THE PATH TO GENOMIC MEDICINE: AN IMPLEMENTATION CHALLENGE

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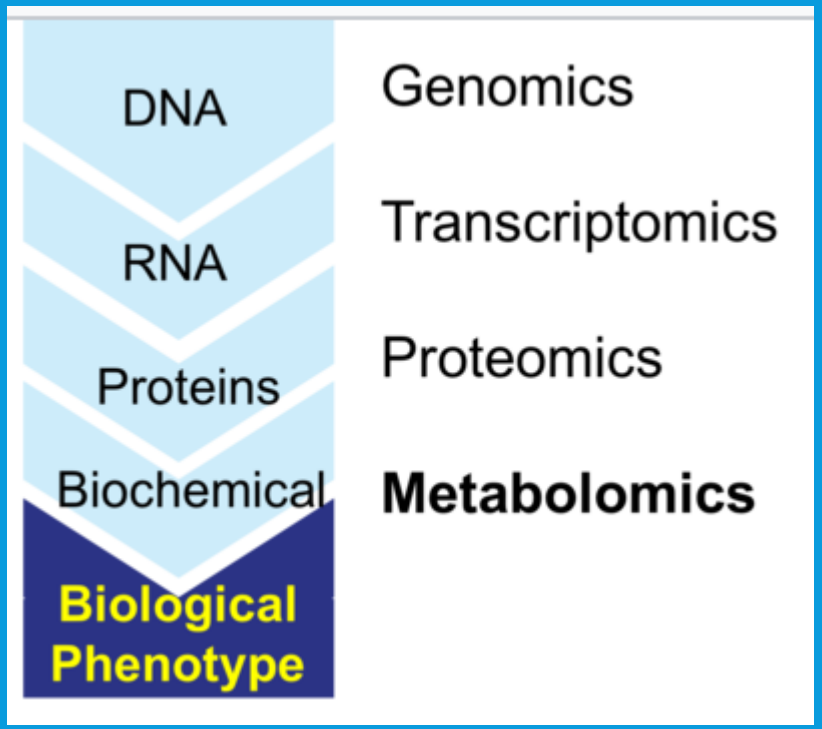
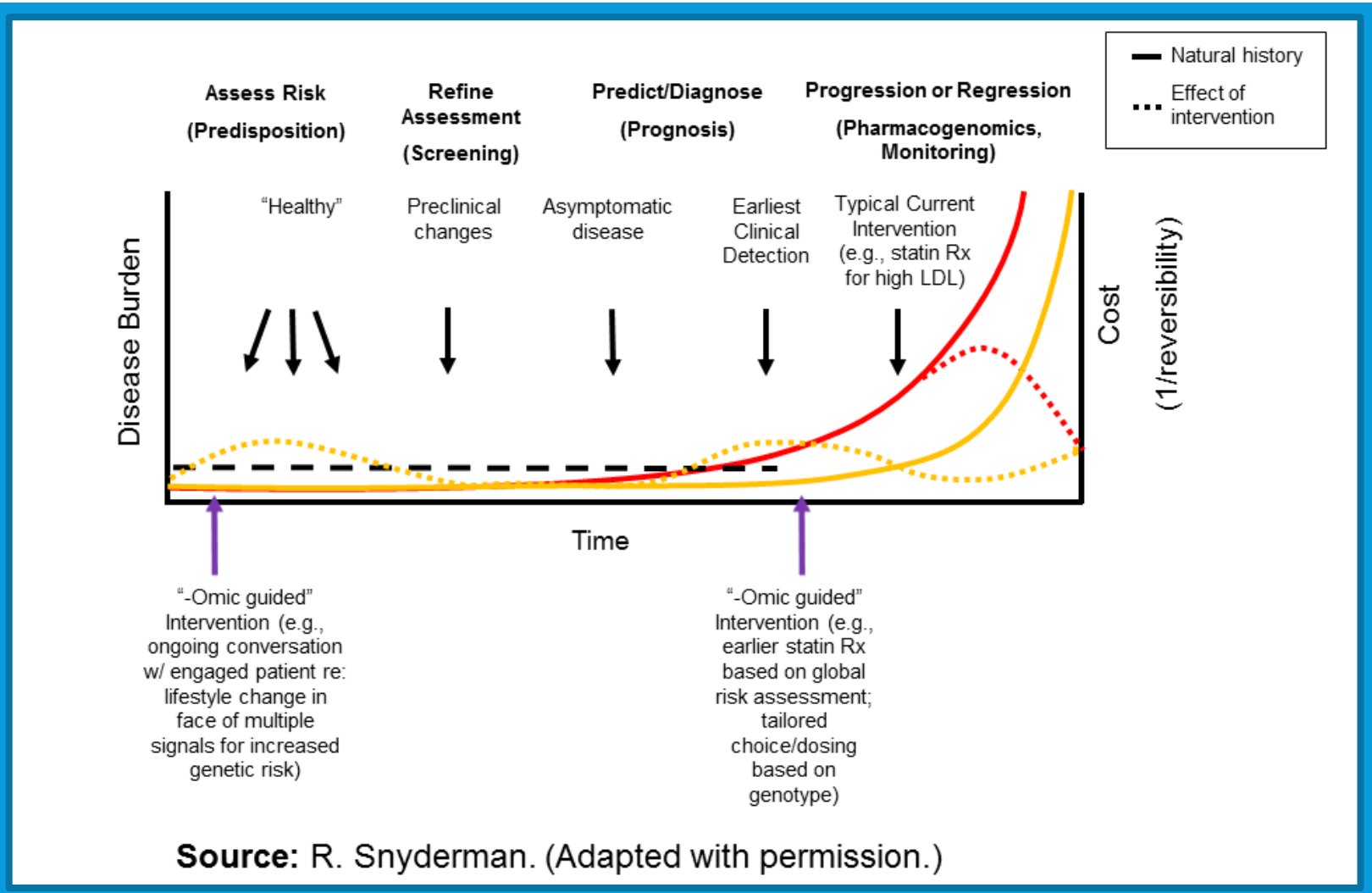
APPLIED GENOMICS & PRECISION MEDICINE

POTENTIAL TO CHANGE THE HEALTHCARE PARADIGM



From https://en.wikipedia.org/wiki/Metabolomics



Source: R. Snyderman. (Adapted with permission.)

