A Role for Social and Behavioral Sciences in Genomic Translation: Making Room at the Table

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Today’s talk

- Notes from the field approach
- Who’s at the genomic translation table & why?
- Obligation to reduce health disparities is an optimal collaboration nexus for genomic translation
- Borrowed recommendations
Publications related to genetics:

PubMed query “gene OR genetic OR genome OR genomic” / limited to human vs. HuGE Navigator, Sep 2016
High Profile Genomics Initiatives

Moonshot to Cure Cancer

All of Us
The Future of Health Begins With You
## Evaluation of Genomic Applications in Practice & Prevention (EGAPP)

### Table. Evidence-based Classification of Genomic Tests and Family Health History

<table>
<thead>
<tr>
<th>Tier</th>
<th>Definition</th>
<th>Example(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Implementation in practice is supported by a base of synthesized evidence.</td>
<td>BRCA-associated hereditary breast and ovarian cancer (U.S. Preventive Services Task Force B recommendation); Lynch syndrome (EGAPP)</td>
</tr>
<tr>
<td>2</td>
<td>May provide information for informed decision making based on existing evidence; however, synthesized evidence is insufficient to support routine implementation in practice.</td>
<td>Family health history in primary care, with few exceptions</td>
</tr>
<tr>
<td>3</td>
<td>Not ready for routine implementation in practice based on synthesized evidence culminating in recommendations against use, OR no relevant synthesized evidence identified.</td>
<td>Direct-to-consumer personal genomic tests</td>
</tr>
</tbody>
</table>

https://www.cdc.gov/egappreviews/about.html
Basic Genomic Science

Social & Behavioral Science
neither here nor there

Epidemiology, Data Science & Clinical Practice
Not Invited to the Banquet

- Focus Group Discussions with SBM members (N=40)
- 90-minute video conferencing

- Difficult to find collaborators in epidemiology & clinical sciences
- Lack of funding incentives for social and behavioral science
- Few opportunities for cross disciplinary discussions

Report to Soc Beh Med, Executive Committee, April, 2018; McBride, Allen, Arredondo, Guan, Kaphingst, Klein, Wang,
Social & Behavioral Scientists Slow to Engage in Genomics

1. Concern that genomics will eclipse social determinants of health

2. Infeasible to disseminate high tech & expensive genomic applications

3. Genomic applications unlikely to improve health promotion interventions

McBride, Transl Beh Med, 2018;
What is a collaboration nexus where everybody wins!

neither here nor there
Not all dissimilarities in care are necessarily a disparity.

Layers of Influence on Disparities Related to Genomic Translation

Science paradigm
  Research pathway

Knowledge base
  Underrepresents diversity

Health applications
  Disparities in benefits
Accepted Translation Paradigm

- **Stage 1:** Basic Research
- **Stage 2:** Treatment Development
- **Stage 3:** Efficacy
- **Stage 4:** Effectiveness
- **Stage 5:** Adaptation to real world

<table>
<thead>
<tr>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>From Gene Discovery to Health Application</td>
<td>From Health Application to Evidence-based Guideline</td>
<td>From Guideline to Health Practice</td>
<td>From Practice to Health Impact</td>
</tr>
</tbody>
</table>
Knowledge Based on European Ancestry Groups

- Risk-allele frequencies modest correlations between ancestry groups

- Effect sizes varied:
  - Particularly for European vs. African groups
  - Some in opposite direction
  - Same direction but differed by 2-fold

Ntzani et al., Hum Genet, 2012

Landry et al., 2018
Health Application: HBOC Genetic testing

- GWAS (59 studies) 5% “underrepresented minorities”
- Inadequate risk models
  - High risk white families
- Understanding of testing benefits
  - Based on European Ancestry (BRCA -- Ashkenazi populations)
- Estimating population prevalence
  - High rates of uncertain significance & novel deleterious mutations among African Americans

Hall & Olopade, 2006
Landry et al., 2018
Back at the banquet...

Genomic Translation faces numerous Social/ Behavioral/ Communication challenges
Recruitment & uptake of genetic services: Social/Behavioral/Communication challenges

- What do communities of color have to gain from research participation?
  - What is lost if they do not participate?
- Comprehension of testing results and appropriate follow-up?
- Decision support for those at high risk
- Family communication about risk
As of May 2002, the CGN contained data on 15,007 participants and 241,948 family members. The majority of CGN participants were of Non-Hispanic White/Caucasian ethnicity (90%), with few numbers of Hispanic (4%), Black (3%), Asian (1%), and other ethnicities (2%). These participation figures did not match those of the general public, nor did they match the catchment areas of the participating sites in the CGN.
Minority recruitment to CGN

Moorman et al., CEBP, 2004

<table>
<thead>
<tr>
<th></th>
<th>Black</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled in CGN</td>
<td>37</td>
<td>58</td>
</tr>
<tr>
<td>Received materials &amp; declined</td>
<td>46</td>
<td>28</td>
</tr>
<tr>
<td>Declined to receive CGN materials</td>
<td>18</td>
<td>15</td>
</tr>
</tbody>
</table>

