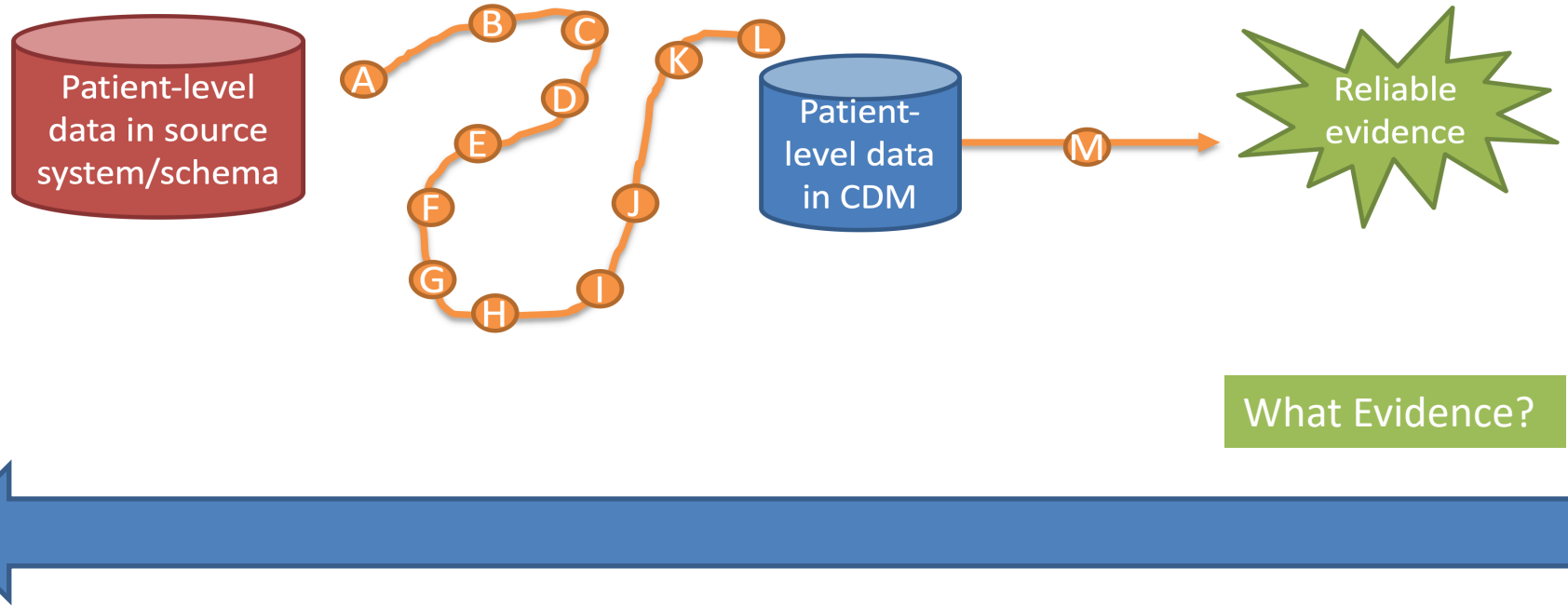


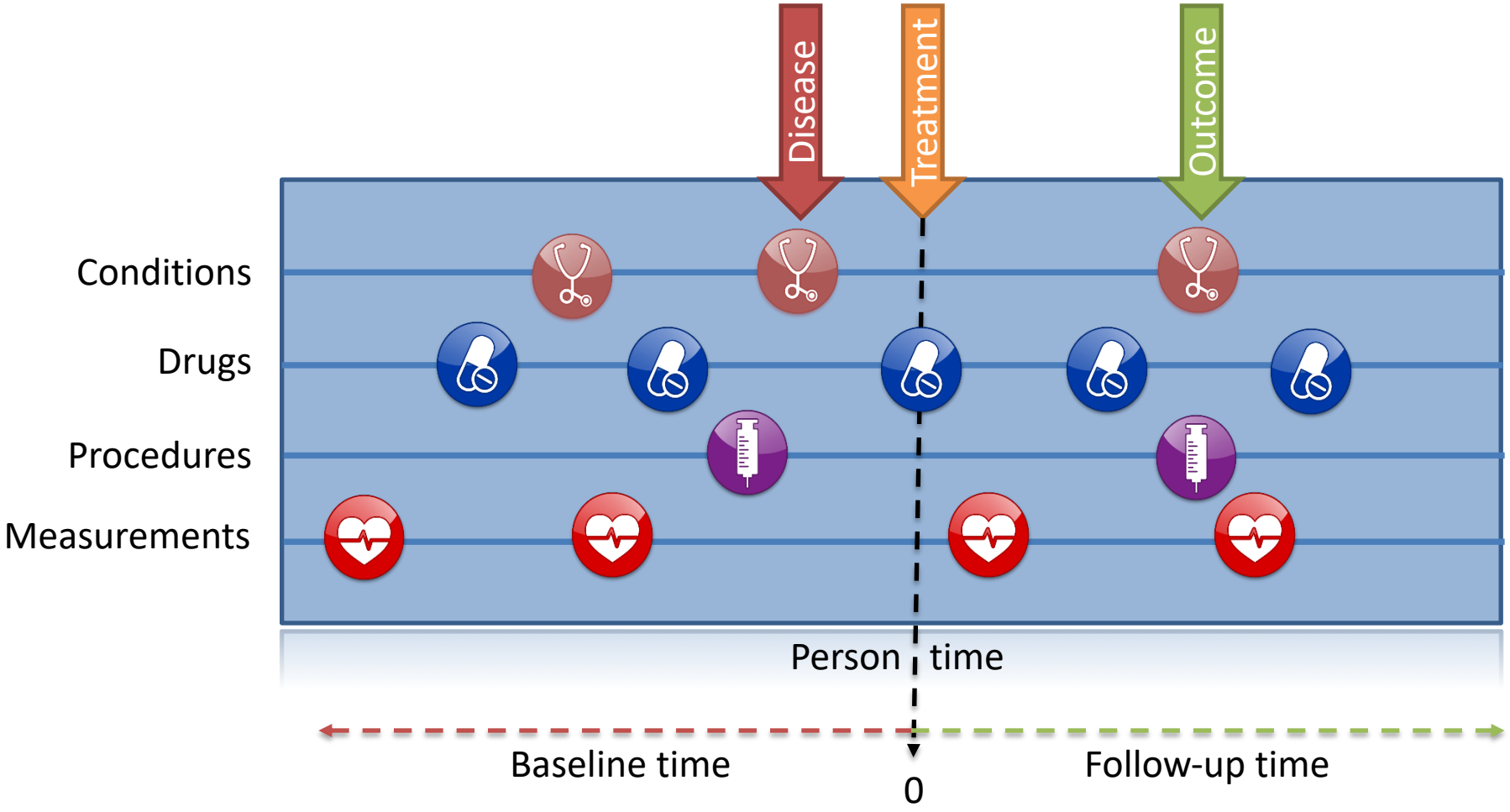
OHDSI

OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

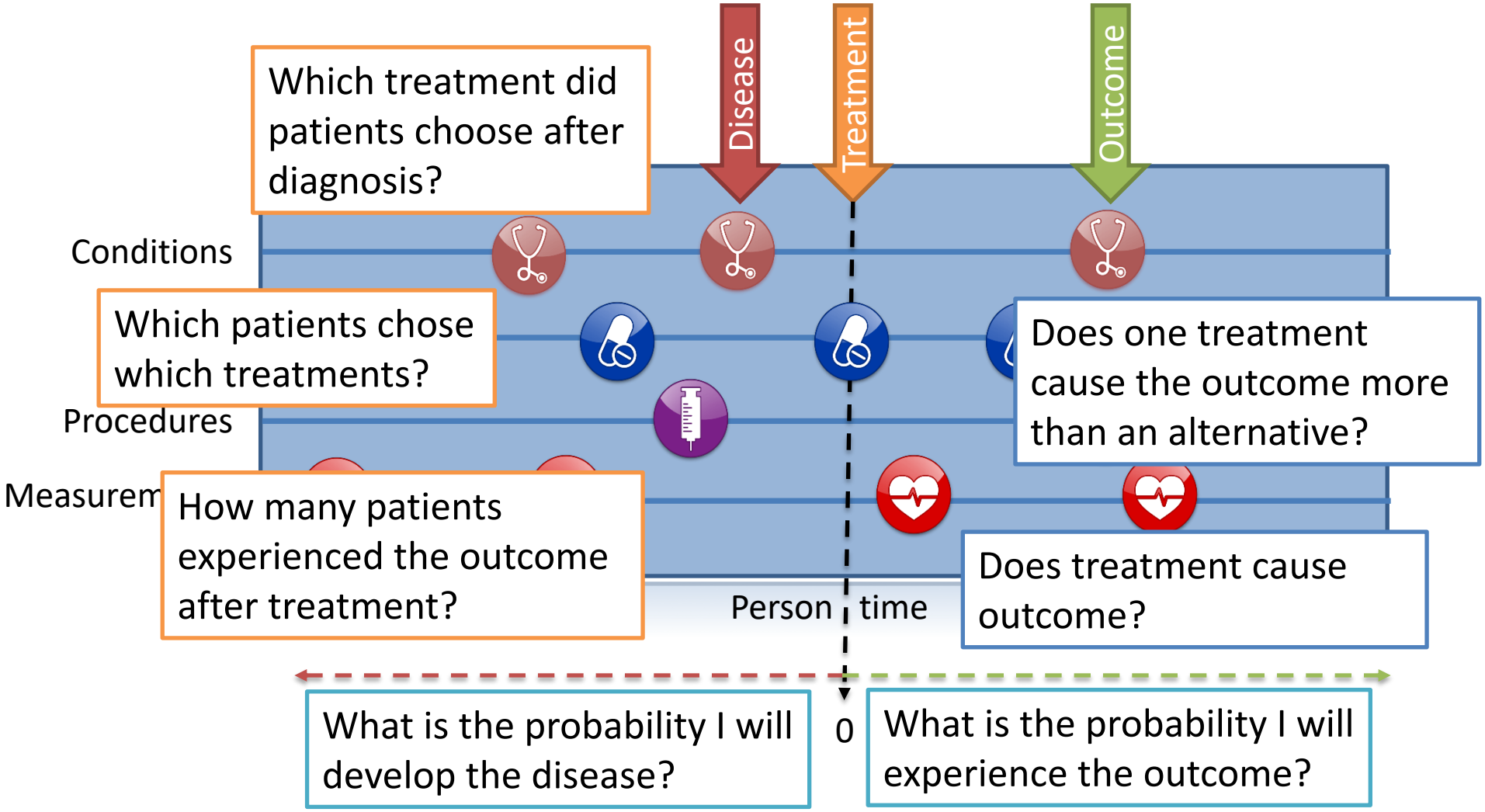
What evidence do we want to generate?

Patrick Ryan, Daniel Prieto Alhambra, Niklas Norén

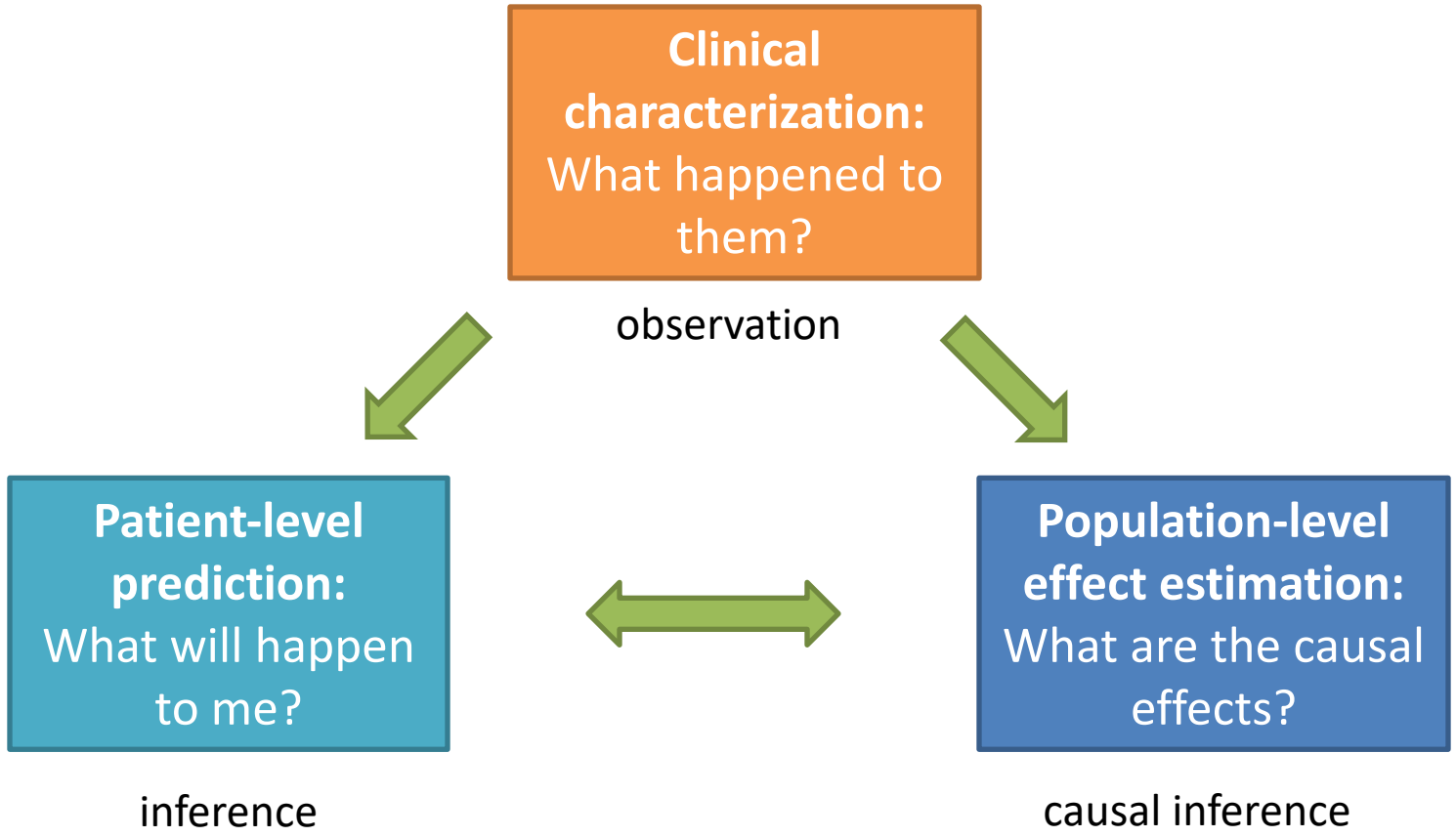
A caricature of the patient journey



Questions asked across the patient journey



Complementary evidence to inform the patient journey



What evidence do we want to generate?

