

What is Public Health Genomics and Why Should we Care?

***A Decade of Public Health Genomics in the
United States: 1997-2007***

**Muin J. Khoury MD, PhD
National Office of Public Health Genomics**



SAFER • HEALTHIER • PEOPLE™



Outline

- Genomics 2007: the gap between scientific excitement and health impact
- Public health genomics: closing the gap between genome discoveries and population health
- The genomics translation highway: medicine-public health partnership
- Updates on major CDC initiatives

“Welcome to the Genomics Era”

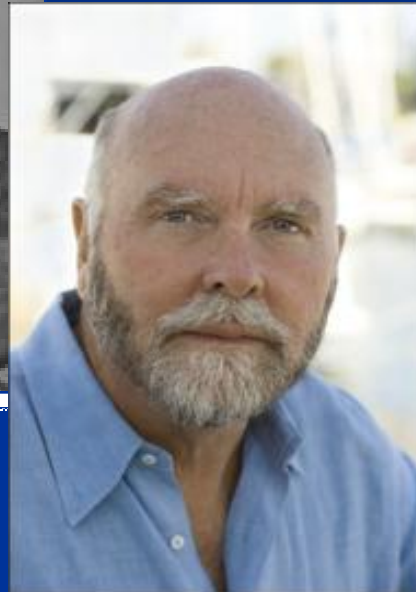
NEJM 2003;349:996



1953 Double Helix

The Diploid Genome Sequence of an Individual Human

PLoS Biology, Sept 3, 2007



Address <http://www.gei.nih.gov/index.asp>

NATIONAL INSTITUTES OF HEALTH
Genes, Environment and Health Initiative (GEI)
Determining Genetic and Environmental Roots of Common Diseases

[GEI Home Page](#)
[Genetics Program](#)
[Exposure Biology Program](#)
[Funding Opportunities](#)
[New Training Grants](#)

The Genes, Environment and Health Initiative (GEI)

On February 8, 2006 Health and Human Services Secretary Michael O. Leavitt announced that the President's 2007 budget proposal includes \$40 million for the National Institutes of Health to plan and implement a Genes and Environment Initiative (GEI). If approved by Congress, federal funding will begin in fiscal year 2007 and continue for four years, with \$26 million annually going to genetic analysis and \$14 million annually designated for the development of new tools to measure environmental exposures that affect health.

The GEI will have two main components:

- The **Genetics Program** is a pipeline for analyzing genetic variation in groups of patients with specific illnesses.
- The **Exposure Biology Program** is an environmental technology.



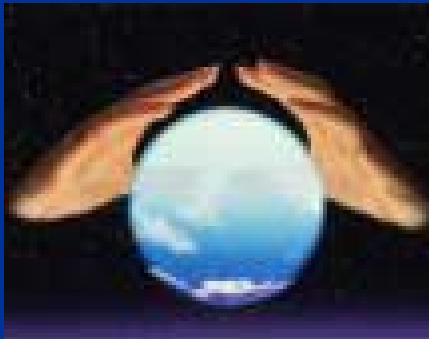
GWAS

Newborn Screening

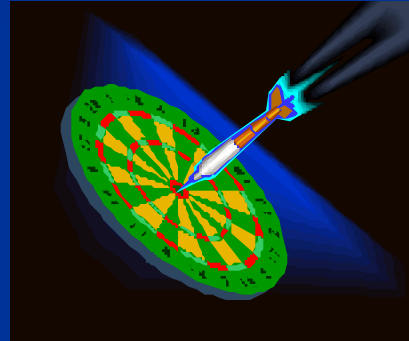
“What do you do with a gene when you find one?”

“Vision for Medicine in the 21st Century”

Predictive



Personalized



Preemptive



“I predict that comprehensive, genomics-based health care will become the norm with individualized preventive medicine and early detection of illnesses” (E. Zerhouni, 2006)

Public Health Challenge 1: Premature Translation

Science May 3, 2007

Scienceexpress

Report

A Common Allele on Chromosome 9 Associated with Coronary Heart Disease

Ruth McPherson,^{1,*†} Alexander Pertsemidis,^{2,*} Nihan Kavaslar,¹ Alexandre Stewart,¹ Robert Roberts,¹ David R. Cox,³ David A. Hinds,³ Len A. Pennacchio,⁴ Anne Tybjaerg-Hansen,¹ Aaron R. Folsom,⁵ Eric Boerwinkle,¹ Helen H. Hobbs,^{1,5} Jonathan C. Cohen^{1,†}

¹Division of Cardiology, University of Ottawa Heart Institute, Ottawa K1Y4W7, Canada. ²Donald W. Reynolds Cardiovascular Clinical Research Center and the Eugene McDermott Center for Human Growth and Development, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA. ³Perlegen Sciences, Mountain View, CA 94043, USA. ⁴Genomics Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA & U.S. Department of Energy Joint Genome Institute, Walnut Creek, CA 94598, USA. ⁵Department of Clinical Biochemistry, Rigshospitalet, Copenhagen University Hospital, Copenhagen DK-2100, Denmark. ⁶Division of Epidemiology and Community Health, University of Minnesota, Minneapolis, MN 55454, USA. ⁷Human Genetics Center and Institute for Molecular Medicine, University of Texas Health Science Center, Houston, TX 77030, USA. ⁸Center for Human Nutrition and the ⁹Howard Hughes Medical Institute at the University of Texas Southwestern Medical Center, Dallas, TX 75390, USA.

