

Real World Evidence

A prática como fonte de evidência

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Estrutura da comunicação

- Agradecimentos
- COI
- Causalidade em medicina
- Tipos de fontes de informação:
MBE + Big Data/RWD/RWE
- Um exemplo: ICHOM.

Causalidade em medicina

Causalidade em medicina

(Critérios de Koch/Bradford Hill)

Temporalidade	<ul style="list-style-type: none"> a causa precede sempre o efeito (tabagismo e cancro do pulmão)
Força	<ul style="list-style-type: none"> é uma associação causa-efeito forte, representada por riscos absolutos e relativos de grandes dimensões (o tabagismo aumenta 4-6 vezes a probabilidade de DC)
Dose-resposta	<ul style="list-style-type: none"> quanto maior for a dimensão do factor causal, maior será o efeito produzido (nº de cigarros fumados e incidência de cancro do pulmão)
Reversibilidade	<ul style="list-style-type: none"> a remoção de um factor etiológico diminui o risco da doença (após 10 anos, a cessação tabágica reduz o risco de cancro do pulmão até ao nível dos não fumadores)
Consistência	<ul style="list-style-type: none"> resultados análogos em estudos diferentes (tabaco e cancro em diversos estudos)
Plausibilidade biológica	<ul style="list-style-type: none"> consistente com o conhecimento biomédico mais actual e com uma base conceptual compreensível (efeito carcinogénico do tabaco)
Especificidade	<ul style="list-style-type: none"> uma causa, um efeito (cancro do pulmão: tabagismo 95% do risco)
Analogia	<ul style="list-style-type: none"> causas idênticas para doenças semelhantes (tabagismo no cancro do pulmão e da laringe)

Relação causa/efeito nos estudos clínicos mais comuns

TIPO DE ESTUDO	CAUSA	EFEITO
ETIOLOGIA/DANO/RISCO	Medicação, genética ou ambiental	Incidência da doença, complicações ou mortalidade
DIAGNÓSTICO	Teste	Precisão diagnóstica
TERAPÊUTICA/PREVENÇÃO	Medicação/outra intervenção, modalidade preventiva	Melhoria de sintomas ou diminuição da mortalidade
PROGNÓSTICO	Doença ou terapêutica	Tempo até ao <i>outcome</i>

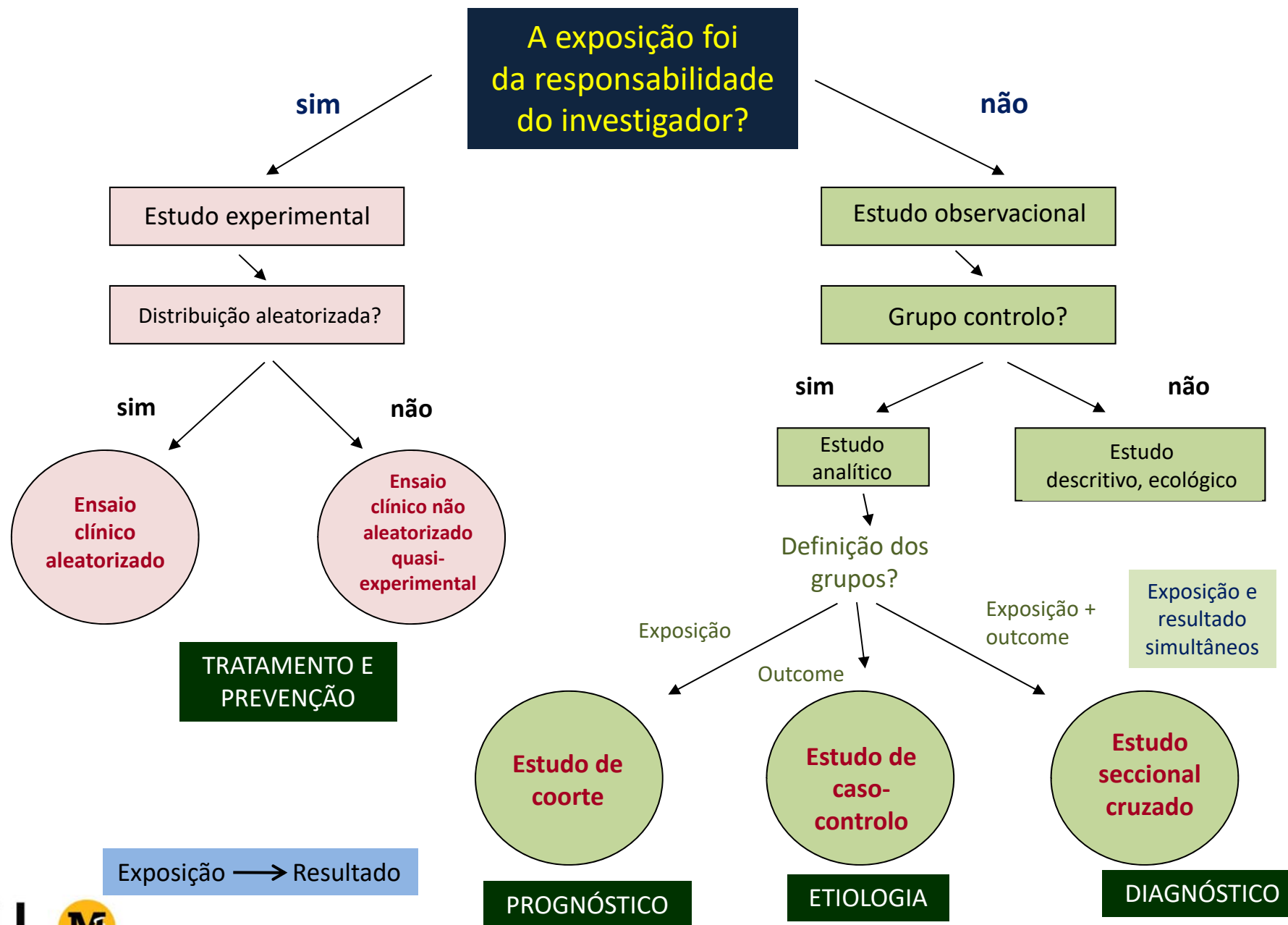


Tabela 2x2 para cálculo das medidas de associação em estudos clínicos

	Outcome presente	Outcome ausente	Total
Expostos	a	b	a+b
Não expostos	c	d	c+d
Total	a+c	b+d	a+b+c+d

TIPOS DE MEDIDAS DE ASSOCIAÇÃO EM ESTUDOS CLÍNICOS

- Caso-controlo: **odds ratio** (OR)
- Coorte: **risco relativo** (RR)
- Seccionais cruzados: **prevalência**
- Ensaio clínico: **Redução do Risco Absoluto** (RRA) e **Relativo** (RRR) e **Número Necessário Tratar** (NNT)

A Medicina Baseada na Evidência

O que é a Medicina Baseada na Evidência

A Medicina Baseada na Evidência (MBE) é a integração:

- da melhor evidência científica com
- a experiência clínica e com
- os valores individuais dos doentes.

O que é a melhor evidência científica?

É a que é clinicamente relevante, proveniente em parte da investigação básica mas sobretudo da investigação clínica, através de estudos centrados em problemas de doentes, nas áreas do diagnóstico, tratamento e prognóstico (entre outras).

O que é a experiência clínica?

É a capacidade que os médicos têm de utilizar as suas capacidades técnicas (em combinação com as suas experiências passadas) na determinação do **estado de saúde** do doente individual, no **diagnóstico** dos seus problemas e na selecção de um **tratamento** que tenha em conta os riscos e benefícios, assim como as suas características únicas.

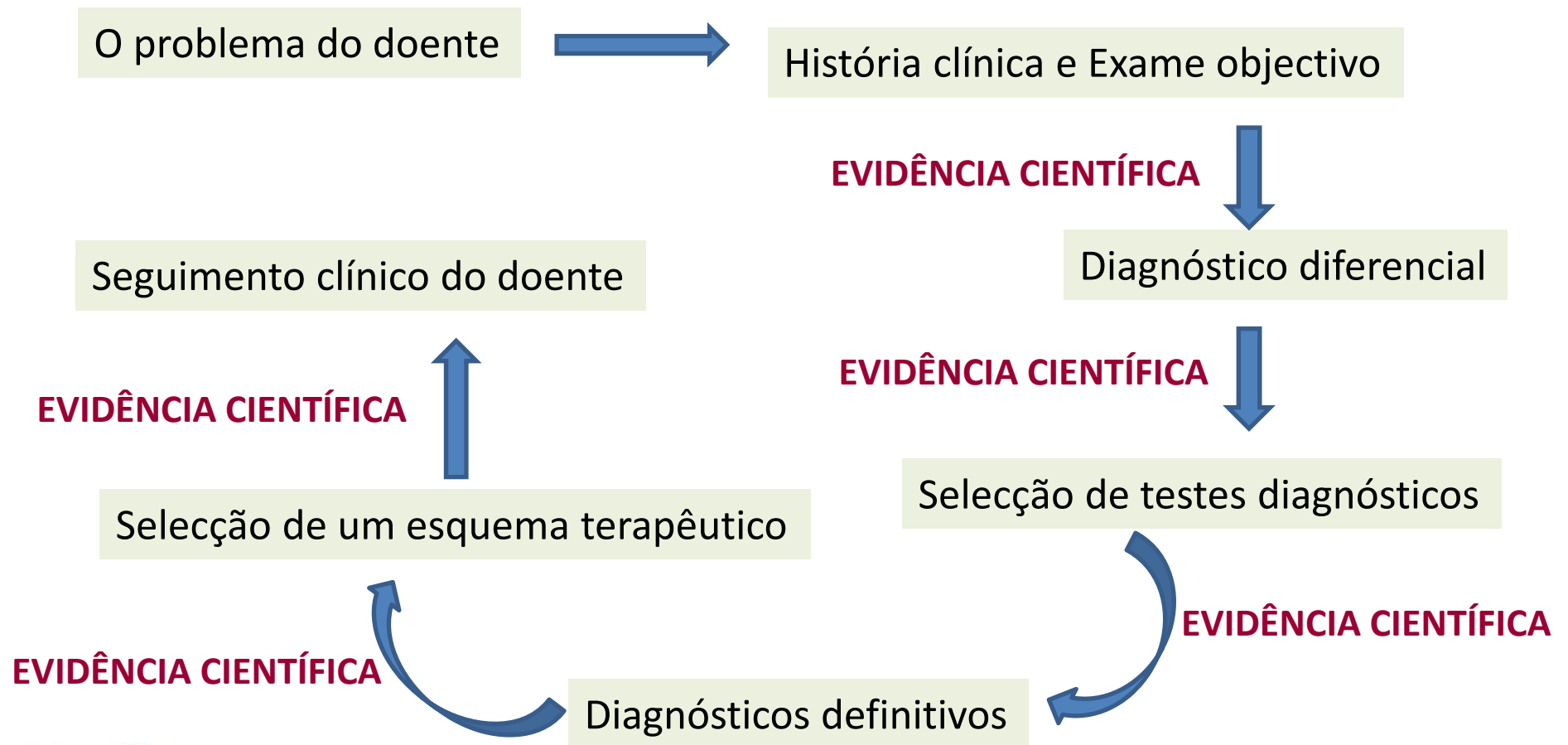
O que são os valores dos doentes?

