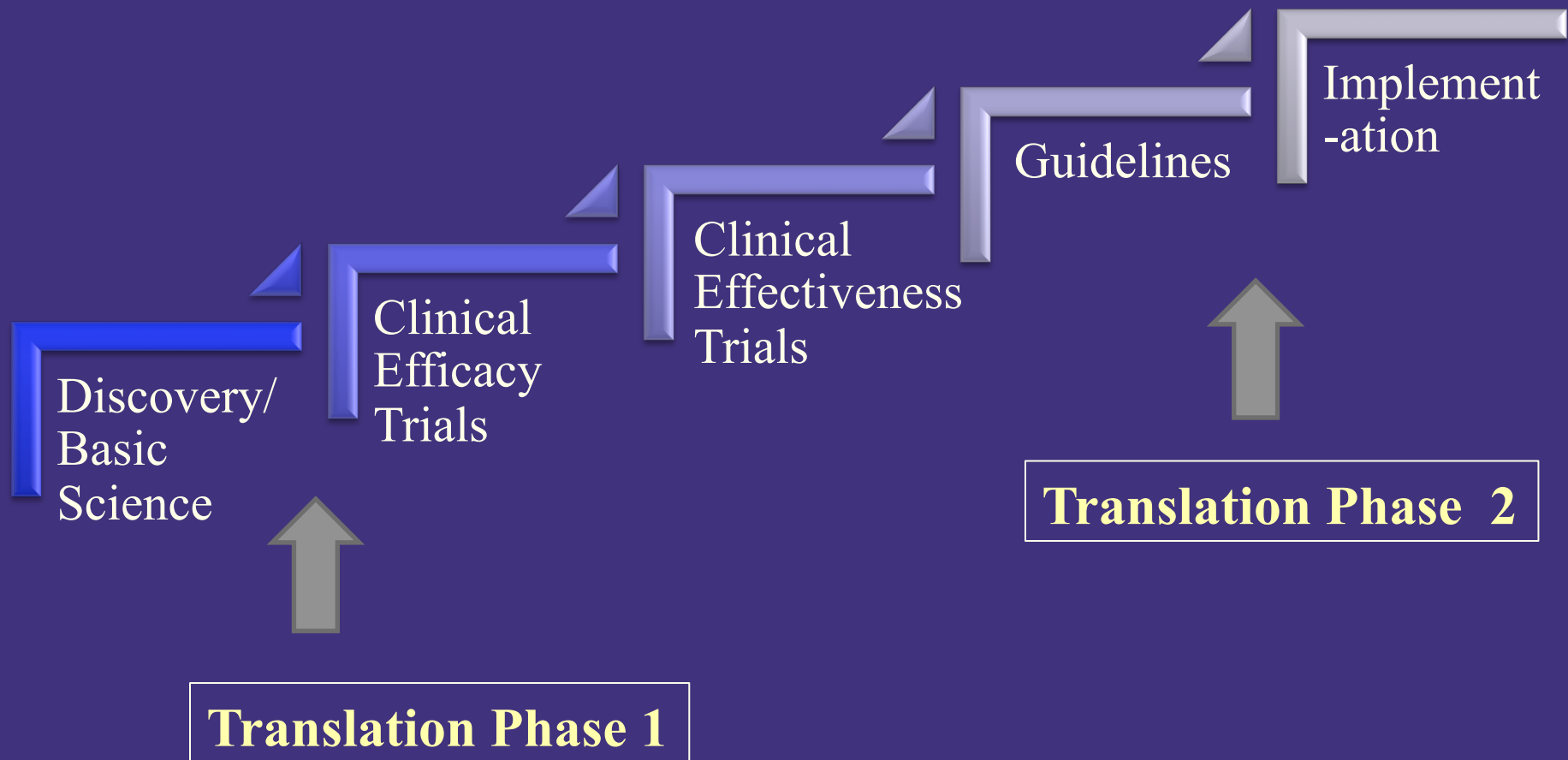


*Implementation Science - An  
Opportunity for Personalized  
Medicine*

Lori A. Orlando, MD MHS

# Presentation Topics

- Overview
- Methodology
- Frameworks
- Opportunities in Personalized Medicine



2001



2003

SPECIAL ARTICLE

SHATTUCK LECTURE

Clinical Research to Clinical Practice —  
Lost in Translation?

