3. Multimorbidity Day, 22.11.2018
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Electronic Phenotyping for Multimorbidity Research and Personalized Health

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Phänotyp

Feedback

Summe aller an einem Einzelwesen vorhandenen Merkmale (Phäne), sein äußeres Bild, seine äußere Erscheinungsform und seine funktionellen Eigenschaften. Der Phänotyp wird geprägt durch das Zusammenwirken von erblichen Merkmalen (Genotyp, Genexpression) und nichterblichen Merkmalen (Innenmilieu und Umwelt). Die Expressivität beschreibt den Grad der phänotypischen Ausprägung.

Autoren / letzte Bearbeiter: Dorit Schöller; Pschyrembel Redaktion
Letzte Aktualisierung dieses Artikels: 04.2016
Publikation: Pschyrembel online
Artikelkategorie: Keine

Feedback zum Artikel

Box 1 | **Electronic phenotyping**

Electronic phenotyping is the process of deriving phenotype information from incomplete sources of data, such as electronic health records. The process of electronic phenotyping can use a variety of data types, including billing and procedure codes, vital signs, laboratory measures and clinical free text. Phenotyping algorithms are often verified by performing a manual review of a subset of records. In the eMERGE network, the development of a phenotype algorithm is an iterative process whereby content experts are consulted to identify the relevant billing codes, procedures, laboratory tests, medications and free text phrases for cases (individuals with the disease) and for controls (individuals free of the disease). An algorithm is then drafted and implemented on the data set to identify potential cases and controls. A fraction of the identified cases and controls are then manually reviewed by content experts to confirm case or control status. The positive predictive value is calculated with these data as the ratio of true positives (TP) over TP + false positive (FP): that is, PPV = TP/(TP + FP). The algorithm can be revised and re-implemented until the study's target positive predictive value has been achieved. To evaluate an algorithm against other established algorithms, a 'gold standard' set of true positives can be created by manual review. This gold standard set can then be used to generate statistics to evaluate algorithm performance.

Nat Rev Genet. 2016 Mar;17(3):129-45.

