Comparative Effectiveness and Patient-Centered Outcomes Research:

Enhancing Uptake and Use by Patients, Clinicians and Payers

January 26-27, 2017

DAY 2

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In Action: Dissemination and Uptake of CER/PCOR

Elaine Morrato

Nilay Shah

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In Action: Dissemination and Uptake of CER/PCOR Evidence

A Guiding Framework from Implementation Science and Case Study Application

Elaine H. Morrato, DrPH MPH CPH
Interim Dean | Associate Dean for Public Health Practice
Associate Professor, Health Systems, Management and Policy

CER/PCOR Conference: Enhancing Uptake and Use by Patients, Clinicians and Payers
January 26-27, 2017

Disclosure

- Colorado Clinical and Translational Sciences Institute (CCTSI) NIH/NCATS UL1TR001082
- CTSA Accrual to Clinical Trials NIH/NCATS UL1TR001857
- Innovation-Corps@CTSA NIH/NCATS UL1TR001417
- Center for American Indian and Alaska Native Diabetes Translational Research NIDDK P30 DK092923
- Problem-Solving Skills Training for Clinicians Providing Psychosocial Care in Pediatric Oncology NCI R25 CA183725
- FDA Special Government Employee, advises on issues of drug safety and risk management implementation.

The content is solely the responsibility of the presenter and does not necessarily represent the official views of the National Institutes of Health or the Food and Drug Administration.

Implementation Science (D/I)

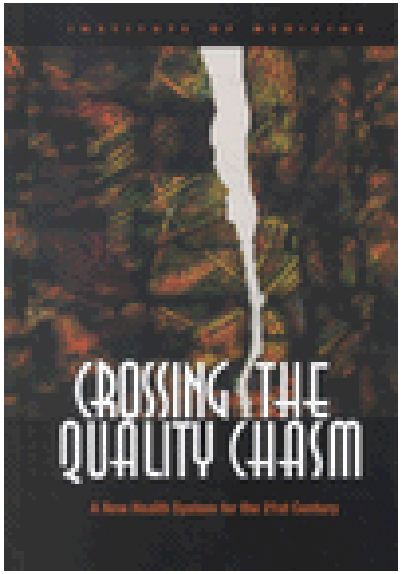
Dissemination (D) is the targeted distribution of information and intervention materials to a specific public health or clinical practice audience.

The intent is to spread knowledge and the associated evidence-based interventions.

Implementation (I) is the use of strategies to adopt and integrate evidence-based health interventions and change practice patterns within specific settings.

The intent is to promote adoption by an individual, organization or community to commit to, initiate, and sustain use of evidence-based practices.

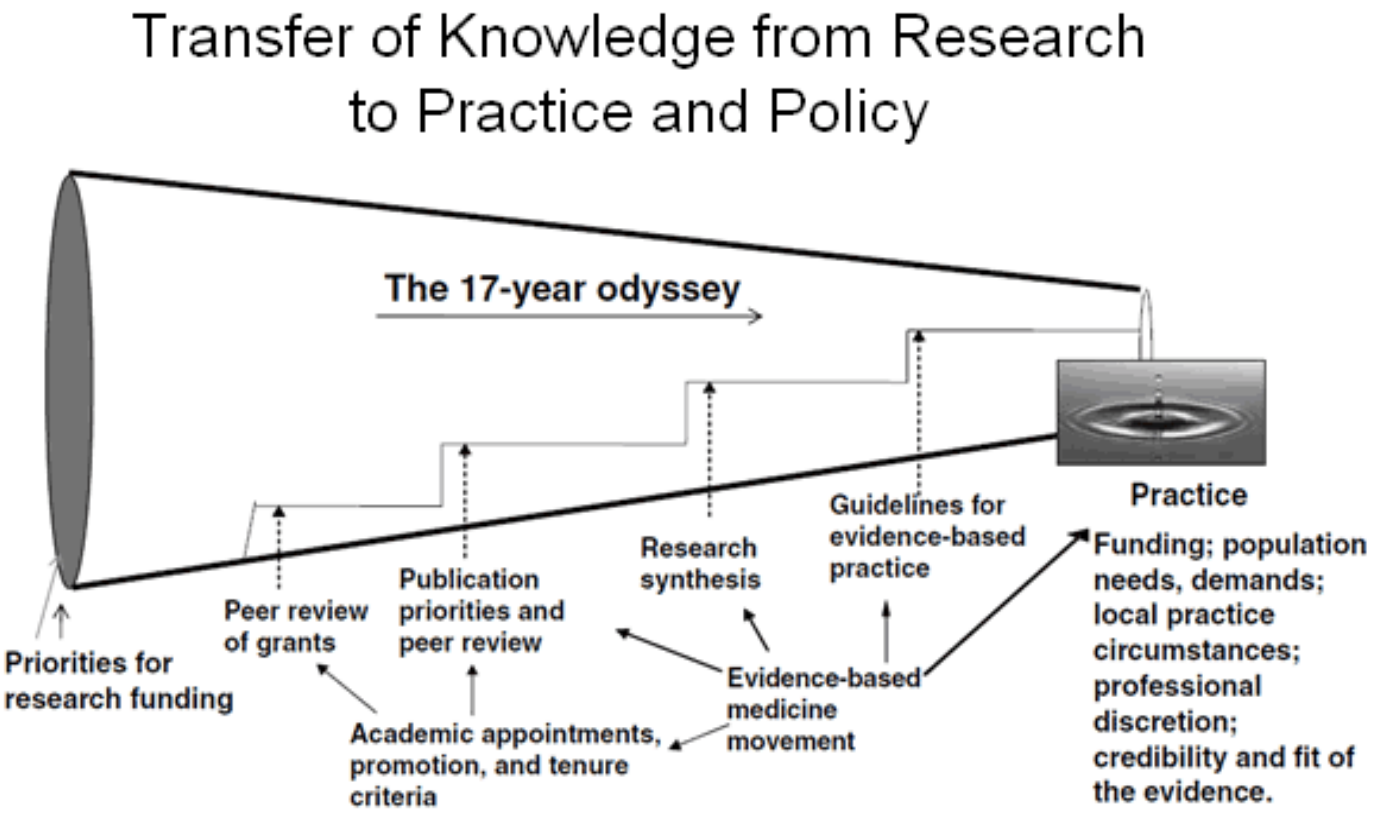
Rabin in Dissemination and Implementation Science in Health (2012)



"Scientific knowledge about best care is not applied systematically or expeditiously to clinical practice. It … takes ***an average of 17 years*** *for new knowledge generated by randomized controlled trials to be incorporated into practice, and even then* ***application is highly uneven****."*

-- Institute of Medicine (2001)

Implementation Challenge: a leaky pipeline



Green LW, Ottoson, J, Garcia C, Robert H. Diffusion Theory and Knowledge Dissemination, Utilization, and Integration in Public Health. *Annu. Rev. Public Health* (2009)

An implementation science framework: Diffusion of Innovation Theory

1. **Innovation.** Perceived value.
2. **Communication Channels.** Mass media vs. interpersonal channels.
3. **Time and the Adoption Process.** Early vs. late adopters.
4. **Social System.** Setting and group norms.

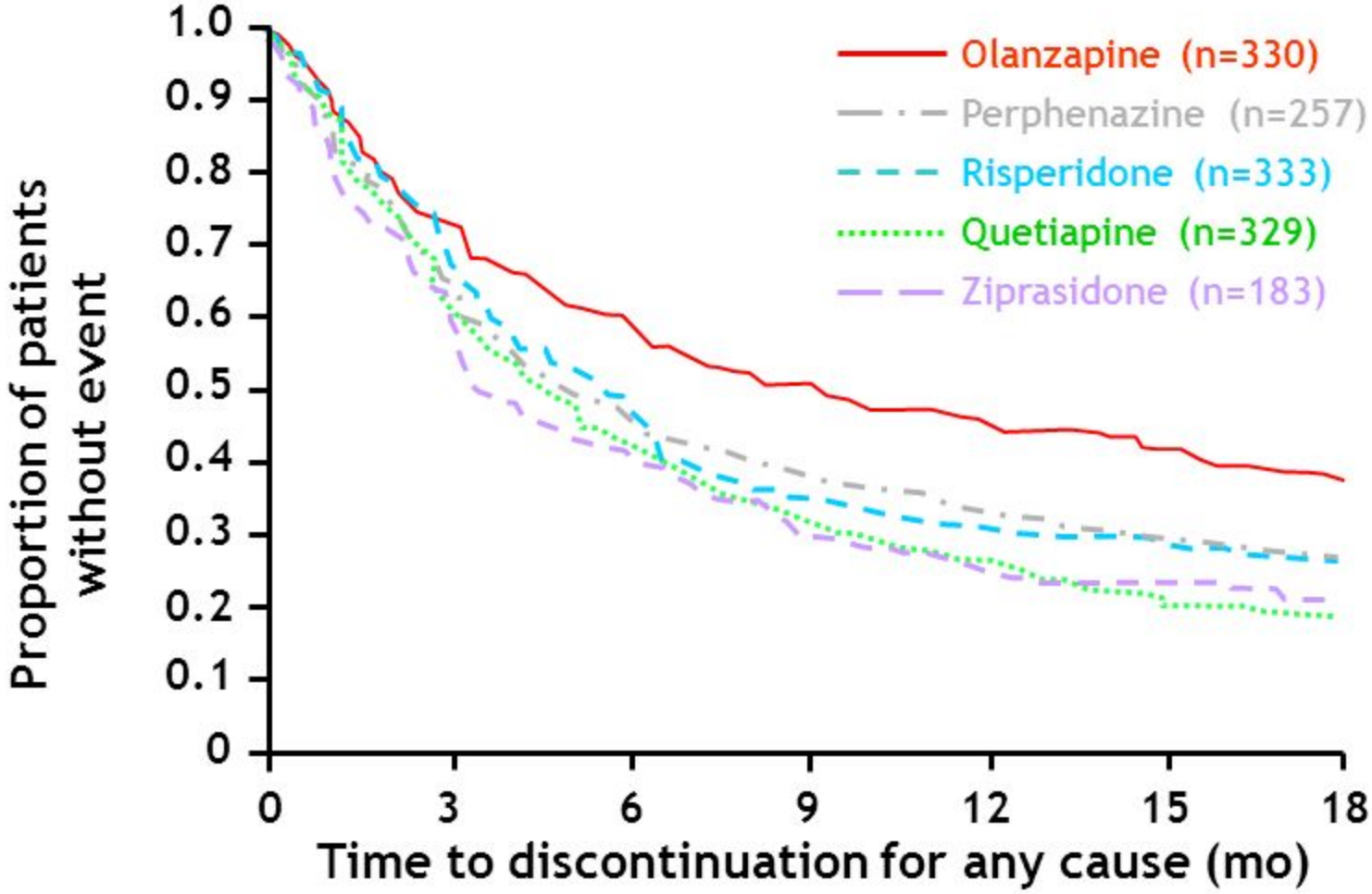
Developed by E.M. Rogers in 1962, is one of the oldest social science theories. It originated in communication to explain how, over time, an idea or product gains momentum and diffuses (or spreads) through a specific population or social system.

CER/PCOR case application

Uptake of metabolic screening and monitoring for patients taking antipsychotic medication

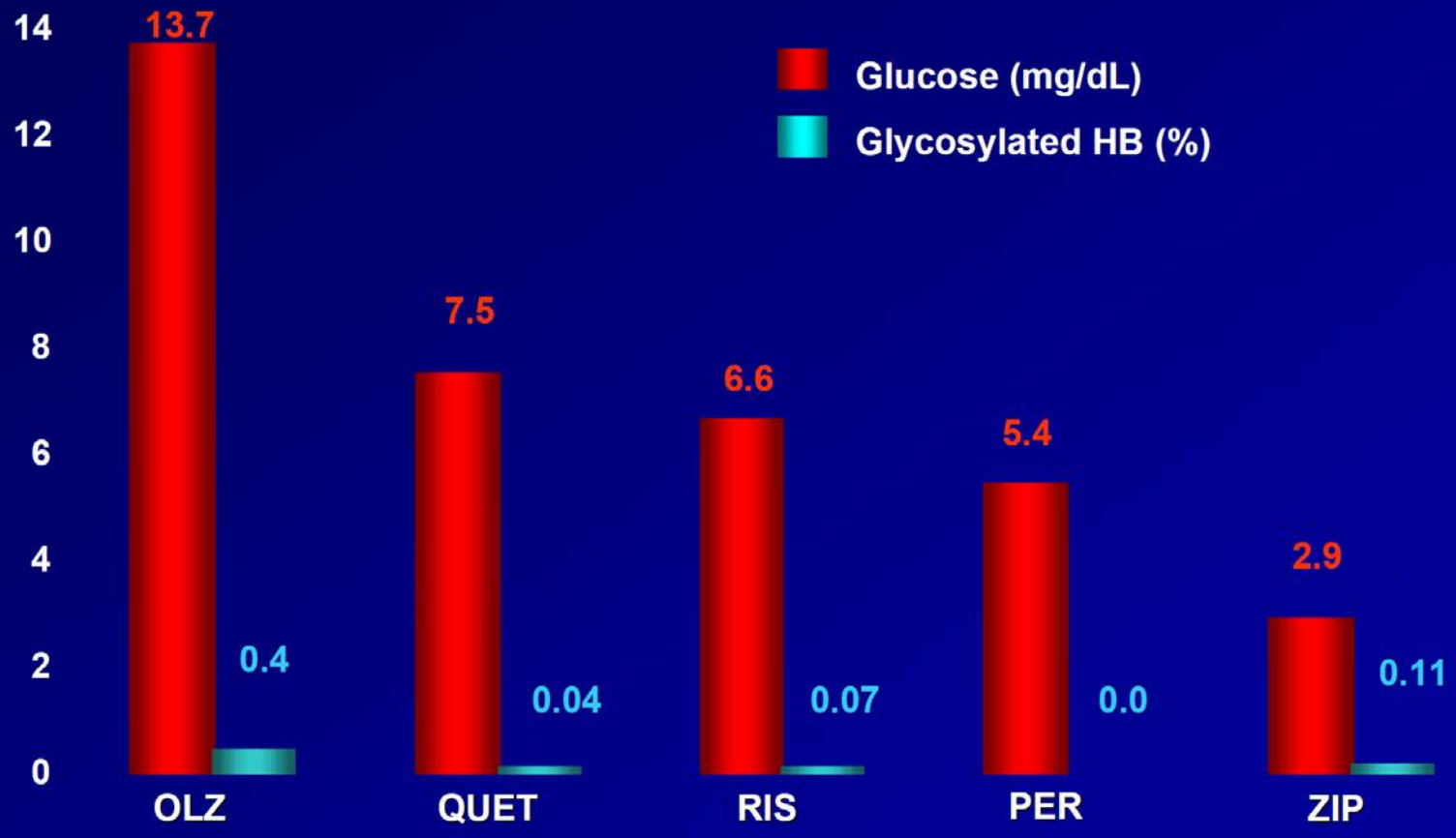
[*derived from the landmark NIMH-funded Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Study*]

CATIE-Schizophrenia Trial: All- Cause Discontinuation



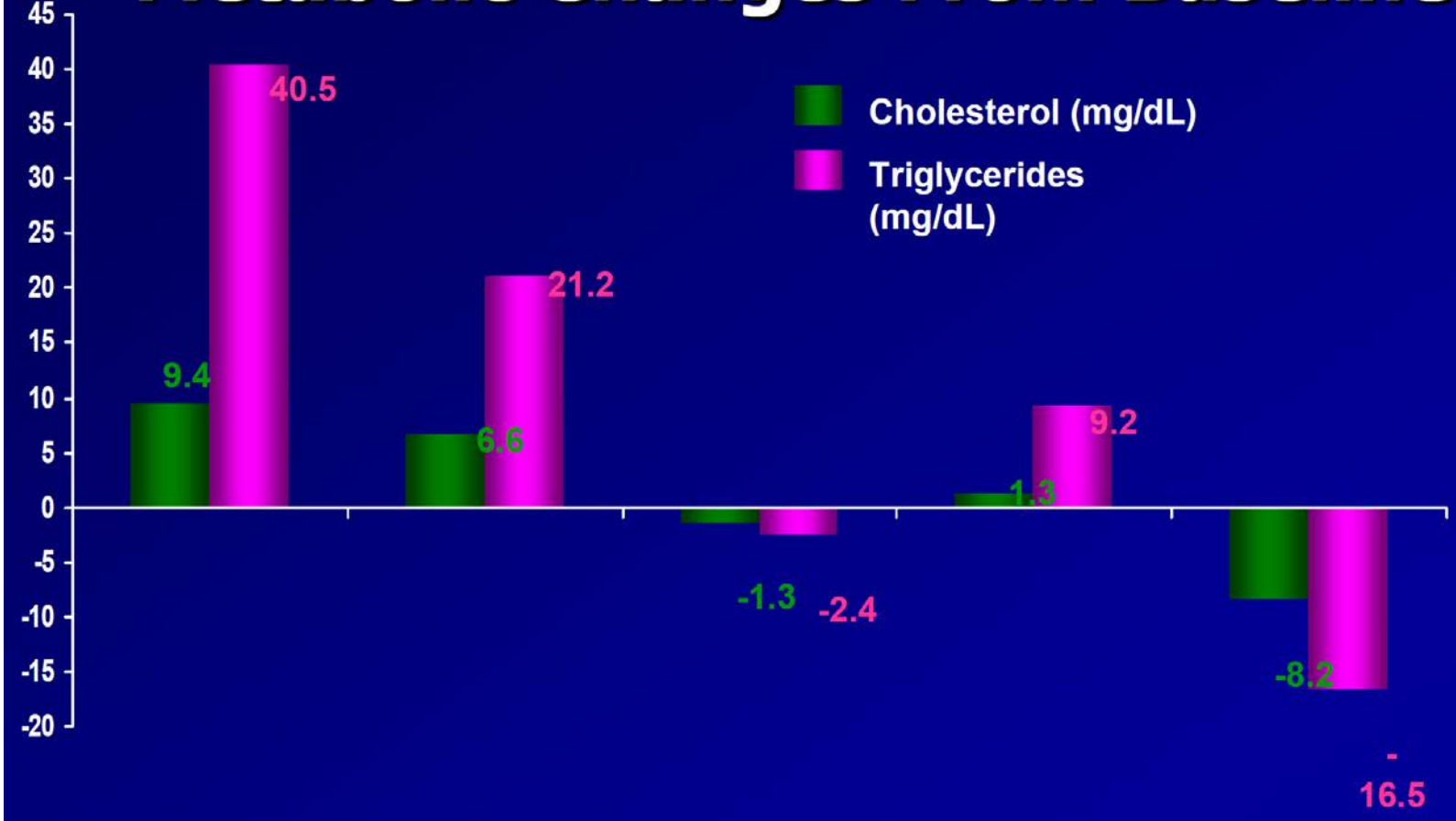
Lieberman JA et al. *N Engl J Med.* 2005;353:1209-1223.

CATIE Results: Metabolic Changes From Baseline



NEJM 2005 353:1209-1223

CATIE Results: Metabolic Changes From Baseline



NEJM 2005 353:1209-1223

Metabolic disorders are highly prevalent. Baseline rates of under-treatment are high.

Diabetes

- Prevalence 10.4%
- Non-treatment 30.2%

Dyslipidemia

- Prevalence 63.3%
- Non-treatment 88.0%

Hypertension

- Prevalence 33.2%
- Non-treatment 62.4%

Schizophrenia Research 86 (2006) 15-22

1. Innovation

Faster adoption with….

- Greater perceived relative advantage
- Compatibility with existing systems & behaviors
- Lower complexity
- Trial use
- Observable behavior

Case application: metabolic screening / antipsychotics

D/I Strategy	D/I Tactics	Lessons Learned
Demonstrate relative advantage.	Increased morbidity and mortality; years of life lost Dissemination of need-gap (scientific + pharma) Synthesized literature (2005+) Medical guidelines (2004+) FDA class language (2008+)	Effective – raised awareness, but… trade-off with efficacy. Focused primarily on patients with schizophrenia; CMHCs. Primarily targeted the psychiatric audience. Inconsistencies in guidelines.
Make compatible. Reduce complexity.	Annual screening. A1C o.k. – fasting not required Integrated care models. 'Health Homes' (ACA, 2012)	Limited reach (VA, Medicaid and public systems). Fragmented - reliant on early adopter systems.
Promote trial use.	Screening fairs (pharma) NIMH funding for interventions. (2012+)	Fragmented – funding not coordinated.
Make behavior observable.	Localized QI initiatives. NCQA HEDIS measure (2014/2015)	Fragmented - reliant on early adopter systems.

2. Communication

- Knowledge transfer precedes behavior (necessary but not sufficient)
- Channels and media mix
  - Mass media channels offer rapid and efficient means of creating awareness & knowledge.
  - Interpersonal communication is more effective in persuading individuals to change behavior.
- Change agents
  - Transfer of ideas occurs faster among individuals with shared professions, education & social status
  - Increases the likelihood of information exchange and adoption.

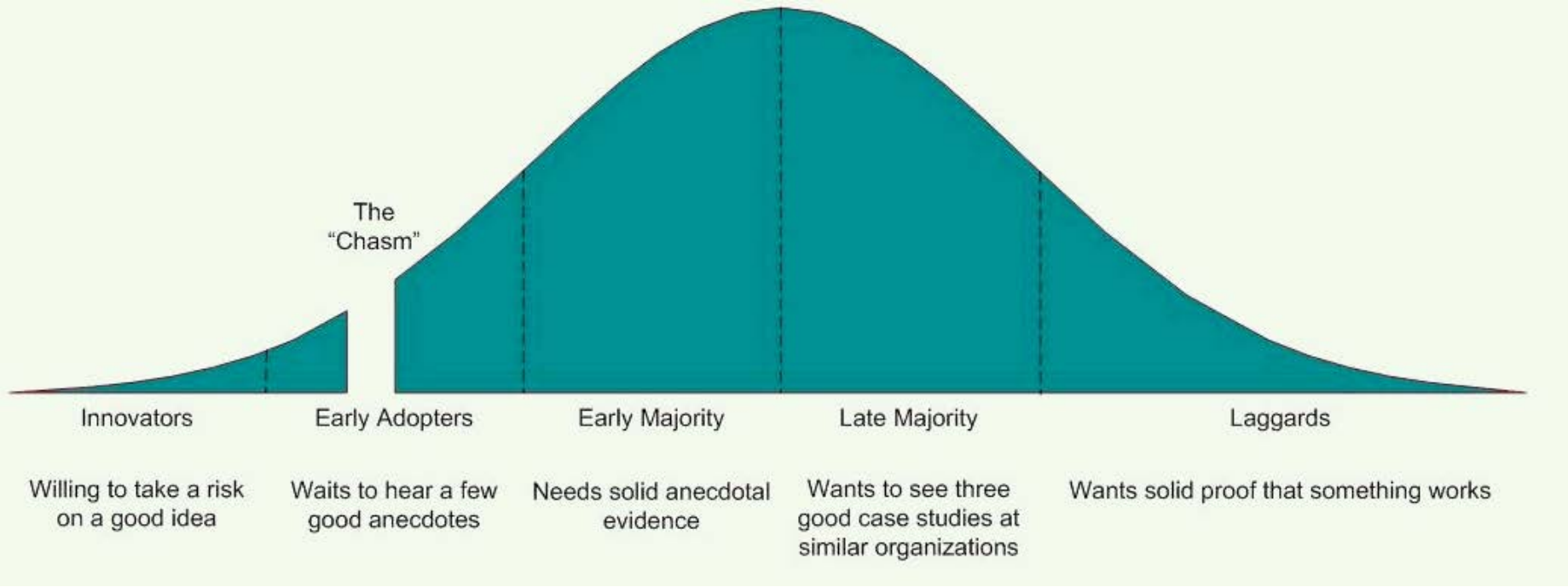
Case application: metabolic screening / antipsychotics

D/I Strategy	D/I Tactics	Lessons Learned
Mass communication.	FDA Warning Scientific literature Pharma advertising (Pfizer, BMS) CME: on-line	Framed as an issue for schizophrenia patients ('on label' usage)
Interpersonal communication.	CME: in-person Pharma promotional activities (Pfizer, BMS).	Primarily targeted individual 'high' prescribers (psychiatric) …. waned over time.
Support change agents to spread evidence.	Medical liaisons: CME and speaker engagements (Pfizer, BMS).	Pharma-supported. Wide-spread use of this strategy has declined over time. 'Academic Detailing' focused more on reducing off-label use and polypharmacy.

3. Time and the adoption process

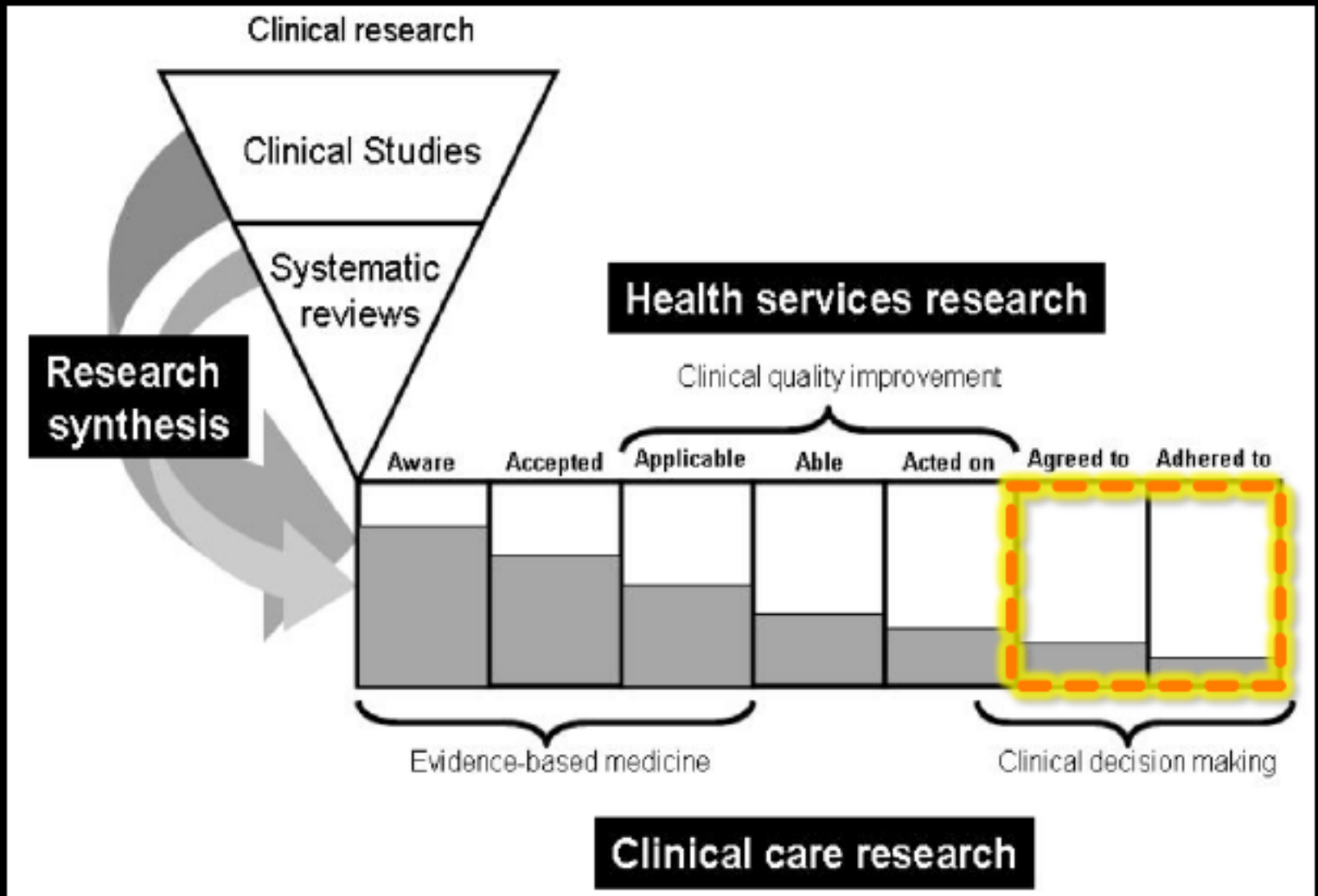
The adoption process involves several phases: (1) knowledge, (2) persuasion, (3) decision, (4) implementation and (5) confirmation.

Individuals in a social system can be categorized based on their relative speed of adoption versus their peers.



Early adopters are:

- More highly interconnected through interpersonal networks
- Better able to cope with uncertainty
- Have greater knowledge and seek information more actively
- More likely to adopt a new behavior based on information from mass communication channels



Glasziou and Haynes ACP JC 2005

Case application: metabolic screening / antipsychotics

Early adopters: Medicaid / state departments of mental health / and VA health systems where rates of serious mental illness are higher and antipsychotics usage greater.

Where there was an organizational champion.

Missouri MO HealthNet (Medicaid)

Population Characteristics	U.S.	Missouri
General Health, %		
Fair or poor health	15	17
Frequent mental distress	10	11
Obesity	26	28
No exercise	23	26
Currently smoking	20	25
Diabetes	8	8
High blood pressure	28	29
High cholesterol	38	40
Medicaid Profile		
Number of enrollees, million	58.4	1.1
Enrollees, % of population	20	21
Type of enrollees, %		
Children	50	54
Adults	26	22
Elderly	10	8
Disabled	14	15

Sources: Centers for Disease Control, Kaiser Family Foundation

Dr. Joe Parks
Director, MO HealthNet
Formerly medical director for
The MO Dept. of Mental Health

2015 APA Achievement
Gold Award for Community-Based Program

Intention to screen for diabetes: MO HealthNet

	CMHC n=156	non-CMHC Psychiatry n=136	Primary Care n=499	Other n=133
Would 'Definitely' Order a Blood Glucose Test, %				
Baseline visit (drug initiation)	56.6	45.6	39.1****	23.5****
One-year Follow-up (continuous use)	78.3	61.0***	60.2****	30.5****
Advocacy for Screening				
Promoters[a]	76.2	61.8	49.4****	32.8****

Significance denotes differences between CMHC and each specialty tested by Pearson's chi-square test of association and adjusted for multiple comparisons with the Bonferroni method ** $p<0.05$, *** $p<0.01$, **** $p<0.001$.

[a] Promoters are defined as providers who responded 9 or 10 (on a 10 point scale, with 10 being "Extremely Likely") to "How likely are you to recommend glucose testing for adults taking antipsychotics to a colleague?".

Morrato, et al. *Psych Serv* (2015)

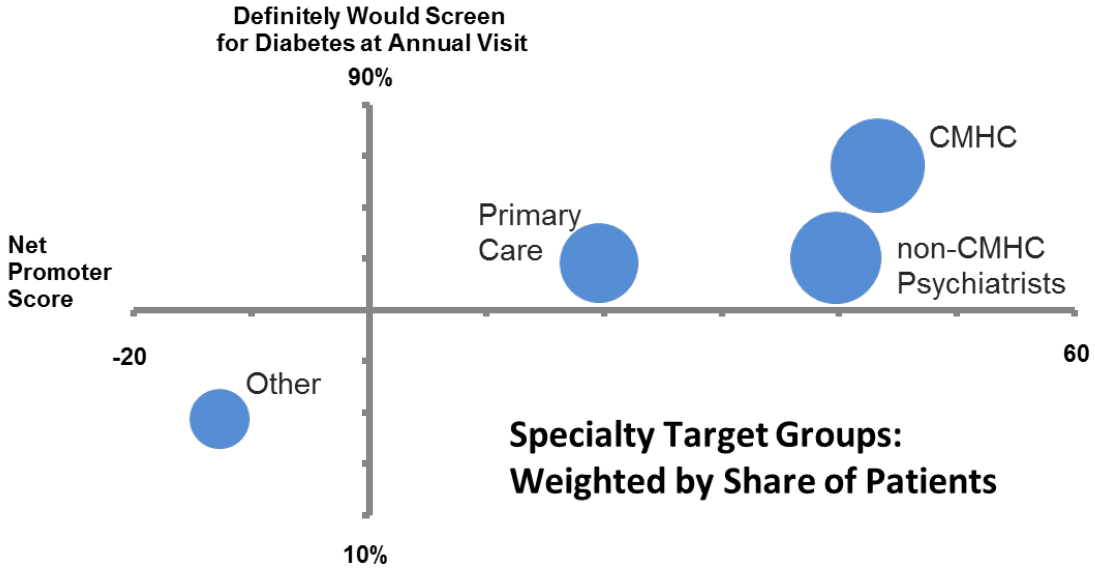
Who to target?

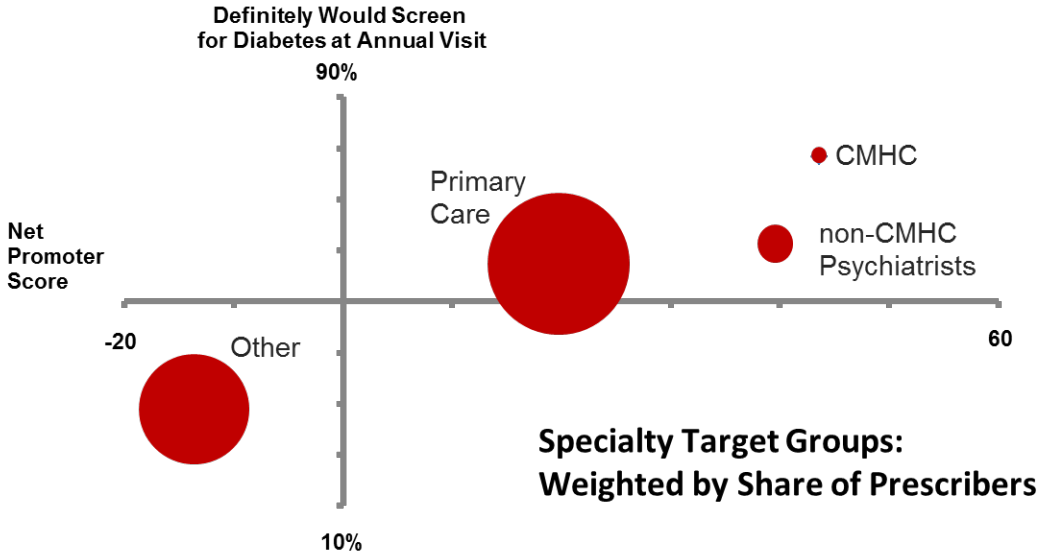
PCPs and Other providers -- greatest potential for population health impact

Lowest intention of screening and advocacy

Large segment

- 42% of patients
- 85% of prescribers





Net Promoter Score is defined as the percent of providers who responded 9 or 10 (on a 10 point scale, with 10 being “Extremely Likely”) to “How likely are you to recommend glucose testing for adults taking antipsychotics to a colleague?” less the percent who responded 6 or lower.

Population-based metabolic testing rates: MO HealthNet

	Primary Cohort *New Users*	Secondary Cohort *Survey Responder*
	Column-% (n/N)	**Column-% (n/N)**
Annual testing rates among new users of antipsychotics		
Glucose	79.6 (7413/9316)	79.0 (1433/1813)
Lipid	41.2 (3841/9316)	43.7 (793/1813)
Annual glucose testing among new users of antipsychotics without diabetes		
No. of ascertainable type 2 diabetes risk factors		
None	68.1 (2296/3373)	65.4 (467/714)
1	76.1 (1789/2350)	79.6 (354/445)
2	87.5 (997/1140)	87.8 (166/189)
3 or more	92.8 (779/839)	94.9 (129/136)

Data source: Missouri Medicaid administrative claims data, 2010-2012.

Annual test period = Index +/- 180 days.

Morrato, et al JAMA Psych (2016)

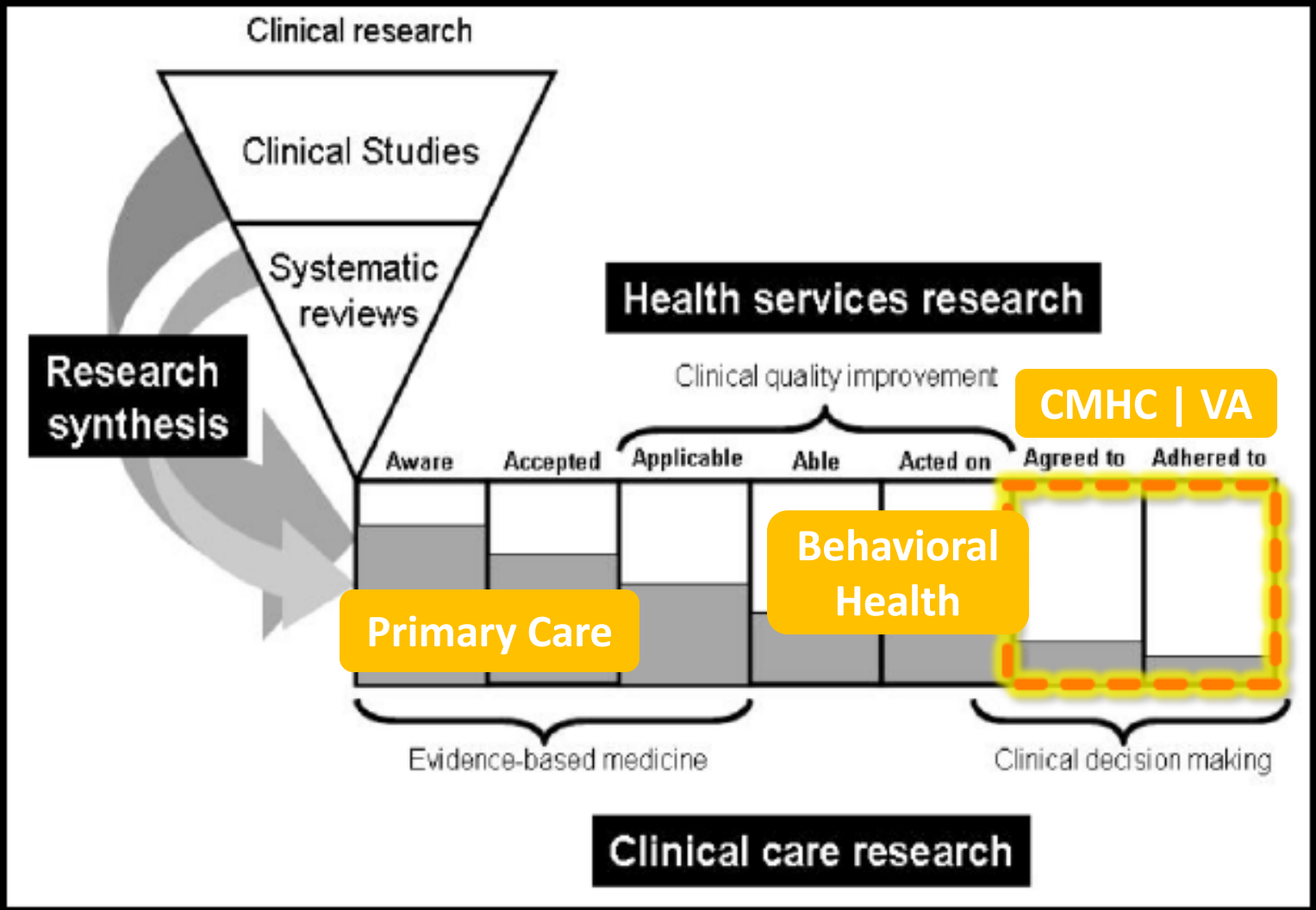
4. Social Setting

Public Health
Prevent. Promote. Protect.

- Individuals are more likely to adopt an innovation if more members of their personal network have adopted.
- Opinion leaders within social systems tend to be early adopters, especially if the system norms favor change.
- Denser social systems generally reflect a cohesive normative environment and may facilitate diffusion.

Case application: metabolic screening / antipsychotics

- **Opinion Leader Professional Society.** National Association of State Mental Health Program Directors Director
- **Opinion Leader Health Systems.**
  - Kansas Medicaid
  - MO HealthNet (2015 APA Gold Award)
  - VA/VISNs
- **Denser Social Systems.** Community Mental Health Centers.



Glasziou and Haynes ACP JC 2005

Implications for CER/PCOR Dissemination

1. **Is there sufficient evidence?**
   - Is 1 rigorous RCT sufficient?
   - Is it a preponderance of evidence?
   - By whose authority? (FDA, professional societies, AHRQ, P&T committees, NCQA HEDIS, PCORI, etc.)

A model for consideration:

AHRQ | USPSTF recommendations (clinical preventive services) [+ increased stakeholder involvement]

Implications for CER/PCOR Dissemination

2. Who "owns" dissemination and implementation?

- Single, national point of accountability?
- Who should be the sustaining 'convening', 'agenda setting' authority?
- Implement multi-stakeholder, public-private partnership, when possible

A model for consideration:

- Pharma brand or product manager
- U.S. Dept. of Health and Human Services.

Implications for CER/PCOR Dissemination

3. Approach as a sustained, dynamic series of D&I campaigns

- Multi-level, multi-channel interventions.
- Identify and target thought leaders and early adopters. Build a contagion effect.
- Identify competing market and behavior forces. Strategize and intervene proactively. Adaptive D/I designs.
- Ensure sustained (and sufficient) funding

A model for consideration:

- Pharma promotion and marketing efforts for a product or therapeutic category

Implications for CER/PCOR Dissemination

4. Adopt time urgency

- Design for dissemination. Broad stakeholder engagement. Anticipate barriers. Provide solutions-value (e.g., I-Corps).
- Work dissemination efforts in parallel with evidence generation. "Soften the market."
- Use real-time data-based D/I surveillance – from Day 1
- Faster-nimbler D/I funding. Eliminate/reduce funding gaps in stages of dissemination.

