Genomics in Public Health

Cascade Screening Working Group Leadership Meeting

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Cascade Screening Working Group Vision

• Identify gaps in research and barriers to implementation of cascade screening in the US

• Identify and enable public health / healthcare interfaces to accelerate cascade screening for all Tier 1 conditions.

• Meaningful, demonstrated pilot results within 1 year.

“....the concept of “cascade” testing, in which at-risk family members of those with pathogenic mutations undergo screening, can be seen as a ‘bridge’ to inform population screening.”

Jim Evans & Sun Hee Rim

GPHAC Leadership Team Feb 2017
Key Takeaways From Year 1

• Outstanding collaboration and keen insights that are informing publications and public policy statements

• We have (and will) seek opportunities to embed Implementation team’s guidance into Cascade Screening Working Group’s deliverables

• We believe our future direction will build upon momentum with individual physicians, health care systems, and public health organizations integrating cascade screening into routine care
Critical Review of Published Cascade Screening Literature

- “Cascade screening delivery: A scoping review of the literature” effort begins in Fall 2017
- Submitted and under review by Health Affairs by Roberts, et. al. in March 2018
- Identify most effective ways of cascade screening through published and identified gaps in literature
- Informs future research why that is and why effective in US (policy issues)
- Provide direction to Policy, ELSI, and Cascade Screening Implementation Framework
Establish a Systematic Policy Reference Document

• Our objective is to develop a systematic policy reference to inform future public health programs and the Cascade Screening Implementation Framework.
  - Answer questions to consider in my state regarding laws on disease reporting, can I collect data, exemptions, database laws, etc.

• Work underway includes the following:
  - 50 state overview and segment examples (e.g., restrictive law, no state genetic law, states with limitations on government entities)
  - Ethical Legal Social Implications (ELSI) may come through patient & family communication survey from FH, Lynch and HBOC communities
  - HIPAA review for states without genetic privacy law

• Special acknowledgement to Christopher Devore & Chris Hammond
Cascade Screening for Familial Hypercholesterolemia and the Use of Genetic Testing


### Case identification

- Ways to identify possible proband
  - Health care visit
  - Lipid screening
  - Database search (electronic health record, laboratory results, billing record)

#### Possible FH

#### Confirm diagnosis

- Repeat lipid testing
- Genotyping
- Family history
- Physical examination

#### Diagnosis

- Proband

### Cascade screening

#### Early onset of ASCVD
- (men, age <50 y; women, age <60 y)

#### High cholesterol
- (LDL >190 mg/dL)

### Potential barriers to cascade screening

- Family structure and dynamics
- Geographic dispersion
- Health care literacy
- Access to care
- Privacy concerns

#### Location

- Oregon (OR)
- Virginia (VA)
- Texas (TX)

#### Cascade cycle

<table>
<thead>
<tr>
<th>Cascade cycle</th>
<th>Location</th>
</tr>
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<tbody>
<tr>
<td>1 (3)</td>
<td>Oregon (OR)</td>
</tr>
<tr>
<td>2 (6)</td>
<td>Virginia (VA)</td>
</tr>
<tr>
<td>3 (8)</td>
<td>Texas (TX)</td>
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<tr>
<td>4 (10)</td>
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Table 1. Recommendations and considerations for genetic testing for familial hypercholesterolemia.

A. Proband (Index Case)

**Genetic testing for FH should be offered** to individuals of any age in whom a strong clinical index of suspicion for FH exists based on examination of the patient’s clinical and/or family histories. This includes the following:

1. Adults with persistent* LDL-C ≥190 mg/dL or children with persistent* LDL-C ≥160 mg/dL and with at least 1 first-degree relative similarly affected or with premature CAD^.
2. Adults with persistent* LDL-C ≥250 mg/dL or children with persistent* LDL-C ≥190 mg/dL (even in the absence of a positive family history) without an apparent secondary cause of hypercholesterolemia^.

**Genetic testing for FH may be considered** in the following clinical scenarios:

1. Adults with no pre-treatment LDL-C levels available but with a personal history of premature CAD^ and family history of both hypercholesterolemia and premature CAD^.
2. Adults with persistent* LDL-C ≥160 mg/dL (without an apparent secondary cause of hypercholesterolemia^) in the setting of a family history of hypercholesterolemia and either a personal history or a family history of premature CAD^.
3. Children with persistent* LDL-C ≥160 mg/dL (without an apparent secondary cause of hypercholesterolemia^) with an LDL-C ≥190 mg/dl in at least one parent or a family history of hypercholesterolemia and premature CAD^.

B. At-Risk Relatives

1. Cascade genetic testing for the specific variant(s) identified in the FH proband (known familial variant testing) should be offered to all first-degree relatives. If first-degree relatives are unavailable, or do not wish to undergo testing, known familial variant testing should be offered to second-degree relatives. Cascade genetic testing should commence throughout the entire extended family until all at-risk individuals have been tested and all known relatives with FH have been identified.

*persistent = 2 or more measurements, including assessment after intensive lifestyle modification / ^premature CAD = males <55, females <65, adapted from the AHA phenotype definition of HeFH / ^hypothyroidism, diabetes, renal disease, nephrotic syndrome, liver disease, medications
FH Quality Improvement Programs Underway
Cascade Screening Implementation Framework

- PRISM framework is ideal for cascade screening
- Key enhancement is addition to patient and family member perspective
- Paper being written with case studies from each of three Tier 1 conditions
- Generalize-able to multiple care settings and levels
- Opportunity to incorporate Implementation deliverables (e.g. Outcome measures)
Summary

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• We have (and will) seek opportunities to embed Implementation team’s guidance into Cascade Screening Working Group’s deliverables

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Ideas for Action

1.) Public Policy
Example: Tier 1 Conditions Reportable

2.) Genetic Counseling Model
Example: State, Regional, National or Tele-health Delivery

3.) Public / Private Partnership
Example: National registry with bidirectional reporting

Benefits
Consent to share health information for benefit of at-risk population
Expand utilization of GC’s despite fragmented hc delivery & dispersed families
Innovative use of multiple stakeholder assets

GPHAC Leadership Team Feb 2017