National Cancer Institute

What Types of Evidence Do We Need to Produce Relevant and Sustainable Interventions??

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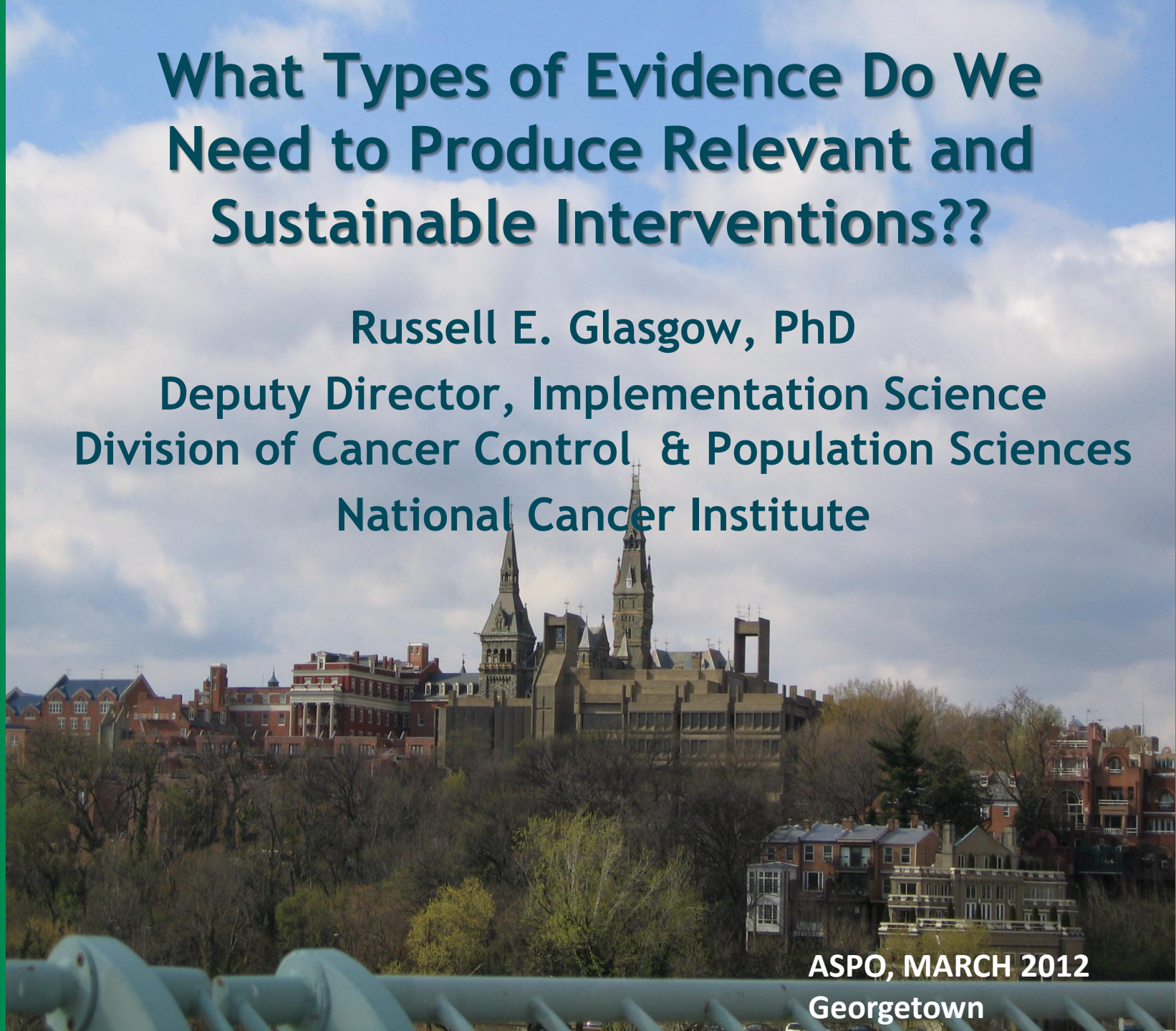