IT IS NOT WITHOUT RISKS

Eugenics
Determinism

REAL QUESTION IS: HOW TO IMPLEMENT?

CHALLENGES

- Complex
- Interventions vary widely
- Context dependent
- Highly diverse stakeholders




IMPLEMENTATION RESEARCH

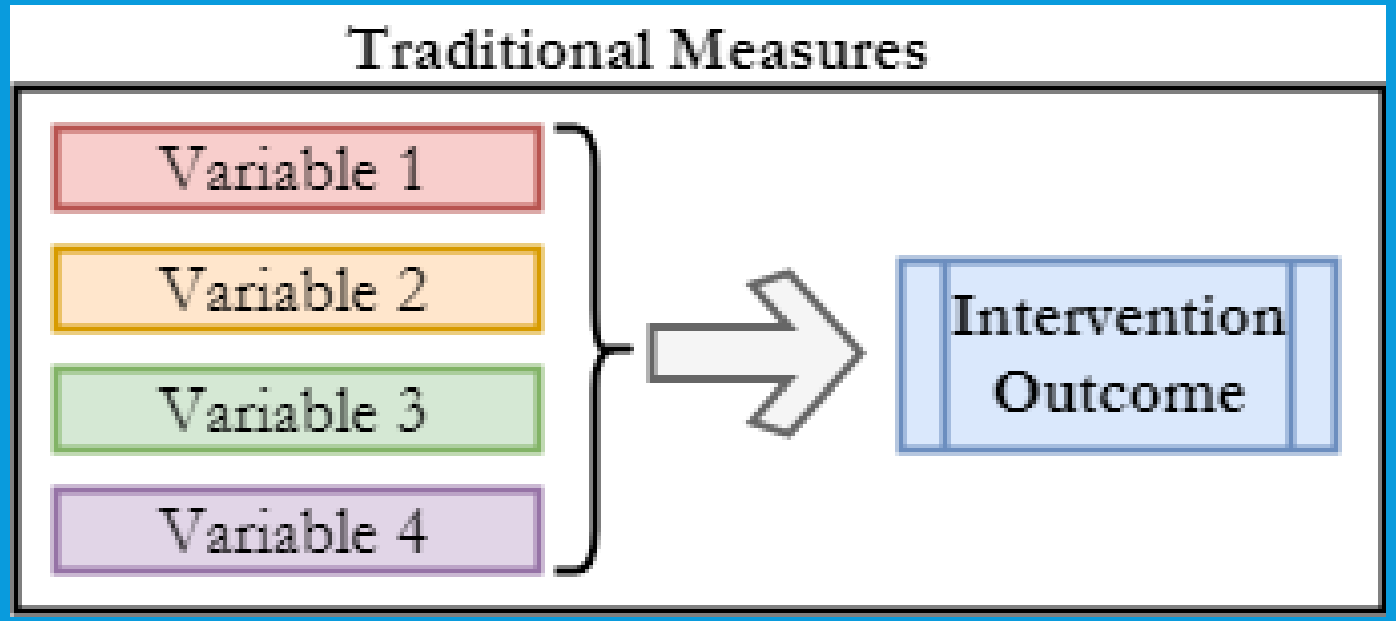
Implementations without structure provide no guidance on implementation in other settings–

- Lack generalizability
- Lack sustainability

EXAMPLE: CENTRAL LINE INFECTIONS

- Peter Pronovost's ICU checklist (NEJM 2006)
- 108 ICUs in Michigan
- Catheter related infections decreased by 80% at all sites

HOW YOU GET TO OUTCOMES IS IMPORTANT



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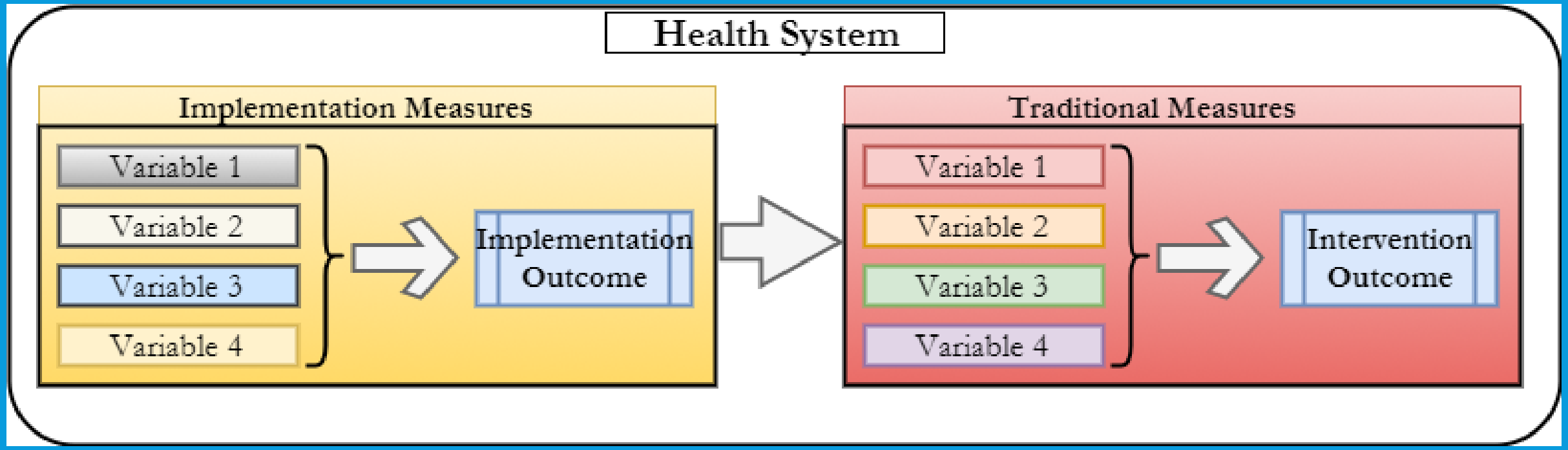