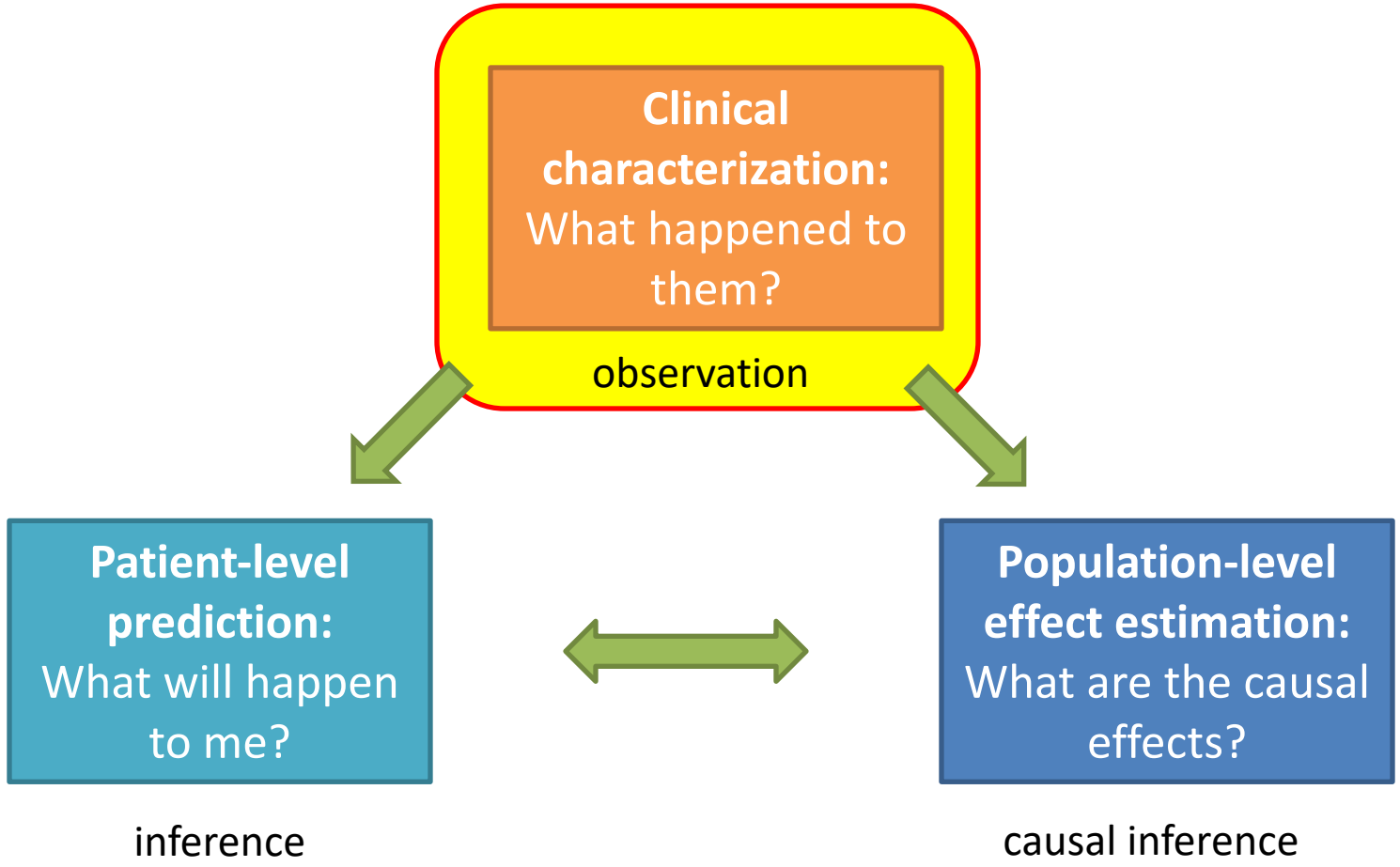
Treatment utilization studies

D Prieto-Alhambra

Prof of Pharmaco- and Device Epidemiology

Centre for Statistics in Medicine, NDORMS, University of Oxford

Complementary evidence to inform the patient journey



AGENDA

- Real World Evidence: Why do I bother?
- Why are treatment utilization studies relevant?
- Multi-country DUS
- Future directions and opportunities

AGENDA

- Real World Evidence: Why do I bother?
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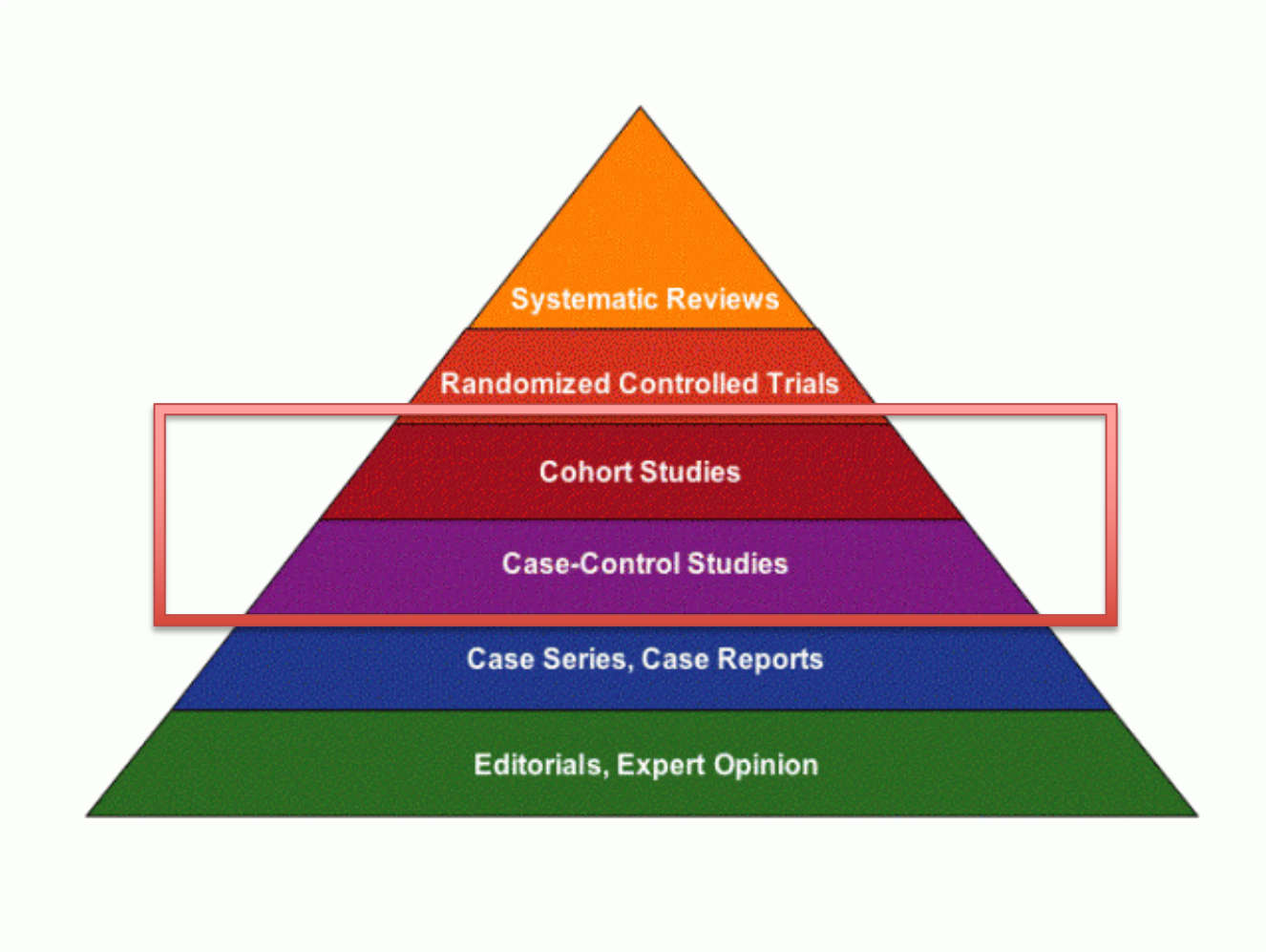
Why should I bother?



Why ‘real world’ evidence?
1.When RCTs are not possible …

Hazard

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

BMJ 2003

Gordon C S Smith, Jill P Pell

What this study adds

No randomised controlled trials of parachute use have been undertaken

The basis for parachute use is purely observational, and its apparent efficacy could potentially be explained by a “healthy cohort” effect

The medicalisation of free fall

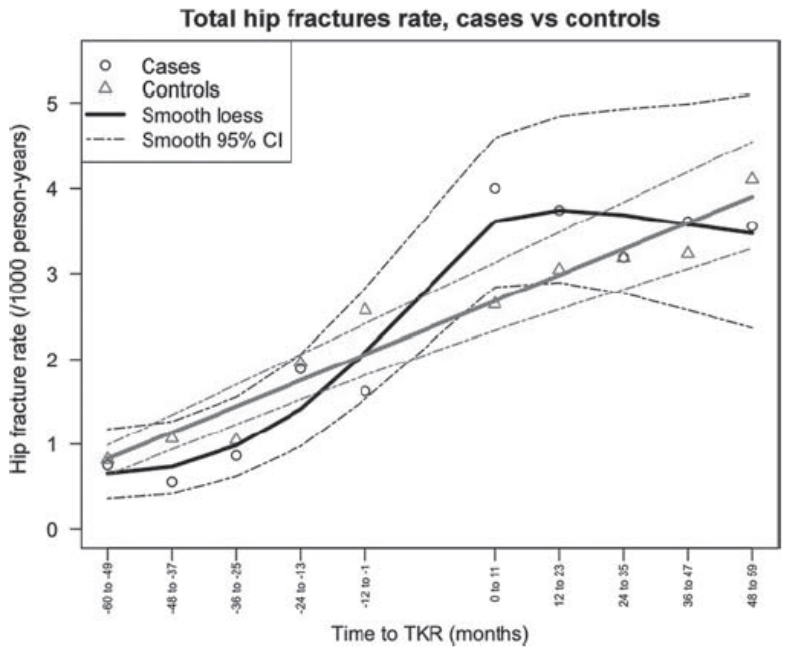
It is often said that doctors are interfering monsters obsessed with disease and power, who will not be satisfied until they control every aspect of our lives (*Journal*

 # OF RCTs = 0

Why ‘real world’ evidence?
2.The data is out there …

Changes in hip fracture rate before and after total knee replacement due to osteoarthritis: a population-based cohort study

Daniel Prieto-Alhambra,[1–3] M Kassim Javaid,[1] Joe Maskell,[1,4] Andrew Judge,[1] Michael Nevitt,[5] Cyrus Cooper,[1,4] Nigel K Arden[1,4]



- Over 20,000 TKA patients
- Over 3y median follow-up

Study completed in just under 1 year …

How long would it take you to recruit and follow-up?

Prieto-Alhambra D et al. Ann Rheum Dis 2011

Why ‘real world’ evidence?
2.The data is out there …

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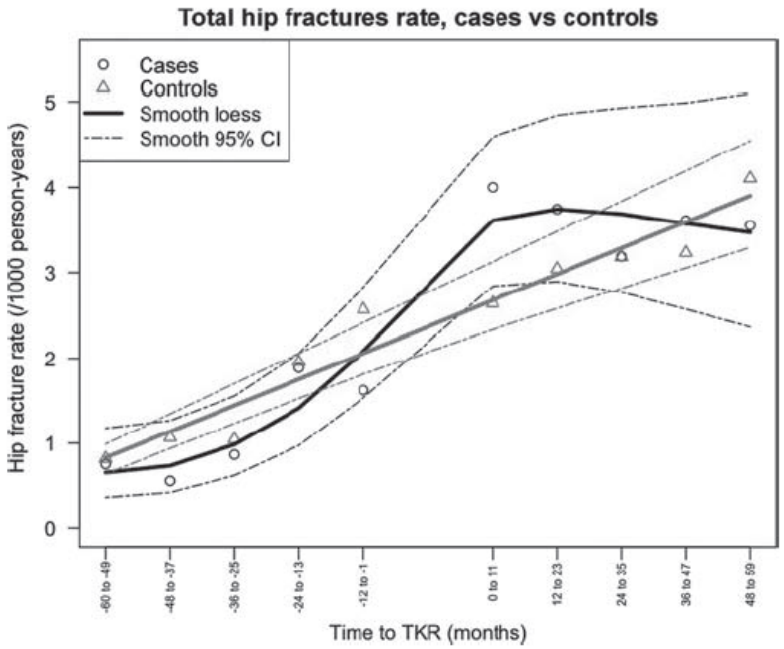
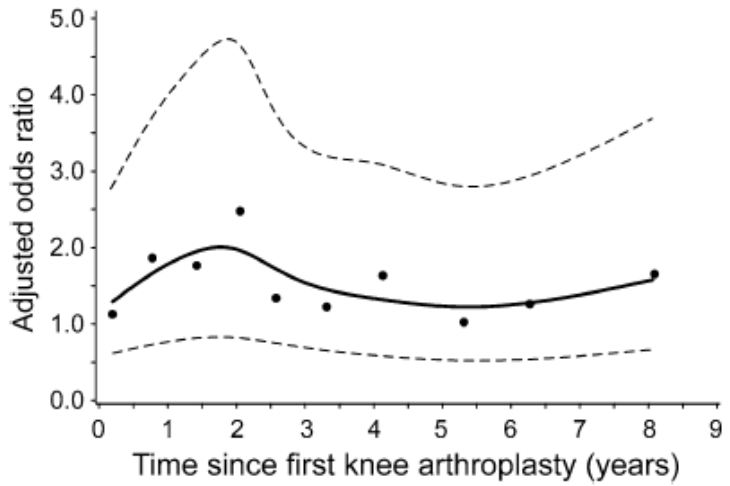


Prieto-Alhambra D et al. Ann Rheum Dis 2011

Knee Arthroplasty and Risk of Hip Fracture: A Population-Based, Case–Control Study

Arief Lalmohamed · Frans Opdam · Nigel K. Arden · Daniel Prieto-Alhambra · Tjeerd van Staa · Hubertus G. M. Leufkens · Frank de Vries



Prieto-Alhambra D et al. CTI 2012

Why ‘real world’ evidence?
3.External validity

ELIGIBILITY CRITERIA

- >70 year old
- Woman
- …

Why ‘real world’ evidence?
3.External validity

AGENDA

- Real World Evidence: Why do I bother?
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REGULATORS HAVE A POINT (OR TWO) ☺

- Lack of evidence on certain population subgroups
- Adherence and persistence in actual practice
- On vs off-label use
- Risk Minimisation Measure/s Effectiveness

None of these can be assessed in RCTs or observational studies other than using ‘real world’ (routinely collected) data

Actual Drug Users vs RCT participants

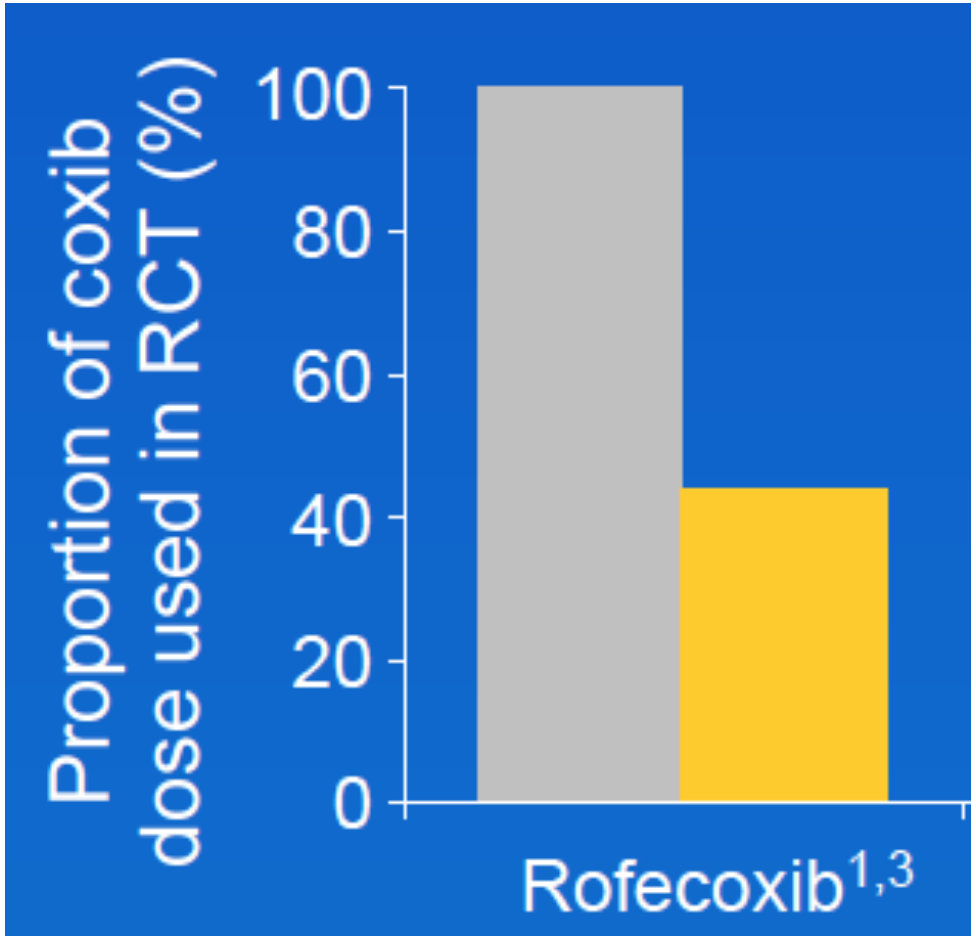
How big is the gap?