ASPO, MARCH 2012

Georgetown

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute

NCI Implementation Science Team Mission

The mission of the Implementation Science (IS) Team is to build and advance the field of Implementation Science by:

- Promoting science that is rigorous, transparent and relevant in the real world;
- Fostering rapid learning strategies for improving individual and population health; and
- Building partnerships for the development, dissemination and implementation of evidence-based measures, initiatives and programs.

http://cancercontrol-dev.cancer.gov/IS/index.html

Evidence Needed: 2R's and 'RCCT'

- **R**elevant
- **R**igorous and

- **R**apid
- **C**ost
- **C**onvergent
- **T**ransparent

Glasgow R, *Annals of Behavioral Medicine, 2008, 35:* 19-25.
Glasgow R, Chambers D. *Clinical and Translational Science*, in press, 2012

Relevant (Contextual and Practical)

- Relevant to *stakeholders* (patients/family, clinicians, administrators, policy makers)
- Relevant *samples*- representative of real world, including patients with co-morbid conditions
- Relevant *settings*- similar to those in practice (not just the most advanced and well resourced)
- Relevant *clinicians*- including those who have other duties and competing demands

RE-AIM Implications: Transparent Reporting

CONSORT Pragmatic Trials Reporting Criteria[1, 2]

- Real-world *stakeholder* questions
- *Multiple outcomes*…of interest to stakeholders—costs and Return on Investment
- Real-world *comparison conditions*- consider "Minimal Intervention Needed for Change" (MINC)
- *Multiple settings*—replications
- CONSORT "PLUS" flow diagram[3]

[1]Glasgow RE, et al. *Health Services Research*, 2011, Nov 2. doi: 10.1111/j.1475-6773.2011.01347.x.
[2]Zwarenstein M, et al. *Br Med J* 2008;(11 November) 337:a2390
[3] http://cancercontrol.cancer.gov/IS/reaim/figures-and-tables.html

Rigorous…. and a word about RCTs

- Address most likely challenges to validity and conclusions for THAT question
- Both external and internal validity are important
- Design should fit the question- NOT vice-versa[1]
- An RCT is not an RCT is not an RCT
- CONSORT delineation of Pragmatic trials is an important advance[2]
- RCT is not the only design that is experimental- and it does NOT guarantee causality [3,4,5]

[1] Mercer S et al. Amer J Prev Med, 2007; 3:, 139-154.

[2] Thorpe et al. J Clin Epidem 2009; 62: 464–475, Can Med Ass J 2009; *180*, E47-E57.

[3] Kessler & Glasgow, Amer J Prev Med, 2011, 40, 637-644;

[4] Cartwright BioSocieties, 2007, 2: 11-20.

[5] Grossman J, MacKenzie FJ. Persp Biol & Med 2005, 48: 516-534.

Rigorous Designs

- Multiple Baseline Across Settings
- Interrupted Time Series (with replication)
- RCT- individual, cluster randomized, mTCT
- N of 1
- Regression-discontinuity
- Cross-over
- Prospective Meta-analyses
- Comparative Case Study
- Natural experiments- with replication and addressing contextual factors
- Preference
- Many hybrid and quasi-experimental designs

Rapid Evidence

- Need rapid learning research- especially for pressing issues such as obesity, HIV, explosion of health care spending, health inequities