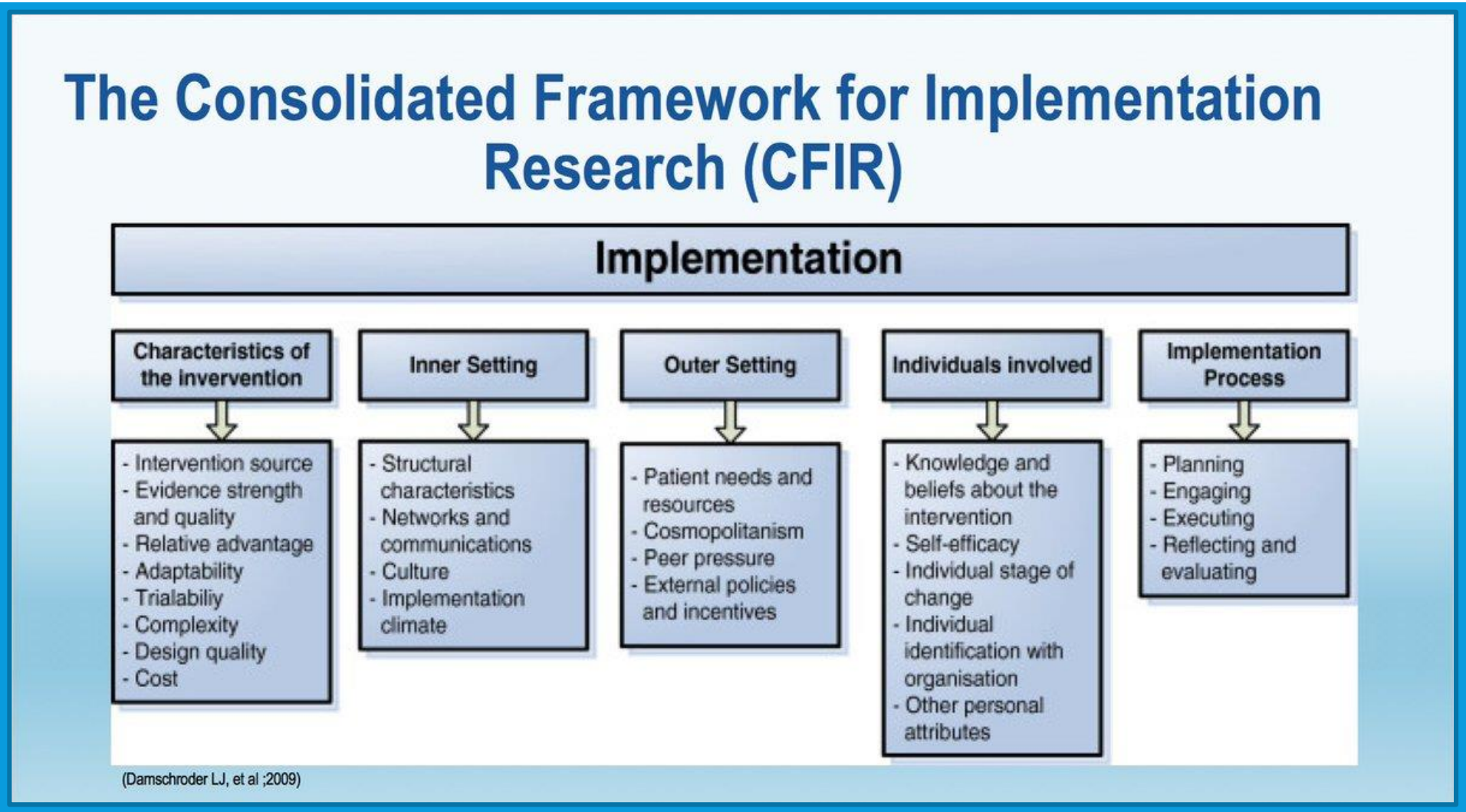
CONSOLIDATED FRAMEWORK FOR IMPLEMENTATION RESEARCH (CFIR)

Overall:

26 constructs

13 sub-constructs

www.dissemination-implementation.org/



Conceptual Framework- Translating Genomic Discoveries in Diverse Populations

Interventions

***Purpose*:** Evaluate
- Disease risk, Dx, Prognosis, Therapy

***Type*:** Family history, SNP-panel, targeted, whole genome, exome sequencing, cascade

***Comparator*:** none, usual care, another intervention

Education:
- patient, family, provider

***Return of Results*:**
-By : clinicians, genetic counselors, lay persons
-To: patient, family, provider
- How: In person, app, EHR, telemedicine
- What: Structure, content of report including what will be returned

***Characteristics*:**
-Cost, relative advantage, evidence strength, adaptability, complexity

IMPLEMENTATION PROCESS
Select steps taken to facilitate uptake using expert recomm. for implementing change study choices (in sparks)

Potential Mitigating Factors

Outer Setting

PHYSICAL CONTEXT

Medical: Access, available quality of care

Built Environment: Housing, poverty, crime, walkability, pollution, food

Unequal Distribution of Resources: Money, Public Policy, Systems, Education

Inner Setting

MEDICAL CONTEXT

Setting Type: in/outpatient, academic/community, rural/urban, private/safety

Health Systems: patient population (#/year, payor mix, EHR type, race/ethnicity, SES)