Table 1 Comparison of the exclusion criteria in the FIT trial with the incident users of alendronate in the SIDIAP and DHR database

FIT exclusion criteria[a]	Operational definition/ICD-10 Codes	Incident users of Alendronate[d]	
		SIDIAP $N = 14{,}316$ (%)	DHR $N = 21{,}214$ (%)
Men	Sex according to administrative data	3818 (26.7 %)	3885 (18.3 %)
Age <55 years old	Age at first ALD dispensation	1844 (12.9 %)	1654 (7.8 %)
Age >80 years old	Age at first ALD dispensation	2347 (16.4 %)	5275 (24.9 %)

C Reyes et al. Osteoporos Int 2014

Adherence in the real world … vs RCT



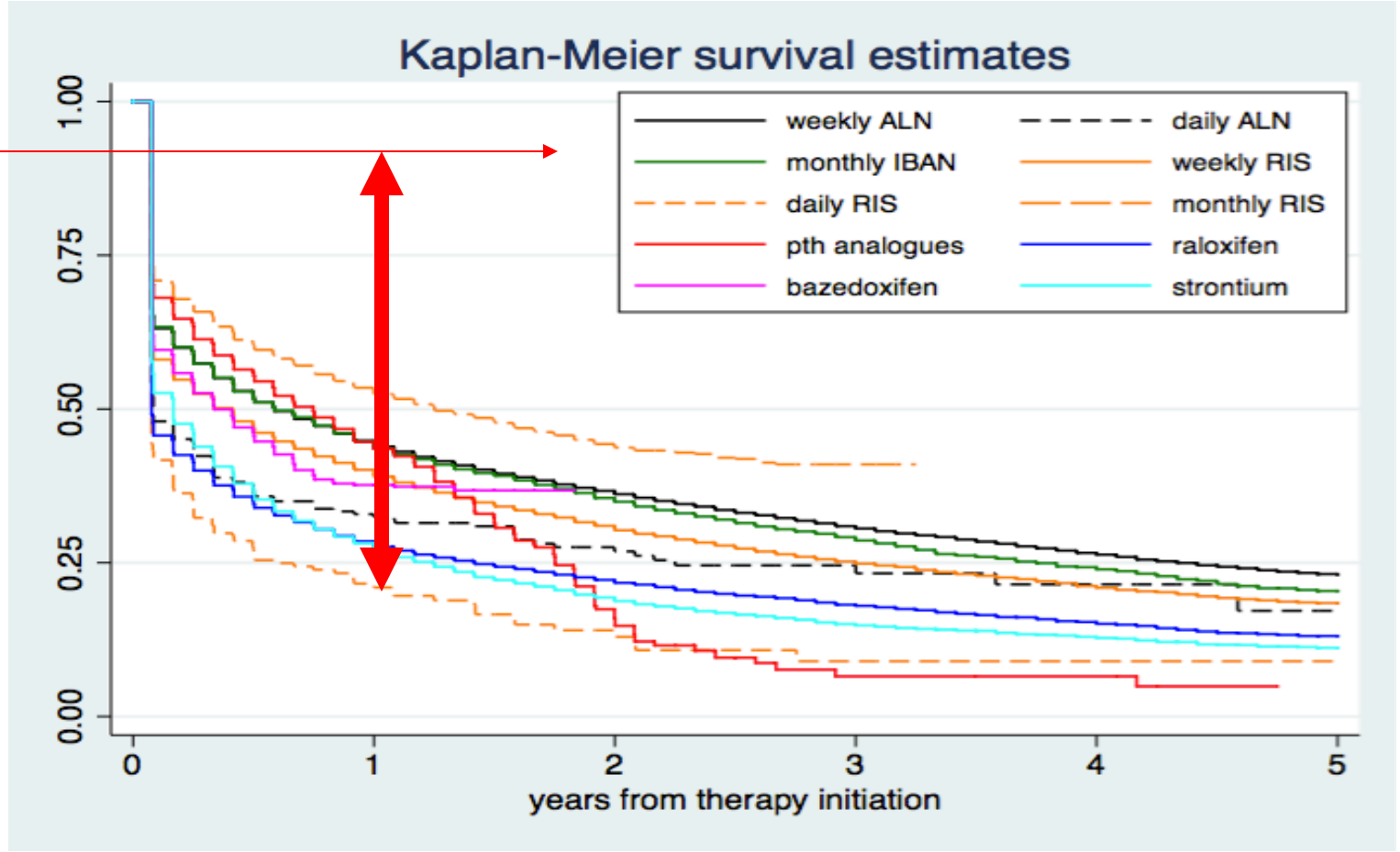
Adherence in RCT (Vigor study) vs "real life"

Rofecoxib users in CPRD

[TV Staa PLoS One '09]

Persistence in actual practice conditions …

3-year persistence
In pivotal RCTs
Was >90% for all these



N = 127,076 SIDIAP participants, Cat, Spain

Carbonell C et al. Calcif Tiss Int 2015.

AGENDA

- Real World Evidence: Why do I bother?
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- Future directions and opportunities

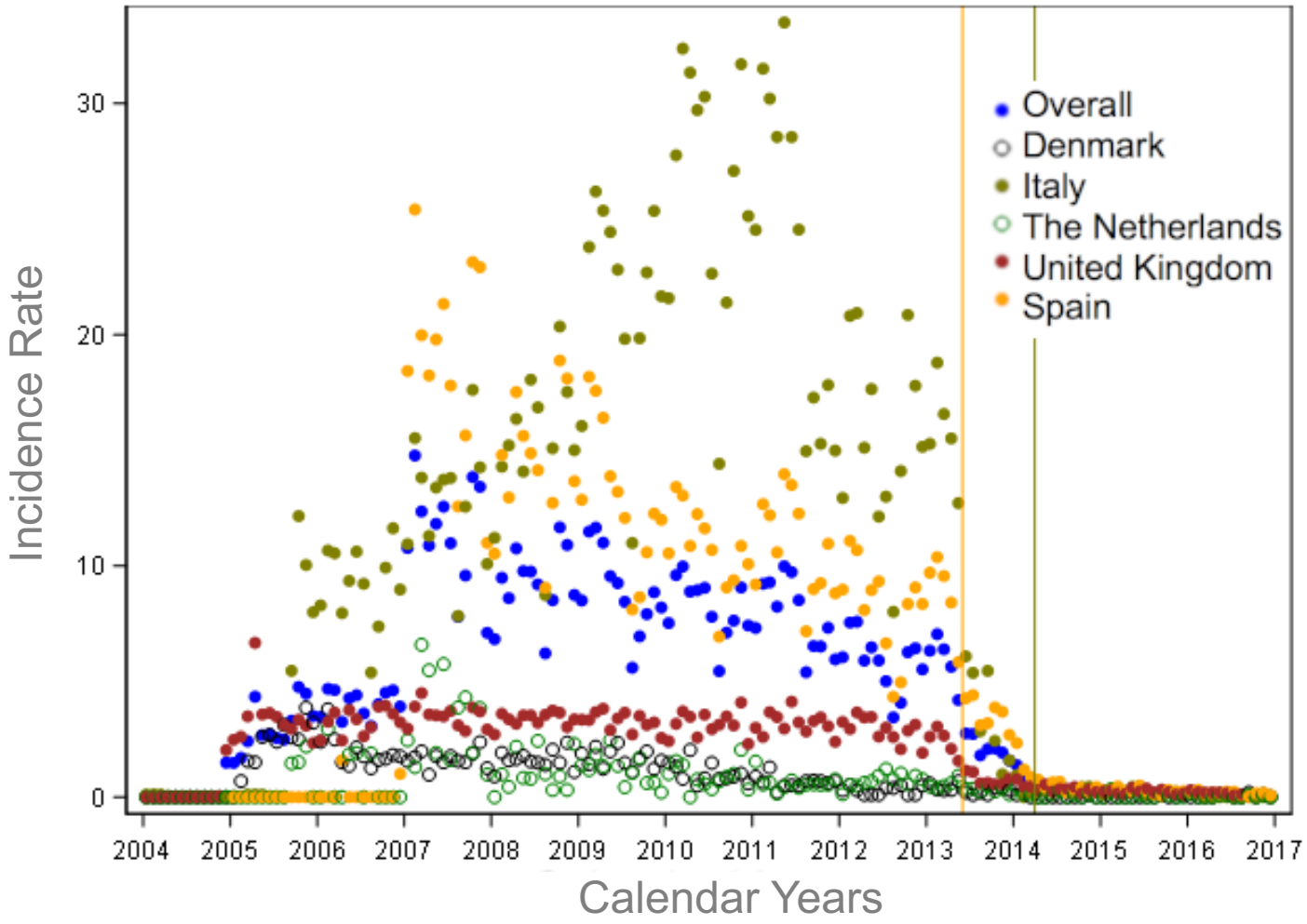
THE NEED - The European context

- Different healthcare settings
- Different funding systems
- Different conditions of use for medicines
- …

- And **hence the importance of EU-wide DUS for the EMA**

A previous example – EU-ADR Alliance Multi-country Population Level DUS

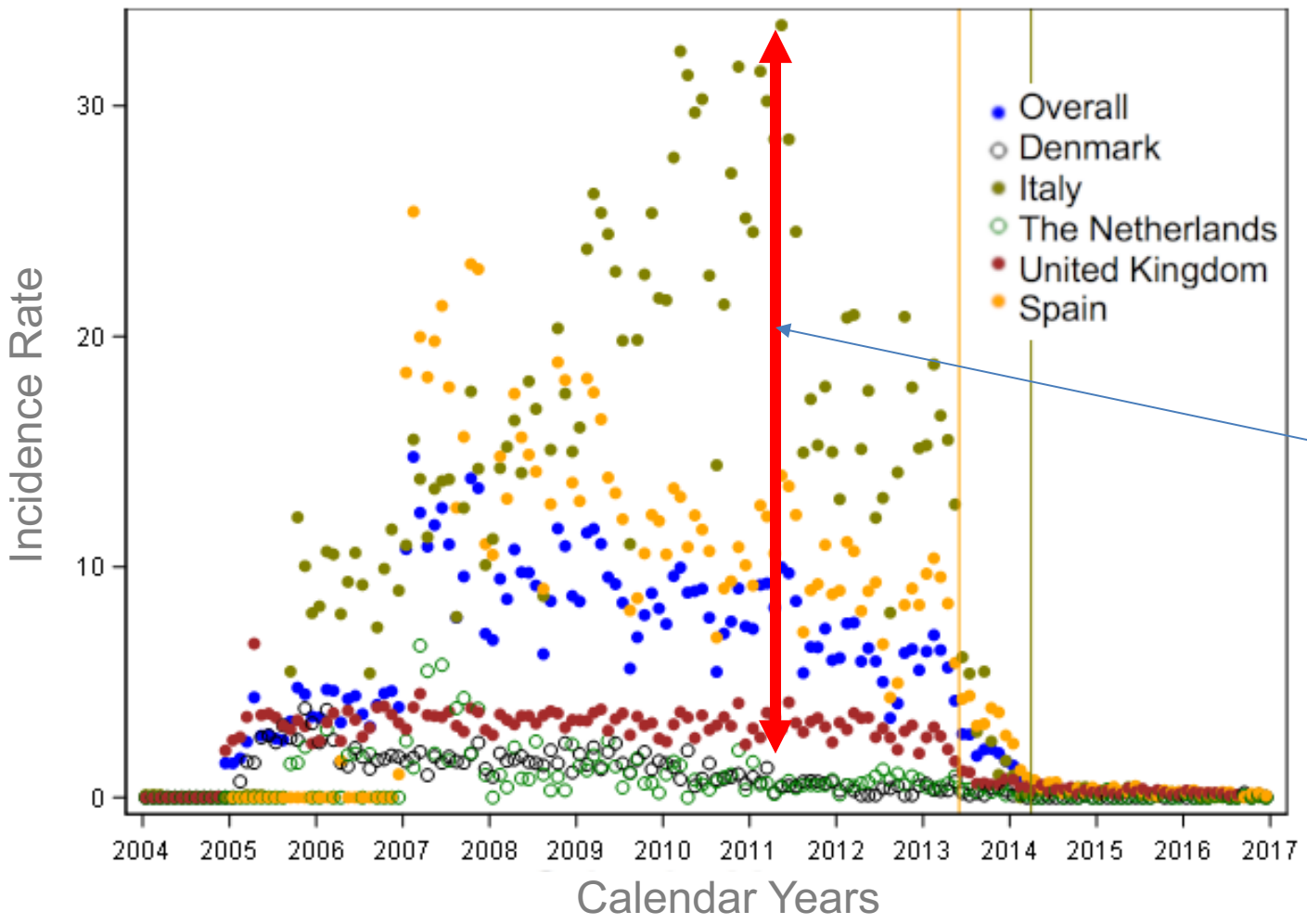
Monthly incidence rates (10,000 PY) of use