Routinely collected electronic health record data on inpatients

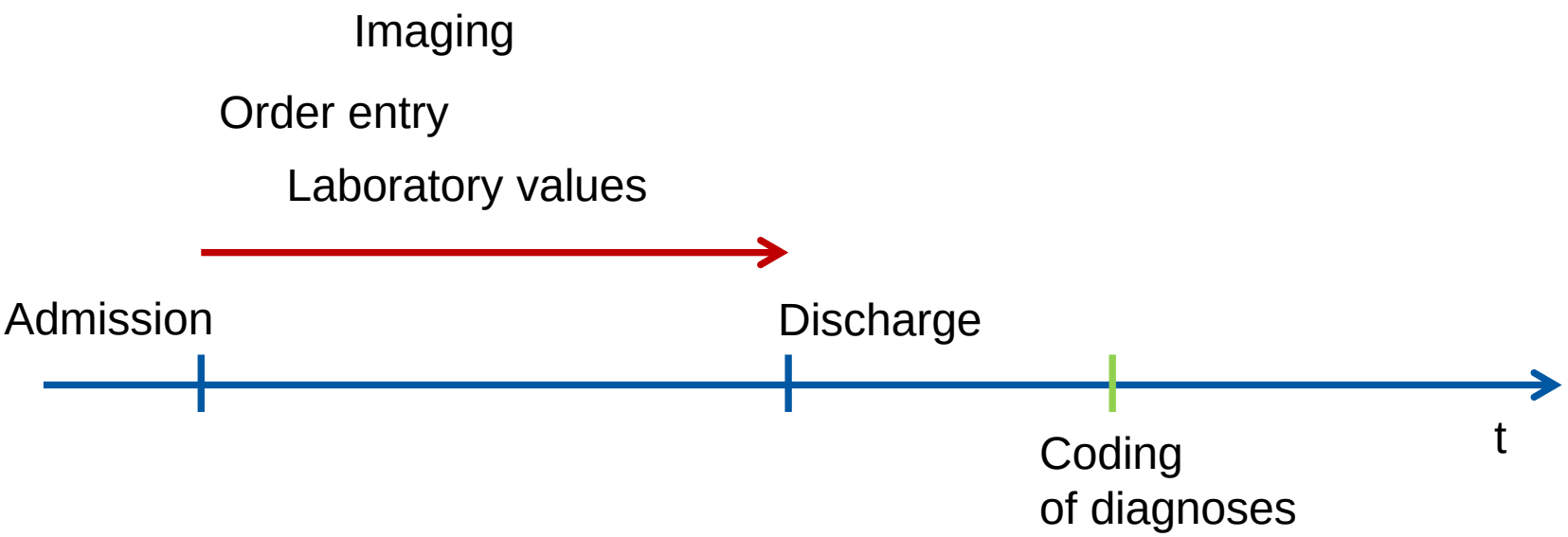


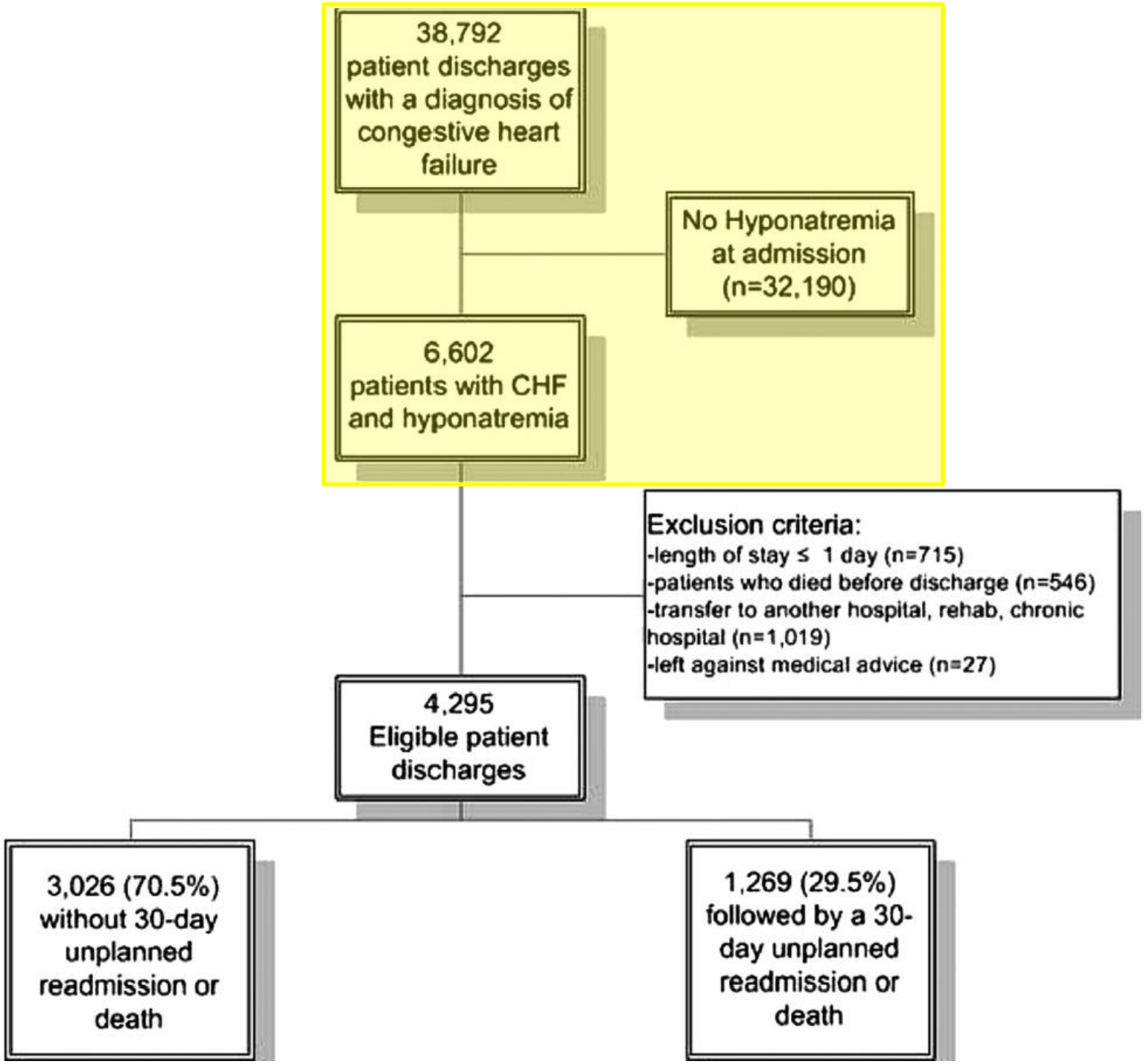
TABLE 1. ICD-9-CM and ICD-10 Coding Algorithms for Charlson Comorbidities

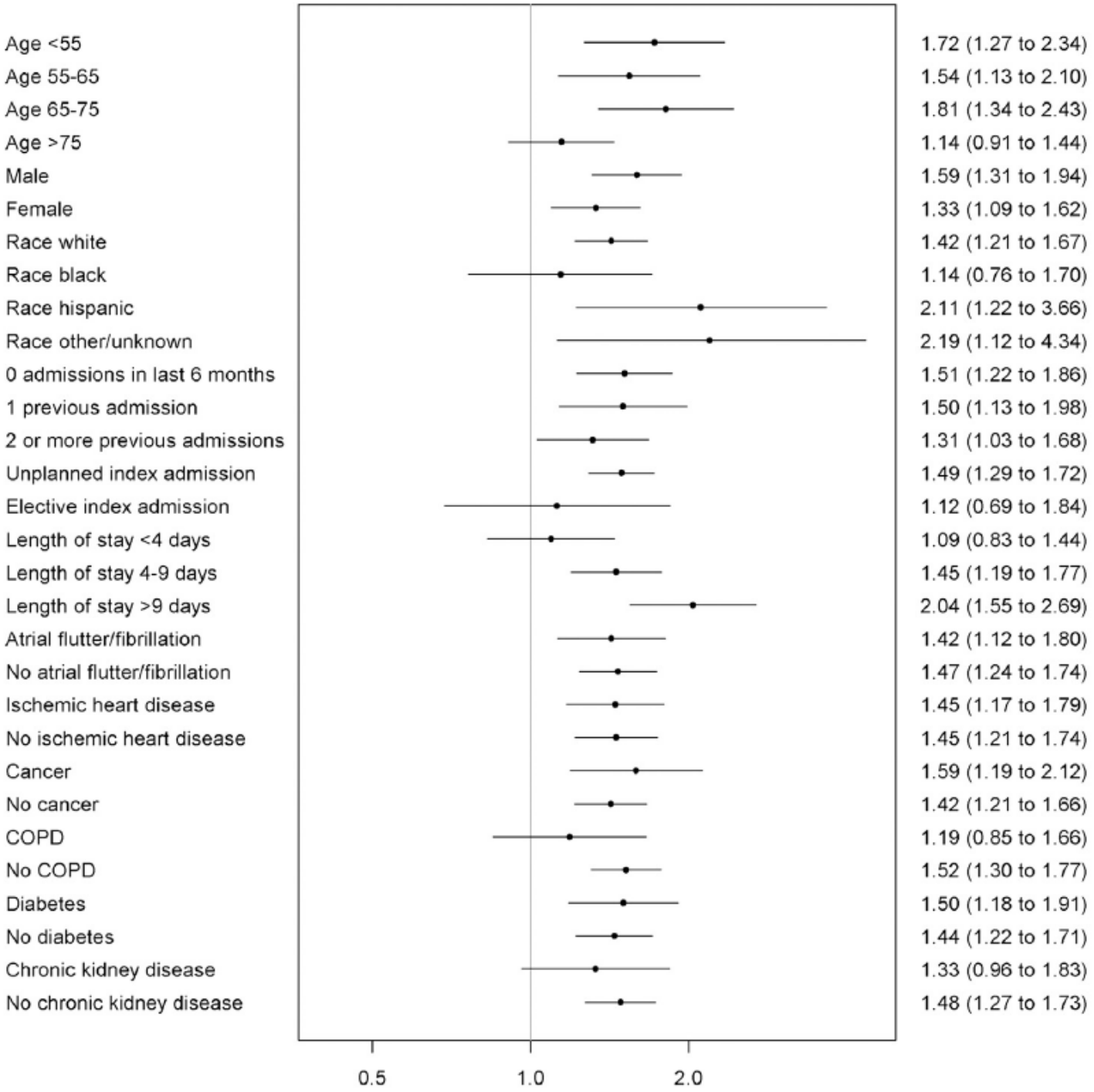
Comorbidities	Deyo's ICD-9-CM	ICD-10	Enhanced ICD-9-CM
Myocardial infarction	410.x, 412.x	I21.x, I22.x, I25.2	410.x, 412.x
Congestive heart failure	428.x	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5–I42.9, I43.x, I50.x, P29.0	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4–425.9, 428.x
Peripheral vascular disease	443.9, 441.x, 785.4, V43.4 Procedure 38.48	I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9	093.0, 437.3, 440.x, 441.x, 443.1–443.9, 47.1, 557.1, 557.9, V43.4
Cerebrovascular disease	430.x–438.x	G45.x, G46.x, H34.0, I60.x–I69.x	362.34, 430.x–438.x
Dementia	290.x	F00.x–F03.x, F05.1, G30.x, G31.1	290.x, 294.1, 331.2
Chronic pulmonary	490.x–505.x, 506.4	I27.8, I27.9, I40.x–I47.x, I60.x–I67.x	416.8, 416.9, 490.x–505.x