Implementation Climate: Readiness, access to resources & information, compatibility with workflow, leader engagement, tension for change

PROCESSES

Communication: Patient, family, provider, lab (nature and quality)

Laboratory: Quality metrics, turn around, structural variant calling, ROR process

Individuals

PATIENT FACTORS

Social: Social network, support, influence, engagement

Demographic: Age, race/ethnicity, sex/gender, lang., literacy, numeracy, income, employment, education, insurance

Psychosocial: Depression, stress, anxiety, self-efficacy, perceived racism, activation, cultural norms, family issues

Stressors/Resources: Family, community, occupational, financial

Behavioral: Lifestyle, self-management, adherence, health seeking

Attitude, Understanding: Genetic testing, return of results, about intervention, trust (in testing, results, providers), expected utility, preference for who returns results

Biological/genetic makeup:
Family history, Health history, Ancestry

PROVIDER FACTORS

Demographic: Age, Race/Ethnicity, Sex/gender, Training, Experience, Specialty

Psychosocial: Stress, satisfaction, anxiety from medical uncertainty

Stressors/Resources: Time, access to information, experts, referrals

Behavioral: Communication style, implicit bias, cultural appropriateness

Attitude, Understanding: Genetic testing, value of intervention, return of results, expected utility, ability to appropriately use the intervention (self-efficacy)

Outcomes

Clinical Utility:
Actionability of intervention
Diagnostic yield
Health Status, QOL, Morbidity Mortality
Patient uptake of intervention recs
Provider uptake of intervention recs
Patient achieves study endpoint

Psychological Utility:
health behaviors, anxiety, distress, depression

Pragmatic Utility:
Life and reproductive planning

Intervention Adoption:
Patient (reach)
Uptake by clinic, health system, provider (adoption)
Adherence to intervention

Social Utility & Maintenance :
Healthcare Utilization
Effectiveness >6 months
Sustained delivery of intervention
Uptake by payors
Cost effectiveness

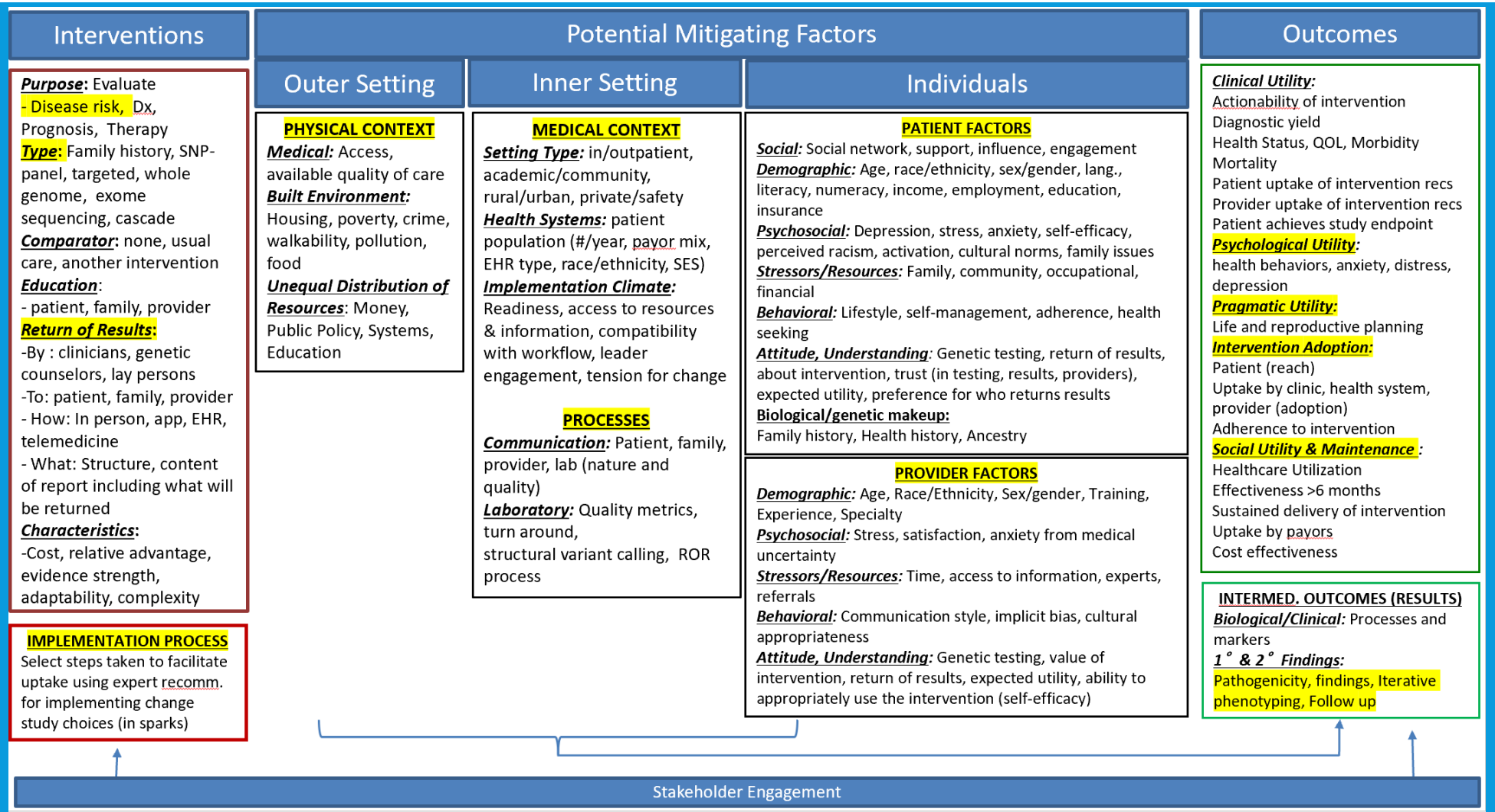
INTERMED. OUTCOMES (RESULTS)

