



Phenotype Aphril Week 2: The Phoundation of Reliable Real World Evidence through Phenotype Evaluation

Patrick Ryan, PhD
Vice President, Observational Health Data Analytics, Janssen
Research and Development
Assistant Professor, Adjunct, Department of Biomedical
Informatics, Columbia University Medical Center



Plans for Phenotype Aphril

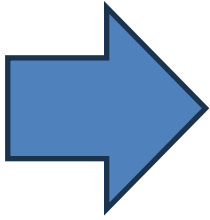
- Week 0: Phenotype Aphril kickoff
 - March 31 community call: Overview of phenotyping and opportunities for LLM
- Week 1: Phenotype development
 - April 7 community call: Demo – building cohorts in ATLAS
- Week 2: Phenotype evaluation
 - April 14 community call: Interactive – case adjudication using KEEPER
- Week 3: Iterative phenotype development
 - No community call: build your own AMI cohort definitions!
- Week 4: Iterative phenotype evaluation
 - April 28 community call: Review performance of submitted AMI cohort definitions



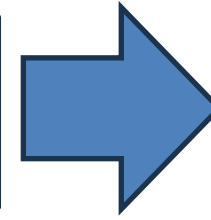
Evaluating the Phenotype Development and Evaluation process

Inputs:

- Clinical idea



Phenotype Development process

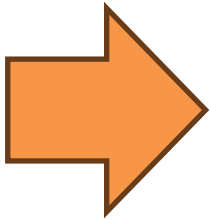


Outputs:

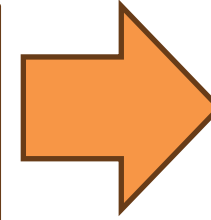
- Cohort definition

Inputs:

- Clinical idea
- Cohort definition
- Database



Phenotype Evaluation process

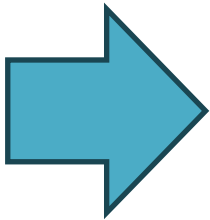


Outputs:

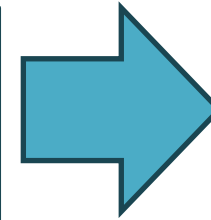
- Measurement error quantification

Inputs:

- Clinical idea
- Cohort definition
- Database
- Measurement error quantification



Phenotype Evaluation Calibration



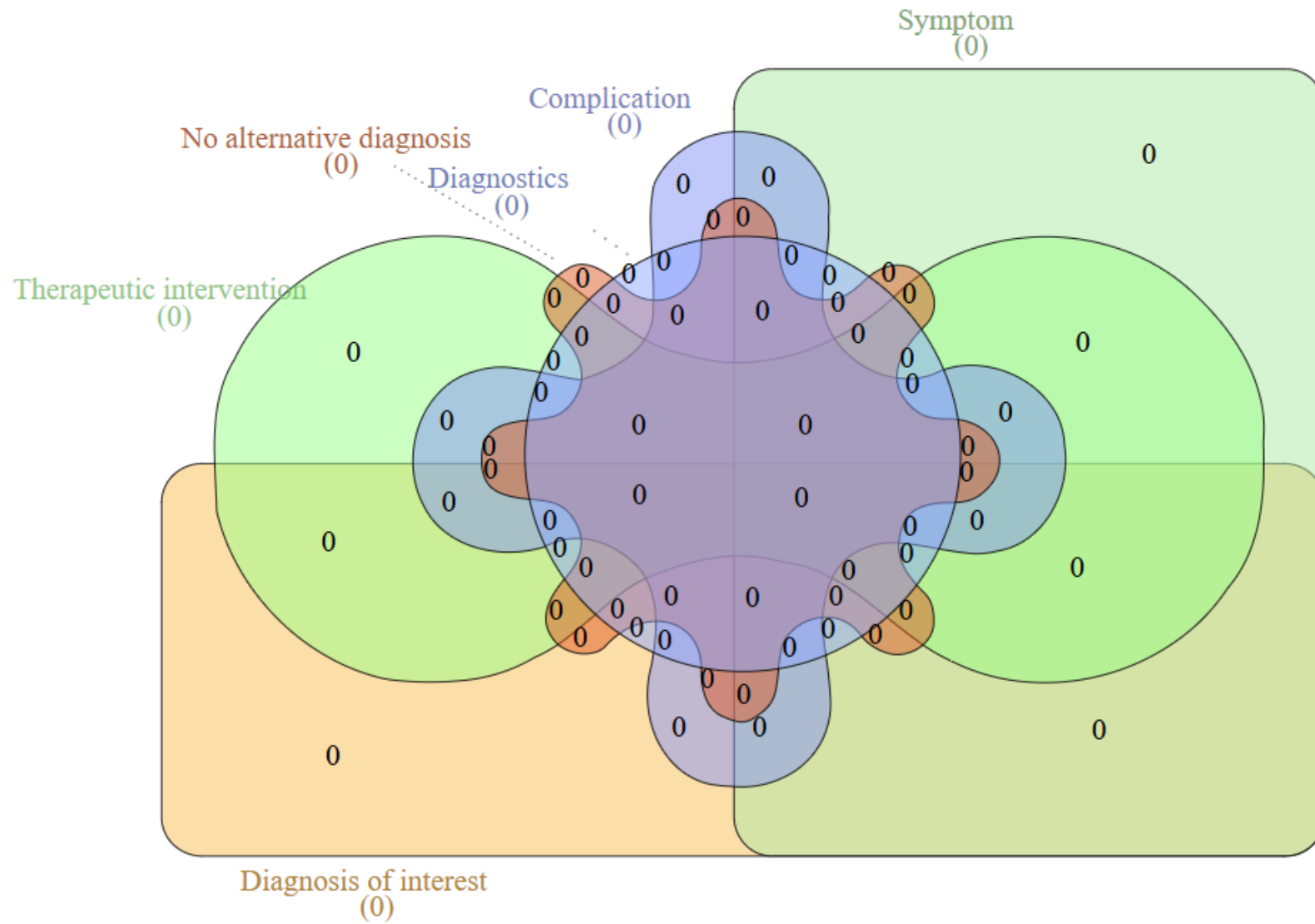
Outputs:

- Measurement error bias assessment



Clinical elements associated with disease status

- **Diagnosis of interest:** 'Acute myocardial infarction'
- **Symptoms:** Chest pain, Difficulty breathing, Sweating, Nausea, ...
- **Diagnostics:**
 - Procedures: Electrocardiography, angiocardiology, ...
 - Measurements: Troponin, creatine kinase, ...
- **Therapeutic interventions:**
 - Drugs: beta blocker, aspirin, heparin, clopidogrel, ...
 - Procedures: percutaneous coronary intervention, coronary artery bypass grafting, insertion of cardiac pacemaker...
- **Complications:** heart failure, cerebral hemorrhage, acute kidney injury, acute pulmonary edema, hepatic failure...
- **Alternative diagnoses:** Aortic aneurysm, panic attack, esophageal reflux...



Heberle, H.; Meirelles, G. V.; da Silva, F. R.; Telles, G. P.; Minghim, R. InteractiVenn: a web-based tool for the analysis of sets through Venn diagrams. *BMC Bioinformatics* 16:169 (2015). [10.1186/s12859-015-0611-3](https://doi.org/10.1186/s12859-015-0611-3)



ATLAS

- Home
- Data Sources
- Search
- Concept Sets
- Cohort Definitions**
- Characterizations
- Cohort Pathways
- Incidence Rates
- Profiles
- Estimation
- Prediction
- Reusables
- Jobs
- Configuration
- Feedback
- Tools

[PhenotypeApril] persons with acute myocardial infarction

Definition

Concept Sets

Generation

Samples

Reporting

Export

Versions

Messages

22

Enter a cohort definition description here

Cohort Entry Events

Events having any of the following criteria:

a condition occurrence of **Diagnosis of interest**

a condition occurrence of **Symptoms**

a procedure occurrence of **diagnostic procedures and mea...**

a measurement of **diagnostic procedures and mea...**

a drug exposure of **therapeutic interventions - drug...**

a procedure occurrence of **therapeutic interventions - drug...**

a condition occurrence of **complications**



Inclusion Criteria



New inclusion criteria

1. has diagnosis of interest

2. has symptom

3. has diagnostic procedure or measurement

4. has therapeutic intervention - drug or procedure

5. has follow-up care or complication

6. has no alternative diagnoses

7. has 2+ categories

8. has 3+ categories

9. has 4+ categories

10. has 5+ categories

has diagnosis of interest

Copy

Delete

enter an inclusion rule description

having of the following criteria:

+ Add criteria to group... ▾

with using occurrences of:

a condition occurrence of

+ Add attribute... ▾

where between

days and days [add additional constraint](#)

The index date refers to the event from the Cohort Entry criteria.