TABLE 2. ICD-9-CM and ICD-10 Coding Algorithms for Elixhauser Comorbidities

Comorbidities	Elixhauser's Original ICD-9-CM	Elixhauser AHRQ-Web ICD-9-CM	ICD-10	Enhanced ICD-9-CM
Congestive heart failure	398.91, 402.11, 402.91, 404.11, 404.13, 404.91, 404.93, 428.x	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.x	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5–I42.9, I43.x, I50.x, P29.0	398.91, 402.01, 402.11, 402.91 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4–425.9, 428.x
Cardiac arrhythmias	426.10, 426.11, 426.13, 426.2–426.53, 426.6–426.8, 427.0, 427.2, 427.31, 427.60, 427.9, 785.0, V45.0, V53.3	—	I44.1–I44.3, I45.6, I45.9, I47.x–I49.x, R00.0, R00.1, R00.8, T82.1, Z45.0, Z95.0	426.0, 426.13, 426.7, 426.9, 426.10, 426.12, 427.0–427.4, 427.6–427.9, 785.0, 996.01, 996.04, V45.0, V53.3
Valvular disease	093.2, 394.0–397.1, 424.0–424.91, 746.3–746.6, V42.2, V43.3	093.2, 394.x–397.1, 397.9, 424.x, 746.3–746.6, V42.2, V43.3	A52.0, I05.x–I08.x, I09.1, I09.8, I34.x–I39.x, Q23.0–Q23.3, Z95.2–Z95.4	093.2, 394.x–397.x, 424.x, 746.3–746.6, V42.2, V43.3
Pulmonary circulation disorders	416.x, 417.9	416.x, 417.9	I26.x, I27.x, I28.0, I28.8, I28.9	415.0, 415.1, 416.x, 417.0, 417.8, 417.9
Peripheral vascular disorders	440.x, 441.2, 441.4, 441.7, 441.9, 443.1–	440. x, 441.x, 442.x, 443.1–443.9, 447.1	I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0	093.0, 437.3, 440.x, 441.x, 443.1–443.9, 447.1, 557.1

Med Care. 2005 Nov;43(11):1130-9.


38,792
patient discharges with a diagnosis of congestive heart failure
No Hyponatremia at admission (n=32,190)
6,602
patients with CHF and hyponatremia
Exclusion criteria:
-length of stay ≤ 1 day (n=715)
-patients who died before discharge (n=546)
-transfer to another hospital, rehab, chronic hospital (n=1,019)
-left against medical advice (n=27)
4,295
Eligible patient discharges
3,026 (70.5%) without 30-day unplanned readmission or death
1,269 (29.5%) followed by a 30-day unplanned readmission or death


Age <55
Age 55-65
Age 65-75
Age >75
Male
Female
Race white
Race black
Race hispanic
Race other/unknown
0 admissions in last 6 months
1 previous admission
2 or more previous admissions
Unplanned index admission
Elective index admission
Length of stay <4 days
Length of stay 4-9 days
Length of stay >9 days
Atrial flutter/fibrillation
No atrial flutter/fibrillation
Ischemic heart disease
No ischemic heart disease
Cancer
No cancer
COPD
No COPD
Diabetes
No diabetes
Chronic kidney disease
No chronic kidney disease
1.72 (1.27 to 2.34)
1.54 (1.13 to 2.10)
1.81 (1.34 to 2.43)
1.14 (0.91 to 1.44)
1.59 (1.31 to 1.94)
1.33 (1.09 to 1.62)
1.42 (1.21 to 1.67)
1.14 (0.76 to 1.70)
2.11 (1.22 to 3.66)
2.19 (1.12 to 4.34)
1.51 (1.22 to 1.86)
1.50 (1.13 to 1.98)
1.31 (1.03 to 1.68)
1.49 (1.29 to 1.72)
1.12 (0.69 to 1.84)
1.09 (0.83 to 1.44)
1.45 (1.19 to 1.77)
2.04 (1.55 to 2.69)
1.42 (1.12 to 1.80)
1.47 (1.24 to 1.74)
1.45 (1.17 to 1.79)
1.45 (1.21 to 1.74)
1.59 (1.19 to 2.12)
1.42 (1.21 to 1.66)
1.19 (0.85 to 1.66)
1.52 (1.30 to 1.77)
1.50 (1.18 to 1.91)
1.44 (1.22 to 1.71)
1.33 (0.96 to 1.83)
1.48 (1.27 to 1.73)
0.5
1.0
2.0

CLINICAL SIGNIFICANCE

- The prognostic impact of persistent hyponatremia in comparison with corrected hyponatremia before hospital discharge is unknown.
- Those who do not have their hyponatremia corrected before discharge have an increased risk of nearly 50% for a 30-day unplanned readmission or death and a 2-fold increased risk for mortality compared with those who have their hyponatremia corrected before discharge.

