**ED Patient**
- 20 to 30 year-old Female
- Presents with headache, nausea, and dizziness

**Flagged by NLP**
- “victim of crime”
- “victim of abuse”

**Human In the Loop**
- Provided summary of EMR, presented info to clinician

**Social Worker Assessment**
- Used a trauma-informed approach
- Allowed patient to share more info

**Resources & impact**
- Patient referred to services for PTSD care and legal assistance

**ED Social Workers assessed 56% more patients for SDOH needs that would not have otherwise been identified.**
"Adverse Event" BERT model captures general medical terms, not true adverse effects.
Adverse Drug Reaction

Adverse chemical reactions as reported in the specified index.

Chemical

Pharmacologic Substance

Effect

Diseases and Symptoms

Description

This query extracts chemical dosages and combinations along with their associated adverse events. It is part of the Chemical Profile query pack.

Example hits:

- with nafamostat mesilate combined with gemcitabine chemotherapy... Cardiac arrest caused by nafamostat mesilate
  - Treatment with dapagliflozin 2.5mg, 5mg, or 10mg once daily is accompanied by an increased risk of vulvovaginitis or balanitis, related to the induction...
  - Skin toxicity induced by gefitinib is common

Parameters:

- Chemical: The chemical name or class for profiling.
- Effect: The class used to identify the adverse event.
Adverse Drug Reaction

Adverse chemical reactions as reported in the specified index.

### Chemical
- Cyclosporine
- Fluorouracil

### Effect
- Diseases and Symptoms
- MedDRA
- AdverseEffect

Description

This query extracts chemical dosages and combinations along with their associated adverse events. It is part of the Chemical Profile query pack.

Example hits:
- ... with nafamostat mesilate combined with gemcitabine chemotherapy... Cardiac arrest caused by nafamostat mesilate
- Treatment with dapagliflozin 2.5mg, 5mg, or 10mg once daily is accompanied by an increased risk of vulvovaginitis or balanitis, related to the induction ...
- Skin toxicity induced by gefitinib is common

