

Public Health Genomics How not to get lost in translation?

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January 25, 2011



Outline

1. Background of Public Health Genomics and applicability to Child and Youth Healthcare
2. Problem of translation
3. Methodologies for assessment and translation (with examples)
4. Conclusions

Background: What is out there?



Background: What is out there?



Public Health Genomics



the responsible and effective translation of genome-based knowledge and technologies into public policy and health services for the benefit of the population health

("Bellagio Statement": Burke, Khoury et al. 2006)



Background: What is out there?

5 key areas of impact according to The Canadian genomics community:

- Childhood cancer
- Neurodevelopmental diseases (autism, mental retardation, schizophrenia, ADHD)
- Auto-immune, inflammatory and allergic disease (type 1 diabetes, asthma)
- Obesity and type 2 diabetes
- Birth defects

Background: What is out there?

The genomic aspects of childhood illness and disease must be addressed as a part within the overall contribution of genomics to the health

Child health genomics is distinct form of health genomics, as the **physiology of children** is inherently different than that of adults

Genome Canada – Strategic Research Themes
Child Health Genomics: An Investment in Canada's Future

Problem

There is a lot of knowledge, but how can we evaluate and integrate it successfully for the benefit of all children?



Existing methodologies

- ACCE (Analytical validity, Clinical validity, Clinical utility, Ethical, legal and social implications),
- EGAPP (Evaluation of Genomic Applications in Practice and Prevention)
- HTA (Health Technology Assessment),
- Continuum of translational research T1 to T4,
- The Public Health Wheel
- The Bellagio Public Health Genomics enterprise.

ASSESSMENT

TRANSLATION

Assessment

Which innovation can be introduced into practice?

- ✓ How reliable is innovation?
- ✓ How useful is it for the patients?
- ✓ Cost-effectiveness, etc

Translation

How to effectively introduce the innovation into the practice?

- ✓ What needs to be done for education of stakeholders?
- ✓ What policy decisions and action should be taken?
- ✓ How to ensure effective use of innovations? Etc.

ACCE

Analytic validity, Clinical validity, Clinical utility, Ethical, legal and social implications

- Analytic Validity

assess the test's performance in the laboratory

- Clinical Validity

define the ability of the genetic test to predict/detect the presence/absence of the disorder

- Clinical Utility

to show the possibilities of the test introduction to influence the health outcome

- Ethical, social and legal implications

Addressing the general considerations for all medical interventions and the specific issues for genetic testing

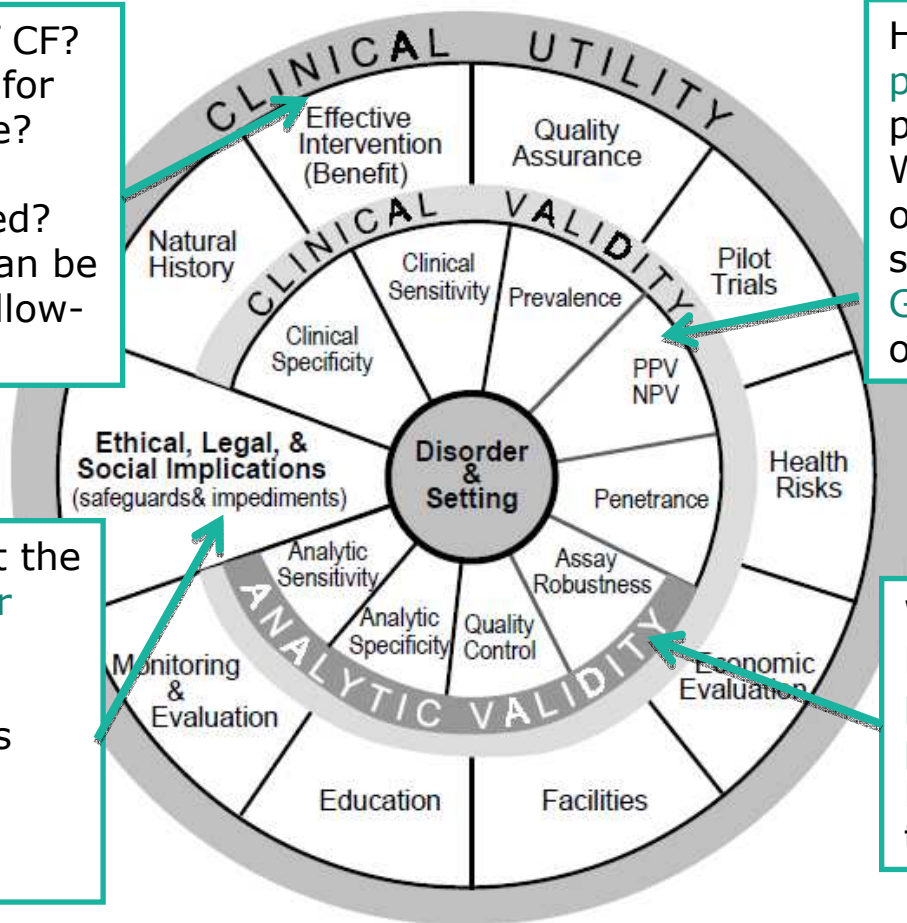
ACCE review of screening for Cystic Fibrosis