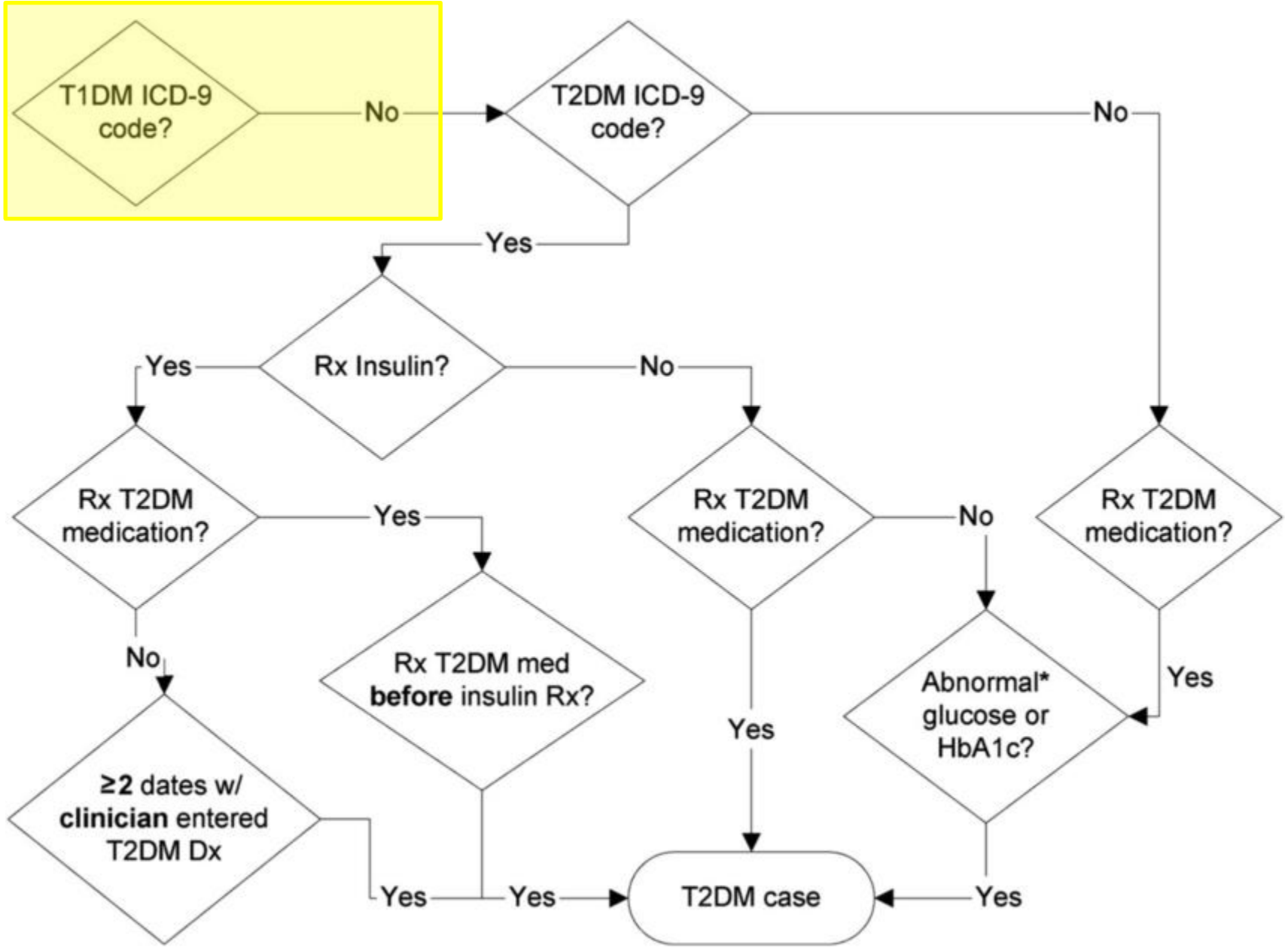
Am J Med. doi: 10.1016/j.amjmed.2016.02.036.

Multimorbidity MeSH Descriptor Data 2018

Details | Qualifiers | MeSH Tree Structures | Concepts

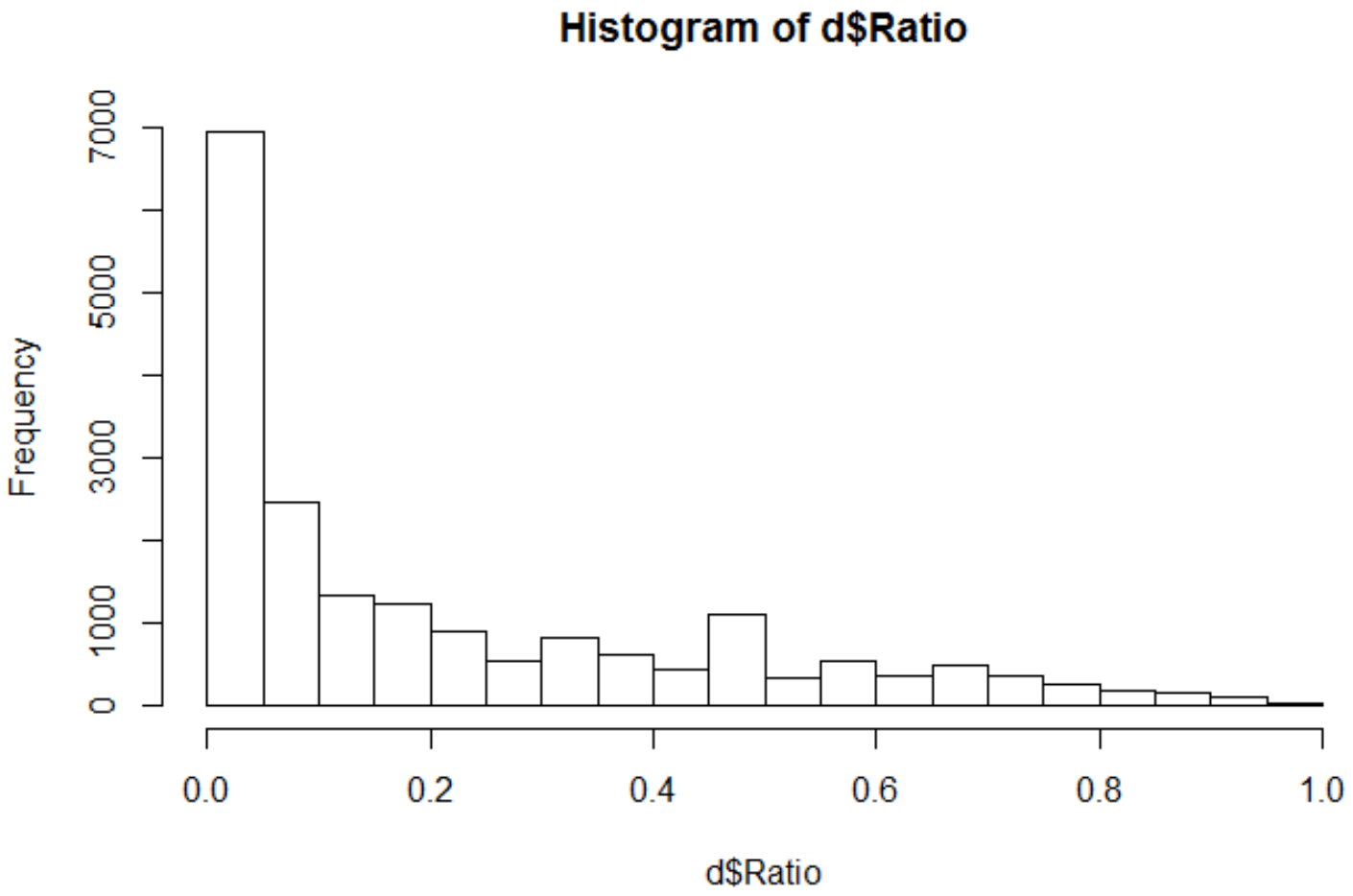
MeSH Heading	Multimorbidity
Tree Number(s)	N05.715.350.225.500
	N06.850.490.687.500
Unique ID	D000076322
Scope Note	The complex interactions of several co-existing diseases.
Public MeSH Note	2018
History Note	2018
Date Established	2018/01/01
Date of Entry	2017/07/11

Medical Subject Headings (MeSH), United States National Library of Medicine (NLM)

