Evolution of Direct-to-Consumer Genetic Testing

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Disclosures

- Employee and Stock Holder in Invitae Corporation
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Evolution of DTC Genetic Testing

- Scope
  - Ancestry
  - Personal traits
  - Multifactorial Genetic Risk Scores (e.g. Type 2 Diabetes, Rheumatoid Arthritis, Dementia)
  - Mendelian Disorders (Hereditary Breast and Ovarian Cancer, Cardiomyopathy)
- Limitations
- Uptake
- Provider Perceptions
- Hybrid Models

Scope: Using Allele-Specific Genotyping

- Ancestry
- Personal traits

} Engagement, Entertainment, Enlightenment, Enlistment

- Multifactorial Genetic Risk Scores: Clinical Utility?
- Single-Gene Disorders (with Heterogeneity)
  - Thrombophilia
  - Hereditary Breast and Ovarian Cancer
  - Familial Hypercholesterolemia
  - MUTYH polyposis
  - Hypertrophic Cardiomyopathy

Multifactorial (Complex) Disease Risk: Crohn Disease

RESULTS:

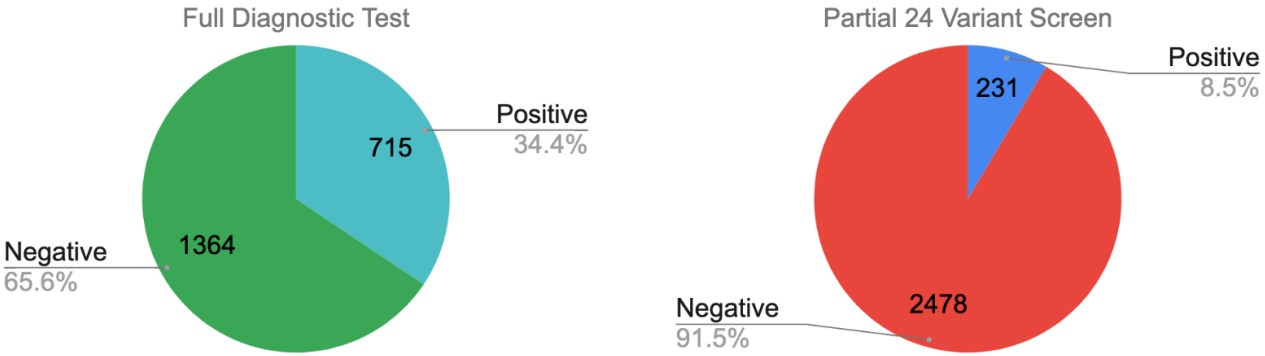
The proportion of participants stopping smoking for 24 hours or longer did not differ between arms: 35% (73/209) in the DNA arm versus 36% (78/217) in the non-DNA arm (difference -1%, 95% confidence interval -10% to 8%, P=0.83). The proportion making a quit attempt within the DNA arm did not differ between those who were told they had mutations putting them at increased risk (36%), those told they had none (35%), and those in the non-DNA arm (36%).

CONCLUSION:

Among relatives of patients with Crohn's disease, feedback of DNA based risk assessments does not motivate behaviour change to reduce risk any more or less than standard risk assessment. These findings accord with those across a range of populations and behaviours. They do not support the promulgation of commercial DNA based tests nor the search for gene variants that confer increased risk of common complex diseases on the basis that they effectively motivate health related behaviour change.

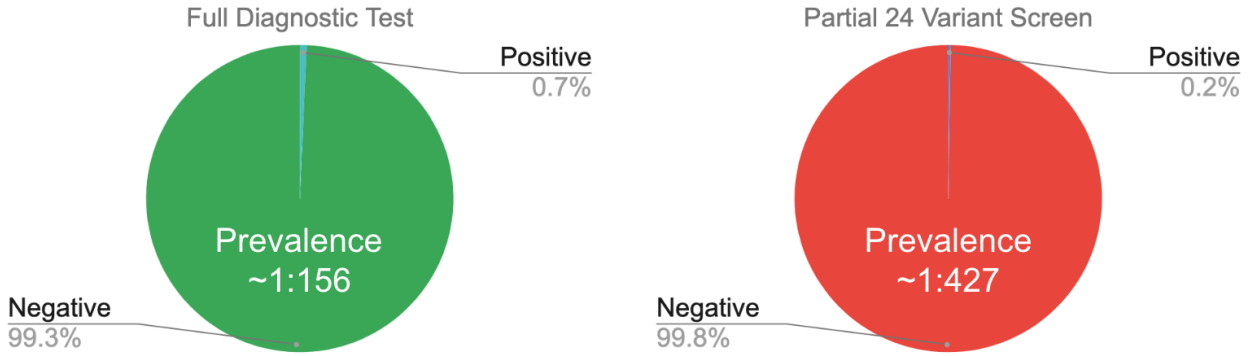
Mendelian Disorders:
24 Variant Screen for Familial Hypercholesterolemia