What is a history of CF?
 What **interventions** for treating are in place?
 What **educational** materials are needed?
 What **health risks** can be identified for the follow-up?

How often the test is **positive** when CF is present?
 What is **birth prevalence** of CF in prenatal settings?
Genetic, environmental, other modifiers

What is known about the **discrimination and/or stigmatisation** of children with CF?
 What are legal issues about **consent, ownership of data, licensing** etc.

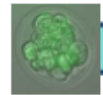
What is CF (clinically)?
 How often the **test is positive** when mutation is present?
 How often does a test fail to give **usable result**?



Continuum of translational research

T1 to T4

TRANSLATIONAL RESEARCH IN PUBLIC HEALTH GENOMICS



FROM CELL TO SOCIETY



KNOWLEDGE GENERATION

TRANSLATIONAL RESEARCH

IMPROVEMENT IN HEALTH

T1

from gene discovery to health application

Basic research
science research
observational studies
preclinical and early clinical studies

T2

from health application to evidence-based guidelines

Policy research
late clinical studies
guidelines formulation
developing policies

T3

from guidelines to health practice

Dissemination research
HTA
communication
education

T4

from practice to health impact

Outcomes research
health priorities
law
education



Genomics of child abuse

nature
neuroscience

Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse

Patrick O McGowan^{1,2}, Aya Sasaki^{1,2}, Ana C D'Alessio³, Sergiy Dymov³, Benoit Labonté^{1,4}, Moshe Szyf^{2,3}, Gustavo Turecki^{1,4} & Michael J Meaney^{1,2,5}



Molecular Psychiatry (2006) 11, 903–913
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www.nature.com/mp

ORIGINAL ARTICLE

MAOA, maltreatment, and gene–environment interaction predicting children’s mental health: new evidence and a meta-analysis

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frontiers in
BEHAVIORAL NEUROSCIENCE

REVIEW ARTICLE
published: 16 November 2009
doi: 10.3389/neuro.08.044.2009



Getting the phenotypes right: an essential ingredient for understanding aetiological mechanisms underlying persistent violence and developing effective treatments

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Translation of genomics of child abuse

TRANSLATIONAL RESEARCH IN PUBLIC HEALTH GENOMICS



FROM CELL TO SOCIETY



KNOWLEDGE GENERATION

T1

from gene discovery to health application

- Is there an established connection between gene variant and the abuse/maltreatment?
- How can it be used?