Science May 3, 2007

Scienceexpress

Report

A Common Variant on Chromosome 9p21 Affects the Risk of Myocardial Infarction

Anna Helgadóttir,^{1,*} Gudmar Thorleifsson,^{1,*} Andrei Manolescu,^{1,*} Solveig Gretarsdóttir,¹ Thorarinn Blondal,¹ Aslaug Jonasdóttir,¹ Adalbjorg Jonasdóttir,¹ Asgeir Sigurdsson,¹ Adam Baker,¹ Arnar Palsson,¹ Gisli Masson,¹ Daniel Gudbjartsson,¹ Kristinn P. Magnusson,¹ Karl Andersen,² Allan I. Levey,³ Valgerdur M. Backman,¹ Sigurborg Matthíasdóttir,¹ Thorbjorg Jonsdóttir,¹ Stefan Palsson,¹ Helga Eimarsdóttir,¹ Steinunn Gunnarsdóttir,¹ Arnaldur Gylfason,¹ Viola Vaccarino,³ W. Craig Hooper,³ Muredach P. Reilly,⁴ Christopher B. Granger,⁵ Harland Austin,³ Daniel J Rader,⁴ Svati H. Shah,⁵ Arshed A. Quyyumi,³ Jeffrey R. Gulcher,¹ Gudmundur Thorgeirsson,³ Unnur Thorsteinsdóttir,¹ Augustine Kong,^{1,†} Kari Stefansson^{1,†}

¹deCODE genetics Inc, Reykjavik, Iceland. ²National University Hospital, Reykjavik, Iceland. ³Emory University School of Medicine, Atlanta, GA 30322, USA. ⁴University of Pennsylvania School of Medicine, Philadelphia, PA 19104, USA. ⁵Duke University School of Medicine, Durham, NC 27710, USA.

*These authors contributed equally to this work.

†To whom correspondence should be addressed. E-mail: augustine.kong@decode.is (A.K.); kstefans@decode.is (K.S.)

The global endemic of cardiovascular diseases calls for chance (fig. S1). Hence, we further explored the SNPs that

- ‘A hunt for genes has found that people of Northern European descent have DNA that raises their risk for heart disease.... **DECODE** plans to bundle this discovery with other genetic variants into a DNA-based test for gauging inherited risk of heart attacks’. The company said in a statement’

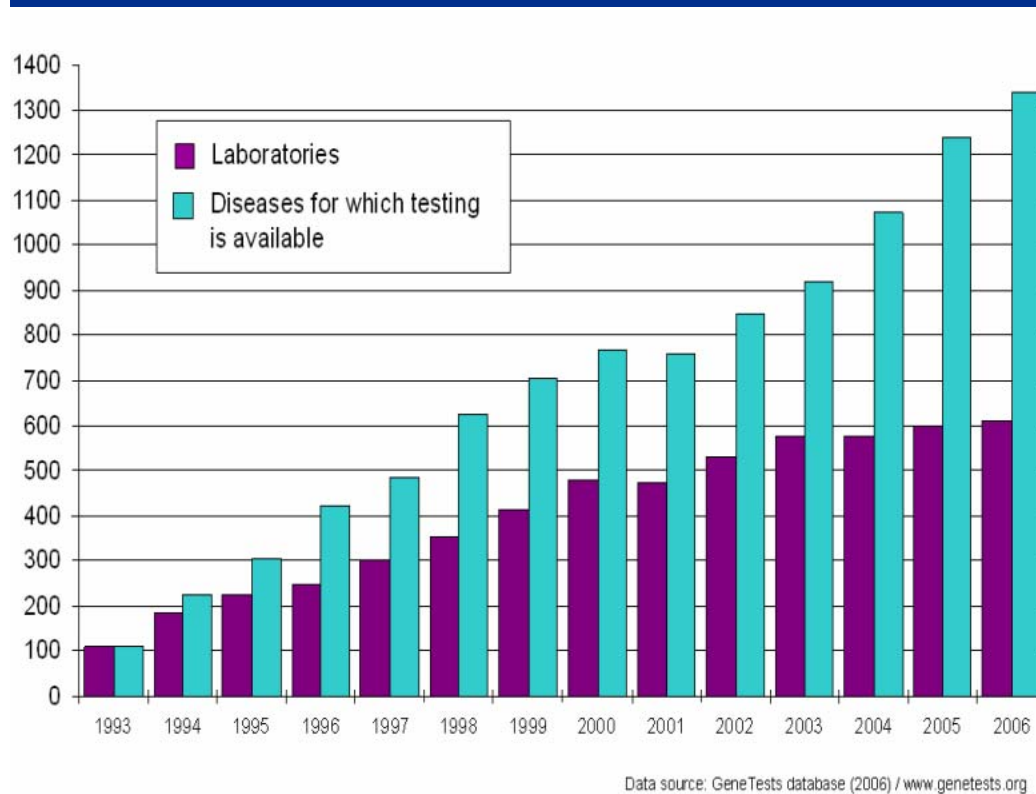
■ Reuters, May 3, 2007

Population level Questions are Important for Using Genetic Information in Practice

- How many people have this genetic variant?
- Is prevalence different in subgroups of the population?
- How much of the population burden of disease does it explain?
- Does the variant interact with other genes and modifiable risk factors?
- Can we construct a risk profile related to genetic and environmental factors?



