Genomic Test Evaluation Frameworks

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Conflicts:
Chair of Medical Services Advisory Committee
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Genomic health alliances in Australia
Focused on implementing genomics in practice
Whole of system change

Discovery Research

Translational Research

Implementation

Routine Practice

Research Institutes and Universities

Australian Genomics Health Alliance

Queensland Genomics Health Alliance

Melbourne Genomics Health Alliance

Clinical Genetics Services and Hospitals
GOOD INTENTIONS
bad results
Overdiagnosis and Overtreatment

"Overdiagnosis"

Overdetection

Over-testing

Over-interpretation

Over-definition

Over-treatment
Overdetection: thyroid “cancer"

Thyroid cancer tripled in 25 years; no more deaths

Screening for Thyroid Cancer

Since South Korea adopted widespread cancer screening in 1999, thyroid cancer has become the most diagnosed cancer in the country. But if this early detection were saving lives, the already-low death rate from thyroid cancer should have fallen, not remained steady.

NEW CASES AND DEATHS FROM THYROID CANCER
Per 100,000 people

Figure 4.73: Yearly trends in incidence, mortality and 5-year relative survival of thyroid cancer, 1982 to 2007

Notes
1. Incidence and mortality rates are age-standardised to the Australian population as at 30 June 2001 and are expressed per 100,000 population.
2. Survival data for this figure are presented in online Table S26.3.
Source: AIHW Australian Cancer Database (2007); AIHW 2010b.

Sources: New England Journal of Medicine; National Cancer Institute
By The New York Times
Options to reduce unnecessary health care expenditure (waste)

1. Restrict uptake (*easy*)
2. Improve efficiency/costs of current services (behavior change – *hard*)
3. Disinvest in unproven technologies (*very hard*)

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**Current Services**

- **Reduce Volume**
- **Reduce Costs; Lower prices**

**New Services**

**Disinvestment**

**HTA**
Goal: International comparative analysis of theoretical and practical genomic test evaluation frameworks

Investigators:
Andrew Mitchell (DoH) and Robyn Ward (UQ)
Sarah Nowak & Jakub Hlavka (RAND Corporation)

Funding: National Health and Medical Research Council through the Australian Genomics Health Alliance
Supported by G2MC – contact lists
Method – literature review + survey

Web of Science Search for terms “genetic testing” “genomic testing”, “gene test”, “genetic test” in Web of Science 4086 articles


Included the terms: “evaluation”, “assessment” or “value” 555 articles

Did not include the terms: “evaluation”, “assessment” or “value” 3531 articles

Were relevant to the assessment of genetic testing based on search result meta data 115 articles

670 abstracts reviewed for relevance, full text obtained where available

15 assessment frameworks identified

18 frameworks identified (17 new)

21 responses indicated no framework to evaluate genomic tests

5 incomplete or duplicate responses (eliminated)

45 responses received within data collection period

Survey – large number of contacts

Very few frameworks published

32 assessment frameworks assessed and discussed

21/48 responses “no framework”
Framework categorisation

- types of decisions the framework informs
  reimbursement, certification, regulation, other
- whether the framework is specific to genetic/genomic testing or more general
- types of test covered by the framework
  single gene, multiple genes/small panel, whole genome scale, RNA expression- single gene/arrays
- test applications covered by the framework
  diagnostic, screening, predictive, prognostic, other
- framework audience
  clinicians, path labs, health ministries, research institutes, commissioning groups, reimbursement organisations, patients
- types of criteria the framework uses to evaluate tests
  purpose, target population and intended use, population impact, seriousness, appropriateness
Framework sources by region

- North America: 13, 41%
- Europe: 11, 34%
- Asia Pacific: 6, 19%
- Latin America: 1, 3%
- Middle East: 1, 3%
Decisions informed by framework

- **Regulation**
  - Europe: 6
  - North America: 8
  - Asia Pacific: 3
  - Middle East
  - Latin America

- **Reimbursement**
  - Europe: 5
  - North America: 7
  - Asia Pacific: 1
  - Middle East: 1
  - Latin America

- **Certification**
  - Europe: 6
  - North America: 4
  - Asia Pacific: 2
  - Middle East: 1
  - Latin America

- **Other**
  - Europe: 3
  - North America: 5
  - Asia Pacific: 2
  - Middle East
  - Latin America
Assessment criteria by different test applications

Clinical validity, utility, analytical validity

Population impact, budget implications
Conclusion

• Poor preparedness for implementing testing
  (50% had draft or complete frameworks)

• Frameworks evaluate genetic and genomic tests
  often consider only benefits and risks common to
  most screening, predictive, diagnostic and
  prognostic medical test

But

• Fail to explicitly consider risks that are specific
  large-scale genomic tests
Assessing value of genomics
Australian government published expectations

- Co-dependent technology

- Clinical utility card including release of economic models
CU card

Supporting innovative genetic testing to improve health outcomes in Australia
Tests need to fulfil the following criteria:

- **analytical validity** can the test measure accurately and reliably the presence or absence of a particular gene or genetic change?
- **clinical validity** can the test identify a genetic predisposition or a particular clinical condition?
- **clinical utility** can the test be used to inform treatment decisions and improve health outcomes?
- **economic evaluation** can the test add value to the health of Australians at an acceptable cost?
- **government budget** can the utilisation and total cost of the test to Australians be justified by the government?
Application of the CUC proforma

- **paediatrics** genetic conditions presenting in infancy or later childhood
- **reproductive planning** families with a history of a particular genetic condition
- **cancer genetics** predisposition to certain cancers or cancer syndromes
- **rare diseases** rare and ultra-rare life-threatening or chronic conditions
- **adult genetics** conditions presenting in adulthood that may have an underlying genetic cause, such as kidney, neurological or cardiac disease
Clinical utility card + economic models

• Scope heritable mutations which predispose to disease
• Started with cancer
• Star performers – best case scenarios
• Complexity with modelling which needs to include:
  ➢ prevention of >1 future disease
  ➢ age specific-relative risks
  ➢ health impact on relatives (joint production)
  ➢ misleading test results
  ➢ parental disutility of caring for disabled children