restrict to the same visit occurrence

allow events from outside observation period

Delete Criteria





Inclusion Report for **Optum Extended DoD (v3787)** using 1 event per person

	Match Rate	Matches	Total Events
Summary Statistics:	0.18%	123,234	68,218,480

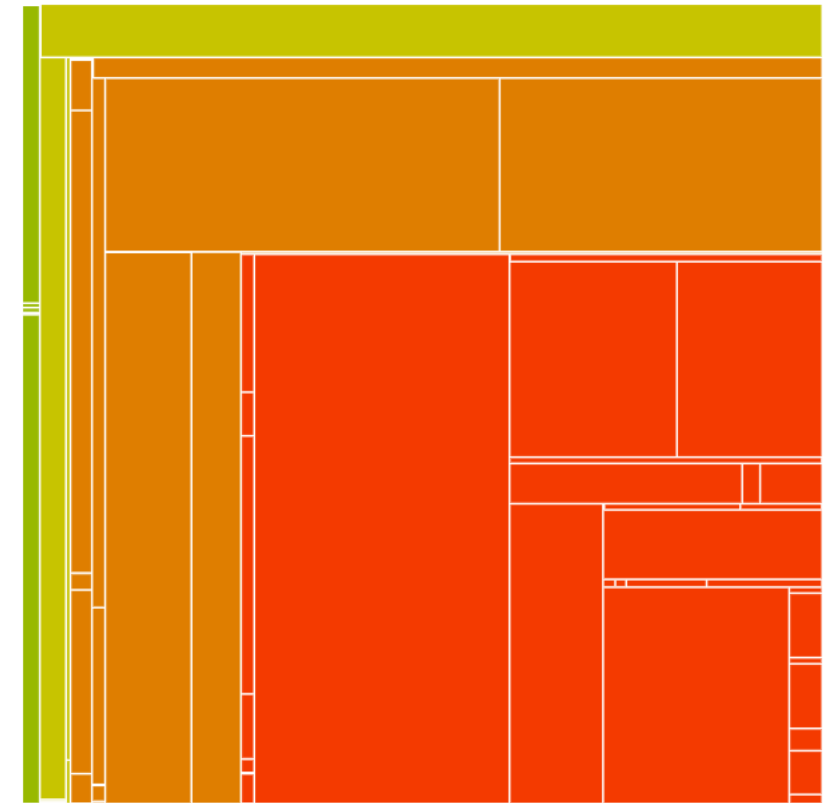
Having of selected criteria

<input checked="" type="checkbox"/>	Inclusion Rule	N	% Satisfied	% To-Gain
<input checked="" type="checkbox"/>	1. has diagnosis of interest	1,529,357	2.24%	0.83%
<input checked="" type="checkbox"/>	2. has symptom	59,083,628	86.61%	0.01%
<input checked="" type="checkbox"/>	3. has diagnostic procedure or measurement	39,491,240	57.89%	0.00%
<input checked="" type="checkbox"/>	4. has therapeutic intervention - drug or procedure	32,715,153	47.96%	0.01%
<input checked="" type="checkbox"/>	5. has follow-up care or complication	17,155,854	25.15%	0.01%
<input checked="" type="checkbox"/>	6. has no alternative diagnoses	41,217,790	60.42%	1.35%
<input checked="" type="checkbox"/>	7. has 2+ categories	67,909,815	99.55%	0.00%
<input checked="" type="checkbox"/>	8. has 3+ categories	61,289,210	89.84%	0.00%
<input checked="" type="checkbox"/>	9. has 4+ categories	25,766,487	37.77%	0.00%
<input checked="" type="checkbox"/>	10. has 5+ categories	6,106,186	8.95%	0.00%

Summary: 68,218,480 events (100.00%)

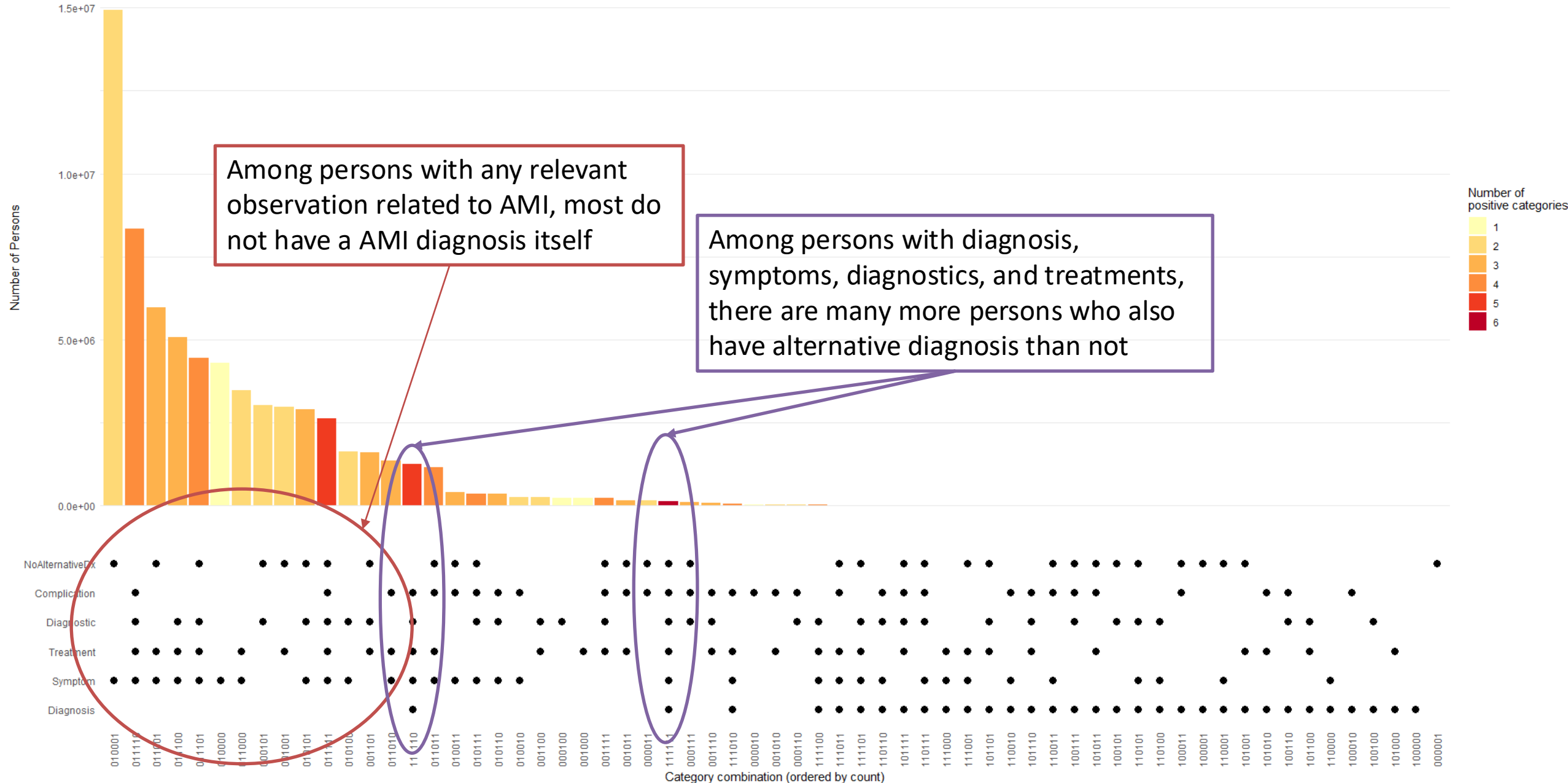
Population Visualization

[Switch to attrition view](#)