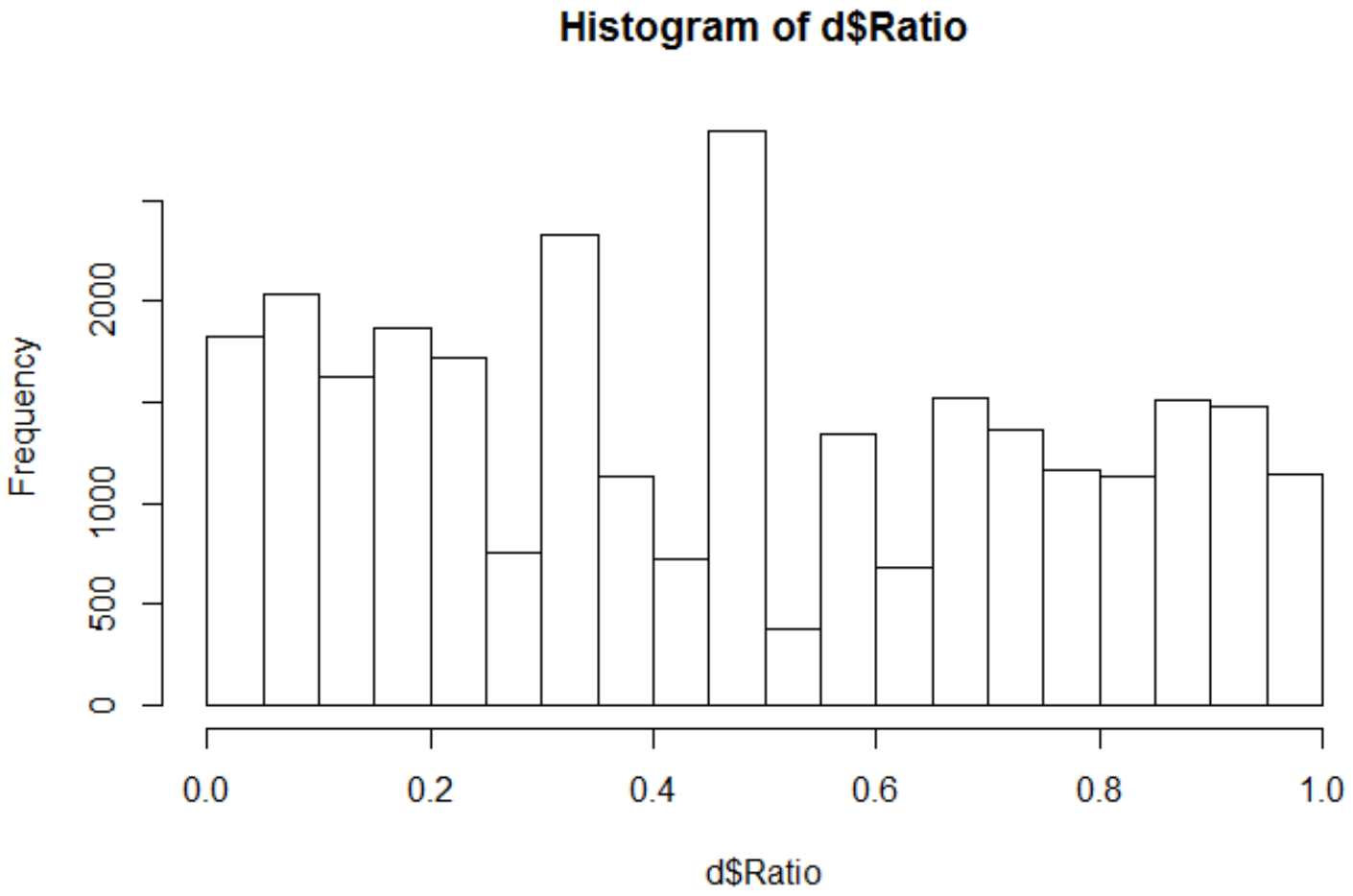


J Am Med Inform Assoc. 2012 Mar-Apr;19(2):212-8.

Proportion of «DM1 encounters» of potential DM2 patients



Proportion of «?» of potential asthma patients



Aspirin-exacerbated respiratory disease (AERD)

- Neither an ICD-9 code nor an ICD-10 code for AERD (ICD-11 beta currently features an "Aspirin-induced asthma" code)
- Partners' sites: Records with allergy information including drug allergies (“PEAR”)
- Routinely collected EHR data from outpatient and inpatient sites
- Long-term longitudinal data

Aspirin-exacerbated respiratory disease (AERD)

Samter's Triad:

- Chronic rhinosinusitis with nasal polyposis
- Asthma
- NSAID allergy: Respiratory reactions to all inhibitors of cyclooxygenase (COX)-1

“Possible AERD” algorithm, intersection of 3 queries

ASTHMA

```
where
LMR_Text_Description = 'asthma' or
LMR_Text_Description = 'H/O Asthma' or
LMR_Text_Description = 'Allergic asthma' or
LMR_Text_Description = 'Cough variant asthma' or
LMR_Text_Description = 'Asthma - resolved' or
LMR_Text_Description = 'Asthma, acute exacerbation'
LMR_Text_Description = 'asthma/allergic rhinitis' or
LMR_Text_Description = 'Moderate persistent asthma'
LMR_Text_Description = 'Severe persistent asthma' or
LMR_Text_Description = 'Asthmatic breathing' or
LMR_Text_Description = 'Extrinsic asthma' or
LMR_Text_Description = 'Asthma - or eosinophilic bro
LMR_Text_Description = 'ASTHMA,SEVERE' or
LMR_Text_Description = 'chronic obstructive asthma'
LMR_Text_Description like '*Asthma, aspirin sensitiv
LMR_Text_Description like '*ASTHMA, FREQUENT STEROII
LMR_Text_Description like '*ASTHMA, INTUBATED*'
```

NASAL POLYPS

```
where
LMR_Text_Description like '*polyp of nasal cavity*'
LMR_Text_Description like '*nasal polyp*' Or
LMR_Text_Description like '*other polyp of sinus*' O
LMR_Text_Description like '*polypoid sinus degenerat
LMR_Text_Description like '*sinus surgery, polyp*' o
LMR_Text_Description like '*sinus polyp*'
or
(
    (
    LMR_Text_Description like '*sinus*' or
    LMR_Text_Description like '*nasal*' or
    LMR_Text_Description like '*allergic rhinitis*'
    )
    and
    (
    Comments like '*polyp*'
    )
```