FH Indication Cohort Results



68% (484/715) of genetically-positive FH patients would test negative by a Partial 24 Variant Screen

Healthy Cohort Results



64% (16/25) of individuals with genetically-positive FH would test negative by a Partial 24 Variant Screen

MUTYH Polyposis

- Cohort of 270,806 patients referred by healthcare providers for gene testing including *MUTYH* for personal/family history of cancer stratified by **self-reported ethnicity**.
- Examined those with positive MUTYH results by sequencing for how many carried Northern European variants on a DTC panel

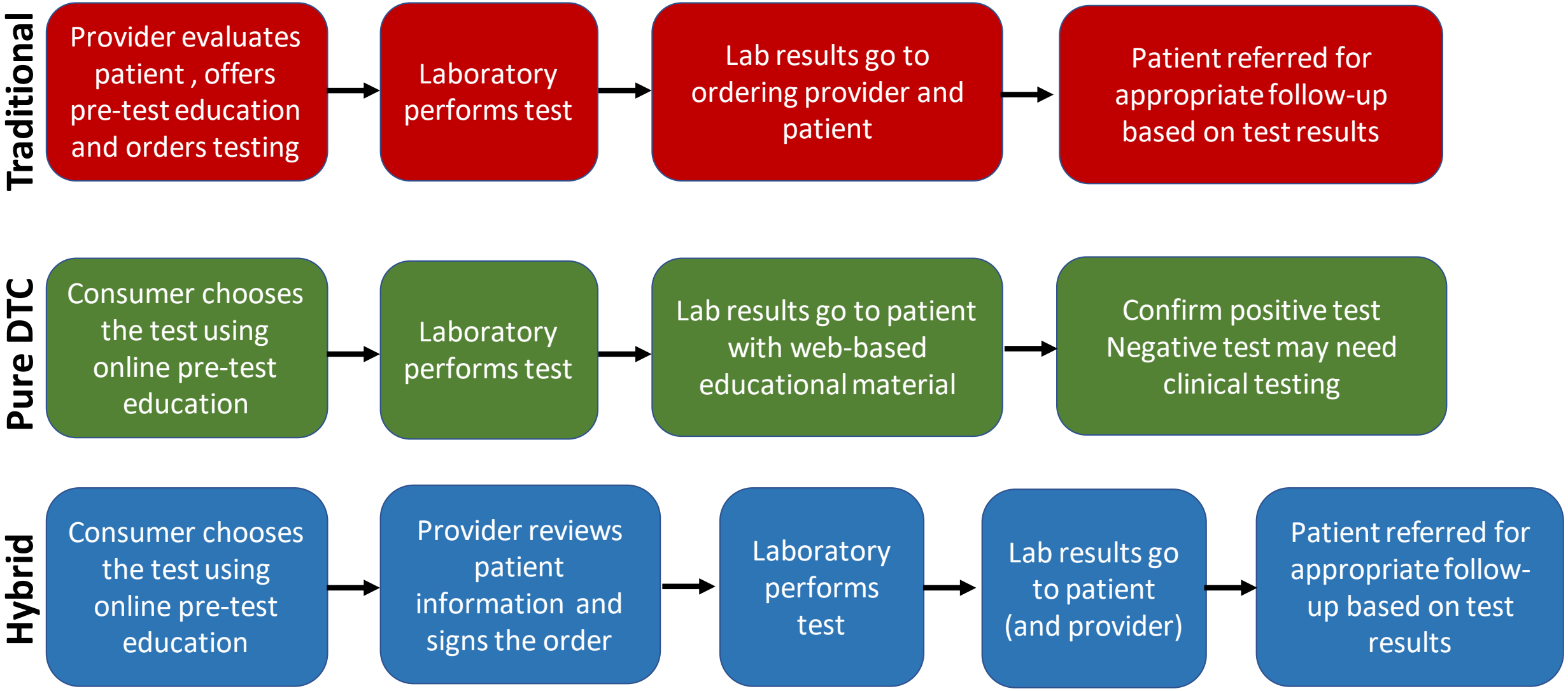
Results

- 5,929 patients had a pathogenic or likely pathogenic (P/LP) variant in *MUTYH*; 4,552 had one of the Northern European (NE) variants on the DTC panels
- By ethnicity, ascertainment was incomplete in
  - 100% for Asians
  - 75% African-American (AA)
  - 46% Hispanic
  - 33% Caucasian

Routes to obtain genetic testing

- Traditional healthcare provider-initiated service delivery
- Direct to consumer (no physician involvement)
- Hybrid models that are consumer driven, but with physician involvement

Models for Genetic Risk Screening and/or Testing



Why Develop a Hybrid Model?