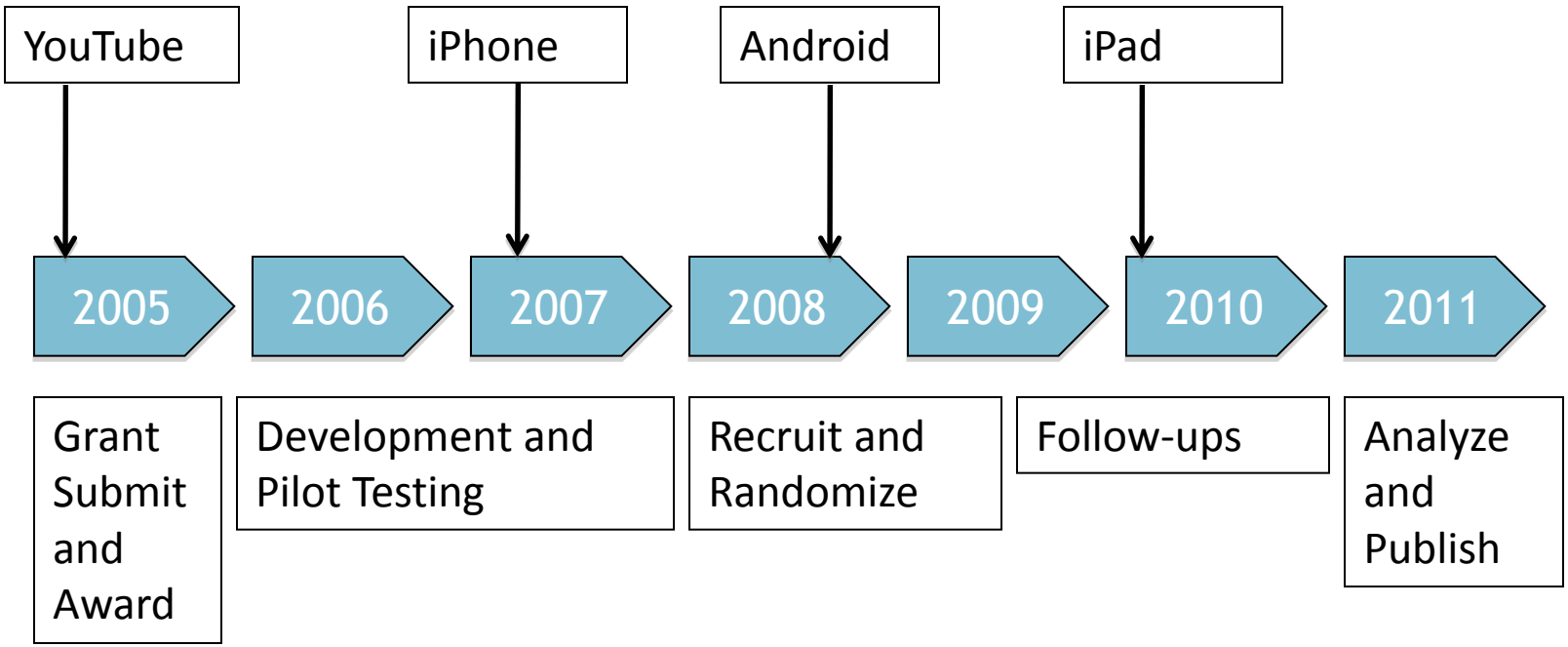
- EMR, and their potential enhancements, make possible 'rapid learning health care systems'*
  - *Real time data on millions of real world patients in real world health care settings, treated under usual conditions*

Institute of Medicine, A Foundation for Evidence-Driven Practice: A Rapid Learning System for Cancer Care, 2010. http://www.iom.edu/Reports/2010/A-Foundation-for-Evidence-Driven-Practice-A-Rapid-Learning-System-for-Cancer-Care.aspx

Etheredge L et al, *Health Affairs, Web Exclusive Collection,* w107-w118, doi:10.1377/hlthaff.26.2.w107)

Glasgow R, Chambers D. Clinical Translational Science, 2012, in press

How to Evaluate Technologies that Outpace Research?



William Riley, NHLBI

Cost Evidence

- Replication costs and scalability costs are arguably most needed
- Perspective- patient and adopting setting
- Costs should be comprehensive and transparent
- 'One persons costs are another's profits'
- Cost-effectiveness analyses need not be overwhelming[1]- cost per incremental unit change
- Should be harmonized and include costs frequently not counted that need to be- e.g., recruitment, overhead, training, preparation and supervision[1]

[1] Ritzwoller et al, Trans Behav Med, 2011, *1,* 427-435.