A model for consideration:

- PCORI's engagement pipeline approach (expand so more intentional in multi-stakeholder involvement)
- A "K00/R99-like" funding mechanism (*A Pathway to Dissemination Award*?)

Thank you.

Elaine.Morrato@ucdenver.edu

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Dissemination and Uptake of Comparative Effectiveness Research

Nilay Shah
Division of Health Care Policy and Research
Center for the Science of Health Care Delivery
Knowledge and Evaluation Research Unit
Mayo Clinic

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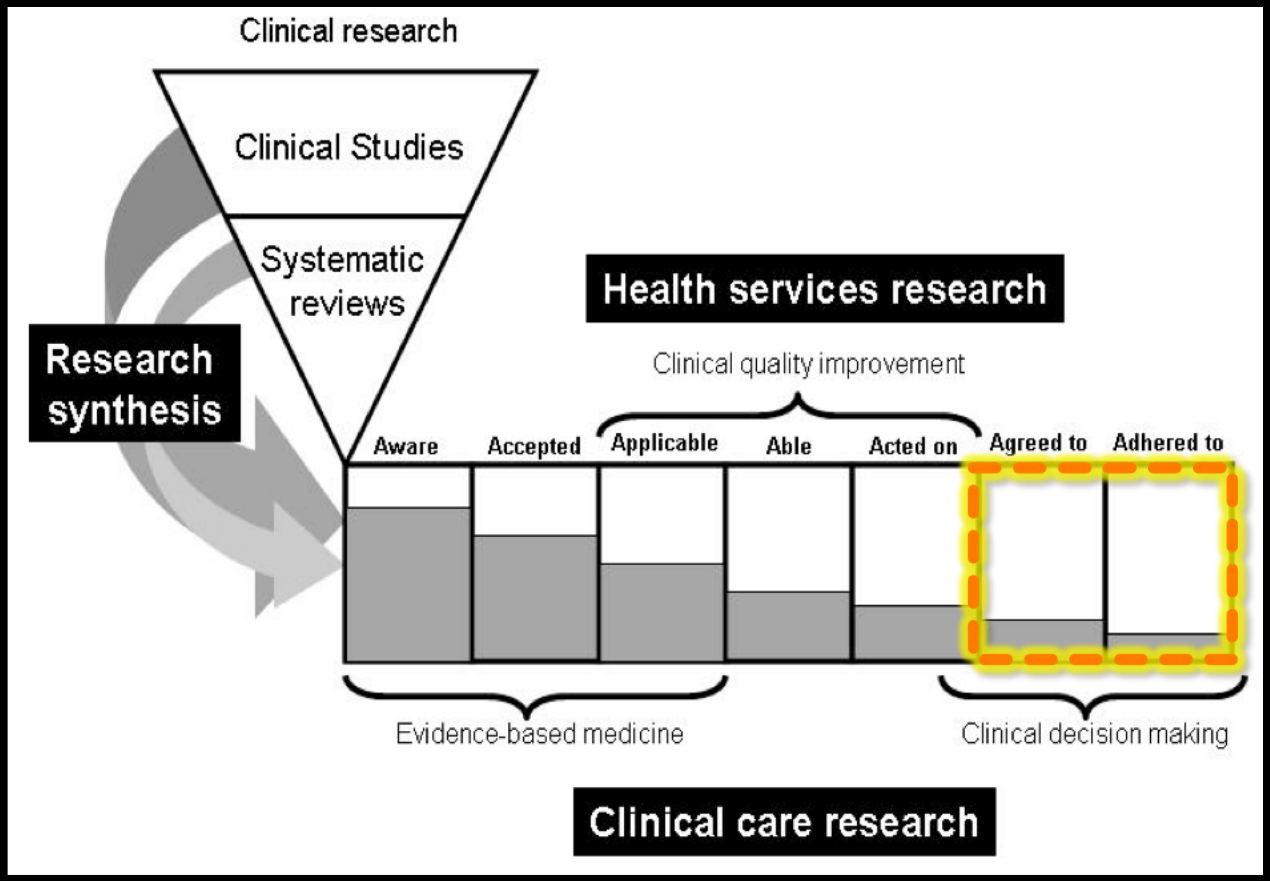
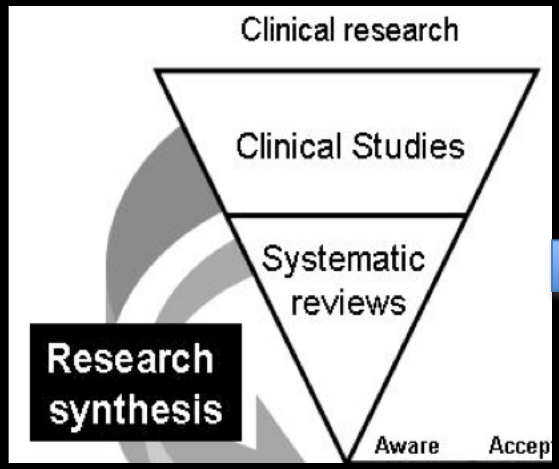
  - Foundation for Informed Medical Decision Making (FIMDM)
  - American Diabetes Association (ADA)
  - Mayo Clinic Foundation for Medical Education and Research
  - Mayo Clinic CCaTS

EBM ⟶ KT



Glasziou and Haynes ACP JC 2005



Systematic Review: Comparative Effectiveness and Safety of Oral Medications for Type 2 Diabetes Mellitus

Shari Bolen, MD, MPH; Leonard Feldman, MD; Jason Vassy, MD, MPH; Lisa Wilson, BS, ScM; Hsin-Chieh Yeh, PhD; Spyridon Marinopoulos, MD, MBA; Crystal Wiley, MD, MPH; Elizabeth Selvin, PhD; Renee Wilson, MS; Eric B. Bass, MD, MPH; and Frederick L. Brancati, MD, MHS

Background: As newer oral diabetes agents continue to emerge on the market, comparative evidence is urgently required to guide appropriate therapy.

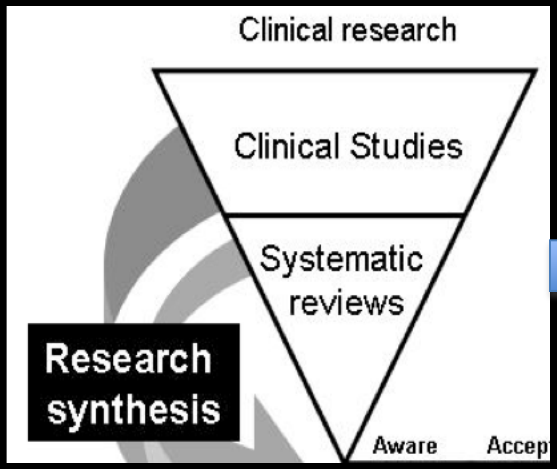
had a beneficial effect on high-density lipoprotein cholesterol levels (mean relative increase, 0.08 to 0.13 mmol/L [3 to 5 mg/dL]) but a harmful effect on low-density lipoprotein (LDL) cholesterol levels (mean relative increase, 0.26 mmol/L [10 mg/dL]) compared with

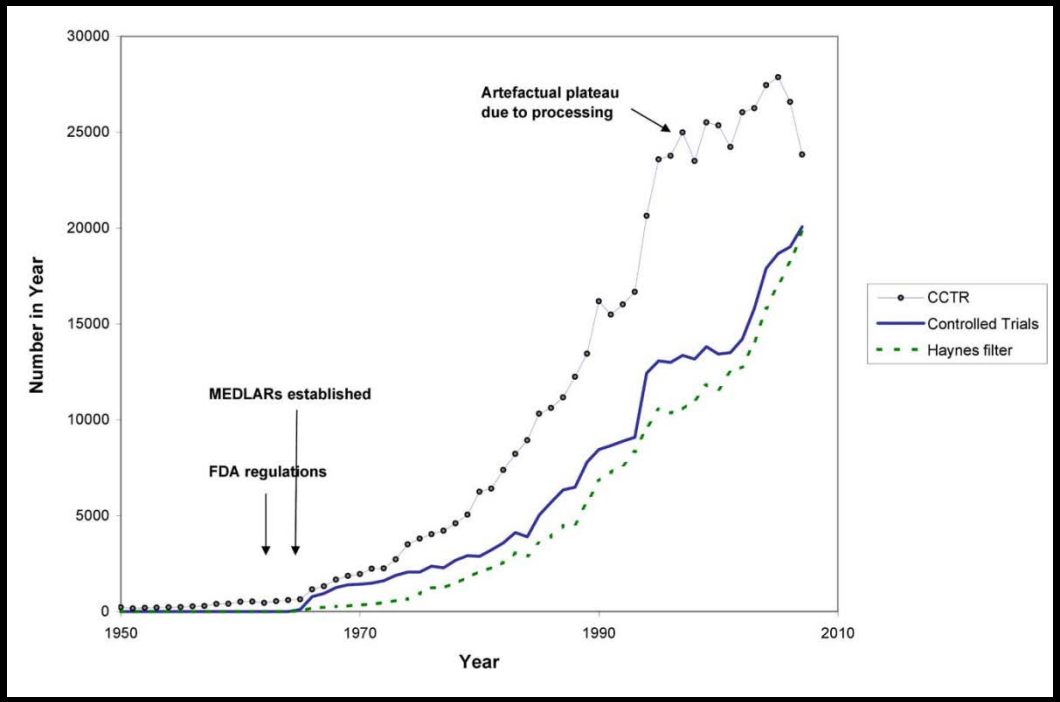
LESS IS MORE

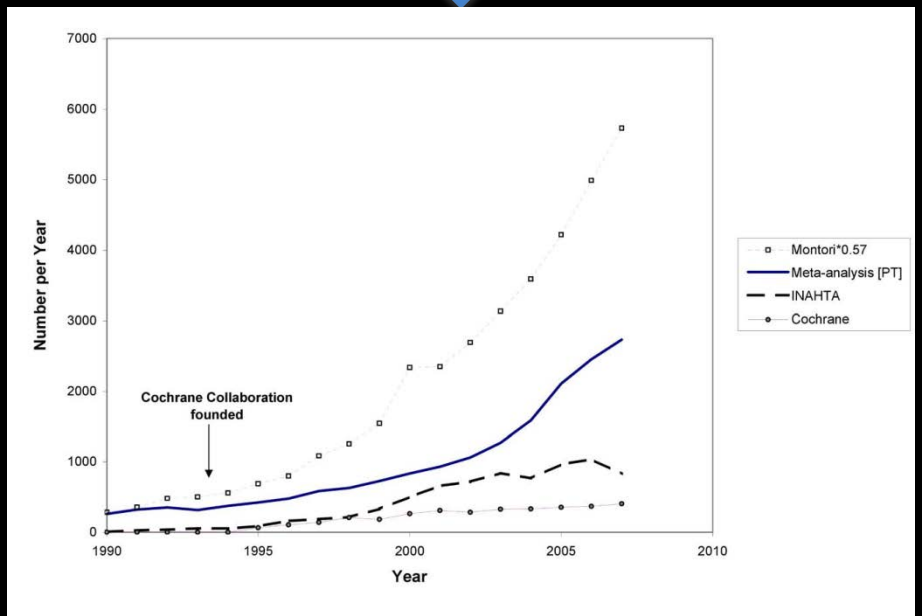
Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

Meta-analysis of Randomized Controlled Trials

Kathleen Stergiopoulos, MD, PhD; David L. Brown, MD

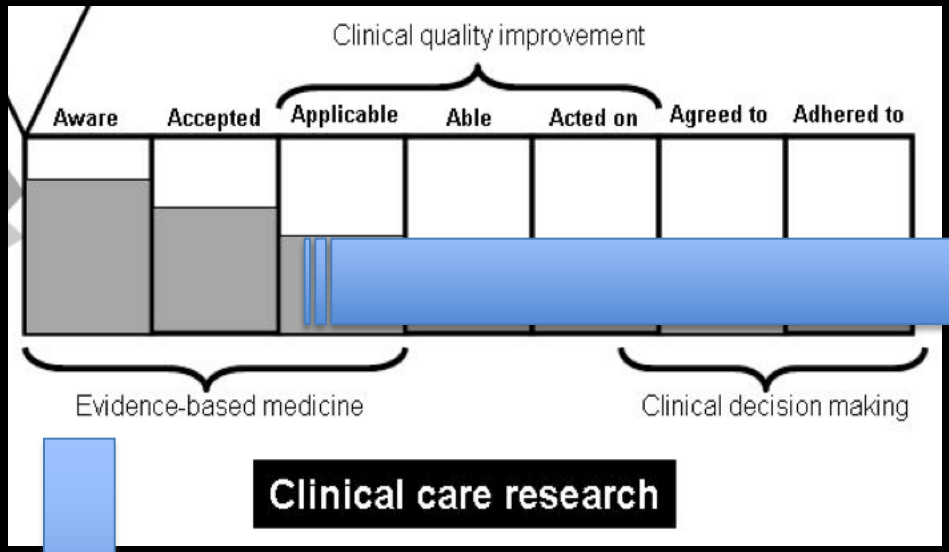


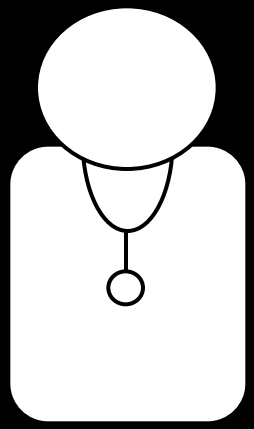




"There are now 75 trials and 11 systematic reviews of trials, per day…"

Bastian et. al, 2010
PLoS Medicine





National Cholesterol Education Program

ATP III Guidelines At-A-Glance Quick Desk Reference

1

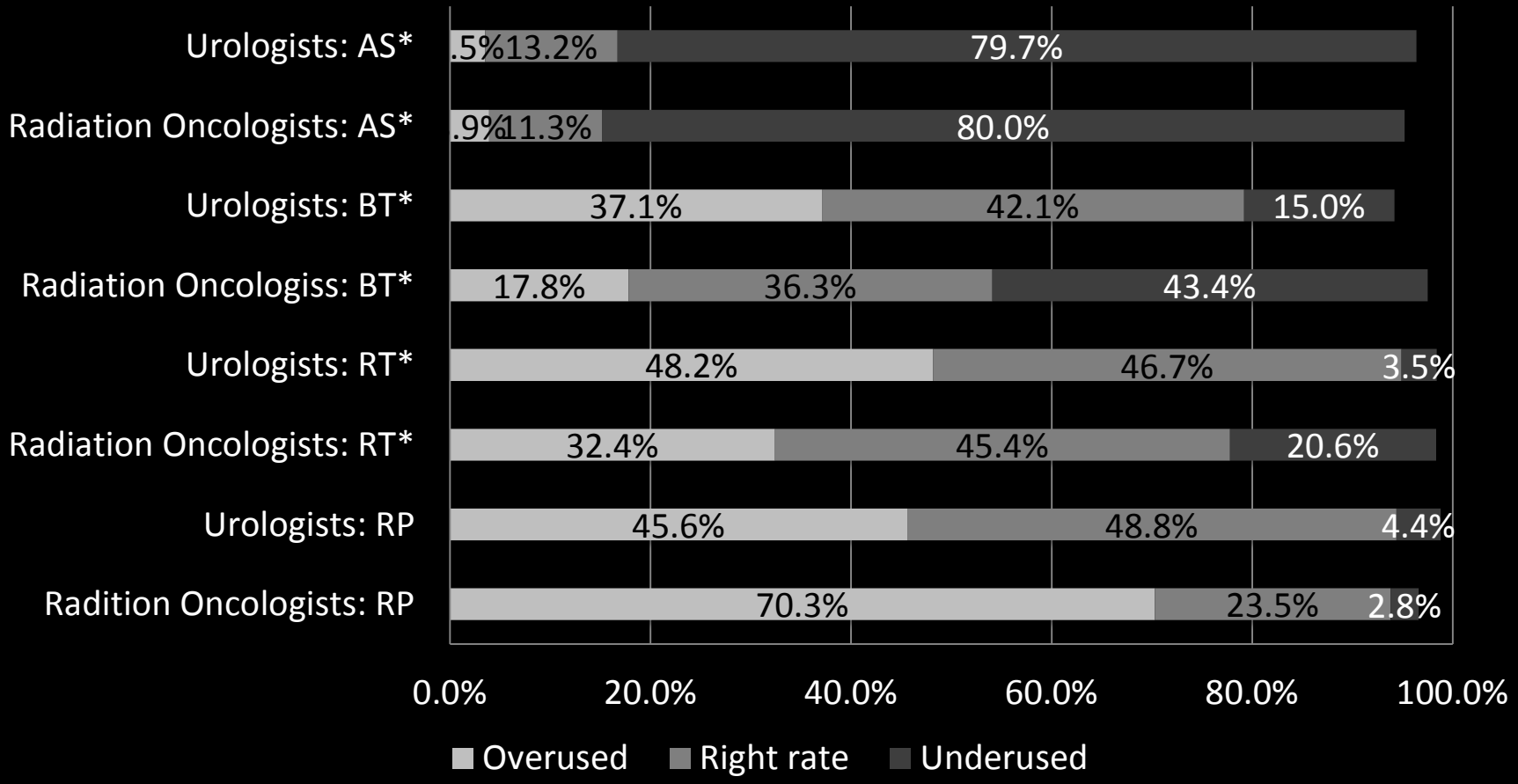
Step 1 **Determine lipoprotein levels–obtain complete lipoprotein profile after 9- to 12-hour fast.**

ATP III Classification of LDL, Total, and HDL Cholesterol (mg/dL)

LDL Cholesterol – Primary Target of Therapy	
<100	Optimal
100-129	Near optimal/above optimal

Source: IOM, *Best Care at Lower Costs*

Treatment of Low Grade Prostate Cancer



Kim SP et al. Prostate Cancer Prostatic Dis 2014

The Translational Challenge

Uneven delivery of effective care well-documented

Only 50% of effective interventions are reliably delivered…and it takes a long time

If we only focus on GENERATING more information on comparative effectiveness, without attending to how to IMPLEMENT it, we will not improve quality or value or provide return on CER investment.

CER Translation Gap

Study	Results	Practice	Translation
ALLHAT	Thiazide diuretics were superior in preventing cardiovascular disease events	ACE-inhibitors	No change
CATIE	Conventional antipsychotics were as effective as atypical antipsychotics for schizophrenia	Atypical Antipsychotics	No change
COMPANION	Compared to optimal medical therapy, both cardiac resynchronization therapy (CRT) and CRT plus defibrillator use improved survival, reduced hospitalization rates, and improved functional status in patients with moderate to severe heart failure	Medical therapy	Minimal change
COURAGE	Optimal medical therapy combined with percutaneous coronary intervention (PCI) had similar survival benefit and angina relief, compared to optimal medical therapy alone	PCI	Minimal/No change
SPORT	Surgery for lumbar spinal stenosis had better outcomes than nonsurgical treatment, according to the cohort study results	Surgical Treatment	No change

Source: Timbie 2012

Why?

Misalignment of financial incentives

Complexity of research

Biases in interpretation of results

Applicability of the evidence

Limited use of decision support

Source: Timbie 2012; Morrato 2013

JAMA Internal Medicine | Review | LESS IS MORE

Clinicians'
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A Systema

Tammy C. Hoffmann, PhD

VIEWPOINT

Surgical Decision Making
Challenging Dogma and Incorporating Patient Preferences

Karan R. Chhabra, MD
Department of Surgery, Brigham and Women's Hospital, Boston, Massachusetts.

Greg D. Sacks, MD, MPH, PhD
Department of Surgery, University of California at Los Angeles.

Justin B. Dimick, MD, MPH
Center for Healthcare Outcomes and Policy, University of Michigan, Ann Arbor; and Department of Surgery,

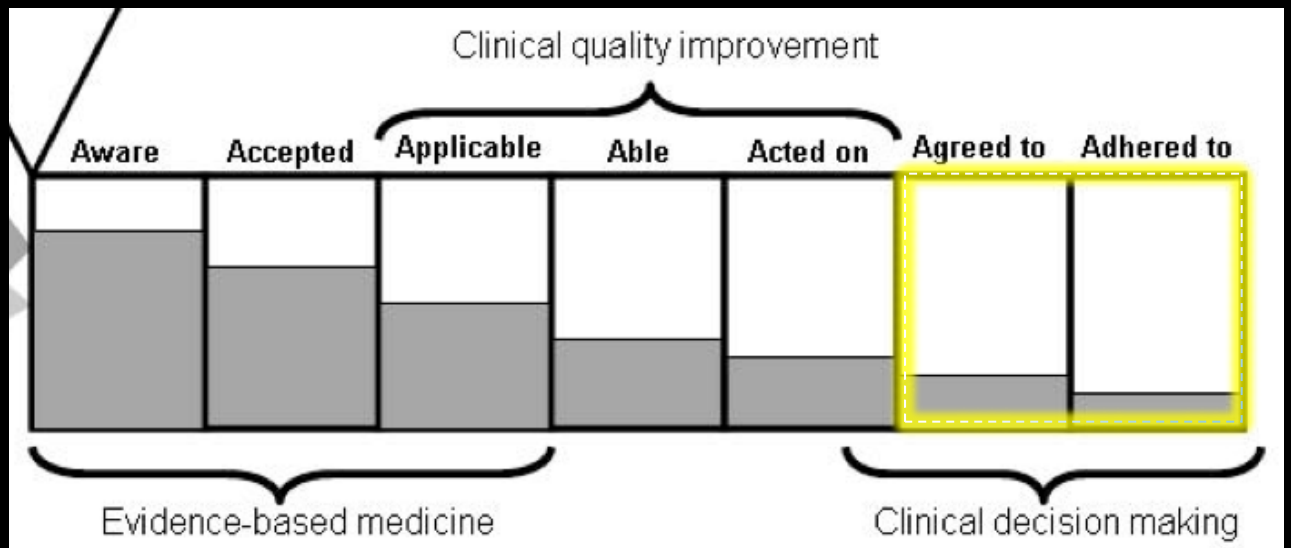
Three recently published randomized trials questioned the primacy of surgical management in 3 widely accepted operations: appendectomy for appendicitis,[1] colectomy for diverticulitis,[2] and knee replacement for osteoarthritis.[3] What these studies had in common—setting them apart from others in the past—is that they, in randomized fashion, compared commonly used operations with significantly less aggressive or nonoperative alternatives. In all 3 trials, the less invasive treatment proved both safe and effective—not necessarily as definitive as a major operation but potentially more desirable in other important ways. All 3 of these trials challenge surgical dogma—shifting accepted treatment approaches away from long-established surgical gold-standard treatments. But when considered more broadly, these trials may begin reshaping how the ing routine appendectomy" for uncomplicated appendicitis,[4] whereas others concluded that "it was a negative trial that should not change practice."[5] So how should clinicians and patients interpret the findings of these trials when not even experts can agree? The answer should involve an appreciation of shared decision making in surgery, which has been conspicuously absent from these debates despite its importance in other specialties. Shared decision making is a collaboration in which the physician explains treatment options, elicits values from the patient, and, importantly, guides the conversation toward a decision consistent with the patient's values and current evidence.

Shared decision making is particularly relevant because in all 3 studies neither treatment was superior across all outcomes. For one outcome, the traditional op-

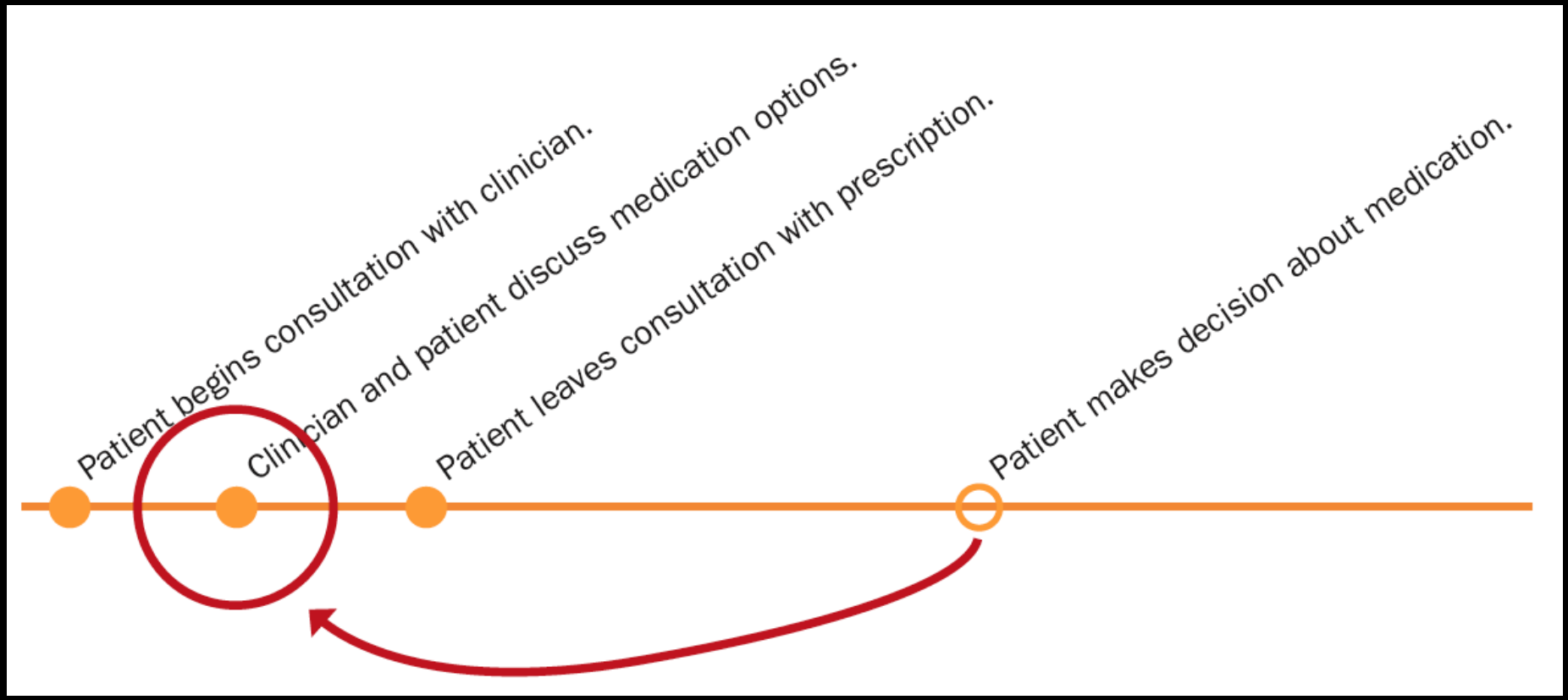
Table. Study Design, Results, and Interpretations of 3 Surgical Clinical Trials

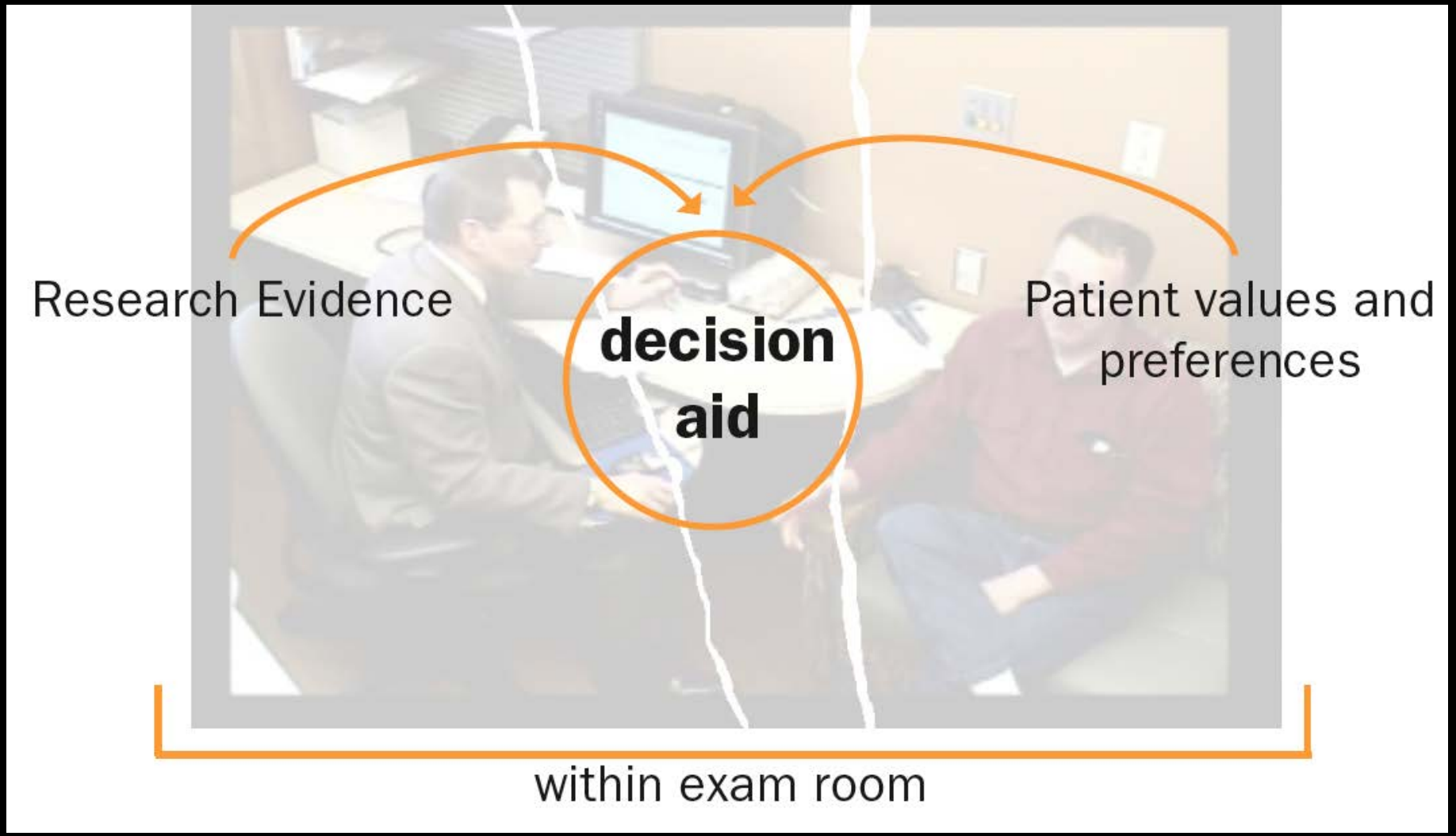
Study Name and Patient Population	Standard Treatment vs Experimental Alternative	Absolute Differences (Standard vs Experimental)		Interpretation	
		Primary Outcome	Secondary Outcomes	Study Authors	Hypothetical Patient
APPAC[1]: Uncomplicated appendicitis in adults	Open appendectomy vs antibiotics (3 d IV, then 7 d PO)	Freedom from recurrence of appendicitis within 1 y; 100% vs 72.7% (95% CI, 67%-78%)	Overall surgical complications (20.5% vs 2.8%, $P < .001$) Length of sick leave (19.0 d vs 7.0 d, $P < .001$)	Relapse rate of 27% with antibiotics did not meet noninferiority threshold of 24%, thus favoring surgery over antibiotics	"Antibiotics may allow me to avoid surgery entirely, or convert it to elective operation without increased risk of complications."
SCANDIV[2]: Perforated diverticulitis without feculent peritonitis	Colectomy (all types) vs laparoscopic lavage and interval colonoscopy	Severe complications within 90 d; 30.7% vs 26.0% ($P = .53$)	Reoperation (5.7% vs 20.3%, $P = .01$) QOL score (0.73 vs 0.75, $P = .32$) Stoma at 90 d (69% vs 16%, $P < .001$)	Colectomy preferable owing to lower reoperation rate	"Lavage would leave me less likely to need stoma but more likely to need a reoperation."
"A Randomized, Controlled Trial of Total Knee Replacement"[3] Moderate-to-severe knee osteoarthritis eligible for unilateral knee replacement	Total knee replacement followed by 12 wk of nonsurgical treatment (exercise, education, diet, insoles, pain medications) vs nonsurgical treatment alone for 12 wk	Clinically significant (15%) improvement in symptom score: 85% vs 68%	Knee replacement within 1 y (98% vs 26%) Serious adverse events: (22% vs 4%, $P = .05$)	Knee replacement associated with greater symptom relief but more adverse events	"Nonsurgical treatment can significantly improve my symptoms, without the risks of surgery."

Abbreviations: IV, intravenous; PO, by mouth; QOL, quality of life.

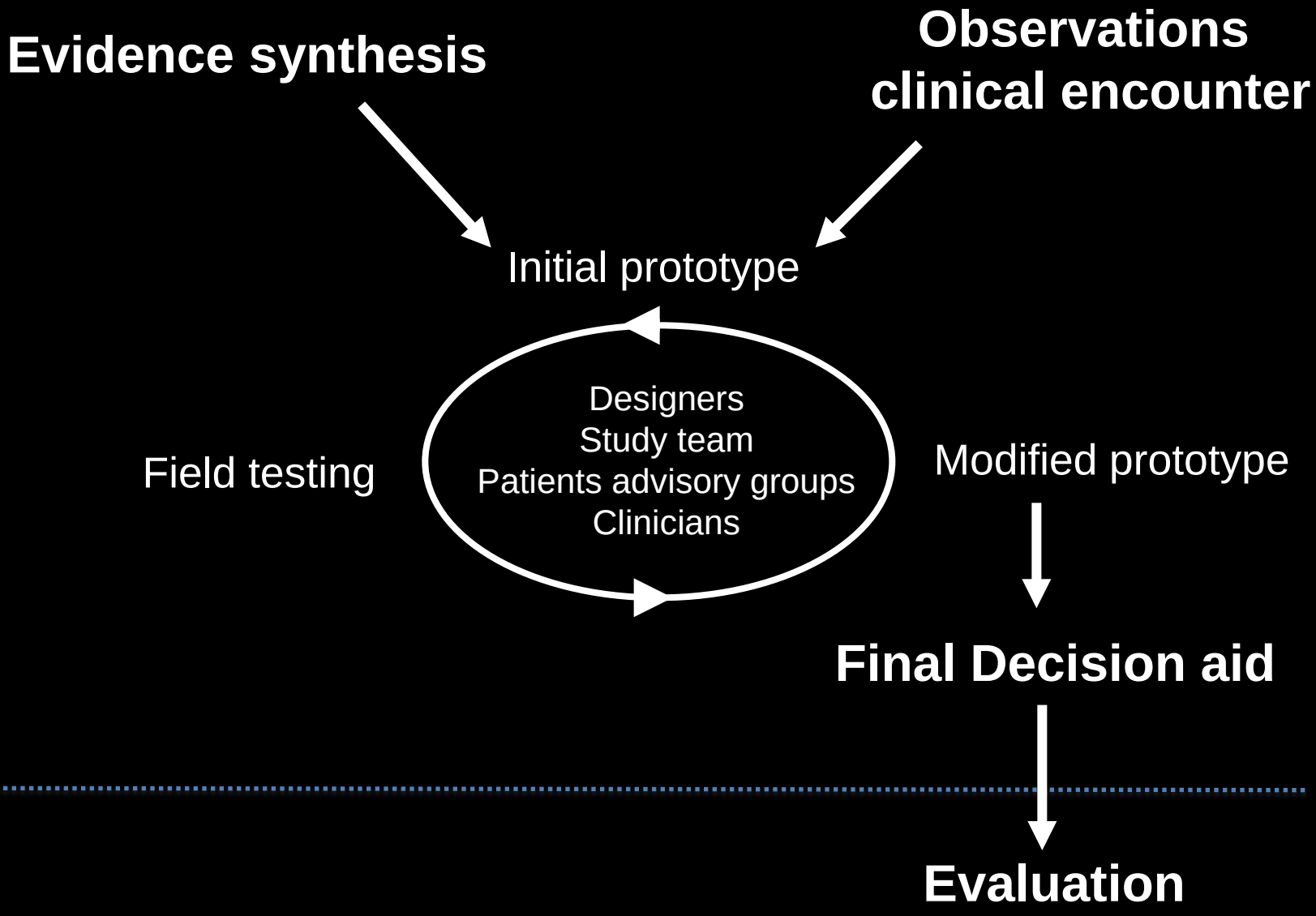


Clinical care research


Patient begins consultation with clinician.
Clinician and patient discuss medication options.
Patient leaves consultation with prescription.
Patient makes decision about medication.

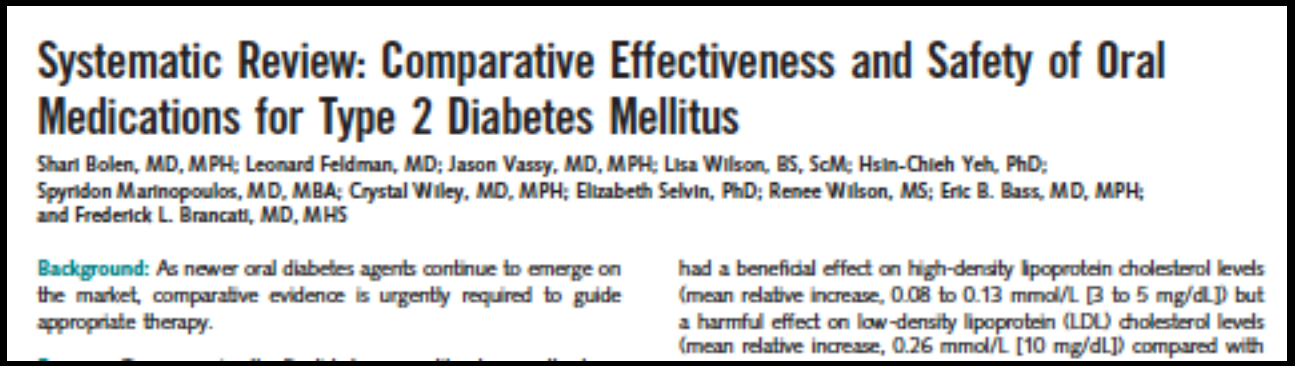

Research Evidence
decision aid
Patient values and preferences
within exam room

User-centered Design meets CER



Diabetes Cards

- Nature of diabetes medication discussions
- Summarizing the research evidence



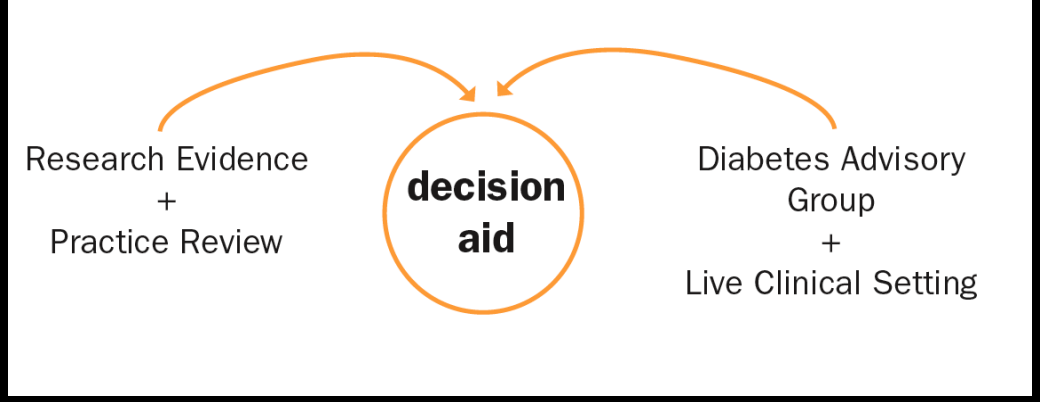
Systematic Review: Comparative Effectiveness and Safety of Oral Medications for Type 2 Diabetes Mellitus

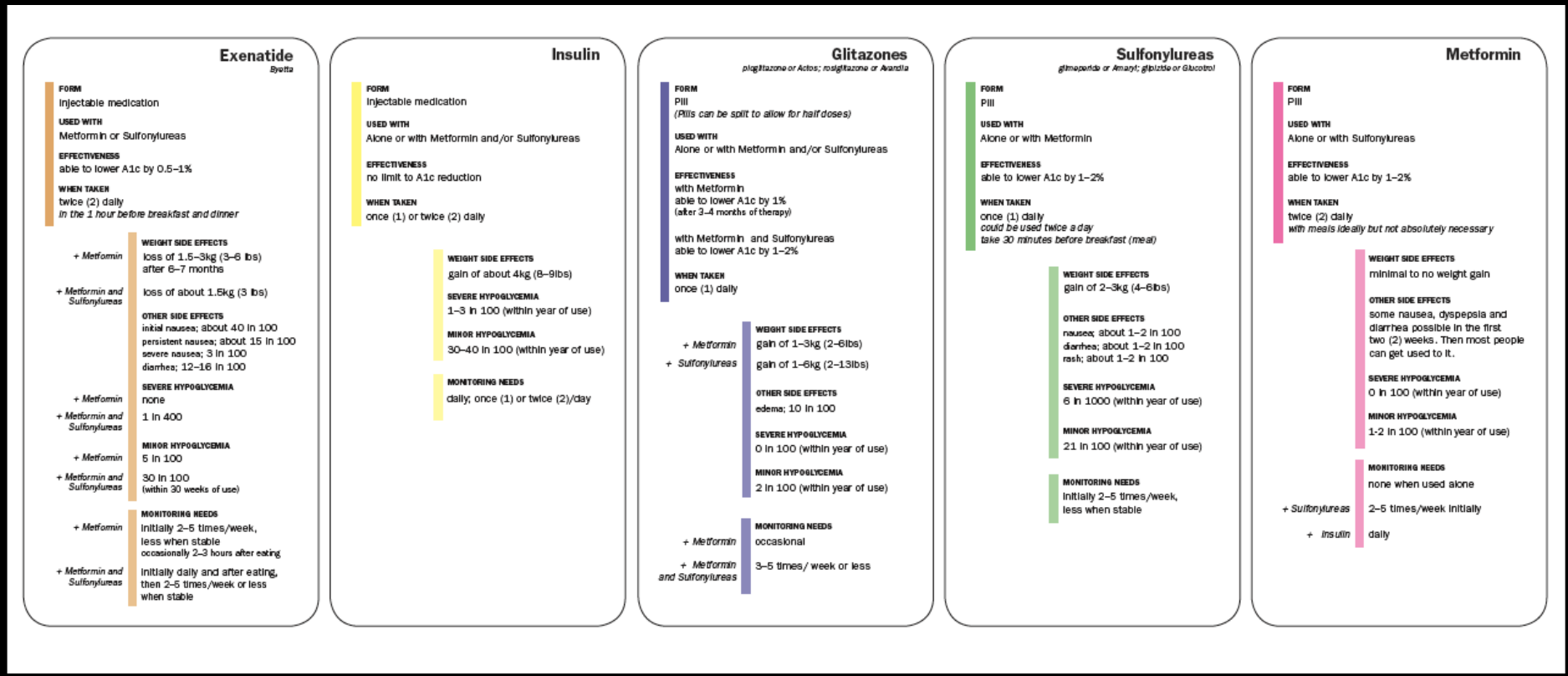
Shari Bolen, MD, MPH; Leonard Feldman, MD; Jason Vassy, MD, MPH; Lisa Wilson, BS, ScM; Hsin-Chieh Yeh, PhD; Spyridon Marinopoulos, MD, MBA; Crystal Wiley, MD, MPH; Elizabeth Selvin, PhD; Renee Wilson, MS; Eric B. Bass, MD, MPH; and Frederick L. Brancati, MD, MHS

Background: As newer oral diabetes agents continue to emerge on the market, comparative evidence is urgently required to guide appropriate therapy.