- Roadblocks to accessing clinically valid genetic testing
  - Provider scarcity leading to long wait times
  - Provider discomfort and ignorance
  - Testing guidelines are slow to change
  - Cost of testing
  - Insurance barriers to ordering a test
  - Logistical barriers

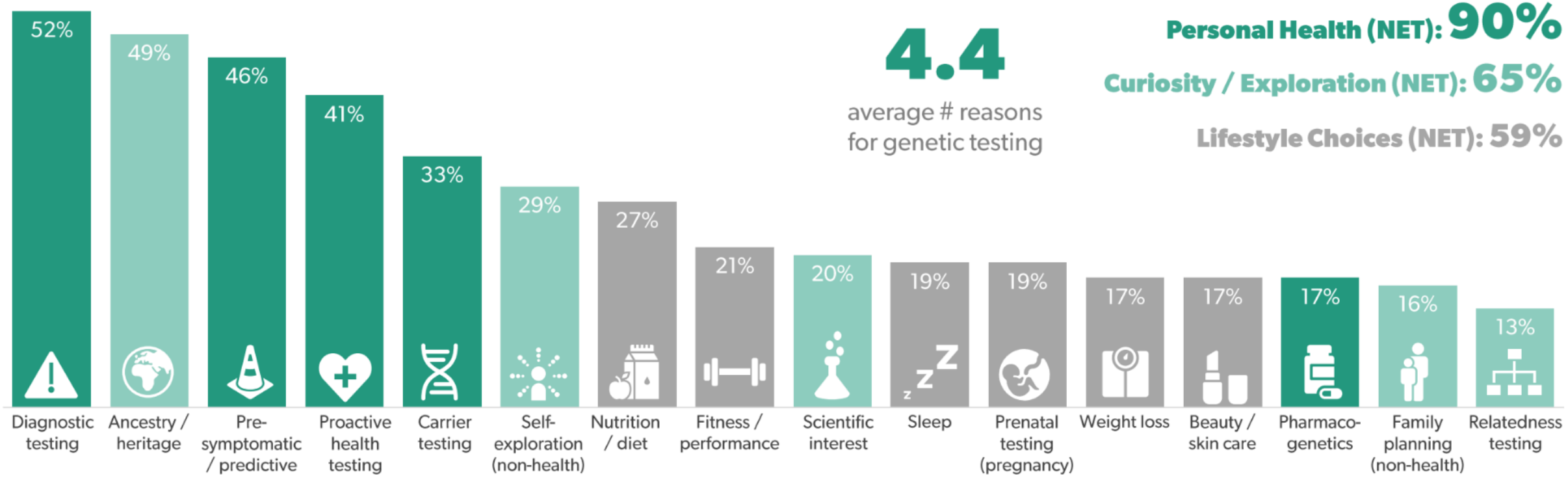
Reasons to consider the Hybrid Model

- Engage with, don’t ignore, Providers.
- Limit “gate-keeping” role of Payers
- Streamline the process of getting testing done

Survey of Consumer Attitudes towards Pure DTC Medical testing and Hybrid “Clinical Grade” Models

Top Motivations for Purchasing a DTC Test

Specific Motivations for Testing



4.4
average # reasons for genetic testing

Personal Health (NET): 90%

Curiosity / Exploration (NET): 65%

Lifestyle Choices (NET): 59%

Diagnostic & predictive testing tend to come from a more medically-oriented place, whereas **proactive health testing** motivation is nearly twice as strongly associated with more **open-ended curiosity / self-exploration**

Kelton

C3. Which of the following best describe your specific reason(s) for purchasing and completing a DNA/genetic testing kit?
Base: Total Respondents (n503)

Paradoxical Concerns Regarding Genetic Risk Screening by New Hybrid DTC Testing Model

Tier 1: Privacy Concerns

Tier 2: Misperception of Actionability and Reticence in taking this kind of genetic test to avoid the psychological burden of unhappy or even terrifying knowledge

Tier 3: Skepticism about quality of the result. (Theranos Effect)

Tier 4: Lack of insurance coverage reduces medical credibility, yet, some view this as a potential benefit of keeping their genetic information private from health insurance

Real fear exists among some consumers around several recurring issues:

- General fear of having their genetic information existing ‘out there’ in the ether
- Identifying pre-existing conditions their insurance won't cover and/or increasing their premium
- The testing company selling their data to unauthorized third parties
- Government or law enforcement agencies getting their hands on their data
- “Bad actors” using their data for nefarious purposes

Summary