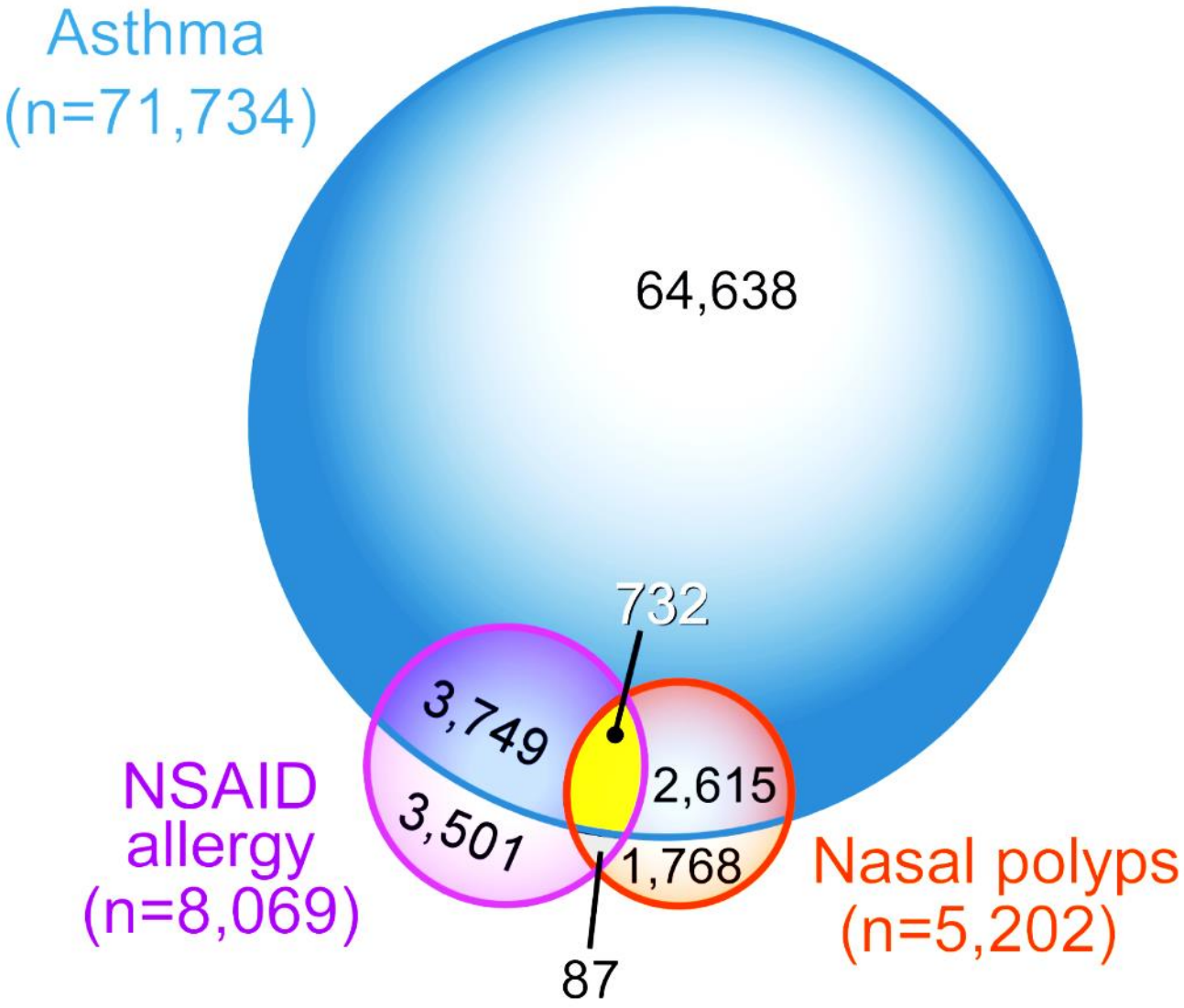
NSAID ALLERGY

```
Allergen like '*sulindac*' Or
Allergen like '*etodolac*' Or
Allergen like '*flurbiprofen*' Or
Allergen like '*ketoprofen*' Or
Allergen like '*fenoprofen*' Or
Allergen like '*oxaprozin*' Or
Allergen like '*mefenamic acid*' Or
Allergen like '*meclofenamic acid*' Or
Allergen like '*piroxicam*' Or
Allergen like '*meloxicam*' Or
Allergen like '*diclofenac*'
```

Focused on respiratory reactions

```
) AND
(
    Reaction like '*bronchospasm*' or
    Reaction like '*brochospasm*' or
    Reaction like '*bronchoconstriction*' or
    Reaction like '*shortness of breath*' or
```