Parameters:
- Chemical: The chemical name or class for profiling.
- Effect: The class used to identify the adverse event.
<table>
<thead>
<tr>
<th>Diseases and Symptoms</th>
<th>Chemical</th>
<th>Relation</th>
<th>Effect</th>
<th>#Docs</th>
<th>Doc</th>
<th>#Hits</th>
<th>Hit</th>
</tr>
</thead>
<tbody>
<tr>
<td>psoriatic lesions</td>
<td>Cyclosporine</td>
<td>induce</td>
<td>psoriatic lesions</td>
<td>10594756</td>
<td>1</td>
<td></td>
<td>... either 1alpha, 25-dihydroxycholecalciferol or <strong>cyclosporine A</strong> to induce psoriatic lesions if they were injected into ...</td>
</tr>
<tr>
<td>Changes in numbers of</td>
<td>Cyclosporine</td>
<td>induce</td>
<td>Changes in numbers of epididermal cell adhesion molecules caused by oral cyclosporin in psoriasis.</td>
<td>7607611</td>
<td>1</td>
<td></td>
<td>Changes in numbers of epididermal cell adhesion molecules induced by oral cyclosporin in psoriasis.</td>
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<td>increase</td>
<td>NMSC</td>
<td>Side effects were a temporary increase in blood pressure during initiation with 200 mg cyclosporin A/day.</td>
<td>11275806</td>
<td>1</td>
<td></td>
<td>Side effects were a temporary increase in blood pressure during initiation with 200 mg cyclosporin A/day.</td>
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<td>produce</td>
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<td>produce</td>
<td>Cyclosporine and prior phototherapy significantly increased the risk of NMSC.</td>
<td>20810486</td>
<td>1</td>
<td></td>
<td>Cyclosporine and prior phototherapy significantly increased the risk of NMSC.</td>
</tr>
<tr>
<td>higher blood concentrations</td>
<td></td>
<td>produce</td>
<td>Cyclosporine and prior phototherapy significantly increased the risk of NMSC.</td>
<td>17584318</td>
<td>1</td>
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<td>Cyclosporine and prior phototherapy significantly increased the risk of NMSC.</td>
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<td>proliferate</td>
<td>human dermal fibroblasts</td>
<td>proliferate</td>
<td>This study thus indicates that CyA influences ECM metabolism and the proliferation of human dermal fibroblasts, and that the effects ...</td>
<td>18559108</td>
<td>1</td>
<td></td>
<td>This study thus indicates that CyA influences ECM metabolism and the proliferation of human dermal fibroblasts, and that the effects ...</td>
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<td>associate</td>
<td>gene expression is modified by CsA through NFAT activity in association with differentiation induction.</td>
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<td>1</td>
<td></td>
<td>gene expression is modified by CsA through NFAT activity in association with differentiation induction.</td>
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<td>develop</td>
<td>a mass in the left maxillary sinus</td>
<td>develop</td>
<td>... months after the discontinuation of cyclosporine, the patient developed a mass in the left maxillary sinus extending to the orbit, ...</td>
<td>1613146</td>
<td>1</td>
<td></td>
<td>... months after the discontinuation of cyclosporine, the patient developed a mass in the left maxillary sinus extending to the orbit, ...</td>
</tr>
<tr>
<td>due</td>
<td>gastrointestinal complications</td>
<td>due</td>
<td>Chlorambucil and cyclosporine A were discontinued due to side effects in 21% ... (nephrotoxicity, 36% and gastrointestinal complications, 21%), respectively ...</td>
<td>20484112</td>
<td>1</td>
<td></td>
<td>Chlorambucil and cyclosporine A were discontinued due to side effects in 21% ... (nephrotoxicity, 36% and gastrointestinal complications, 21%), respectively ...</td>
</tr>
<tr>
<td>exacerbate</td>
<td>an aggravation of the joint condition</td>
<td>exacerbate</td>
<td>... in whom the withdrawal of cyclosporin A induced a generalised pustular exacerbation and an aggravation of the joint condition.</td>
<td>12218252</td>
<td>1</td>
<td></td>
<td>... in whom the withdrawal of cyclosporin A induced a generalised pustular exacerbation and an aggravation of the joint condition.</td>
</tr>
<tr>
<td>implicate</td>
<td>BM component production</td>
<td>implicate</td>
<td>... effect of immunomodulation determined by CsA in the regulation of the functional activity of cells implicated in BM component production.</td>
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<td>... effect of immunomodulation determined by CsA in the regulation of the functional activity of cells implicated in BM component production.</td>
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<td>prolonged therapeutic 5-FU concentrations</td>
<td>prolong</td>
<td>... fatal but in addition to typical 5-FU related adverse effects, the patient developed bilateral incomplete lid closure, secondary corneal exposure and ...</td>
<td>21077799</td>
<td>1</td>
<td></td>
<td>... fatal but in addition to typical 5-FU related adverse effects, the patient developed bilateral incomplete lid closure, secondary corneal exposure and ...</td>
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<td>associate</td>
<td>5-FU and prolonged therapeutic 5-FU concentrations compared with continuous infusion of ...</td>
<td>19398145</td>
<td>1</td>
<td></td>
<td>5-FU and prolonged therapeutic 5-FU concentrations compared with continuous infusion of ...</td>
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<td>higher</td>
<td>irregular pits</td>
<td>higher</td>
<td>... history of ever use of 5-FU and present AKs was strongly associated with worse QoL.</td>
<td>19566817</td>
<td>1</td>
<td></td>
<td>... history of ever use of 5-FU and present AKs was strongly associated with worse QoL.</td>
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<tr>
<td>meddra</td>
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<td>... showed that the surfaces of 5-FU-PGSs with higher concentration of 5-FU had irregular pits.</td>
<td>12602996</td>
<td>1</td>
<td></td>
<td>... showed that the surfaces of 5-FU-PGSs with higher concentration of 5-FU had irregular pits.</td>
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</table>
A bilateral cicatricial ectropion and bilateral upper lid shortening caused by 5-fluorouracil toxicity in a patient with dihydropyrimidine dehydrogenase deficiency.

Obi, Ekhe E; McDonald, Alec; Kemp, Ewen.

Author Info [a]

Abstract

CONTEXT (BACKGROUND): Well-known causes of a cicatricial ectropion are chemical/thermal injuries, dermatitis, cutaneous diseases, malignancies, and trauma. We add to this preceding list a systemic cause of a cicatricial ectropion as a result of a rare side effect of 5-fluorouracil (5-FU), a commonly and frequently used chemotherapeutic agent.

METHODS (METHODS): A case report demonstrating the clinical presentation of a cicatricial ectropion caused by 5-FU chemotherapy toxicity in a patient with dihydropyrimidine dehydrogenase deficiency. We also describe the subsequent investigations and management of this case.