Biological/Clinical: Processes and markers

1° & 2° Findings:
Pathogenicity, findings, Iterative phenotyping, Follow up

Stakeholder Engagement

EX. IMPLEMENT RISK ASSESSMENT PROGRAM



KEY CHALLENGES FOR GENOMIC MEDICINE

There are many but will highlight 4 areas:

1) Intervention complexity
2) Disparities
3) Data (type and ownership)
4) Implementation outcomes

INTERVENTION COMPLEXITY

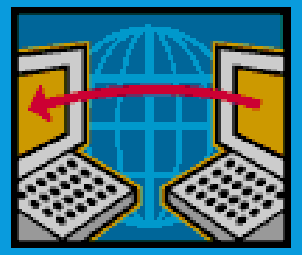
- Family health history, genotyping, WES/WGS ?
  - Current guidelines recommend using FHH to guide testing
  - ~ 50% with pathogenic BRCA do not meet testing criteria
  - New knowledge makes genotyping results outdated in few years
  - Monogenic highly pathogenic variants are not 100% penetrant (why?)
  - FHH x gene interactions (PALB2) *(Antioniu. N Engl J Med 2014; 371:497-506)*
- Who will collect the FHH?
- Who will analyze FHH to know when to test?
- Who will perform the testing and explain the testing to the patient?
- Who and how will results be documented and returned to patient?

PROPOSED FHH-BASED RISK ASSESSMENT

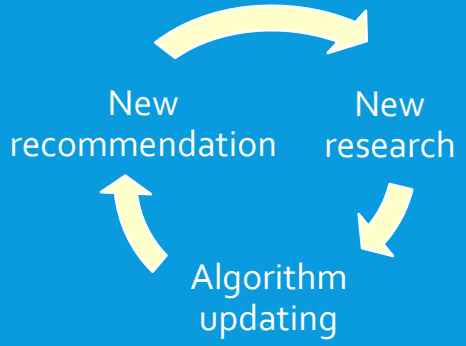
Patient entry from home or clinic *

Prepare with worksheet to talk with relatives

Contact available for questions or problems



Data sent to medical record, processed and report generated

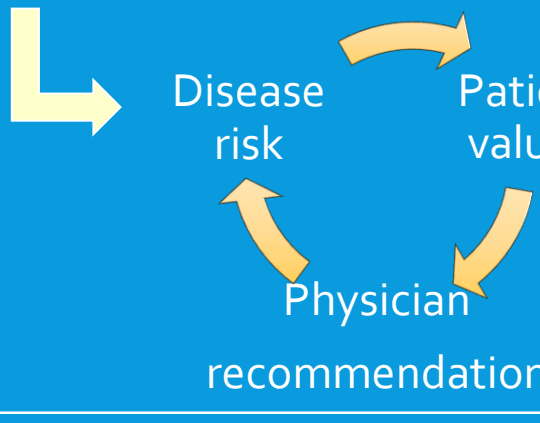


Appointment

Patient-Physician

*

Healthcare Plan



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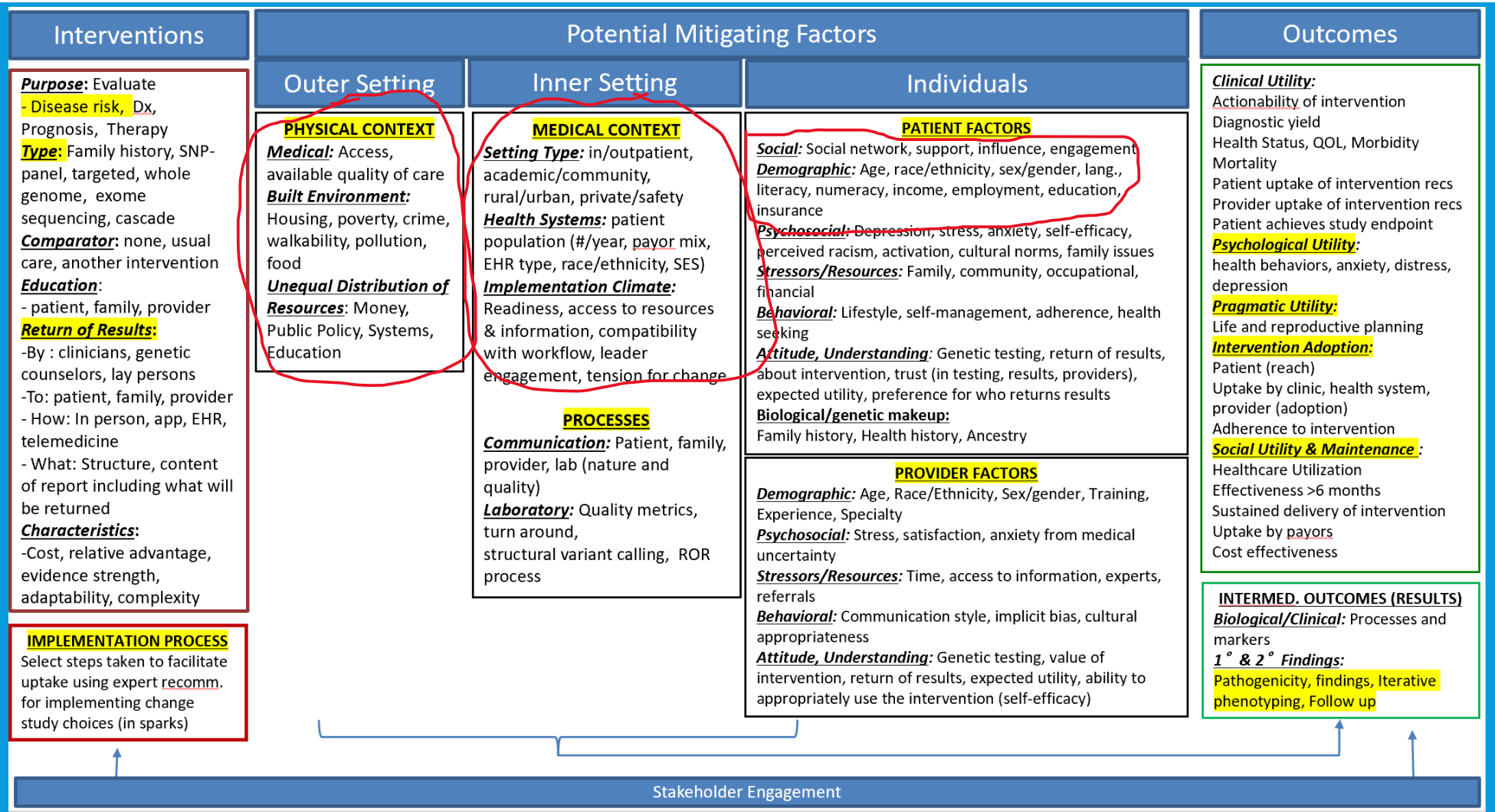