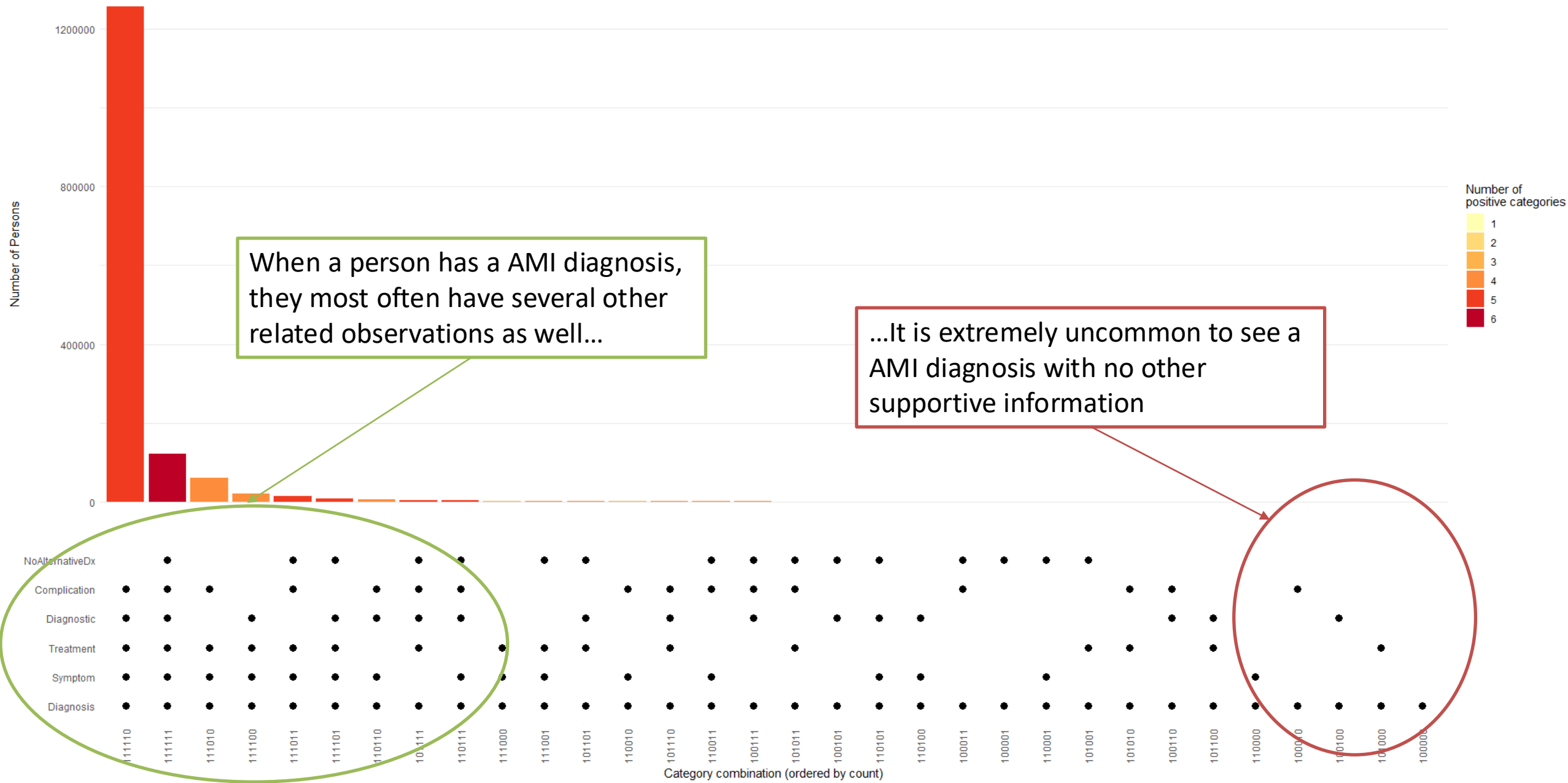


Intersection sizes (precomputed) colored by degree





Intersection sizes (precomputed) colored by degree





Research and Applications

Scalable and interpretable alternative to chart review for phenotype evaluation using standardized structured data from electronic health records

Anna Ostropolets , MD, PhD^{*1}, George Hripcsak , MD, MS^{1,2}, Syed A. Husain , MD, MPH³, Lauren R. Richter , MD, MS¹, Matthew Spotnitz , MD, MPH¹, Ahmed Elhussein, MD, MS¹, Patrick B. Ryan, PhD^{1,4}

¹Department of Biomedical Informatics, Columbia University Irving Medical Center, New York, NY 10032, United States, ²Medical Informatics Services, New York-Presbyterian Hospital, New York, NY 10032, United States, ³Division of Nephrology, Department of Medicine, Vagelos College of Physicians and Surgeons, Columbia University Irving Medical Center, New York, NY 10032, United States, ⁴Observational Health Data Analytics, Janssen Research and Development, Titusville, NJ 08560, United States

*Corresponding author: Anna Ostropolets, MD, PhD, Columbia University Medical Center, 622 West 168th Street, PH-20, New York, NY 10032, USA (ao2671@cumc.columbia.edu)

Abstract

Objectives: Chart review as the current gold standard for phenotype evaluation cannot support observational research on electronic health records and claims data sources at scale. We aimed to evaluate the ability of structured data to support efficient and interpretable phenotype evaluation as an alternative to chart review.

Materials and Methods: We developed Knowledge-Enhanced Electronic Profile Review (KEEPER) as a phenotype evaluation tool that extracts patient's structured data elements relevant to a phenotype and presents them in a standardized fashion following clinical reasoning principles. We evaluated its performance (interrater agreement, intermethod agreement, accuracy, and review time) compared to manual chart review for 4 conditions using randomized 2-period, 2-sequence crossover design.

Results: Case ascertainment with KEEPER was twice as fast compared to manual chart review. 88.1% of the patients were classified concordantly using charts and KEEPER, but agreement varied depending on the condition. Missing data and differences in interpretation accounted for most of the discrepancies. Pairs of clinicians agreed in case ascertainment in 91.2% of the cases when using KEEPER compared to 76.3% when using charts. Patient classification aligned with the gold standard in 88.1% and 86.9% of the cases respectively.

Conclusion: Structured data can be used for efficient and interpretable phenotype evaluation if they are limited to relevant subset and organized according to the clinical reasoning principles. A system that implements these principles can achieve noninferior performance compared to chart review at a fraction of time.



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Table 1. Conceptual elements and corresponding data elements in KEEPER, example for acute appendicitis phenotype

Conceptual element	Conceptual element in the context of the disease of interest	Data element
Clinical presentation	Presence of relevant [known to be associated with the outcome] symptoms on the encounter (index date, day 0) and absence of competing symptoms	Condition codes [day 0] <i>Nausea, vomiting, epigastric pain</i>
Clinical plausibility	Appropriate demographics	Age, gender, race, and ethnicity [day 0] <i>Male, 37 yo, race = White</i>
	Presence of relevant symptoms, diagnoses, or treatment prior to the index date, especially recurring	Condition, drug, and observation codes [before day 0] <i>None expected</i>
	Presence of relevant co-morbidities and (or) predisposing risk factors	Condition and observation codes [before day 0] <i>Family history of acute appendicitis</i>
	Absence of competing diagnoses after the index date, especially if followed by treatment	Condition, procedure, measurement, and drug codes [after day 0] <i>Absence of diagnosis of Crohn's disease, cancer of colon, etc</i>
Diagnostic procedures		
Treatment procedures and medications		
Follow-up care and complications		

Outstanding challenge:
 How do we create the input
 conceptsets for each of
 these clinical elements?

Multiple alternative directions to explore:

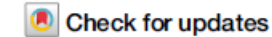
1. Expert manual curation
2. Create a knowledge graph containing all concept-concept relationships to enable standard extraction (see S Bandeian & M Overhage, 2025 OHDSI Symposium)
3. Create LLM-agent pipeline to create conceptsets dynamically construction based on phenotype of interest

Table 3. Comparison of manual chart review and KEEPER profiles: intermethod agreement, interrater agreement, and accuracy

	Intermethod agreement		Interrater agreement			Accuracy		
	Cases, n (%)	Kappa (95% CI)	Chart, n (%)	Kappa (95% CI)	KEEPER, n (%)	Kappa (95% CI)	Chart, n (%)	KEEPER, n (%)
DM type I	32 (80.0)	0.58 (0.34-0.82)	14 (70.0)	0.40 (<0.1 to 0.78)	18 (90.0)	0.77 (0.47 to 1.00)	34 (85.0)	35 (87.5)
Acute appendicitis	38 (95.0)	0.87 (0.69-1.00)	19 (95.0)	0.86 (0.56 to 1.00)	19 (95.0)	0.88 (0.64 to 1.00)	39 (97.5)	39 (97.5)
COPD	34 (85.0)	0.67 (0.44-0.90)	16 (80.0)	0.60 (0.28 to 0.92)	20 (100.0) ^a	1.00 (1.00 to 1.00)	34 (85.0)	32 (80.0)
ESRD	37 (92.5)	0.78 (0.54-1.00)	12 (60.0)	-0.1 (-0.3 to 0.1)	15 (75.0)	0.34 (-0.01 to 0.72)	32 (80.0)	35 (87.5)
Overall	141 (88.1)	0.71 (0.59-0.83)	61 (76.3)	0.45 (0.23 to 0.67) ^b	73 (91.2) ^a	0.74 (0.52 to 0.96) ^b	139 (86.9)	141 (88.1)

<https://doi.org/10.1038/s41746-025-01433-4>

Standardized patient profile review using large language models for case adjudication in observational research



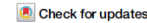
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Using administrative claims and electronic health records for observational studies is common but challenging due to data limitations. Researchers rely on phenotype algorithms, requiring labor-intensive chart reviews for validation. This study investigates whether case adjudication using the previously introduced Knowledge-Enhanced Electronic Profile Review (KEEPER) system with large language models (LLMs) is feasible and could serve as a viable alternative to manual chart review. The task involves adjudicating cases identified by a phenotype algorithm, with KEEPER extracting predefined findings such as symptoms, comorbidities, and treatments from structured data. LLMs then evaluate KEEPER outputs to determine whether a patient truly qualifies as a case. We tested four LLMs including GPT-4, hosted locally to ensure privacy. Using zero-shot prompting and iterative prompt optimization, we found LLM performance, across ten diseases, varied by prompt and model, with sensitivities from 78 to 98% and specificities from 48 to 98%, indicating promise for automating phenotype evaluation.