Genetic Testing as a Public Health Issue



- How good is the genetic test?
- What are the benefits?
What are the harms?
- How can we ensure quality testing and access?
- How can we educate providers and consumers?
- Information on appropriate use to providers, policy makers and the public
- Monitoring use and evaluating health impact
- Addressing complex social issues

***Public Health Challenge 2:
"Lost in Translation"
C. Lenfant NEJM 2003;349:868***

**< 33% of patients with
coronary artery
disease are
prescribed aspirin**

**"Let's be realistic: If
we didn't do it with
aspirin, how can
we expect to do it
with DNA?"**

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- Updates on CDC major initiatives

Who needs genomics research when it is obvious what we need to do to prevent common diseases?

- “If a minor fraction of the billions spent on technological research were spent instead on simpler things like, yes, early health education to improve diet and promote exercise, the benefits could grossly dwarf even the greatest plausible genetic successes”
- A Buchanan et al. IJE 2006

Int. J. Epidemiol. Advance Access published September 19, 2006

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doi:10.1093/ije/dyl214

Letter to the Editor

Genomics, epidemiology, and common complex diseases: let's not throw out the baby with the bathwater!

From MUIN J KHOURY and MARTA GWINN

As
ge
to



Volume 161

Number 9

May 1, 2005

American Journal of
EPIDEMIOLOGY

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Bloomberg School of Public Health

Sponsored by the Society for Epidemiologic Research

Published by Oxford University Press

SPECIAL ARTICLE

Do We Need Genomic Research for the Prevention of Common Diseases with Environmental Causes?

Muin J. Khoury, Robert Davis, Marta Gwinn, Mary Lou Lindegren, and Paula Yoon

From the Office of Genomics and Disease Prevention, Coordinating Center on Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA

“Sick Individuals and Sick Populations”

G Rose (1986)

- Population approach vs. high risk approach
- “Realistically, many diseases will long continue to call for both approaches, and fortunately competition between them is usually unnecessary”

Can Genomics Heal the “Schism” between Medicine and Public Health?

■ Medicine

- Health care
- Individuals
- Treatment
- Biomedical research
- Genes

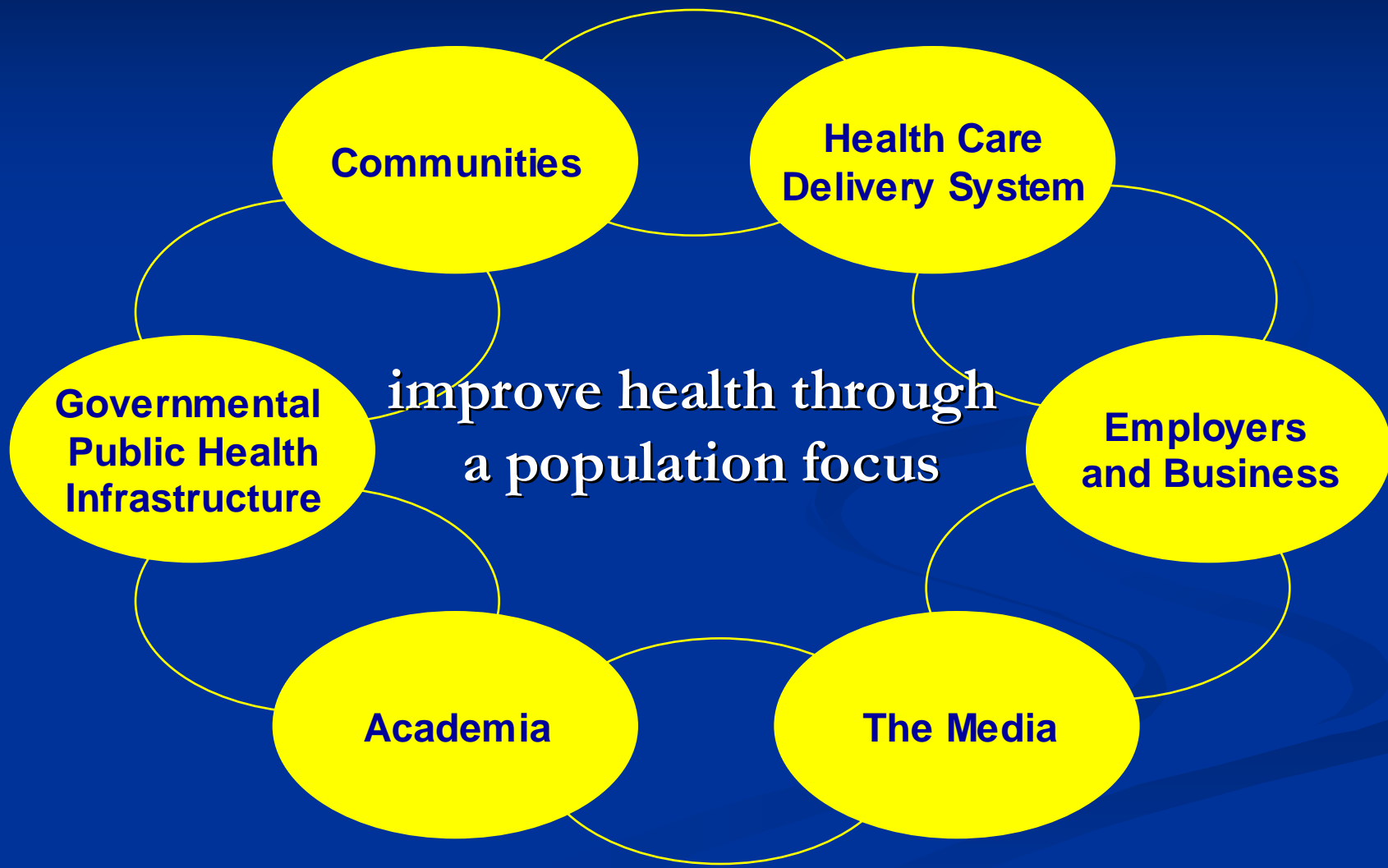
■ Public Health

- Health
- Populations
- Prevention
- Behavioral/Social/Policy
- Environment

Khoury MJ et al. Am J Prev Med 2007

Actors in the Public Health System (IOM, 2002)

“Public Health” as “Population Health”



“Can Public Health and Medicine Partner in the Public Interest?”