Claude Lenfant, M.D.

2007

**Khoury MJ, Gwinn M, Yoon PW, et al. The continuum of translation research in genomic medicine: how can we accelerate the appropriate integration of human genome discoveries into health care and disease prevention?**

# Why is Implementation Uptake Low

- Forgetting about the pipeline continuum
  - Assuming that clinical effectiveness studies = victory
  - Intervention is ready for wide dissemination
- Forgetting that ALL implementations require **behavior change!**
- Implementation is **complex** (multiple barriers and stakeholders)
  - Patient (ex. culture, health activation)
  - Provider (ex. knowledge, time)
  - Clinic (ex. resources, workflow)
  - Health System (ex. IT, organizational culture)
  - Policy (ex. reimbursement, guidelines)

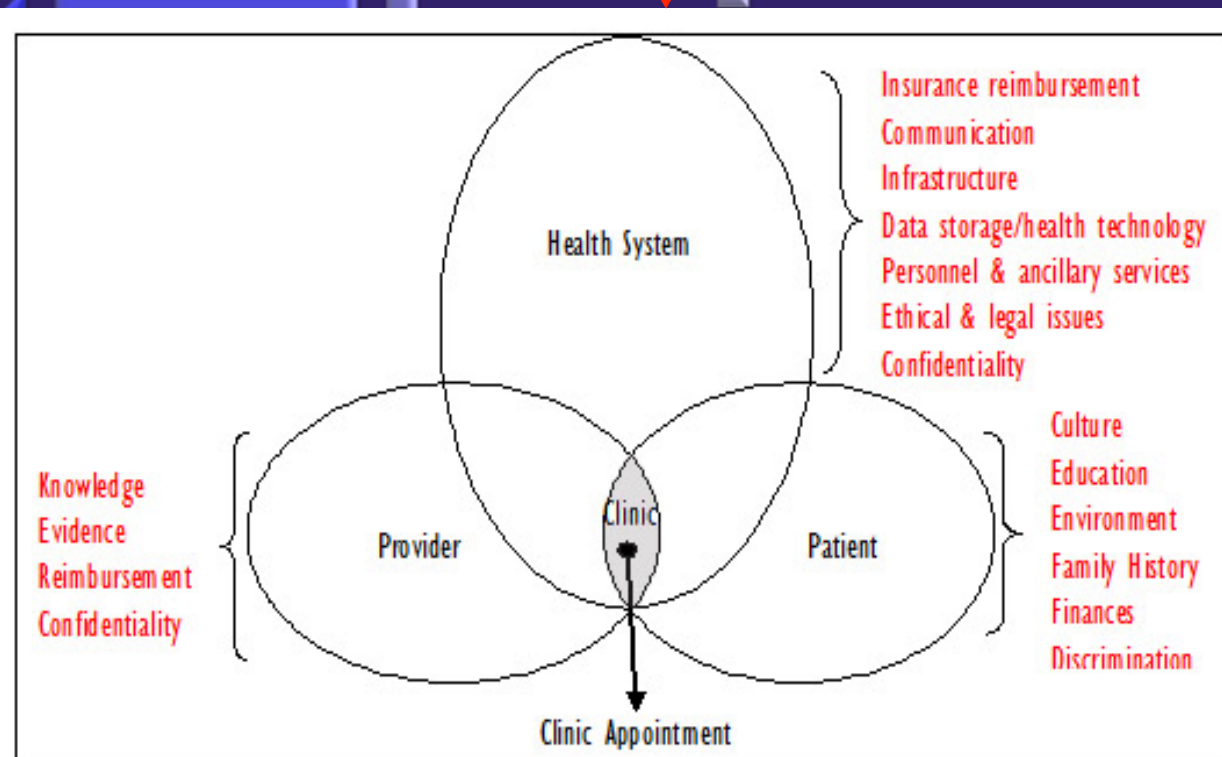
Discovery/  
Basic  
Science

Tra

Clinical

Guidelines

Implement  
-ation



2

# Methodology

# Implementation Studies

- Actively encourage uptake of evidence-based care
- Facilitate widespread adoption/dissemination (generalizability)
- Increase methodologic understanding of implementation
  - Barriers, facilitators
  - Strategies
  - Theories
  - Measures