Public Health Cost Questions to Ask….

- In this world of "the 4 P's" of personalized medicine…. ALSO ask the 4 "W's":
  - ✓ **Who Benefits**
  - ✓ **Who Suffers**
  - ✓ **Who Pays**
  - ✓ **Who Profits**

Glasgow RE, Fisher EB, Haire-Joshu D, Goldstein MG. NIH Science Agenda: A Public Health Perspective. Am J Public Health 97(11):1936-1938

Convergent Evidence

- Much to learn from well conducted *observational studies*
- Huge amount of potential for *simulation modeling*- esp. re: interactions and unintended consequences[1,2]
- *Evaluability*[3]- aka initial 'sniff test'
- Mixed methods[4] and *qualitative*
- Practice-based evidence on *efficiency and feasibility*
- Emphasis on *replication and consistency*
- Combine with *experimental*

[1] Stern M, Williams K, Eddy D, Kahn R.Diabetes Care. 2008 Aug;31(8):1670-1.
[2] Mabry, P .Am J Prev Med. 2011 May; 40 (5 Suppl 2):S159-61
[3] Leviton, L. Ann Rev Public Health, 2010, 3:, 213-233.
[4] Creswell J, Klassen A, Plano-Clark V, Smith, LC. 2011, NIH-OBSSR. Mixed Methods Summary: http://obssr.od.nih.gov/scientific_areas/methodology/mixed_methods_research/pdf/Best_Practices_for_Mixed_Methods_Research.pdf

Transparent Evidence on…..

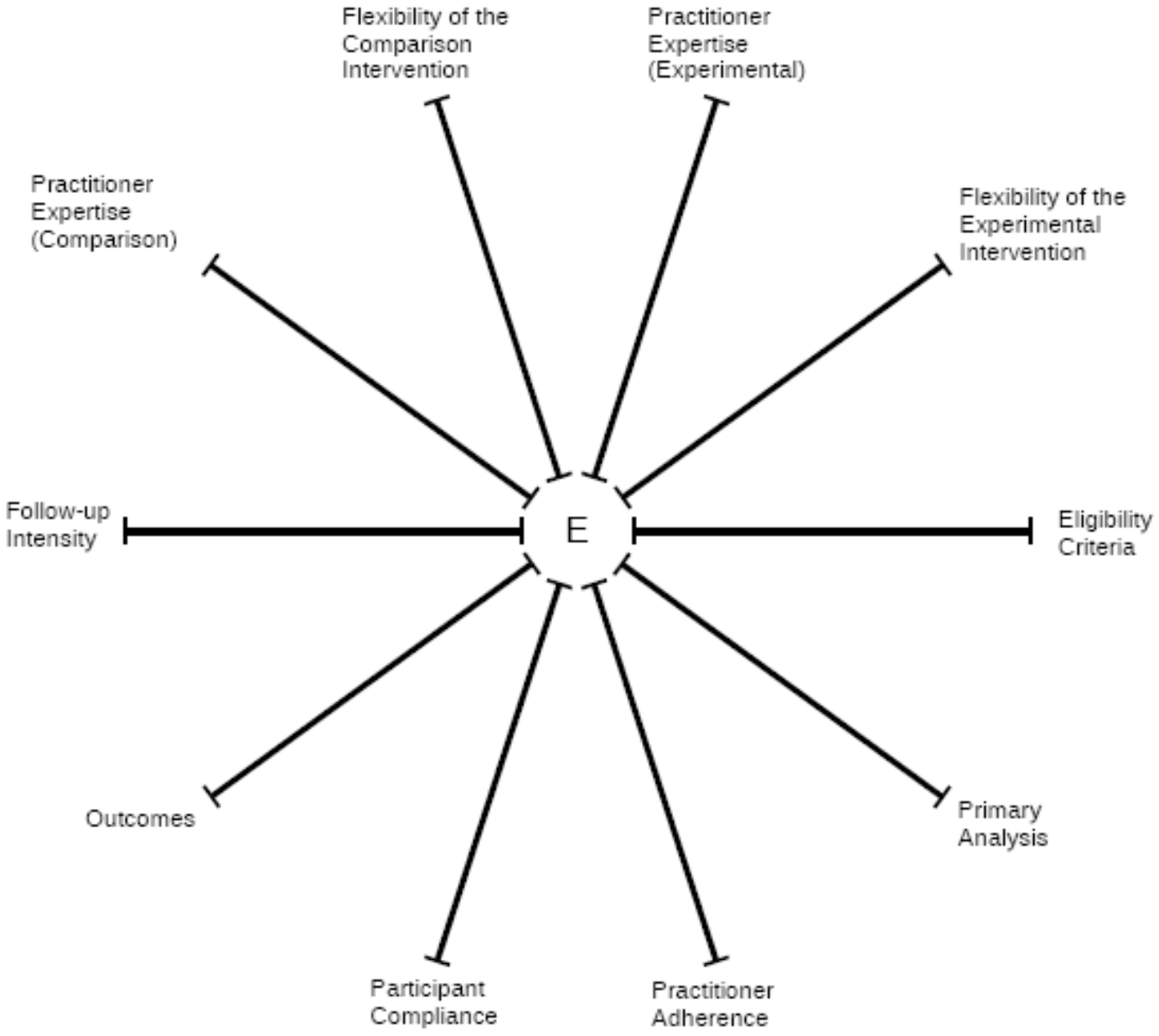
- Info needed to replicate or implement
- Resources required- costs for patients and delivery setting perspectives
- How were settings, clinicians, and patients selected- (*who was excluded and why*)
- *Adaptation*- changes made to protocol, to intervention, to recruitment, etc.
- *Differences across settings*