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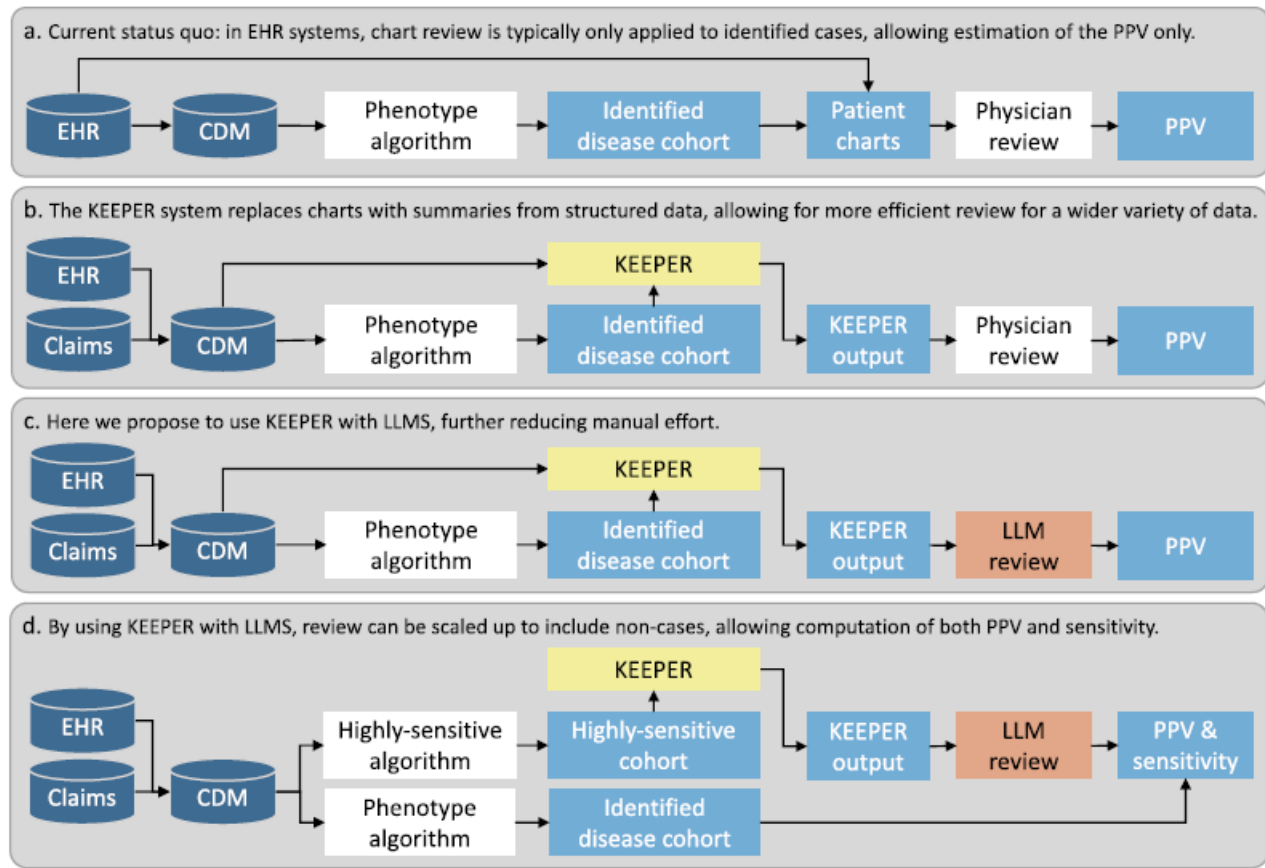
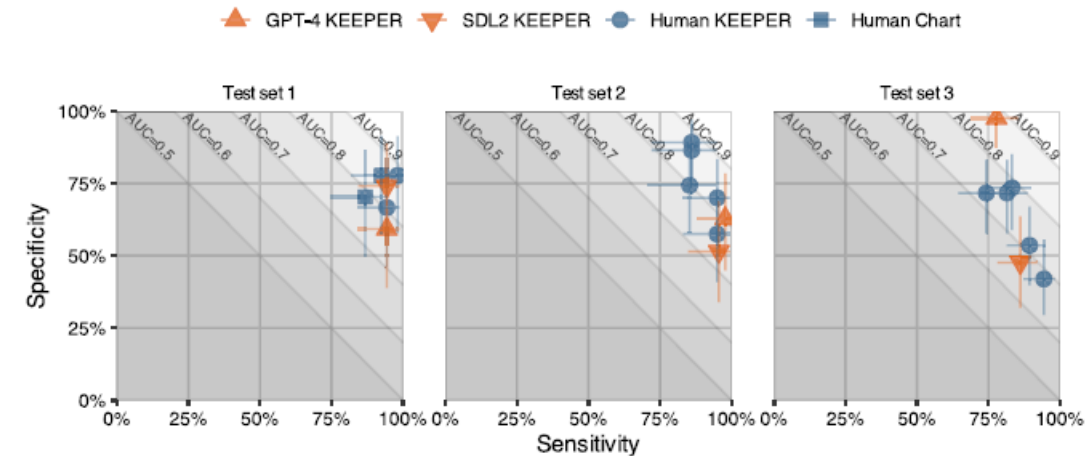





Fig. 3 | Sensitivity and specificity of reviewers for the three test sets. Points indicate sensitivity and specificity of each human or LLM reviewer against the gold standard. Error bars indicate 95% confidence intervals. For test set 1, the gold standard was created by external reviewers. For test set 2 and 3, the gold standard was the majority vote of human reviewers using a leave-one-out approach. Slanted lines denote iso-AUC contours, spaced 0.1 apart.





Knowledge-Enhanced Electronic Profile Review (KEEPER)

 R-CMD-check  passing  codecov.io

KEEPER is part of [HADES](#).

Introduction

An R package for reviewing patient profiles for phenotype validation.

Features

- Extracts patient level data for a) a random sample of patients in a cohort or b) patients in a user-specified list and formats it according to the KEEPER principles.
- Supports review of patient profiles by humans through an interactive Shiny app.
- Supports review of patient profiles by large language models.

Examples

```
keeperConceptSets <- generateKeeperConceptSets(  
  phenotype = "Gastrointestinal bleeding",  
  client = ellmer::chat_openai_compatible(),  
  vocabConnectionDetails = connectionDetails,  
  vocabDatabaseSchema = "cdm"  
)  
  
keeper <- generateKeeper(  
  connectionDetails = connectionDetails,  
  cdmDatabaseSchema = "cdm",  
  cohortDatabaseSchema = "results",  
  cohortTable = "cohort",  
  cohortDefinitionId = 1234,  
  sampleSize = 100,  
  removePii = TRUE,  
  phenotypeName = "Gastrointestinal bleeding",  
  keeperConceptSets = keeperConceptSets  
)
```

Links

[Browse source code](#)

[Report a bug](#)

[Ask a question](#)

License

[Apache License](#)

Citation

[Citing Keeper](#)

Developers

[Ostropolets Anna](#)

Author, maintainer

[Schuemie Martijn](#)

Author

[More about authors...](#)



Let's play:

Phinding Phenotypes With Phriends



Rules for Phinding Phenotypes with Phriends

- I will show you a KEEPER profile, and you will adjudicate the case to determine if you believe the person has had an Acute Myocardial Infarction.
- Cast your vote on: pollev.com/patrickryan800 for one of four options:
 - Decision: Case; Certainty: High
 - Decision: Case; Certainty: Low
 - Decision: Not a case; Certainty: Low
 - Decision: Not a case; Certainty: High
- I will reveal the community's results. If you answered the most common response, give yourself two points. If you got only the case decision right, then give yourself one point.
- I will then reveal the LLM adjudication results. If you answered the most common response, give yourself two points. If you got only the case decision right, then give yourself one point.
- We will repeat 10 times. Keep your own score, honor system. Highest score wins!



Adjudicating Person 2751

Knowledge-Enhanced Electronic Profile Review (KEEPER)



Profile Timeline

Demographics ⓘ

Age: 81
Sex: FEMALE
Observation period: day -871 - day 40
Race: White
Ethnicity: Not Hispanic or Latino

Presentation ⓘ

- Acute non-ST segment elevation myocardial infarction (Claim, Primary admission diagnosis)
- Acute non-ST segment elevation myocardial infarction (Inpatient claim header, Primary diagnosis)
- Cardiomyopathy (Claim, Admission diagnosis)
- Cardiomyopathy (Inpatient claim header, Secondary diagnosis)
- Acute on chronic combined systolic and diastolic heart failure (Claim, Secondary diagnosis)
- Acute on chronic combined systolic and diastolic heart failure (Inpatient claim header, Secondary diagnosis)
- Chest pain (Claim, Primary diagnosis)
- Congestive heart failure (Claim, Secondary diagnosis)
- Congestive heart failure (Inpatient claim header, Secondary diagnosis)
- Paroxysmal atrial fibrillation (Claim, Admission diagnosis)
- Hypoxemia (Claim, Secondary diagnosis)
- Low blood pressure (Claim, Secondary diagnosis)
- Old myocardial infarction (Claim, Secondary diagnosis)
- Acquired absence of cervix and uterus (Claim, Secondary diagnosis)
- Alzheimer's disease (Claim, Admission diagnosis)
- Anemia of chronic disease (Claim, Admission diagnosis)

Phenotype:

Acute myocardial infarction

Decision ⓘ

Decision
 Case
 Non-case

Certainty
 High
 Low

Correct index day

Patient selection



275 / 10000



When poll is active respond at PollEv.com/patrickryan800 Send [patrickryan800](https://t.me/patrickryan800) to 22333



How would you adjudicate person 2751 on whether they have had an Acute Myocardial Infarction?