# Key Characteristics

- Real world sites and heterogeneous populations
  - Strong external validity
- Contextual
- Adaptive
- Formative Evaluation (usually)
- Complex:
  - Multi-component programs
  - Extensive stakeholder involvement
  - Multi-disciplinary

## Practical Clinical Trials

- 1) Representative patients
- 2) Multiple clinical settings representing broad cross-section of care
- 3) Comparator is the standard of care (not usual care)
- 4) Outcomes include measures relevant to clinicians and decision makers
  - Cost
  - Quality of life, behavior

## Quality Improvement Studies

- 1) Contextual
- 2) Formative and other evaluations guide intervention development
- 3) Rapid cycles of stakeholder feedback used to adapt intervention

Tunis SR, Stryer DB, Clancey CM. Practical clinical trials. Increasing the value of clinical research for decision making in clinical and health policy. JAMA 2003;290:1624–32.

|                      | <u>Effectiveness Study</u>     | <u>Implementation Study</u>                                     |
|----------------------|--------------------------------|---|
| <b>INTERVENTION</b>  | Evaluate clinical outcome      | Facilitate organizational change and individual adoption of EBM |
| <b>RANDOMIZATION</b> | Patient                        | Cluster (practice, physician)                                   |
| <b>MEASURES</b>      | Summative                      | Formative   |
| <b>OUTCOMES</b>      | Patient level data are primary | Adoption, Fidelity  |
|                      | Clinical effectiveness         | Process measures, Efficiency                                    |
|                      | Quality of life                | Stakeholder satisfaction  |
|                      | +/- Costs                      | Costs   |
|                      |                                | Sustainability  |

# Complexities

- Multiple stakeholders- payers, administrators, patients, providers
- Choosing an implementation strategy
- Multiple levels of analysis- policy, organization, practice, patient
- Selecting and measuring implementation outcomes
- Design challenges in testing effects of practice change
  - Small N with cluster randomization
  - Contamination
- Adaptation vs Generalizability
  - Which features are core to the intervention?
  - Which features have to be present to maintain effectiveness?

Hybrid Studies  
(Implementation-Effectiveness)

|                          | <u>Type 1</u>                                   | <u>Type 2</u>   | <u>Type 3</u>   |
|--------------------------|---|---|---|
| <b>Primary Outcome</b>   | Effectiveness                                   | Effectiveness   | Implementation  |
| <b>Secondary Outcome</b> | Pre-implementation data gathering               | Implementation  | Effectiveness   |
| <b>Rationale</b>         | Expedites transition to implementation stage    | Implementation feasibility pilot                        | Complete spectrum of effectiveness data not yet available |
| <b>Randomization</b>     | Patient   | Patient or Cluster                                      | Cluster   |
| <b>Measures</b>          | Effectiveness                                   | Effectiveness   | Adoption/Fidelity   |
|                          | Potential barriers/facilitators & modifications | Unanticipated barriers that emerge after implementation | Sustainability & Adaptation                               |
|                          | Staff/workflow capabilities                     | Adaptations to improve uptake and/or simplify           | Costs & Utilization                                       |
|                          | +/- Costs                                       | +/- Costs   | Effectiveness   |

# Formative evaluation

“A rigorous assessment process designed to identify potential and actual influences on the progress and effectiveness of implementation efforts before, during, and after implementation to optimize the potential for success.”

- Data gathered from multiple stakeholders (interviews, SC notes..)
- Identifies barriers and facilitators throughout implementation phases
- Identifies what did / did not happen in implementation plan
- Identifies factors that influenced implementation
- Measures success

Stetler CB, Legro MW, Wallace CM, et al. The role of formative evaluation in implementation research and the QUERI experience. *J Gen Intern Med* 2006;21 Suppl 2:S1-8. 16637954.