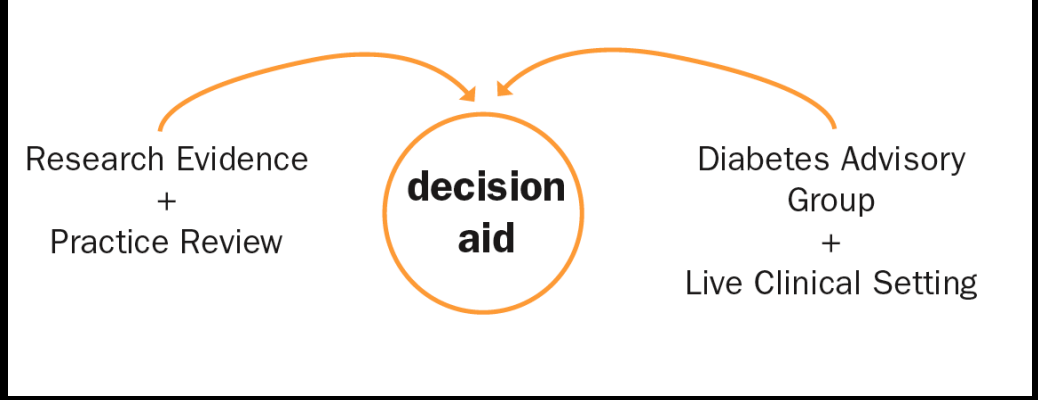
had a beneficial effect on high-density lipoprotein cholesterol levels (mean relative increase, 0.08 to 0.13 mmol/L [3 to 5 mg/dL]) but a harmful effect on low-density lipoprotein (LDL) cholesterol levels (mean relative increase, 0.26 mmol/L [10 mg/dL]) compared with

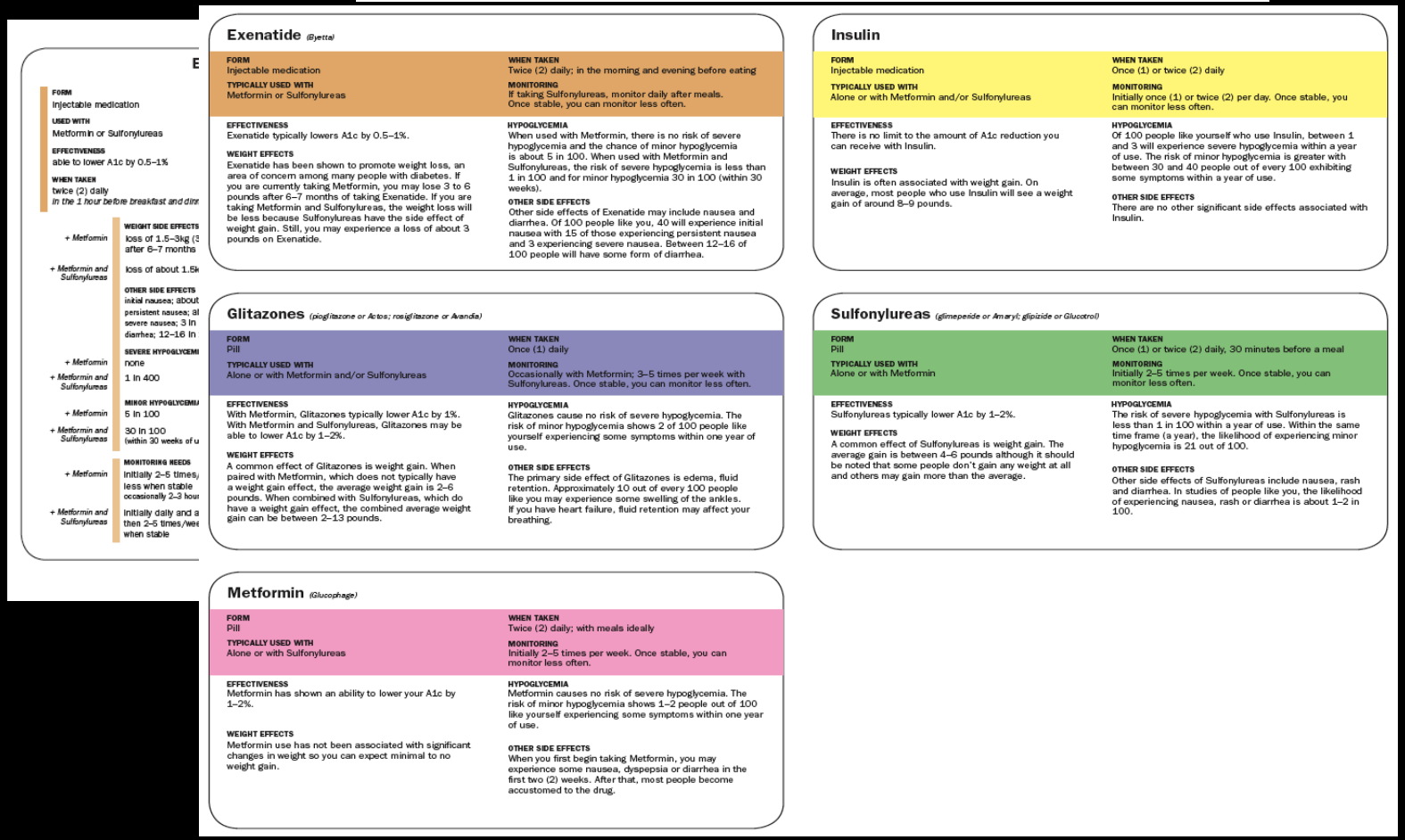
- Iterative process – *Choice Architecture*





"Baseball Cards"





FORM
Injectable medication

USED WITH
Metformin or Sulfonylureas

EFFECTIVENESS
able to lower A1c by 0.5–1%

WHEN TAKEN
twice (2) daily
in the 1 hour before breakfast and din

+ Metformin	**WEIGHT SIDE EFFECTS** loss of 1.5–3kg (after 6–7 months
+ Metformin and Sulfonylureas	loss of about 1.5k
	OTHER SIDE EFFECTS initial nausea; about persistent nausea; al severe nausea; 3 in diarrhea; 12–16 in
+ Metformin	**SEVERE HYPOGLYCEMI** none
+ Metformin and Sulfonylureas	1 in 400
+ Metformin	**MINOR HYPOGLYCEMIA** 5 in 100
+ Metformin and Sulfonylureas	30 in 100 (within 30 weeks of u
+ Metformin	**MONITORING NEEDS** initially 2–5 times/ less when stable occasionally 2–3 hou
+ Metformin and Sulfonylureas	initially daily and a then 2–5 times/wee when stable

Exenatide *(Byetta)*

FORM
Injectable medication

TYPICALLY USED WITH
Metformin or Sulfonylureas

EFFECTIVENESS
Exenatide typically lowers A1c by 0.5–1%.

WEIGHT EFFECTS
Exenatide has been shown to promote weight loss, an area of concern among many people with diabetes. If you are currently taking Metformin, you may lose 3 to 6 pounds after 6–7 months of taking Exenatide. If you are taking Metformin and Sulfonylureas, the weight loss will be less because Sulfonylureas have the side effect of weight gain. Still, you may experience a loss of about 3 pounds on Exenatide.

WHEN TAKEN
Twice (2) daily; in the morning and evening before eating

MONITORING
If taking Sulfonylureas, monitor daily after meals. Once stable, you can monitor less often.

HYPOGLYCEMIA
When used with Metformin, there is no risk of severe hypoglycemia and the chance of minor hypoglycemia is about 5 in 100. When used with Metformin and Sulfonylureas, the risk of severe hypoglycemia is less than 1 in 100 and for minor hypoglycemia 30 in 100 (within 30 weeks).

OTHER SIDE EFFECTS
Other side effects of Exenatide may include nausea and diarrhea. Of 100 people like you, 40 will experience initial nausea with 15 of those experiencing persistent nausea and 3 experiencing severe nausea. Between 12–16 of 100 people will have some form of diarrhea.

Glitazones *(pioglitazone or Actos; rosiglitazone or Avandia)*

FORM
Pill

TYPICALLY USED WITH
Alone or with Metformin and/or Sulfonylureas

EFFECTIVENESS
With Metformin, Glitazones typically lower A1c by 1%. With Metformin and Sulfonylureas, Glitazones may be able to lower A1c by 1–2%.

WEIGHT EFFECTS
A common effect of Glitazones is weight gain. When paired with Metformin, which does not typically have a weight gain effect, the average weight gain is 2–6 pounds. When combined with Sulfonylureas, which do have a weight gain effect, the combined average weight gain can be between 2–13 pounds.

WHEN TAKEN
Once (1) daily

MONITORING
Occasionally with Metformin; 3–5 times per week with Sulfonylureas. Once stable, you can monitor less often.

HYPOGLYCEMIA
Glitazones cause no risk of severe hypoglycemia. The risk of minor hypoglycemia shows 2 of 100 people like yourself experiencing some symptoms within one year of use.

OTHER SIDE EFFECTS
The primary side effect of Glitazones is edema, fluid retention. Approximately 10 out of every 100 people like you may experience some swelling of the ankles. If you have heart failure, fluid retention may affect your breathing.

Metformin *(Glucophage)*

FORM
Pill

TYPICALLY USED WITH
Alone or with Sulfonylureas

EFFECTIVENESS
Metformin has shown an ability to lower your A1c by 1–2%.

WEIGHT EFFECTS
Metformin use has not been associated with significant changes in weight so you can expect minimal to no weight gain.

WHEN TAKEN
Twice (2) daily; with meals ideally

MONITORING
Initially 2–5 times per week. Once stable, you can monitor less often.

HYPOGLYCEMIA
Metformin causes no risk of severe hypoglycemia. The risk of minor hypoglycemia shows 1–2 people out of 100 like yourself experiencing some symptoms within one year of use.

OTHER SIDE EFFECTS
When you first begin taking Metformin, you may experience some nausea, dyspepsia or diarrhea in the first two (2) weeks. After that, most people become accustomed to the drug.

Insulin

FORM
Injectable medication

TYPICALLY USED WITH
Alone or with Metformin and/or Sulfonylureas

EFFECTIVENESS
There is no limit to the amount of A1c reduction you can receive with Insulin.

WEIGHT EFFECTS
Insulin is often associated with weight gain. On average, most people who use Insulin will see a weight gain of around 8–9 pounds.

WHEN TAKEN
Once (1) or twice (2) daily

MONITORING
Initially once (1) or twice (2) per day. Once stable, you can monitor less often.

HYPOGLYCEMIA
Of 100 people like yourself who use Insulin, between 1 and 3 will experience severe hypoglycemia within a year of use. The risk of minor hypoglycemia is greater with between 30 and 40 people out of every 100 exhibiting some symptoms within a year of use.

OTHER SIDE EFFECTS
There are no other significant side effects associated with Insulin.

Sulfonylureas *(glimeperide or Amaryl; glipizide or Glucotrol)*

FORM
Pill

TYPICALLY USED WITH
Alone or with Metformin

EFFECTIVENESS
Sulfonylureas typically lower A1c by 1–2%.

WEIGHT EFFECTS
A common effect of Sulfonylureas is weight gain. The average gain is between 4–6 pounds although it should be noted that some people don't gain any weight at all and others may gain more than the average.

WHEN TAKEN
Once (1) or twice (2) daily, 30 minutes before a meal

MONITORING
Initially 2–5 times per week. Once stable, you can monitor less often.

HYPOGLYCEMIA
The risk of severe hypoglycemia with Sulfonylureas is less than 1 in 100 within a year of use. Within the same time frame (a year), the likelihood of experiencing minor hypoglycemia is 21 out of 100.

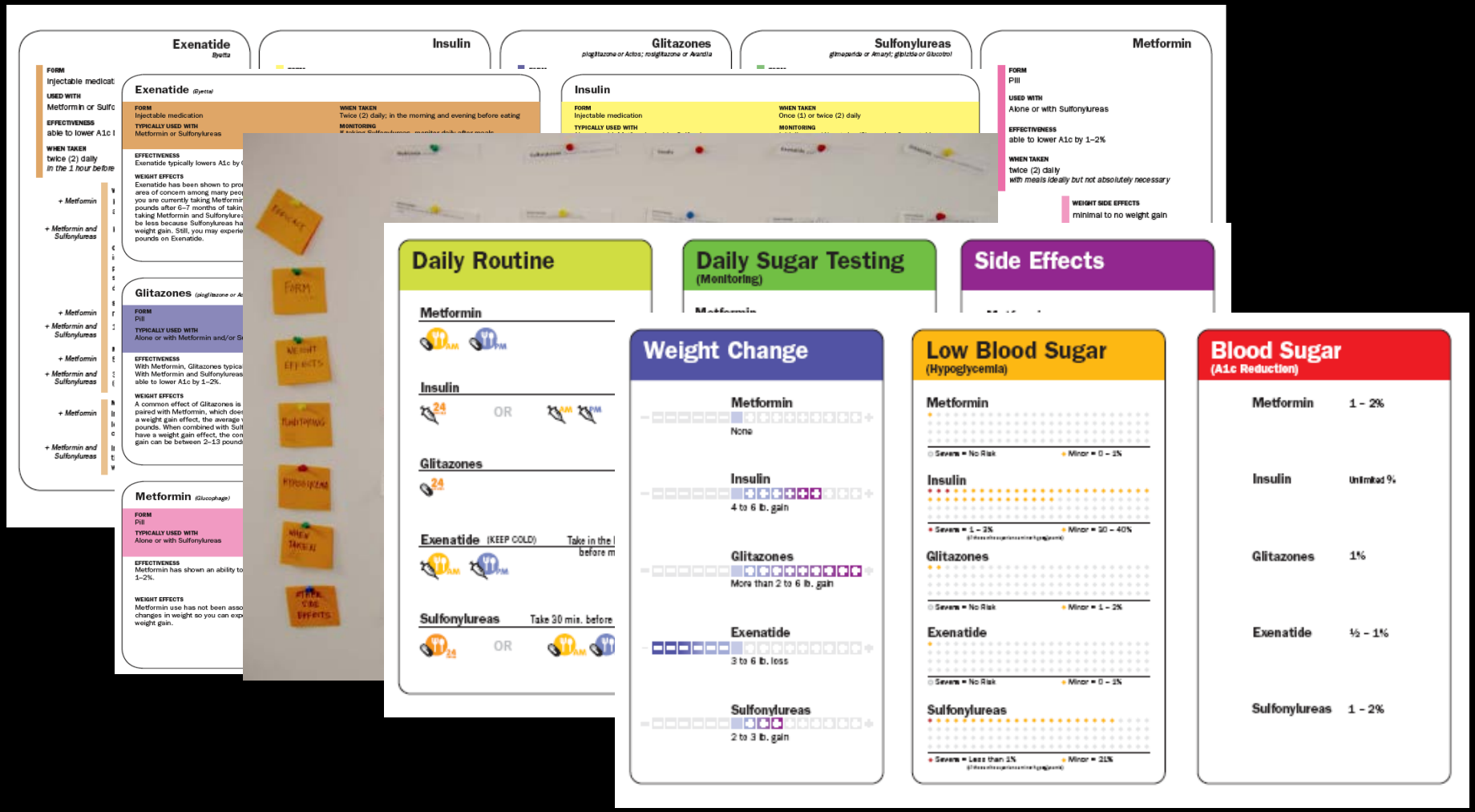
OTHER SIDE EFFECTS
Other side effects of Sulfonylureas include nausea, rash and diarrhea. In studies of people like you, the likelihood of experiencing nausea, rash or diarrhea is about 1–2 in 100.

"Narrative Cards"

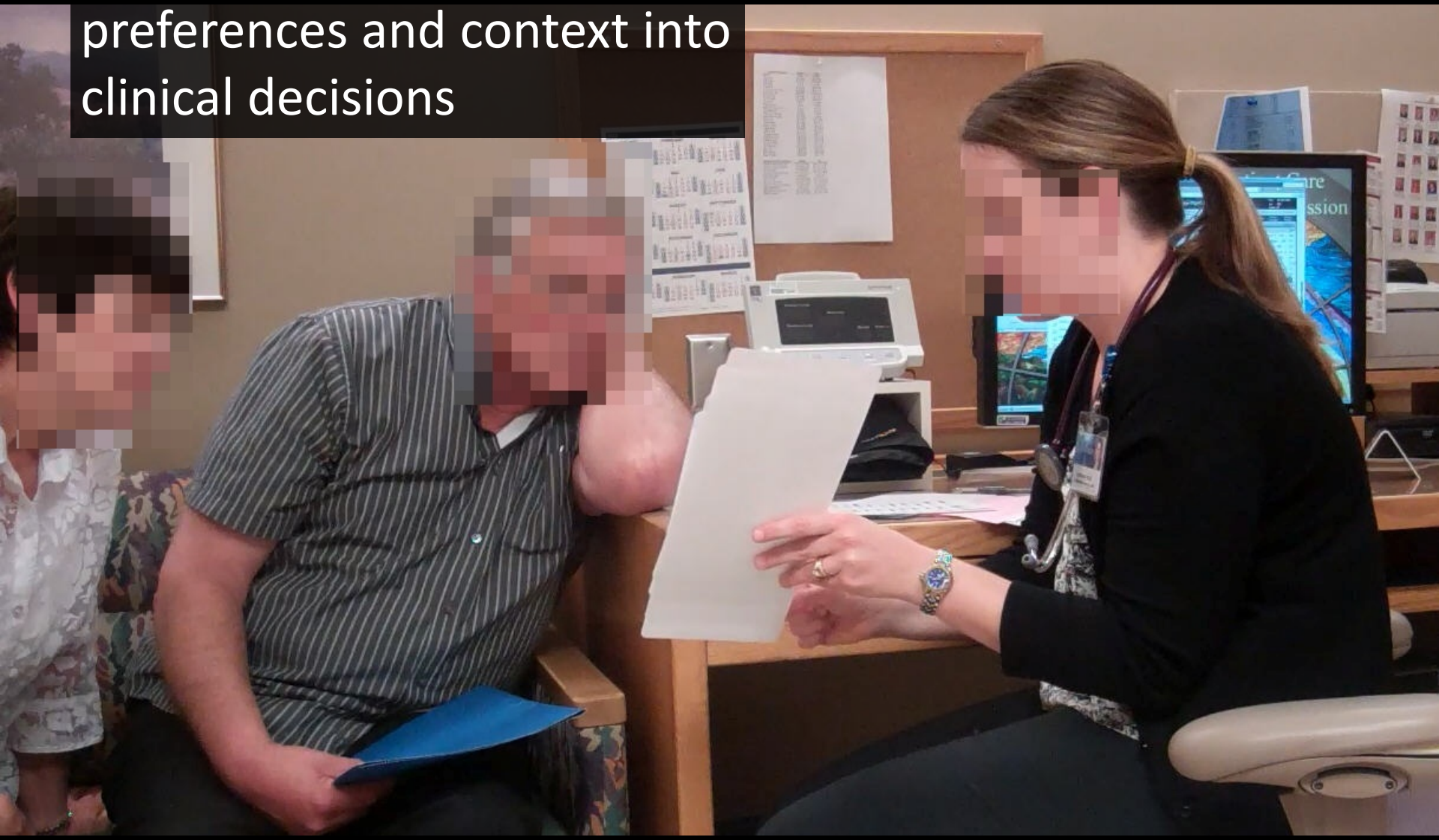
Research Evidence
+
Practice Review

decision aid

Diabetes Advisory Group
+
Live Clinical Setting



Incorporate patient preferences and context into clinical decisions




Incorporate research evidence and clinician's expertise into patient decisions

MAYO CLINIC

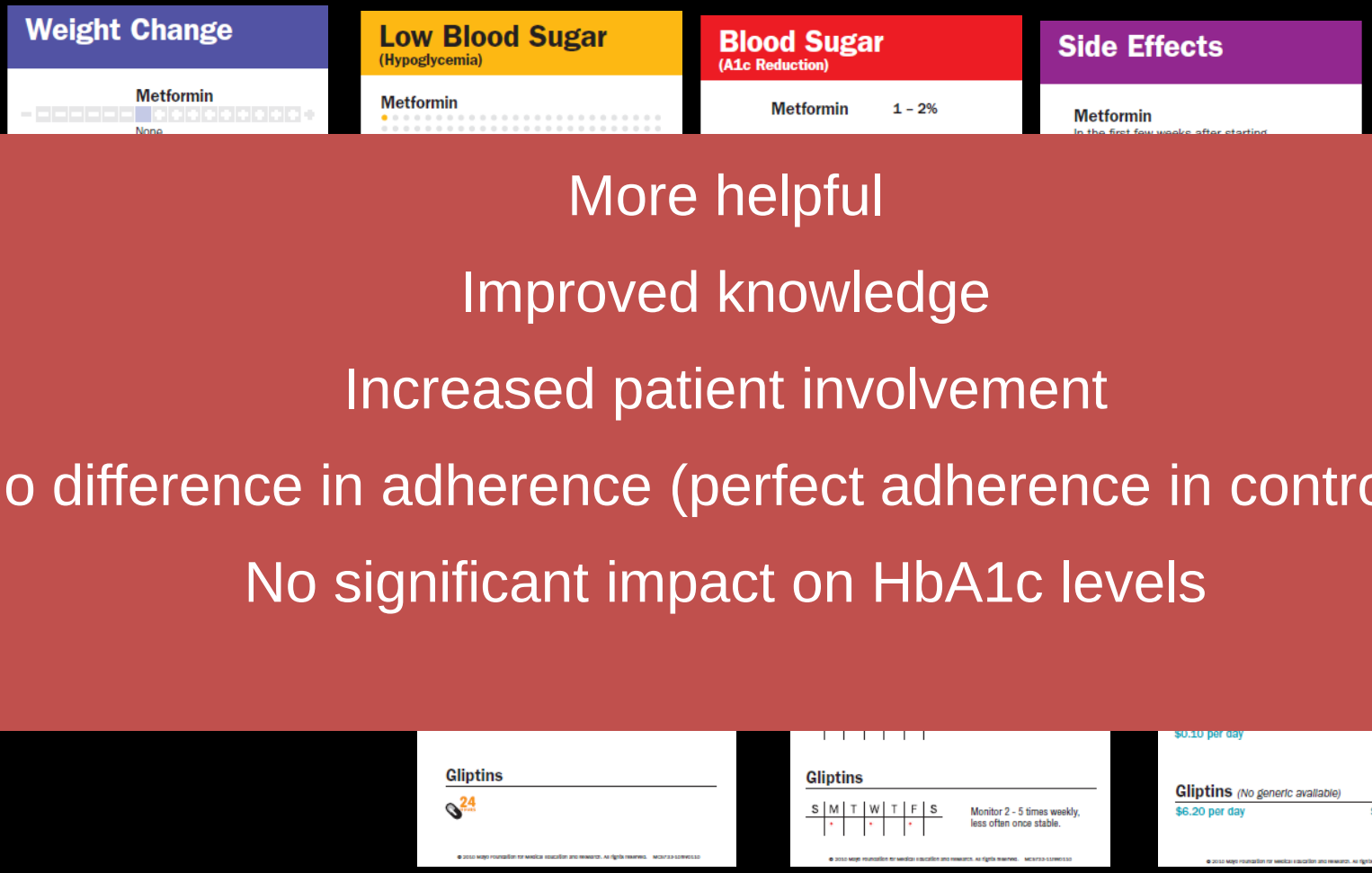
Diabetes Medication Choice
Decision Aid

Welcome to the **Diabetes Medication** Choice Decision Aid.

This guide provides information on medications c
to treat type-2 diabetes.

Let's get started

Caution: This application is for use exclusively during the clinical encounter with your clinician



More helpful

Improved knowledge

Increased patient involvement

No difference in adherence (perfect adherence in control gr)

No significant impact on HbA1c levels

Mullan RJ et al. Archives of Internal Medicine 2009


CURRENTLY ON
EXIT 58A-B
95
1
Zoloft
9
Prozac
Paxil
LAST EXIT
BEFORE TOLL
Buspar
Wellbutrin
Celexa
Xanax


Comparative effectiveness research
Patient centered translation into action
Decision aid
Patient-centered decision making

Effective Health Care Program

Comparative Effectiveness Review Number 46

Second-Generation Antidepressants in the Pharmacologic Treatment of Adult Depression:

An Update of the 2007 Comparative Effectiveness Review

AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care • www.ahrq.gov

Evidence Table 1. Randomized controlled

Study Characteristics	Research Intervention
Author, Year	Research

Table E. S
effectiven

Figure 14. Odds ratios of response rates comparing SSRIs and SNRIs with SNRIs and SSNRIs

Favors first drug Favors second drug

SSRI vs. SSNRI

0.38 (0.10, 3.07)
0.74 (0.56, 0.98)
1.14 (0.87, 1.46)
0.46 (0.13, 2.87)
0.93 (0.72, 1.22)
0.93 (0.70, 1.20)
0.43 (0.11, 3.45)
0.81 (0.56, 1.22)
1.27 (0.89, 1.76)
0.51 (0.14, 3.25)
1.07 (0.73, 1.51)
1.04 (0.72, 1.44)
0.48 (0.12, 4.14)
0.99 (0.57, 1.59)
1.48 (0.91, 2.27)
0.57 (0.16, 3.65)
1.24 (0.76, 1.89)
1.21 (0.73, 1.88)
0.49 (0.13, 3.91)
0.93 (0.67, 1.33)
1.46 (1.16, 1.83)
0.58 (0.17, 3.67)
1.18 (0.86, 1.65)
1.17 (0.88, 1.53)
1.13 (0.80, 1.55)
1.25 (0.92, 1.73)
1.32 (0.78, 2.09)
1.12 (0.78, 1.67)
0.84 (0.50, 1.50)
0.96 (0.58, 1.65)

1 2 5

w conclusions about treating depression in
isting low energy. Results from head-to-
t available.

Antidepressant Medicines*

Brand Name	Generic Available?	Drug Name
Wellbutrin®; Wellbutrin [illegible] Wellbutrin XL®		
Celexa®		
Pristiq®		
Cymbalta®		

What did research find about specific antidepressants?

Research has found some specific information about the benefits of a few medicines:

ed feeling better
lemeron® took about
ntidepressants
s.
as regular Prozac®

exor®, Effexor XR®)
her antidepressants.
ed it because of side

ms related

ments in their
ut the same amount

balta®) both helped
the same amount.
Fluoxetine (Prozac®),
d sertraline (Zoloft®)
ount, but there is not

5

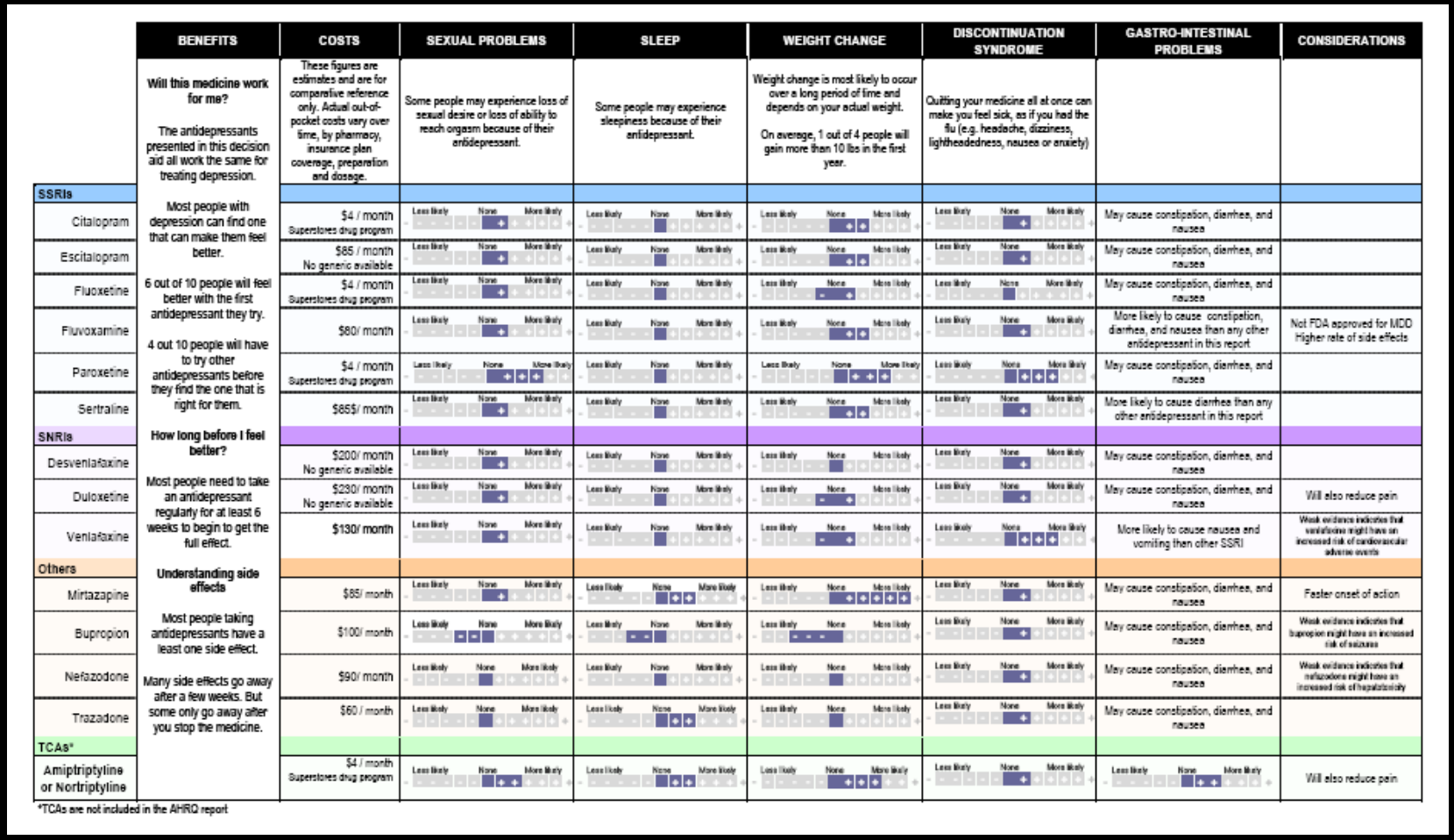
Effective Health Care Program

Medicines for Treating Depression

A Review of the Research for Adults

AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care • www.ahrq.gov

Comparative Effectiveness Research



	BENEFITS	COSTS	SEXUAL PROBLEMS	SLEEP	WEIGHT CHANGE	DISCONTINUATION SYNDROME	GASTRO-INTESTINAL PROBLEMS	CONSIDERATIONS
	Will this medicine work for me? The antidepressants presented in this decision aid all work the same for treating depression. Most people with depression can find one that can make them feel better. 6 out of 10 people will feel better with the first antidepressant they try. 4 out 10 people will have to try other antidepressants before they find the one that is right for them. **How long before I feel better?** Most people need to take an antidepressant regularly for at least 6 weeks to begin to get the full effect. **Understanding side effects** Most people taking antidepressants have a least one side effect. Many side effects go away after a few weeks. But some only go away after you stop the medicine.	These figures are estimates and are for comparative reference only. Actual out-of-pocket costs vary over time, by pharmacy, insurance plan coverage, preparation and dosage.	Some people may experience loss of sexual desire or loss of ability to reach orgasm because of their antidepressant.	Some people may experience sleepiness because of their antidepressant.	Weight change is most likely to occur over a long period of time and depends on your actual weight. On average, 1 out of 4 people will gain more than 10 lbs in the first year.	Quitting your medicine all at once can make you feel sick, as if you had the flu (e.g. headache, dizziness, lightheadedness, nausea or anxiety)		
SSRIs								
Citalopram		$4 / month Superstores drug program	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	May cause constipation, diarrhea, and nausea	
Escitalopram		$85 / month No generic available	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	May cause constipation, diarrhea, and nausea	
Fluoxetine		$4 / month Superstores drug program	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	May cause constipation, diarrhea, and nausea	
Fluvoxamine		$80/ month	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	More likely to cause constipation, diarrhea, and nausea than any other antidepressant in this report	Not FDA approved for MDD Higher rate of side effects
Paroxetine		$4 / month Superstores drug program	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	May cause constipation, diarrhea, and nausea	
Sertraline		85/ month	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	More likely to cause diarrhea than any other antidepressant in this report	
SNRIs								
Desvenlafaxine		$200/ month No generic available	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	May cause constipation, diarrhea, and nausea	
Duloxetine		$230/ month No generic available	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	May cause constipation, diarrhea, and nausea	Will also reduce pain
Venlafaxine		$130/ month	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	More likely to cause nausea and vomiting than other SSRI	Weak evidence indication that venlafaxine might have an increased risk of cardiovascular adverse events
Others								
Mirtazapine		$85/ month	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	May cause constipation, diarrhea, and nausea	Faster onset of action
Bupropion		$100/ month	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	May cause constipation, diarrhea, and nausea	Weak evidence indication that bupropion might have an increased risk of seizures
Nefazodone		$90/ month	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	May cause constipation, diarrhea, and nausea	Weak evidence indication that nefazodone might have an increased risk of hepatotoxicity
Trazadone		$60 / month	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	May cause constipation, diarrhea, and nausea	
TCAs*								
Amiptriptyline or Nortriptyline		$4 / month Superstores drug program	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	Less likely None More likely	Will also reduce pain

*TCAs are not included in the AHRQ report

Stakeholders meetings

24 participants /12 organizations

(Health systems, patients, clinicians, buyers)

Clinical observations

2 primary care practices

(Patients, family physicians, care managers)

Focus groups/ Discussion

Family physicians, care managers

Patients Advisory Groups

Keep in Mind

Sexual Issues

Sleep

Cost

Weight Change

Stopping Approach

What You Should Know

Will this medicine work for me?

- The antidepressants presented in this decision aid all work the same for treating depression.
- Most people with depression can find one that can make them feel better.
- 6 out of 10 people will feel better with the first antidepressant they try and the rest will have to try other antidepressants before they find the one that is right for them.

How long before I feel better?

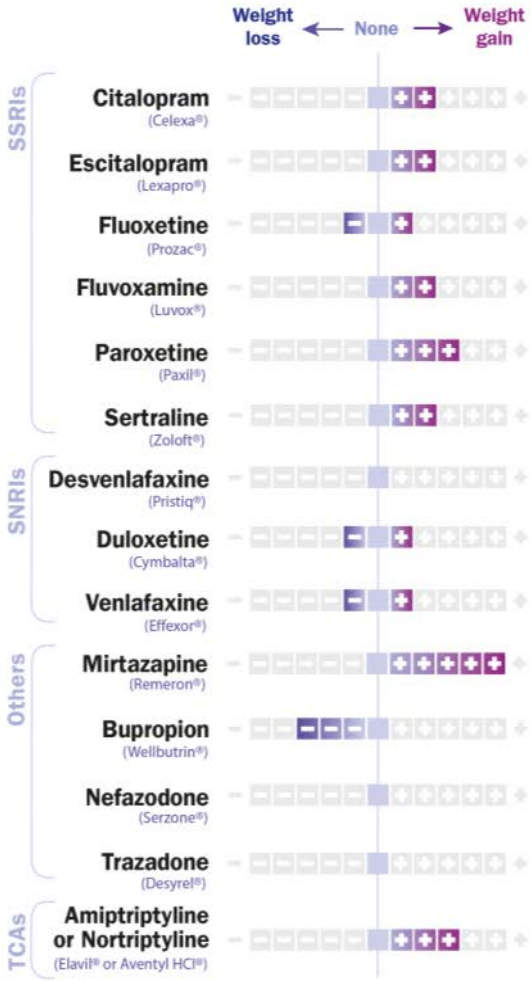
- Most people need to take an antidepressant regularly for at least 6 weeks to begin to get the full effect.

Understanding side effects

- Most people taking antidepressants have at least one side effect.
- Many side effects go away after a few weeks, but some only go away after you stop the medicine.

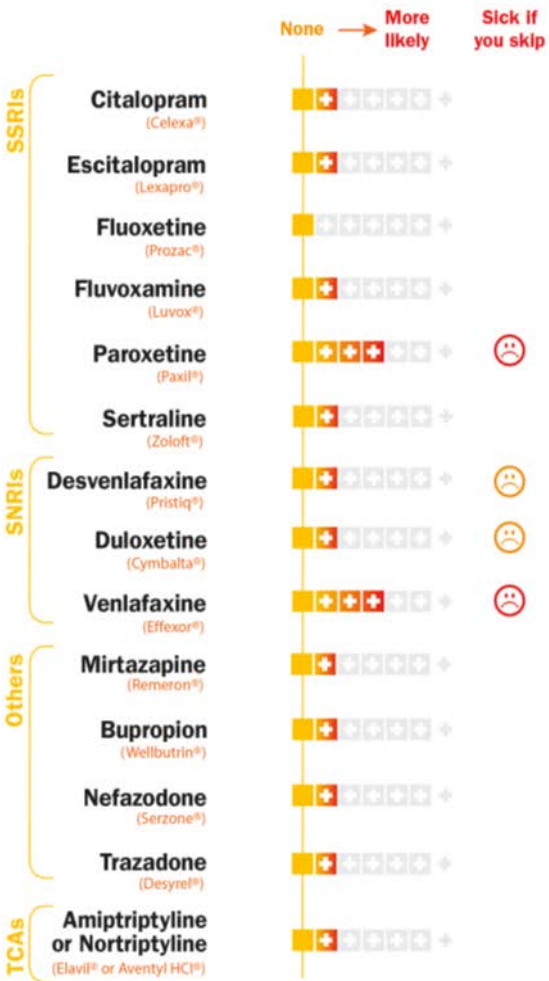
Weight Change

Weight change is most likely to occur over a long period of time and depends on your actual weight.



Stopping Approach

Quitting your medicine all at once can make you feel sick, as if you had the flu (e.g. headache, dizziness, light-headedness, nausea or anxiety).



