Healthy NV Project℠

Personalized Medicine on a Statewide Scale
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What is the Healthy Nevada Project?

• Large scale population genetics and health determinants study
• Recruiting as many Nevadans as possible
  • Current IRB approval is 250,000 participants
  • Current cohort = ~47,000 sequenced individuals
• Two components:
  • Clinical
    • Reporting on Incidental Findings - currently, CDC Tier 1
    • Risk awareness of **autosomal dominant** inherited conditions
  • Research
    • Investigator focused
    • Leveraging a data-lake of health determinants
Self-reported demographics

- 30% reside in five most impoverished zip codes in Reno/Sparks
- 47% of zip codes in NV represented
Northern Nevada is a unique catchment for studying population health

- One primary hospital system
- Multi-generational population
- >1 M Patient EHR since 2007
- 600k person catchment area
- 62k square miles
Healthy Nevada Project structure

3 CONSENTS: STUDY, RECONTACT, RESULTS

SURVEY PLATFORM: BEHAVIOR/ SOCIAL

RECALL: BLOOD/IMAGING

RETURN OF RESULTS
Recruitment Pathways

OUTREACH VIA PHONE
OUTREACH VIA EMAIL
EVENTS/POP-UPS
TOUCH POINTS VIA RENOWN SYSTEM
Necessity of Tier 1 population screening

- Are we effectively ascertaining Tier 1 cases using best practices?
- Are there outcome improvements of broad-based screening?
- How to accomplish population level screening?
  - Without bias
  - Effective results disclosure / follow up
  - Limit false positives
Population genetic screening efficiently identifies carriers of autosomal dominant diseases


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2409 Accesses | 1 Citations | 151 Altmetric | Metrics
CDC Tier 1 Findings:

- 1:80 prevalence of known pathogenic/likely pathogenic findings
- 26,906 participants Exome+ results
- Results analyzed for 358 carriers (no correction for relatedness)
  - Hereditary Breast and Ovarian Cancer Syndrome (HBOC): 178 (1:150)
  - Lynch Syndrome: 80 (1:340)
  - Familial Hypercholesterolemia: 102 (1:260)
90% of participants screening positive were not previously identified.

19.8% of these had documentation in their medical records of inherited genetic disease risk, including family history.
Case Study 1

Female 64y/o

\textit{BRCA1}

Rt. Ovarian malignancy (dx @ 63y/o)
Secondary spread to large intestine and retroperitoneum as well as malignant pleural effusion
Scant evidence of prior mammography (1x, 6Y before diagnosis)
No medical record documentation of family history
No medical documentation of \textit{BRCA1}
Case Study 2

Male 28y/o
Lynch (*MSH2*)
Metastatic colon cancer (dx @26)
Family history of digestive organs and bladder malignancies.
No medical record documentation of genetic diagnosis.
Why we need to ascertain CDC Tier 1 carrier status
But, falling within guidelines confers excess risk
Earlier intervention for ASCVD based on lipid screening?
## Overall results return (updated since paper)

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<tr>
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<th>HBOC &amp; LYNCH</th>
<th>FH</th>
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<tbody>
<tr>
<td>Informed of Results</td>
<td>231</td>
<td>143</td>
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<tr>
<td>Results pending delivery</td>
<td>72</td>
<td>68</td>
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<tr>
<td>Results Lost to Follow Up</td>
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<td>20</td>
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<td>Total Results not received</td>
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<td>88</td>
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<tr>
<td><strong>Totals</strong></td>
<td><strong>326</strong></td>
<td><strong>231</strong></td>
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>98% consent to return of results, yet 70% success rate returning results
Future steps

- Used a 313 SNPs PGS from Mavaddat et al., AJHG, 2019
- Score was calculated using SNPs directly sequenced or imputed
- All participants were assigned to one genetic ancestry (6 different groups total) based on ADMIXTURE results
- Distributions were made for each genetic ancestry group
- Participants were assigned a polygenic risk based on the distribution of the scores for their specific genetic ancestry
High polygenic risk for breast cancer is in-between monogenic risk and average risk
<table>
<thead>
<tr>
<th>Renown Health</th>
<th>Desert Research Institute</th>
<th>Helix</th>
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<tbody>
<tr>
<td>• Anthony Slonim</td>
<td>• Karen Schlauch</td>
<td>• Alex Bolze</td>
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<td>• Christos Galanopoulos</td>
<td>• Gai Elhanan</td>
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<td>• Amberly Diets</td>
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Questions