JM McGinnis. Health Affairs 2006;25:1044

“...no important health problem will be solved by clinical care alone, or research alone, or by public health alone- But rather by all public and private sectors working together.....”

**JS Marks. Managed Care 2005;14:p11
Supplement on “The Future of Public Health”**

The Emergence of Public Health Genomics

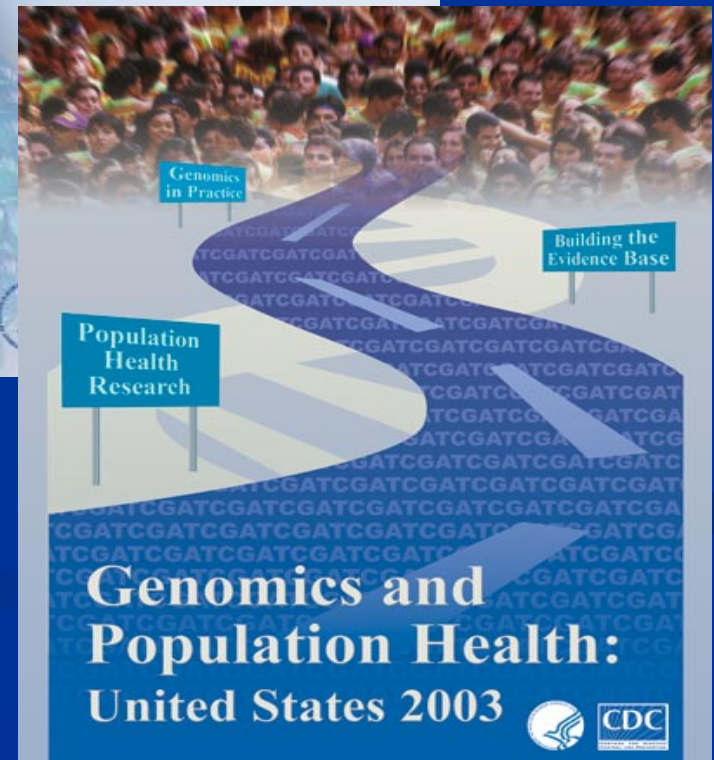
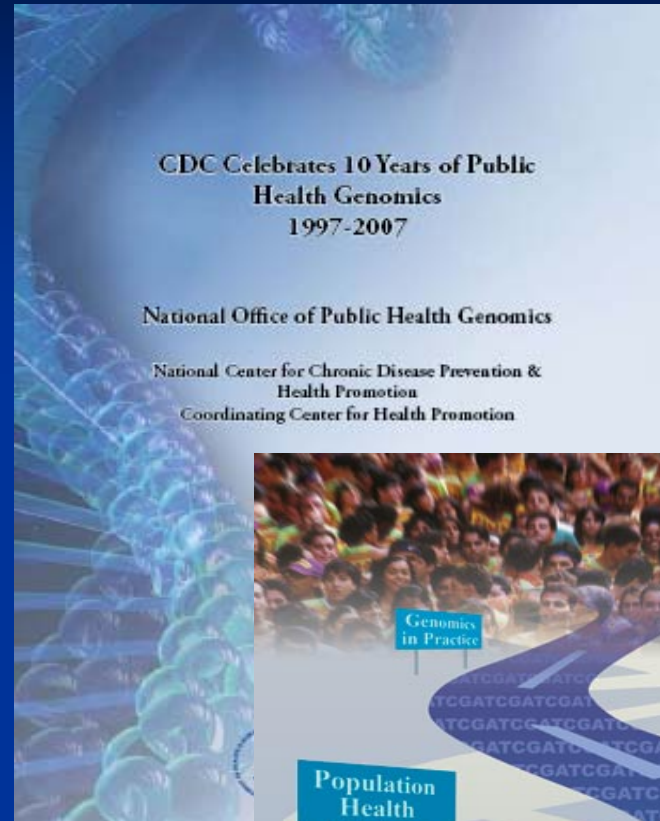
The population health approach provides the best strategy for the appropriate applications of genomics in health practice in the 21st century

What is “Public Health Genomics?”