São as preferências, preocupações e expectativas próprias dos doentes, que devem ser tomadas em conta se se quiser obter um resultado equilibrado na sua interacção com o sistema de saúde e seus profissionais.

Prática da Medicina Baseada na Evidência

1. Definição da questão clínica
2. Selecção da evidência científica
 1. Fontes primárias
 2. Fontes secundárias
3. Avaliação crítica metodológica da evidência científica
4. Síntese e aplicação.

A prática da MBE



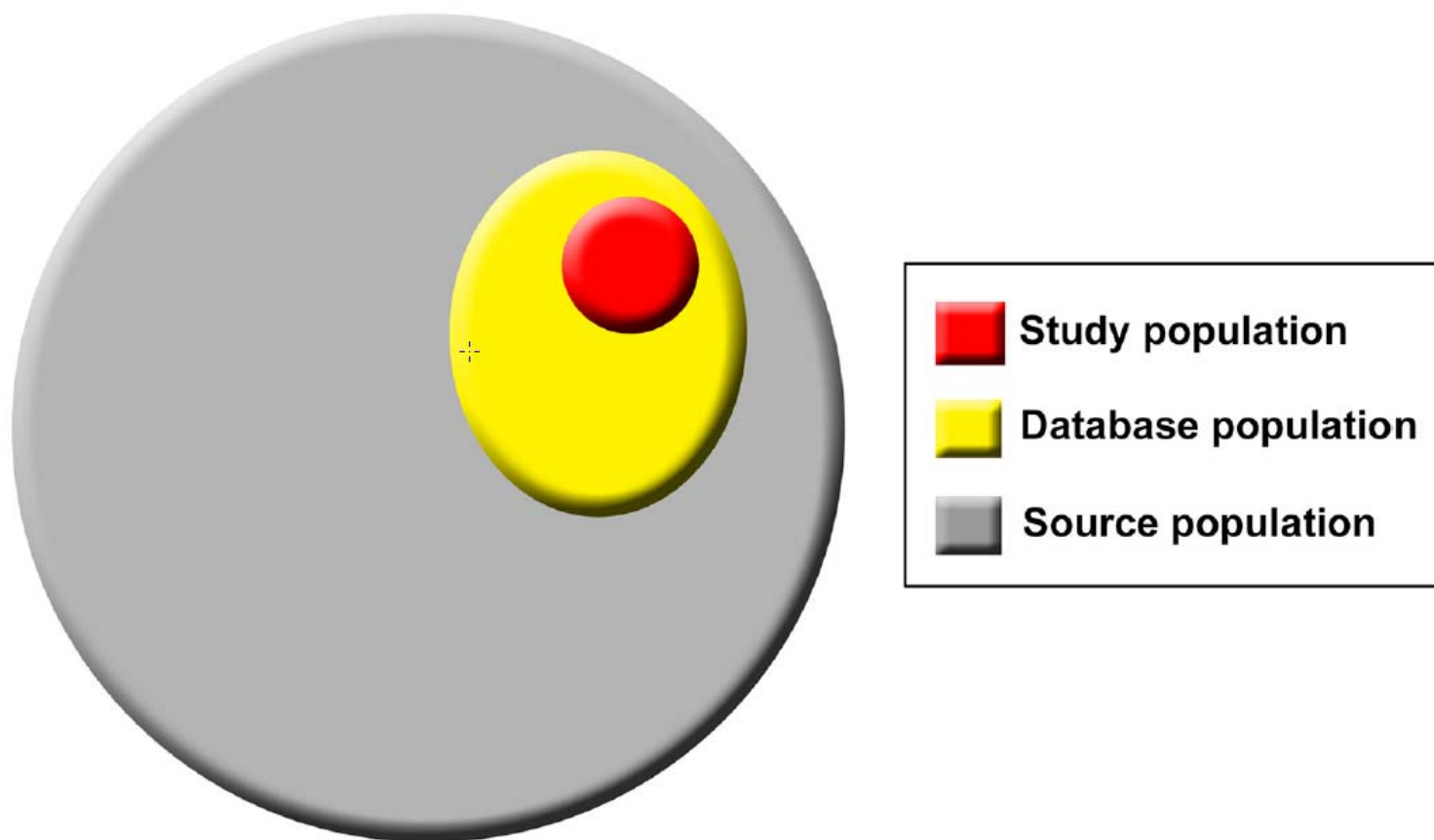
Big data em saúde

Definições

- Big Data
- Real World Data
- Real World Evidence.

Population hierarchy in studies using routinely collected data sources

- PLOS Medicine DOI:10.1371/journal.pmed.1001885 - October 6, 2015 -



“Big data” em saúde

- Grande quantidade de factos aglomerados em bases de dados, obtidos de propósito ou não
- Três conceitos/base:
 1. Capacidade de análise de grande quantidade de dados (em vez de dados parcelares)
 2. Aceitação de alguma desordem, em vez de precisão
 3. Correlação em vez de causalidade.

Caracterização de big data: 3 Vs

- **Volume** is the amount of data generated by organizations or individuals
- **Velocity** is the frequency and speed at which data is generated, captured and shared
- **Variety** is the proliferation of new data types including those from social, machine and mobile sources.

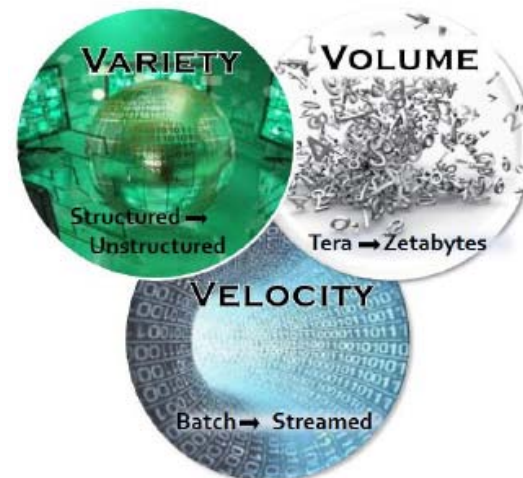
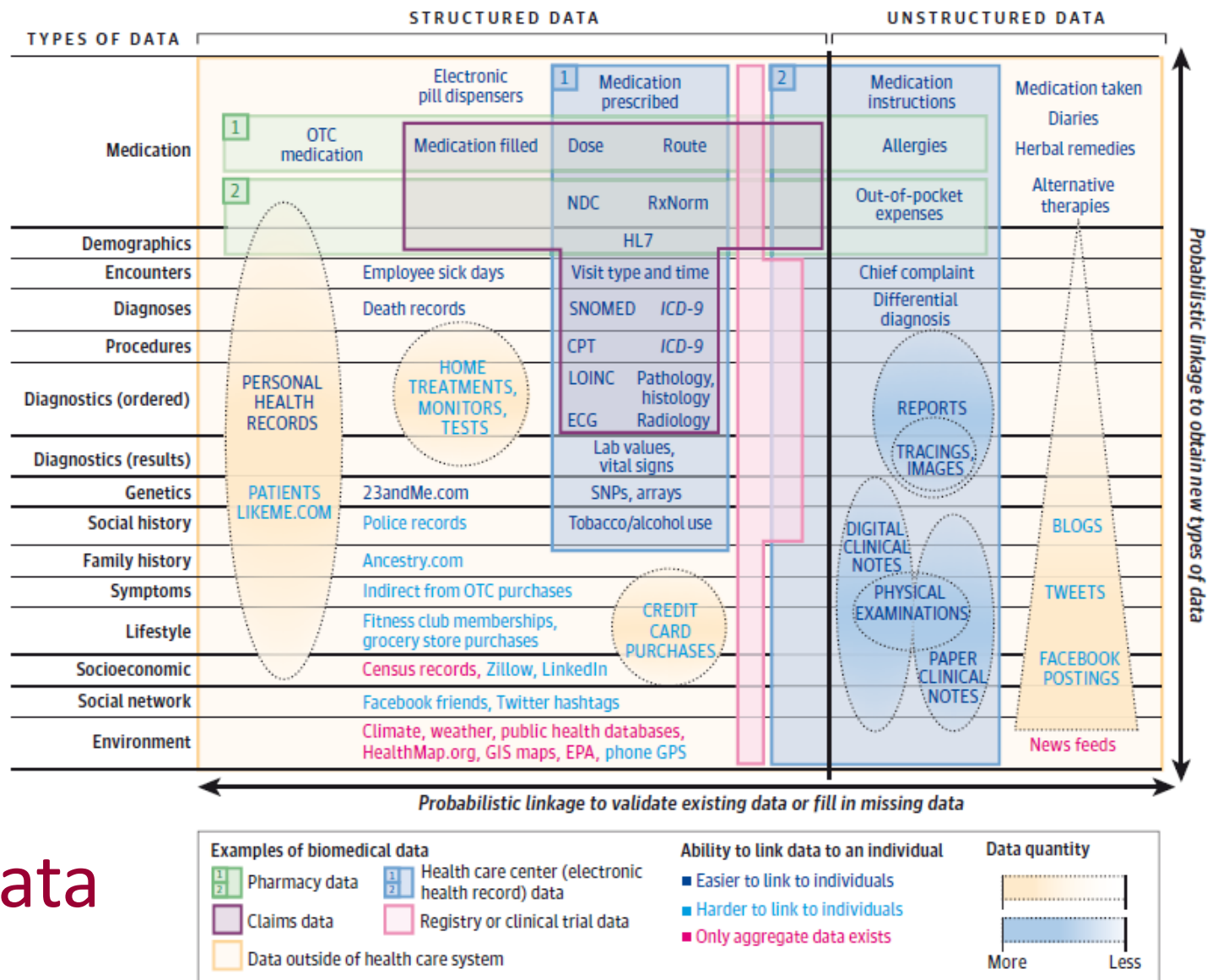
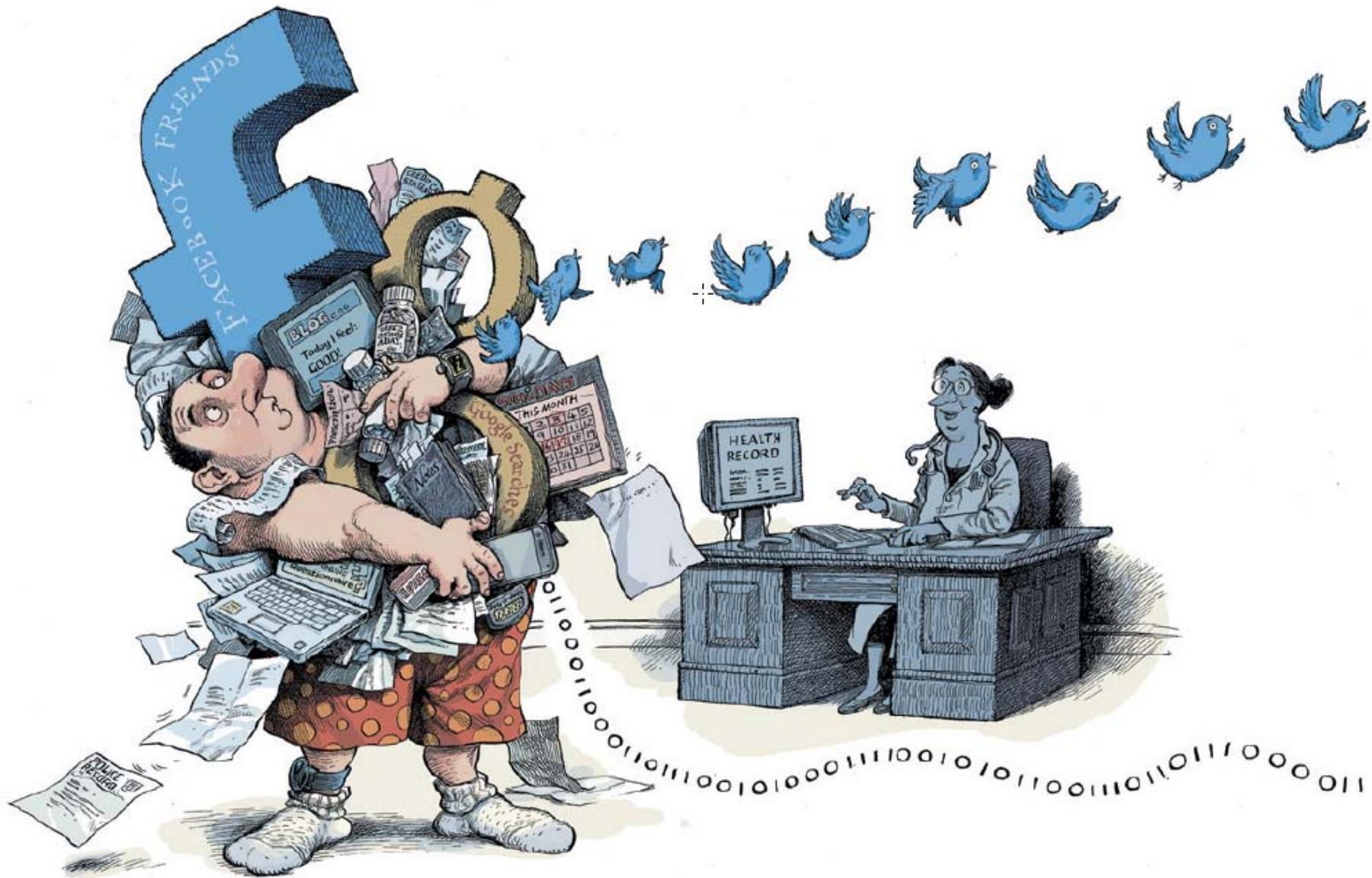


