Challenges and Opportunities with Rapidly-Changing Biomedical Technologies:

Insights from Genetic Testing for Colorectal Cancer

2016 CADTH Symposium

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Disclosure

• The views expressed here are solely those of mine in my private capacity and do not in any way represent the views of CADTH.

• I have no actual or potential conflict of interest in relation to this topic or presentation.
Background
What is Personalized Medicine?

“tailoring of preventive, diagnostic, and therapeutic interventions to the characteristics of individuals using advanced biomedical technologies”

From Genetics to Genomics

Ernst Rüdin

“single-gene disorder”

Schizophrenia 100 years

Progress in identifying associated genes

## Types of Genetic Testing

<table>
<thead>
<tr>
<th>Setting</th>
<th>First Generation</th>
<th>Next Generation</th>
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<tbody>
<tr>
<td></td>
<td>• Health care</td>
<td>• Direct-to-consumer (DTC)</td>
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<tr>
<td>Population</td>
<td>• Clinical populations</td>
<td>• General populations</td>
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<tr>
<td>Intervention</td>
<td>• Single genes for monogenic conditions</td>
<td>• Multiple genes for common complex conditions</td>
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<td></td>
<td>• Specific mutations</td>
<td>• Single-nucleotide polymorphisms (SNPs)</td>
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<td></td>
<td>• Causality</td>
<td>• Association</td>
</tr>
<tr>
<td></td>
<td>• High penetrance</td>
<td>• Low penetrance</td>
</tr>
<tr>
<td></td>
<td>• High clinical utility</td>
<td>• Low clinical utility</td>
</tr>
<tr>
<td></td>
<td>• Mandatory counselling</td>
<td>• Optional counselling</td>
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<tr>
<td>Outcome</td>
<td>• Carrier/non-carrier</td>
<td>• Elevated/average risk</td>
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<td></td>
<td>• 10-20x average risk (high)</td>
<td>• 2-3x average risk (low)</td>
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Get to know you.
Health and ancestry start here.

- View reports on over 100 health conditions and traits
- Find out about your inherited risk factors and how you might respond to certain medications
- Discover your lineage and find DNA relatives

4.2 (366)

$199
Price increasing to $249 on March 30th

order now
What your DNA says about you.

Find out how your genetics relate to things like celiac disease, cystic fibrosis or response to certain medications. You can also see if your body metabolizes caffeine quickly or if you're likely lactose intolerant. We believe the more you know about your DNA, the more you know about yourself. Learn more →

Keep in mind that many conditions and traits are influenced by multiple factors. Our reports are intended for informational purposes only and do not diagnose disease.

Because genetic information is hereditary, knowing something about your genetics also tells you something about those closely related to you. Your family may or may not want to know this information as well, and relationships with others can be affected by learning about your DNA.

**Inherited Conditions**
40+ reports
Find out if you are at risk for passing on an inherited condition.

**Drug Response**
10+ reports
Learn information about how your genetics might affect your response to certain medications.

**Genetic Risk Factors**
10+ reports
Understand your genetic risk factors. Change what you can, manage what you can't.

**Traits**
40+ reports
Explore your genetic traits for everything from lactose intolerance to male pattern baldness.
Research

• **Question:**
  • Does predictive genetic information change individual health behaviours?

• **Colorectal cancer (CRC) as an example:**
  • 3rd/2nd most common cancer in men/women
  • Hereditary in 5% of all cases
  • Genetic testing available in clinics and DTC
  • Prevention and early detection possible
Literature Review
Search & Selection Methods

• **Search Terms:**
  - genetic screening/service/testing/predisposition to disease/information
  - behaviour, lifestyle, alternative medicine, complementary therapy
  - change, modify, alter, effect, impact
  - neoplasm, cancer

• **Databases:**
  - MEDLINE, EMBASE, PsycINFO, CINAHL, Cochrane Library, EconLit, NBER
  - Initial search in 2011, updates in 2013 and 2015, continuous alerts ongoing