2,647,842 records searched and 168,126 of them further analyzed



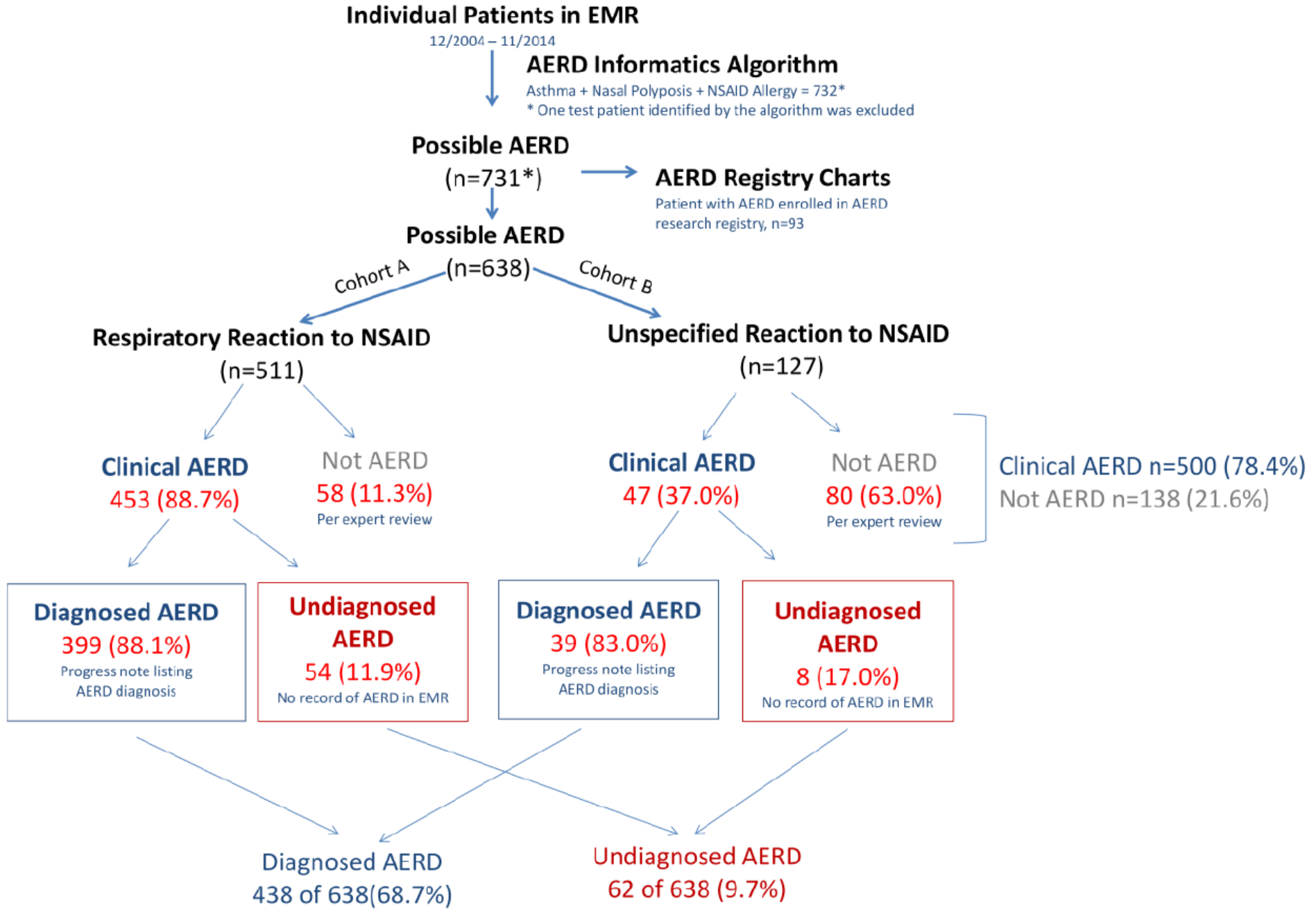

Individual Patients in EMR
12/2004 – 11/2014
AERD Informatics Algorithm
Asthma + Nasal Polyposis + NSAID Allergy = 732*
* One test patient identified by the algorithm was excluded
Possible AERD
(n=731*)
AERD Registry Charts
Patient with AERD enrolled in AERD research registry, n=93
Possible AERD
(n=638)
Cohort A
Cohort B
Respiratory Reaction to NSAID
(n=511)
Unspecified Reaction to NSAID
(n=127)
Clinical AERD
453 (88.7%)
Not AERD
58 (11.3%)
Per expert review
Clinical AERD
47 (37.0%)
Not AERD
80 (63.0%)
Per expert review
Clinical AERD n=500 (78.4%)
Not AERD n=138 (21.6%)
Diagnosed AERD
399 (88.1%)
Progress note listing AERD diagnosis
Undiagnosed AERD
54 (11.9%)
No record of AERD in EMR
Diagnosed AERD
39 (83.0%)
Progress note listing AERD diagnosis
Undiagnosed AERD
8 (17.0%)
No record of AERD in EMR
Diagnosed AERD
438 of 638(68.7%)
Undiagnosed AERD
62 of 638 (9.7%)

TABLE I. Allergist/immunologist involvement in undiagnosed and diagnosed clinical AERD

	AERD		
	Diagnosed	**Undiagnosed**	**Total**
Allergist/immunologist involvement	408	24	
No allergist/immunologist involvement	30	38	
Total, n	438	62	500
Allergy involvement (%)	93.2	38.7	

The charts of undiagnosed (n = 62) and diagnosed AERD (n = 438) cases were assessed for involvement by allergy/immunology specialists.

TABLE II. Demographic characteristics of diagnosed and undiagnosed AERD cases and the BWH AERD registry

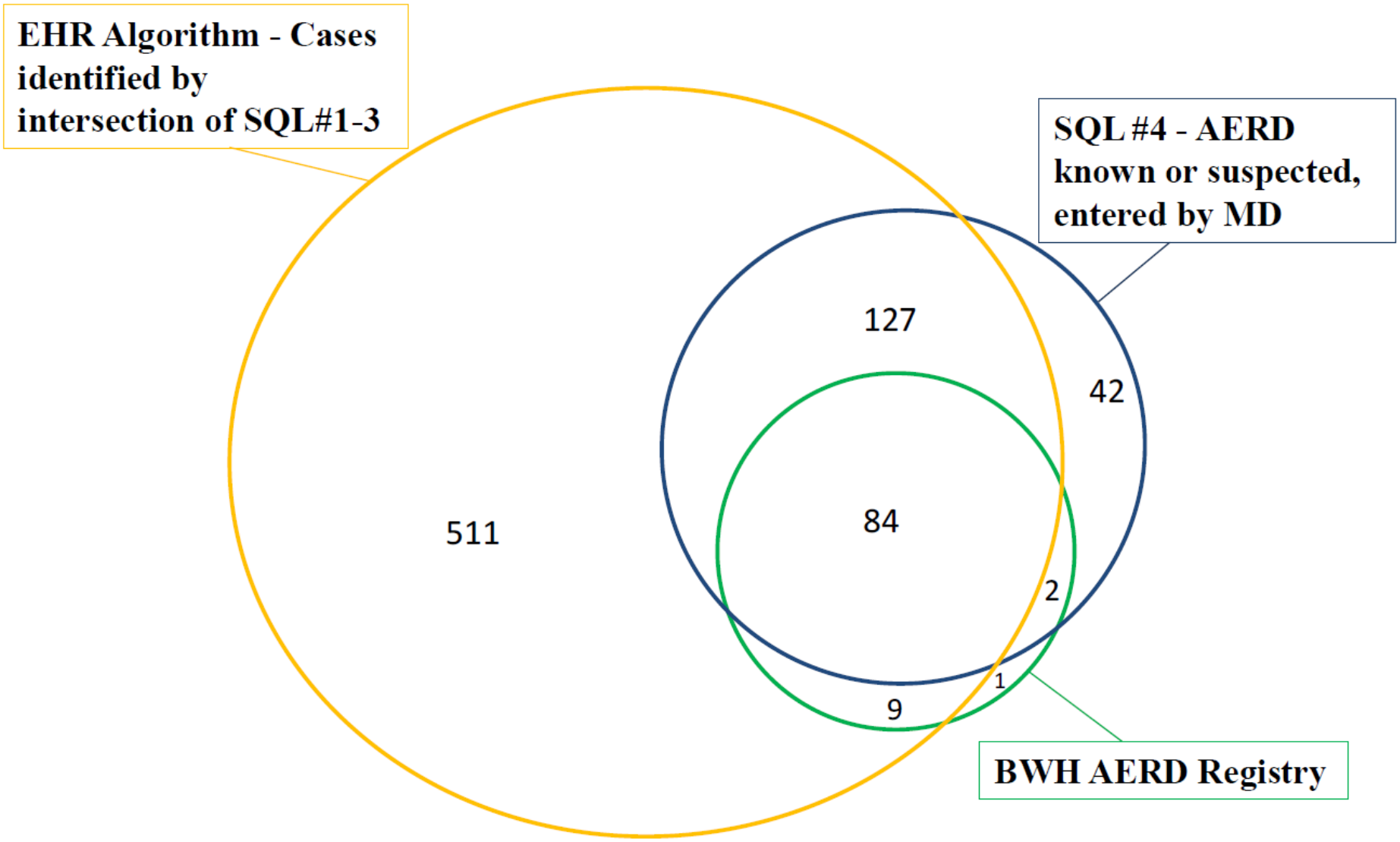
Characteristic	Diagnosed AERD	Undiagnosed AERD	*P* value	AERD registry
Sample size, n	438	62		96
Sex: male, n (%)*	179 (40.9)	26 (41.9)	.9	42 (43.8)
Median age (y) (IQR)†	54 (45-65)	58 (51-72)	<.01	52 (42-60)
Race, n (%)*			.7	
White/Caucasian	356 (81.3)	53 (85.5)		87 (90.6)
Black/African American	27 (6.2)	2 (3.2)		3 (3.1)
Hispanic/Latino	16 (3.7)	3 (4.8)		2 (2.1)
Asian	5 (1.1)	1 (1.6)		3 (3.1)
Other/unknown	34 (7.8)	3 (4.8)		1 (1.0)
Encounters, total, median (IQR)‡	37.5 (11-101)	54.5 (19-126)	.3	