- A multidisciplinary field concerned with the effective and responsible translation of genome-based knowledge and technologies to improve population health

- **Focus:**

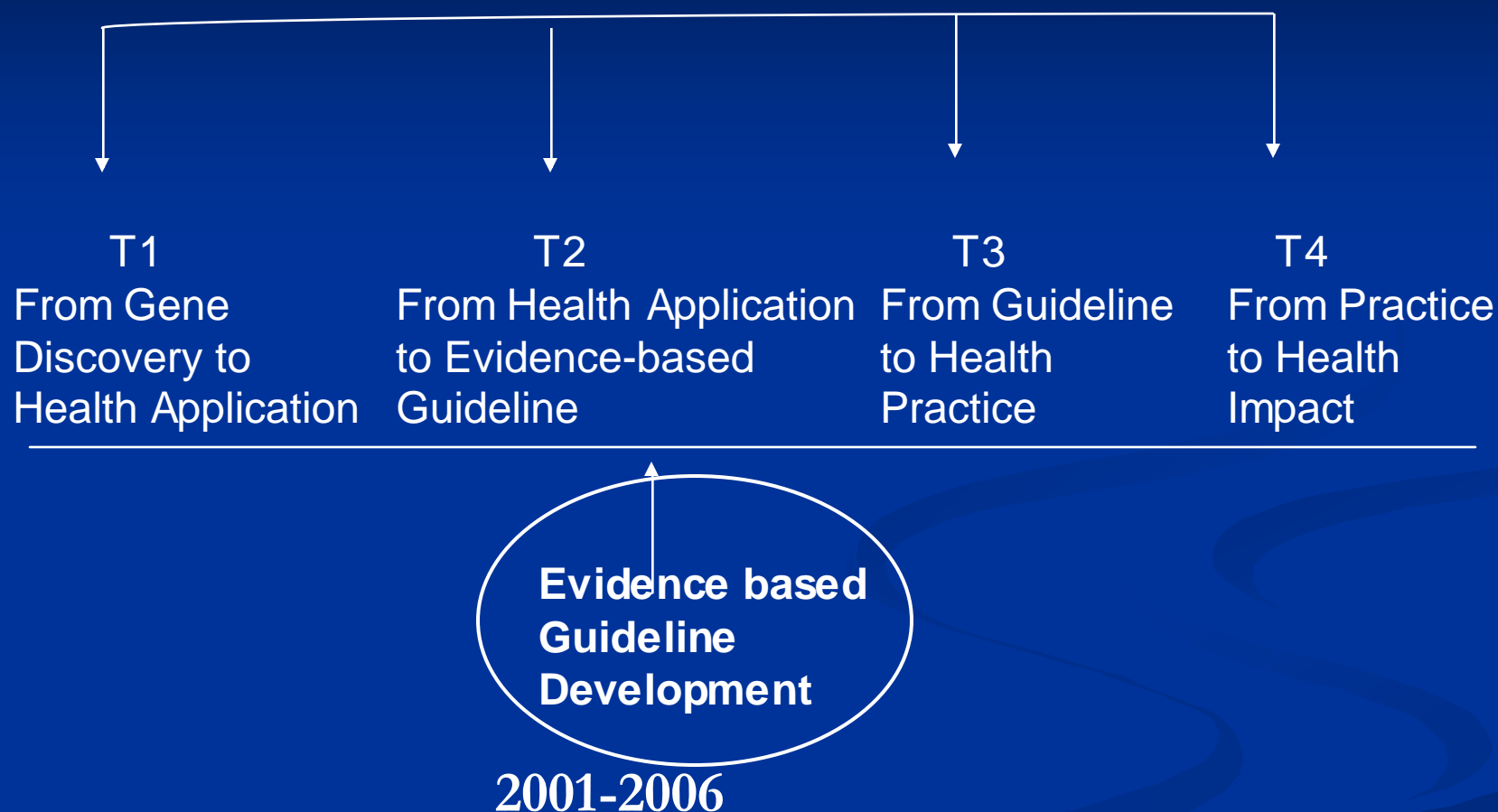
- Populations
- Gene-environment Interaction
- Prevention
- Evidence-based applications
- ELSI integration
- Health disparities



Outline

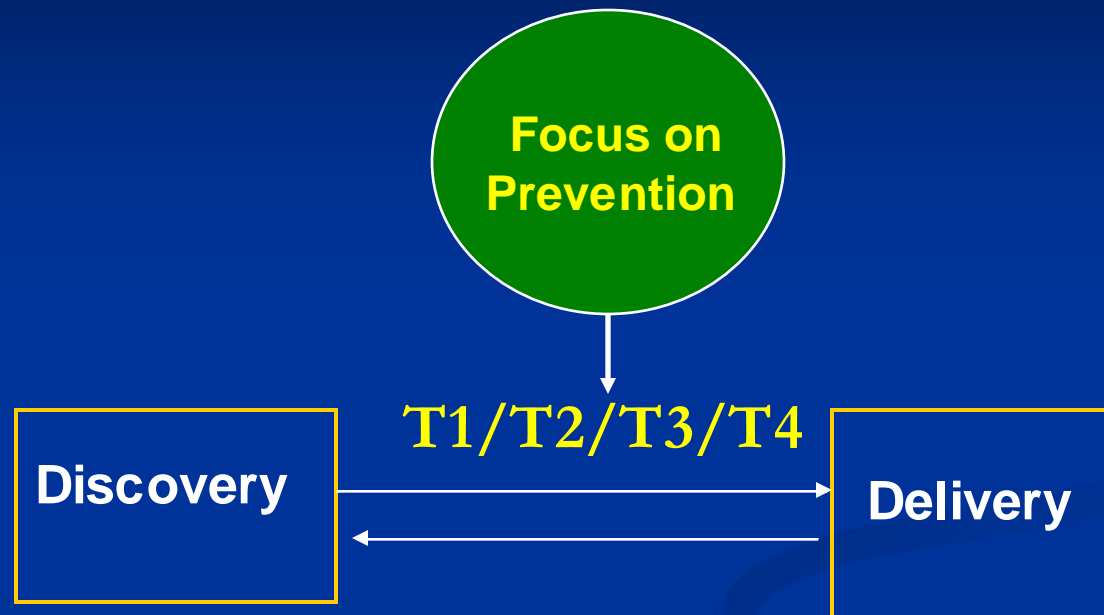
- Genomics 2007: the gap between scientific excitement and health impact
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The Four Phases of Translation For Genomic Applications in Population Health



Less than 3% of published genomics research is T2 and beyond
Only 2 USPSTF evidence based guidelines (BRCA1 & HFE)
Khoury MJ et al. Genet Med 2007

A “Population Health” Approach to Genomics Translation



Khoury MJ et al. Am J Prev Med 2007

Gene-Based Medicine in 2010?