Comfortable

Knowledgeable

Satisfied

(feel better)

Comfortable

Satisfied

Use tool/like it

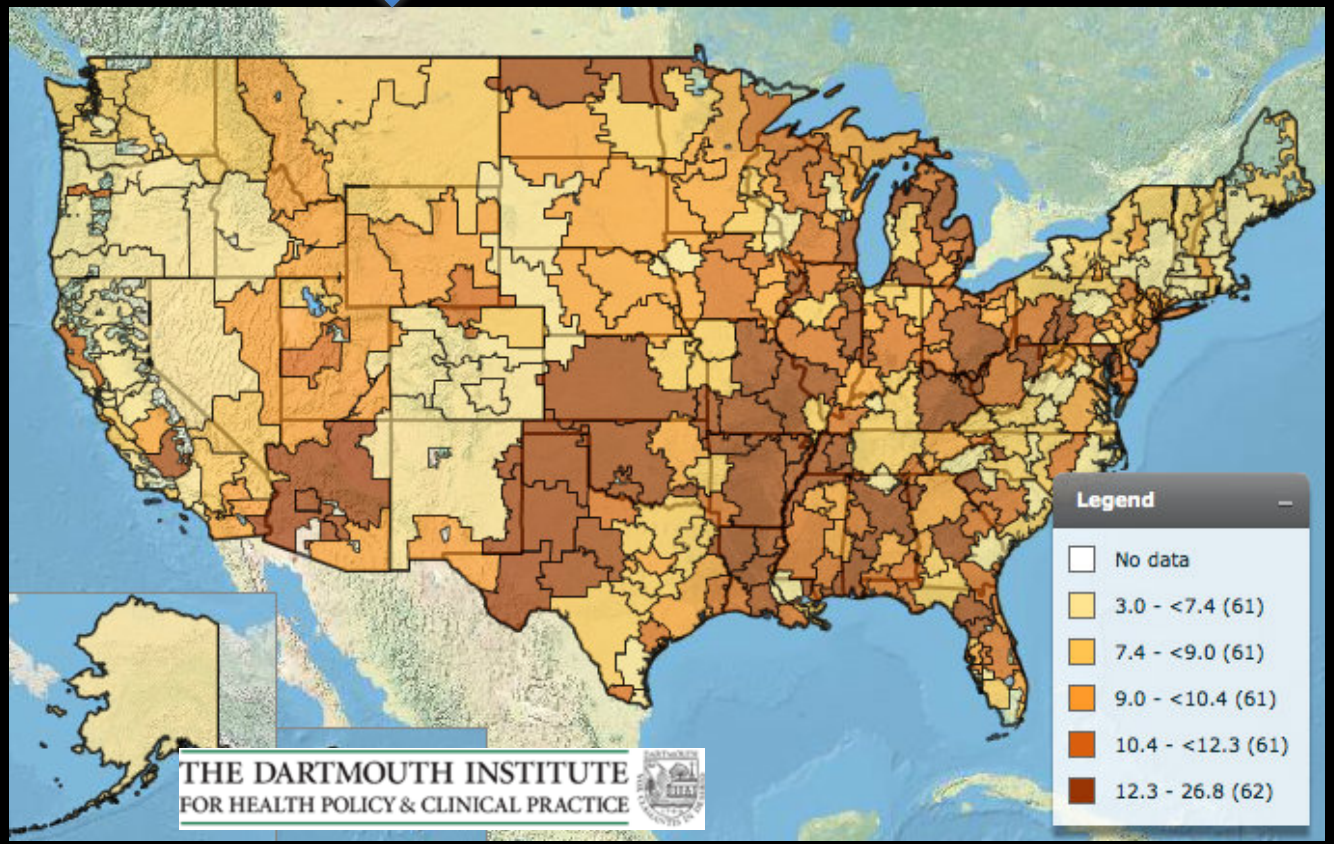
Engaged in decision making process

LESS IS MORE

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

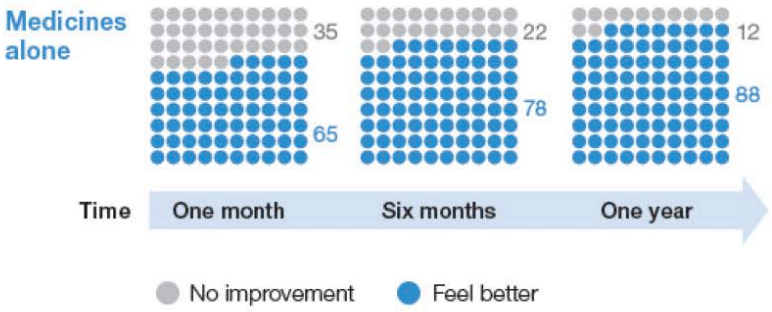
Meta-analysis of Randomized Controlled Trials

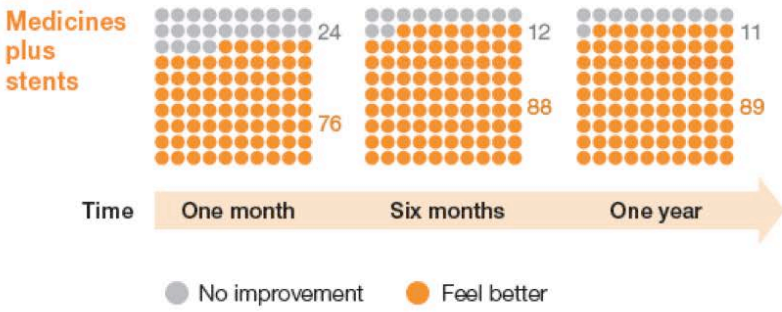
Kathleen Stergiopoulos, MD, PhD; David L. Brown, MD



Benefits

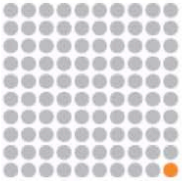
Improvement of symptoms in 100 people like you after treatment:



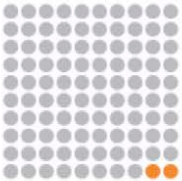


Risks

During stent procedure

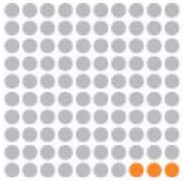


In 100 people like you:
ONE will have a heart attack, stroke or other major complication,
99 will not.

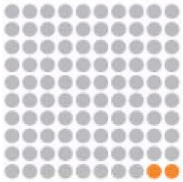


In 100 people like you:
TWO will have bleeding or damage to a blood vessel,
98 will not.

Bleeding and clotting within one year



In 100 people like you:
THREE will have a bleeding event from the additional blood thinner needed with a stent,
97 will not.



In 100 people like you:
TWO will develop a clot that forms in the stent leading to a heart attack,
98 will not.

PCI Choice

Coronary artery disease is a CHRONIC disease.

If you don't choose to have a stent placed now,
it's possible that you could still have one later.

MEDICINES

In 15 people like you:
THREE will need a stent within one year, 12 will not.

MEDICINES + STENTS

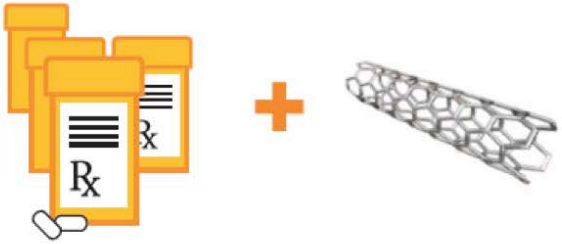
In 15 people like you:
ONE will need another stent within one year, 14 will not.

Based upon this shared information...

What is most important to *you*?

MEDICINES

MEDICINES + STENTS



Did you know...

Use of stents for stable coronary artery disease will **NOT** lower your risk of heart attack or death when compared to using medicines alone.

PCI Choice

The Medical Letter on Drugs and Therapeutics

FROM ISSUE 1492

April 11, 2016

Which Oral Anticoagulant for Atrial Fibrillation?

Download PDF: US English

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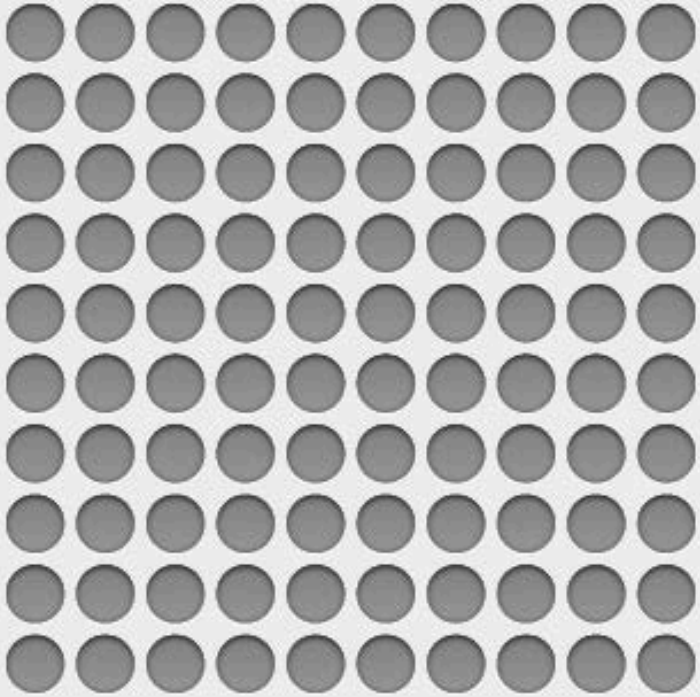
Send Article Feedback

Direct-to-consumer advertisements continue to urge patients who take warfarin (*Coumadin*, and others) for atrial fibrillation to ask their doctors about the benefits of one or another of the newer oral anticoagulants.

WARFARIN — In patients with nonvalvular atrial fibrillation, warfarin reduces the risk of thromboembolic stroke by about 60%.[1] If necessary, vitamin K, prothrombin complex concentrate, or fresh frozen plasma can reverse its anticoagulant effect.[2] Drawbacks of warfarin include unpredictability and variability in dosage requirements, dietary restrictions, interactions with many other drugs, and the need for close monitoring to keep the international normalized ratio (INR) in the therapeutic range (2-3).



Welcome to the **Anticoagulation Choice** Decision Aid.

This tool will help you and your doctor discuss how to manage your Atrial Fibrillation

Let's get started

Caution: This application is for use exclusively during the clinical encounter with your clinician

1 Year Risk
5 Year Risk

Medical Situation | Risk of Stroke | Anticoagulation | Issues

CHA_2DS_2-VASC **0**

To begin, let's review your medical situation

Gender	M F
Age	?
History of Hypertension	III No
Congestive Heart Failure	III No
Stroke / TIA / Thromboembolism	III No
History of Vascular Disease	III No
Diabetes Mellitus	III No

Continue to consider your risk of stroke

Over the next 5 years

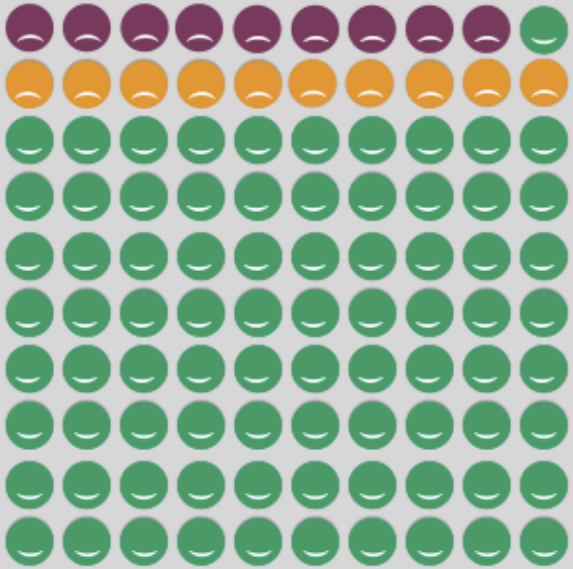
81 people will have no stroke

9 people will have a fatal or disabling stroke

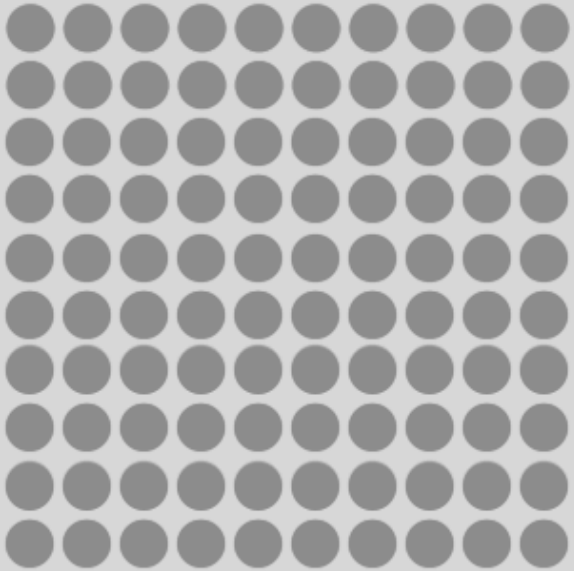
10 people will have a non-disabling stroke

Current Risk
of Stroke without Anticoagulation

In 100 people like you who **are not** taking an anticoagulant



With Anticoagulation



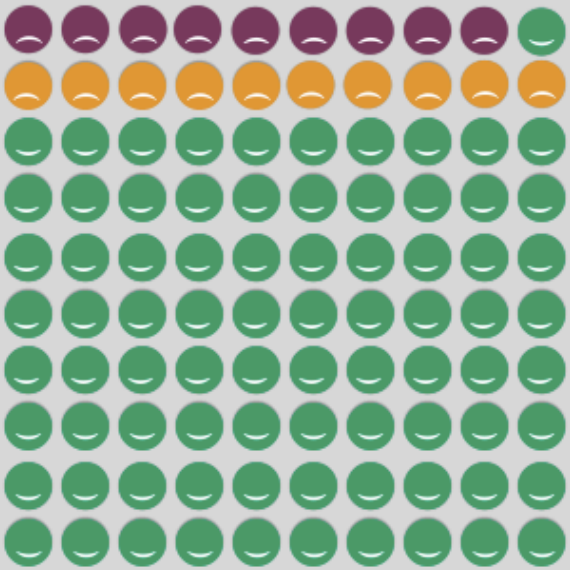
1 Year Risk
5 Year Risk

Medical Situation | Risk of Stroke | **Anticoagulation** | Issues

CHA_2DS_2-VASC **3**

Current Risk
of Stroke without Anticoagulation

In 100 people like you who **are not** taking an anticoagulant



Over the next 5 years

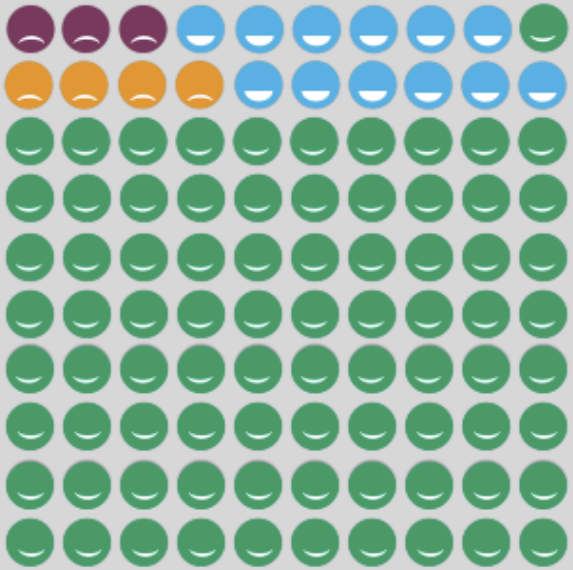
81 people will have no stroke

9 people will have a fatal or disabling stroke

10 people will have a non-disabling stroke

Future Risk
of Stroke with Anticoagulation

In 100 people like you who **are** taking an anticoagulant



Over the next 5 years

93 people will have no stroke

3 people will have a fatal or disabling stroke

4 people will have a non-disabling stroke

12 people will avoid a stroke by taking anticoagulation

Risk of Bleeding
Anticoagulation Routine
Reversing Anticoagulation
Cost
Diet & Medication Interactions

Anticoagulation Routine

Warfarin

Once daily

Regular blood tests

Direct Anticoagulants

Apixaban	*Eliquis*	AM PM
Dabigatran	*Pradaxa*	AM PM
Edoxaban	*Savaysa*	Once daily
Rivaroxaban	*Xarelto*	Once daily

Are you available to do the regular blood tests that Warfarin requires?

Lessons learnt

User-centered design happens in the field, takes multiple iterations and expertise

Challenges with evidence synthesis and changing evidence

Multipronged approaches to translating CER into practice may be necessary

Engaging the patients as part of the translation process critical

Uptake of CER into Practice

Diffusion of Innovations

Culture

Implementation matters – a bit…

Role of informatics

Perceived need – driven by users

Training and education

Contextualize to the practice

MAYO CLINIC

KERUNIT
KNOWLEDGE AND EVALUATION RESEARCH

shah.nilay@mayo.edu

http://shareddecisions.mayoclinic.org

Addressing Barriers and Strategies to Enhance the use of CER/PCOR

A Look at Pre-Conference Survey Results

Ernest Law

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Outline

- Survey Objectives
- Methods
- Results
- Limitations
- Discussion*

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Survey objectives

- To identify the needs and gaps in the uptake and use of PCOR/CER evidence by patients, clinicians, payers
- To identify the best methods or approaches to enhance the uptake and use of PCOR/CER evidence by patients, clinicians, payers
- To stimulate discussion among attendees representing each perspective
- To assist in the development of a consensus document or other enduring material that provides benefit beyond the conference

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Methods

- Survey development
  - Focused literature search for barriers and strategies to evidence implementation
  - Reviewed and refined by planning committee
  - Pre-tested with three non-invitees

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Methods

- Survey instrument
  - Section 1: **perspective** and **work setting**
  - Section 2: Likert rating scale
    - **10 barriers**: "*…. extent that the barrier is an issue*"
      - 1: None of the time → 4: All of the time
    - **6 strategies**: "*…effectiveness of the strategy*"
      - 1: Not effective → 4: Extremely effective
  - Section 3: Free-text
    - **Additional** barriers & strategies

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Methods

- Survey administration
  - Web-based platform (Qualtrics)
  - Individual links emailed to registrants
  - Final cut-off for survey submission January 18th
    - 2-3 reminders to complete survey
- Respondents:
  - Conference invitees (selected by members of planning committee)

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Methods

- Analysis
  - Descriptive statistics
  - Summary score with Likert responses to rank barriers and strategies
    - 1-None of the time/Not effective
    - 2-Some of the time/Somewhat effective
    - 3-Most of the time/Very effective
    - 4-All of the time/Extremely effective
  - Reported for all respondents & stratified by perspectives

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Results

- 64 registrants (as of Jan 18th) emailed
- 46 surveys completed
- 73% response rate

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Primary Work Setting (n=46)

Setting	n (%)
Academia	25 (54%)
Industry	5 (11%)
Payer	4 (8%)
Patient advocacy	3 (7%)
Government	3 (7%)
Clinical practice	0 (0%)
Other*	6 (13%)

*non-profits, consultancy, professional organization, policy research, technology company

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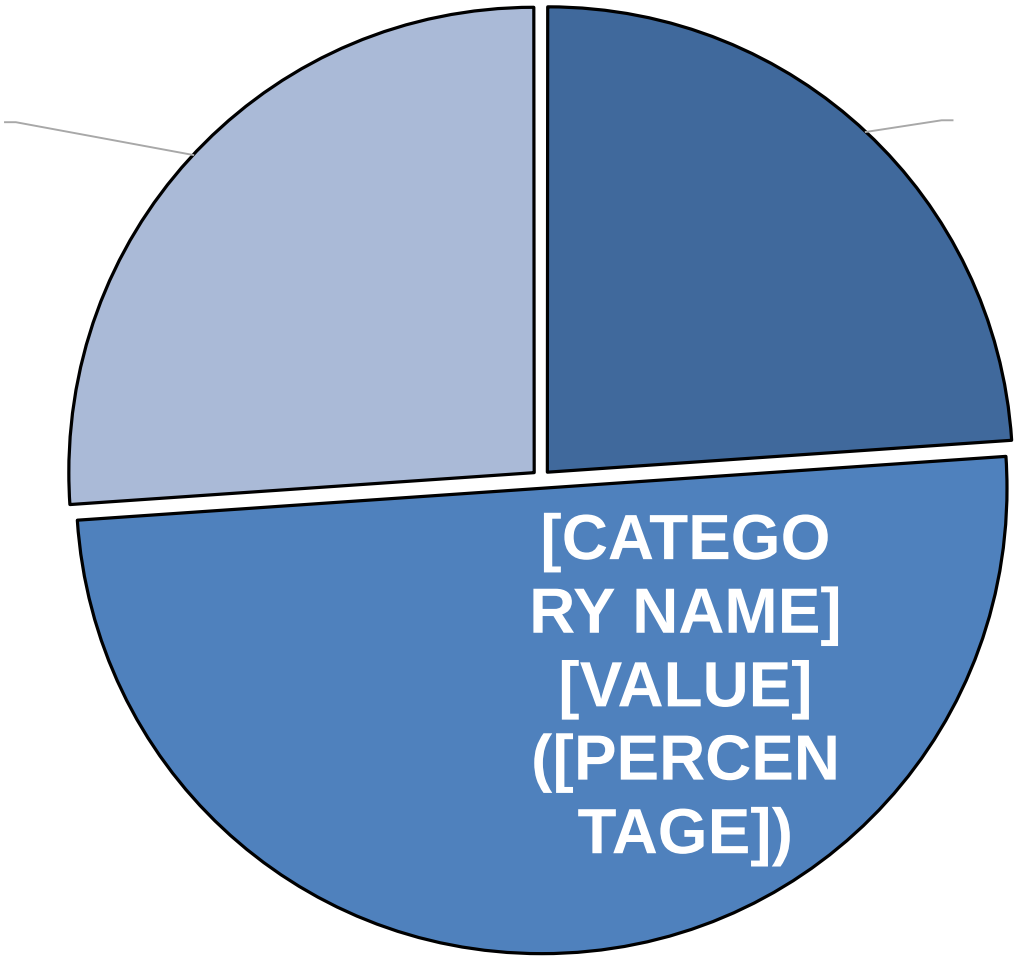
Perspective (n=46)

Please choose one of the following stakeholder perspectives ***you feel you can best represent****.*



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Barriers to CER/PCOR uptake: Ranking*

Barrier	Overall	Patient	Clinician	Payer
CER evidence not applicable/lacks relevance.	**10**	10	10	10
Access to CER studies difficult	**9**	3	9	9
CER poorly understood concept	**8**	5	8	6
Lack of trust of CER methods & results	**7**	8	6	5
Uncertainty with regulations for unpublished data for public use	**6**	9	7	1

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*10 = least encountered barrier; 1 = most extensively encountered barrier

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Barriers to CER/PCOR uptake: Ranking*

Barrier	Overall	Patient	Clinician	Payer
CER not applicable to patient subpopulations	5	4	4	8
Lack of CER studies to support decision-making	4	1	2	4
Insufficient education on how to interpret/apply CER results	3	2	5	3
Lack of tools to incorporate CER into decision-making	2	7	3	2
There is not enough CER studies to support decision-making	1	6	1	7

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*10 = least encountered barrier; 1 = most extensively encountered barrier

Selected additional barriers

- Patient perspective (9 responses):
  - *Peer reviewed manuscripts are intimidating to read, peer reviewed lay person summaries would help*
  - *It is difficult to know which sources of information to trust, e.g., NIH web sources vs. Industry web promotion*
  - *I am in a setting where access to publications is not a problem, but I know from anecdotal evidence that it is a big struggle for others.*

Selected additional barriers

- Clinician perspective (19 responses):
  - *Difficulty delivering findings at the point of care in EHRs and clinical systems*
  - *Lack of an agreed upon systems perspective of the health condition that is being studied*
  - *Many clinicians who are implementers of CER do not understand the vagaries, biases, and limitations of CER when they have access to the results.*
  - *Time*

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Selected additional barriers

- Payer perspective (11 responses):
  - *Timeliness of evidence as it relates to when P&T decisions need to be made*
  - *Traditional marketing and social medial influence patients and clinicians, thereby undermining evidence-based approaches to care.*
  - *Changing the mindset that the RCT is the best way to evaluate a product*

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Strategies to CER/PCOR uptake: Ranking*

Strategy	Overall	Patient	Clinician	Payer
More interactive workshops and conferences that explain CER	6	6	6	4
Provision of direct-to-patient CER-based education materials	5	4	5	6
Face-to-face academic detailing	4	5	4	5
Creation of a registry/repository of CER evidence	3	2	3	3
High quality summaries with direct recommendations for decision-making	2	3	2	1
Direct practice guideline incorporation	1	1	1	2

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*6= least effective strategy; 1 = most effective strategy

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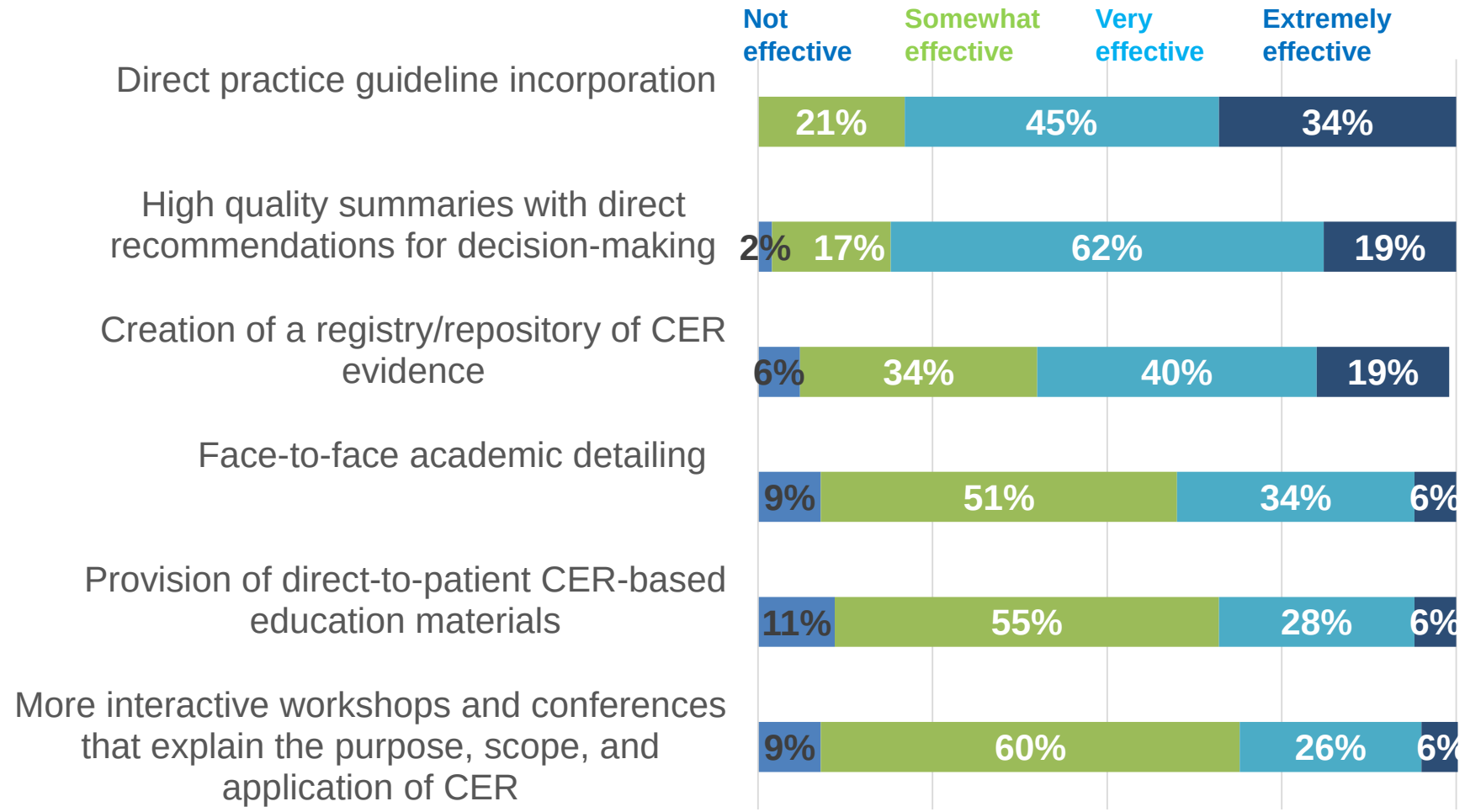
Strategies to improve CER/PCOR uptake (overall, 46 responses)



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Selected additional strategies

- Patient perspective (8 responses):
  - *In choosing among treatment options, my radiation oncologist sent me copies of recent journal articles.*
  - *Take data to clinician before decision on treatment*
  - *Provide plain language explanations underlying treatment decisions*
  - *"Research Club" for patients*

Selected additional strategies

- Clinician perspective (19 responses):
  - *Keep away from new drugs for a period of time*
  - *Elicit patient goals; build patient relationship/trust*
  - *Dear Doctor letters with post-marketing updates*
  - *Enhanced methods regarding lining of different types of data (EMR, claims, PRO, social determinants)*

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Selected additional strategies

- Payer perspective (10 responses):
  - *Outcomes researchers in P&T*
  - *Having mechanisms for payors to identify research questions that can be studied by CER investigators.*
  - *Offer CER certification course scholarships for payer representatives from small plans and/or Medicaid plans*
  - *Ability to sort through data and determine level of applicability, thus infer level of reproducibility in my patient population*

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Discussion

- Limitation to the survey:
  - Selection bias and generalizability
  - Small (unbalanced) stakeholders subgroups
  - Validity of perspective taken

To be continued in the breakout sessions!

DISCUSSION

What We've Learned: Overview of NPC Work on Stakeholder Views and Addressing Barriers to Use

Jennifer Graff

PhRMA FOUNDATION

AMCP Academy of Managed Care Pharmacy®

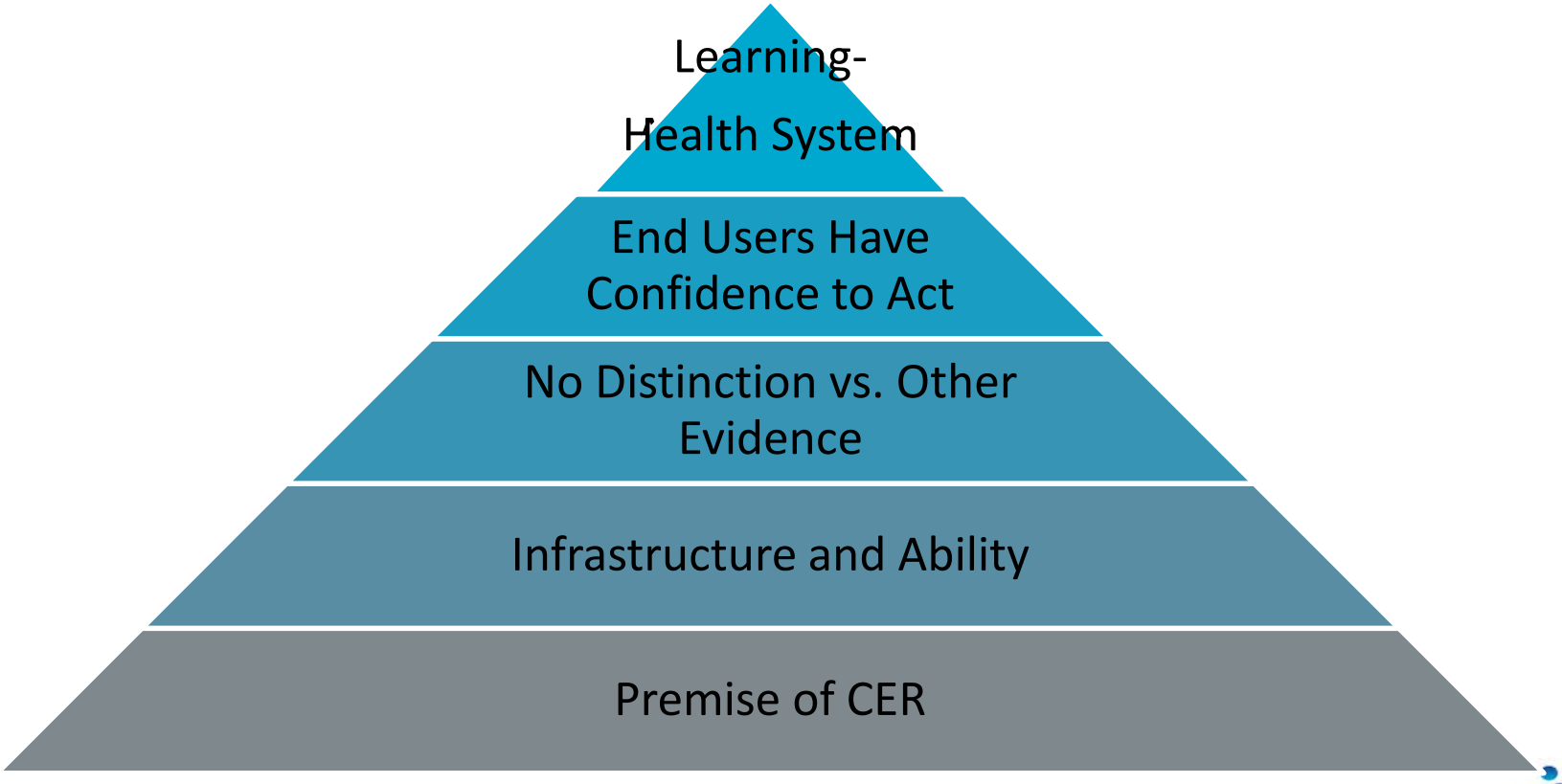
What We've Learned: NPC Research on Stakeholder Views and Barriers to Use

January 27, 2017

National Pharmaceutical Council®

What PCOR and CER Can Be, It Must Be!

Are PCOR and CER fully developed research approaches? Where are we on the journey? What are the opportunities?



Maslow's Hierarchy of needs

Insights Today Based On Research Portfolio on Generation, Use and Acceptance of CER

Standards

Journal Editors (Perfetto et al)

Clinical Practice Guidelines (Wallace et al)

Medicaid views (Weissman)

Fit for Use (AcademyHealth)

NPC Annual CER Survey

Employer, Insurer, Industry View (RAND)

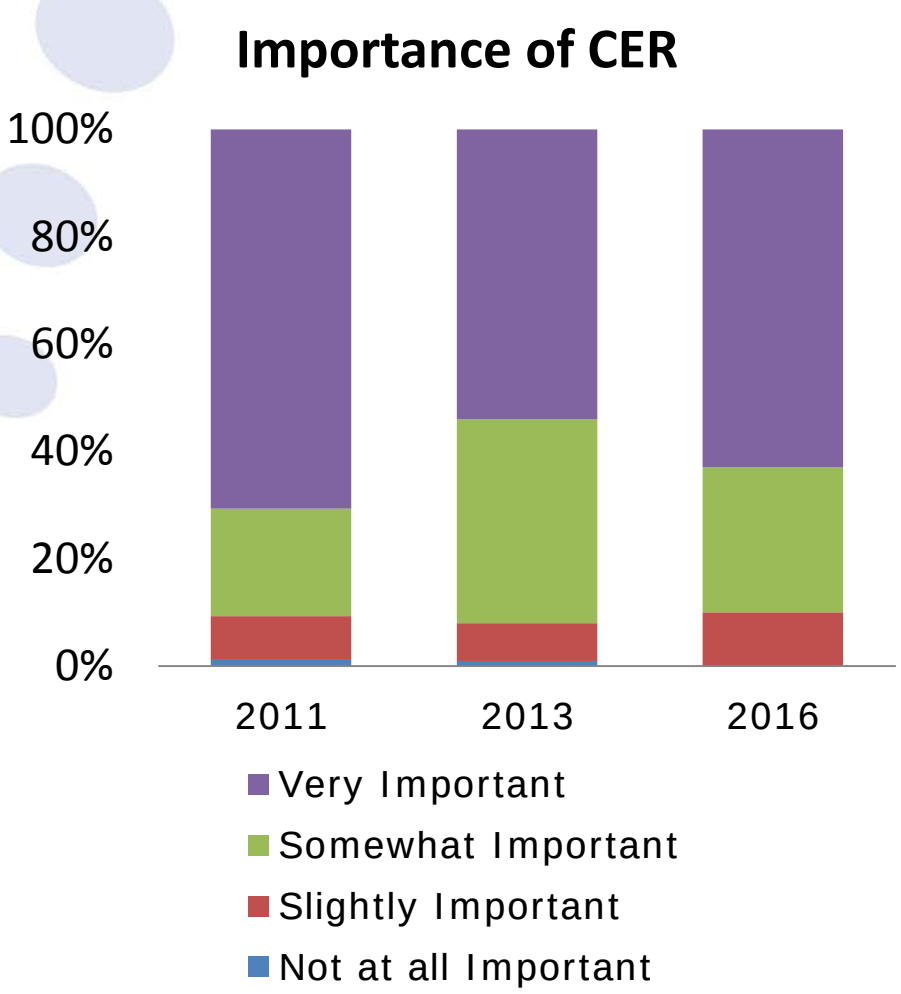
Employers (Reynolds et al)

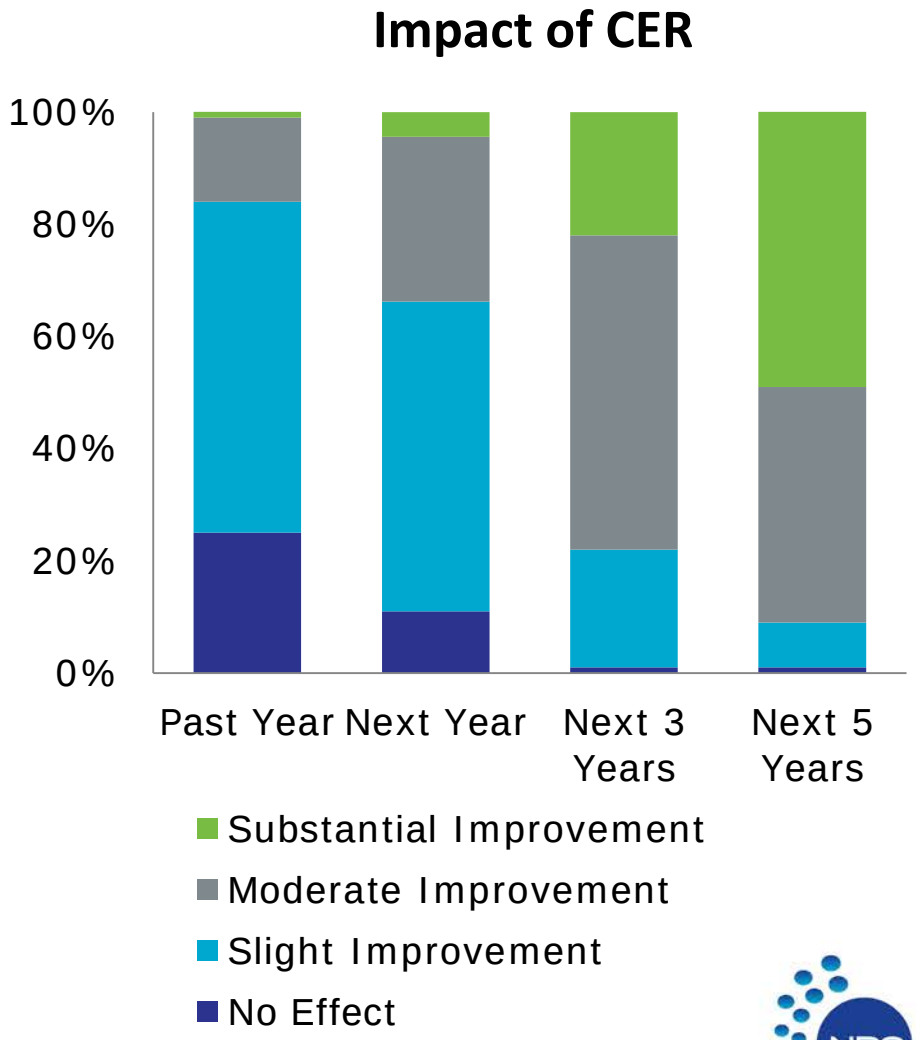
CER Collaborative

P&T use (Malone et al)

Medical Policy (Chambers)

CER Remains Important but Impact Remains 3-5 Years Out





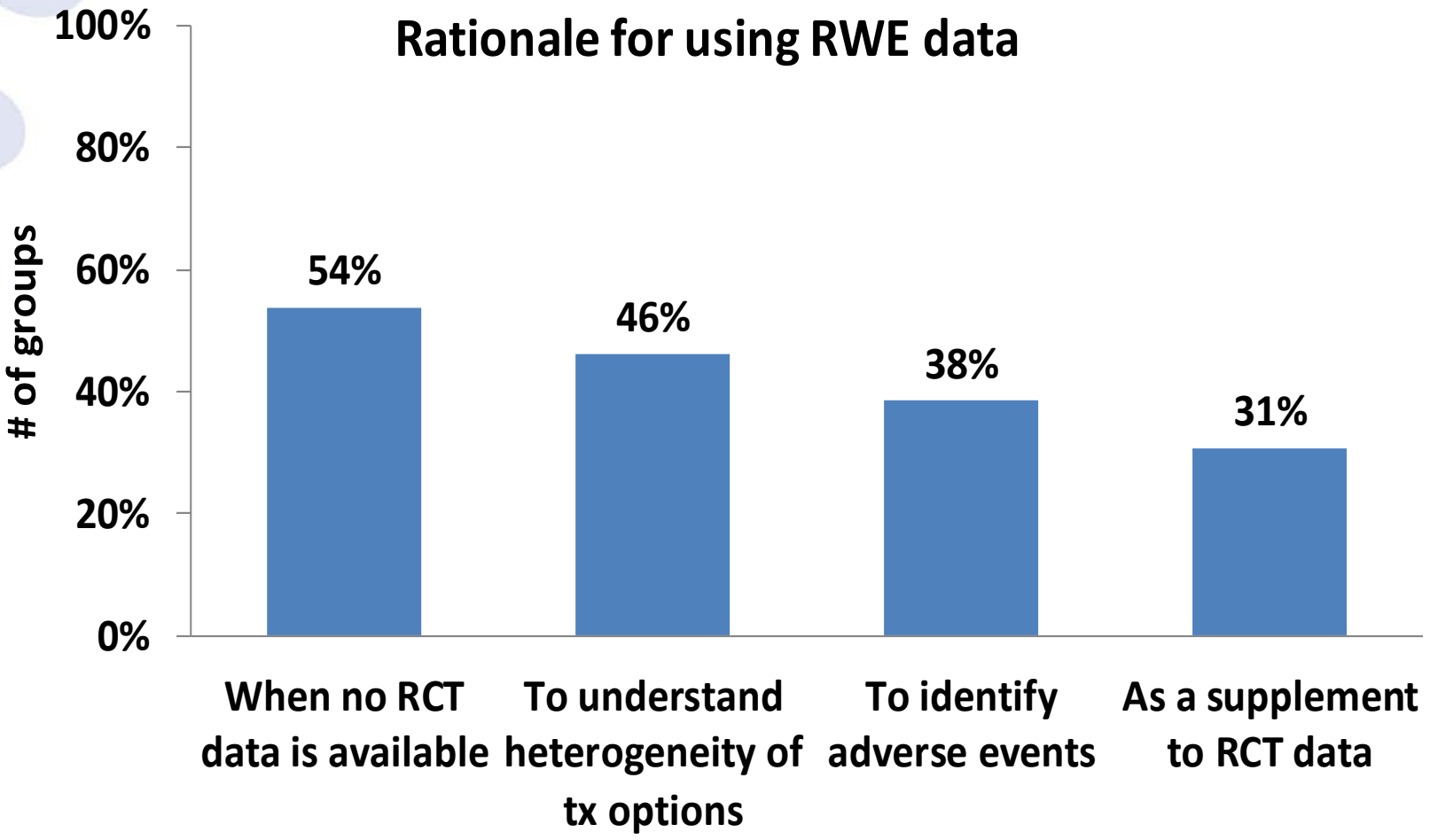
2016 Annual NPC CER Survey

Journal Editors Use the Same Criteria (ALMOST) for Reviewing Different Types of Studies

"Big data is more data. More bad 'data' cannot possibly make better data"

"We always get fewer RCTs than we want, so maybe we have a lower bar. But for RWE, we know we will get enough papers, so "was there an interesting question" becomes more important" - RT participant

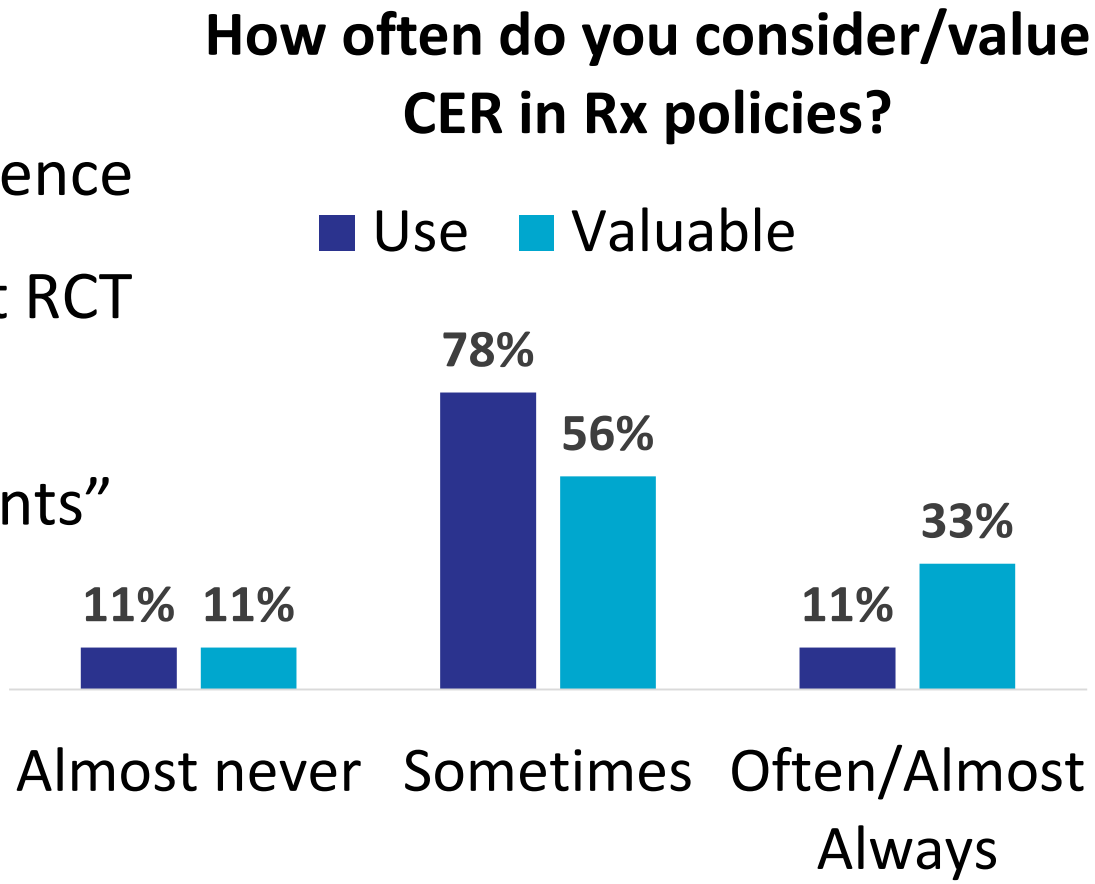
Acceptance Varies by Clinical Practice Guideline Group



Rangaro S. et al. Are Clinical Practice Guidelines Being Informed by Real-world Data? In review.