Statistical analyses run between diagnosed and undiagnosed AERD. The BWH AERD registry's demographic characteristics have been included for reference. *n* represents sample size.

*Fisher exact test.

†Mann-Whitney *U* test.

‡*T* test.



J Allergy Clin Immunol. 2017 Mar;139(3):819-825.e6.

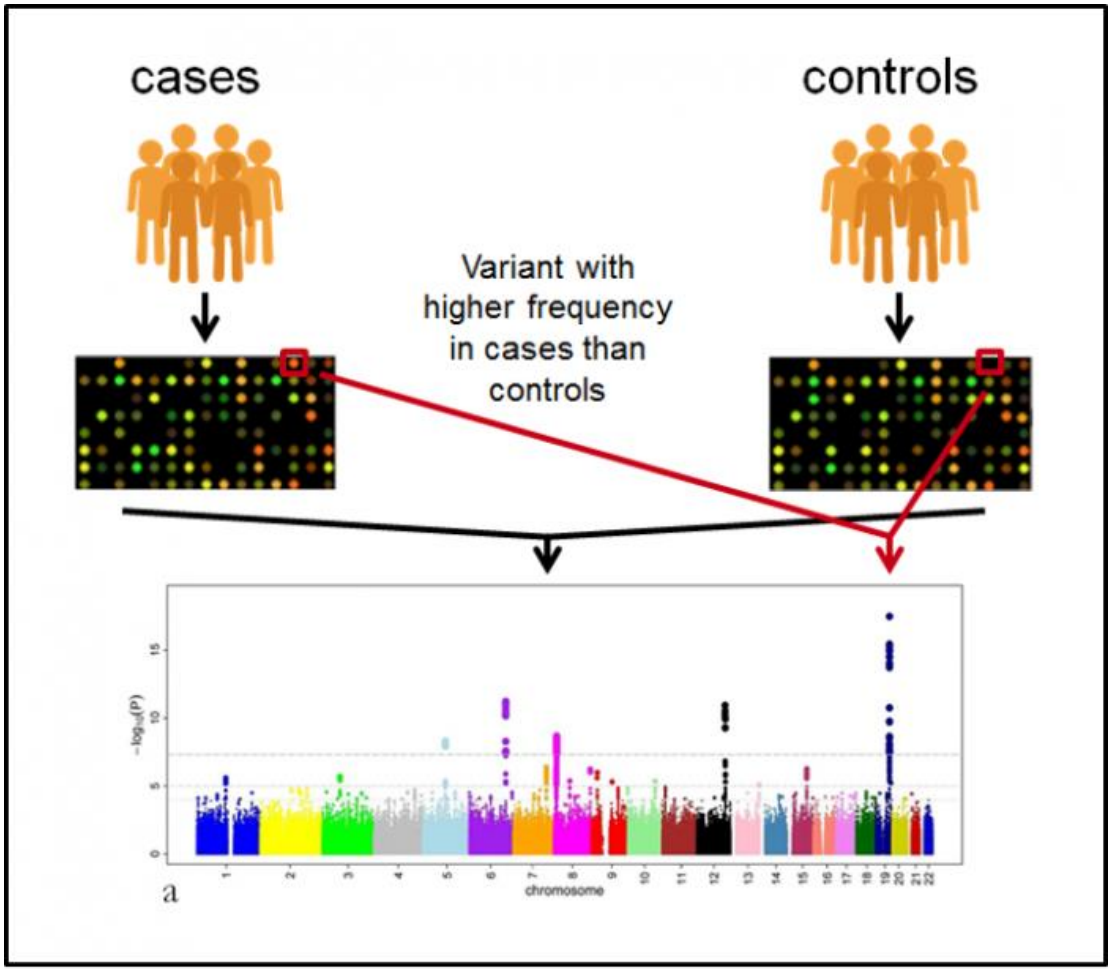
AERD project key messages

- An informatics algorithm can be used to search EHRs to identify diagnosed and previously undiagnosed cases of clinical AERD
- Incomplete recording of drug reaction data by caregivers limits the PPV of this algorithm
- Involvement of allergy/immunology specialists in the care of subjects with asthma, nasal polyposis, and NSAID allergy increases the likelihood that a diagnosis of AERD will be made

And last but not least

- There is effective treatment
- The project helped enrolling more patients
- Increased the number of patients in the AERD registry from ca. 100 to ca. 1000

Genome-wide association studies (GWAS)



https://www.ebi.ac.uk/training/online/sites/ebi.ac.uk.training.online/files/resize/GWAS/GWAS3-700x614.png, accessed on Nov 21, 2018

Science Home News Journals Topics

Lisa Bastarache & Joshua Denny

RESEARCH ARTICLE

Phenotype risk scores identify patients with unrecognized Mendelian disease patterns

Lisa Bastarache[1], Jacob J. Hughey[1], Scott Hebbring[2], Joy Marlo[1], Wanke Zhao[3], Wanting T. Ho[3], Sara L. Van Driest[4,5], Tracy L. McGregor[5], Jonathan D. Mosley[4], Quinn S. Wells[4,6], Michael Temple[1], Andrea H. Ramirez[4], Robert Carroll[1], Travis Osterman[1,4], Todd Edwards[4], Douglas Ruderfer[4], Digna R. Velez Edwards[7], Rizwan Hamid[5], Joy Cogan[5], Andrew Glazer[4], Wei-Qi Wei[1], QiPing Feng[6], Murray Brilliant[2], Zhizhuang J. Zhao[3], Nancy J. Cox[4], Dan M. Roden[1,4,6], Joshua C. Denny[1,4,*]

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The *All of Us* Research Program is a historic effort to gather data from one million or more people living in the United States to accelerate research and improve health. By taking into account individual differences in lifestyle, environment, and biology, researchers will uncover paths toward delivering precision medicine.

Thank you!

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