TRANSLATIONAL RESEARCH

T2

from health application to evidence-based guidelines

- Creation of clinical guidelines on detection of child abuse through saliva test

T3

from guidelines to health practice

- Assessment of the test for the use in hospitals
- HTA including cost-effectiveness
- Education of the medical staff

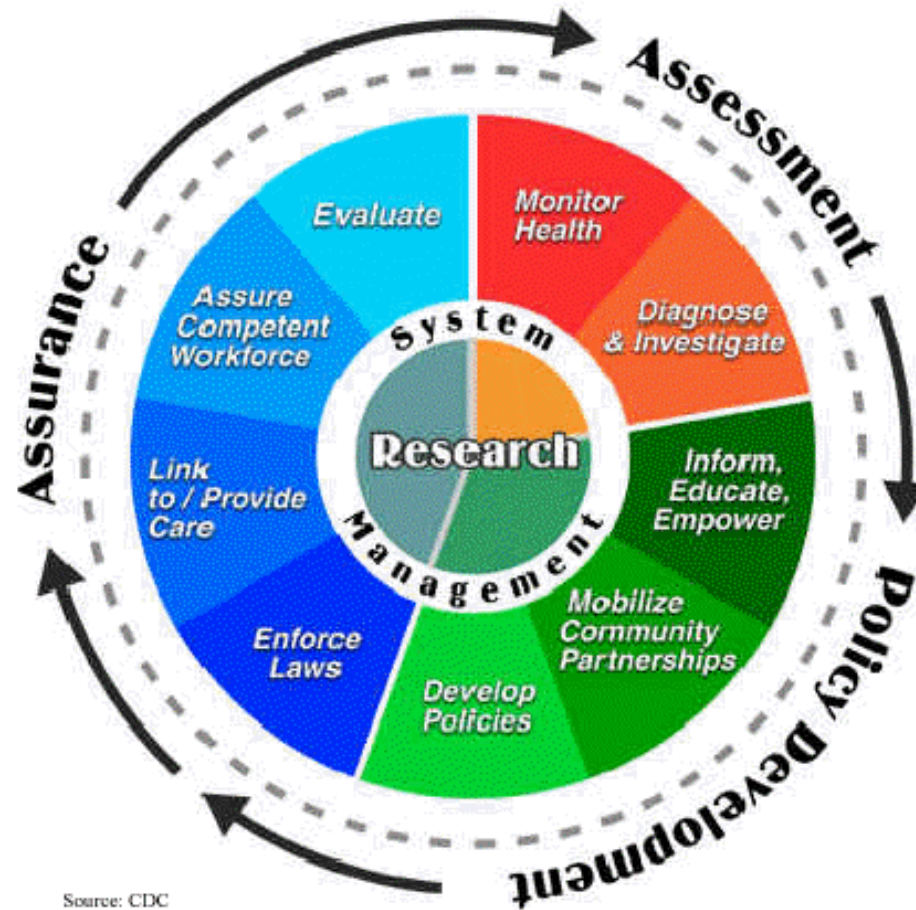
IMPROVEMENT IN HEALTH

T4

from practice to health impact

- How can the "test" on child abuse change the health outcomes
- Policy design and design of laws
- Communication to the public

The Public Health Wheel



Source: CDC

Genomics and Asthma in Children

Variants of *DENND1B* Associated with Asthma in Children

Patrick M.A. Sleiman, Ph.D., James Flory, Ph.D., Marcin Irmielinski, M.D., Ph.D., Jonathan P. Bradfield, B.S., Kiran Annaiah, M.Sc., Saffron A.G. Willis-Owen, Ph.D., Kai Wang, Ph.D., Nicholas M. Rafaels, M.S., Sven Michel, Ph.D., Klaus Bonnelykke, M.D., Ph.D., Haitao Zhang, Ph.D., Cecilia E. Kim, B.A., Edward C. Frackelton, B.A., Ioseph T. Glessner, M.Sc., Cuiding Hou, M.Sc.