Figure. The Tapestry of Potentially High-Value Information Sources That May be Linked to an Individual for Use in Health Care



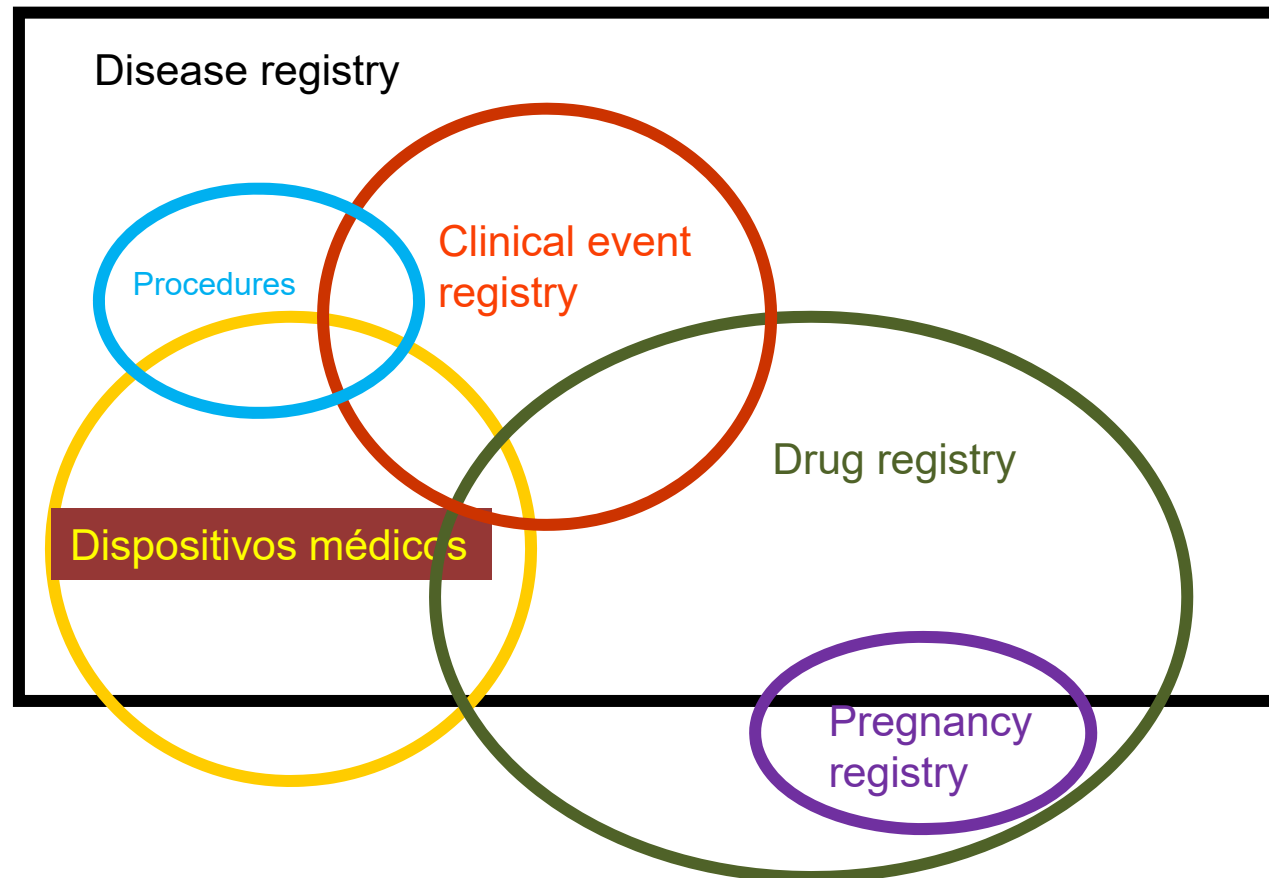
Big data



Exemplos de RWD

- Estudos observacionais
- Ensaaios clínicos suplementares
- PROM, ICHOM
- Bases de dados administrativas
- Processos clínicos electrónicos
- Redes sociais
- Registos de doentes
- ...

Real world data: registos de doentes



Registos de doentes

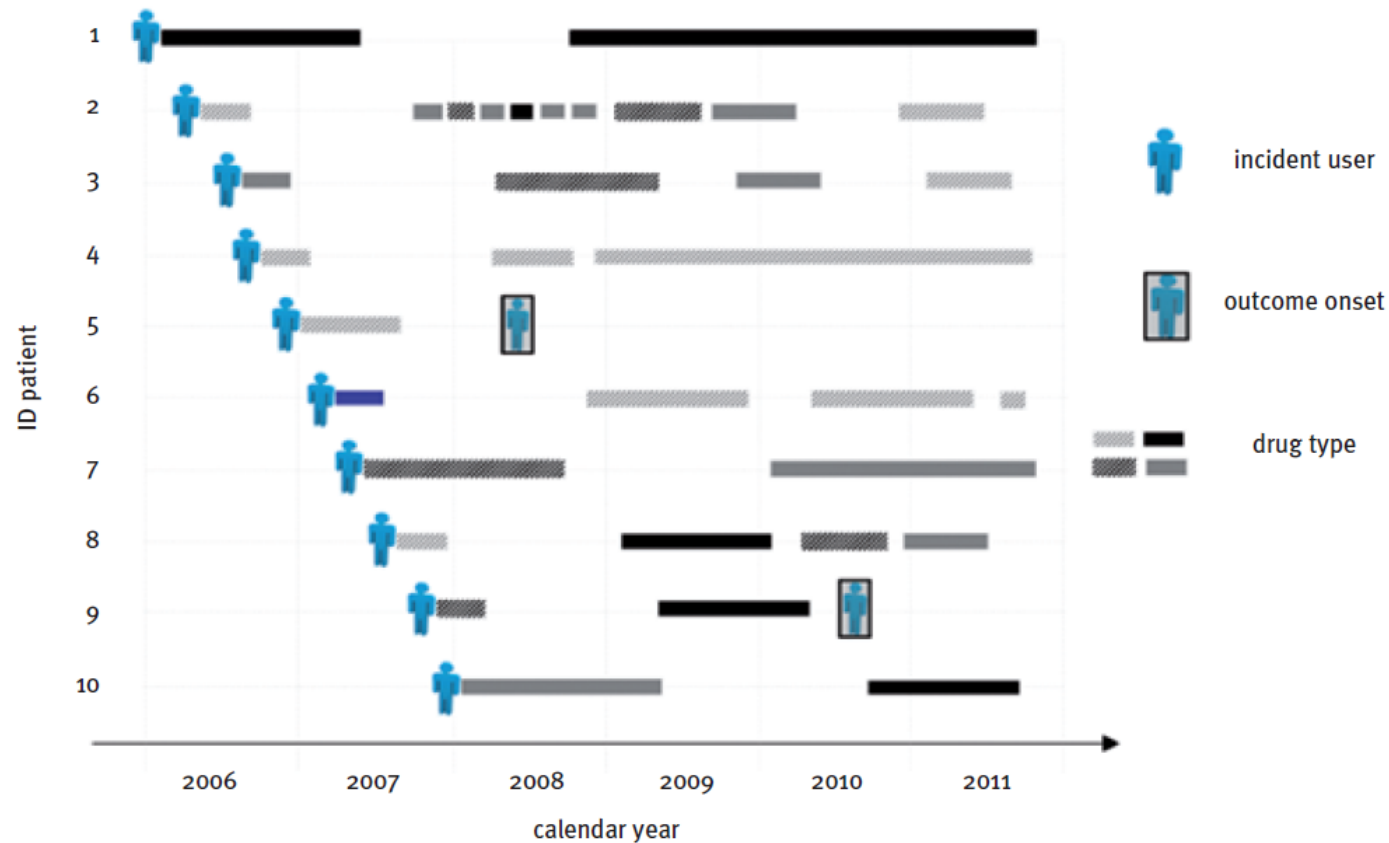
- Sistemas organizados que usam métodos de estudo observacionais para recolher dados uniformes (clínicos ou outros)
- Avalia os resultados específicos para uma população definida por uma determinada doença/condição/exposição e
- Destina-se a servir objectivos clínicos, de investigação, de gestão e de políticas.