Most, But Not All, Payers Use RWE For Some Decisions

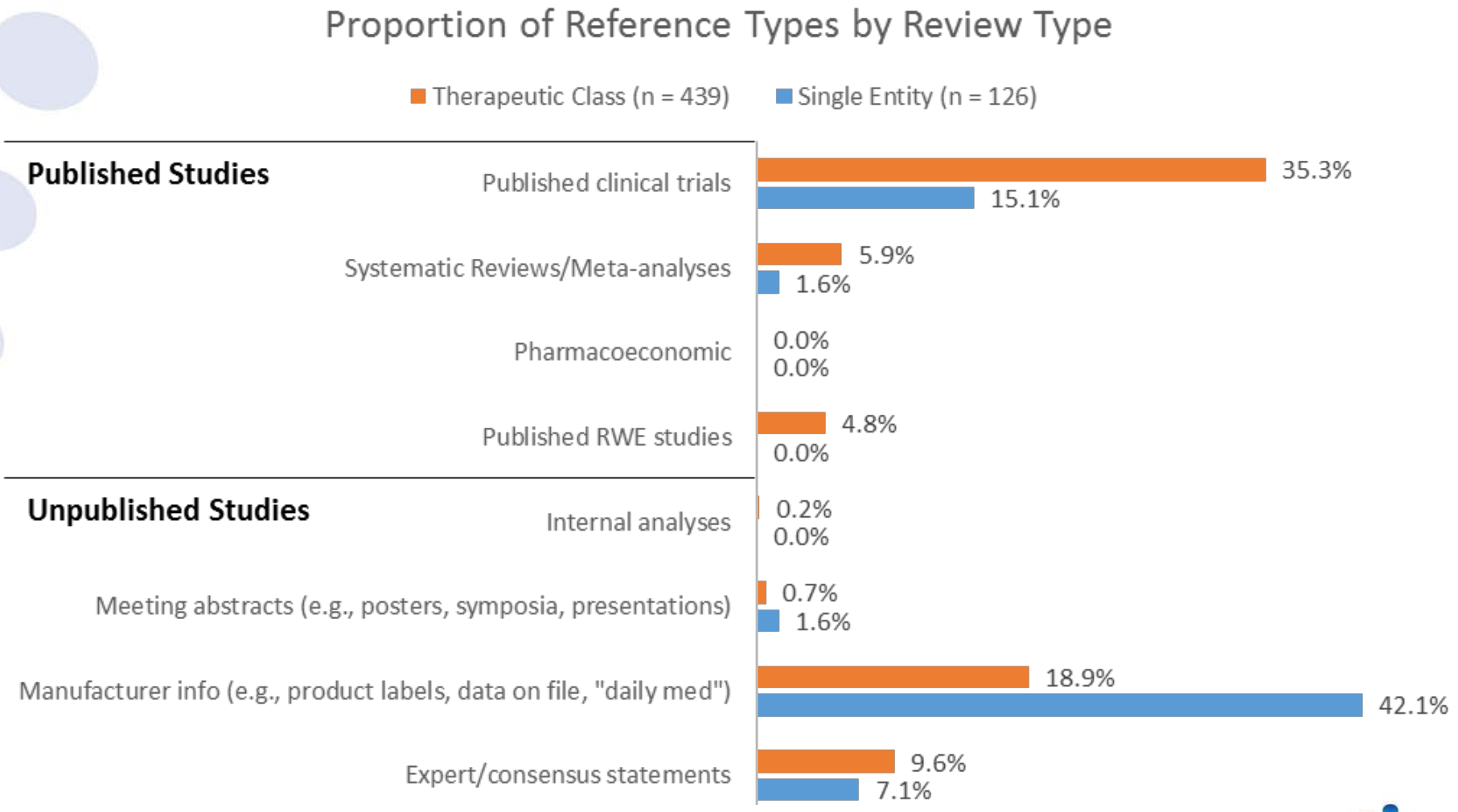
- Best Available Evidence
- Use to Supplement RCT Findings
- Value of "My Patients"
- Do not Use



N=17

Hurwitz et al. Is There Evidence in the Real World that Real World Evidence is Used in P&T Monographs and Therapeutic Class Reviews? JMCP. In press.

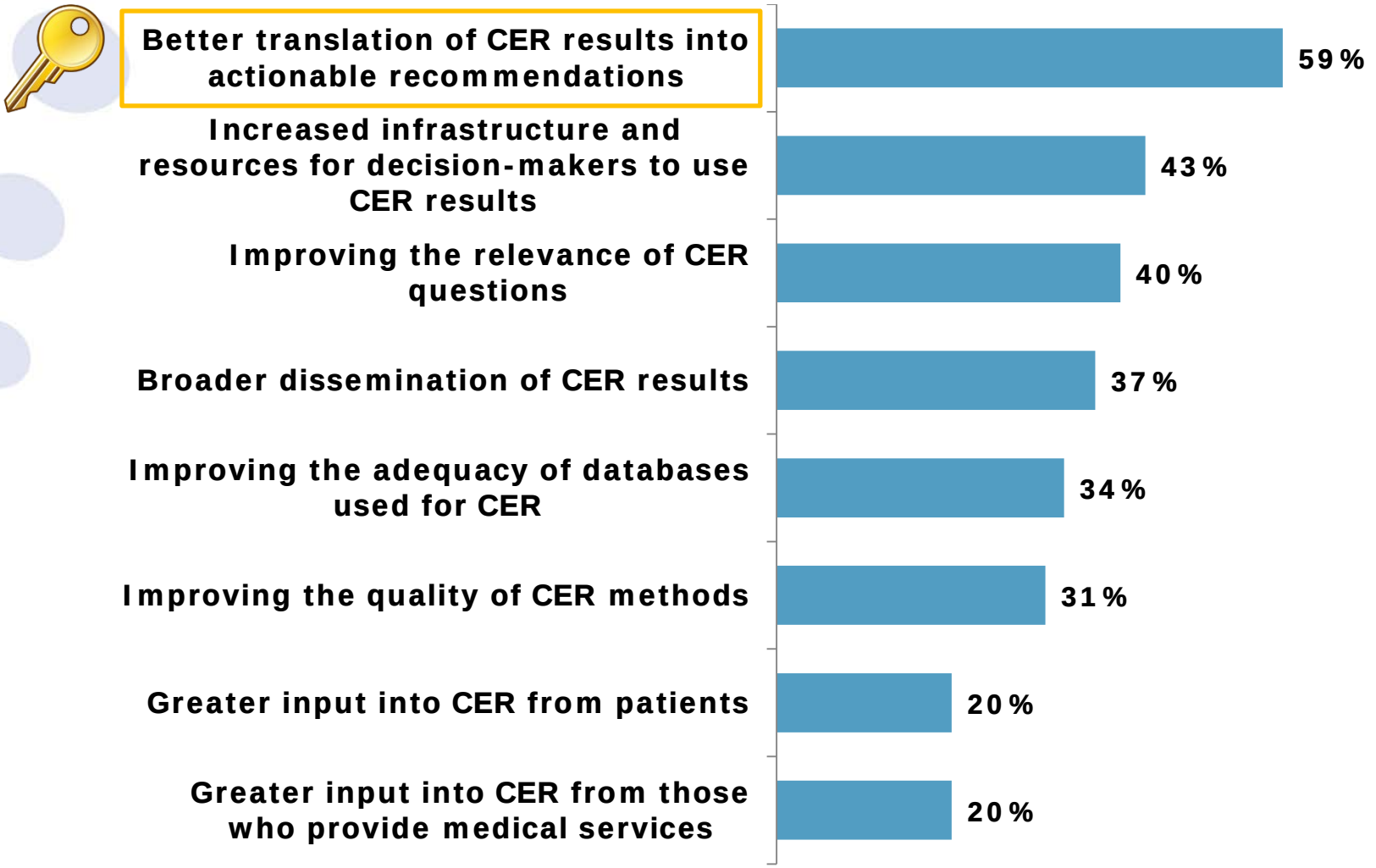
Many Types of Evidence Cited in P&T Monographs; Findings Replicated in Medical Policy Review



N=17

Hurwitz et al. Is There Evidence in the Real World that Real World Evidence is Used in P&T Monographs and Therapeutic Class Reviews? JMCP. In press.

Recommendations to Increase CER's Impact



N=137

2016 NPC Annual CER and the Environment for Health Care Decision-Making Survey

1. Ask An Important Question

- Question:
  - Delivery system reform, care coordination, wellness programs
- Endpoints
  - Long-term safety, impact on performance measures
- Comparators (usual care vs. optimal usual care)
- Population

Reynolds et al. 2010;
Sabharwal RK. AJMC 2015:21(9): Malone et al

2. Understand Who CARES?

"Who's the audience they're trying to influence and what's important to them? And so, if you want a payer to pay attention you have to have economic endpoints in the study." - Payer

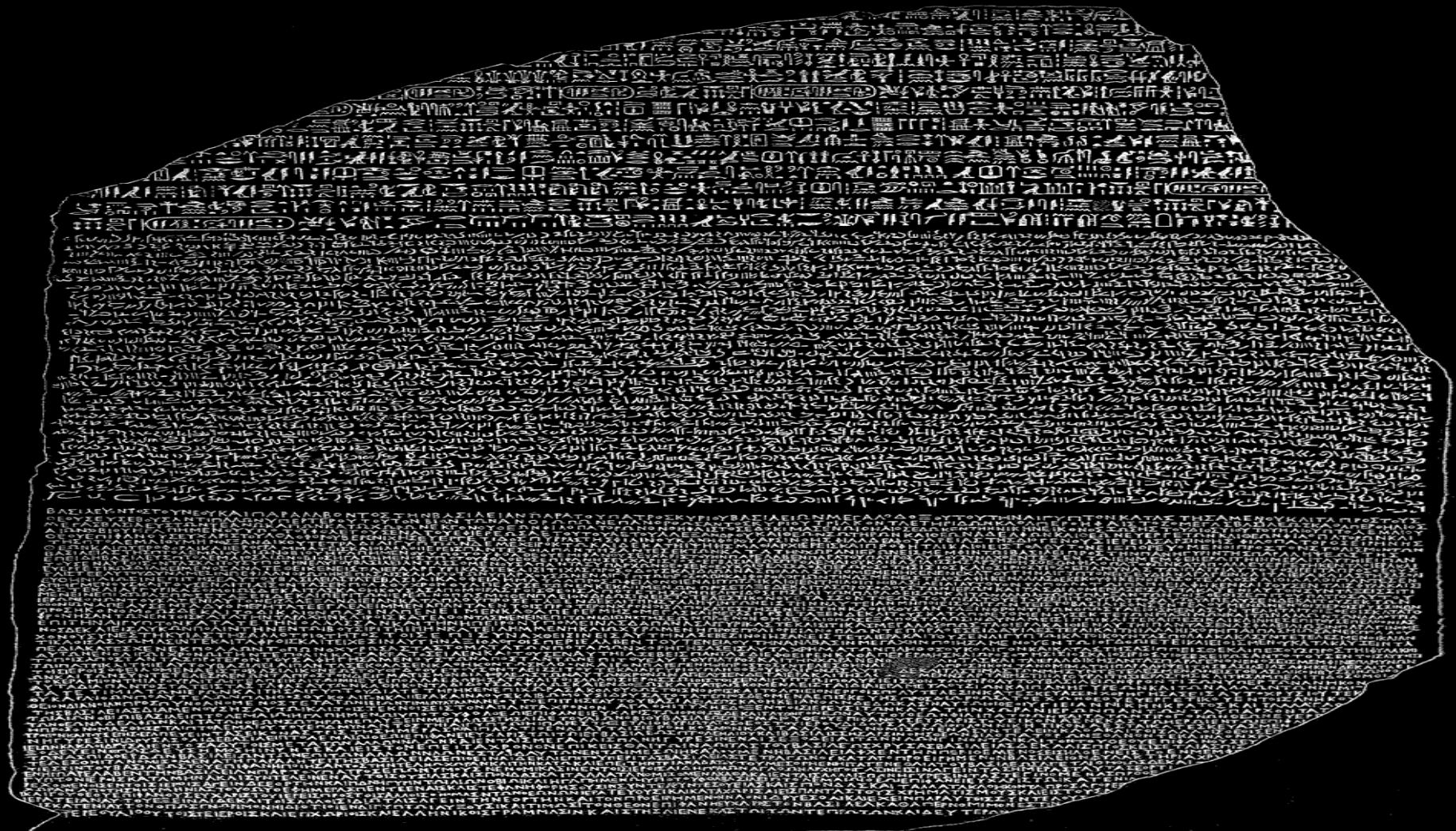
- Report break down of composite endpoints (Major CV event, total cost of care vs. individual endpoints or costs)
- Make the endpoints translatable to practice (post index costs vs. Per member/per month; return to work for stroke)
- Ability to apply to work force vs. retirees (Employers)
- Simplify the language

3. When? How Much?

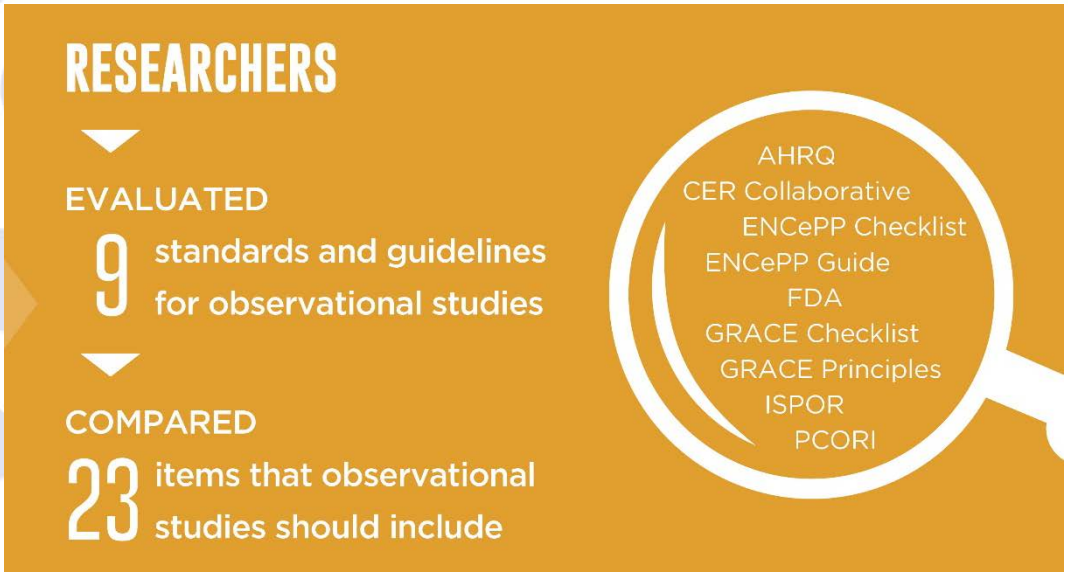
- Timing Matters
- Evidence needed when uncertainty exists (changing patterns of use, clinical practice guidelines)
- More Impact — Not Just More Evidence
- Impact must justify the resources required to change practice (cost for administration etc.).

Sabharwal RK, Graff JS, Holve E, Dubois RW. AJMC 2015;21(9)

No Rosetta Stone Exists For Observational Studies



5. Lack of Standards Impacts All Stakeholders; Policies Are Needed to Gain Consensus



39% addressed by less th
half of the best practices

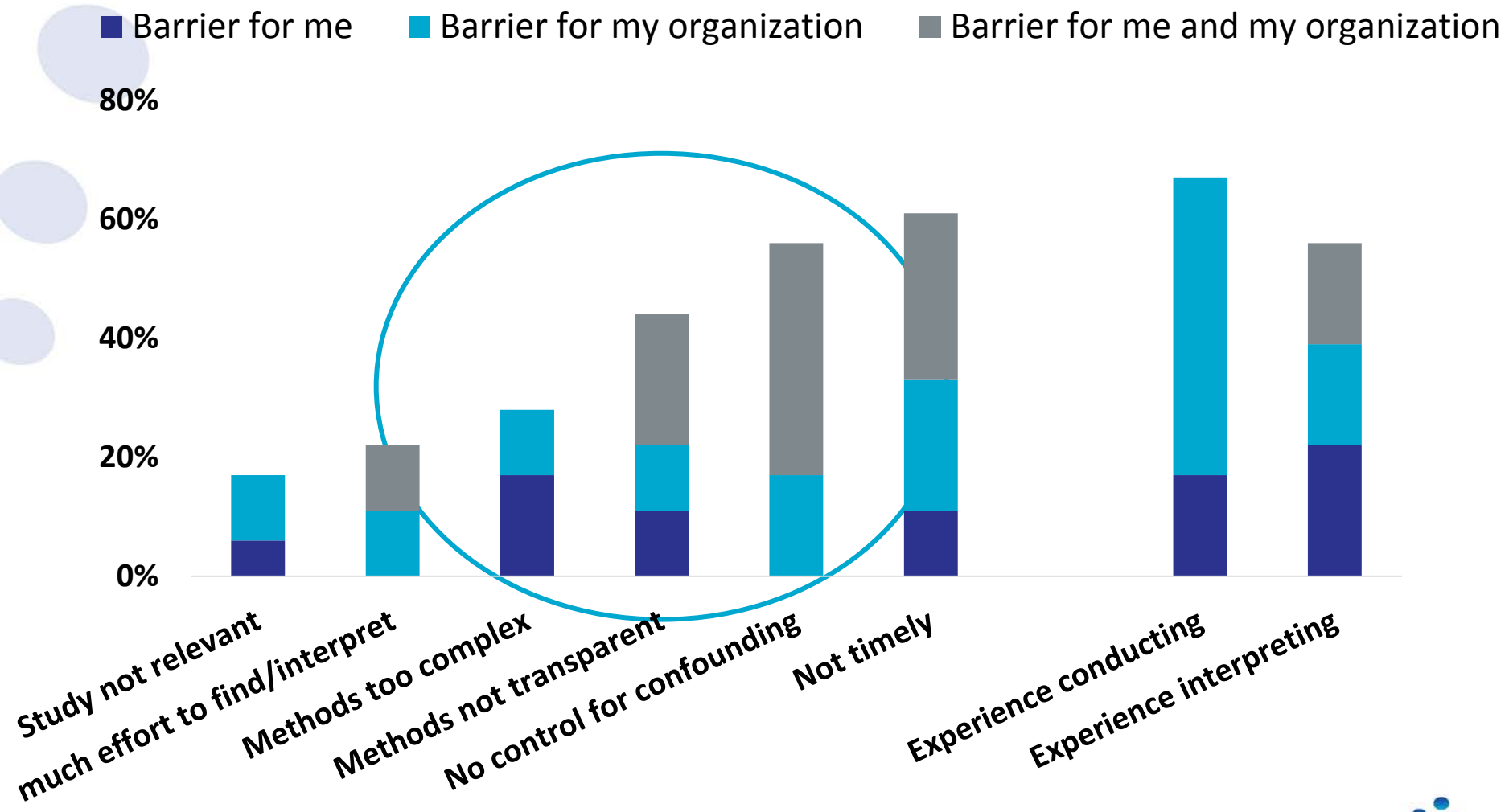
61% addressed by most best practices

- 2 agree on how to do
- 12 disagree on how to do

Policies Needed:

Morton SC. Journal of Clinical Epidemiology. 2015; online.

Barriers to Use – Payers
Mix of Systematic and Research Issues



N=18; Barriers to use of observational studies in decision-making

6. Improve the Transparency of Methods

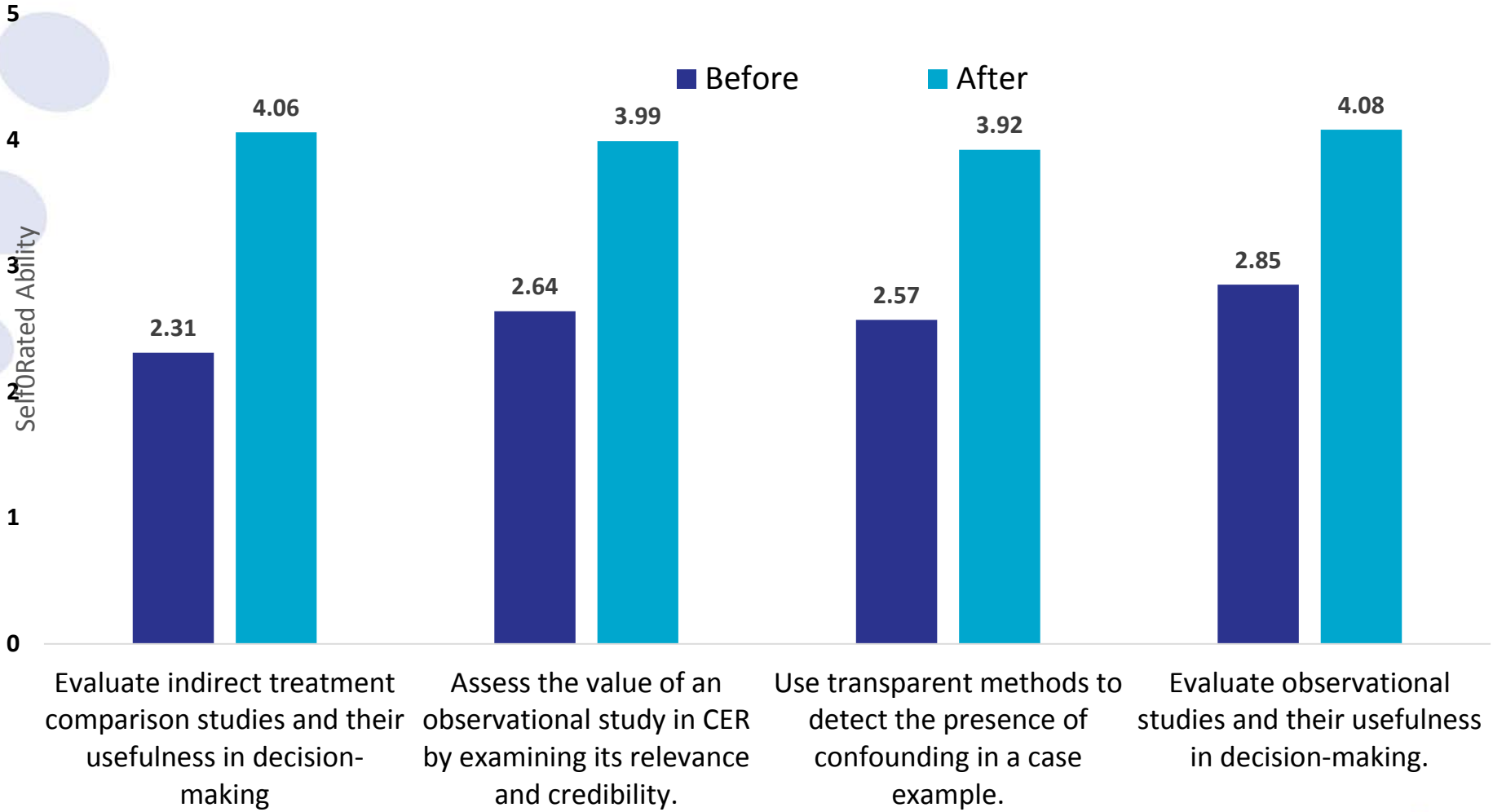
Share the population and generalizability

- Are they like my patients?
- Are the sites like my site? .

Be transparent in the study analysis and processes

- Methods are too complex (CPGs, Payers)
- Methods insufficiently explained (CPGs; Payers)
- **Is it the first or the 12th analysis?**
- Can this be recorded in a time box/lock registration?

7. Training and Tools Can Help… Experts, Others Etc.



Perfetto EM et al. JMCP 2016;22(6):609-16

8. Trust…in Data, Research, and Communication

- Trust the data?
  - Is it accurate, complete, and validate? (Kahn et al)
  - *"I know where the holes (in the data) are" – Payer*
  - *"If they don't know the datasets, can reviewers really evaluate those studies?" –Journal editor*
- Trust the research type/validity?
  - Clinician acceptance?
  - Funding source/affiliation
- Trust and intermediary?
  - Employee health benefits consultant ?
  - Clinical Practice Guidelines
  - Seal of approval on good studies?

Reynolds 2010.
Rangaro S. et al. Are Clinical Practice Guidelines Being Informed by Real-world Data? In review.

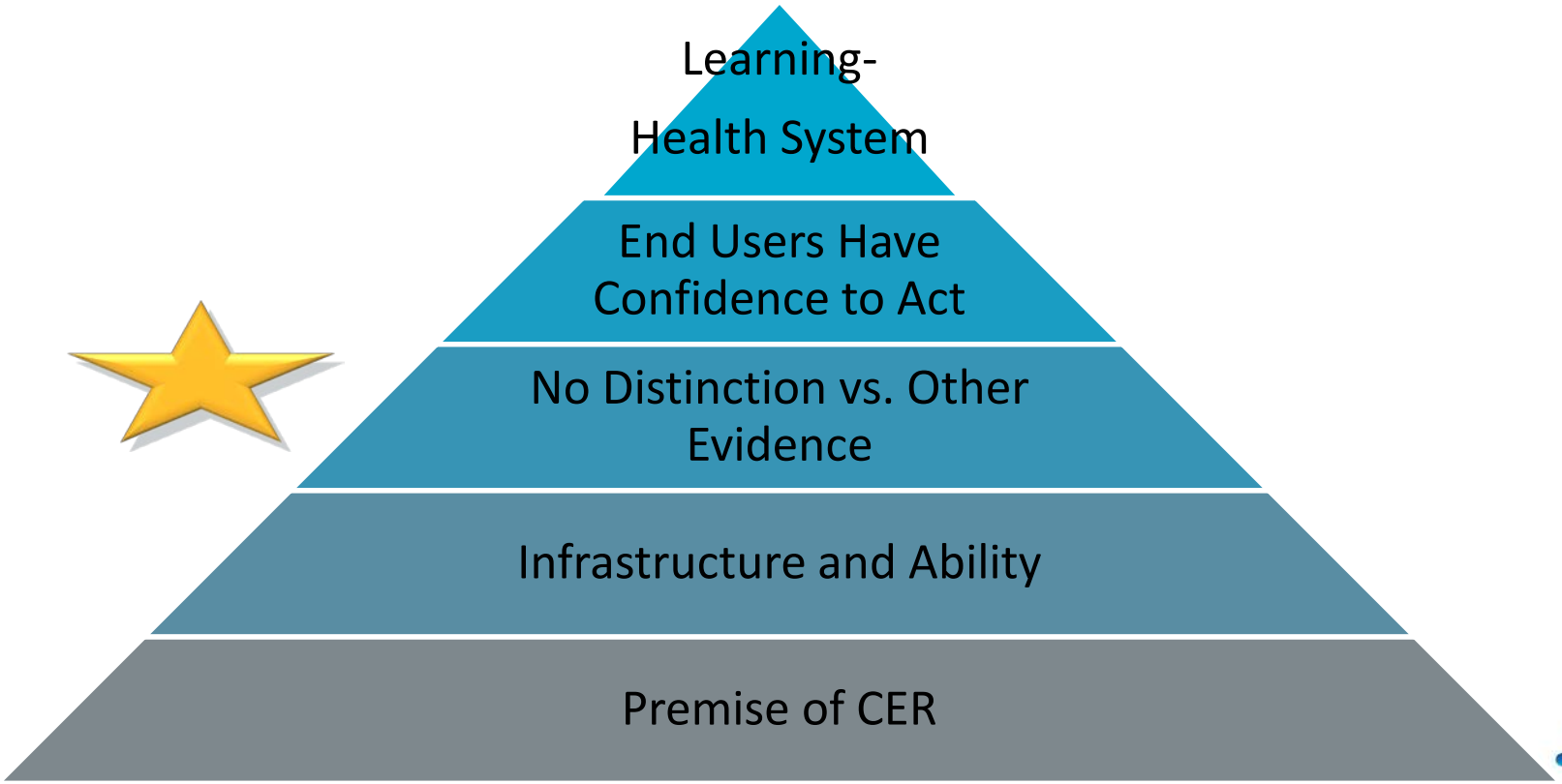
9. Build Infrastructure to Make it Easy

- Easier to communicate results
- Easier to access data
- Easier to interpret data
  - More evidence= more time and resources
  - Expertise not typically on guideline development group
- Easier to understand impact to specific patients

10. CER should be *collaborative*… Not *comparative* between disciplines and stakeholders

What PCOR and CER Can Be, It Must Be!

Are PCOR and CER fully developed research approaches? Where are we on the journey? What are the opportunities?



Maslow's Hierarchy of needs

Break

A Deeper Dive: Small Group Discussions

Observations: Reports from Small Group Discussions and Overall Consensus

Lunch and Presentation: A Learning Network - Improving the Dissemination of PCOR-Based Clinical Decision Support

Barry Blumenfeld, RTI International

PhRMA FOUNDATION

AMCP Academy of Managed Care Pharmacy®

The Patient Centered Outcomes Research Clinical Decision Support Learning Network (PCOR CDS-LN)

Transforming Patient Centered Research into Action

Barry Blumenfeld, MD, MS
bhb@rti.org

Learning Objectives for Today

- What is the PCOR CDS Learning Network?
- Some Key Concepts
- What We Have Learned So Far?
- What We are Doing Next

Motivation for the PCOR CDS-LN

Translating knowledge gained from Patient-Centered Outcomes Research (PCOR) into clinical practice is key to healthcare quality improvement. A promising way to ensure that PCOR informs clinical care is through clinical decision support (CDS), which uses technical and non-technical approaches to make it easier for care teams – including patients – to make decisions and take actions known to enhance outcomes

Definitions we are Using

PCOR IS…

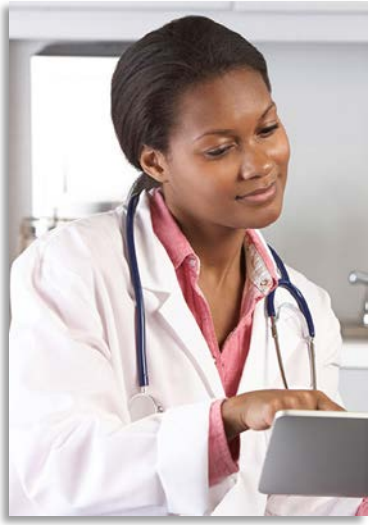
The ACA defines PCOR as, “comparative clinical effectiveness research on the impact of patient health outcomes of two or more preventive, diagnostic, treatment, or health care delivery approaches.”

CDS is…

Clinical Decision Support (CDS) is a process for enhancing health-related decisions and actions with pertinent, organized clinical knowledge and patient information to improve health and healthcare delivery. Information recipients can include patients, clinicians and others involved in patient care delivery; information delivered can include general clinical knowledge and guidance, intelligently processed patient data, or a mixture of both; and information delivery formats can be drawn from a rich palette of options that includes data and order entry facilitators, filtered data displays, reference information, alerts and others.*

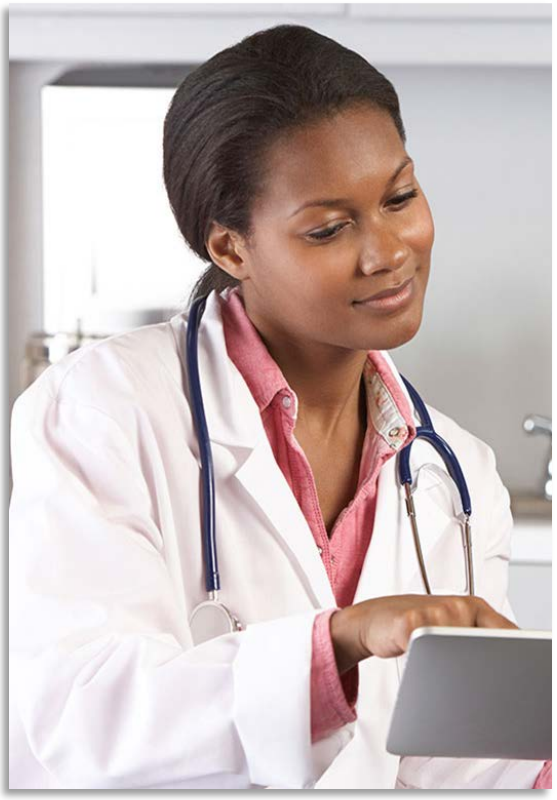
A Short Story - Patient-Centered CDS

A Short Story - Patient Centered CDS



What is the evidence for self-measured BP monitoring?