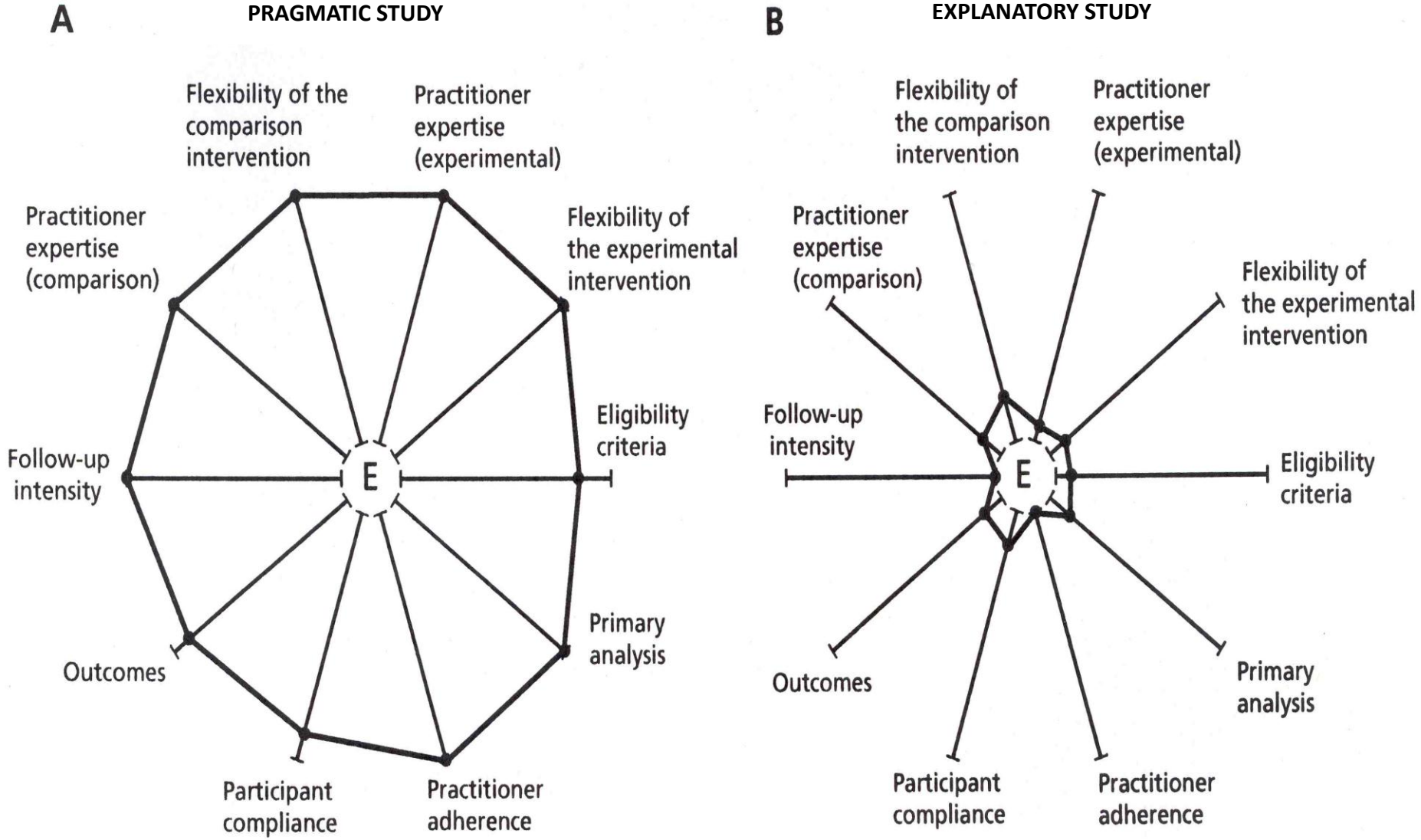
The Pragmatic-Explanatory Continuum Indicator Summary (*PRECIS*)