DISPARITIES

- Social determinants of health
- Trust
- Ancestry
- Insurance coverage
- Type of accessible medical providers and clinics
- Resources for performing testing or return of results

(Manrai N Engl J Med 2016; 375:655-665)

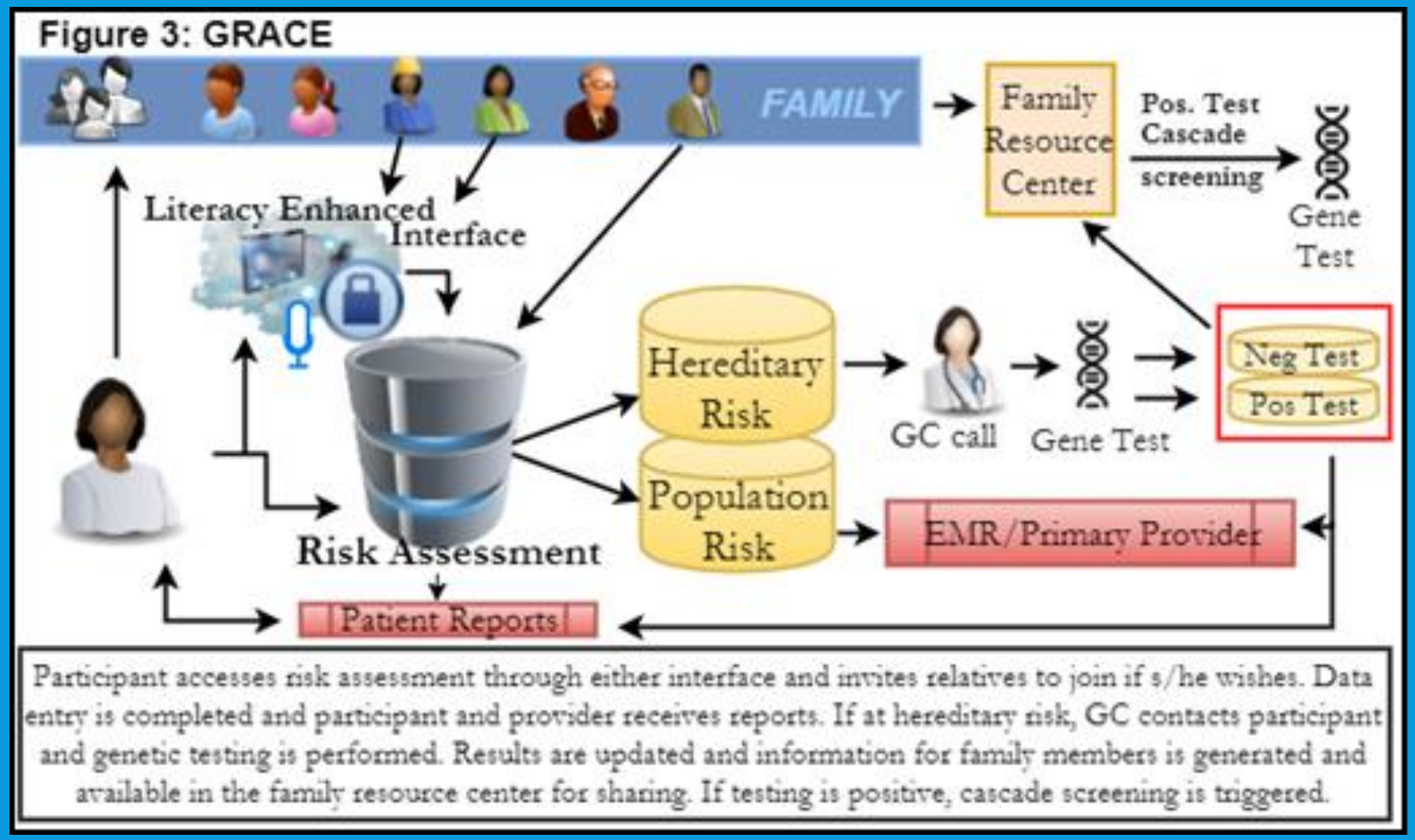
FHH IMPLEMENTATION ADAPTATION

Each step contains several implementation strategies that each site could select based upon their context.