K Berencsi et al. ICPE 2018

A previous example – EU-ADR Alliance Multi-country Population Level DUS

Monthly incidence rates (10,000 PY) of use

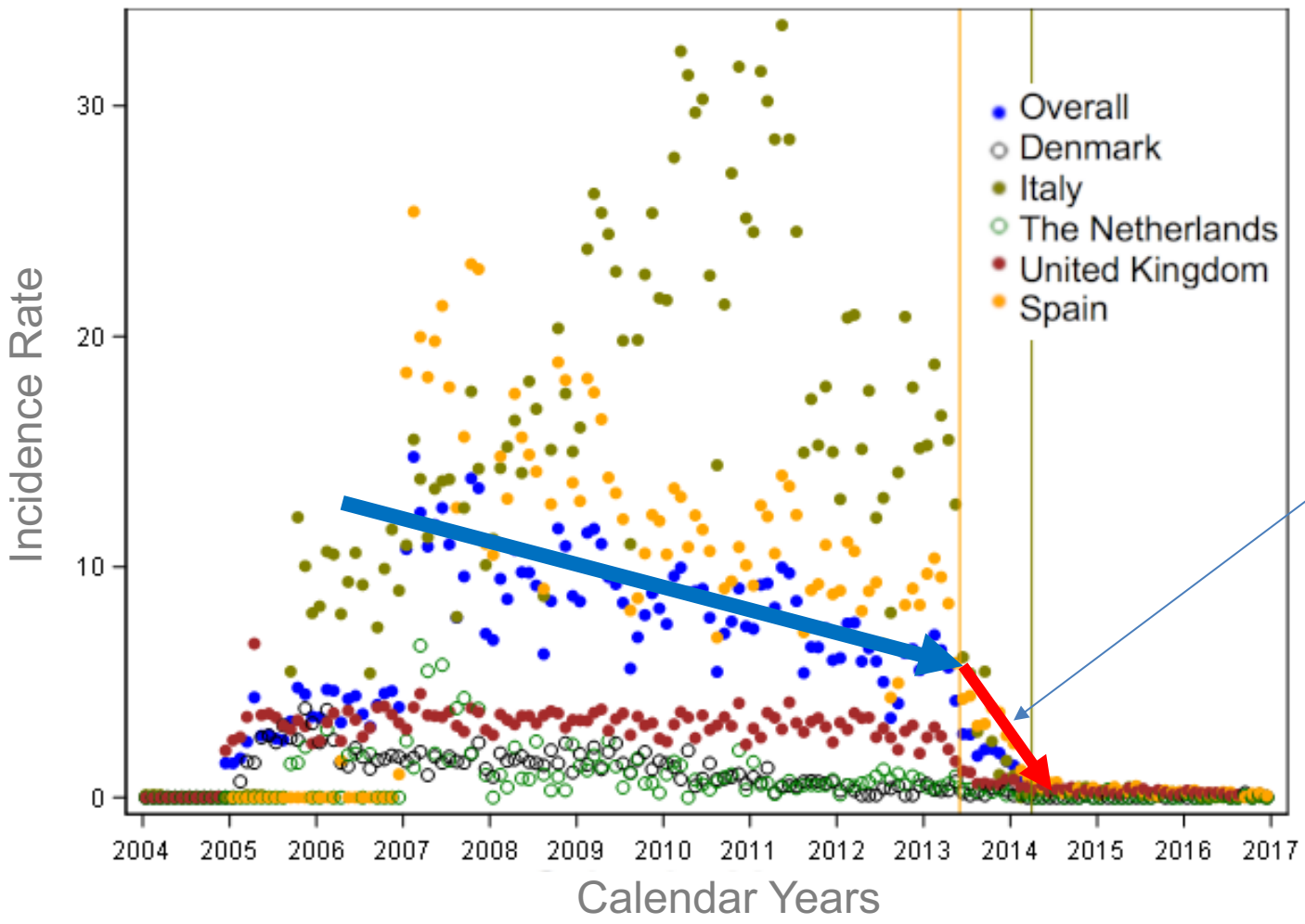


Between-country differences

K Berencsi et al. ICPE 2018

A previous example – EU-ADR Alliance Multi-country Population Level DUS

Monthly incidence rates (10,000 PY) of use



RMM Effectiveness

K Berencsi et al. ICPE 2018

AGENDA

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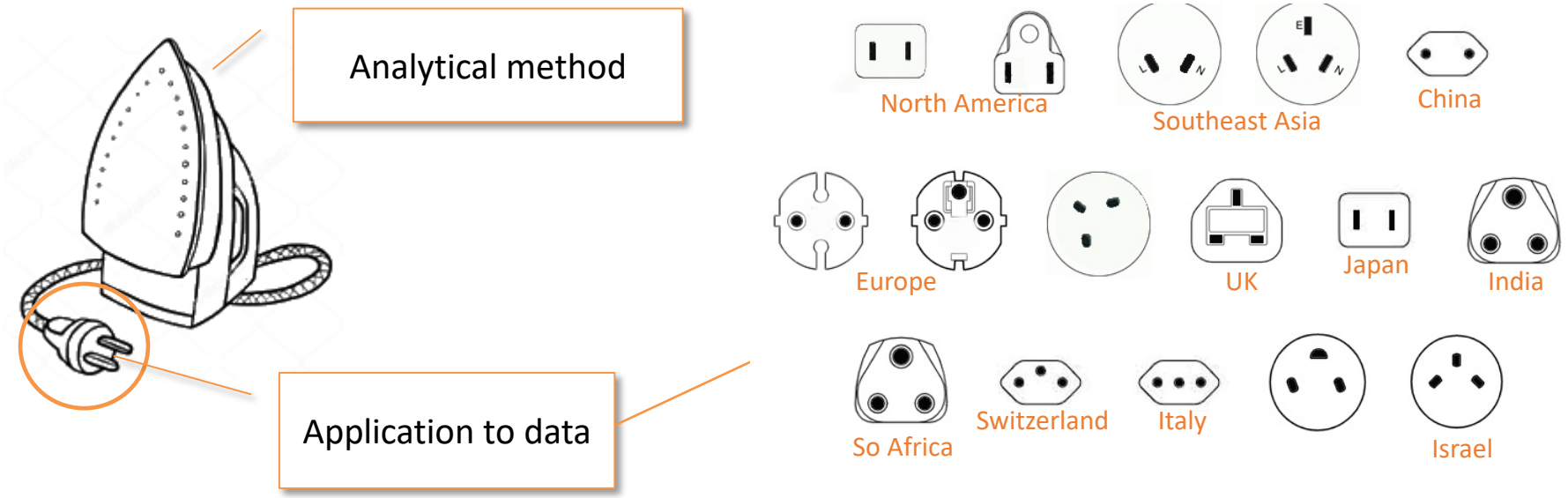


The EU DUS challenge

Interoperability

What can (and should) be improved?

- Automation of common processes
  - Data curation, analyses
- Speed -> from 1-2 years to 1-2 days
- Reproducibility
- More complex analytics
- Visualisation/s

EHDEN Use case 1 - DUS

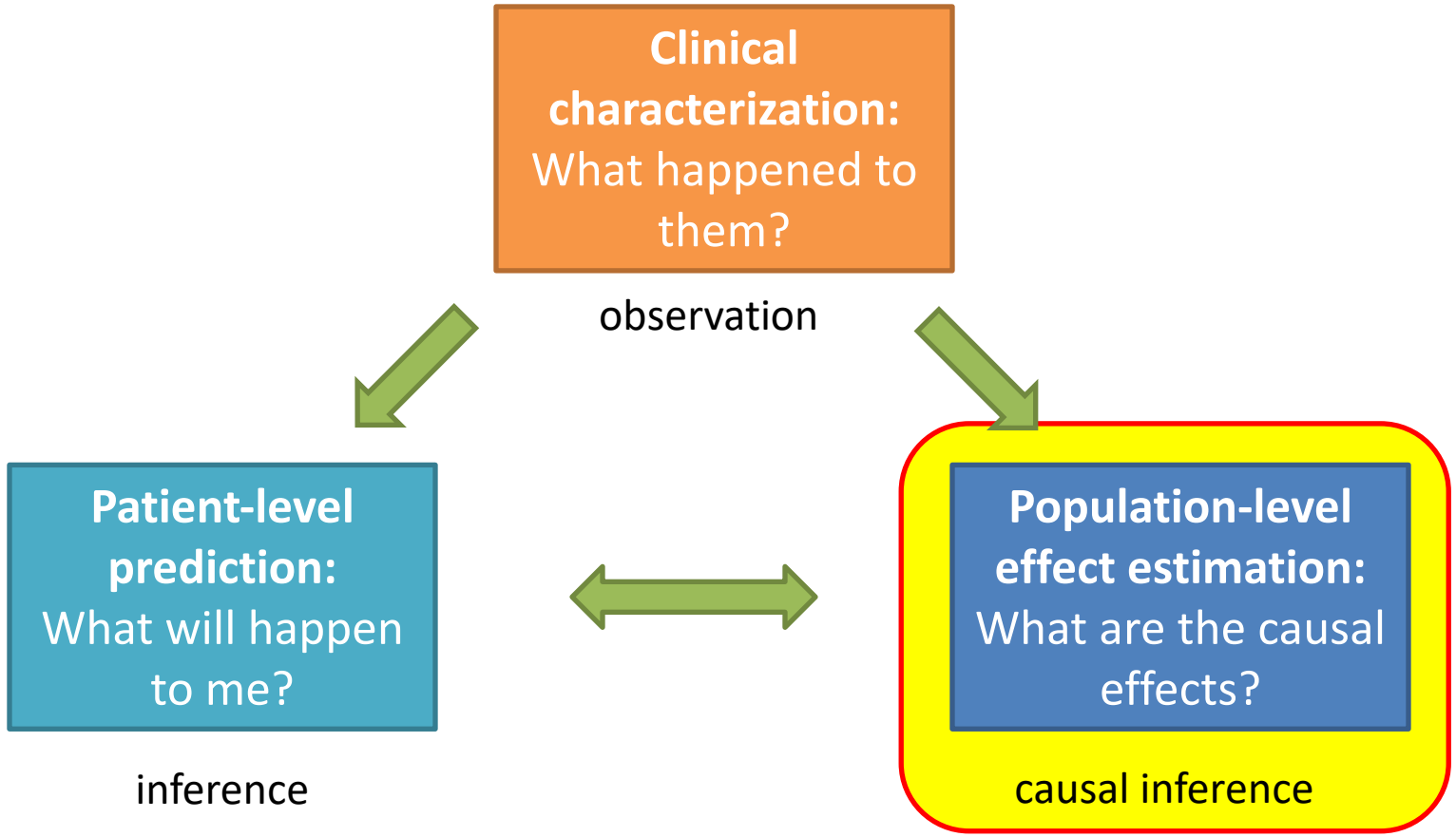
	UC1 – DUS
ANALYSES/ TOOLS	- Population level (incidence, prevalence) - Patient level (adherence, % with contra/indications) - Treatment pathways - Dose / Indication: NLP - Secular trends (RMM)
DASHBOARD/S VISUALISATION	- Sunburst / Sankey plots - Interactive filters/zoom - Subgroup stratification - Patterns over time

What evidence do we want to generate?

Pharmacovigilance

Niklas Norén
Chief Science Officer
Uppsala Monitoring Centre

Complementary evidence to inform the patient journey



On the **lookout** for the **un**expected

Broad scope

Generic analysis strategies

Humility

Individual case reports

Report of Suspected Adverse Drug Reaction including Birth Defects 224289

(**Note:** Identities of Reporter, Patient and Institution will remain **Confidential**)

Patient (Initials or Record only)	Age	Sex	Weight	Height
[redacted] 05 DEC 2006	55	M	80	168

Adverse Reaction Description: DESC Date of Onset of Reaction: 29/11/06

PATIENT WITH A NON ST ELEVATION MI HAD DIAGNOSTIC ANGIOGRAM SHOWING SEVERE STENOSIS IN LAD. THE SAME DAY HAD PCI TO LAD DURING WHICH EXPERIENCED PROFOUND AND SUSTAINED HYPOTENSION NOT RELIEVED WITH ANAMINE 6mg (SEVERAL 0.5mg SOLUSES) AND IABP. IMPROVED AFTER HYDROCORTISONE 200mg + PHENERGAN GIVEN. ??ALERGIC REACTION TO CONTRAST (ISOVUE 370)

All Drug Therapy Prior to Reaction Asterisk Suspected Drug(s) (please use trade names)	Daily Dosage and Route	Date Begun	Date Stopped	Reason for Use
ASPIRIN	300mg O	29/11/06	—	NSTEMI
CLOPIDOGREL	300mg LOADING DOSE	29/11/06	—	NSTEMI
TEMAZEPAM	10mg	29/11/06		SEDATION
TIROFIBAN	IV BOLUS + INFUSION	29/11/06	29/11/06	NSTEMI
MIDAZOLAM	2mg IV	29/11/06	29/11/06	SEDATION
OMNIPAQUE	90 ml IC	29/11/06	29/11/06	} ANGIOGRAM
ISOVUE 370		29/11/06	29/11/06	} ANGIOPLASTY

Treatment (of reaction): ANAMINE, HYDROCORTISONE PHENERGAN

Outcome: Recovered ☒ Not Yet Recovered ☐ Unknown ☐ Fatal ☐ Date of Death / /

Sequelae: No ☒ Yes ☐ (describe) MYOCARDIAL INFARCTION

Comments (eg. relevant history, allergies, previous exposure to this drug):

NO KNOWN ALLERGIES before the episode. HAD ANGIOGRAM IN another hospital. then PCI SAME DAY. REACTION DURING PCI

POSS

Reporting Doctor, Pharmacist, etc:

Name: [redacted]

Address: [redacted]

Signature [redacted] 30/11/06

Headache	62%
Fatigue	56%
Dizziness	53%
Nausea	41%
Arthralgia	31%
Syncope	22%
Pain	22%
Asthenia	22%
Dyspnoea	21%
Malaise	21%

585 reports 14.6 AE per report

Dizziness	30%
Vomiting	20%
Pain	13%
Myalgia	11%
Fatigue	10%
Malaise	9%
Abdominal pain	8%

9938 reports 3.8 AE per report

Pain in extremity	10%
Hypoaesthesia	9%
Paraesthesia	8%
Oedema peripheral	8%
Pain	7%
Arthralgia	6%

7088 reports 4.3 AE per report

Expected local reactions

Injection site pain	75%
Injection site swelling	53%
Injection site erythema	40%
Injection site pruritis	13%
Asthenia	12%
Pain	9%
Injection site warmth	9%
Headache	8%
Pyrexia	8%
Muscular weakness	7%

4959 reports 3.1 AE per report

Vasovagal reactions

Syncope	46%
Dizziness	28%
Loss of consciousness	28%
Pallor	24%
Seizure	17%
Fall	15%
Immediate post injection reaction	12%
Nausea	9%
Presyncope	8%
Hyperhidrosis	8%

6517 reports 4.1 AE per report

Clusters of interest

694 cases

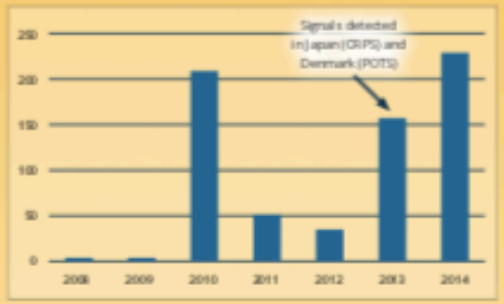
62% serious

Postural orthostatic tachycardia syndrome:	64 reports
Chronic fatigue syndrome:	30 reports
Post viral fatigue syndrome:	18 reports
Complex regional pain syndrome:	12 reports

Please note that one case report may include two or more of these terms

85% of cases without one of these diagnoses

VigiBase entry over time



The large total in 2010 reflects the entry into VigiBase of a backlog of reports from the USA

The map below displays the countries of origin and their totals of cases which are included in the cluster of interest

Headache	75%
Nausea	63%
Dizziness	50%
Fatigue	50%
Arthralgia	38%
Pain in extremity	38%
Palpitations	38%
Disturbance in attention	38%
Quality of life decreased	25%

8 reports 1.5 AE per report

Fatigue	100%
Dizziness	92%
Headache	88%
Nausea	80%
Arthralgia	71%
Myalgia	69%
Disturbance in attention	67%
Memory impairment	63%
Muscular weakness	59%
Pain	59%

83 reports 41.7 AE per report

Vaccination exposure during pregnancy

Exposure during pregnancy	90%
Pregnancy test positive	19%
Abortion spontaneous	18%
Human chorionic gonadotropin positive	18%
Caesarean section	11%
Abortion induced	10%
Ultrasound scan normal	9%
Foetal disorder	9%

Medication errors

No adverse event	89%
Inappropriate schedule of drug administration	48%

Dizziness	61%
Headache	61%
Syncope	56%
Postural orthostatic tachycardia syndrome	39%
Tremor	33%
Heart rate increased	33%
Electroencephalogram normal	33%
Fatigue	33%
Blood test normal	33%

Lack of effectiveness

Smear cervix abnormal	44%
Human papilloma virus test positive	38%
Cervical dysplasia	38%
Papilloma viral infection	31%
Anogenital warts	13%
Vaccination failure	13%
Smear cervix	7%
Biopsy cervix abnormal	6%
Cervix carcinoma stage 0	6%
Colposcopy abnormal	5%

660 reports 3.3 AE per report

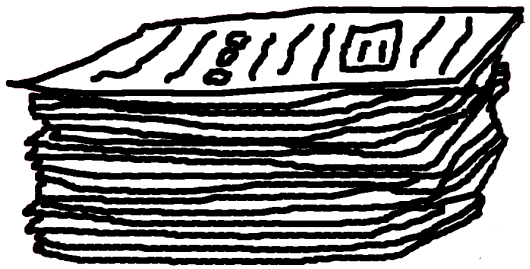
By the millions

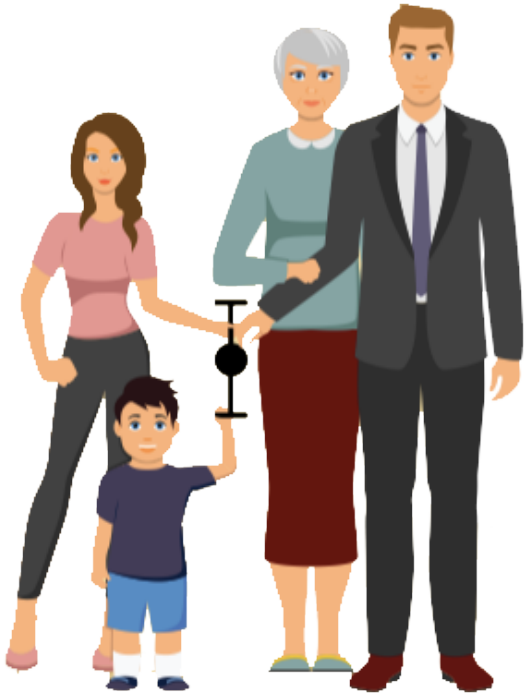

Hard to spot


Hard to assess

Whose risk?