# Stages of Formative Evaluation

*Pre-Implementation*

*Implementation*

*Post-Implementation*

## Developmental

“Diagnostic” of the existing context (baseline assessment)

- organizational readiness for change
- expectations of project
- existing services and structure of care

## Implementation-Focused

“Actuality” of implementation

- barriers to change
- adjustments to interventions

## Progress-Focused

“Monitoring impacts & indicators of progress toward goals”

- dose & intensity of intervention

## Interpretive

“Uses results of all other FE stages”

- key stakeholder experiences
- could “re-diagnose” the context

# FE: Developmental (needs assessment)

- Baseline assessment of practice pattern (related to intervention)
- Determinants of current practice
- Potential barriers / facilitators to change
- Potential barriers / facilitators to implementation
- Feasibility
- Gauge buy-in / engagement of stakeholders
- Encourage stakeholders to participate in identifying and solving barriers

**End result is an implementation strategy**

# FE: Implementation-Focused

- Assesses differences between implementation plan and execution
- Identify barriers arising during initial implementation
- Identify adaptations that optimize success
- Identify core components and those that are unnecessary to allow wider adoption

# FE: Progress-Focused

- Assess success of intermediate goals along timeline
- Continuous adaptation for optimization
- Provides performance feedback for providers/clinics (whatever the randomization unit is)

# FE: Interpretive Evaluation

- Final evaluation of stakeholders
- Final evaluation of strategy for adaptation
- Final evaluation of success
- Identify reasons for success / failure

# Formative Evaluation Methods

## Quantitative

- Organizational culture, readiness to change, provider receptivity
  - ORCA, OCM, etc.
- Fidelity measures
  - Administrative data on clinical performance and quality

## Qualitative

- Semi-structured stakeholder interviews
- Focus groups
- Direct observation of workflow and clinic processes/responsibilities

# Summative Evaluation

“systematic process of collecting and analyzing data on impacts, outputs, products, outcomes and costs” that are used to assess success, effectiveness, or goal achievement of an intervention”

- Assess intervention effectiveness of implementation with process of care measures
- Assess intervention effectiveness on clinical care (patient outcomes)
- Can use administrative data, chart review, primary data collection
- Assess costs of implementation

Stetler CB, Legro MW, Wallace CM, et al. The role of formative evaluation in implementation research and the QUERI experience. J Gen Intern Med 2006;21 Suppl 2:S1-8. 16637954.

# Framework

# RE-AIM

TABLE 1  
RE-AIM Perspectives on Policy Translation Issues

| <i>RE-AIM Dimension</i> | <i>Key Issues</i>   | <i>Policy Issues, Questions, and Examples</i>   |
|-------------------------|---|---|
| Reach                   | How many people are impacted and are they representative or those most at risk?   | Extent that populations most exposed to environmental risks are reached   |
| Effectiveness           | Impact/risk reduction results<br>Robustness and impact on quality of life<br>Unanticipated consequences                               | How robust or consistent are outcomes?<br>Impact on other prevention activities or environmental risks  |
| Adoption                | How many (what %) of target settings will participate especially if voluntary?<br>Diffusion or adoption curves for different policies | How many and which coal burning power plants will decrease emissions under Policy A?  |
| Implementation          | Cost (and different types of cost)<br>Level of enforcement or delivery variability  | What happens to adherence over time?<br>Are some parts of a policy implemented and enforced more consistently than others?<br>What are the economic implications of Policy A in terms of both development and outcomes? |
| Maintenance             | Long-term effects and sustainability<br>Re-invention and variation in policy interpretation   | Policy may lose impact over time, policy may be rescinded in difficult economic times.<br>New scientific findings may require policy revisions over time  |

Jilcott, S, Ammerman, A, Sommers, J and Glasgow, RE (2007). "Applying the RE-AIM framework to assess the public health impact of policy change." *Ann Behav Med* 34(2): 105-14.

# RE-AIM Purpose

- To standardize criteria to evaluate programs
- To evaluate issues relevant to adoption, implementation, and sustainability
- To inform design of interventions and selection of key outcome measures