• **Selection Criteria:**
  - Primary research on pre- and post-behaviours in asymptomatic adults who underwent predictive genetic testing for CRC and learned of their results
Search & Selection Results

• Current literature on first generation:
  • # of primary studies: 8 observational (n=42-98)
  • Population: CRC families
  • Intervention: genetic testing for hereditary CRC (carrier/non-carrier)
  • Behaviour: % of participants undergoing colonoscopy
  • Follow-up: 1-3 years
  • Countries: Australia, Belgium, Netherlands, US

• Current literature on next generation:
  • # of primary studies: 1 RCT (n=783)
  • Population: general population
  • Intervention: genetic testing for SNPs + folate level (elevated/average risk)
  • Behaviour: % of participants undergoing fecal immunochemical test
  • Follow-up: 6 months
  • Country: US
Colon Screening Results

Change in % of participants undergoing colon screening before and after genetic testing

- Carriers
- Non-carriers
- Non-testers/Test-decliners
- Elevated risk
- Average risk
- Non-testers
Nuanced Interpretations

“The study nurse explained that an elevated result did not guarantee disease but was only one potential risk factor for CRC, suggesting modestly increased risk compared with that of a similarly aged person”

“Conversely, the nurse stated that an average result did not ensure protection against CRC now or in the future but simply indicated the absence of this risk factor”

“Regardless of study group or risk, all participants were encouraged to have screening”

Discussion
Concerns about DTC Services

• **Test quality:**
  • No standardization on test accuracy and applicability

• **Advertising:**
  • Exaggerated claims and promises of health benefits

• **Test process:**
  • Bypassing health professionals and optional counselling

• **Privacy:**
  • Selling data to researchers and companies

• **Consequences:**
  • Misinformed individual health decisions and increased health care costs

Current Evidence

• **Little benefit:**
  - Predispositions are marginally predictive and unactionable
  - Personal or family histories influence more than genetic testing results
  - Behaviour change is difficult

• **Little harm:**
  - Psychological impacts are short-lived
  - Genetic discrimination appears limited
  - Little concern exists over overuse of health care

Ongoing Challenges

• **Evolution of genetic testing:**
  • Rapidly-changing biomedical technologies
  • Constantly-emerging DTC companies
  • Aggressive marketing centred on autonomy and empowerment

• **Genetic literacy in customers and health providers:**
  • Increasing public curiosity and inquiry
  • Health providers as caregivers and gatekeepers
  • Need and desire to improve genetic literacy

• **“Foot-loose” DTC companies:**
  • Governed by one jurisdiction but operating in others
  • Questionable applicability of one test for many populations

Regulation in Canada

• **Current status:**
  - In 2014, Health Canada determined 23andMe is not a medical device
  - Medical information and privacy issues are a provincial responsibility

• **Calls for regulation:**
  - July 2015 Canadian College of Medical Geneticists:
    - Letter to Health Minister
    - “We ask you to protect the population by recognizing health-related DTC genetic testing as a medical service and instituting a regulatory framework that will hold the providers of such testing to the appropriate professional performance standards”
  - September 2015 Doctors of British Columbia (BC):
    - Position statement
    - “Doctors of BC calls for: federal regulation of marketing and health-related claims in connection with DTC genetic testing...; the development of national standards for reliability and validity of DTC genetic testing; and public education initiatives...” and physician guidelines, education, and training

Regulation Elsewhere

• **Check test quality and/or advertising:**
  - US FDA requires clearance for marketing and selling genetic testing (2016)
  - Maryland bans DTC advertising of genetic testing (2012)
  - New York requires state-approved laboratories for genetic testing (2012)

• **Manage test process:**
  - Connecticut, Maryland, and Michigan require physicians to order genetic testing (2010)

• **Ban DTC services:**
  - France, Germany, Portugal, and Switzerland require medical doctors to perform genetic testing for the practice of medicine (2012)

Conclusion

• Biomedical technologies are rapidly changing and entering the consumer market

• While current evidence suggests little benefit and little harm, there are ongoing challenges

• Opportunities and options exist to ensure quality and manage the process of DTC genetic testing