Objectivos dos registos

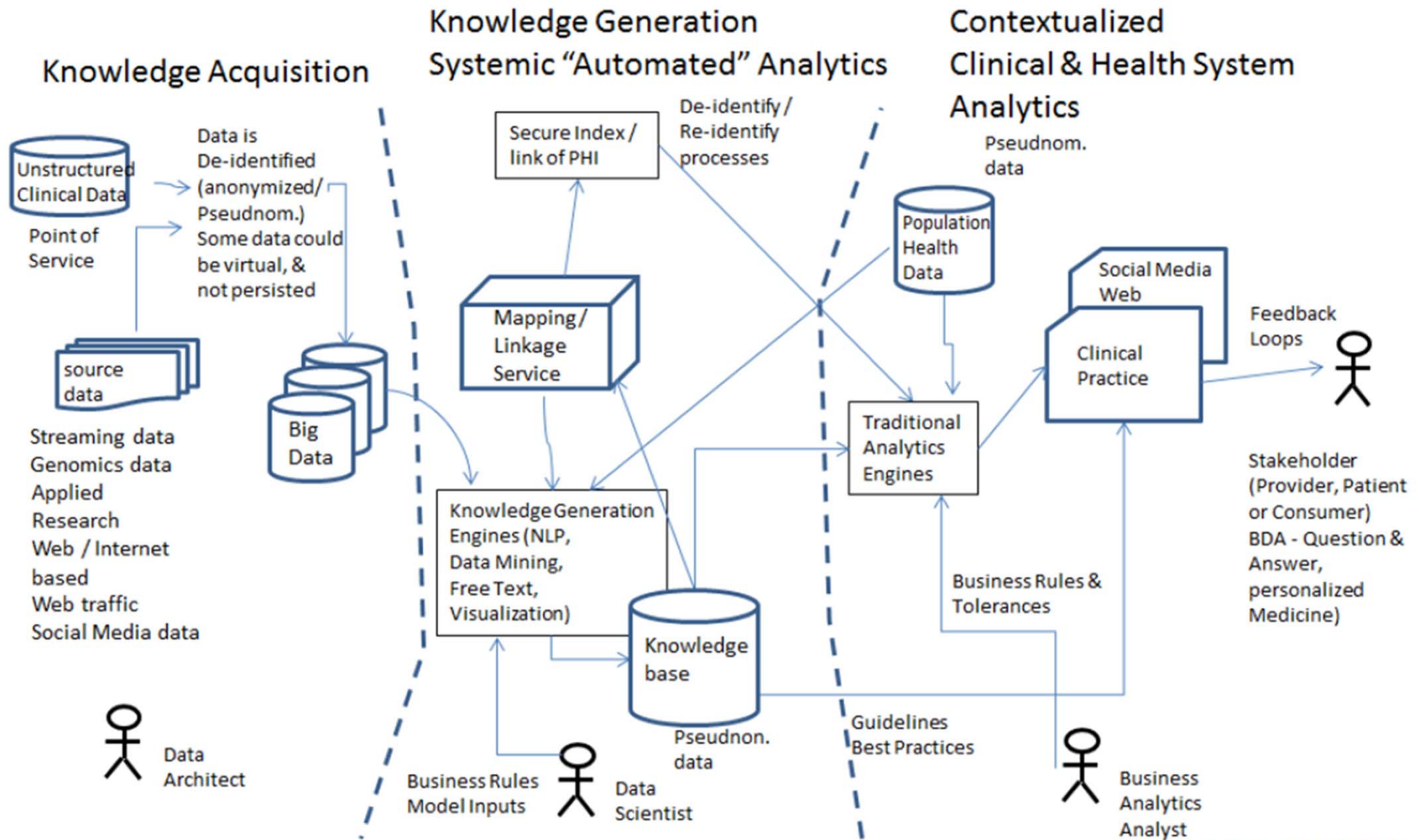
- Estudar a história natural da doença
- Monitorizar o benefício e o dano das intervenções
- Avaliar custo-efectividade de testes diagnósticos ou esquemas terapêuticos
- Medir e melhorar a qualidade de vida
- Identificar variação da prática clínica
- ...

Real World Evidence

ILLUSTRATION OF A FIXED COHORT OF TEN INCIDENT USERS OF A GIVEN DRUG THERAPY WHO WERE GENERATED FROM A WELL-DEFINED DYNAMIC POPULATION FROM 2006 THROUGH 2007



Operacionalização



ICHOM was formed to drive the industry towards value-based health care by defining global outcome standards that matter most to patients

ICHOM's three founders...



ICHOM mission:

*Unlock the potential of Value-Based Health Care by **defining global standard sets of outcome measures that really matter to patients** for the most relevant medical conditions and by **driving adoption and reporting** of these measures worldwide.*

What is value-based healthcare?

(Porter M. NEJM 2010;363:2477-81)

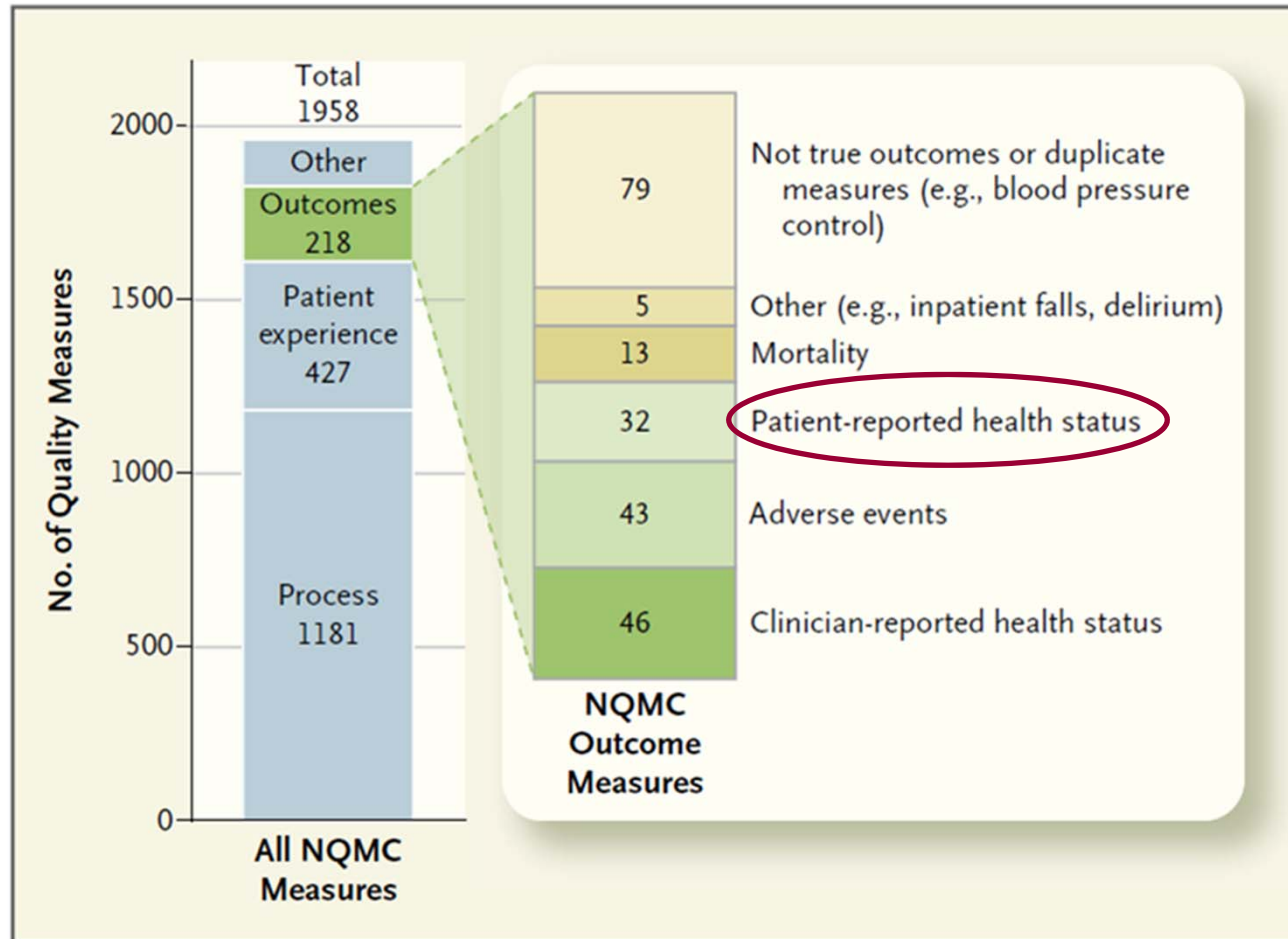
- Value is defined as **outcomes** relative to **costs**
$$\text{VBHC} = \text{outcomes} / \text{costs}$$
- **Outcomes** are inherently condition-specific and multidimensional
- **Cost** refers to the total costs of the full cycle of care for the patient's medical condition, not the cost of individual services.