# RE-AIM Example

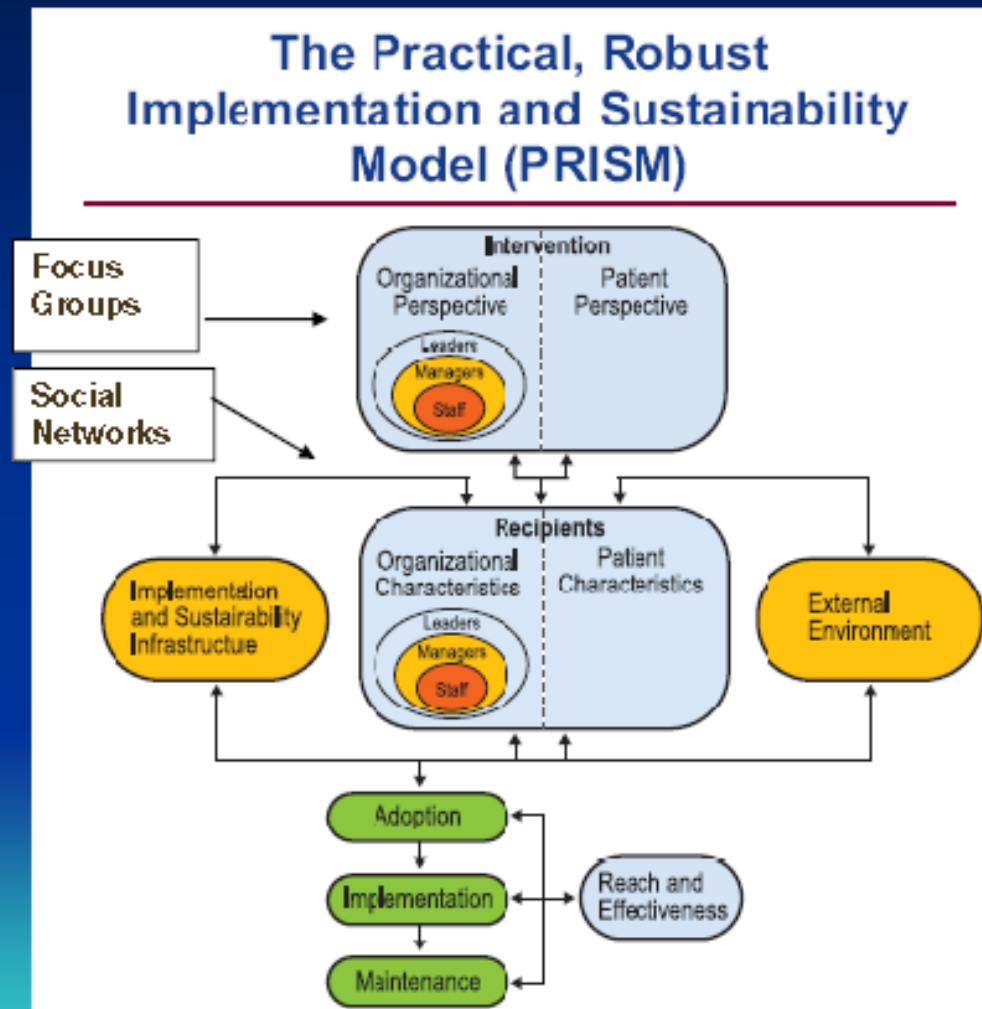
|   | Concept        | Level                | Impact       |
|---|----------------|----------------------|--------------|
| Guideline recommended                           |                | Public health/system | 100%         |
| Health system has access to necessary resources | Adoption       | System/Clinic        | 50%          |
| Provider adherence                              | Adoption       | Provider             | 50%          |
| Patient has access                              | Reach          | Patient              | 50%          |
| Patient outcome improves                        | Effectiveness  | Patient              | 50%          |
| <u>Public health impact</u>                     |                |                      | <u>6.25%</u> |
| Implementation effort                           | Implementation | Single stakeholder   | 12.5%        |
|   |                | Two stakeholders     | 25%          |
|   |                | Three stakeholders   | <u>50%</u>   |

Adapted from Glasgow, R. presentation at SGIM 2011

# Theoretical Models

- Organizational Change Management (OCM)
- Promoting Action on Research Implementation in Health Services Research (PARIHS)
- Diffusion of Innovation (DoI)
- Simpson's Transfer Conceptual Model
- Fully Immersive Team Training (FITT)
- Practical, Robust, Implementation, and Sustainability Model (PRISM)
- Consolidated Framework for Advancing Implementation Research (CFIR)
- Organizational transformation model
- Precede-Proceed