Describes ten domains that affect the degree to which a trial is pragmatic or explanatory.

1. Participant eligibility criteria
2. Experimental intervention flexibility
3. Practitioner expertise (experimental)
4. Comparison intervention
5. Practitioner expertise (comparison) outcome
6. Follow-up intensity
7. Primary trial outcome
8. Participant compliance
9. Practitioner adherence
10. Analysis of primary outcome

Thorpe KE, et al. *J Clin Epidemiol* 2009; 62: 464–475, Can Med Assoc J 2009; 180(10)

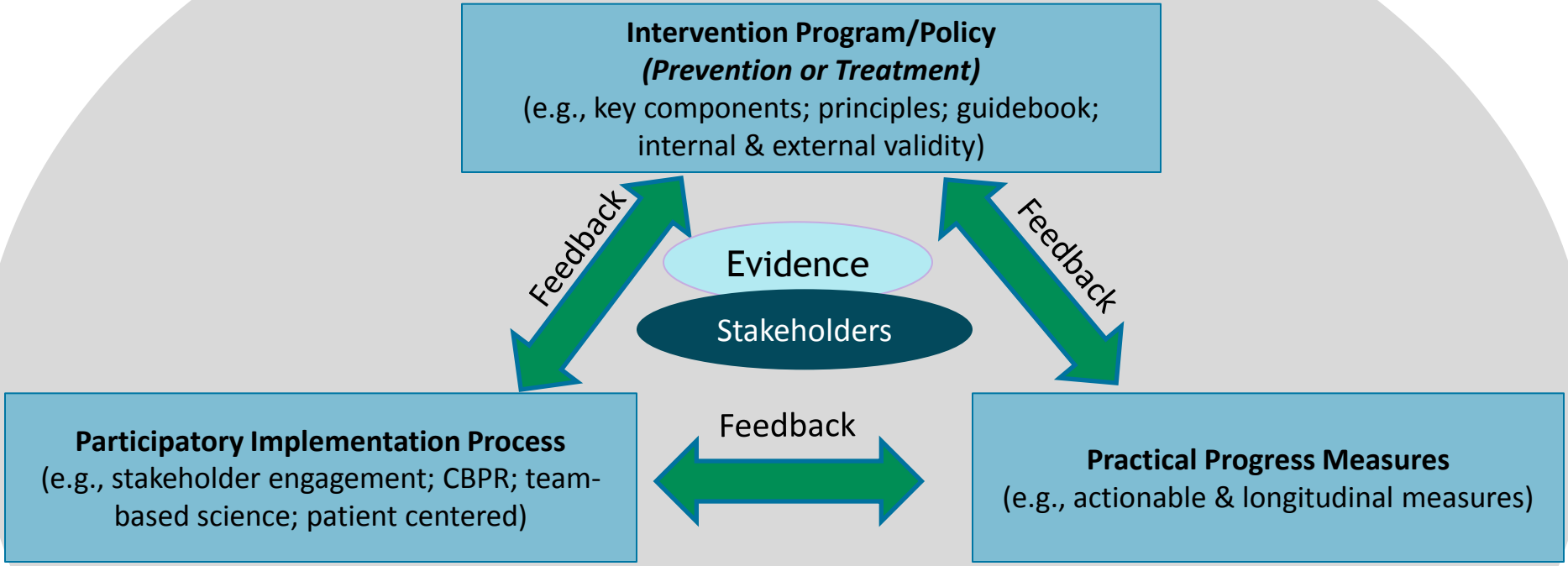

Flexibility of the Comparison Intervention
Practitioner Expertise (Experimental)
Practitioner Expertise (Comparison)
Flexibility of the Experimental Intervention
Follow-up Intensity
E
Eligibility Criteria
Outcomes
Primary Analysis
Participant Compliance
Practitioner Adherence


A
PRAGMATIC STUDY
Flexibility of the comparison intervention
Practitioner expertise (experimental)
Practitioner expertise (comparison)
Flexibility of the experimental intervention
Eligibility criteria
Follow-up intensity
E
Primary analysis
Outcomes
Participant compliance
Practitioner adherence
B
EXPLANATORY STUDY
Flexibility of the comparison intervention