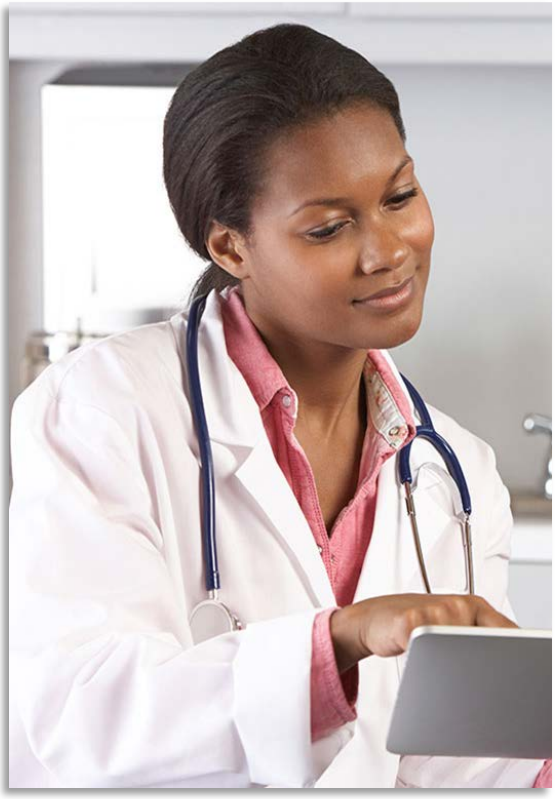
A Short Story - Patient Centered CDS



The Clinician:

1. Has difficulty finding specific evidence among multiple sources
2. Questions which evidence is most reliable
3. Needs to know about evidence that is actionable both for her and the patient
4. Wonders what the evidence says around what is measurable

A Short Story - Patient Centered CDS



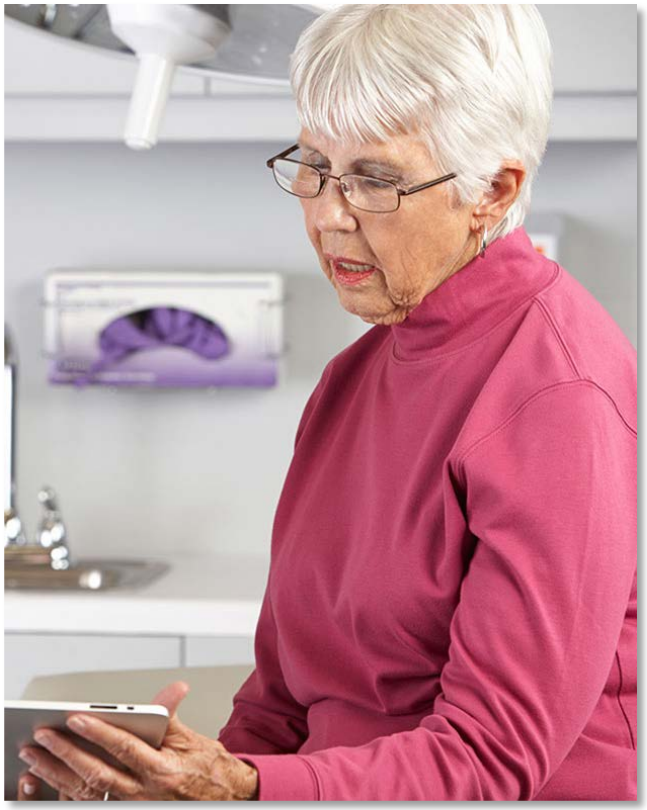
The Clinician Wants:

1. One or more repositories with PCOR-enabled CDS tools
2. Embedded clinical care and patient engagement that generate secure and reliable data
3. Confidence that any CDS tool fits into the EHR and workflow
4. Clinically meaningful results for her care and reimbursement

A Short Story - Patient Centered CDS

The Patient:

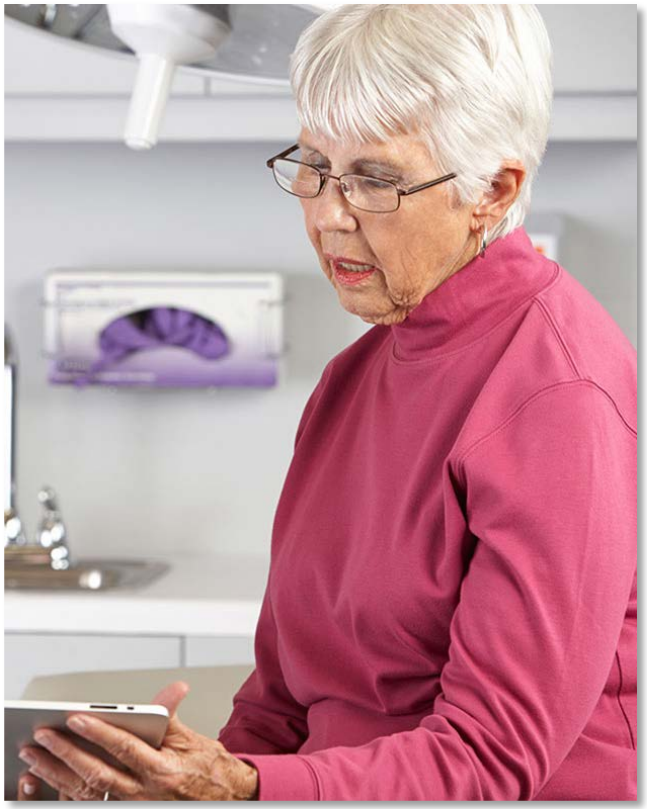
1. Has concerns with the side effects of her meds
2. Knows that her pen and paper logs are inconsistently used
3. Is open to the idea of sharing data with her MD “in theory”
4. Agrees technology could be helpful but “not good with computers”



A Short Story - Patient Centered CDS

The Patient Wants:

1. To learn how she can mitigate side effects
2. Support to improve how she tracks her data from the convenience of home
3. Her safety, privacy, and reliability concerns to be addressed
4. Usable tools and data that help her self-measure her BP for improved decision-making



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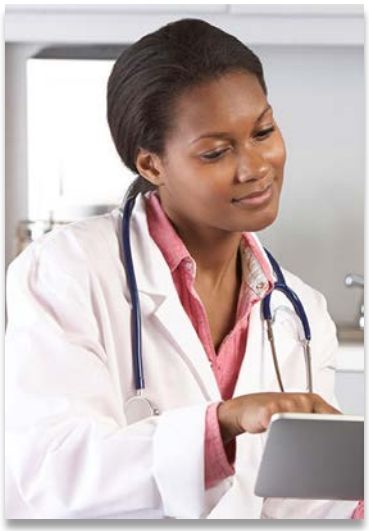
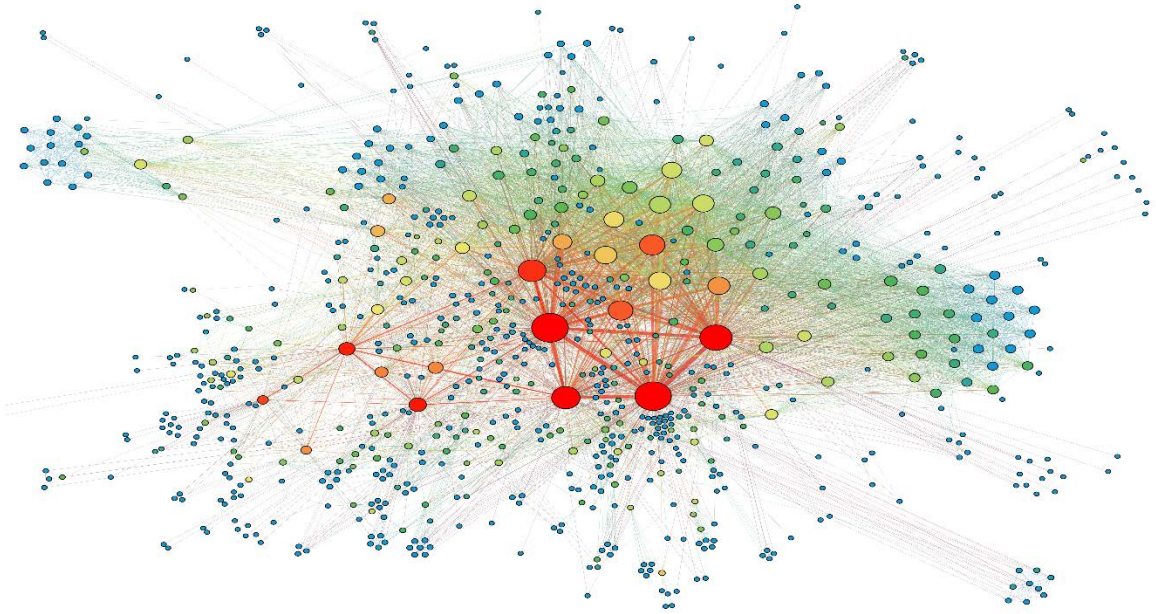
A Short Story - Patient Centered CDS



Delivering evidence through CDS…

A Short Story - Patient Centered CDS

to promote patient-centered care…



Requires collaboration among multiple stakeholders.

Patients. Care Givers. Vendors. Providers. Payers. Researchers. QI Organizations. Societies. And more…

The PCOR CDS Learning Network

Our Mission

To create a learning network that allows stakeholders to turn knowledge from patient-centered evidence and practices* into clinical decision support (CDS) that improves care and outcomes.

Inform **Connect** **Advance**

- 4 year Cooperative agreement awarded by AHRQ
- Period of performance: 4/2016 – 1/31/2020
- PI: Barry Blumenfeld, MD, MS, (bhb@rti.org)
- Senior Investigators: Blackford Middleton, MD, MPH, MSc and Jerome Osheroff, MD, Robert Greenes, MD, PhD, and Kensaku Kawamoto, MD, PhD, MHS

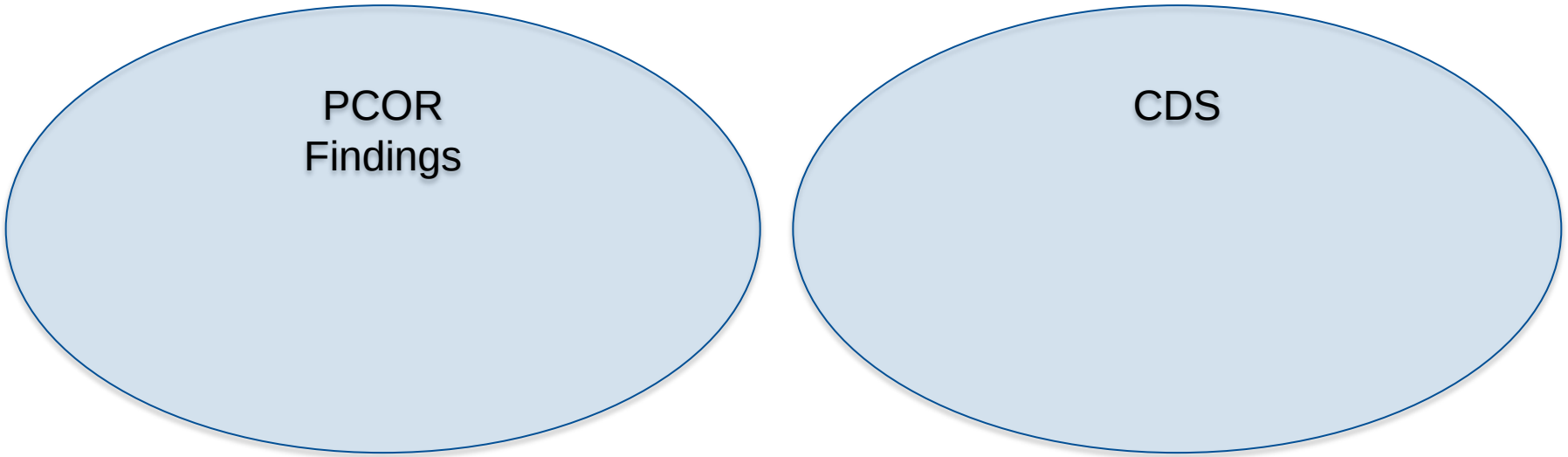
*Includes CER and PCOR

PCOR CDS Learning Network Strategies

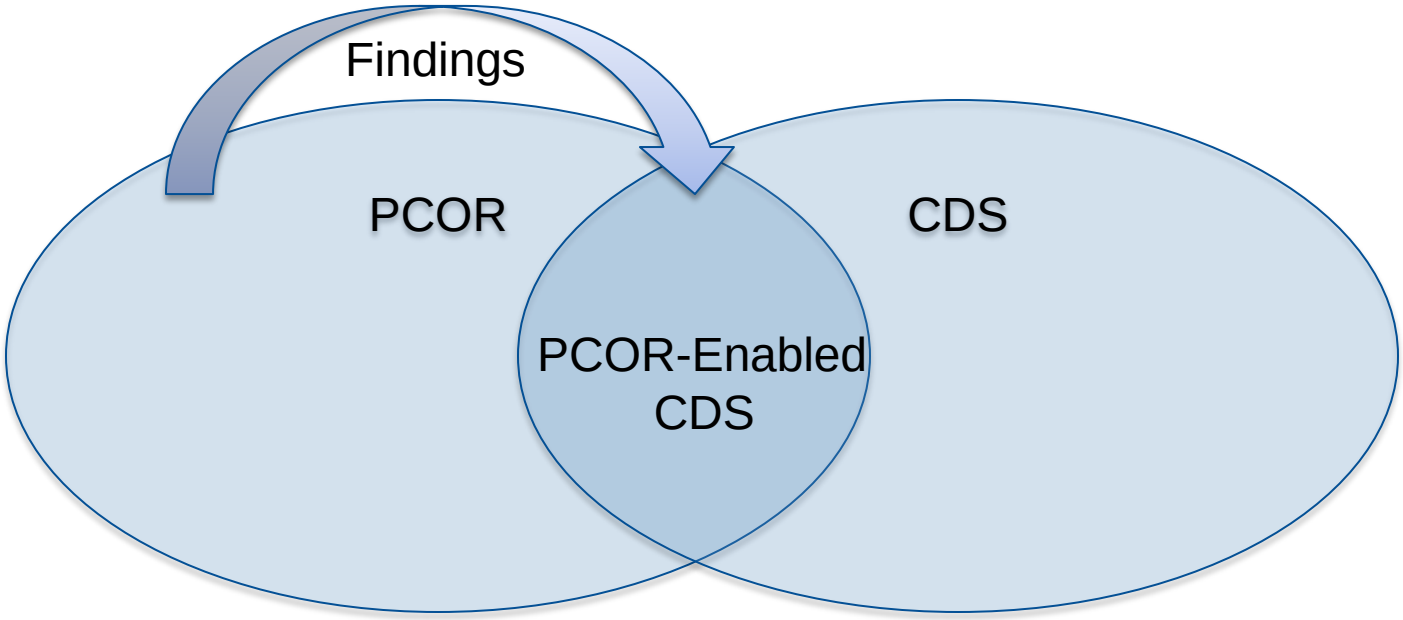
- **Inform**
  - Provide Stakeholders with a broad array of up-to-date information germane to Patient-Centered CDS
- **Connect**
  - Provide information and services that allow stakeholder to connect and collaborate
- **Advance**
  - Foster the collaborative development of concepts, frameworks, policies and standards for Patient-Centered CDS

What We've Learned so far…

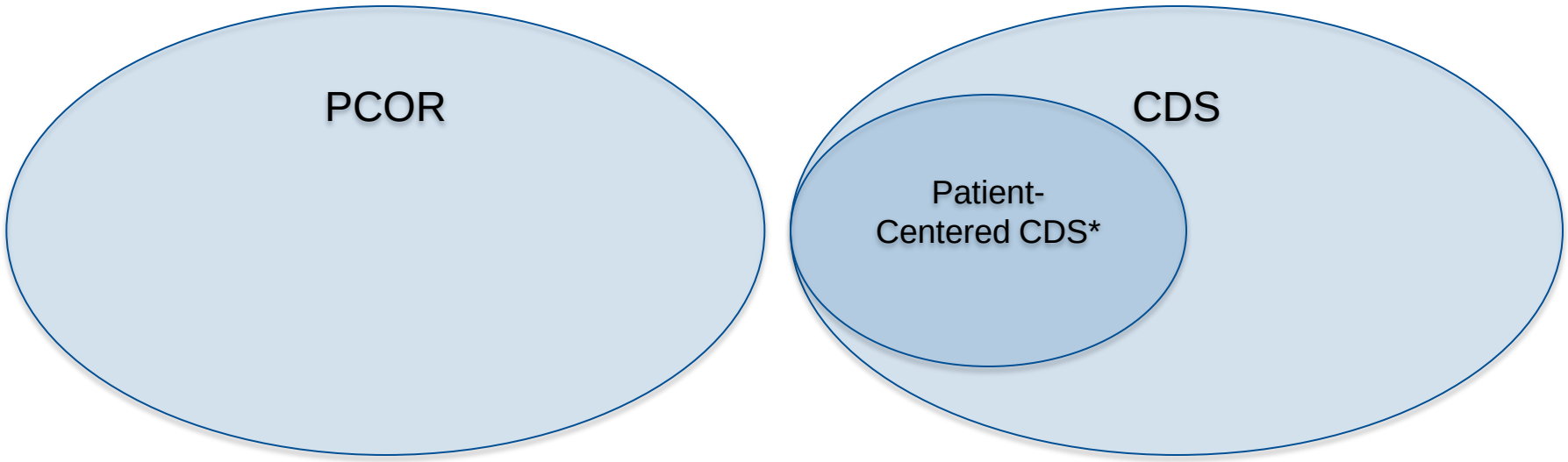
Key Concepts



Key Concepts: PCOR-Enabled CDS

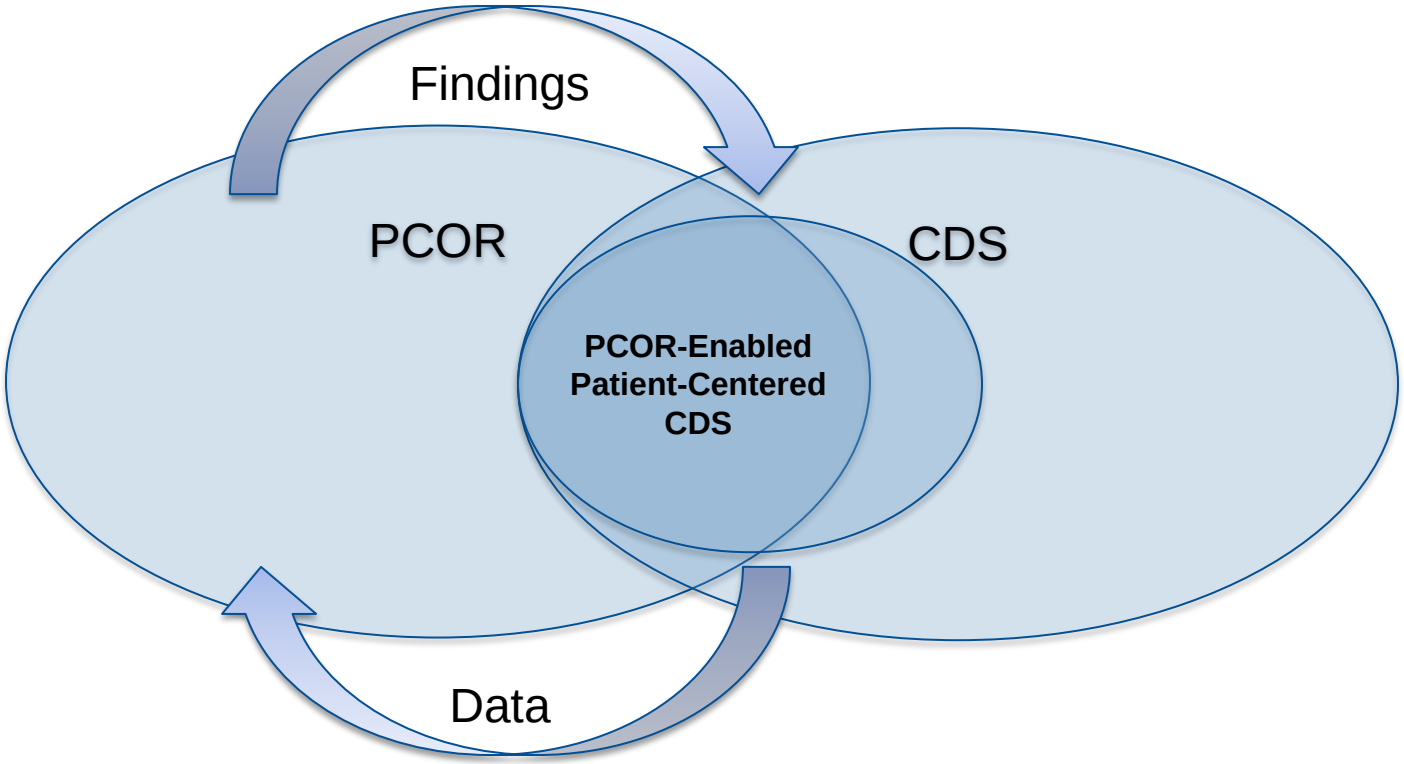


Key Concepts: Patient-Centered CDS



*This is a new term and is still being defined

Key Concepts: PCOR–Enabled, Patient-Centered CDS



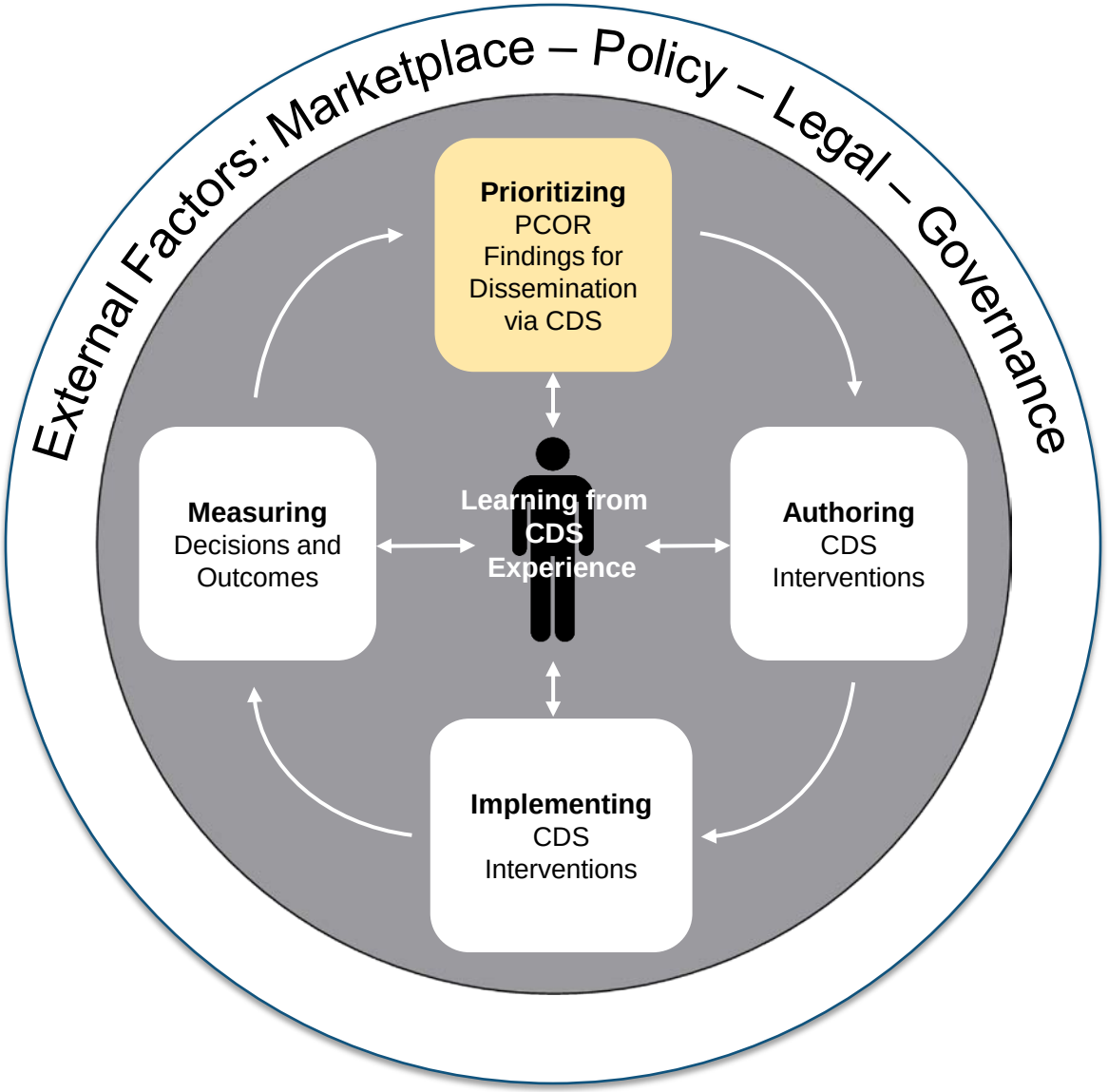
- Patient Centered CDS is a broader concept and subsumes PCOR-Enabled CDS
- Patient Centered CDS Is both a channel for PCOR findings and a source of data for research

The Analytic Framework for Action (AFA)

*One of the first activities of the PCOR CDS-LN was to identify barriers and facilitators to the dissemination of PCOR-Based CDS. A critical artifact that grew out of this effort is the **Analytic Framework for Action (AFA)**.*

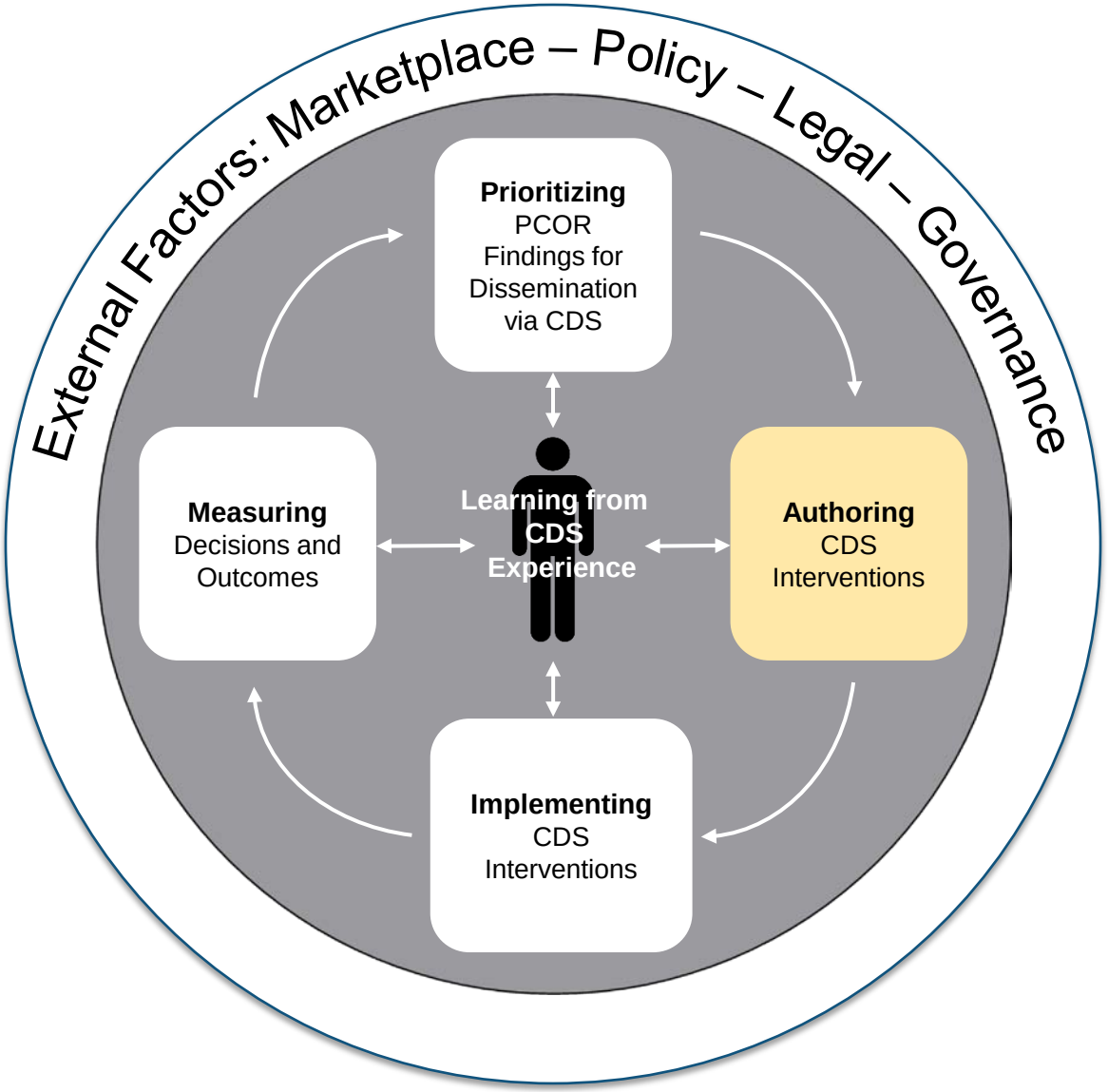
*The **AFA** provides a means by which we can organize the findings and recommendations of the PCOR CDS-LN. It represents the lifecycle of activities that must occur to disseminate POCR through CDS, measure impact, and create a learning system*

The AFA



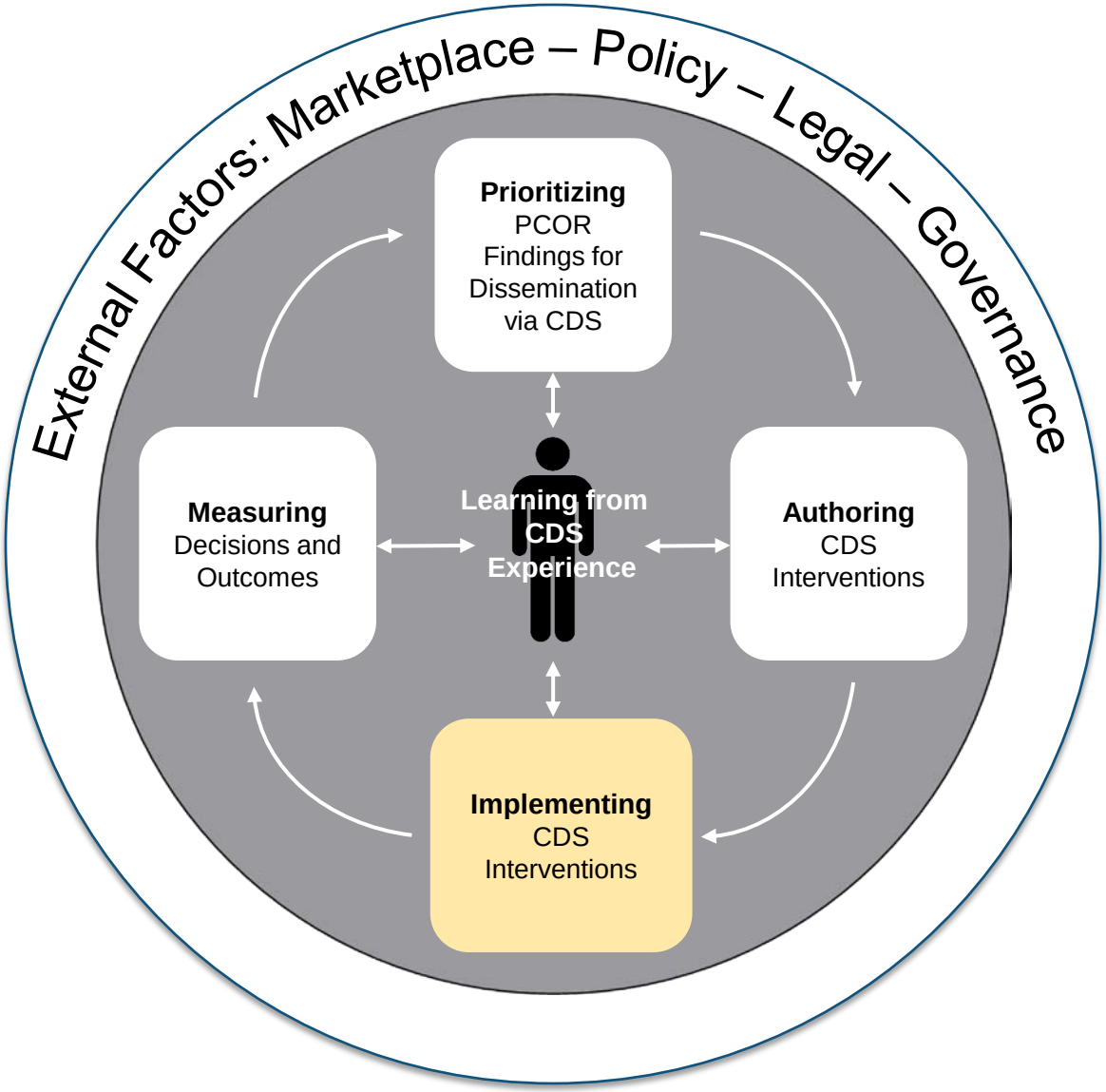
Step 1: *Applying objective measures of evidence for identifying and prioritizing PCOR findings that are to be transformed and disseminated via Patient –Centered CDS, assessing or defining their implementability, and defining stewardship and governance requirements.*

The AFA



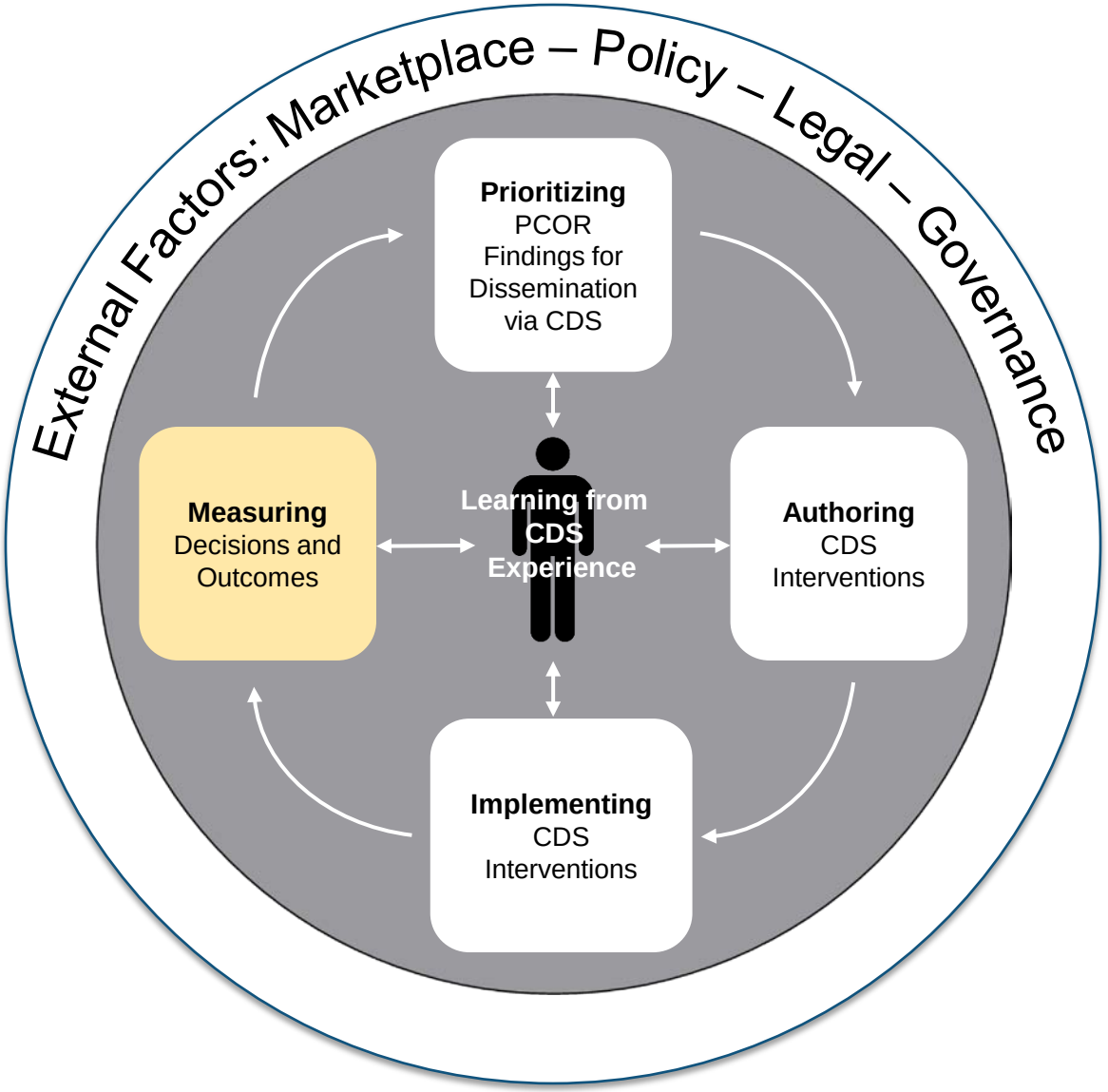
Step 2: *Applying consensus-based data and knowledge standards for translating PCOR findings into CDS interventions that support comparative and/or patient-centered decision-making (i.e. risk calculators, cognitive aides).*

The AFA



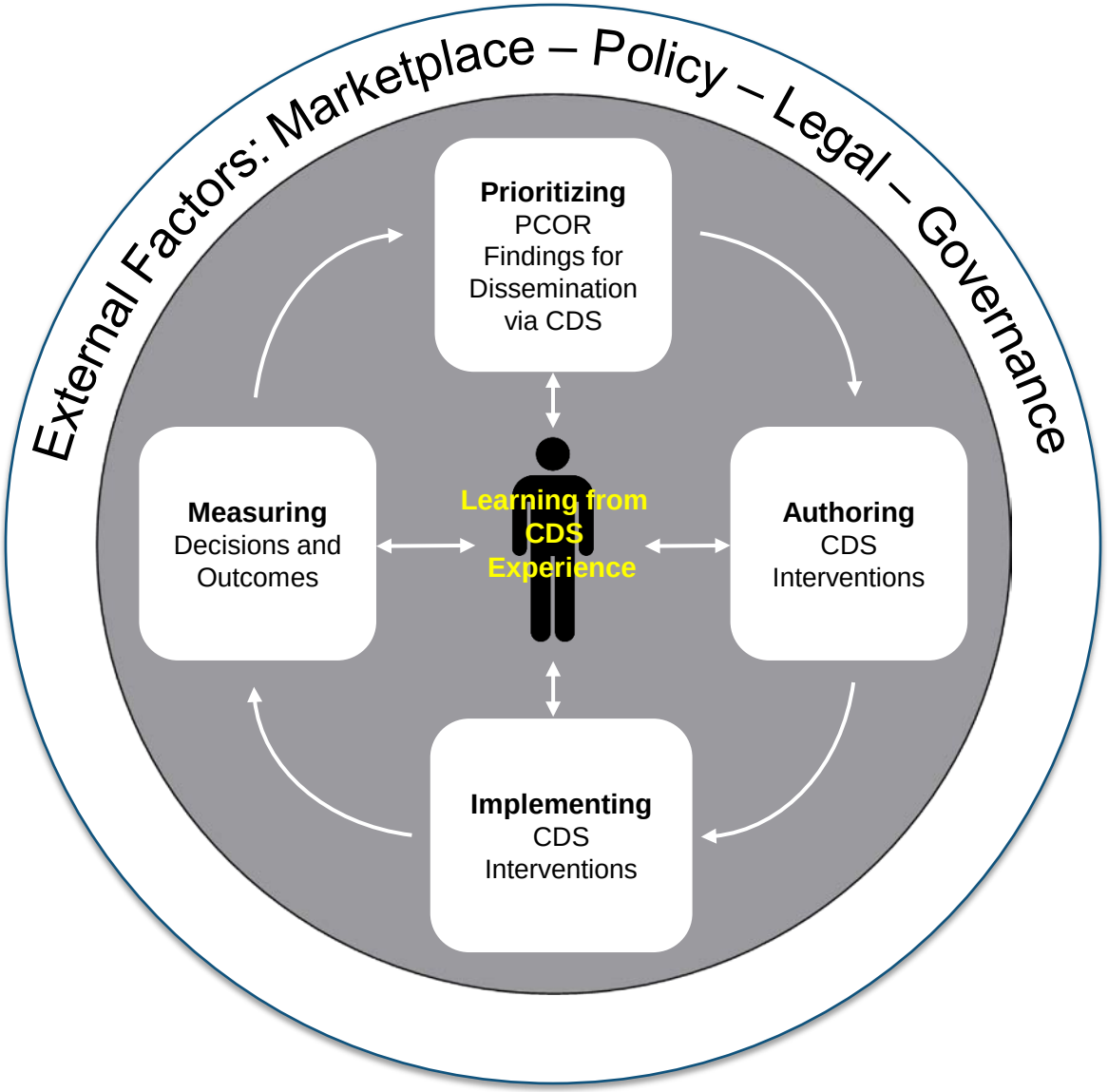
Step 3: *Applying standardized methods and architectures for operationalizing CDS interventions into clinical workflows, which deliver the right information to the right people in the right formats through the right channels at the right times ("CDS Five Rights").*

The AFA



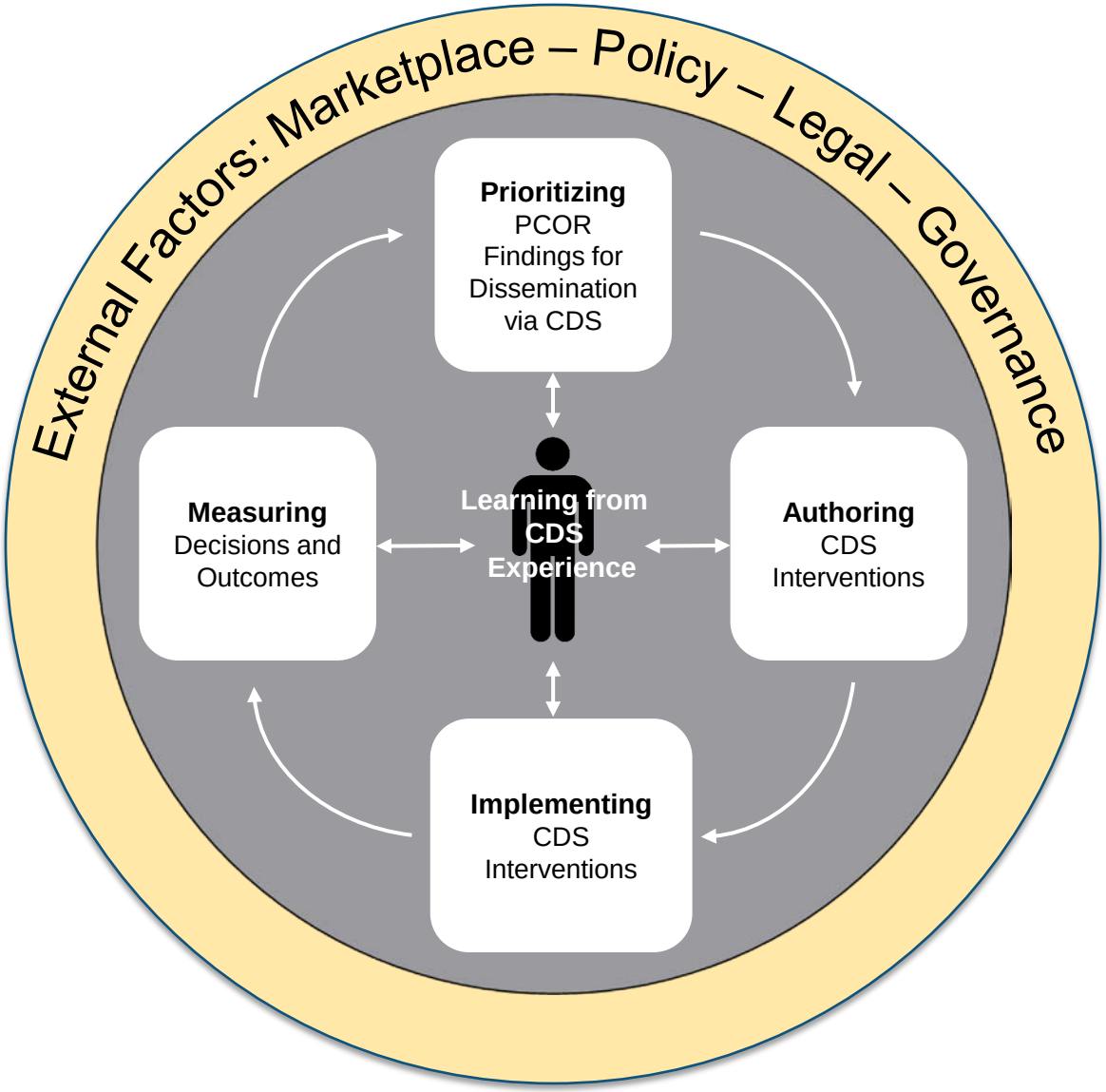
Step 4: *Ensuring that CDS interventions measurably improve clinician and patient decision-making, care processes, and outcomes.*

The AFA



Step 5: *Aggregating local CDS-related outcomes and effectiveness measures to facilitate patient-centered, system level learning from identified gaps in PCOR knowledge, clinical practice, and patient outcomes.*

The AFA



Throughout the Process: *Recognize and Manage External factors including the marketplace, policy, legal, and governance factors that impact development, dissemination, and implementation processes for Patient – Centered CDS.*

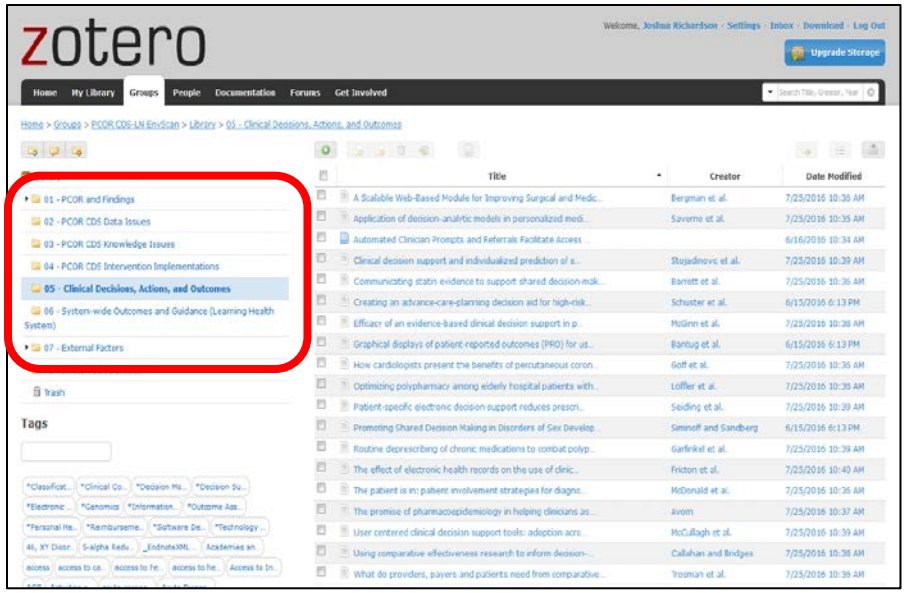
The Environmental Scan: A "Springboard for Action"

- Purpose: Examine the barriers and facilitators to the use of CDS as a vehicle for putting PCOR findings into practice to improve outcomes.