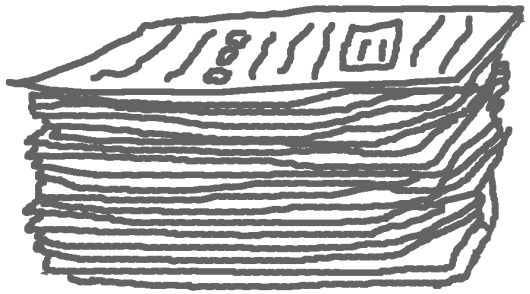
228



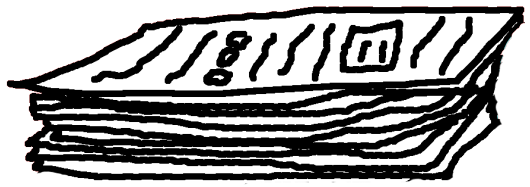


vs

267



67



VS

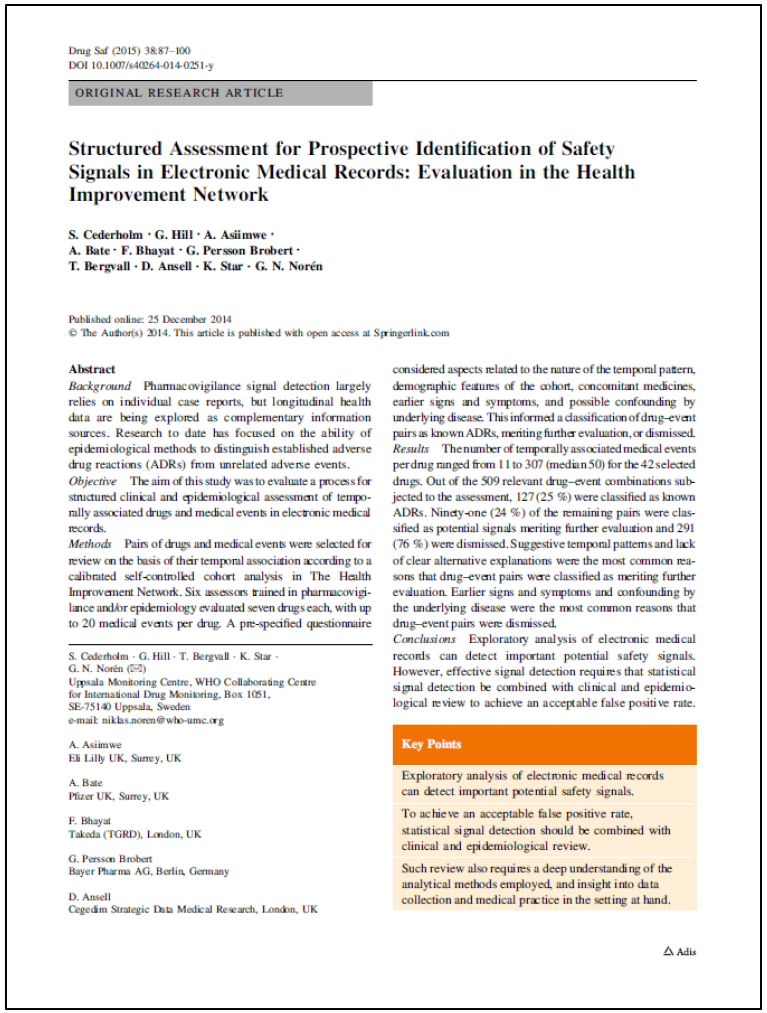
39

Observational health data

\+ Denominators
Longitudinal

\- Secondary use
No causality assessment

Signal detection in electronic health records



Drug Saf (2015) 38:87–100
DOI 10.1007/s40264-014-0251-y

ORIGINAL RESEARCH ARTICLE

Structured Assessment for Prospective Identification of Safety Signals in Electronic Medical Records: Evaluation in the Health Improvement Network

S. Cederholm · G. Hill · A. Asiimwe · A. Bate · F. Bhayat · G. Persson Brobert · T. Bergvall · D. Ansell · K. Star · G. N. Norén

Published online: 25 December 2014

Abstract

Background Pharmacovigilance signal detection largely relies on individual case reports, but longitudinal health data are being explored as complementary information sources. Research to date has focused on the ability of epidemiological methods to distinguish established adverse drug reactions (ADRs) from unrelated adverse events.

Objective The aim of this study was to evaluate a process for structured clinical and epidemiological assessment of temporally associated drugs and medical events in electronic medical records.

Methods Pairs of drugs and medical events were selected for review on the basis of their temporal association according to a calibrated self-controlled cohort analysis in The Health Improvement Network. Six assessors trained in pharmacovigilance and/or epidemiology evaluated seven drugs each, with up to 20 medical events per drug. A pre-specified questionnaire considered aspects related to the nature of the temporal pattern, demographic features of the cohort, concomitant medicines, earlier signs and symptoms, and possible confounding by underlying disease. This informed a classification of drug–event pairs as known ADRs, meriting further evaluation, or dismissed.

Results The number of temporally associated medical events per drug ranged from 11 to 307 (median 50) for the 42 selected drugs. Out of the 509 relevant drug–event combinations subjected to the assessment, 127 (25 %) were classified as known ADRs. Ninety-one (24 %) of the remaining pairs were classified as potential signals meriting further evaluation and 291 (76 %) were dismissed. Suggestive temporal patterns and lack of clear alternative explanations were the most common reasons that drug–event pairs were classified as meriting further evaluation. Earlier signs and symptoms and confounding by the underlying disease were the most common reasons that drug–event pairs were dismissed.

Conclusions Exploratory analysis of electronic medical records can detect important potential safety signals. However, effective signal detection requires that statistical signal detection be combined with clinical and epidemiological review to achieve an acceptable false positive rate.

Key Points

Exploratory analysis of electronic medical records can detect important potential safety signals.

To achieve an acceptable false positive rate, statistical signal detection should be combined with clinical and epidemiological review.

Such review also requires a deep understanding of the analytical methods employed, and insight into data collection and medical practice in the setting at hand.

S. Cederholm · G. Hill · T. Bergvall · K. Star · G. N. Norén (✉)
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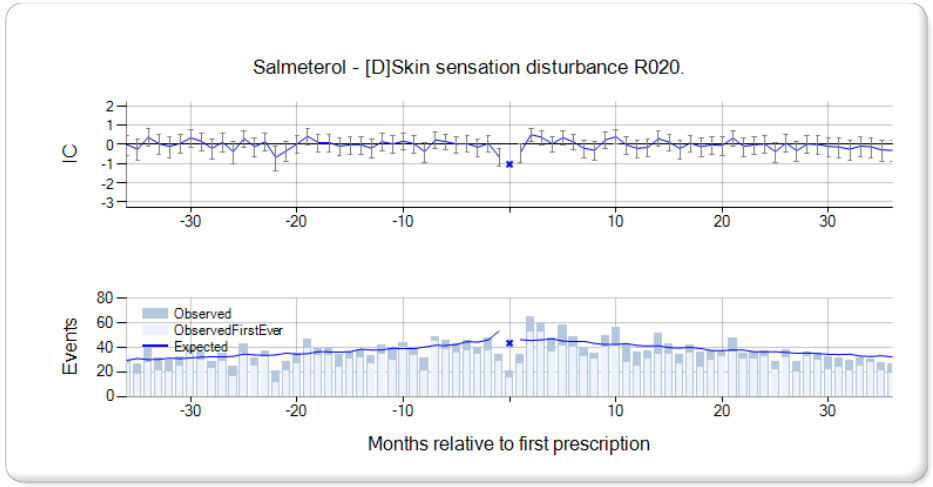
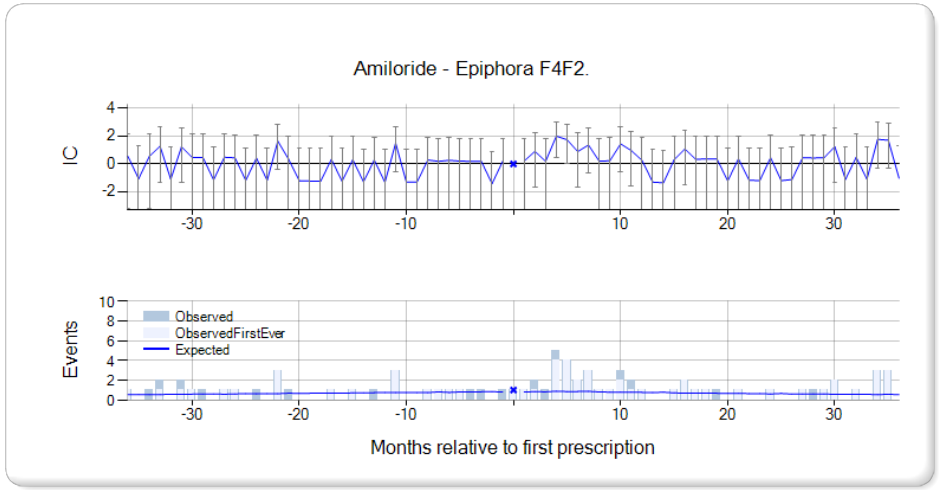
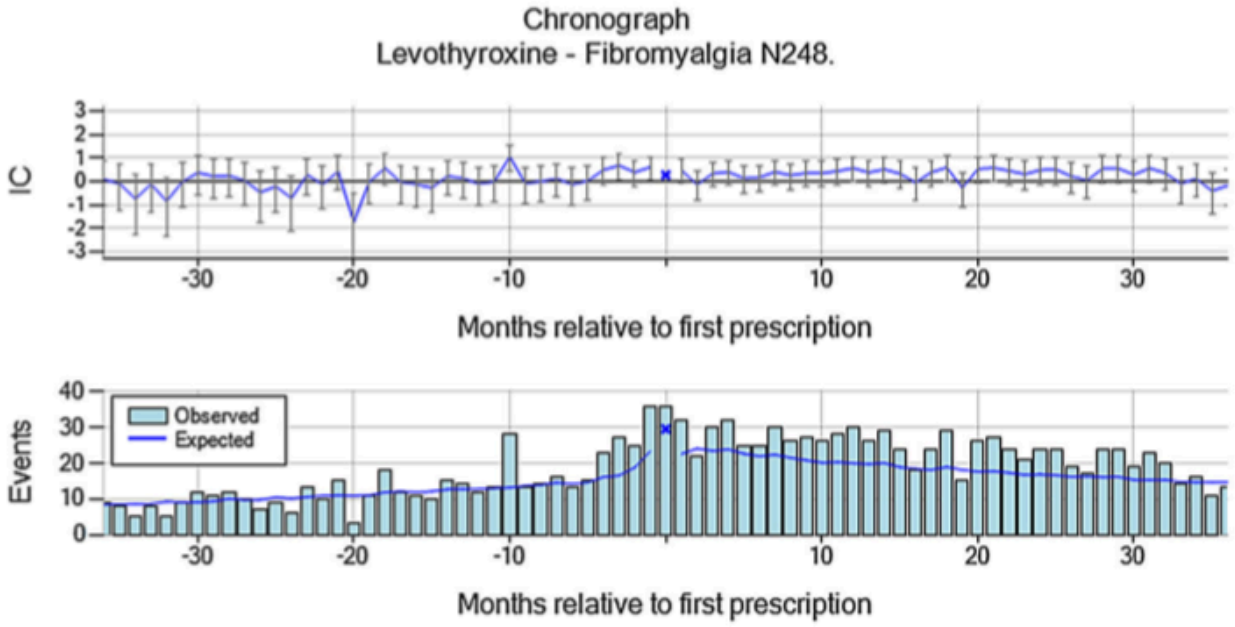




Signal strengthening in electronic health records



PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2015; **24**: 486–494
Published online 27 January 2015 in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.3739

ORIGINAL REPORT

Longitudinal medical records as a complement to routine drug safety signal analysis†

Kristina Star*, Sarah Watson, Lovisa Sandberg, Jeanette Johansson and I. Ralph Edwards

Uppsala Monitoring Centre, WHO Collaborating Centre for International Drug Monitoring, Uppsala, Sweden

ABSTRACT

Purpose To explore whether and how longitudinal medical records could be used as a source of reference in the early phases of signal detection and analysis of novel adverse drug reactions (ADRs) in a global pharmacovigilance database.
Methods Drug and ADR combinations from the routine signal detection process of VigiBase® in 2011 were matched to combinations in The Health Improvement Network (THIN). The number and type of drugs and ADRs from the data sets were investigated. For unlabelled combinations, graphical display of longitudinal event patterns (chronographs) in THIN was inspected to determine if the pattern supported the VigiBase combination.
Results Of 458 combinations in the VigiBase data set, 190 matched to corresponding combinations in THIN (after excluding drugs with less than 100 prescriptions in THIN). Eighteen percent of the VigiBase and 9% of the matched THIN combinations referred to new drugs reported with serious reactions. Of the 112 unlabelled combinations matched to THIN, 52 chronographs were inconclusive mainly because of lack of data; 34 lacked any outstanding pattern around the time of prescription; 24 had an elevation of events in the pre-prescription period, hence weakened the suspicion of a drug relationship; two had an elevated pattern of events exclusively in the post-prescription period that, after review of individual patient histories, did not support an association.
Conclusions Longitudinal medical records were useful in understanding the clinical context around a drug and suspected ADR combination and the probability of a causal relationship. A drawback was the paucity of data for newly marketed drugs with serious reactions.

KEY WORDS—electronic medical records; temporal pattern discovery; adverse drug reactions; post-marketing surveillance; signal detection and analysis; individual case safety reports; pharmacoepidemiology

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INTRODUCTION

To evaluate the implications of suspected harm from a drug, as in safety signal analysis,[1,2] the fullest description of the clinical setting is essential. Too often, this information is incomplete in individual case safety reports (ICSRs) of suspected adverse drug reactions (ADRs).

The identification of signals in large collections of ICSRs often starts by selecting drug-ADR combinations that are reported disproportionally more frequently than expected.[3–7] Decisions need to be made whether the statistical signal should be subject to in-depth investigation and whether a signal should be communicated. Sometimes decisions in this process must be based on dubious or very limited information being available.[8] Randomized clinical trials, on which a drug's marketing approval is based, are not always publically available, and supportive published case reports might not yet exist.