Patient Outcomes Measurement

(Porter M. NEJM 2016;374:504-6)

- Health care is shifting focus from the **volume** of services delivered to the **value** created for patients
- **First**, measurement of **outcomes** that matter to patients, aside from survival, remains limited
- For many conditions, **death** is a rare outcome whose measurement fails to differentiate excellent from merely competent care.

Measures of performance



Measures of performance

- **Second**, the limited outcomes measurement that has occurred has been led overwhelmingly by specialty societies
- **Third**, efforts at outcomes measurement have overwhelmingly focused on clinical status (e.g., survival and “objective” outcomes that are readily captured by laboratory tests) and left out functional status, even though improving functional status is why patients seek care.

Measures of performance

- **Finally**, progress on outcomes measurement has been slowed dramatically by the fact that each organization has ones of their own
- Stakeholders can come together to create a process to agree on a minimum sufficient set of outcomes for each important medical condition - including rigorous definitions, risk-adjustment factors and methods.

Variation in health outcomes is a worldwide problem

2X variation in 30-day mortality rate from heart attack in US hospitals



4X variation in bypass surgery mortality in the UK hospitals



5X Variation of major obstetrical complications among US hospitals



9X variation in complication rates from radical prostatectomies in the Dutch hospitals



18X variation in reoperation rates after hip surgery in German hospitals



20X variation in mortality after colon cancer surgery in Swedish hospitals

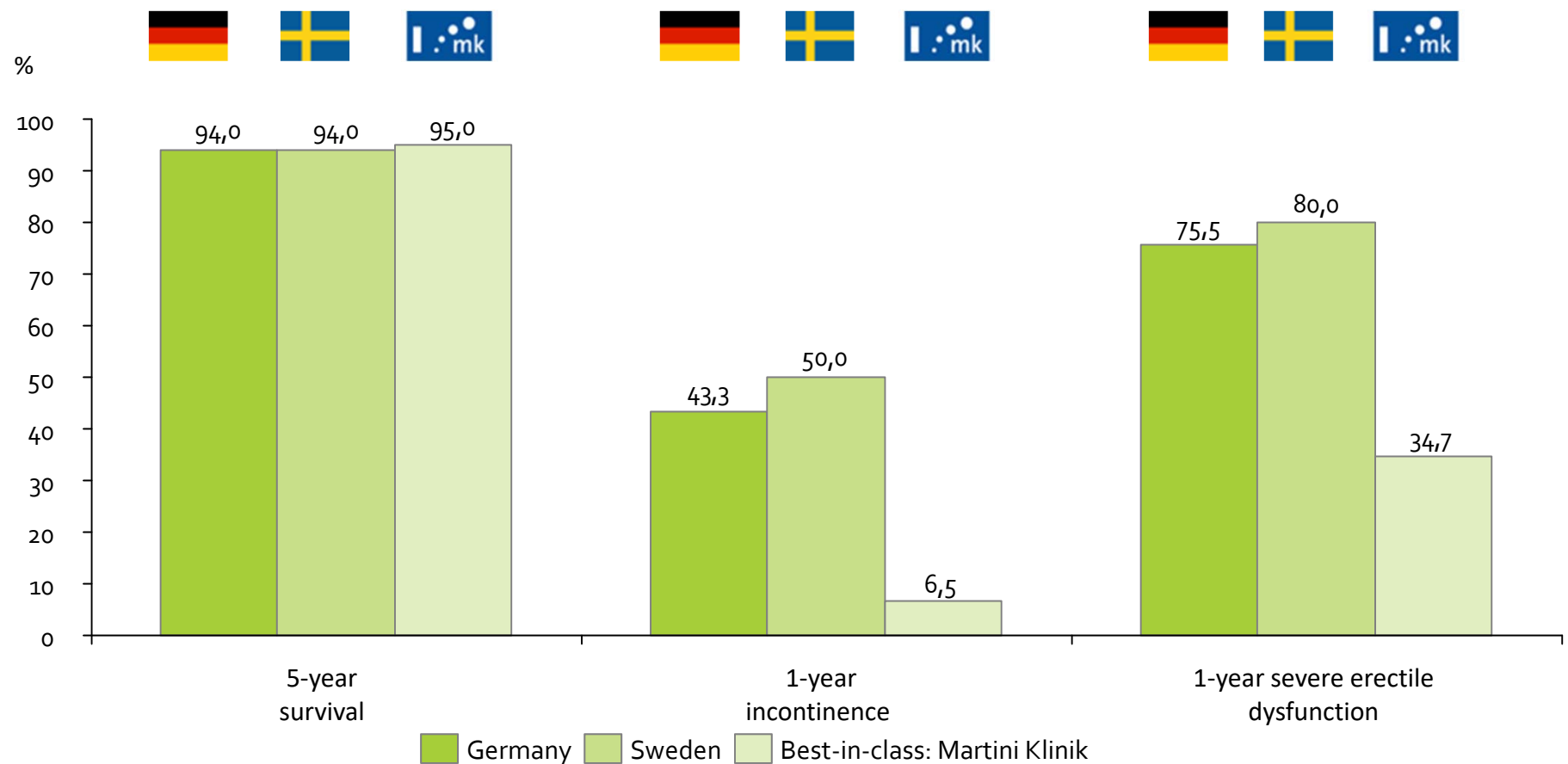


36X variation in capsule complications after cataract surgery in Swedish hospitals

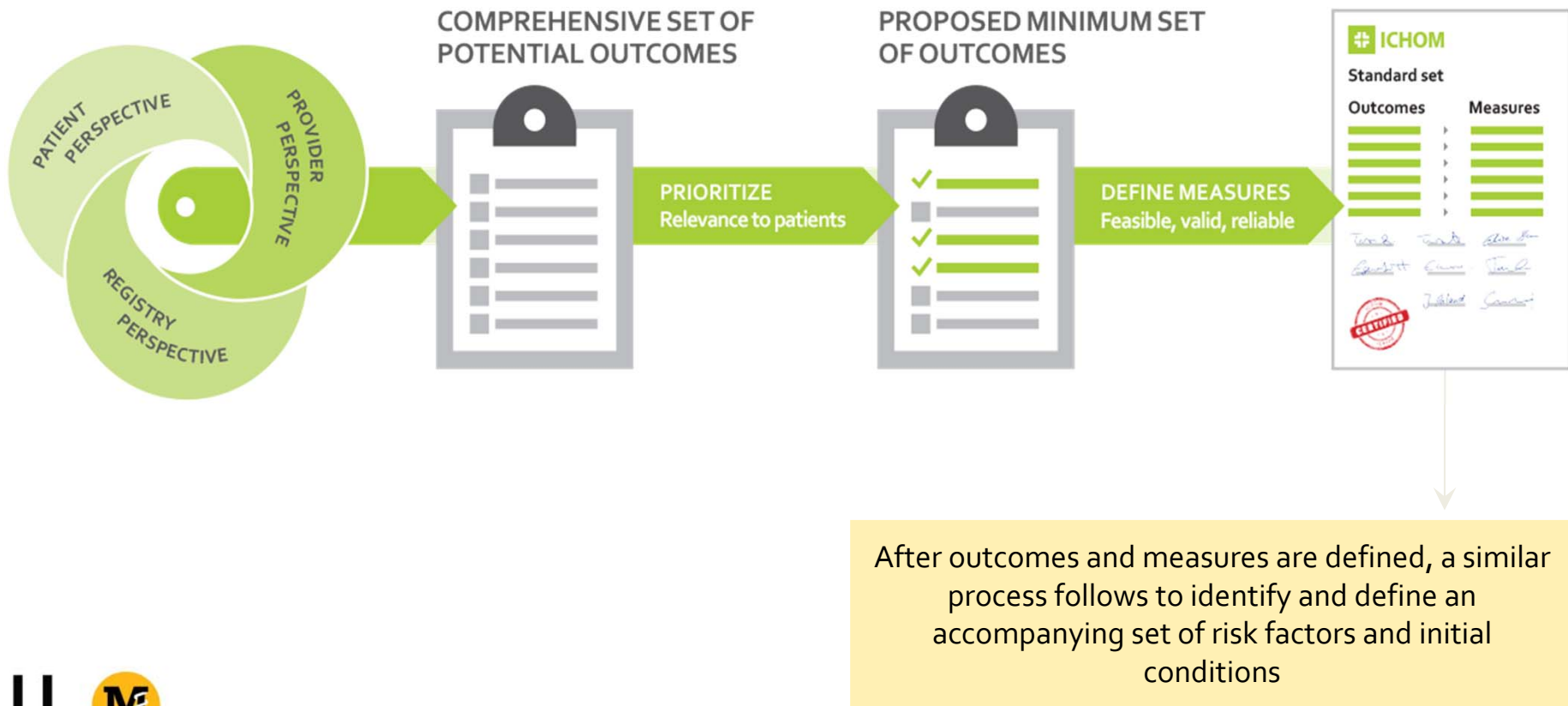


But, for outcomes that matter most to patients – improvement in their symptoms, functioning, and well-being – this only begins to describe the magnitude of the problem.