A hypothetical 23 year old patient named John...

■ Condition	Genes	RR	Lifetime
■ Prostate Ca	HPC1, 2, 3	0.5	7%
■ Alzheimer's	APOE,FAD3,XAD	0.3	10%
■ Heart disease	APOB,CETP	2.5	70%
■ Colon Cancer	FCC4,APC	4.0	23%
■ Lung Cancer	NAT2	6.0	40%

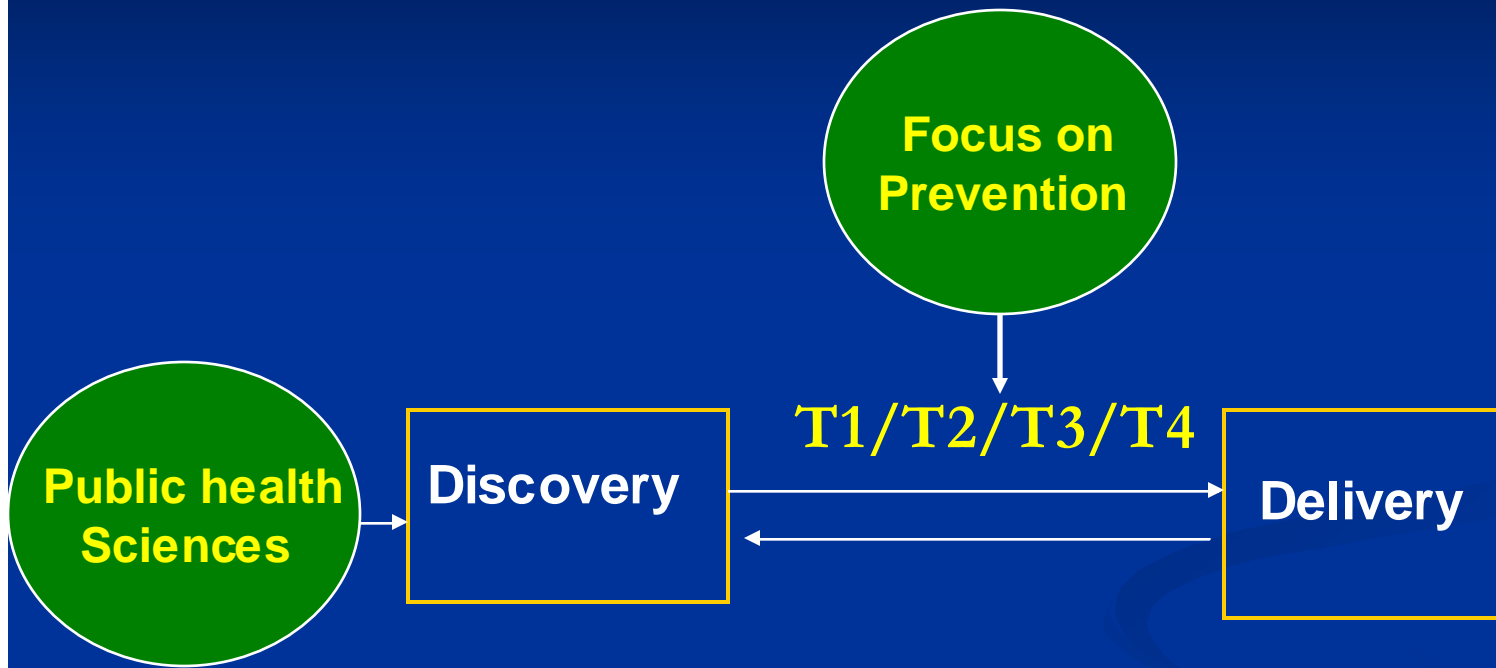
Collins FC, New Engl J Med 1999;341:28-37.

Gene-Based Medicine in 2010?

Prevention Strategies Based on Gene-Environment Interaction

- Increased Risk for
 - Heart disease
 - Colon Cancer
 - Lung Cancer
- Prevention Strategies
 - **Tertiary:** Cholesterol drugs + Lifestyle changes
 - **Secondary:** Increased surveillance for early detection
 - **Primary:** Behavior modification for smoking cessation