Electronic medical record (EMR) databases contain clinical data—diagnoses, observations, laboratory results, treatments, and other useful information—collected longitudinally over substantial parts of a patient's life. Longitudinal data might help us understand the relative chronology of drug use and the relationships between clinical events. They present opportunities for further insight into drug safety problems and have been used primarily in confirmatory studies. Recently, several initiatives have investigated

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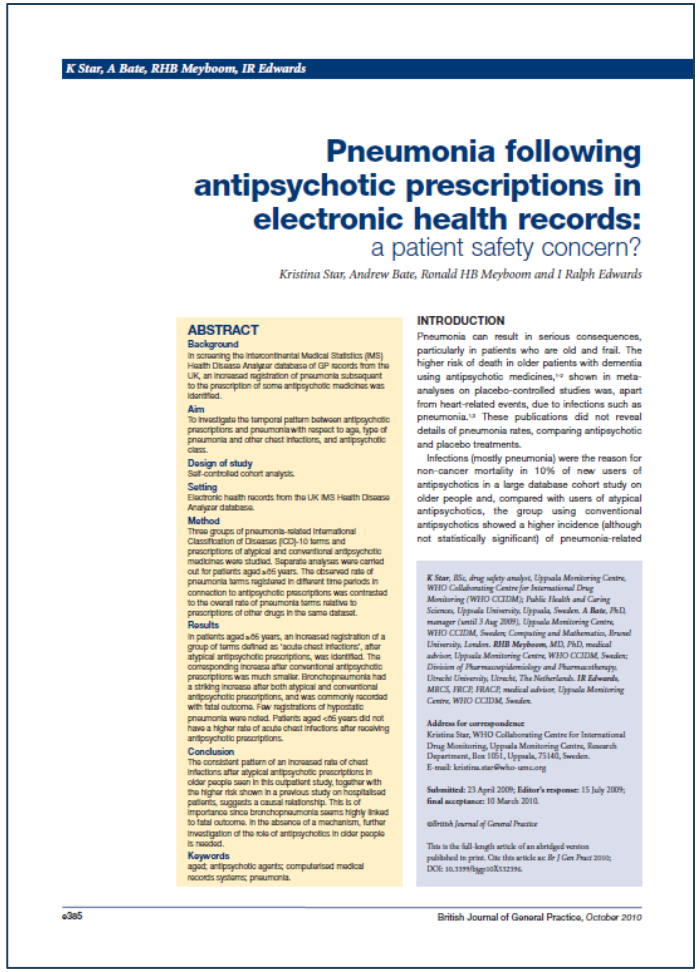
†An abstract based on parts of the content in this paper was presented at the 28th International Conference on Pharmacoepidemiology and Therapeutic Risk Management in 2012.

Risk group identification in electronic health reccords



K Star, A Bate, RHB Meyboom, IR Edwards

Pneumonia following antipsychotic prescriptions in electronic health records:
a patient safety concern?

Kristina Star, Andrew Bate, Ronald HB Meyboom and I Ralph Edwards

ABSTRACT

Background
In screening the Intercontinental Medical Statistics (IMS) Health Disease Analyzer database of GP records from the UK, an increased registration of pneumonia subsequent to the prescription of some antipsychotic medicines was identified.

Aim
To investigate the temporal pattern between antipsychotic prescriptions and pneumonia with respect to age, type of pneumonia and other chest infections, and antipsychotic class.

Design of study
Self-controlled cohort analysis.

Setting
Electronic health records from the UK IMS Health Disease Analyzer database.

Method
Three groups of pneumonia-related International Classification of Diseases (ICD)-10 terms and prescriptions of atypical and conventional antipsychotic medicines were studied. Separate analyses were carried out for patients aged ≥65 years. The observed rate of pneumonia terms registered in different time periods in connection to antipsychotic prescriptions was contrasted to the overall rate of pneumonia terms relative to prescriptions of other drugs in the same dataset.

Results
In patients aged ≥65 years, an increased registration of a group of terms defined as 'acute chest infections', after atypical antipsychotic prescriptions, was identified. The corresponding increase after conventional antipsychotic prescriptions was much smaller. Bronchopneumonia had a striking increase after both atypical and conventional antipsychotic prescriptions, and was commonly recorded with fatal outcome. Few registrations of hypostatic pneumonia were noted. Patients aged <65 years did not have a higher rate of acute chest infections after receiving antipsychotic prescriptions.

Conclusion
The consistent pattern of an increased rate of chest infections after atypical antipsychotic prescriptions in older people seen in this outpatient study, together with the higher risk shown in a previous study on hospitalised patients, suggests a causal relationship. This is of importance since bronchopneumonia seems highly linked to fatal outcome. In the absence of a mechanism, further investigation of the role of antipsychotics in older people is needed.

Keywords
aged; antipsychotic agents; computerised medical records systems; pneumonia.

INTRODUCTION

Pneumonia can result in serious consequences, particularly in patients who are old and frail. The higher risk of death in older patients with dementia using antipsychotic medicines,[1,2] shown in meta-analyses on placebo-controlled studies was, apart from heart-related events, due to infections such as pneumonia.[1,2] These publications did not reveal details of pneumonia rates, comparing antipsychotic and placebo treatments.

Infections (mostly pneumonia) were the reason for non-cancer mortality in 10% of new users of antipsychotics in a large database cohort study on older people and, compared with users of atypical antipsychotics, the group using conventional antipsychotics showed a higher incidence (although not statistically significant) of pneumonia-related

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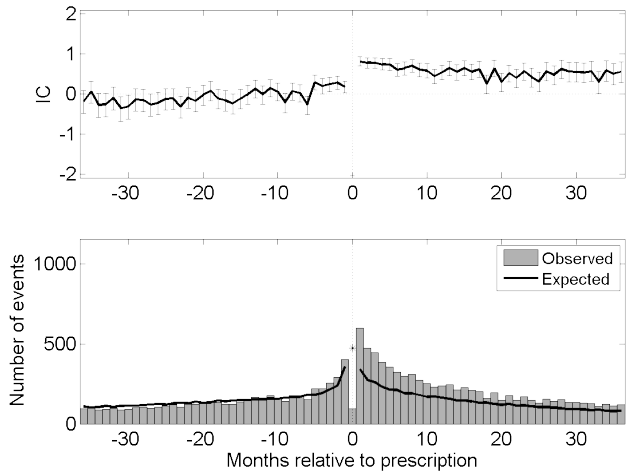
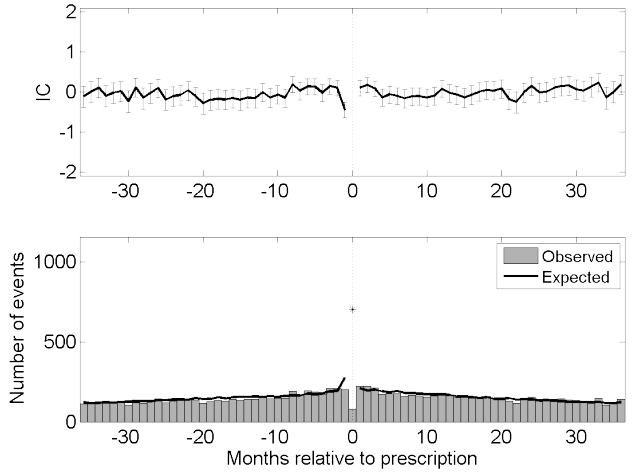




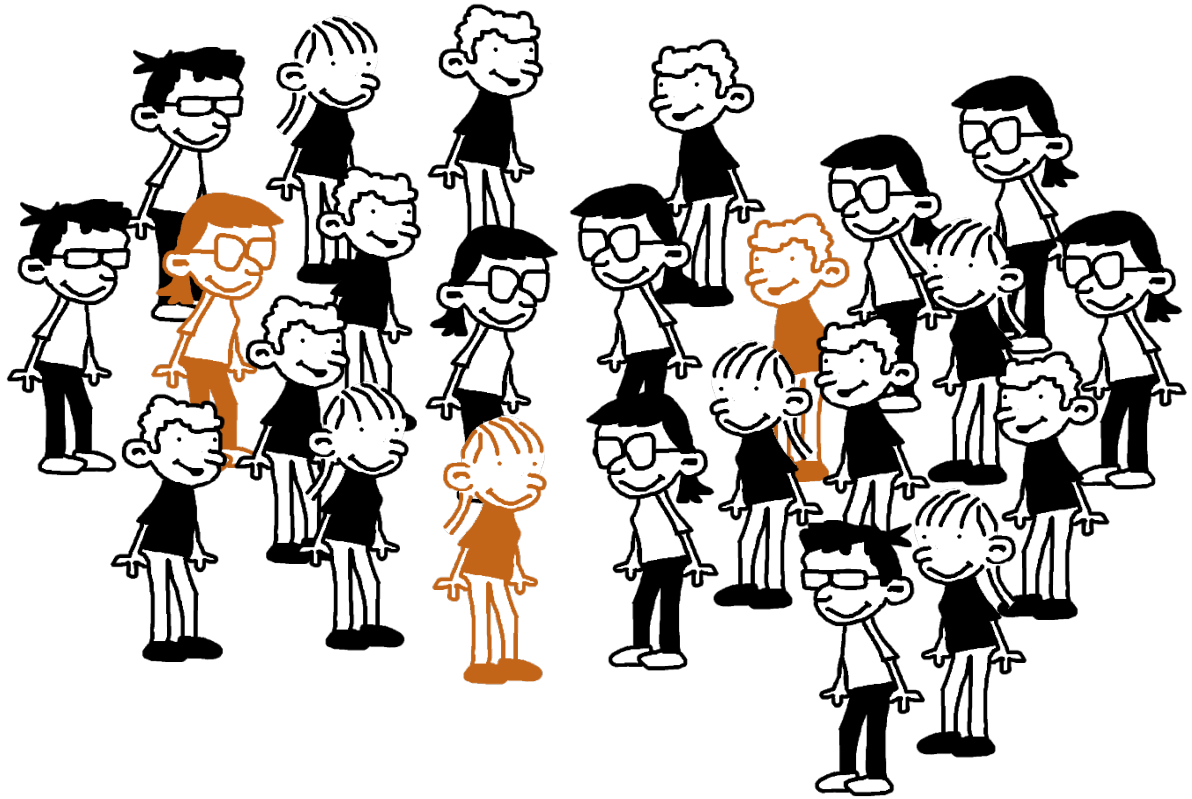
Over the counter

Primary vs secondary care

Recorded?

On the market?