Genome-wide transcriptional profiling linked to social class in asthma

E Chen,¹ G E Miller,¹ H A Walker,¹ J M Arevalo,² C Y Sung,^{3,4} S W Cole^{2,3,4}

ABSTRACT

Objectives: Low socioeconomic status (SES) is one of the most robust social factors associated with disease morbidity, including more severe asthma in childhood. However, our understanding of the biological processes that explain this link is limited. This study tested whether the social environment could get “under the skin” to alter genomic activity in children with asthma.

circulating inflammatory markers, such as C reactive protein and interleukin (IL)6.⁹⁻¹⁰ In children with asthma, low SES has been associated with greater eosinophil counts as well as heightened in vitro stimulated production of inflammatory cytokines implicated in asthma, such as IL5 and IL13.¹¹⁻¹² Another social factor associated with low SES—stress—has been linked to heightened

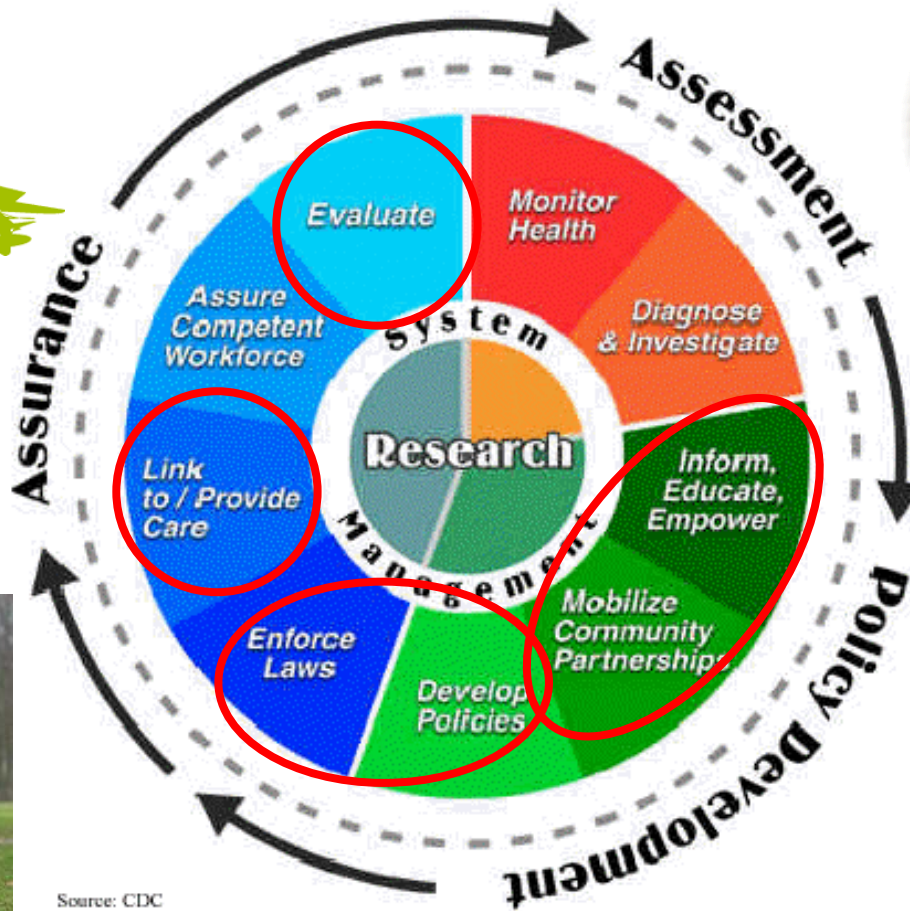
Genomics and Asthma in Children

- In children, asthma is often linked to allergies, which were assumed to trigger the condition

However!

- International research team, incl. researchers from Karolinska Institute, found six gene variants that can explain nearly 40 percent of all cases of asthma in children
- Researchers from GABRIEL consortium proved that allergies are rather a consequence, not a cause

The Public Health Wheel and Asthma



Source: CDC



Conclusions

- The translational models now do not fulfill both aims: evaluation and integration, thus more research is needed
- All models of translation existing now are focused on the adult patients, thus more input from pediatricians about their and their patients needs is needed
- More awareness of the issue among different stakeholder groups will facilitate the job

Questions?



"That concludes my prepared remarks. I will now evade your questions."