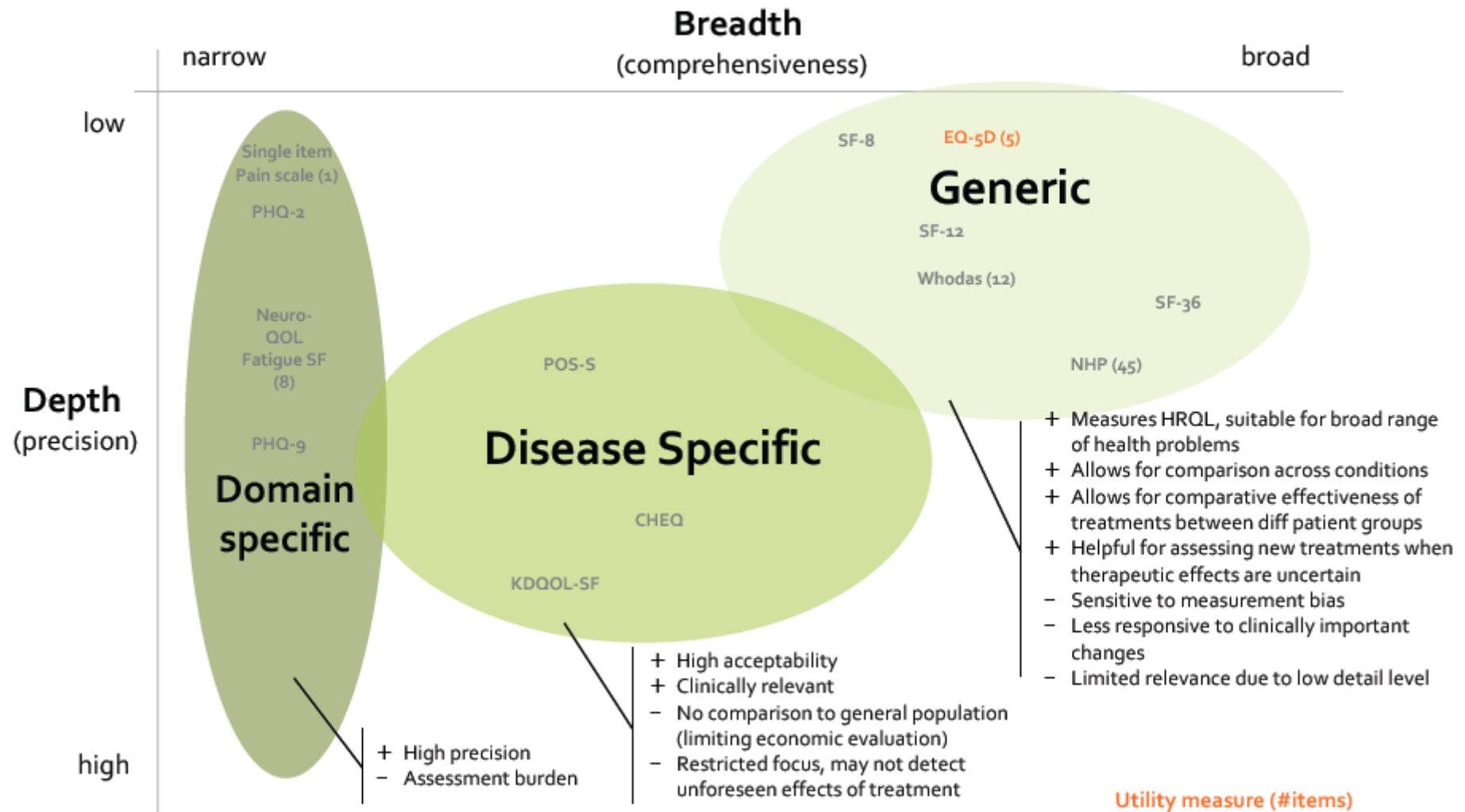
Why measuring and reporting meaningful outcomes matters



Working Group led through a structured process to reach agreement on Standard Set of outcomes and case-mix factors



PROM types are: Domain, Disease, or Generic. The ideal (combination of) PROM is determined by specific needs/goals

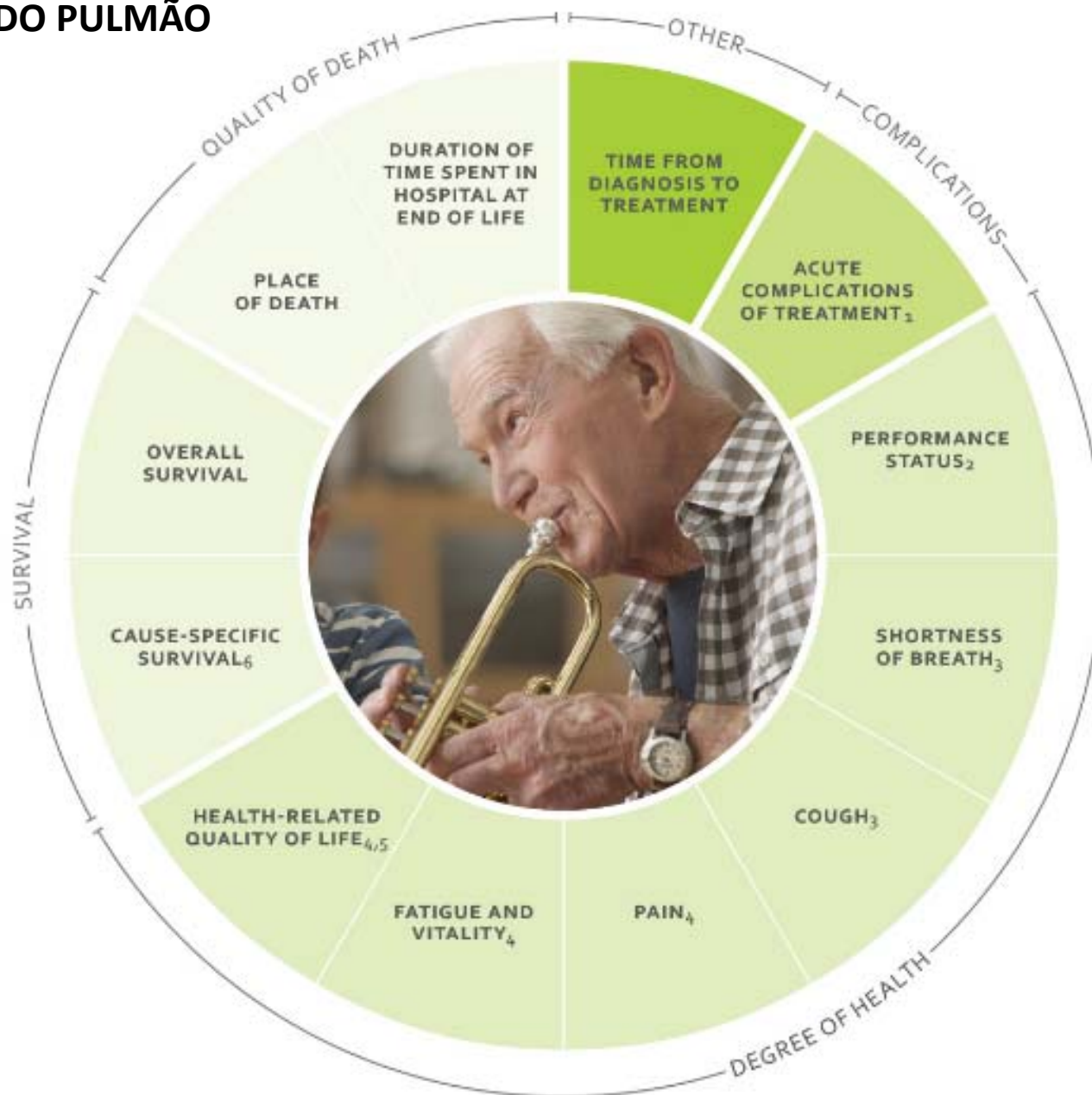


We have already developed 23 Standard Sets, covering 47% of the global disease burden



Etc....

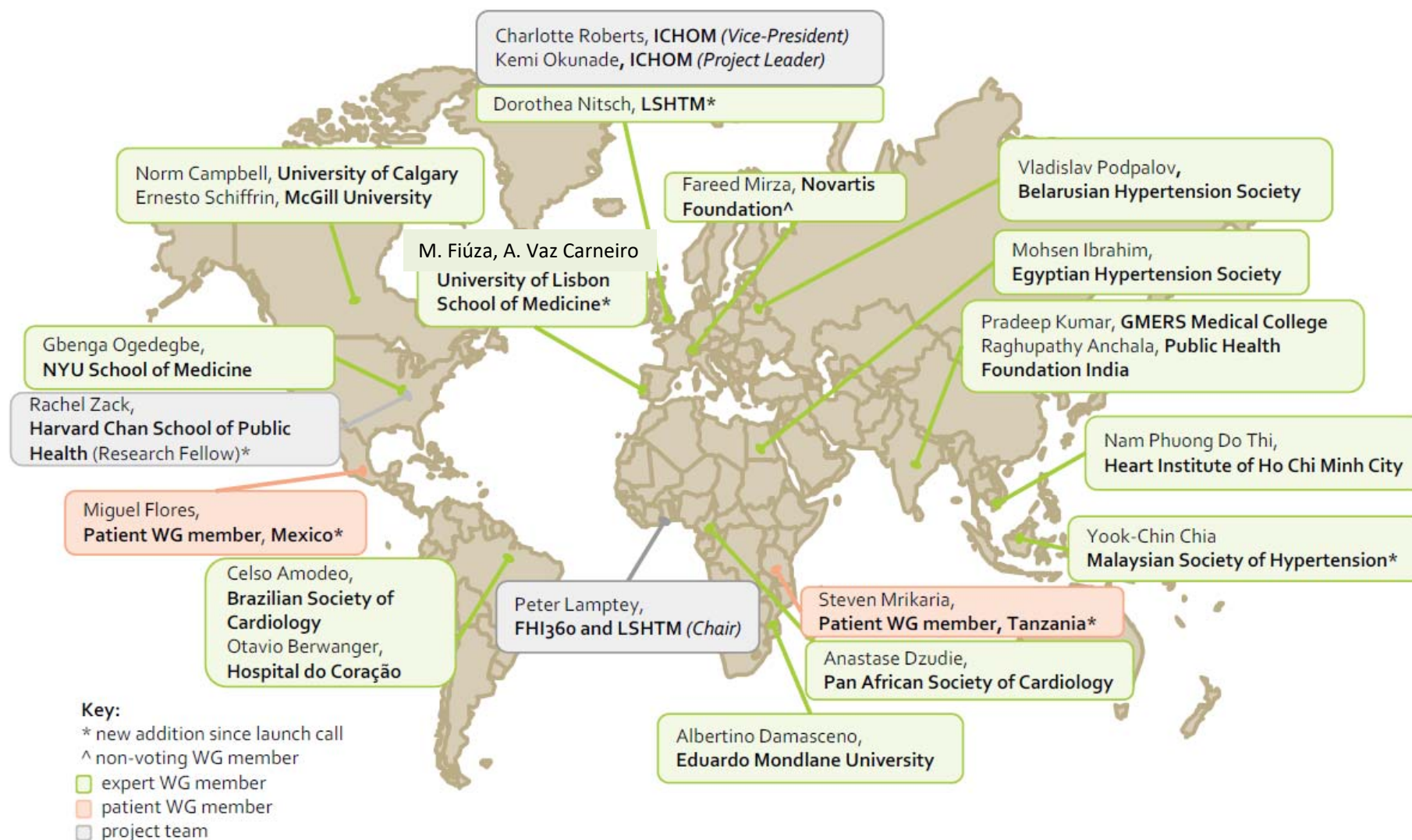
CANCRO DO PULMÃO



The arterial hypertension standard set

<http://www.ichom.org/medical-conditions/hypertension-in-low-and-middle-income-countries/>