- Goal: Give the PCOR CDS-LN a comprehensive review of the current state of the field to include: technologies and architectures; user needs; policy; and more.

Online Bibliography

- 316 citations
- PubMed, PCORI, Executive Committee recommendations
- Organized by Analytical Framework for Action
- Collection to be curated and disseminated
- Citations to be appended to the Environmental Scan



https://www.zotero.org/groups/pcor_cds-ln_envscan/items

Some Barriers and Facilitators

Barrier	Facilitator
Defining PCOR	Refine definition of PCOR
Defining and Describing Patient- Centered CDS	Generate a use cases
Access to Literature Around Patient-Centered CDS	Online bibliography
Costs and Competing Priorities for development and implementation	Estimate development and implementation costs in use case
Identifying PCOR to be disseminated via CDS	Build and/or extend partnerships with AHRQ and PCORI
Means for Evaluating PCOR for Patient-Centered CDS	Develop a resource with evaluation tools
Access to PCOR for Patient Centered CDS	Plan with AHRQ for development and dissemination of a repository
Patient-Centered CDS Not Aligned with Payer Priorities	Involve payers to insure payer perspectives

Full report available at: http://www.pcorcds-ln.org

The Barriers and Facilitators Workgroup

- Propose criteria for selecting PCOR findings to be used as use cases
- Determine PCOR findings to be applied in use cases
- Populate a use case matrix (see below), which is organized by the Analytic Framework for Action
- Disseminate findings

Million Hearts Initiative: SMBP Monitoring

http://millionhearts.hhs.gov/tools-protocols/smbp.html

Identifying Barriers and Facilitators

	Current State	Barriers	Facilitators	Recommendations	ACTION
Addressing External Factors (Marketplace, Policy, Legal, Governance)	Uncertain marketplace	Marketplace has been and remains challenging in that vendors don't implement CDS in any standardized way	MITRE Corp developing repository and PCOR CDS artifact	Build personalized patient medical/pharmacy coverage into CDS (antihypertensive tiering/preferred Rx etc.)	?
Prioritizing PCOR (What findings are appropriate given level of evidence, priorities, available data, etc.)	PCOR has a new dissemination group to potentially prioritize PCOR	Differences between the inclusion criteria and methodology of clinical trials/observational data and "real-life" application	"High quality" and "scientifically sound" PCOR evidence	Publicly available criteria for prioritizing PCOR	?
Authoring CDS (Intervention Types, Knowledge issues, Data issues)	A host of API-based services and approaches increasingly available	Access to Reliable PCOR Measures When Authoring PCOR-Based CDS	NA	Publish a library of approved patient-reported data sets and measures	?
Implementing CDS Interventions (Localization issues, architecture/methods, workflow integration,)	Variable degrees of monitoring the status of implementation and maintenance	Providers not trained to integrate PCOR into workflow	Leadership commitment to CDS as an intervention	Identify known implementation strategies and tools for improving care delivery that are transferable to PCOR-based CDS	?
Measuring Decisions and Actions (Measuring CDS efficacy and impact as well as value delivered and ROI/cost-benefit)	Ad hoc recording between home and clinic settings muddies measurement	Uncertainty as to how the patient's role in the intervention captured	Providers already reporting BP control for a number of measures and so there is momentum for expanding to this guideline	Publish a use case that identifies barriers and opportunities for measuring the effects of PCOR-based CDS	?
Learning from PCOR-based CDS Experience (Feeding results back to broadly enhance care/ outcomes/guidance faster)	CDS monitored within HCOs	Unknown how to integrate PCOR-Based CDS into a Learning Health System	Hardwired CQI process at team, department, organization, insurer, gov levels	Evaluate whether specific patient subgroups respond to different CDS approaches	?

Takeaway One…

Finding: There is a need to help both patients and clinicians navigate to PCOR findings suitable for CDS implementation

Our Experience:

- Current resources (e.g. guidelines.gov) didn't help to narrow
- The BFWG arrived at SMBP Monitoring through our network of experts rather than a particular source

Recommendation: Invent or build on a repository with vetted PCOR by levels of implementability

Takeaway Two…

Finding: PCOR-based patient-centered information is not offered in any type of machine-readable format

Our Experience:

- The SMBP Monitoring guideline is a narrative handout geared to clinicians and patients
- The SMBP Monitoring guideline and others elsewhere don't provide machine-readable logic

Recommendation: Work with CDC to plan and develop its SMBP Monitoring guideline as CDS

Takeaway 3…

Finding: Unclear how SMBP monitoring data will be accurately and consistently reported in the patient record

Our experience:

- What, if any, PCOR evidence is there around reminders for patients at home to self measure BP?
- How do data in SMBP reflect factors such as device type (ambulatory BP monitor vs home BP monitor), patient position (supine vs sitting), etc.?

Recommendation: Collaborate with researchers and vendors around ways to structure and capture SMBP monitoring data

Where We Are Going…

PCOR CDS-Learning Network Collaboration Hub

www.pcorcds-ln.org

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Activities in 2017

Informing, Connecting, Advancing

- Key Topic Workgroups
  - Barriers and Facilitators (in progress)
  - Dissemination
  - Technical Standards
  - Evaluation
  - Sustainability
- Enhancing the Collaboration Hub www.pcorcds-ln.org

- Annual Meeting
  - 2nd Annual Meeting in September 2017, Washington DC (open attendance)
- Planning E-Journal focused on Patient-Centered CDS in 2017
- Developing consensus recommendations and reports
- Promoting Patient-Centered CDS research

Engaging and Collaborating with You!

Questions?

- Contact Information
  - Barry Blumenfeld, MD, MS (bhb@rti.org)
  - Collaboration Hub: http://www.pcorcds-ln.org

The PCOR CDS Learning Network

Transforming Patient Centered Research into Action

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What Is the Future of CER and CER Education? How Will CER Be Integrated Into Practice?

Diana Brixner, University of Utah & President-Elect, Academy of Managed Care Pharmacy (AMCP)

Bill Galanter, University of Illinois at Chicago

Lou Garrison, University of Washington & President, International Society of Pharmacoeconomics and Outcomes Research (ISPOR)

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Perspectives on the Future of Comparative Effectiveness in Research, Education and Practice

Diana Brixner, RPh, PhD
Professor, Department of Pharmacotherapy
Executive Director of Pharmacotherapy
Outcomes Research Center
Director of Outcomes, Program in Personalized Health
Academy of Managed Care Pharmacy President Elect

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The opportunity for CER has never brighter

- CER is being considered for regulatory decisions for medical devices
- Data sources available to conduct CER is growing
- Research methods for CER are rapidly improving
- CER education is being integrated into medical/pharmacy schools and for health care decision makers
- Health plans and systems are increasingly using CER evidence in decision making
- Significant efforts to increase information exchange between manufacturers and health care decision makers are ongoing
- Value based care in infiltrating health care practice

What more could we want???

CER and Medical Devices

- The Center for Biologics Evaluation and Research (CBER) has recognized the following in evaluation of medical devices for regulatory decisions
  - There is limited clinical trial evidence
  - Evidence for medical devices often exists in the HER
  - Such data may be supportive in evaluating benefit-risk
- Could such evidence also support regulatory decisions for Drugs? Time will tell..
- We are currently conducting an observational study within a health plan to evaluate the cost-effectiveness of a MBDA test in RA to better target use of biologics

http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm513027.pdf

CER and Big Data

- PCORnet, the National Patient-Centered Clinical Research Network, is designed for faster, easier, and less costly clinical research http://www.pcornet.org
- Clinical and Translational Science Awards (CTSA) program is incorporating emerging data and technology into its vision statement https://www.ncbi.nlm.nih.gov/books/NBK169207/
- Biologics and Biosimilars Collective Intelligence Consortium is a managed care organizational infrastructure to enable active surveillance of biosimilars in distributed research networks (DRNs). http://www.amcp.org/BBCIC/
- CancerLinQ, HMO Network, Vizient (UHC) and others.

But there are challenges!

Improving CER Methods

- ISPOR Good Practice Guidelines[1]
  - Comparative effectiveness research methods
  - Observational study methods
  - Economic evaluations and modeling
  - Clinical Outcomes Assessment
  - Use of Outcomes Research in Health Care Decision Making
- More sophisticated methodologies in CER
  - Indirect treatment comparisons
  - Multi criteria decision analysis
  - Causal inference
  - Predictive analytics
  - Dynamic Treatment Regimes

[1] https://www.ispor.org/workpaper/practices_index.asp

Addressing CER Educational Needs

- AMCP-NPC-ISPOR CER Certificate Program[1]
- PhRMA Foundation CER Education Grants[2]
- CER Study checklists
  - STROBE[3]
  - GRACE Principles[4]
- The perspective of the learner is very important
  - Students/Fellows
  - Researchers
  - HCDMS
  - HCPs
- ISPOR and AMCP working together on education and expertise exchange between researchers and payers

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[1]http://www.amcp.org/CERCertificate/ [2]http://www.phrma.org/press-release/phrma-foundation-awards-comparative-effectiveness-research-grants-to-top-universities [3]http://www.strobe-statement.org/fileadmin/Strobe/uploads/checklists/STROBE_checklist_v4_combined.pdf
[4]https://www.graceprinciples.org

Increasing the Exchange of Health Care Economic Information (HCEI) between Manufacturers and Health Care Decision Makers (HCDMs)

- The AMCP Partnership Forums
  - *Improving the Exchange of Pharmacoeconomic Data,* to clarify and update FDAMA section 114[1]
  - *Enabling the Exchange of Clinical and Economic Data Pre-FDA Approval,* to more easily share information on products awaiting FDA approval for forecasting, benefit design and efficient formulary decision making[2]
- AMCP Format 4.0[3]
  - Value Framework for the evaluation of new products
  - Continuous adaptation to accommodate information exchange
- All this work has led to draft guidance on drug and device communications[4]

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[1]http://www.jmcp.org/doi/abs/10.18553/jmcp.2016.22.7.826 [2]http://www.jmcp.org/doi/abs/10.18553/jmcp.2016.16366 [3]http://www.amcp.org/FormatV4/ [4]*draft guidance on drug and device manufacturer communications with payors, formulary committees, and similar entities*

Getting CER Imbedded into Practice

- Going from Volume to Value Driven Health Care[1]

- Value Based Insurance Design[2]
  - encourages the use of services when the clinical benefits exceed the cost and likewise discourages the use of services when the benefits do not justify the cost

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[1] http://www.chqpr.org/goals.html

[2] http://content.healthaffairs.org/content/26/2/w195.abstract

Getting CER Imbedded into Practice

- Bring researchers and HCDMs closer together
  - Outcomes researchers on P&T committees
  - Joint positions between academia and health plans to support relevant research
  - CER conducted in health plans and systems
    - Validate models with health plan data
    - Conduct observational studies within health plans
- Value Driven Outcomes in Health Systems
  - Understanding costs and related outcomes across system
  - Identify High Variability in Clinical Costs and Outcomes and Association With Reduced Cost and Improved Quality

http://jamanetwork.com/journals/jama/article-abstract/2552208

The opportunity for CER has never been brighter ?

ME

My daughter

Thank you!

How Will CER Be Integrated Into Practice?

-Use of Clinical Decision Support and EHR's to promote use of CER by clinicians, past & future

Bill Galanter, PhD, MD, MS
Chair, P & T Committee
Associate Chief Health Information Officer
Faculty, Colleges of Medicine & Pharmacy
Associate Professor of Medicine
University of Illinois at Chicago

January 27, 2017

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Disclosure of Conflicts

None

Funding

AHRQ: *U19HS021093, U18HS016967,* U18HS016973

Attorney General Consumer and Prescriber Education Grant Program

NPSF

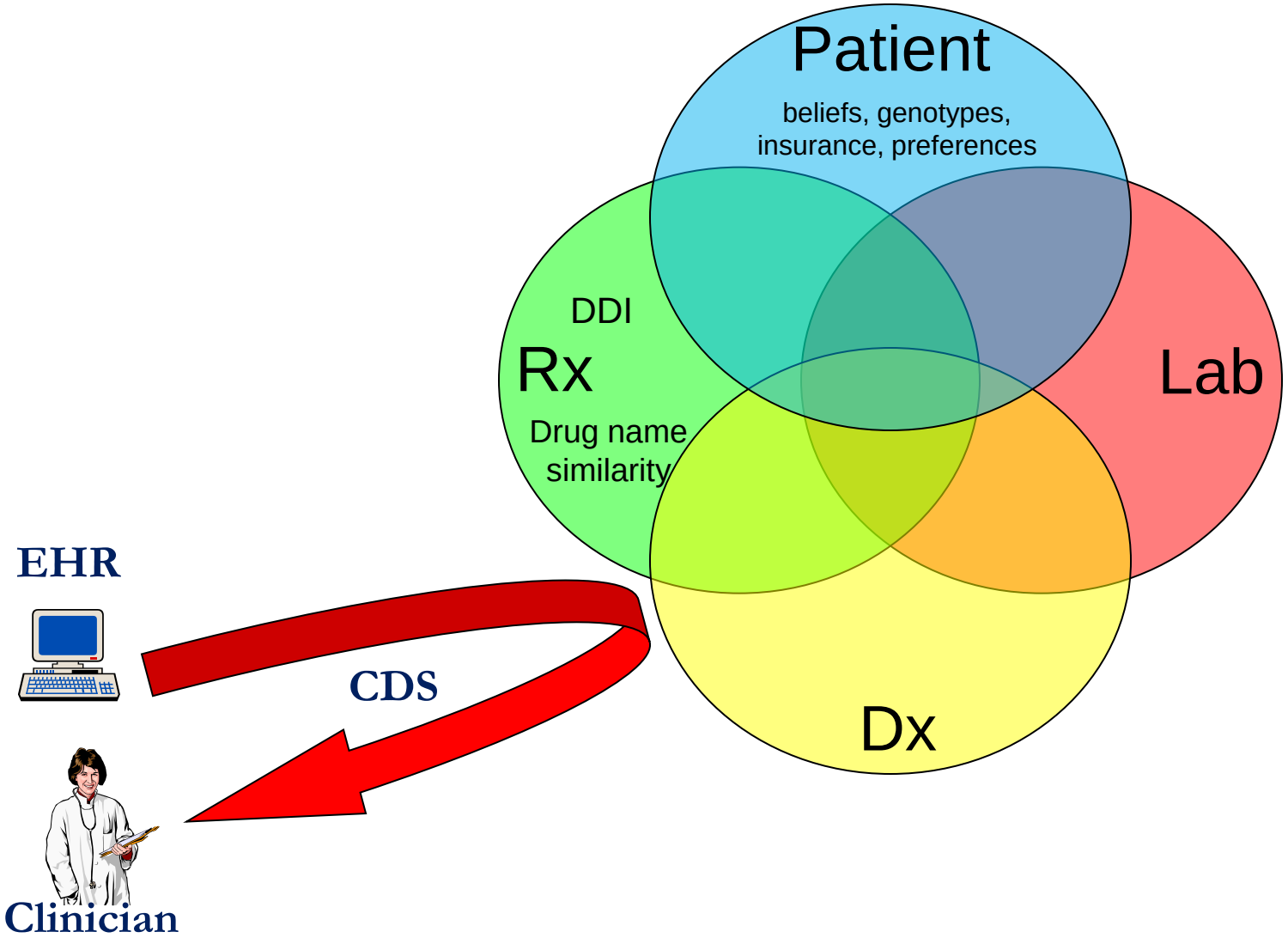
CER, PCOR & Clinical Decision Support

Goal is the best treatment for the particular patient at the specific time

CDS can assist in many area's of medication use;

-Therapeutic decisions
-Prompting Use
-Shared decision making
-Dosing
-Patient education
-Monitoring

Targets for medication use CDS



Evidence/CER Based CDS Intervention Governance

Evidence/CER Based Guidelines

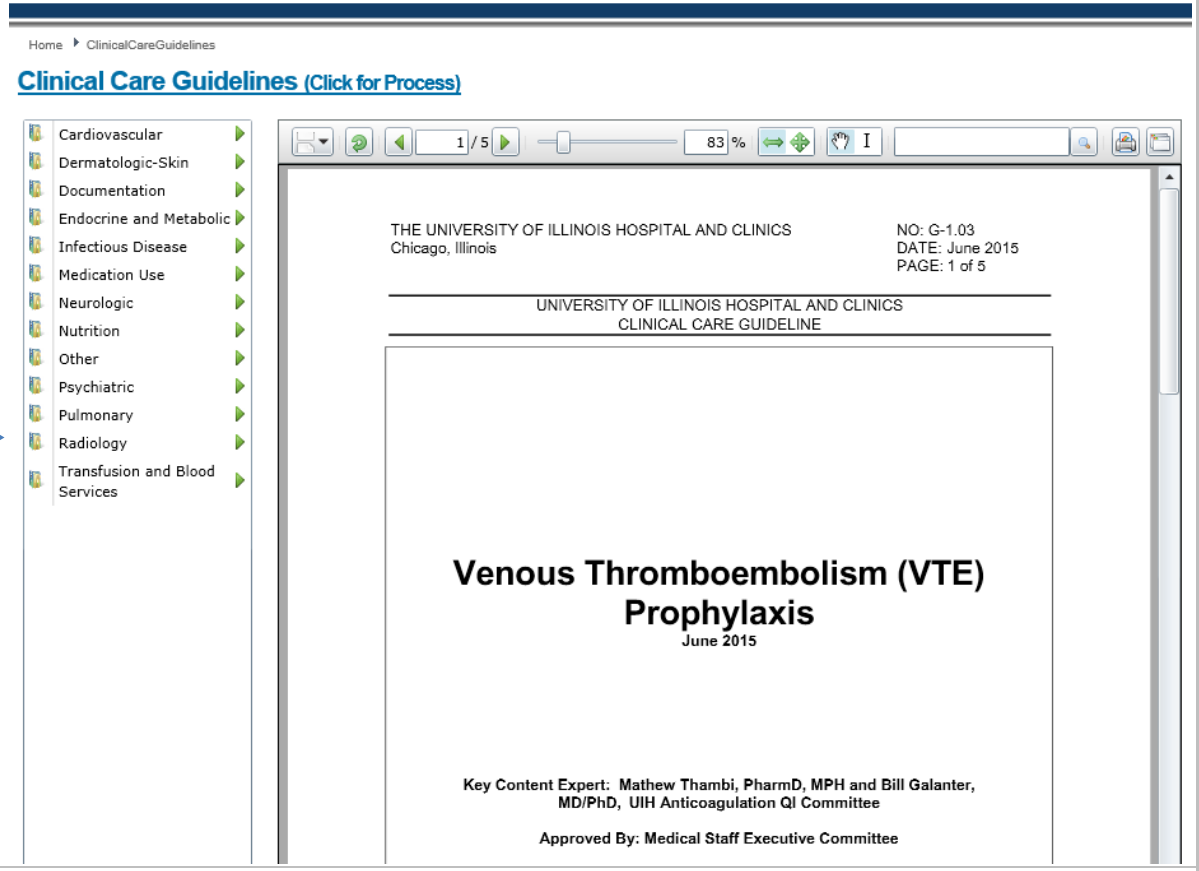
Anticoagulation Committee

P&T/Pharmacy

MSEC
GUIDELINE

IS

EHR/CDS



Evidence/CER Based Order Set

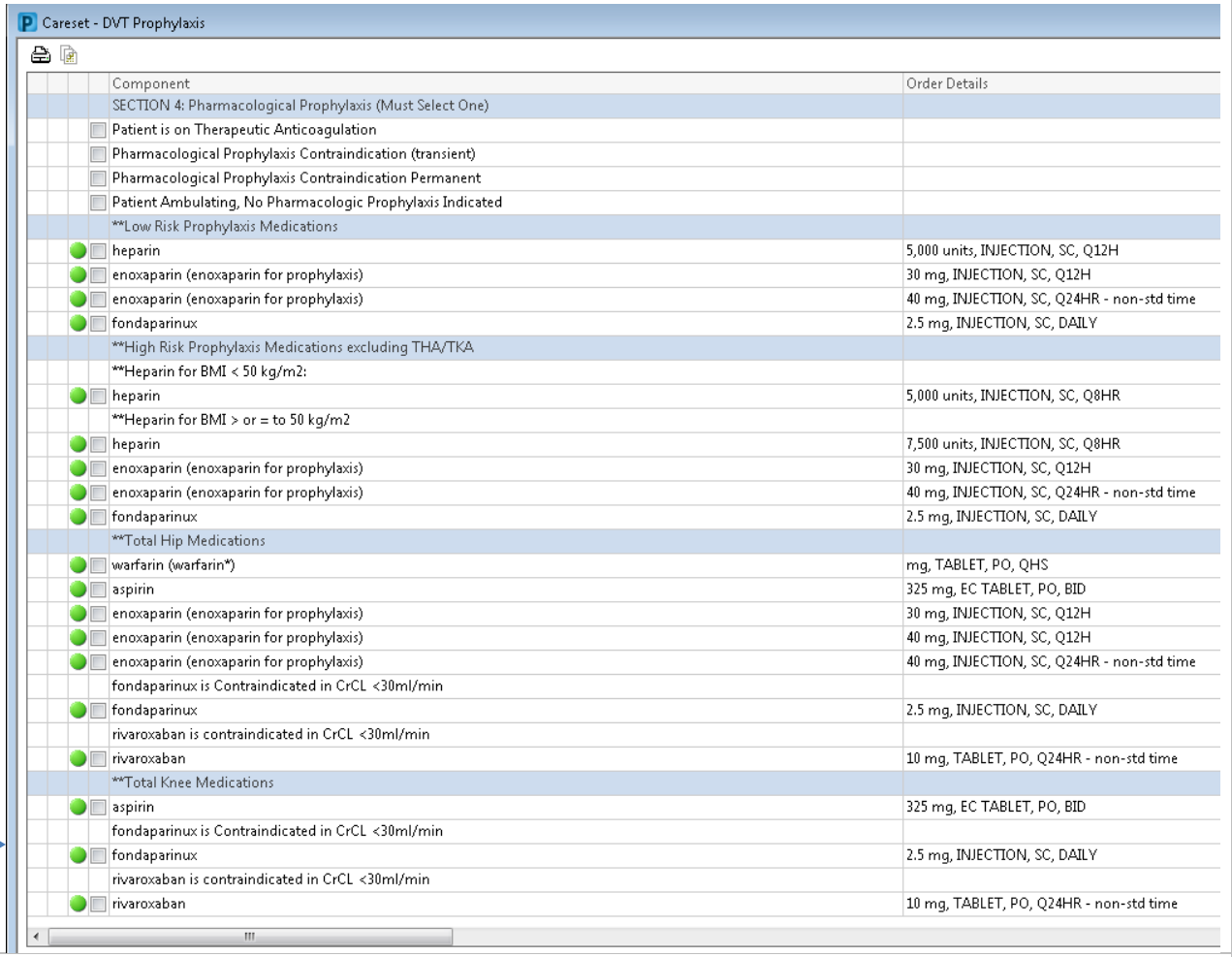
Anticoagulation Committee

P&T/Pharmacy

MSEC
GUIDELINE

IS

EHR/CDS
(Order Set)



Component	Order Details
SECTION 4: Pharmacological Prophylaxis (Must Select One)	
Patient is on Therapeutic Anticoagulation	
Pharmacological Prophylaxis Contraindication (transient)	
Pharmacological Prophylaxis Contraindication Permanent	
Patient Ambulating, No Pharmacologic Prophylaxis Indicated	
**Low Risk Prophylaxis Medications	
heparin	5,000 units, INJECTION, SC, Q12H
enoxaparin (enoxaparin for prophylaxis)	30 mg, INJECTION, SC, Q12H
enoxaparin (enoxaparin for prophylaxis)	40 mg, INJECTION, SC, Q24HR - non-std time
fondaparinux	2.5 mg, INJECTION, SC, DAILY
**High Risk Prophylaxis Medications excluding THA/TKA	
**Heparin for BMI < 50 kg/m2:	
heparin	5,000 units, INJECTION, SC, Q8HR
**Heparin for BMI > or = to 50 kg/m2	
heparin	7,500 units, INJECTION, SC, Q8HR
enoxaparin (enoxaparin for prophylaxis)	30 mg, INJECTION, SC, Q12H
enoxaparin (enoxaparin for prophylaxis)	40 mg, INJECTION, SC, Q24HR - non-std time
fondaparinux	2.5 mg, INJECTION, SC, DAILY
**Total Hip Medications	
warfarin (warfarin*)	mg, TABLET, PO, QHS
aspirin	325 mg, EC TABLET, PO, BID
enoxaparin (enoxaparin for prophylaxis)	30 mg, INJECTION, SC, Q12H
enoxaparin (enoxaparin for prophylaxis)	40 mg, INJECTION, SC, Q12H
enoxaparin (enoxaparin for prophylaxis)	40 mg, INJECTION, SC, Q24HR - non-std time
fondaparinux is Contraindicated in CrCL <30ml/min	
fondaparinux	2.5 mg, INJECTION, SC, DAILY
rivaroxaban is contraindicated in CrCL <30ml/min	
rivaroxaban	10 mg, TABLET, PO, Q24HR - non-std time
**Total Knee Medications	
aspirin	325 mg, EC TABLET, PO, BID
fondaparinux is Contraindicated in CrCL <30ml/min	
fondaparinux	2.5 mg, INJECTION, SC, DAILY
rivaroxaban is contraindicated in CrCL <30ml/min	
rivaroxaban	10 mg, TABLET, PO, Q24HR - non-std time

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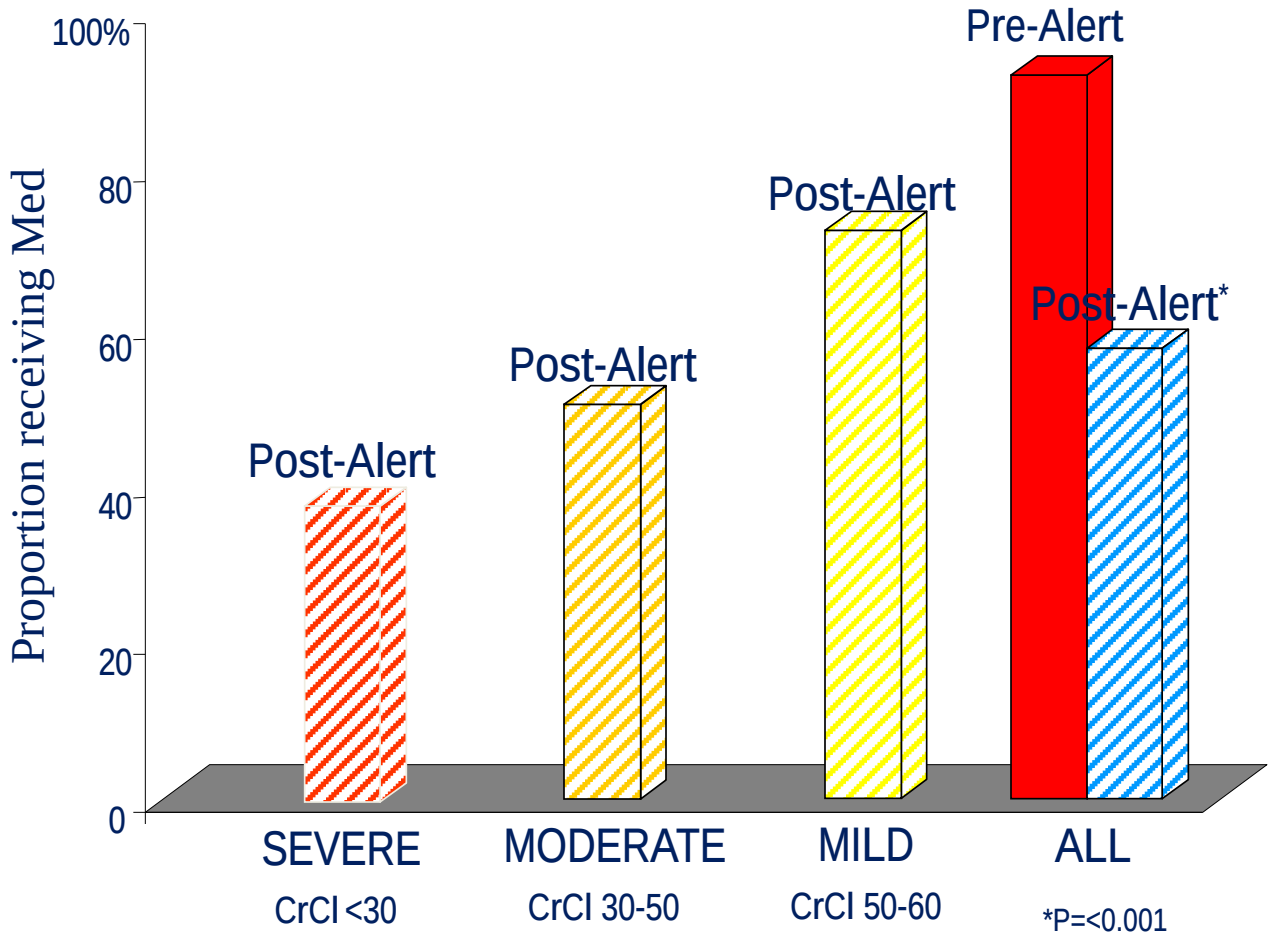
CDS for Metformin Contraindication

(Can you change behavior with pop-up's?)



Galanter W, Didomenico R, Polikaitis A. A trial of automated decision support alerts for contraindicated medications using computerized physician order entry. J Am Med Inform Assoc. 2005 May-Jun;12(3):269-74

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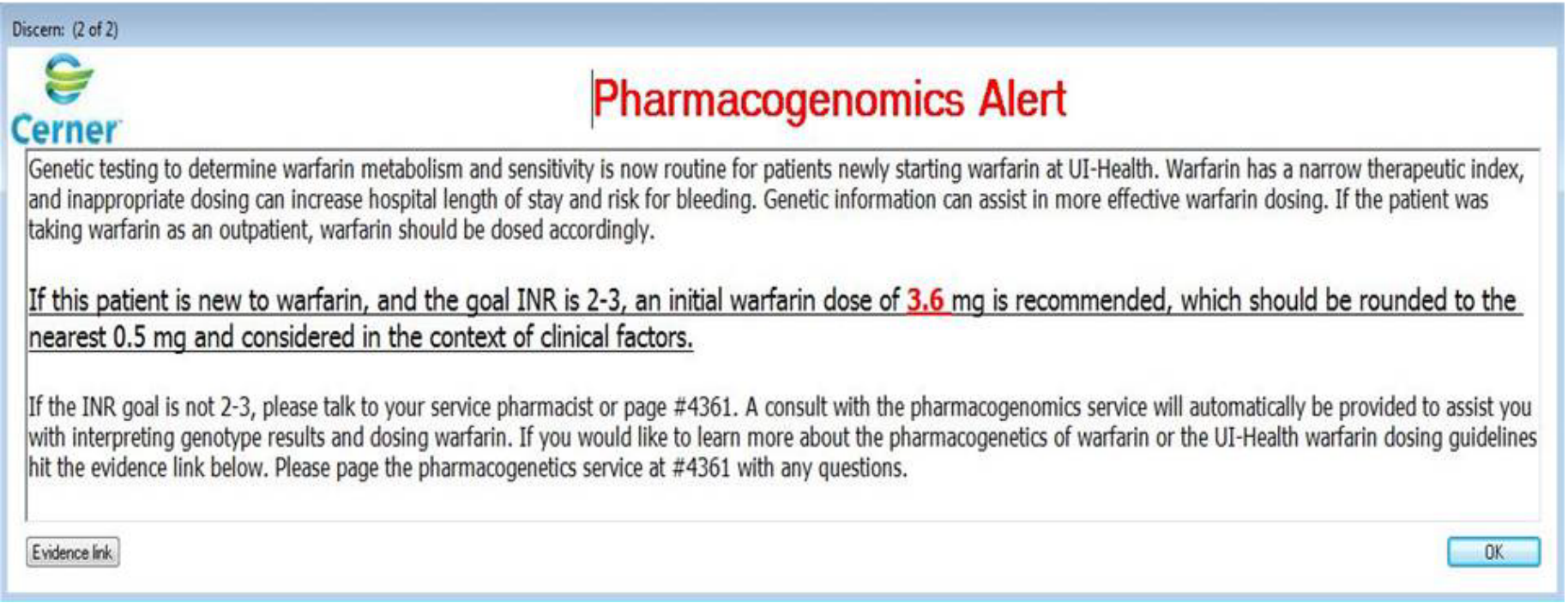
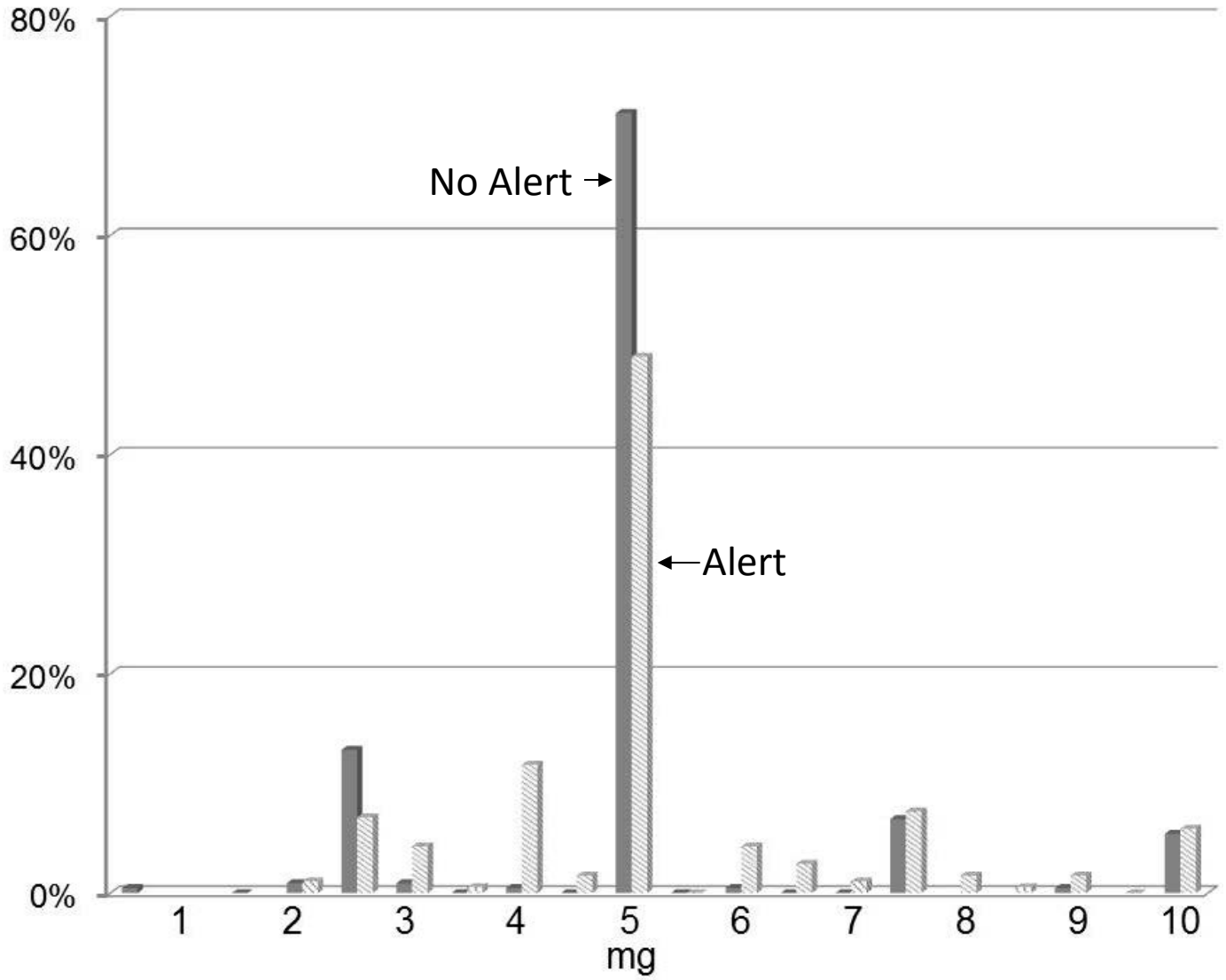
Individualized dosing of warfarin



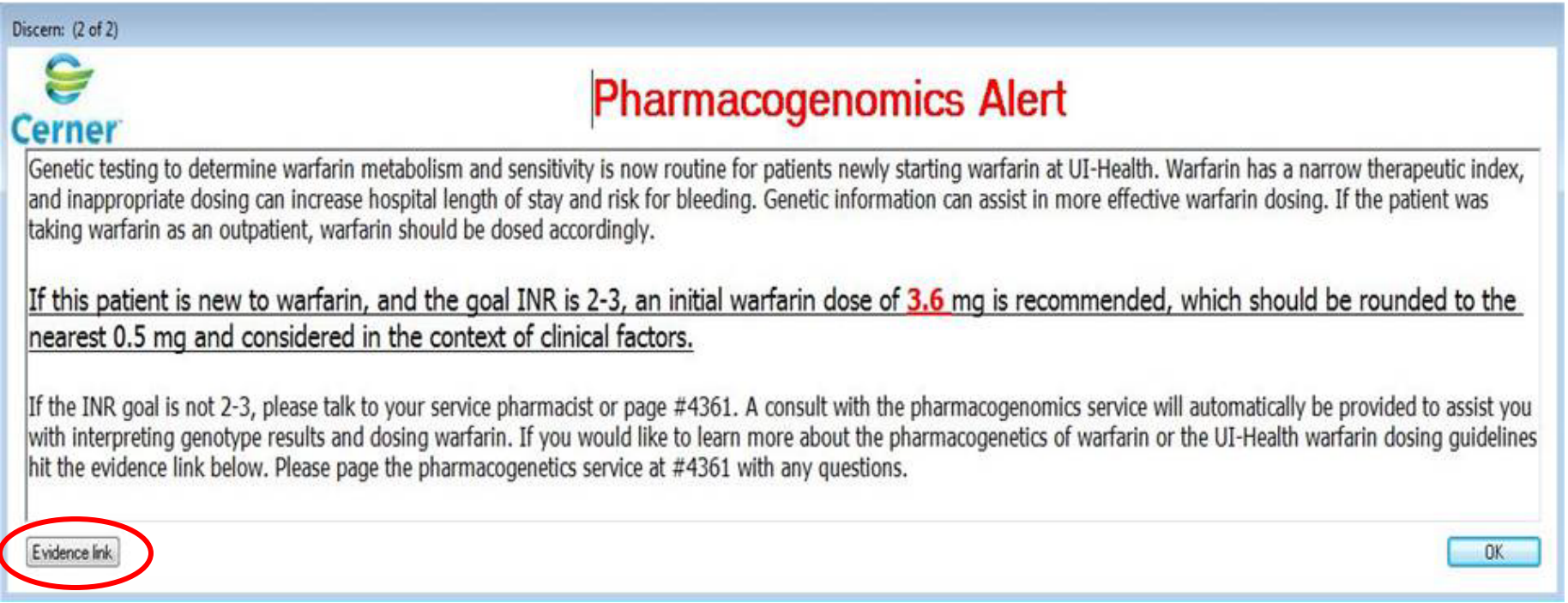
$$Dose = \exp[0.613 + (0.425 * BSA) - (0.0075 * age) + (0.156 * African\ America\ race) + (0.216 * target\ INR) - (0.257 * amiodarone) + (0.108 * smokes)$$

Nutescu E, Drozda K, Bress A, Galanter W, Stevenson J, Stamos T, Desai A, Duarte J, Gordeuk V, Peace D, Kadkol A, Dodge C, Saraf S, Garofalo J, Krishnan J, Garcia J, Cavallari L. Feasibility of implementing a comprehensive warfarin pharmacogenetics service. Pharmacotherapy. 2013 Nov;33(11):1156-64

Initial dose of warfarin



CDS Directed Education



CDS Directed Education

University of Illinois Hospital & Health Sciences System
Changing medicine. For good.