Legend:
- Purple: Enrolled in CGN
- Orange: Received materials & declined
- Green: Declined to receive CGN materials
**Observational study**

**NCI-funded Cancer Research Network**
- Henry Ford Health System clinical recruitment site

**Multiplex genetic test for 8 common health conditions**
- Removed access barriers

**Sample: Healthy adults** (25-40/ without health condition)
## Multiplex Testing Uptake

<table>
<thead>
<tr>
<th></th>
<th>Gender (Men vs. Women) Adjusted+ OR (95% CI)</th>
<th>Education (Low vs. High) Adjusted+ OR (95% CI)</th>
<th>Race (AA vs. White) Adjusted+ OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline survey</strong></td>
<td>.65 (0.58, 0.72)**</td>
<td>0.86 (0.79, 0.97)*</td>
<td>0.88 (0.80, 0.99)*</td>
</tr>
<tr>
<td><strong>Visited website</strong></td>
<td>.81 (0.67, 0.99)*</td>
<td>1.07 (0.88, 1.32)</td>
<td>0.52 (0.43, 0.63)**</td>
</tr>
<tr>
<td><strong>Tested</strong></td>
<td>1.02 (0.73, 1.42)</td>
<td>0.80 (0.57, 1.11)</td>
<td>0.36 (0.25, 0.50)**</td>
</tr>
</tbody>
</table>

+adjusted for other two categories

Alford et. al. Public Health Genomics, 2010
Health Applications

Genetic testing

- Enhanced screening
- Risk-reducing surgery
- Chemoprevention
  - Tamoxifen
  - Oral contraceptives
- Family member benefits
Health Applications con.

- **Identifying & Offering Genetic Testing to Cancer Patients**
  - Tumor registries to identify probands
    - Tertiary specialty centers
    - Over-represents white & high SES
  - Efforts to increase reach
    - Few efforts at community engagement
    - Telegenetics

![Graph showing incidence and mortality rates from 1975 to 2014, with separate lines for white and black populations.](image-url)
Declined genetic testing by race

- Used outreach approaches to increase reach
- DC site: 13.6 (n=91) “nonwhite”
- Whites 2x more likely to undergo genetic testing (Butrick)
- New Mexico trial cite 5.8% were hispanic or “nonwhite” (Kinney, 2014)

Butrick et al., 2015
Uptake of genetic testing by genetic counseling approach & race

Figure 2 Race by group interaction in intention-to-treat sample.

Butrick et al., 2015
HBOC Population Screening Tradeoffs for Communities of African Ancestry

Benefits
- Women of AAn > advanced disease and > mortality
- Women of AAn > likelihood for mutations
- At risk family members can benefit
- Mutations inform risk for other cancers

Limitations
- Healthy individuals with information
  - Increased anxiety & existential concerns
  - More likely to have VUS
  - No clear treatment course
  - Family members diffusion
- 85-95% will not be at risk
  - Misunderstanding

ACR recommends all women of AAn be screened for breast cancer risk < 30
Ongoing in 13 districts

Approached in women’s health clinics; ages 25-49

Nov 2012 - Dec 2013 screened 2,159 women (3% of eligible patients)

Majority of patients AA

Traxler et al., Ann Surg Oncol, 2014
Understanding of BRST results among those with negative results: Georgia Experience

Guan Y et al., in preparation
Mismatch of Genetic Counseling Audiences with Low Literacy

- English, Spanish, Chinese-speaking (N=124)
- 170 genetic counseling appointments
- Mismatch
  - Too much information
  - Complex terminology
  - Information not perceived relevant
  - Unintentional inhibition of patient engagement
  - Vague descriptions of prevention

Probability of Not Being Counseled by Study Arm

Joseph et al., 2017; Pasick, Joseph et al., 2016
BRIDGING THE TRANSLATION GAP
Envisioning (Post)Genomic Translation Research as an Interlocking Loop

Callard et al., 2011
Scientific Inclusion

- Appropriate reach of “precision public health”
  - Uptake individuals & families
  - Outside of clinical settings
  - SBC challenges intersect with basic science, epidemiology & clinical

- Averting disparities, an opportunity for interdisciplinary collaborations
  - Problem-based discussions
  - National forums needed to foster cross disciplinary conversations
  - Must include community partners

- Need incentives for collaboration
  - NIH and other funders to incentivize interdisciplinary collaborations
Genomics to reduce disparities
recommendations

- Minority-focused genetic research
  - Framing basic science research benefits to minority communities

- Community-based participatory research
  - Bring novel engagement approaches to the table

- GxE Research aligned with social determinants of health -- epigenetics
  - Study health issues of concern to communities

- Public education
  - Clinical settings
  - Community settings

Smith et al., Health Affairs, 2016
Landry et al., 2018
THANK YOU!