Decision: Case; Certainty: High

0%

Decision: Case; Certainty: Low

0%

Decision: Not a Case; Certainty: Low

0%

Decision: Not a Case; Certainty: High

0%



KEEPER-LLM rationale for person 2751

- Is a Case? = **YES**
- Certainty = **HIGH**
- Justification:

The patient was admitted on day 0 with a PRIMARY inpatient diagnosis of acute non-ST elevation myocardial infarction (NSTEMI). During that same hospitalization she underwent definitive infarct-related therapy: coronary angiography followed by percutaneous coronary intervention with drug-eluting stent placement (records: "Dilation of Coronary Artery â€¦ with Drug-eluting Intraluminal Device" on day 0 and PCI code on day 2). Post-procedure she was started on appropriate secondary-prevention pharmacotherapy (clopidogrel, nitrates, diuretics, etc.). Additional NSTEMI diagnosis appears again on day 40 in follow-up, supporting that the earlier event was confirmed rather than ruled out. The presence of chest pain preceding admission, acute heart-failure decompensation, multiple ECGs, stress testing and invasive management all align with treatment of an actual acute MI rather than mere evaluation. No evidence suggests the diagnosis was later overturned. Therefore, the preponderance of evidence strongly supports a true acute myocardial infarction occurring at the index admission.



Adjudicating Person 225

Knowledge-Enhanced Electronic Profile Review (KEEPER)



Profile

Timeline

Demographics i

Age: 83
Sex: MALE
Observation period: day -470 - day 1171
Race: White
Ethnicity: Not Hispanic or Latino

Presentation i

- Acute ST segment elevation myocardial infarction (Claim, Primary diagnosis)
- Acute non-ST segment elevation myocardial infarction (Claim, Admission diagnosis)
- Acute non-ST segment elevation myocardial infarction (Inpatient claim header, Secondary diagnosis)
- Angina co-occurrent and due to coronary arteriosclerosis (Claim, Primary diagnosis)
- Gastroesophageal reflux disease without esophagitis (Claim, Admission diagnosis)
- Gastroesophageal reflux disease without esophagitis (Inpatient claim header, Secondary diagnosis)
- Hypertensive emergency (Claim, Primary admission diagnosis)
- Hypertensive emergency (Inpatient claim header, Primary diagnosis)
- Chest pain (Claim, Primary admission diagnosis)
- Chest pain (Claim, Primary diagnosis)
- Chest pain (Claim, Secondary diagnosis)
- Chronic pulmonary edema (Claim, Primary diagnosis)
- Dyspnea (Claim, Secondary diagnosis)
- Jaw pain (Claim, Secondary diagnosis)
- Right bundle branch block (Claim, Secondary diagnosis)
- Tachycardia (Claim, Secondary diagnosis)
- Old myocardial infarction (Claim, Secondary diagnosis)
- Anemia (Claim, Admission diagnosis)
- Aortocoronary bypass graft present (Claim, Secondary diagnosis)
- Atherosclerosis of coronary artery without angina pectoris (Claim, Admission diagnosis)
- Atherosclerosis of coronary artery without angina pectoris (Inpatient claim header, Secondary diagnosis)
- Essential hypertension (Claim, Admission diagnosis)

Phenotype:

Acute myocardial infarction

Decision i

Decision

Case

Non-case

Certainty

High

Low

Correct index day

Patient selection

<
225 / 10000
 >

Color legend i

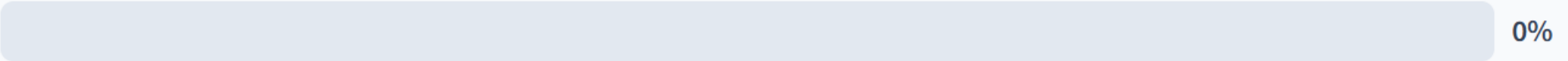
- Disease of interest
- Both
- Alternative diagnoses
- Other

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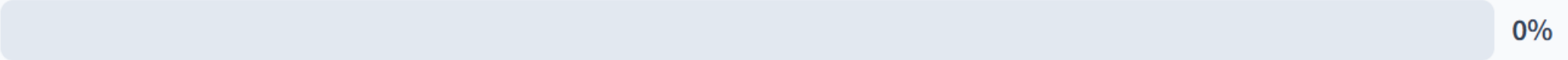


How would you adjudicate person 225 on whether they have had an Acute Myocardial Infarction?

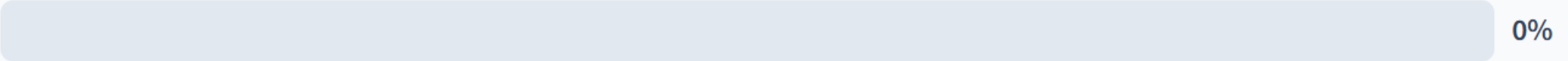
Decision: Case; Certainty: High



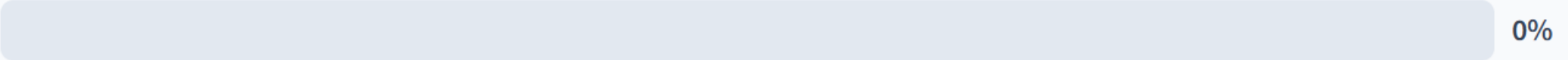
Decision: Case; Certainty: Low



Decision: Not a Case; Certainty: Low



Decision: Not a Case; Certainty: High





KEEPER-LLM rationale for person 225

- Is a Case? = **YES**
- Certainty = **HIGH**
- Justification:

Evidence for true acute myocardial infarction is strong. 1) Day 0 admission carries primary diagnoses of both STEMI and NSTEMI and is an emergent interventional-cardiology hospitalization with left-heart catheterization and coronary angiography, accompanied by ECGs and troponin testing exactly the diagnostic work-up for an acute MI. 2) Within the same hospitalization window (days 14-17) the patient underwent percutaneous coronary intervention (PCI) with drug-eluting stent placement, an MI-specific therapeutic procedure that would not be performed merely to rule out disease. 3) Subsequent hospitalizations on day 183 and day 1125 again list acute STEMI/NSTEMI as primary diagnoses and include repeat left-heart catheterizations, PCI, and complications such as cardiogenic shock and acute heart failure all typical of true infarction. 4) Long-term secondary codes for old MI appear, consistent with prior infarction. 5) The medication profile after each event includes dual antiplatelet therapy (clopidogrel), high-dose statin, nitrates, and beta-blockers standard post-MI management. The repeated combination of acute MI diagnoses, characteristic symptoms/complications, invasive coronary revascularization, and post-MI pharmacotherapy across several admissions makes it overwhelmingly likely the patient truly experienced acute myocardial infarctions rather than mere evaluation for chest pain. No alternative explanation fits this consistent pattern.



Adjudicating Person 1816

Knowledge-Enhanced Electronic Profile Review (KEEPER)



Profile

Timeline

Demographics i

Age: 66
Sex: MALE
Observation period: day -272 - day 92
Race: White
Ethnicity: Hispanic or Latino

Presentation i

Acute gastritis (Claim, Admission diagnosis)
Acute gastritis (Claim, Secondary diagnosis)
Acute myocardial infarction (Claim, Primary admission diagnosis)
Acute myocardial infarction (Claim, Primary diagnosis)
Chest pain (Claim, Secondary diagnosis)

Visits i

Emergency Room Visit (day 0)
Outpatient Visit (day 0)
Outpatient Visit - Internal Medicine (day 30)
Pharmacy visit - Family Medicine Physician (day 1, day 30)

Symptoms i

NA

Phenotype:

Acute myocardial infarction

Decision i

Decision
 Case
 Non-case

Certainty
 High
 Low

Correct index day

Patient selection

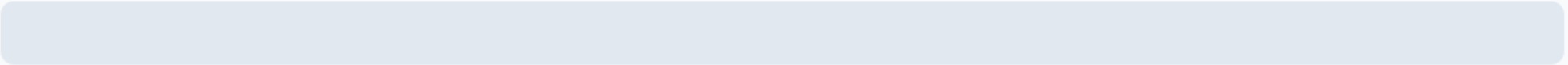
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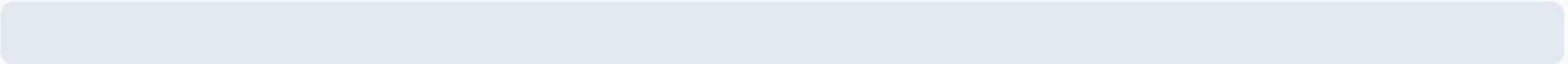
How would you adjudicate person 1816 on whether they have had an Acute Myocardial Infarction?