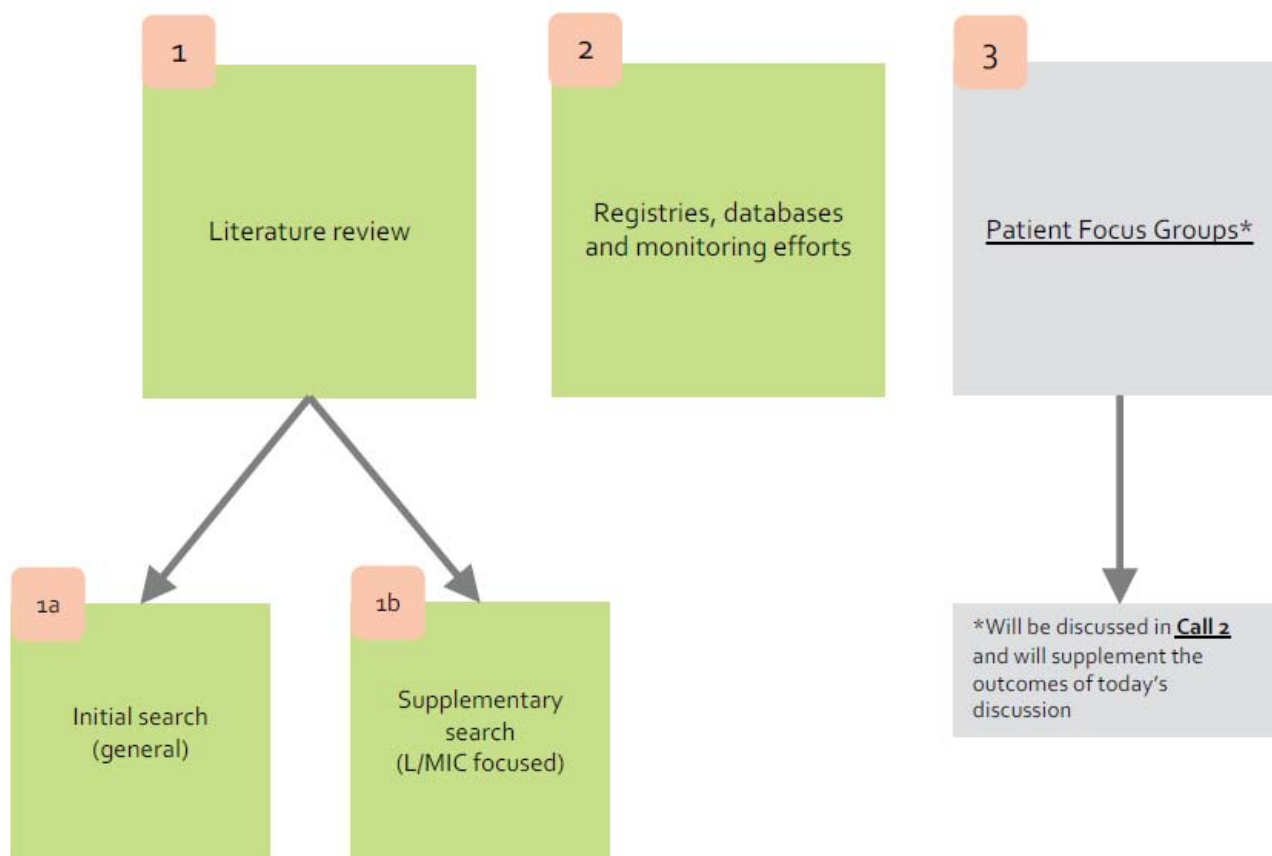
The ICHOM Hypertension in L/MIC Working Group



Proposed scope: to define a standard set of outcome measures for adult patients with hypertension in L/MIC

	Patient population	Treatment options	Examples of outcomes
Include	<p>An adult (≥ 16 years) diagnosed with hypertension :</p> <ul style="list-style-type: none"> • I10 Essential (primary) hypertension • I11 Hypertensive heart disease • I12 Hypertensive chronic kidney disease • I13 Hypertensive heart and chronic kidney disease • I15 Secondary hypertension (I15.0 Renovascular HTN, I15.1 HTN secondary to other renal disorders, I15.2 HTN secondary to endocrine disorders, I15.8 Other secondary hypertension) 	<ul style="list-style-type: none"> • Pharmacological • Life style modifications • Other 	<ul style="list-style-type: none"> • All cause mortality • Cardiac-cause mortality • Major cardiovascular events (e.g. fatal / nonfatal myocardial infarctions, stroke and cardiovascular death), minor cardiovascular events (hospitalized heart failure, angina, atrial fibrillation, and claudication) • Renal failure/renal function • Adverse drug effects • Health-related quality of life • Physical activity levels • Physical function • Fatigue • Depression, anxiety, psychosocial stress
Exclude	<ul style="list-style-type: none"> • Persons aged <16 years and neonatal hypertension • Hypertensive disease complicating pregnancy, childbirth and the puerperium • I27.0 Primary pulmonary hypertension 		

Framework of methodology and presenting outcomes



Appendix 1: Detailed search phrase (general search)

PubMed Search Terms

- (hypertension[Majr] OR "blood pressure"[Majr] OR hypertension[ti] OR "blood pressure"[ti])
- NOT ("pulmonary hypertension"[ti] OR "pulmonary arterial hypertension"[ti] OR child*[ti] OR maternal[ti] OR pregnant[ti])
- NOT (animals [mh] NOT humans [mh])

AND

((("Quality of Life"[Mesh] OR "Quality Indicators, Health Care"[Mesh] OR "Patient Outcome Assessment"[Mesh] OR "Treatment Outcome"[Mesh] OR Quality of life[tiab] OR QOL[tiab] OR quality indicator*[tiab] OR patient reported outcome*[tiab] OR patient related outcome*[tiab] OR patient outcome*[tiab] OR patient assessment*[tiab] OR treatment outcome*[tiab] OR outcome*[ti])

AND

(index[tiab] OR indices[tiab] OR instrument[tiab] OR instruments[tiab] OR measure*[tiab] OR questionnaire*[tiab] OR profile*[tiab] OR scale*[tiab] OR scor*[tiab] OR status[tiab] OR survey*[tiab] OR rating*[tiab] OR tool[tiab] OR tools[tiab] OR metric*[tiab] OR reporting[tiab])

AND

(randomized controlled trial[All Fields] OR randomized controlled trials[All Fields] OR randomised controlled trial[All Fields] OR randomised controlled trials[All Fields] OR randomized controlled trial[pt] OR Review[pt] OR systematic[sb])

OR

("Quality Indicators, Health Care"[Mesh] OR "Patient Outcome Assessment"[Mesh] OR quality indicator*[tiab] OR patient reported outcome*[tiab] OR patient related outcome*[tiab] OR patient outcome*[tiab] OR patient assessment*[tiab] OR outcome report*[tiab] OR "Patient Outcome Assessment"[Mesh:NoExp] OR "Patient-Centered Care"[Mesh] OR "Patient Satisfaction"[Mesh] OR "Physician-Patient Relations"[Mesh] OR "Nurse-Patient Relations"[Mesh] OR patient centered[tw] OR patient participation[tw] OR patient involvement[tw] OR patient preference*[tw] OR patient's preference*[tw] OR patients' preference*[tw] OR patient satisfaction[tw] OR patient's satisfaction[tw] OR patients' satisfaction[tw] OR patient expectation*[tw] OR patient's expectation*[tw] OR patients' expectation*[tw] OR (patient reported[tw] AND outcome*[tw]) OR shared decision*[tw] OR physician patient[tw] OR doctor patient[tw] OR clinician patient[tw] OR nurse patient[tw]))

OR

((("randomized controlled trials as topic"[MeSH Terms] OR ("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomized controlled trial"[All Fields] OR "randomised controlled trial"[All Fields]) OR randomized controlled trial,[All Fields] OR ("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomized controlled trials"[All Fields] OR "randomised controlled trials"[All Fields]))) OR ("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomised controlled trial"[All Fields] OR "randomized controlled trial"[All Fields]) OR ("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomised controlled trials"[All Fields] OR "randomized controlled trials"[All Fields])) OR randomized controlled trial[Publication Type])

AND (((("Quality of Life"[Mesh] OR "Outcome Assessment (Health Care)"[Mesh]) OR "Outcome and Process Assessment (Health Care)"[All Fields]) OR "Quality Indicators, Health Care"[Mesh]))

- AND ("2005/01/01"[PDAT] : "3000/12/31"[PDAT])

- AND (English[la])

Summary of Literature and Registries search

1a	Literature search (general outcomes)	
Number of papers identified		2,543
Total excluded		1,429
Total included		1,114

1b	Literature search (LMIC-focused outcomes)	
Number of papers identified		139
Total excluded		87
Total included		52