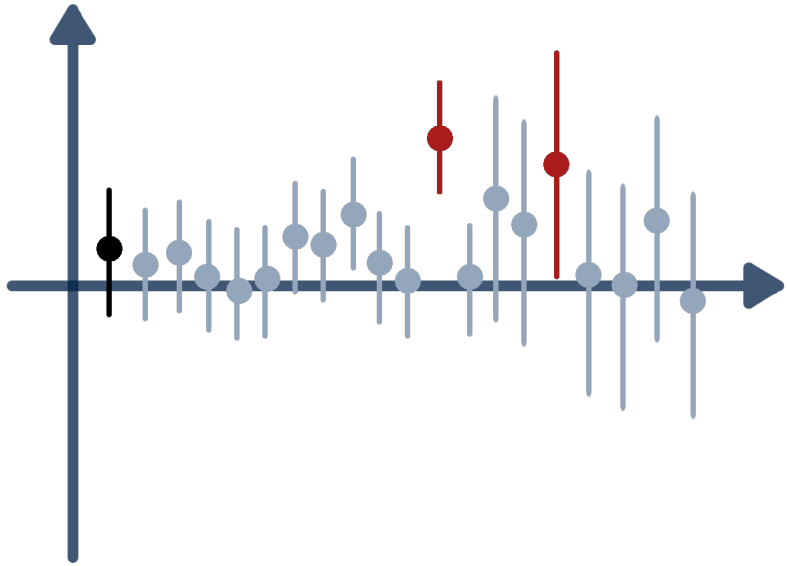
Enough data

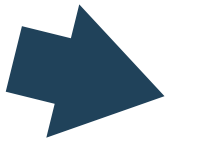


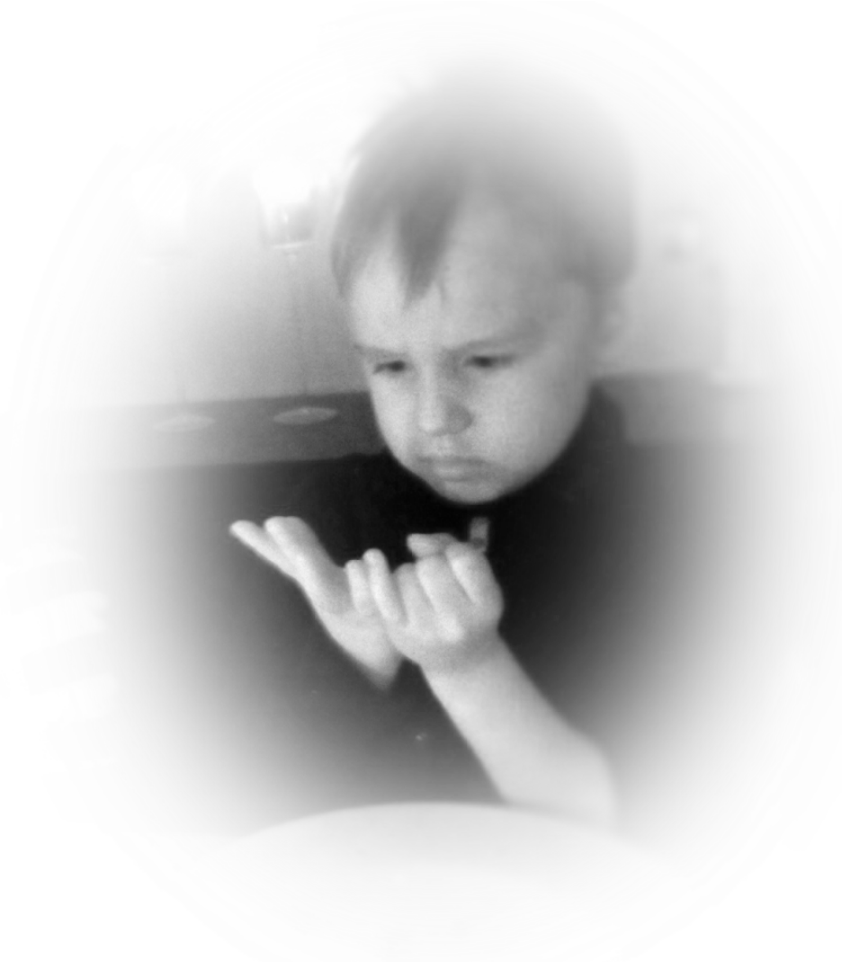
on patients

at risk

Iteration and exploration





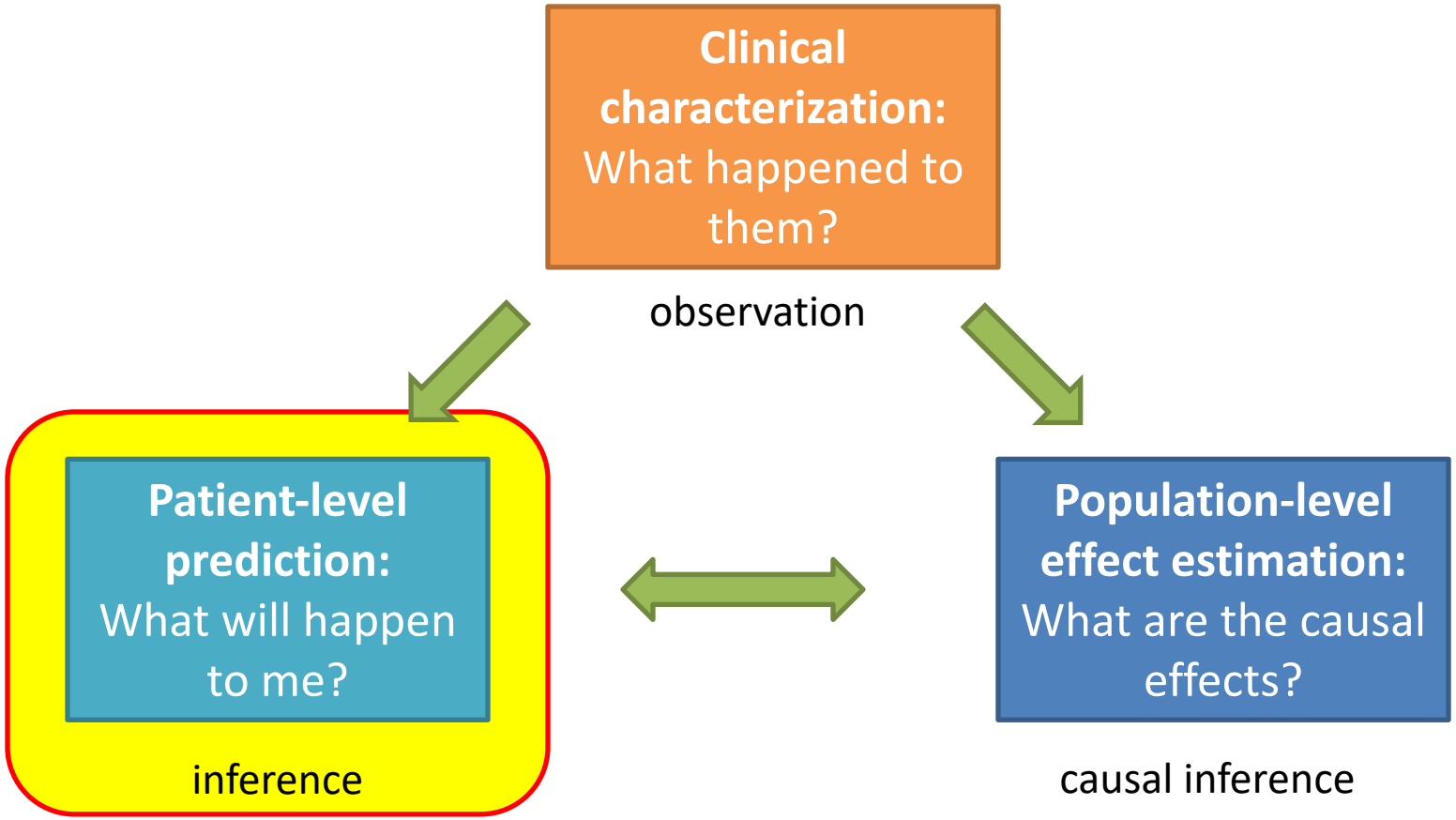


What evidence do we want to generate?

Patient-level prediction

Patrick Ryan
Janssen Research and Development
Columbia University Medical Center

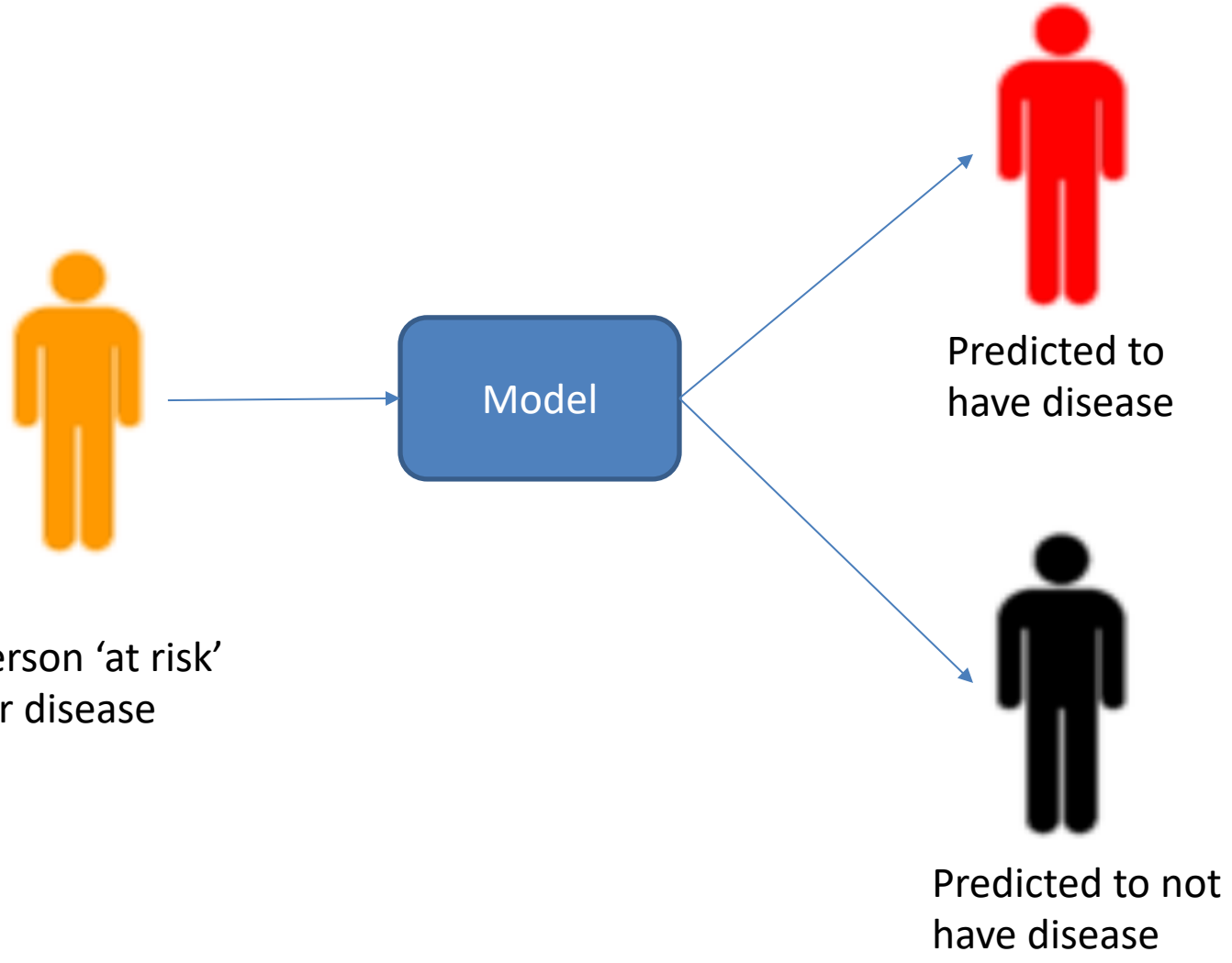
Complementary evidence to inform the patient journey



A candidate for predictive modeling?

- Fairly common disease (~80-110 cases per 100,000 person-years; lifetime risk ~5-13%)
- Serious prognosis following initial diagnosis
  - Though technical advances have greatly decreased mortality and improved quality of life
- The earlier the diagnosis, the higher likelihood of an effective treatment

Would you use this model in clinical practice?



Opportunity:

- Patients predicted to have disease who are confirmed and can obtain more timely treatment, reducing disease-related mortality

Challenges:

- Prediction is imperfect
  - 10% False positives – induces unnecessary worry and results in extra tests to refute model finding
  - 20% False negatives – provides inappropriate reassurance, potentially delaying timely treatment
- Model is not interpretable by a non-expert
- Results can be uncertain

CURRENT ONCOLOGY
A Canadian Cancer Research Journal

REVIEW ARTICLE

Screening for breast cancer in 2018—what should we be doing today?

J.M. Seely MD* and T. Alhassan MD*

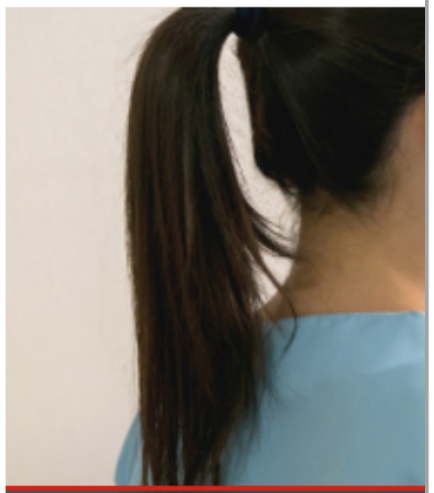
ABSTRACT

Although screening mammography has delivered many benefits since its introduction in Canada in 1988, questions about perceived harms warrant an up-to-date review. To help oncologists and physicians provide optimal patient recommendations, the literature was reviewed to find the latest guidelines for screening mammography, including benefits and perceived harms of overdiagnosis, false positives, false negatives, and technologic advances.

For women 40–74 years of age who actually participate in screening every 1–2 years, breast cancer mortality is reduced by 40%. With appropriate corrections, overdiagnosis accounts for 10% or fewer breast cancers. False positives occur in about 10% of screened women, 80% of which are resolved with additional imaging, and 10%, with breast biopsy. An important limitation of screening is the false negatives (15%–20%). The technologic advances of digital breast tomosynthesis, breast ultrasonography, and magnetic resonance imaging counter the false negatives of screening mammography, particularly in women with dense breast tissue.

Key Words Breast cancer, screening mammography, digital breast tomosynthesis, overdiagnosis

Curr Oncol. 2018 Jun;25(S1):S115-S124 www.current-oncology.com



Mammography: Wh

Learn how the FDA's prop
patients better understand

News & Events

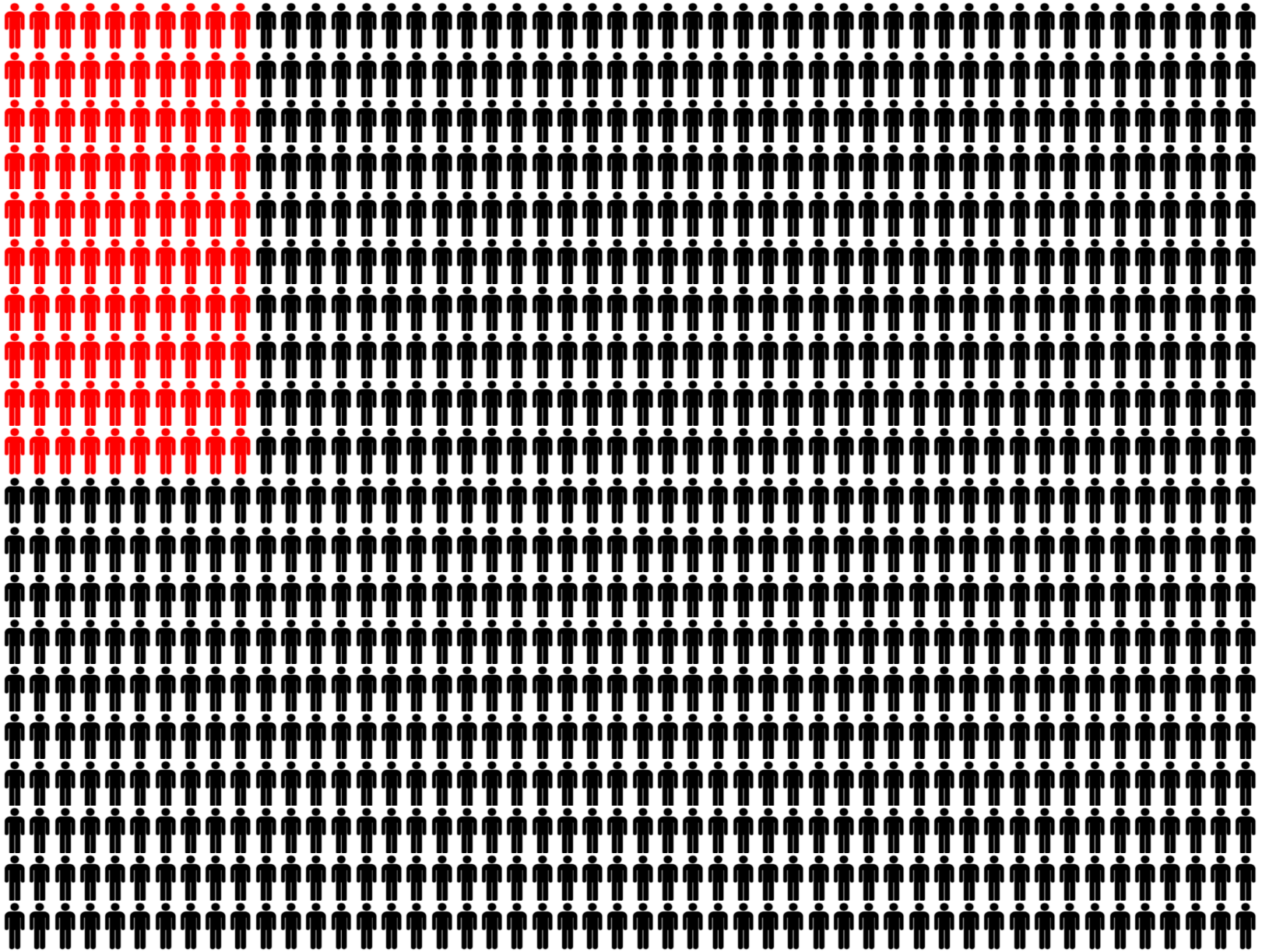
FDA News Release

FDA advances landmark policy changes to modernize mammography services and improve their quality

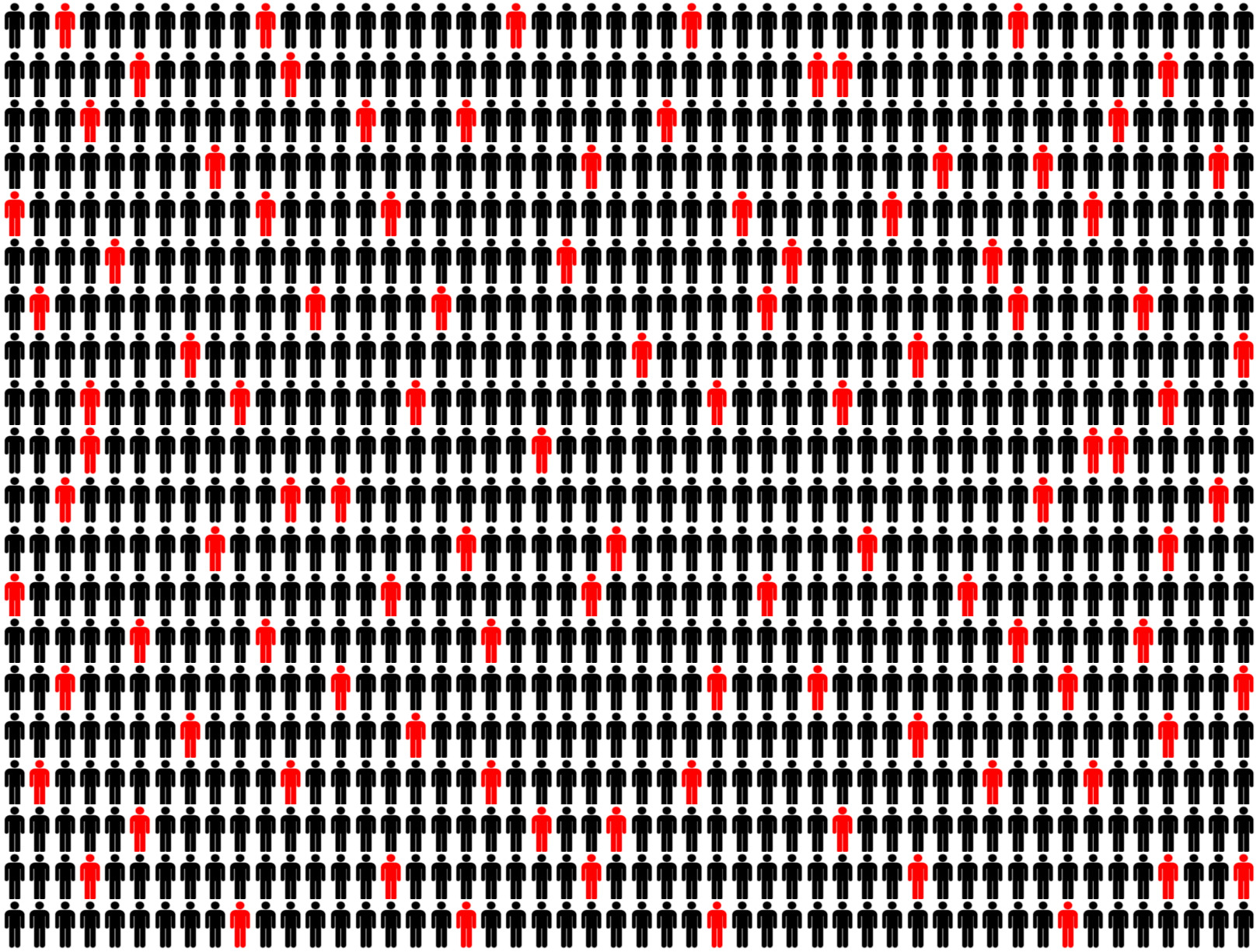
Proposed rule would require breast density reporting, enhance the FDA's ability to enforce mammography facilities' compliance with standards