Decision: Case; Certainty: High



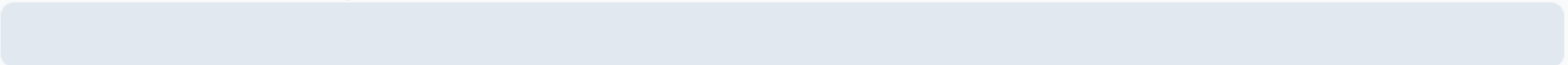
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Decision: Case; Certainty: Low



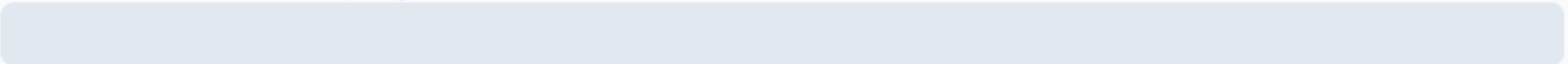
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Decision: Not a Case; Certainty: Low



0%

Decision: Not a Case; Certainty: High



0%



KEEPER-LLM rationale for person 1816

- Is a Case? = **NO**
- Certainty = **HIGH**
- Justification:

Only a single-day encounter (ED/outpatient) lists Acute myocardial infarction as an admission/primary diagnosis but is accompanied by typical rule-out MI work-up (ECG, troponin, D-dimer) without any MI-specific treatment or downstream care. No admission to an inpatient cardiology service, no cardiac catheterization/PCI, no antiplatelet/anticoagulation, beta-blocker, statin, ACE-I, or long-term cardiac follow-up appear during the 3-month observation window. Instead, patient receives only esomeprazole and carries concurrent diagnosis of acute gastritis, suggesting chest pain was ultimately attributed to gastritis rather than infarction. The pattern (single evaluation day, diagnostic testing only, no continued MI management) strongly indicates a rule-out scenario, not a true AMI.



Adjudicating Person 129

Knowledge-Enhanced Electronic Profile Review (KEEPER)



Profile **Timeline**

Demographics ⁱ

Age: 68
Sex: FEMALE
Observation period: day -206 - day 1254
Race: Black or African American
Ethnicity: Not Hispanic or Latino

Presentation ⁱ

Chest pain (Claim, Secondary diagnosis)
Insomnia (Claim, Secondary diagnosis)
Sjögren's syndrome (Claim, Secondary diagnosis)
Type 2 diabetes mellitus (Claim, Primary diagnosis)

Visits ⁱ

Outpatient Visit (day 6, day 13)
Outpatient Visit - Internal Medicine (day -26)
Outpatient Visit - Nurse Practitioner (day 0, day 13)
Outpatient Visit - Physician / Diagnostic Radiology (day 6)
Outpatient Visit - Rheumatology (day -19)
Pharmacy visit - Nurse Practitioner (day -19, day 0, day 5, day 14, day 15)
Pharmacy visit - Rheumatology (day -17)

Symptoms ⁱ

Phenotype:

Acute myocardial infarction

Decision ⁱ

Decision

Case

Non-case

Certainty

High

Low

Correct index day

Patient selection

< 129 / 10000 >



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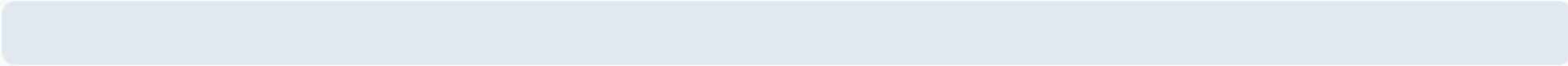
How would you adjudicate person 129 on whether they have had an Acute Myocardial Infarction?

Decision: Case; Certainty: High



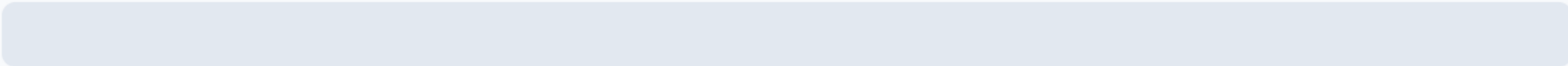
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Decision: Case; Certainty: Low



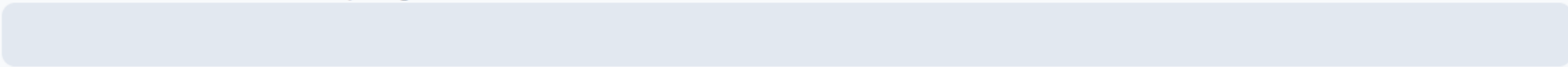
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Decision: Not a Case; Certainty: Low



0%

Decision: Not a Case; Certainty: High



0%



KEEPER-LLM rationale for person 129

- Is a Case? = **YES**
- Certainty = **HIGH**
- Justification:
Three separate encounters (days 383, 591, 1049) carry the specific diagnosis code Old myocardial infarction, which physicians only document when they have firm evidence (history, prior cath report, imaging or old record) that an MI truly occurred in the past. This code is not used for a rule-out situation. Around the same time the patient is placed on a comprehensive post-MI / coronary artery disease regimen: high-intensity statins (atorvastatin, later rosuvastatin), dual antiplatelet therapy with clopidogrel, beta-blocker (metoprolol), ACE/ARB (lisinopril then valsartan), nitrates (isosorbide, nitroglycerin) and ezetimibe. On day 406 she undergoes diagnostic coronary angiography with percutaneous coronary stent placement, and receives procedural heparin and sedation treatments entirely consistent with known prior MI and established coronary disease. No acute MI code or biomarker data appear during the observation window, but the repeated old MI codes plus disease-specific long-term secondary-prevention therapy and PCI make it extremely unlikely that the history of MI is spurious. Thus, the preponderance of evidence supports that the patient truly had a past acute myocardial infarction (now classified as old MI) even though the acute event itself occurred before the observation window and its exact date cannot be determined.



Adjudicating Person 626



Knowledge-Enhanced Electronic Profile Review (KEEPER)

Profile

Timeline

Demographics ?

Age: 84
Sex: FEMALE
Observation period: day -5611 - day 1573
Race: White
Ethnicity: Not Hispanic or Latino

Presentation ?

Acute non-ST segment elevation myocardial infarction (Claim, Primary diagnosis)

Visits ?

Home Visit (day -21, day -20, day -15, day -13, day -9, day -6, day -1, day 1, day 6, day 8, day 13, day 15, day 20, day 27)
Non-hospital institution Visit - Gerontology Nurse Practitioner (day -30, day -28, day -23)
Outpatient Visit (day 16)
Outpatient Visit - Family Medicine Physician (day -22)
Outpatient Visit - General Practice Registered Nurse (day -16)
Outpatient Visit - Internal Medicine (day 0)
Outpatient Visit - Orthopaedic Trauma Physician (day -2)
Pharmacy visit (day 27)
Pharmacy visit - Family Medicine Physician (day 8, day 16, day 22)
Pharmacy visit - Gerontology Nurse Practitioner (day -22, day 18)
Pharmacy visit - Internal Medicine (day 0)
Pharmacy visit - Orthopaedic Trauma Physician (day -2)

Symptoms ?

NA

Prior Disease ?

Phenotype:

Acute myocardial infarction

Decision ?

Decision
 Case
 Non-case

Certainty
 High
 Low

Correct index day

Patient selection

< 626 / 10000 >

Color legend ?

- Disease of interest
- Both
- Alternative diagnoses
- Other

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How would you adjudicate person 626 on whether they have had an Acute Myocardial Infarction?

Decision: Case; Certainty: High

0%

Decision: Case; Certainty: Low

0%

Decision: Not a Case; Certainty: Low

0%

Decision: Not a Case; Certainty: High

0%



KEEPER-LLM rationale for person 626

- Is a Case? = **NO**
- Certainty = **HIGH**
- Justification:

Only two diagnosis codes for Acute non-ST segment elevation myocardial infarction are present (day 0 and day 90). On day 0 the code appears during a routine outpatient Internal Medicine visit with a 12-lead ECG and a same-day pharmacy refill there is no emergency department or inpatient admission, no cardiac catheterization, PCI/CABG, no troponin/CK-MB labs, and no initiation of MI-specific acute therapies (e.g., heparin, P2Y12 inhibitor, high-dose aspirin, IV nitroglycerin, β^2 -blocker titration). Subsequent care consists of home visits and routine outpatient/pharmacy encounters, again without MI-directed acute management. The repeat acute NSTEMI code at day 90 occurs alongside outpatient diagnoses of persistent atrial fibrillation, suggesting administrative/problem-list carry-forward rather than a new infarction. The patient does carry prior codes for old MI fitting a remote event but not supporting a new acute infarct.
- In contrast, true acute MI in an 84-year-old almost invariably triggers hospitalization, serial cardiac enzymes, and disease-specific treatments all absent here. Thus the weight of evidence favors that the recorded NSTEMI codes were used for evaluation/risk-coding rather than documenting a bona-fide acute myocardial infarction.