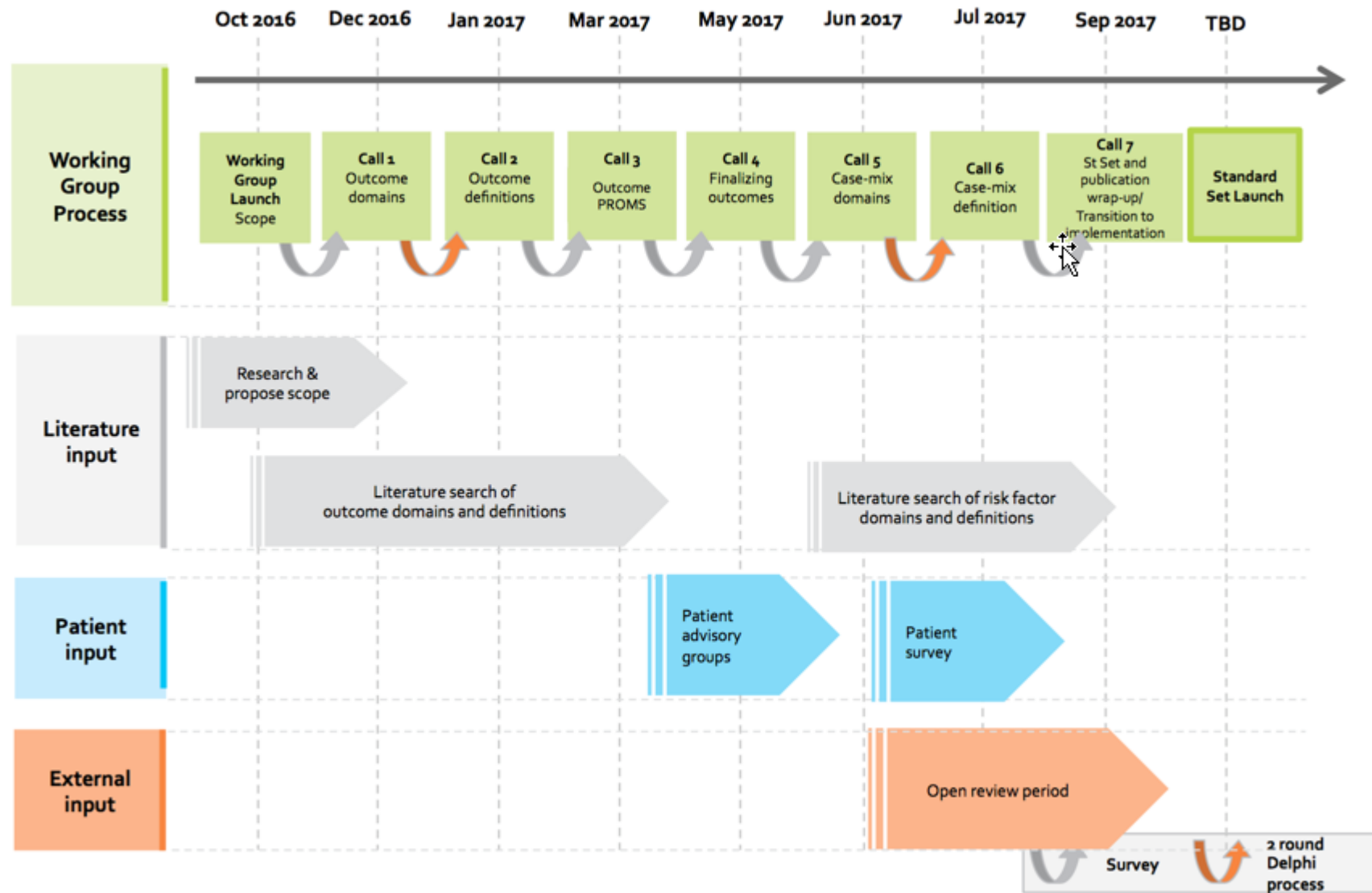
2	Registries search	
Number of hypertension specific registries/databases identified		15
Total inaccessible		3
Total included		12

Outcome domains to consider (patient-centred):

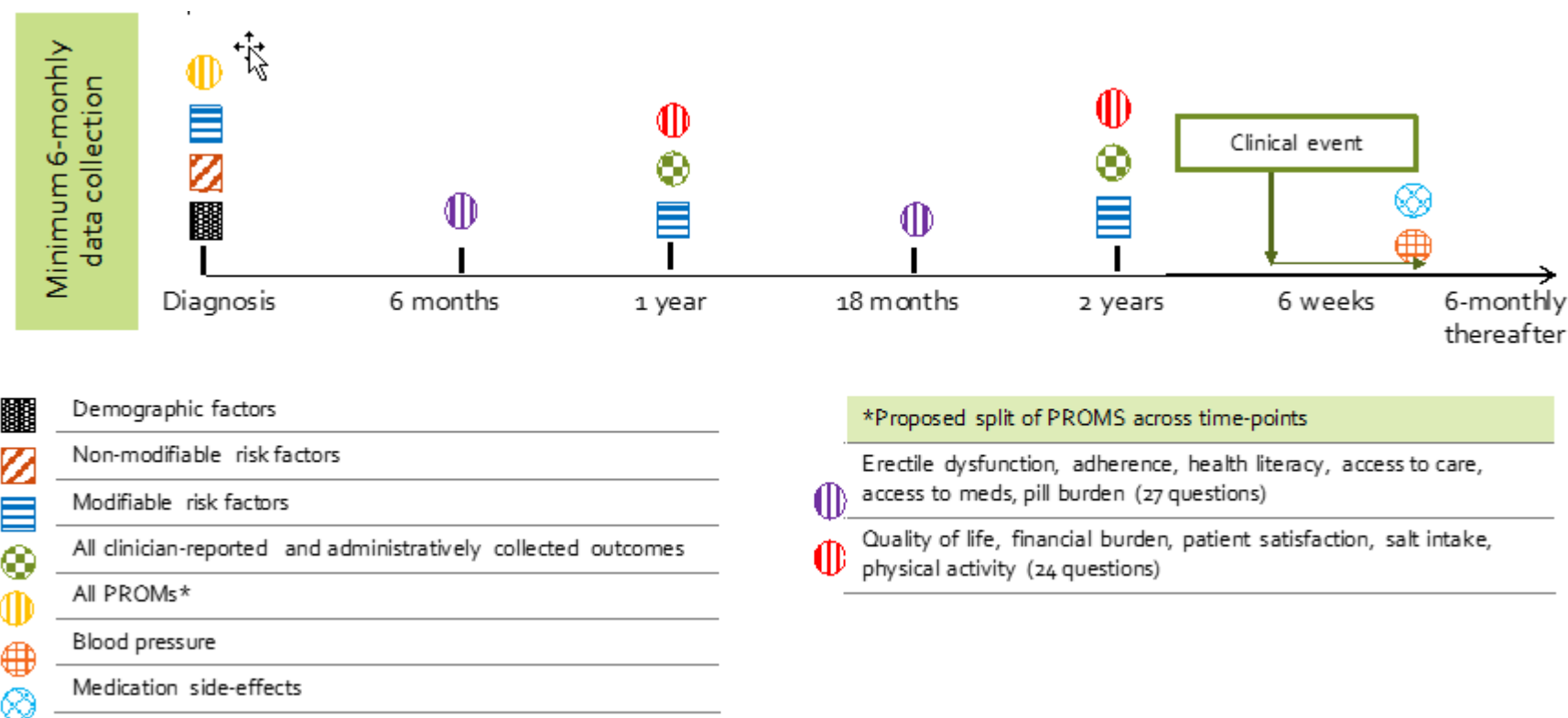
We need to recommend a *minimum* set of outcomes for all providers to track in routine care

Category	Include?	Nice to have?	Not recommended?
Tier 1 Health status achieved or retained	<ul style="list-style-type: none"> • Patient survival (cardiovascular) • Blood pressure • Global cardiovascular risk • HRQoL • Satisfaction • Mood / Anxiety / Depression • Sexual dysfunction • Empowerment / Autonomy • Self-efficacy/ Self-management • Social role disability • Discontinuation of treatment 	<ul style="list-style-type: none"> • Independence • Wellbeing 	<ul style="list-style-type: none"> • Physical functioning • Patient survival (all cause)
Tier 2 Process of Recovery	<ul style="list-style-type: none"> • Adherence • Falls • Acute adverse events from treatment / medication side effects • Hospitalisation • Hypertensive crisis • Smoking cessation 	<ul style="list-style-type: none"> • Bradycardia / Heart rate / • Hypotension • Dizziness • Fatigue • Cough • Urinary problems • Oedema • Sleep quality • Carotid artery damage • Abdominal aortic aneurysm 	<ul style="list-style-type: none"> • Arthralgia • Arrhythmia • Myalgia • GI complaints • Cold symptoms • Headaches • Palpitations • Back pain • Bronchitis • Nausea • Flushing • Diarrhoea • Dyspnoea • Urticaria

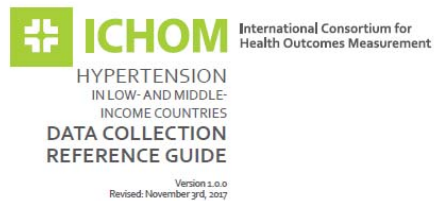
Timeline of Standard Set development



Recommended timeline of data collection for outcomes and case-mix factors for patients with hypertension







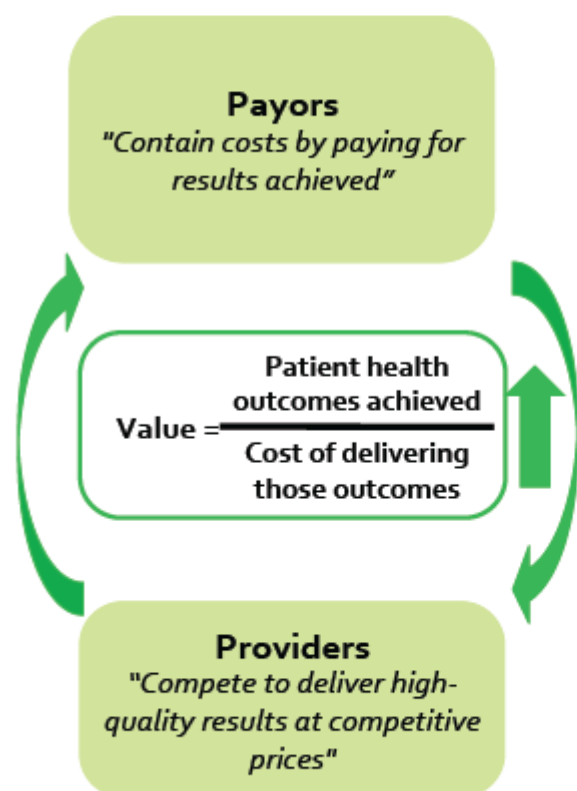
Reference guide



Flyer

ICHOM is founded on the principle of value-based health care

We believe in a model where value is
at the center of health care...



... which will impact every stakeholder



Patients will **choose their provider** based on its expected outcomes and their share of the cost



Providers will **compete** to deliver superior outcomes at competitive prices



Payors will **negotiate contracts based on results** and encourage innovation to achieve those results



Suppliers will **market their products on value**, showing improved outcomes relative to costs

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