A “Population Health” Approach to Genomics Translation



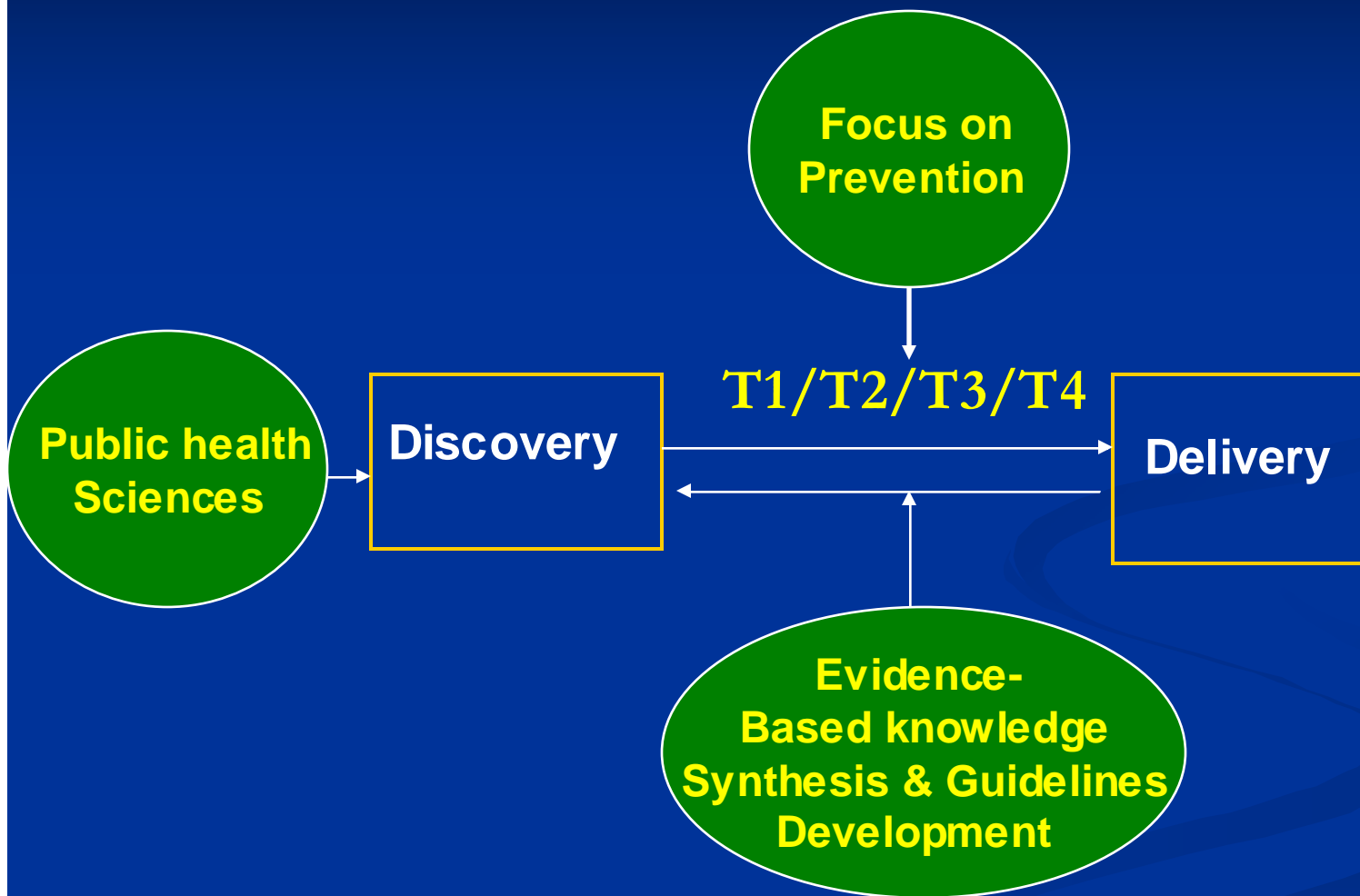
Khoury MJ et al. Am J Prev Med 2007

Gene-Based Medicine in 2010?

Role of Public Health Sciences

- Increased Risk for
 - Heart disease
 - Colon Cancer
 - Lung Cancer
- **Public Health**
 - **Epidemiology-Get the numbers**
 - Intervention trials
 - Behavioral research
 - Delivery research
 - Outcome Research
 - Economic research
 - ELSI research.....
 - Etc..

A “Population Health” Approach to Genomics Translation



Khoury MJ et al. Am J Prev Med 2007

Genetic Prediction of Future Type 2 Diabetes

Valeriya Lyssenko^{1*}, Peter Almgren¹, Dragi Anevski^{1,2}, Marju Orho-Melander¹, Marketa Sjögren¹, Carola Saloranta^{3,4}, Tiinamaija Tuomi^{3,4}, Leif Groop¹, the Botnia Study Group

¹ Department of Clinical Sciences, Diabetes and Endocrinology, Lund University, University Hospital Malmö, Malmö, Sweden, ² School of Mathematical Sciences, Chalmers University of Technology, Gothenburg, Sweden, ³ Department of Medicine, Division of Diabetology, Helsinki University Hospital, Helsinki, Finland, ⁴ Folkhälsan Research

Does Genetic Testing Really Improve the Prediction of Future Type 2 Diabetes?

A. Cecile J. W. Janssens, Marta Gwinn, Subramony Subramonia-Iyer, Muin J. Khoury

From their study on the genetic prediction of future type 2 diabetes (T2D), Lyssenko and colleagues conclude “genetic testing might become a future approach to individuals at risk of developing T2D” [1]. One of the most striking findings is an impressive 21.2-fold increase in risk for T2D in obese carriers of the *PPARG* PP and SNP43/44 GG/TT genotypes with elevated fasting plasma glucose (FPG).