1. Access to risk assessment via linkage from EMR, stand alone web server, phone

2. Testing via health system lab, mailed samples to lab, online servicing

3. Genetic counseling via GC or lay person trained in returning results, in person vs tele-counseling



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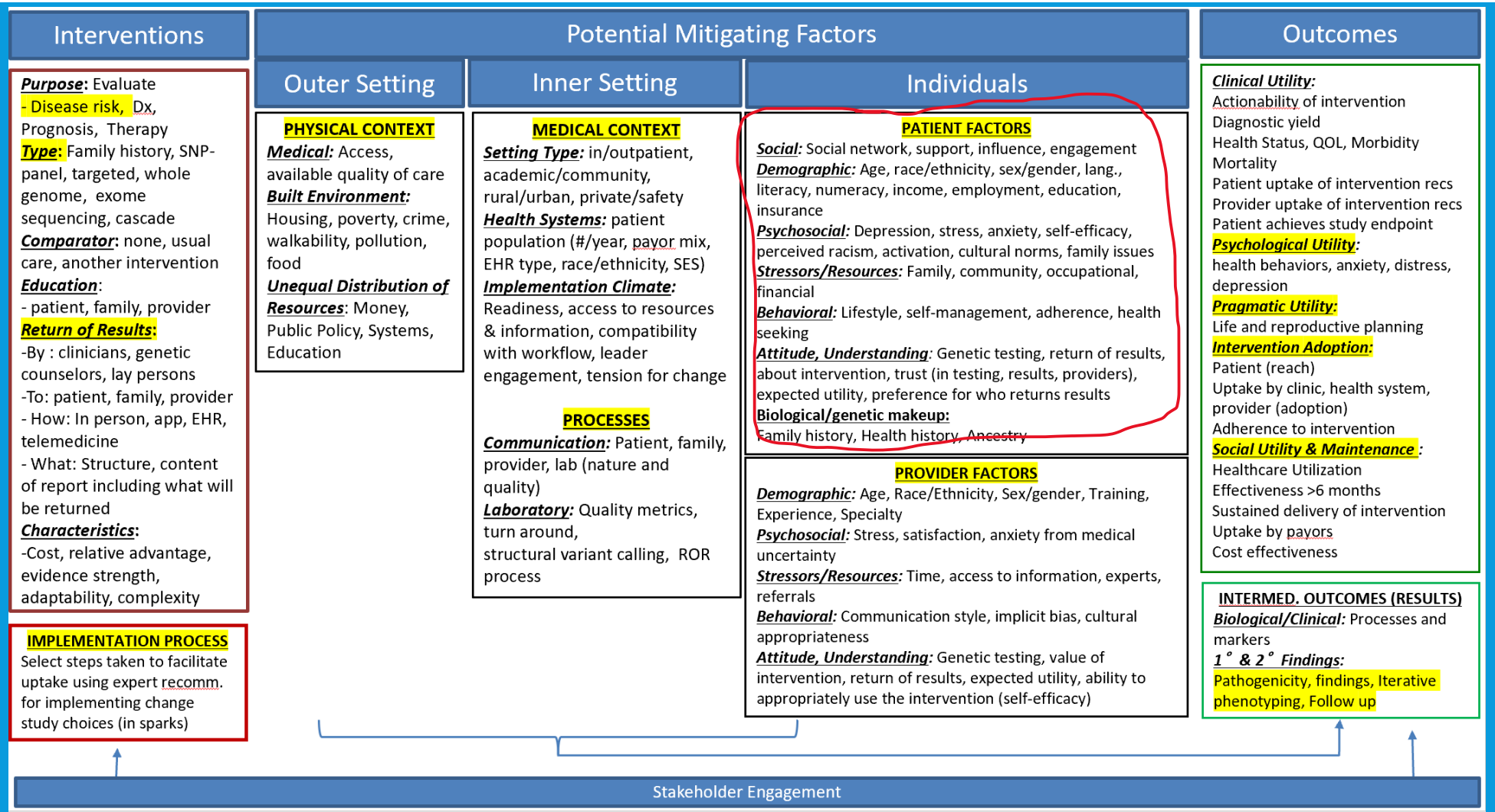


PATIENT DATA (RISK INFORMATION)

- Are risks interpreted differently if it is family history or DNA?
- Does sharing with relatives change for family history vs DNA?
- Do relatives react differently to family history vs DNA?
- Does it change their likelihood of acting on risk information?

Who prefers which method and how do we predict response

PATIENT DRIVEN CLOUD PLATFORM

PATIENTS SHOULD HAVE THE OPTION To OWN THEIR DATA

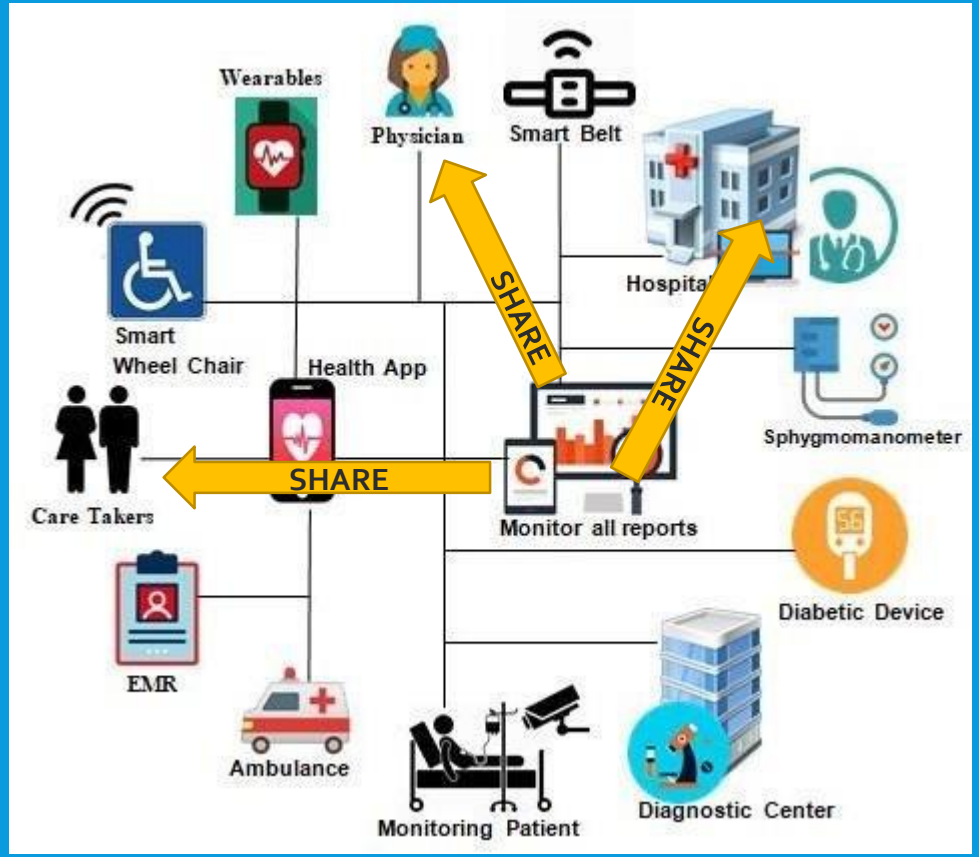
Not all patients want their data but those who do, should