Adjudicating Person 7824

Knowledge-Enhanced Electronic Profile Review (KEEPER)



Profile **Timeline**

Demographics ⓘ

Age: 53
Sex: MALE
Observation period: day -331 - day 520
Race: White
Ethnicity: Not Hispanic or Latino

Presentation ⓘ

Acute myocardial infarction (Claim, Secondary diagnosis)
Essential hypertension (Claim, Secondary diagnosis)
Hyperlipidemia (Claim, Primary diagnosis)
Type 2 diabetes mellitus (Claim, Secondary diagnosis)

Visits ⓘ

Non-hospital institution Visit (day -9, day 19)
Non-hospital institution Visit - Adult Health Nurse Practitioner (day -30, day 0, day 21)
Non-hospital institution Visit - Psychiatry (day 7)
Pharmacy visit - Internal Medicine (day -18, day -4, day 10, day 15, day 17)
Pharmacy visit - Psychiatry (day -29, day -2, day 26)

Symptoms ⓘ

Asthenia (day -30)
Fatigue (day -30)

Phenotype:

Acute myocardial infarction

Decision ⓘ

Decision

- Case
- Non-case

Certainty

- High
- Low

Correct index day

Patient selection



782 / 10000



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How would you adjudicate person 7824 on whether they have had an Acute Myocardial Infarction?

Decision: Case; Certainty: High

0%

Decision: Case; Certainty: Low

0%

Decision: Not a Case; Certainty: Low

0%

Decision: Not a Case; Certainty: High

0%



KEEPER-LLM rationale for person 7824

- Is a Case? = **NO**
- Certainty = **HIGH**
- Justification:
Only a single outpatient claim code for acute myocardial infarction appears on day 0, marked as a secondary diagnosis. There is no inpatient or ER visit, no cardiac catheterization, PCI, thrombolytics, EKG/troponin data, or MI-specific medications (e.g., dual antiplatelet therapy, IV heparin). No subsequent follow-up MI codes, cardiac rehab, or long-term antiplatelet/statin initiation beyond pre-existing therapies are present. Management of a true AMI virtually always includes hospitalization and aggressive cardiac interventions; their absence strongly suggests the code was used for rule-out or clerical reasons rather than a true event. Therefore, the preponderance of evidence indicates the patient did not truly experience an acute myocardial infarction.



Adjudicating Person 5189

Knowledge-Enhanced Electronic Profile Review (KEEPER)



Profile **Timeline**

Demographics i

Age: 68
Sex: FEMALE
Observation period: day -100 - day 19

Presentation i

Atrial fibrillation (Claim, Admission diagnosis)
Atrial fibrillation (Claim, Secondary diagnosis)
Cardiac arrest (Claim, Primary admission diagnosis)
Cardiac arrest (Claim, Primary diagnosis)
Dependence on respirator (Claim, Admission diagnosis)
Tobacco dependence syndrome (Claim, Admission diagnosis)
Tobacco dependence syndrome (Claim, Secondary diagnosis)

Visits i

Emergency Room and Inpatient Visit - Physician / Diagnostic Radiology (days 0 to 1)

Symptoms i

NA

Prior Disease i

NA

Phenotype:

Acute myocardial infarction

Decision i

Decision

- Case
 Non-case

Certainty

- High
 Low

Correct index day

Patient selection



518 / 10000



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How would you adjudicate person 5189 on whether they have had an Acute Myocardial Infarction?

Decision: Case; Certainty: High

0%

Decision: Case; Certainty: Low

0%

Decision: Not a Case; Certainty: Low

0%

Decision: Not a Case; Certainty: High

0%



KEEPER-LLM rationale for person 5189

- Is a Case? = **YES**
- Certainty = **HIGH**
- Justification:

Although no explicit ICD code for acute myocardial infarction (AMI) appears, the clinical picture on day 0 is highly characteristic of an AMI event: 1) sudden cardiac arrest with subsequent cardiogenic shock and anoxic encephalopathy; 2) emergent measurement of cardiac biomarkers (troponin, CK-total, CK-MB) and 12-lead ECG classic AMI work-up; 3) immediate administration of tenecteplase (a fibrinolytic used almost exclusively for ST-elevation MI in contemporary U.S. inpatient practice) plus heparin anticoagulation on day 0; 4) absence of alternative diagnoses (no pulmonary embolism, stroke, or other thrombotic disorder coded). Recurrent atrial fibrillation and tobacco dependence fit the cardiovascular risk profile. The downstream course ventilator dependence, acute respiratory failure, cardiogenic shock, and death aligns with complications of a large myocardial infarction complicated by cardiac arrest. The convergence of a cardiac arrest presentation, targeted cardiac biomarker testing, STEMI-specific thrombolysis, and cardiogenic shock strongly outweighs any counter-evidence. Therefore, the preponderance of evidence indicates the patient did experience an acute myocardial infarction on day 0.



Adjudicating Person 1100



Knowledge-Enhanced Electronic Profile Review (KEEPER)

Profile | **Timeline**

Demographics ?

Age: 38
Sex: MALE
Observation period: day -183 - day 280
Race: White
Ethnicity: Not Hispanic or Latino

Presentation ?

- Acute myocardial infarction (Claim, Secondary diagnosis)
- Angina pectoris (Claim, Primary diagnosis)
- Generalized ischemic myocardial dysfunction (Claim, Secondary diagnosis)
- Hypertensive emergency (Claim, Secondary diagnosis)
- Refractory angina (Claim, Secondary diagnosis)
- Unstable angina co-occurrent and due to coronary arteriosclerosis (Claim, Primary diagnosis)
- Dyspnea (Claim, Primary diagnosis)
- Heart failure (Claim, Secondary diagnosis)
- Hypertensive heart failure (Claim, Secondary diagnosis)
- Syncope and collapse (Claim, Primary diagnosis)
- Complication due to diabetes mellitus (Claim, Secondary diagnosis)
- Coronary atherosclerosis (Claim, Secondary diagnosis)
- Essential hypertension (Claim, Secondary diagnosis)
- Hyperlipidemia (Claim, Secondary diagnosis)
- Hypothyroidism (Claim, Secondary diagnosis)
- Nicotine dependence (Claim, Secondary diagnosis)
- Obesity (Claim, Secondary diagnosis)
- Type 2 diabetes mellitus (Claim, Secondary diagnosis)

Visits ?

- Inpatient Visit - Internal Medicine (days 0 to 2)
- Laboratory Visit (day 19)
- Outpatient Visit (day -9, day -9, day 22, day 22, day 22, day 30, day 30)

Phenotype:

Acute myocardial infarction

Decision ?

Decision

Case

Non-case

Certainty

High

Low

Correct index day

Patient selection

<
110 / 10000
 >

Color legend ?

- Disease of interest
- Both
- Alternative diagnoses
- Other

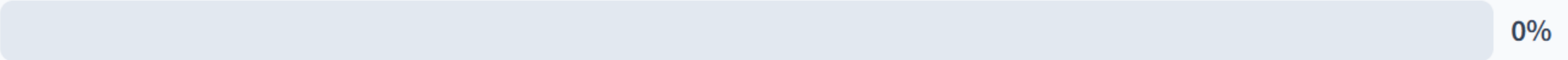


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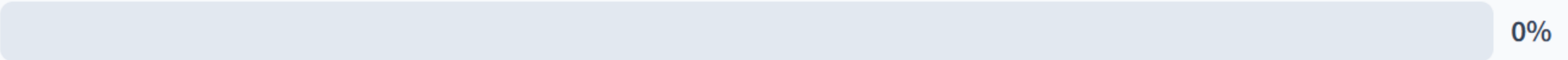


How would you adjudicate person 1100 on whether they have had an Acute Myocardial Infarction?

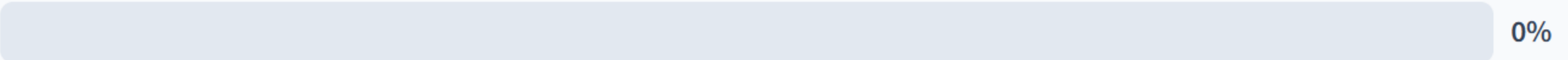
Decision: Case; Certainty: High



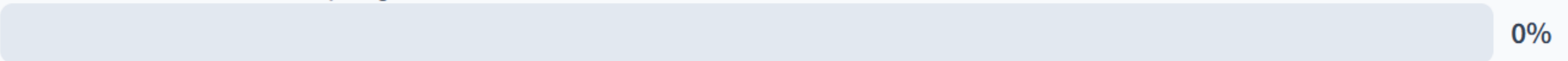
Decision: Case; Certainty: Low



Decision: Not a Case; Certainty: Low



Decision: Not a Case; Certainty: High





KEEPER-LLM rationale for person 1100

- Is a Case? = **NO**
 - Certainty = **LOW**
 - Justification:
Index admission (day 0-2) was for chest pain/angina with many ACS-related secondary codes including acute myocardial infarction but the clinical course looks like a rule-out ACS rather than a confirmed infarction:
 - Diagnosis pattern: Only a single MI code, listed as SECONDARY; primaries were angina pectoris and unstable angina. Subsequent encounters over the 9-month follow-up never again list an acute or recent MI code.
 - Testing pattern: Serial troponins and ECGs, plus diagnostic coronary angiography with left-heart cath (day 2). No PCI, stent placement, CABG, thrombolysis, or other reperfusion therapy was performed, suggesting no culprit occlusion was found.
 - Treatment pattern: Short courses of heparin, nitroglycerin, morphine while inpatient typical of empiric management while ruling out MI/ACS; clopidogrel was not started until day 39 (well after the episode) rather than during hospitalization, arguing against a confirmed MI that would mandate immediate dual antiplatelet therapy.
 - Follow-up: No documentation of acute recent, or history of MI later; care focuses on chronic heart failure and angina.
- Altogether, the evidence fits an evaluation for suspected ACS/unstable angina with MI ultimately not confirmed. Thus, the preponderance of evidence is against a true acute myocardial infarction.