For Immediate Release March 27, 2019

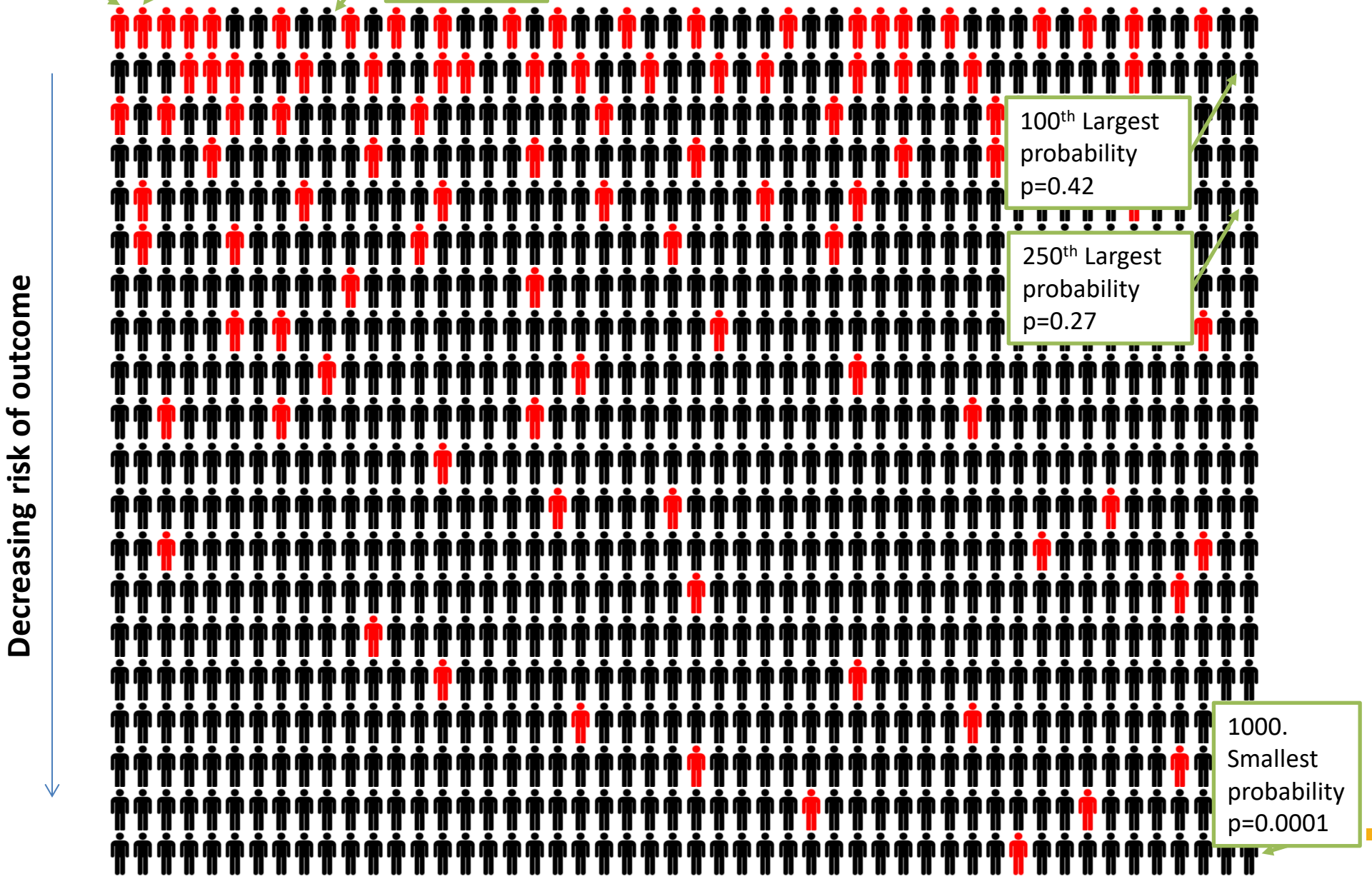
Amongst a target population of 1000 patients, 10% of the patients experience the outcome during the time-at-risk



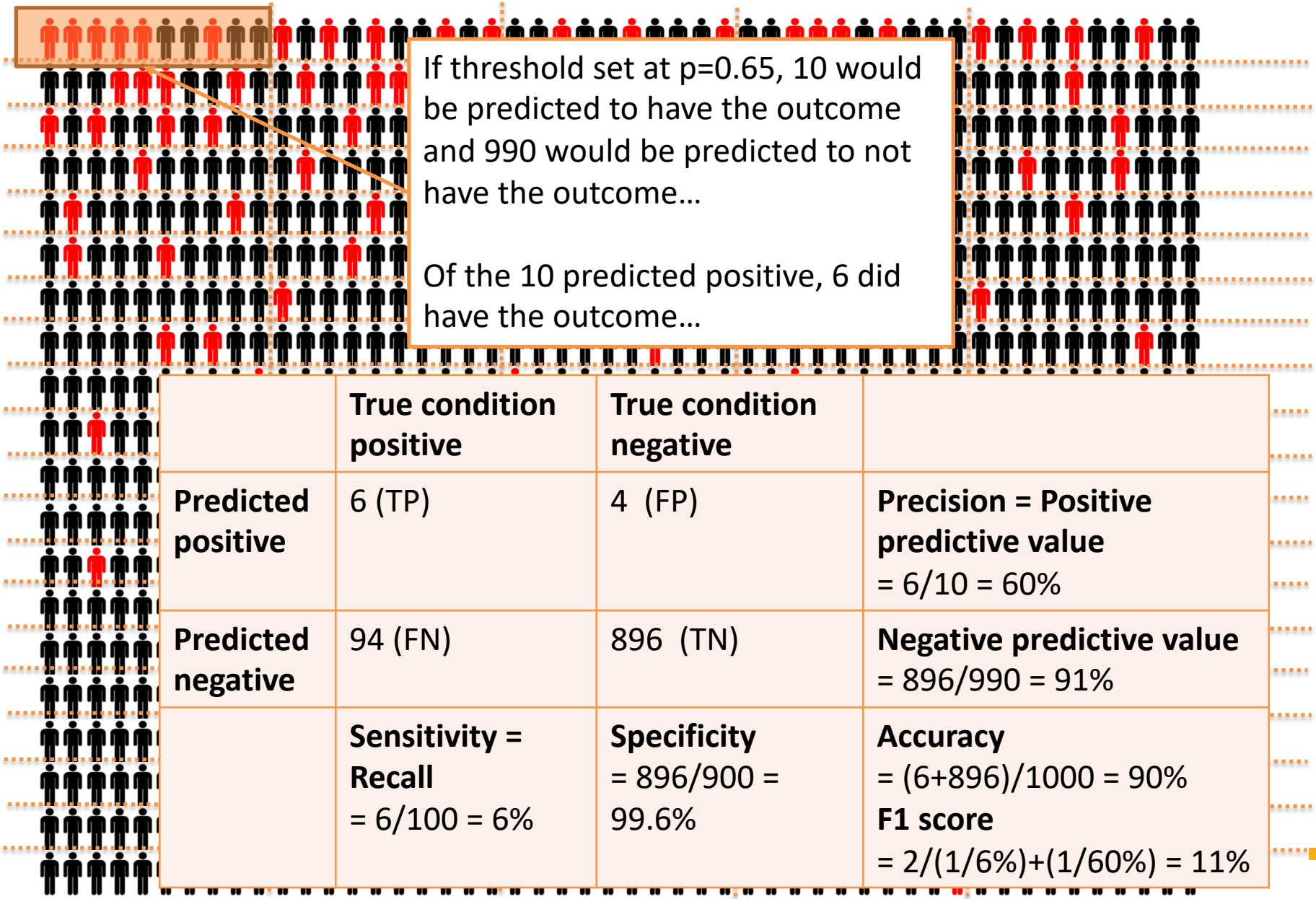
Without predictive modeling, EVERYONE has a 10% risk and outcomes are randomly distributed across the population



re…no…rank all 1000 patients by their predicted …ob… experiencing the outcome



Choosing a threshold on the predicted probability can operationalize the model results into a decision-making criteria

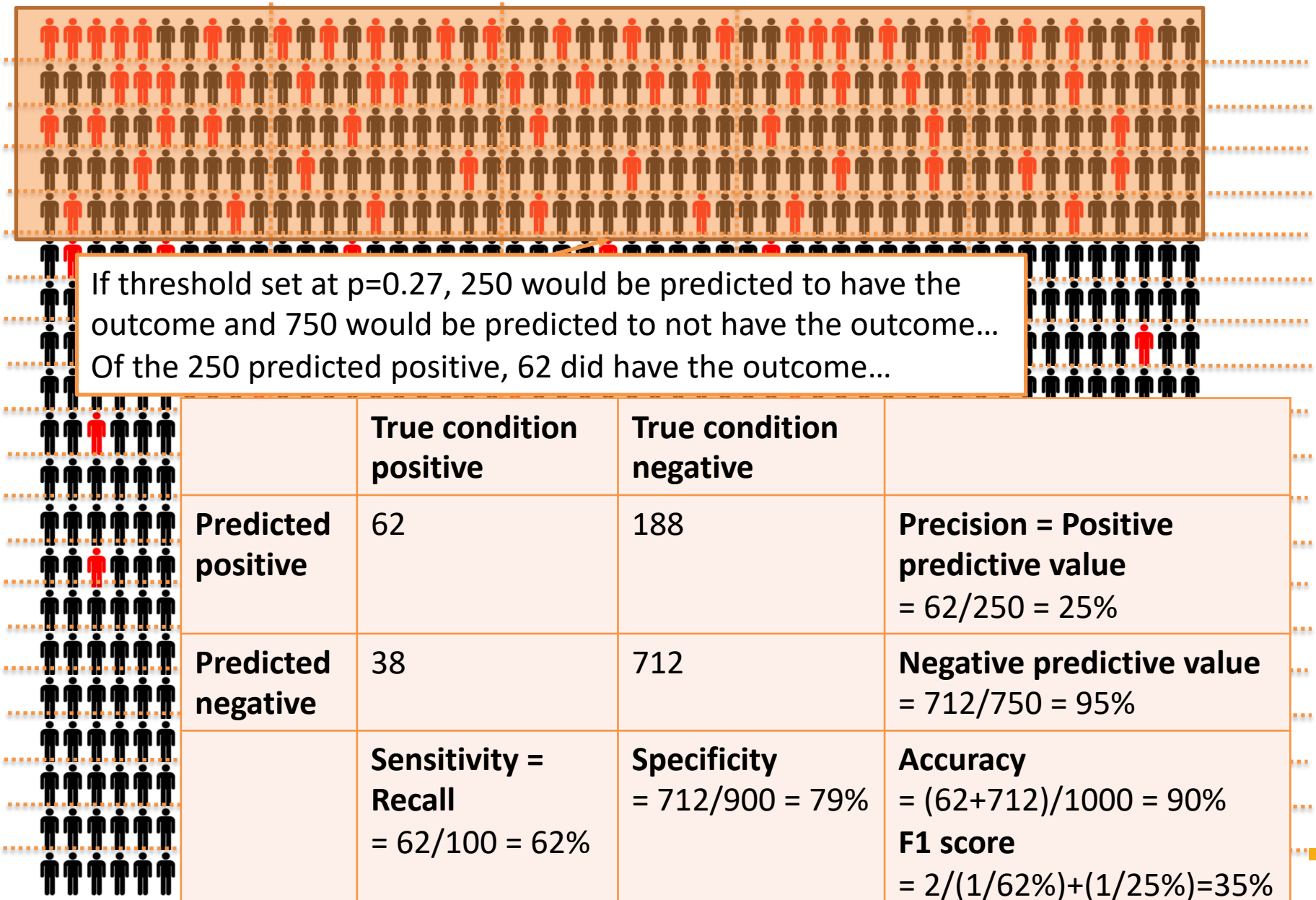


If threshold set at p=0.65, 10 would be predicted to have the outcome and 990 would be predicted to not have the outcome…

Of the 10 predicted positive, 6 did have the outcome…

	True condition positive	**True condition negative**	
Predicted positive	6 (TP)	4 (FP)	**Precision = Positive predictive value** = 6/10 = 60%
Predicted negative	94 (FN)	896 (TN)	**Negative predictive value** = 896/990 = 91%
	Sensitivity = Recall = 6/100 = 6%	**Specificity** = 896/900 = 99.6%	**Accuracy** = (6+896)/1000 = 90% **F1 score** = 2/(1/6%)+(1/60%) = 11%

Different thresholds offer different tradeoffs in operating characteristics



If threshold set at p=0.27, 250 would be predicted to have the outcome and 750 would be predicted to not have the outcome…
Of the 250 predicted positive, 62 did have the outcome…

	True condition positive	**True condition negative**	
Predicted positive	62	188	**Precision = Positive predictive value** = 62/250 = 25%
Predicted negative	38	712	**Negative predictive value** = 712/750 = 95%
	Sensitivity = Recall = 62/100 = 62%	**Specificity** = 712/900 = 79%	**Accuracy** = (62+712)/1000 = 90% **F1 score** = 2/(1/62%)+(1/25%)=35%

What are the key inputs to a patient-level prediction study?

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Research and Applications

Research and Applications

Design and implementation of a standardized framework to generate and evaluate patient-level prediction models using observational healthcare data

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Input parameter	Design choice
Target cohort (T)	
Outcome cohort (O)	
Time-at-risk	
Model specification -which model(s)? -which parameters? -which covariates?	

Types of prediction problems in healthcare

Type	Structure	Example
Disease onset and progression	Amongst patients who are newly diagnosed with <insert your favorite disease>, which patients will go on to have <another disease or related complication> within <time horizon from diagnosis>?	Among newly diagnosed AFib patients, which will go onto to have ischemic stroke in next 3 years?
Treatment choice	Amongst patients with <indicated disease> who are treated with either <treatment 1> or <treatment 2>, which patients were treated with <treatment 1> (on day 0)?	Among AFib patients who took either warfarin or dabigatran, which patients got warfarin? (as defined for propensity score model)
Treatment response	Amongst patients who are new users of <insert your favorite chronically-used drug>, which patients will <insert desired effect> in <time window>?	Which patients with T2DM who start on metformin stay on metformin after 3 years?
Treatment safety	Amongst patients who are new users of <insert your favorite drug>, which patients will experience <insert your favorite known adverse event from the drug profile> within <time horizon following exposure start>?	Among new users of warfarin, which patients will have GI bleed in 1 year?
Treatment adherence	Amongst patients who are new users of <insert your favorite chronically-used drug>, which patients will achieve <adherence metric threshold> at <time horizon>?	Which patients with T2DM who start on metformin achieve >=80% proportion of days covered at 1 year?

Coffee Break


Second Annual
EUROPEAN OHDSI SYMPOSIUM
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