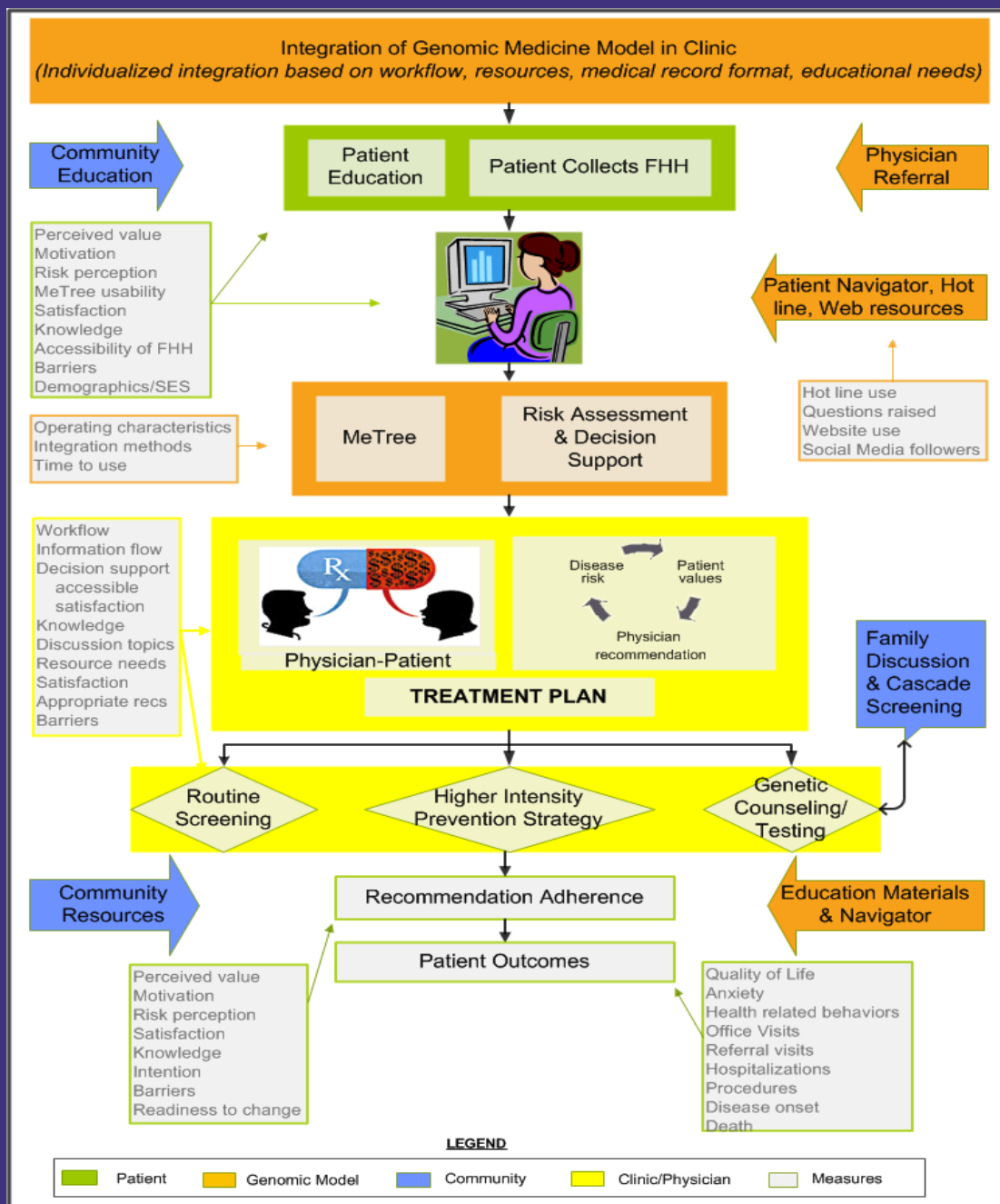
# PRACTICAL, ROBUST, IMPLEMENTATION AND SUSTAINABILITY MODEL (PRISM)



Feldstein A, Glasgow RE. A practical, robust Implementation... *Jt Comm J Qual Safety* 2008;34:228-243

# Personalized Medicine Opportunities

## Information, Participant and Evaluation Flow



- Pharmacogenomics
  - Hybrid Type 1, 2, or 3 study
  - Type 1 or 2 for new markers
  - Type 3 for FDA recommended
- Patient preferences/values
  - Guidelines recommending discuss options with patient
  - Tamoxifen for primary prevention in high risk patients
  - PSA screening