Pharmacogenetics Service

The Pharmacogenetics Service is supported by the Office of the Vice President for Health Affairs and serves as a consult service with Clinical Directorship provided by PharmDs experienced in warfarin pharmacogenetics and anticoagulation, Medical Directorship provided by physicians from Cardiology and Medicine, and Laboratory support provided by the CLIA and CAP accredited Molecular Pathology Laboratory.

The service is responsible for validating and reporting pharmacogenetic test results, providing patient assessment and warfarin dose estimations, serving as a source within the medical center for education and information on warfarin pharmacogenetics, and providing quality assurance assessment of warfarin–pharmacogenetic testing.

Warfarin Genetics	Clinical Utility of Warfarin Pharmacogenetics
Guidelines for Warfarin Dosing based on Genotype	Genetic Information in the Warfarin Labeling
Pharmacogenetics Service Team	For More Information about Warfarin Genetics

UI-HEALTH Warfarin Use Guideline G-13.23
Dosing Procedure

College of Pharmacy Seminar 7/25/12 (Video)

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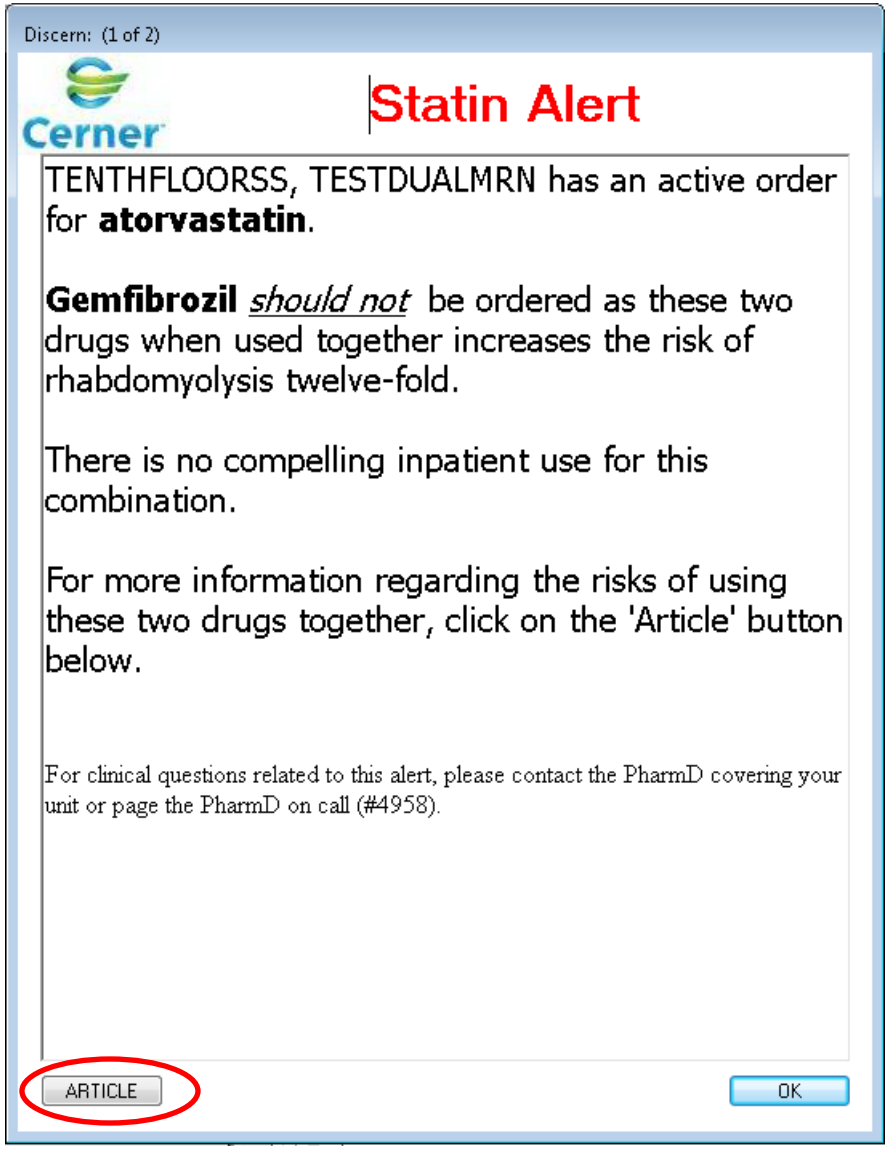


CDS Directed Education

Context Lipid-lowering agents are widely prescribed in the United States. Reliable estimates of rhabdomyolysis risk with various lipid-lowering agents are not available.

Objective To estimate the incidence of rhabdomyolysis in patients treated with different statins and fibrates, alone and in combination, in the ambulatory setting.

Design, Setting, and Patients Drug-specific inception cohorts of statin and fibrate users were established using claims data from 11 managed care health plans across the United States. Patients with at least 180 days of prior health plan enrollment were entered into the cohorts between January 1, 1998, and June 30, 2001. Person-time was classified as monotherapy or combined statin-fibrate therapy.

Main Outcome Measure Incidence rates of rhabdomyolysis per 10 000 person-years of treatment, number needed to treat, and relative risk of rhabdomyolysis.

Results In 252 460 patients treated with lipid-lowering agents, 24 cases of hospitalized rhabdomyolysis occurred during treatment. Average incidence per 10 000 person-years for monotherapy with atorvastatin, pravastatin, or simvastatin was 0.44 (95% confidence interval [CI], 0.20-0.84); for cerivastatin, 5.34 (95% CI, 1.46-13.68); and for fibrate, 2.82 (95% CI, 0.58-8.24). By comparison, the incidence during unexposed person-time was 0 (95% CI, 0-0.48; $P = .056$). The incidence increased to 5.98 (95% CI, 0.72-216.0) for combined therapy of atorvastatin, pravastatin, or simvastatin with a fibrate, and to 1035 (95% CI, 389-2117) for combined cerivastatin-fibrate use. Per year of therapy, the number needed to treat to observe 1 case of rhabdomyolysis was 22 727 for statin monotherapy, 484 for older patients with diabetes mellitus who were treated with both a statin and fibrate, and ranged from 9.7 to 12.7 for patients who were treated with cerivastatin plus fibrate.

Conclusions Rhabdomyolysis risk was similar and low for monotherapy with atorvastatin, pravastatin, and simvastatin; combined statin-fibrate use increased risk, especially in older patients with diabetes mellitus. Cerivastatin combined with fibrate conferred a risk of approximately 1 in 10 treated patients per year.

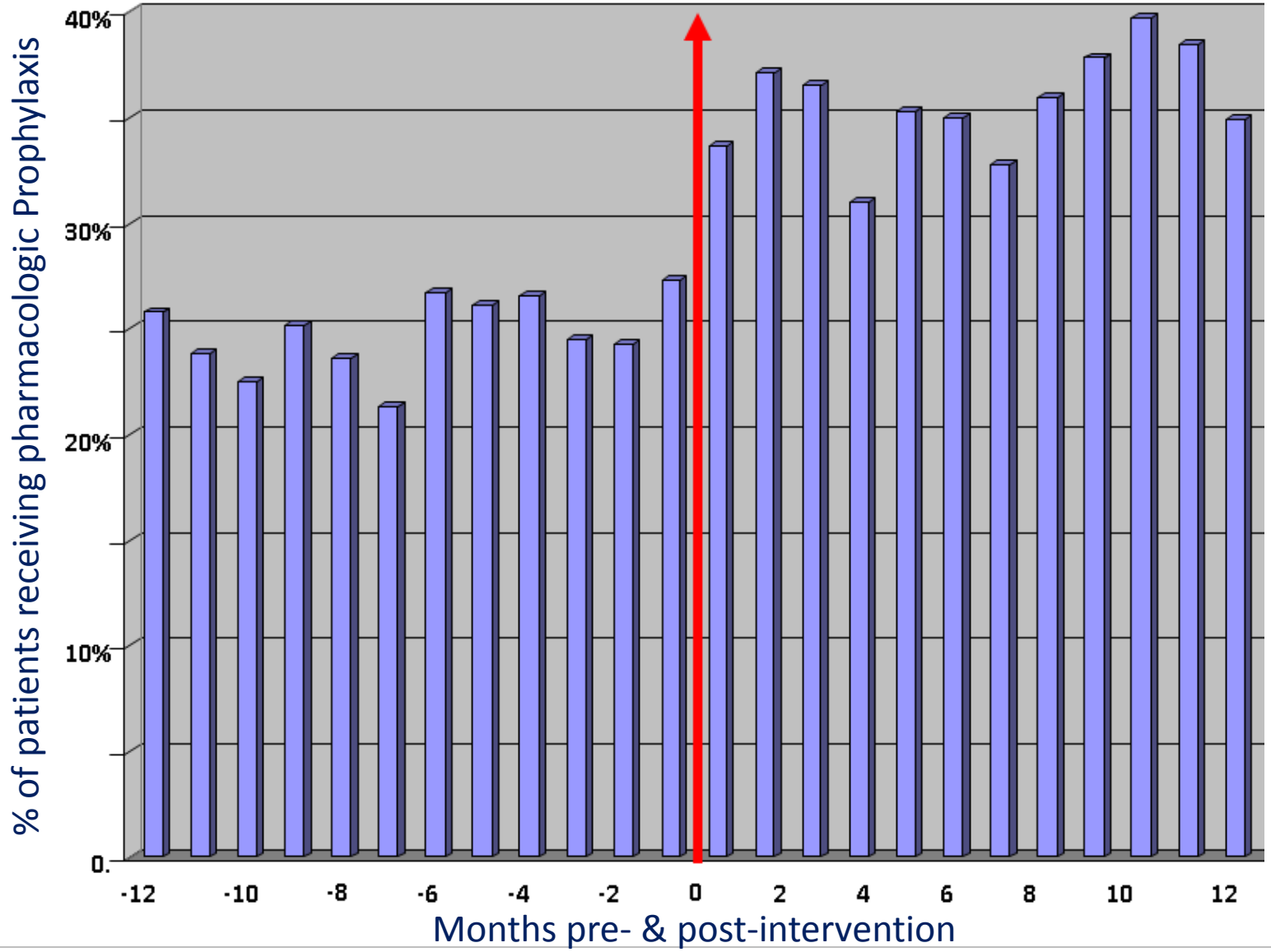
Conclusions Published online November 22, 2004 (doi:10.1001/jama.292.21.2585).

Disorders of muscle, ranging in severity from asymptomatic creatine kinase elevation to rhabdomyolysis, are among the most discussed adverse effects associated with use of lipid-lowering agents, especially 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins).[1-5] Fibric acid derivatives (fibrates) have also been associated with primary muscle injury, especially when used in combination with a statin.[6-11]

The epidemiology of statin-associated and fibrate-associated myopathy is poorly described, with most attention focused on rhabdomyolysis. Based on review of case reports, older age, female sex, low body mass index, hypothyroidism, diabetes mellitus, and impaired renal or hepatic function have been cited as potential risk factors for rhabdomyolysis,[10,11] but these have not been confirmed by clinical trials or observational studies. Myopathy, defined as a serum creatine kinase level of more than 10 times the upper limit of normal, has been estimated to occur in 0.1% to 0.5% of patients treated with statins during randomized controlled trials.[10] However, the incidence of rhabdomyolysis has not been reliably estimated. The product labeling for some statins presents incidence estimates for myopathy and rhabdomyolysis combined, although in labeling for other statins the occurrence of rhabdomyolysis is described as rare.[12,13] One epidemiologic study estimated the incidence of myopathy associated with lipid-lowering drugs at 2.3 per 10 000 person-years of treatment and suggested that fibrate use as monotherapy conferred a 5.5-fold increased risk compared with statin use.[14] Another study reported 1 case of rhabdomyolysis among 2935 patients treated concurrently with a statin and fibrate.[15] Two separate analyses, based on case reports submitted to the US Food and Drug Administration, found that reporting of rhabdomyolysis was greater for simvastatin and cerivastatin than for other statins,[16] and that reporting of fatal rhabdomyolysis was 17- to 79-fold greater for cerivastatin than for other statins.[17]

Following the withdrawal of cerivastatin from the US market in August 2001 because of high reporting of rhabdomyolysis in association with its use,[18] we conducted this study to estimate the incidence of rhabdomyolysis in patients treated with statins and fibrates, alone and in combination, in the ambulatory setting.

CDS (Reminders/Order Set) effect on VTE Prophylaxis rates



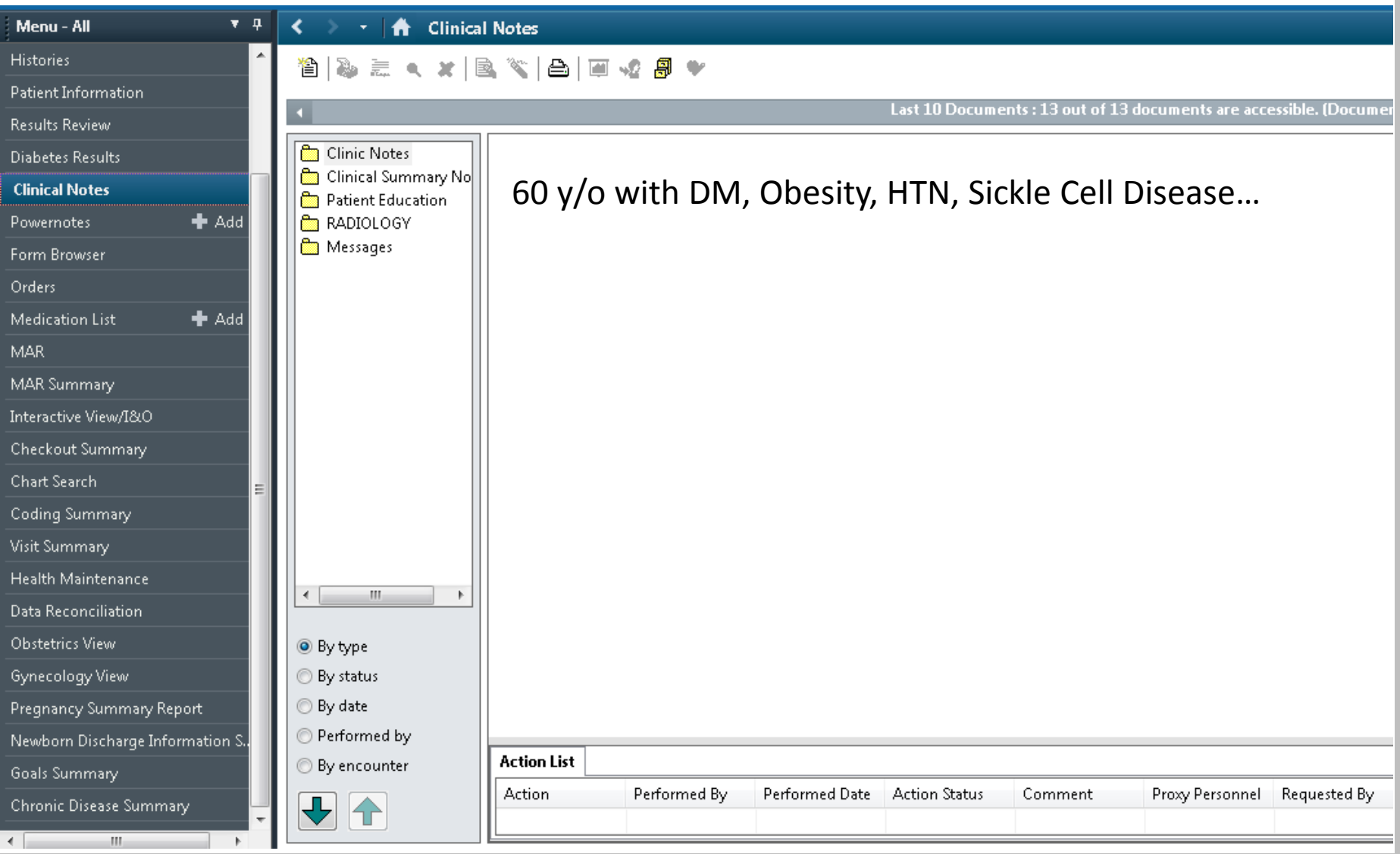
CDS effect on VTE event rates

Rates of Venous Thromboembolism (VTE) and Bleeding

Variable	No. Events/ No. Admissions (%)		Relative Change[a] %	*p*
	Control Group	Intervention Group		
Total VTE	94/18,317 (0.51)	87/20,330 (0.43)	−15.7	0.22
VTE by discharge service type				
Medical	47/8,516 (0.55)	33/9,981 (0.33)	−40.0	0.02
Neurology	3/690 (0.43)	7/706 (0.99)	NA[b]	0.34
Neurosurgery	29/1,533 (1.89)	27/1,731 (1.56)	NA	0.47
Obstetrics/gynecology	1/2,844 (0.04)	3/3,011 (0.10)	NA	0.63
Orthopedics	4/487 (0.82)	6/456 (1.32)	NA	0.54
Surgical	10/4,247 (0.24)	11/4,445 (0.25)	NA	0.91
Total major bleeding	232/18,317 (1.27)	266/20,330 (1.31)	3.15	0.72
Medical service	103/8,516 (1.21)	133/9,981 (1.33)	9.92	0.46
Total minor bleeding	320/18,317 (1.75)	326/20,330 (1.60)	−8.57	0.27
Medical service	203/8,516 (2.38)	221/9,981 (2.21)	−7.14	0.44

Galanter WL, et al.. Am J Health Syst Pharm. 2010 Aug;67(15):1265-73

EHR Embedded Disease Management



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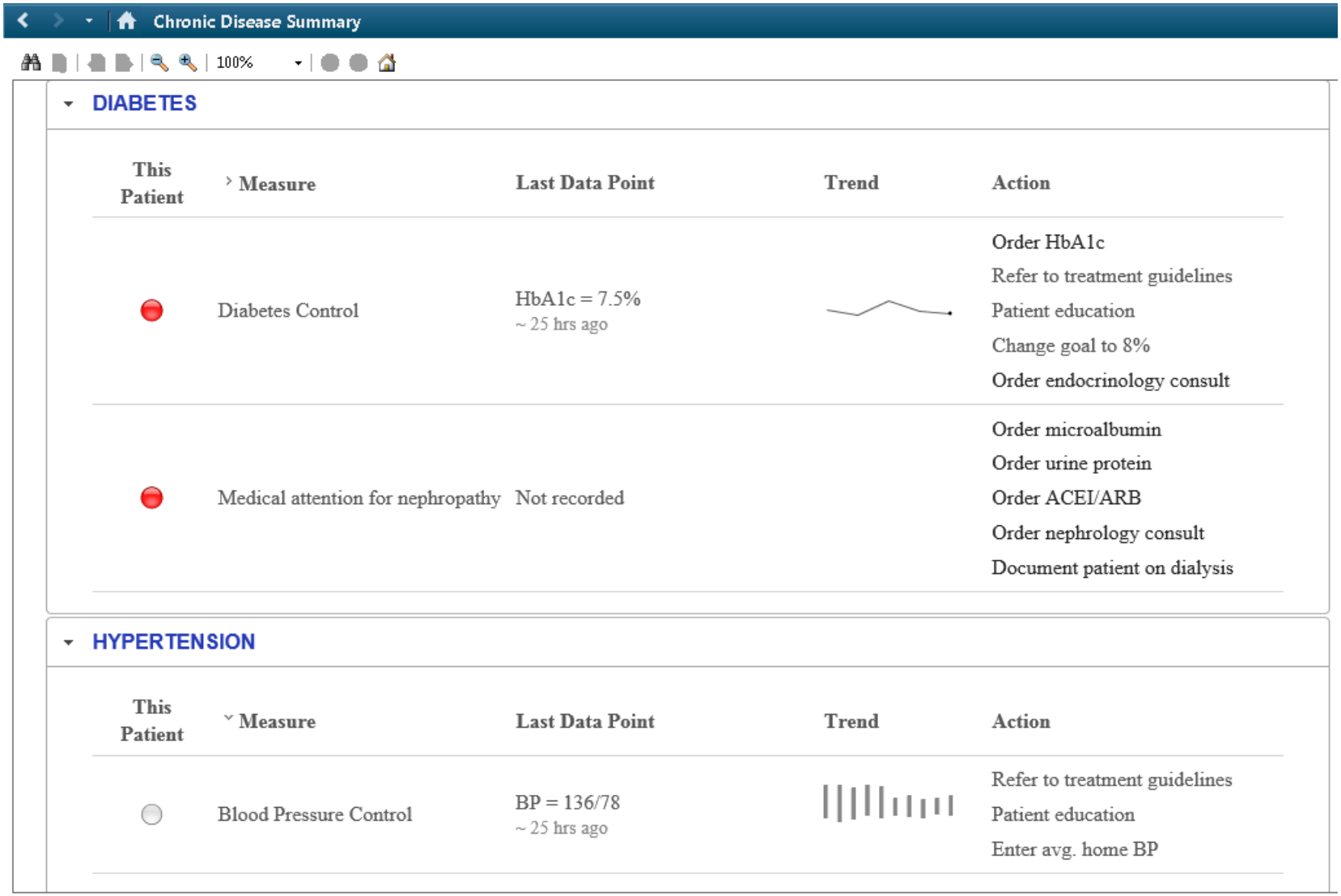
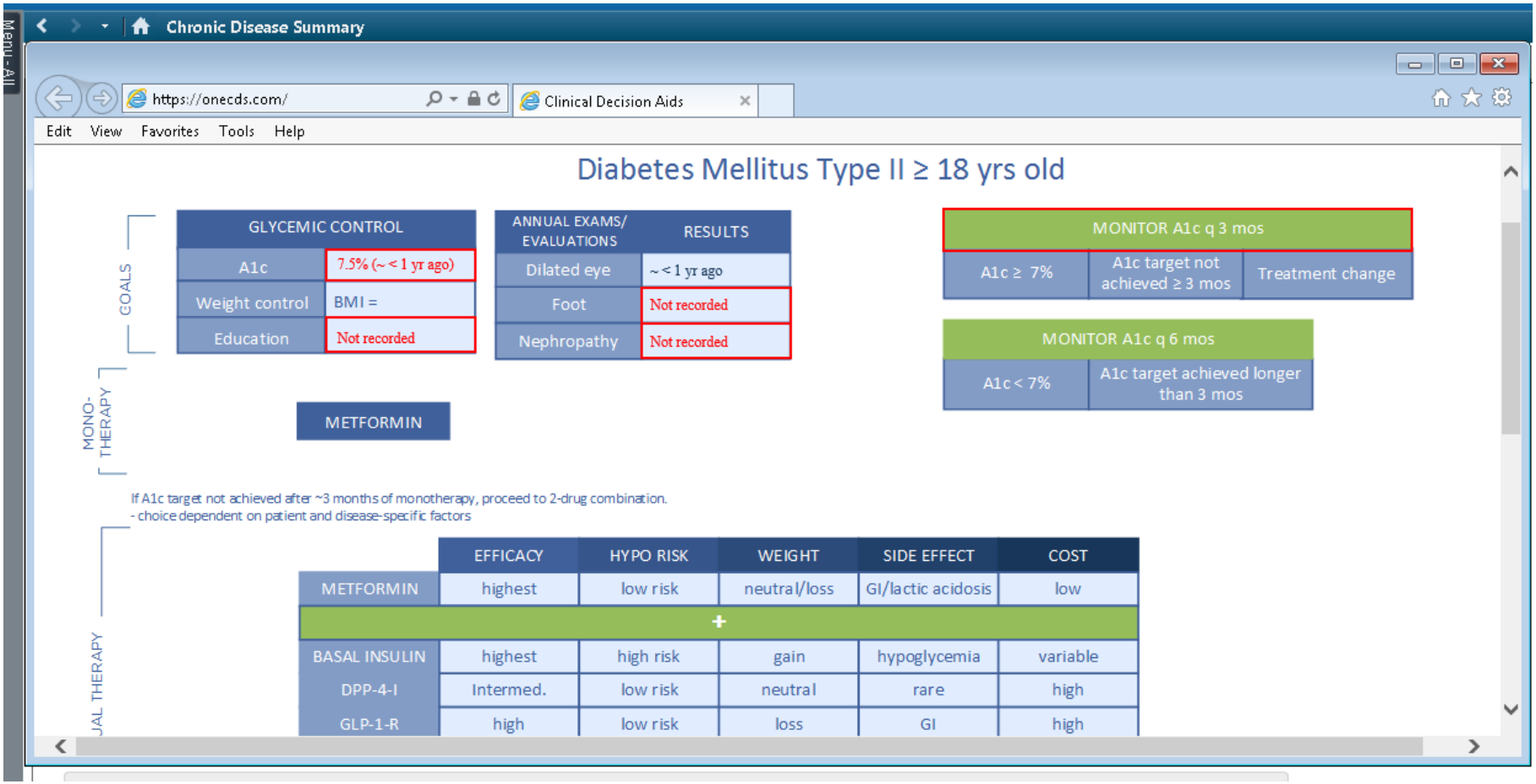
EHR Embedded Disease Management



EHR Embedded Disease Management



Using your institutions own data to help make decisions & selected topics for CER

History of Present Illness: 60 yr old**,** metformin is not working well enough.

Problem list:

DIABETES MELLITUS
HTN
Sickle Cell Dz

Home Medications:
-metformin 1000 extended release PO twice a day

Results review: HGB A1C 8.8%

Impression and Plan

Diagnosis

Diabetes mellitus E11.9

Course: not well treated.

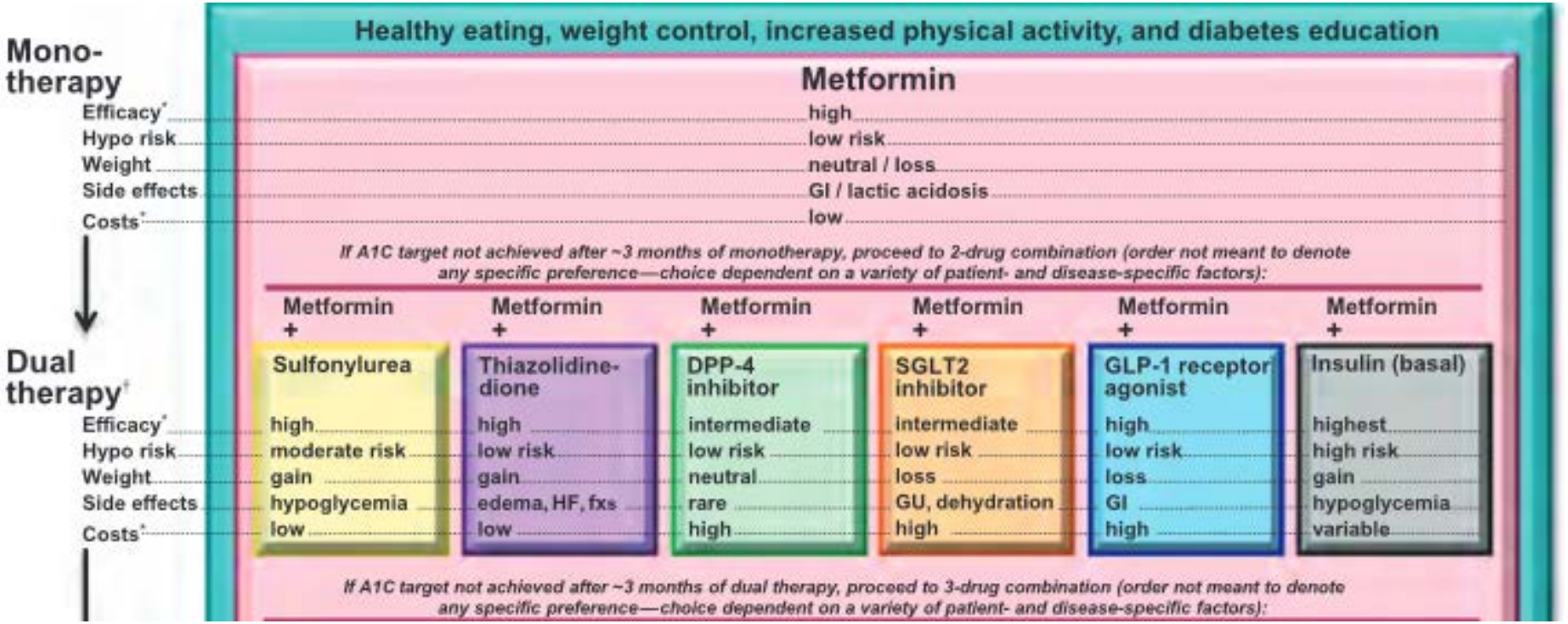
Orders

Pharmacy:

glipizide 10 mg oral tablet ***OR*** insulin glargine 100 units/mL subcutaneous solution

?

Diabetes Mellitus 2nd Med Conundrum



http://care.diabetesjournals.org/content/suppl/2015/12/21/39.Supplement_1.DC2/2016-Standards-of-Care.pdf

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Longhurst C, Robert A. Harrington and Nigam H. Shah. A 'Green Button' For Using Aggregate Patient Data At The Point Of Care. *Health Affairs*, 33, no.7 (2014):1229-1235

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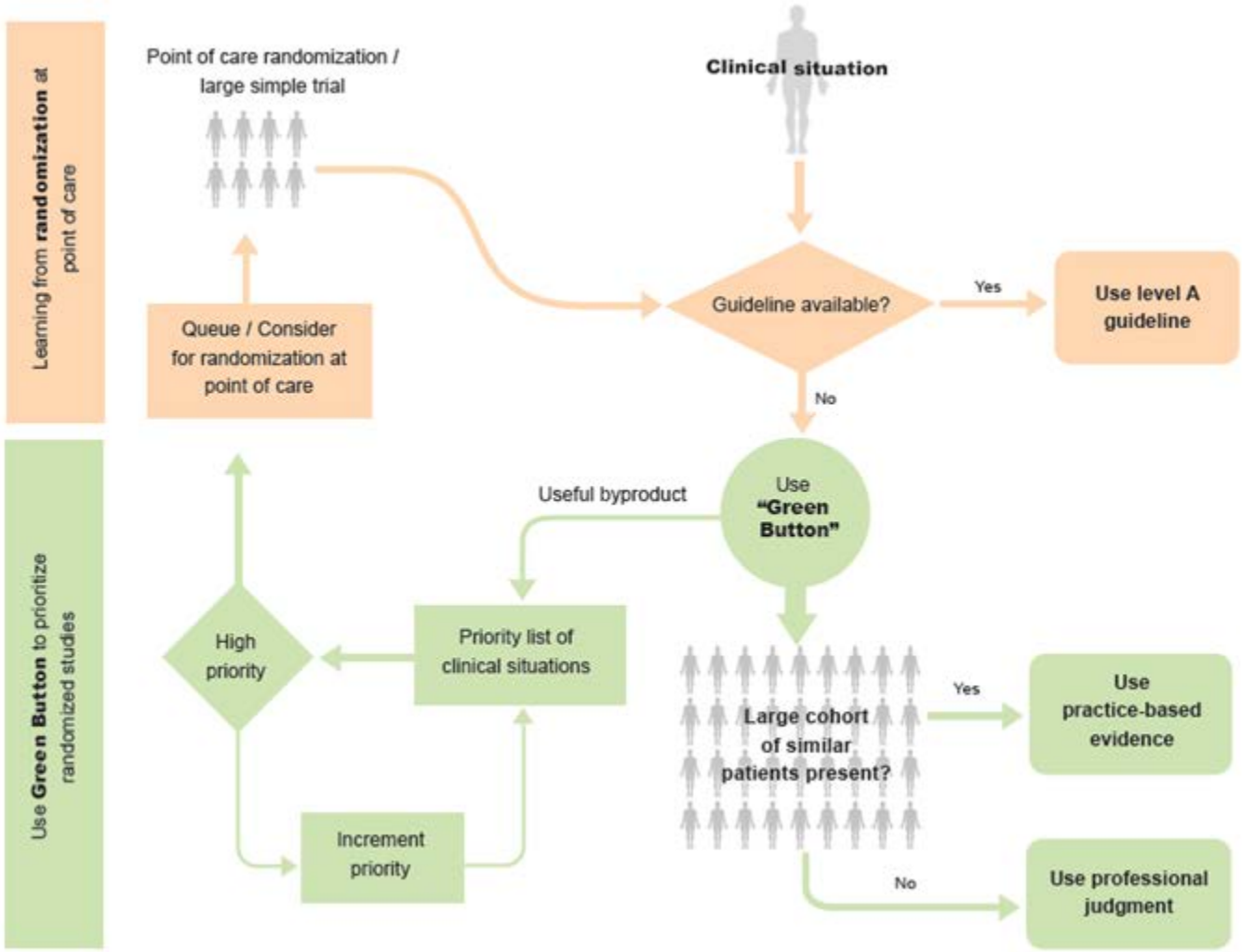
When to Use Retrospective Aggregate Data



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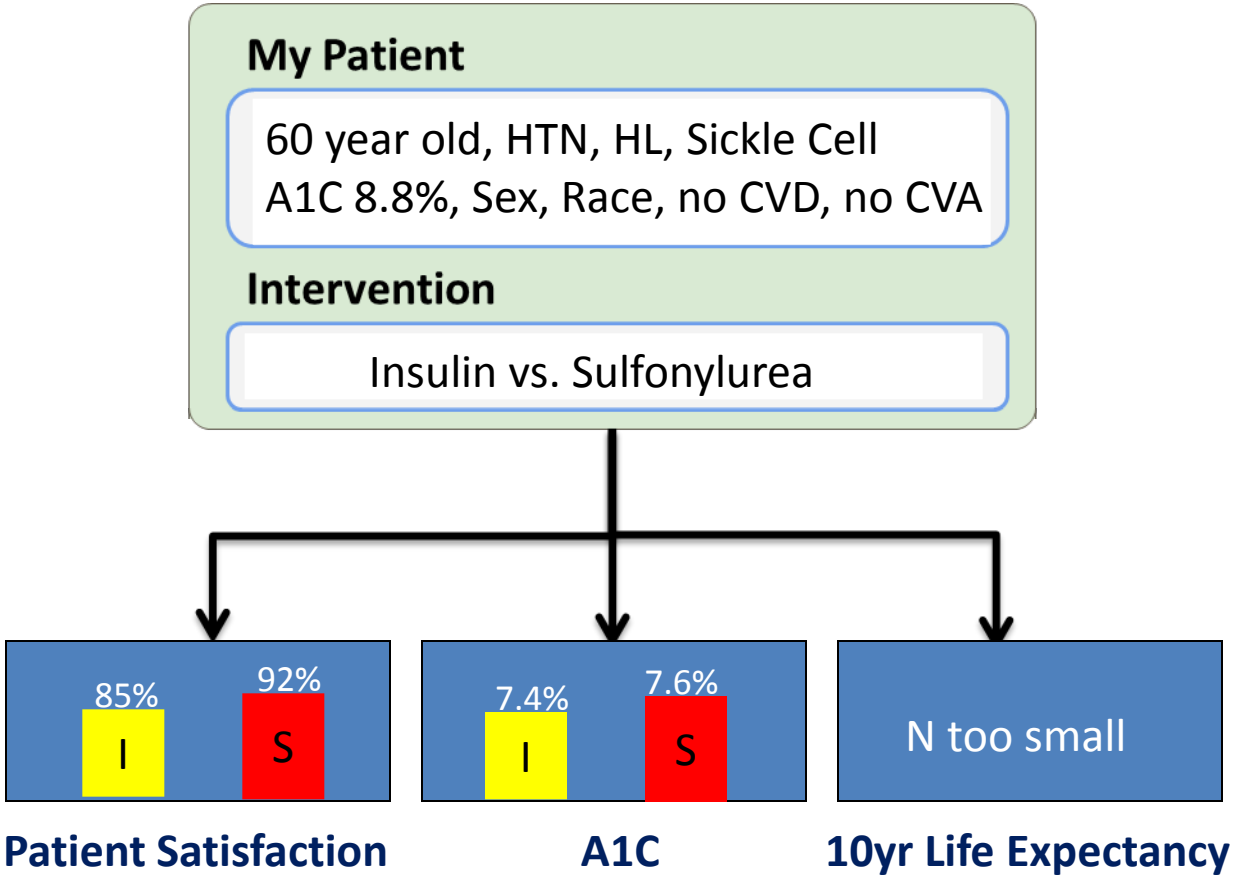
Using your institutions own data to help make decisions



Longhurst C, Robert A. Harrington and Nigam H. Shah. A 'Green Button' For Using Aggregate Patient Data At The Point Of Care. *Health Affairs*, 33, no.7 (2014):1229-1235

Summary

-CER can/should be used to develop the clinical guidelines that inform care and CDS design

-CDS can increase appropriate drug use through alerts, order sets and reminders

-CDS can provide clinician and patient education to promote better decisions and outcomes

-Future EHR and CDS design should be able to provide data on important clinical questions that need CER

-Future EHR and CDS design should be able to help clinicians to leverage their own institutions data for therapeutic decisions and to become *"learning healthcare systems"*

Comparative Effectiveness and Patient-Centered Outcomes Research:

Enhancing Uptake and Use by Patients, Clinicians and Payers

Session: What is the Future of CER and CER Education? How Will CER Be Integrated Into Practice?

January 26, 2017

Lou Garrison, PhD.

Professor Emeritus, University of Washington

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On the other hand . . .

- Cost pressures continue: high and growing share of GDP
- Worsening life expectancy in some groups, e.g., opioid addiction epidemic.
- Repeal of ACA—Cadillac tax; PCORI, etc.
- Inability to move quickly to value-based payment systems for the entire system.
- System inertia: 17-year diffusion curve

An Economic Perspective

- **Generation:** CER is a "public good" will be undersupplied by a "free market", implying that we will need to subsidize or incentivize it some way to approach the optimal amount.
- **Value of Information**: More CER information is needed and desirable, but it is costly to produce and we need to weigh the costs and benefits.
- **Uptake and Use:** Incentives to use CER information appropriately are critical.

Three Questions

1. What is the future of CER?
2. What is the future of CER education?
3. How will CER be integrated into practice?

1. What is the future of CER?

- CER:
  - Intervention compared to SoC
  - Real-world outcomes (=effectiveness); not efficacy
  - Patient-focused
- It is undersupplied: there will be excess demand for it.
  - Can we regulate it? FDA can, e.g., by requiring longer or additional studies.
  - Can we reward its production: e.g., performance-based risk-sharing agreements.
  - "Endogenous" vs. "Exogenous"/Learning health care system.
- If we can reduce the costs of producing it (e.g., via big data, etc.), we will get more.

2. What is the future of CER education?

- Demand is rising as a part of HTA
  - ISPOR has over 20,000 members in 115 countries.
- Methodological advances: value of information, network meta-analysis, patient engagement; implementation science [these need to be taught]
- Need for more than CER/clinical evidence base: we need it for benefit-risk analysis and for CEA/CUA.

3. How will CER be integrated into practice?

- It depends on incentives (intrinsic vs. extrinsic) to use the information
  - Kavita Patel cited challenges of FFS medicine
  - Choosing Wisely has had limited success
- Rise of dissemination/implementation science: guidelines not sufficient
  - Incentives: "greater perceived relative advantage" (Morrato)
  - "Misalignment of financial incentives" (Shah)
- Incorporation into clinical guidelines and pathway development is key.
- How can delivery systems and providers signal that they are providing higher-quality care based on the use of CER?
- Challenge: Why do EU health systems outperform US—with the same CER information?

Frameworks use different attributes of value: Where Does CER Fit In?

	ACA/AHA	ASCO	ICER	Sloan Kettering	NCCN
Clinical benefit	X	X	X	X	X
Toxicity / safety		X	X	X	X
Treatment novelty				X	
Condition rarity and condition burden				X	
Affordability			X		X
Cost effectiveness	X		X		

Context/ Perspective	Clinical Treatment Guidelines	Shared Decision-Making	Coverage & Payment	Shared Decision-Making & Pricing	Shared Decision-Making

Source: Adapted from P. Neumann, May 25, 2016

Thank you!

lgarrisn@uw.edu

Conference Summary and Next Steps?

Glen Schumock, University of Illinois at Chicago

Thank You For Attending!