RESULTS (RESULTS): A bilateral cicatricial lower lid ectropion, bilateral upper lid shortening, cicatricial and sclerosing facial skin changes occurred in an 80-year-old male undergoing preoperative chemoradiotherapy, incorporating Cetuximab, an oral 5-FU produg for a locally advanced rectal carcinoma. Severe 5-FU toxicity ultimately proved fatal but in addition to typical 5-FU related adverse effects, the patient developed bilateral incomplete lid closure, secondary corneal exposure, and keratopathy. Due to the patient’s extreme ill health, he was managed conservatively with a moist chamber.

CONCLUSION (CONCLUSIONS): 5-fluorouracil chemotherapy in patients with dihydropyrimidine dehydrogenase deficiency, can give rise to ocular and cutaneous toxicity. We also present the complex management problems that have to be anticipated in treating such systemically compromised patients.

PMID: 21677739
ISSN: 1556-9535
Publication Types:
Case Reports
Journal Article
MeSH Terms:
Aged, 80 and over
Antineoplastic.
Adverse effects
Drug therapy
Carcinoma
Drug therapy
Dehydropyrimidine Dehydrogenase Deficiency
Ectropion
chemically induced
Classification
Fluorouracil
adverse effects
therapeutic use
Humans
Male
Rectal Neoplasms
drug therapy
Substances:
We are capturing unique hits with each ontology: “ectropion” with Diseases and Symptoms “bilateral incomplete lid enclosure” and “second corneal exposure” with SciBERT “keratopathy” with MedDRA
If we search for “lid closure” in the class searcher – we do not have any ontologies that match, this hit is uniquely picked up by the ML model.
Out of the 88 documents the query hit, SciBERT had unique hits in over 1/3 of them. However, Diseases and Symptoms and MedDRA still matched the greatest number of documents, and are still necessary for high precision and recall. The ML model is ideal for picking up unique or unexpected hits not defined in the ontologies. The NLP rules help us set the context for the ML hits and ensure our results are meaningful.
<table>
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<tr>
<th>Diseases and Symptoms</th>
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<th>Relation</th>
<th>Effect</th>
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<tr>
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...either 1alpha, 25-dihydroxycholecalciferol or cyclosporine A, to induce psoriatic lesions if they were injected into... Changes in numbers of epidermal cell adhesion molecules caused by oral cyclosporin in psoriasis. Side effects were a temporary increase in blood pressure during initiation with 200 mg cyclosporin A/day. Cyclosporine and prior phototherapy significantly increase the risk of NMSC. Therapeutic drug monitoring indicated that cyclosporin administered before meals produces higher blood concentrations than an equivalent dose administered... This study thus indicates that CyA influences ECM metabolism and the proliferation of human dermal fibroblasts, and that the effects... Gene expression is modified by CsA through NFAT activity in association with differentiation induction. Cyclosporin A induced augmentation of the beta-adrenergic adenylate cyclase response of pig epidermis. Chlorambucil and cyclosporine A were discontinued due to side effects in 21%... (nephrotoxicity, 36% and gastrointestinal complications, 21%), respectively... In whom the withdrawal of cyclosporin A induced a generalised pustular exacerabation and an aggravation of the joint condition... Effect of immunomodulation determined by CsA in the regulation of the functional activity of cells implicated in BM component production. Egr-1 and TSP-1 mRNA by 5-FU, while LV increased the expression of Egr-1 and TSP-1 mRNA in KB... Fatality but in addition to typical 5-FU related adverse effects, the patient developed bilateral incomplete lid closure, secondary corneal exposure and... Higher peak plasma concentrations of 5-FU and prolonged therapeutic 5-FU concentrations compared with continuous infusion of... History of ever use of 5-FU and present AKs was strongly associated with worse QoL... Showed that the surfaces of 5-FU-PGSs with higher concentration of 5-FU had irregular pits... Multiple cutaneous squamous carcinoma in a psoriatic associated with cyclosporin, alcohol abuse and ulcerated...
Summary
Natural Language Processing has evolved over the years

IQVIA NLP has kept pace with these evolutions

**Accuracy**
- Aim for client desired precision and recall – often achieving >95% F Score

**Cost**
- For the desired accuracy – what is the most cost effective way of getting there?

**Convenience**
- Within the budget, and for the desired accuracy – what is the easiest way of getting there?

- Continue to use a blend of methods to ensure that our clients get the best result possible within their needs
- LLMs are the latest example of NLP methods that can be used within the IQVIA NLP toolkit
QA
End