PHRs so far have been limited and dysfunctional

- E-patient Dave in 2009 lead to Google Health's closure in 2011

Advances in informatics and data standards

- SMART – FHIR
- Blockchain



Blockchain: Securing Internet of Medical Things (IoMT) - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Internet-of-Medical-Things-IoMT_fig1_330883527 [accessed 21 Jun, 2019]

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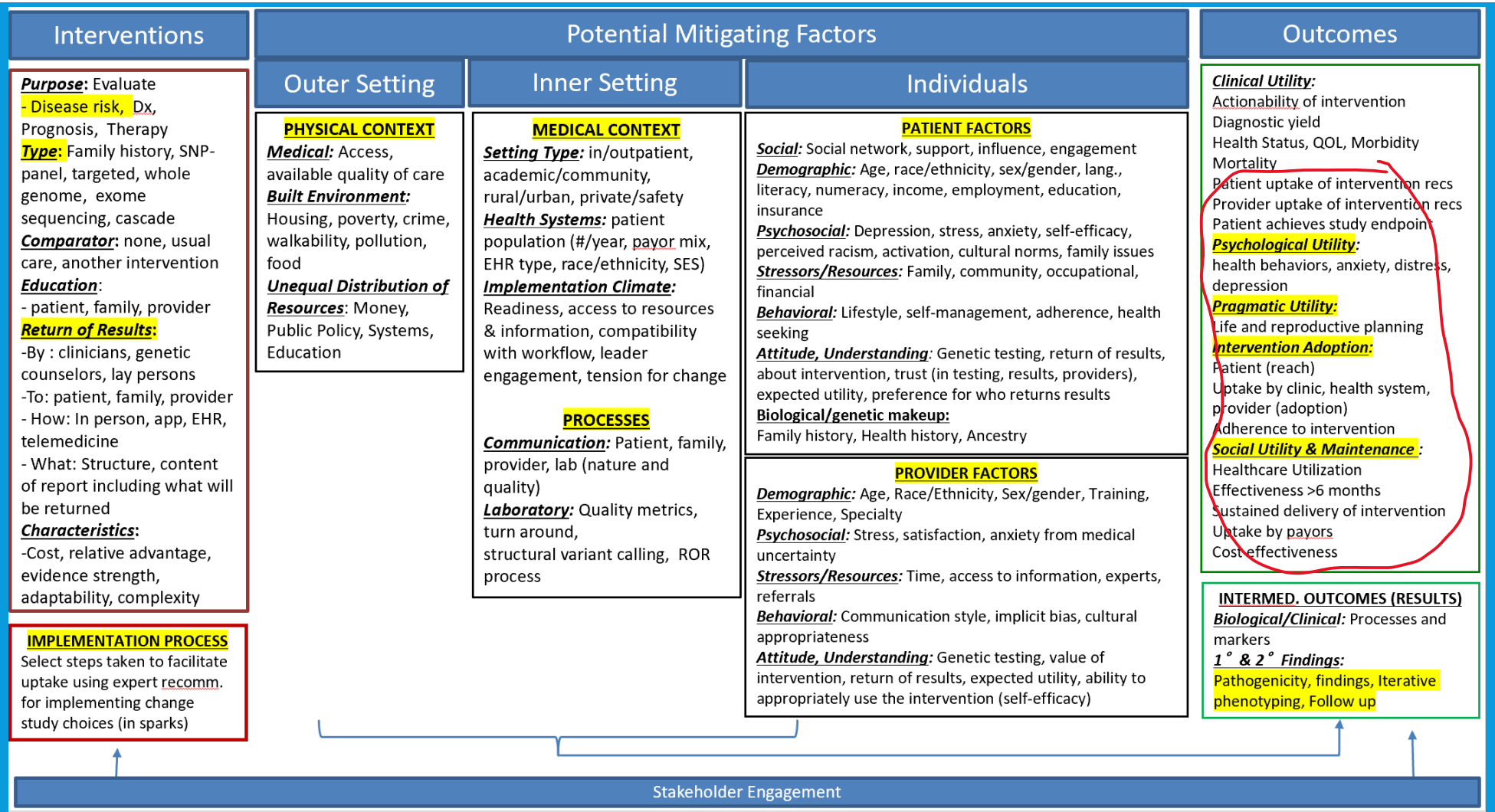

OUTCOMES TO EVALUATE IMPACT

Reach (patient uptake)	80%
Effectiveness	80%
Adoption (provider uptake)	80%
Implementation fidelity	80%
Maintenance	80%

End result: intervention helps 32% of those who could benefit from it

Context: will further mediate this impact (most likely for the worse)

SUMMARY

- Genomic Medicine has tremendous potential to transform healthcare for the better
- There are numerous pitfalls that could lead to misuse, misalignment, and the possibility of harm
- An implementation sciences framework can help anticipate, evaluate, and understand facilitators and barriers to clinical use of genomics and help guide optimal implementations that are tailored to the setting