Practitioner expertise (experimental)
Practitioner expertise (comparison)
Flexibility of the experimental intervention
Follow-up intensity
E
Eligibility criteria
Outcomes
Primary analysis
Participant compliance
Practitioner adherence

Future Evidence Needs- Keys to Advance Translation

- Context- key factors that may be moderators
- Scalability
- Sustainability
- Health inequities impacts
- Patient/citizen/consumer and community perspective
- Multi-level interactions, especially between policy and practice

Evidence Integration Triangle (EIT)



Multi-Level Context

- Intrapersonal/Biological
- Interpersonal/Family
- Organizational
- Policy
- Community/Economic
- Social/Environment/History

Glasgow, R, Green, Taylor, Stange, Am J Prev Med, in press

EIT Conclusions

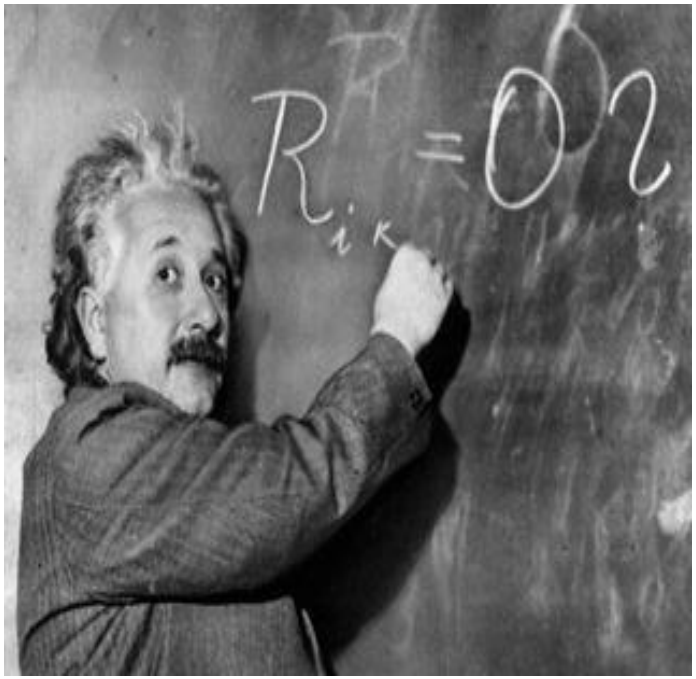
- The evidence-based movement is a good start, but only gets us so far
- To make greater progress, two other elements also need attention:
  - Practical MEASURES to track progress, and
  - Implementation PROCESSES that use partnership principles
  - These 3 legs of the 'EIT" are each necessary but not sufficient by themselves