Adjudicating Person 7282

Profile **Timeline**

Demographics

Age: 66
Sex: MALE
Observation period: day -219 - day 419
Race: White
Ethnicity: Not Hispanic or Latino

Presentation


- Acute ST segment elevation myocardial infarction (Claim, Primary diagnosis)
- Chest pain (Claim, Primary admission diagnosis)
- Chest pain (Claim, Primary diagnosis)
- Dizziness and giddiness (Claim, Admission diagnosis)
- Dyspnea (Claim, Admission diagnosis)
- Cough (Claim, Admission diagnosis)
- Bronchiectasis (Claim, Admission diagnosis)
- Bronchiectasis (Claim, Primary diagnosis)
- Clinical finding (Claim, Primary diagnosis)
- Electrocardiogram abnormal (Claim, Admission diagnosis)
- Essential hypertension (Claim, Admission diagnosis)
- Essential hypertension (Claim, Secondary diagnosis)
- Nicotine dependence in remission (Claim, Admission diagnosis)

Visits

- Ambulance Visit - Ambulance (day 0)
- Emergency Room Visit (day 0)
- Outpatient Visit (day 0, day 10, day 29)
- Outpatient Visit - Adult Health Nurse Practitioner (day 3)
- Outpatient Visit - Cardiology (day 10, day 29)
- Outpatient Visit - General Practice (day 0)

Phenotype:

Acute myocardial infarction

Decision 

Decision

Case

Non-case

Certainty


High

Low

Correct index day

Patient selection

< 728 / 10000 >

Color legend 

- Disease of interest
- Both
- Alternative diagnoses
- Other

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How would you adjudicate person 7282 on whether they have had an Acute Myocardial Infarction?

Decision: Case; Certainty: High

0%

Decision: Case; Certainty: Low

0%

Decision: Not a Case; Certainty: Low

0%

Decision: Not a Case; Certainty: High

0%



KEEPER-LLM rationale for person 7282

- Is a Case? = **YES**
- Certainty = **LOW**
- Justification:

There is a single encounter (day 0) coded as Acute ST-segment elevation myocardial infarction listed as the primary diagnosis of an Emergency Room/Ambulance visit for chest pain with abnormal ECG. A troponin test was ordered the same day exactly what is done when an MI is suspected/confirmed. After this event the patient was started on long-term high-intensity secondary-prevention therapy (atorvastatin) that had not been used before, and underwent a treadmill stress test 4 weeks later a pattern typical of post-MI follow-up. Arrhythmia codes (atrial/ventricular ectopy, SVT) began appearing soon after, which is also consistent with myocardial injury. Although there is no explicit record of PCI/thrombolysis, claims data are often incomplete with respect to inpatient procedures; a single hospitalization for STEMI commonly has only one MI diagnosis code. Taken together, the clinical presentation, confirmatory testing, emergency transport, and subsequent cardiac management make a true AMI more likely than a mere rule-out work-up. The evidence against MI (absence of PCI, only one aspirin dose) is not strong enough to outweigh the above administrative data often omit such details. Overall, the preponderance of evidence supports that the patient did experience an acute MI on day 0.



Adjudicating Person 4081



Knowledge-Enhanced Electronic Profile Review (KEEPER)

Profile **Timeline**

Demographics i

Age: 64
Sex: MALE
Observation period: day -156 - day 956
Race: White
Ethnicity: Not Hispanic or Latino

Presentation i

Acute myocardial infarction (Claim, Secondary diagnosis)
Abnormal results of cardiovascular function studies (Claim, Secondary diagnosis)
Coronary arteriosclerosis (Claim, Primary diagnosis)
Essential hypertension (Claim, Secondary diagnosis)
Hyperlipidemia (Claim, Primary diagnosis)
Obesity (Claim, Secondary diagnosis)

Visits i

Inpatient Visit (days 22 to 27)
Laboratory Visit - Independent Laboratory (day 30)
Outpatient Visit - Internal Medicine (day -5)
Outpatient Visit - Physician / Diagnostic Radiology (day 8)
Outpatient Visit - Thoracic Surgery (Cardiothoracic Vascular Surgery) Physician (day 0)
Pharmacy visit - General Surgery (day -2, day 16, day 20)
Pharmacy visit - Interventional Cardiology (day 4)
Pharmacy visit - Nephrology (day -17, day 13)

Symptoms i

Dyspnea (day -5)

Phenotype:

Acute myocardial infarction

Decision i

Decision
 Case
 Non-case

Certainty
 High
 Low

Correct index day

Patient selection

< 408 / 10000 >

Color legend i

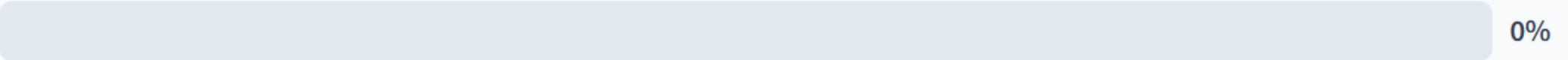
- Disease of interest
- Both
- Alternative diagnoses

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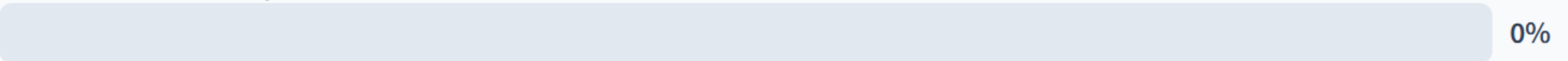


How would you adjudicate person 4081 on whether they have had an Acute Myocardial Infarction?

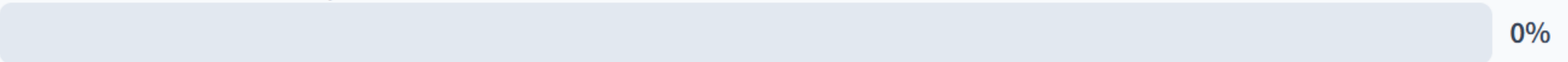
Decision: Case; Certainty: High



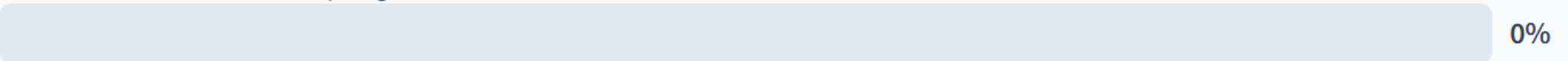
Decision: Case; Certainty: Low



Decision: Not a Case; Certainty: Low



Decision: Not a Case; Certainty: High





KEEPER-LLM rationale for person 4081

- Is a Case? = **YES**
- Certainty = **LOW**
- Justification:

Only a single code for Acute myocardial infarction appears (day 0), but it is accompanied by: 1) coronary angiography performed the same day, 2) initiation of beta-blocker (metoprolol) within a few days, 3) an inpatient admission three weeks later with CABG (2-vessel arterial grafts) and an ECG diagnosis of Old MI. A code for old MI would not be assigned unless the chart documented a prior infarction (e.g., Q-waves, prior imaging or discharge summary). The overall clinical picture new angiography, subsequent surgical revascularisation, long-term antiplatelet therapy (clopidogrel), and the Old MI diagnosis strongly suggests the patient truly had an MI sometime shortly before or at the time of the catheterisation. No troponin values are present, but absence of lab data in claims is common. Conversely, if the MI had merely been ruled out, one would expect multiple subsequent rule-out encounters rather than definitive revascularisation and a coded old MI. Therefore, preponderance of evidence supports that an acute MI occurred, most plausibly around day 0.



Plans for Phenotype Aphril

- Week 0: Phenotype Aphril kickoff
 - March 31 community call: Overview of phenotyping and opportunities for LLM
- Week 1: Phenotype development
 - April 7 community call: Demo – building cohorts in ATLAS
- Week 2: Phenotype evaluation
 - April 14 community call: Interactive – case adjudication using KEEPER
- Week 3: Iterative phenotype development
 - No community call: build your own AMI cohort definitions!
- Week 4: Iterative phenotype evaluation
 - April 28 community call: Review performance of submitted AMI cohort definitions



Join the Journey!

<https://www.ohdsi.org/join-the-journey/>

Looking forward to collaborating with all of you!

Email me: ryan@ohdsi.org