http://cancercontrol-dev.cancer.gov/IS/presentations/

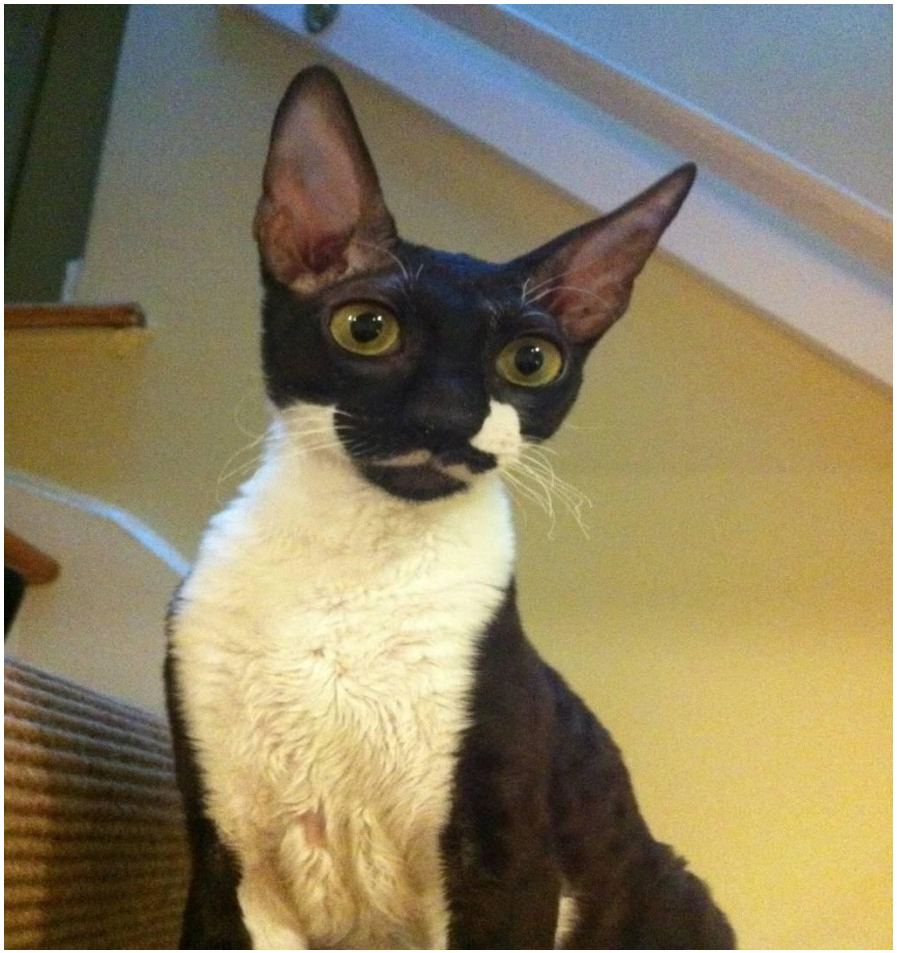
The same research methods, policies, paradigms and approaches that produced today's inequities are not likely to reduce them

"The significant problems we face cannot be solved by the same level of thinking that created them."

A. Einstein



Questions? Comments?



I am all ears

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NCI Implementation Science Website: http://cancercontrol.cancer.gov/IS/