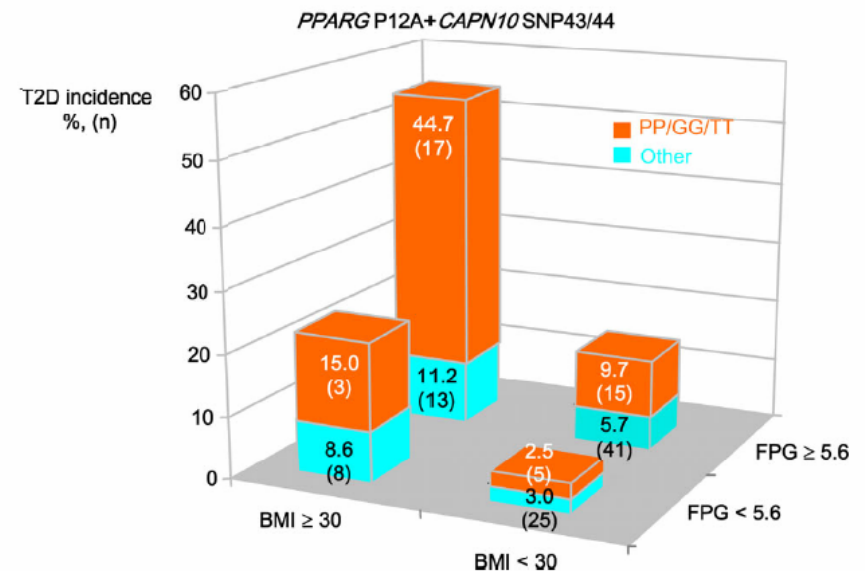
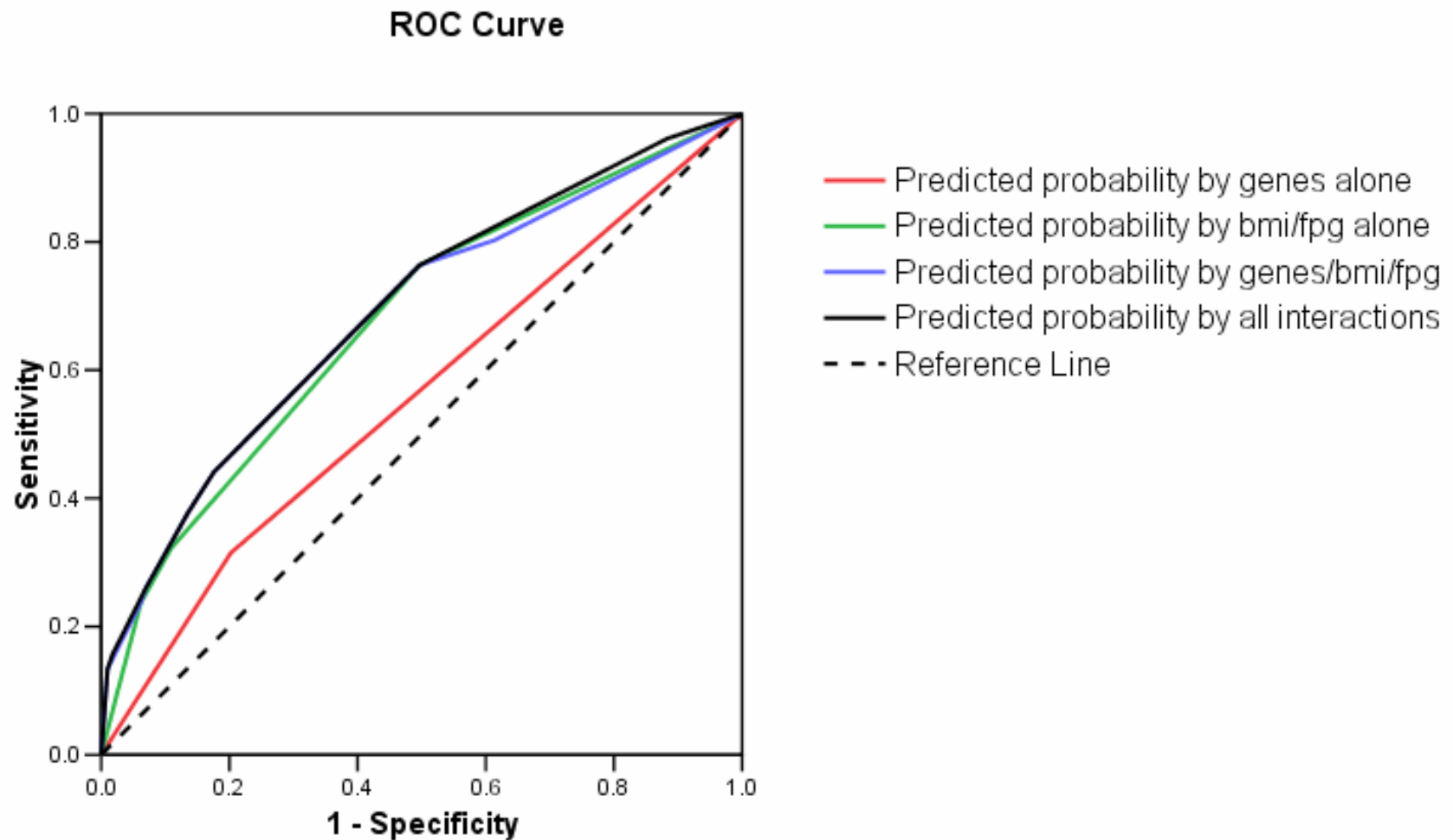
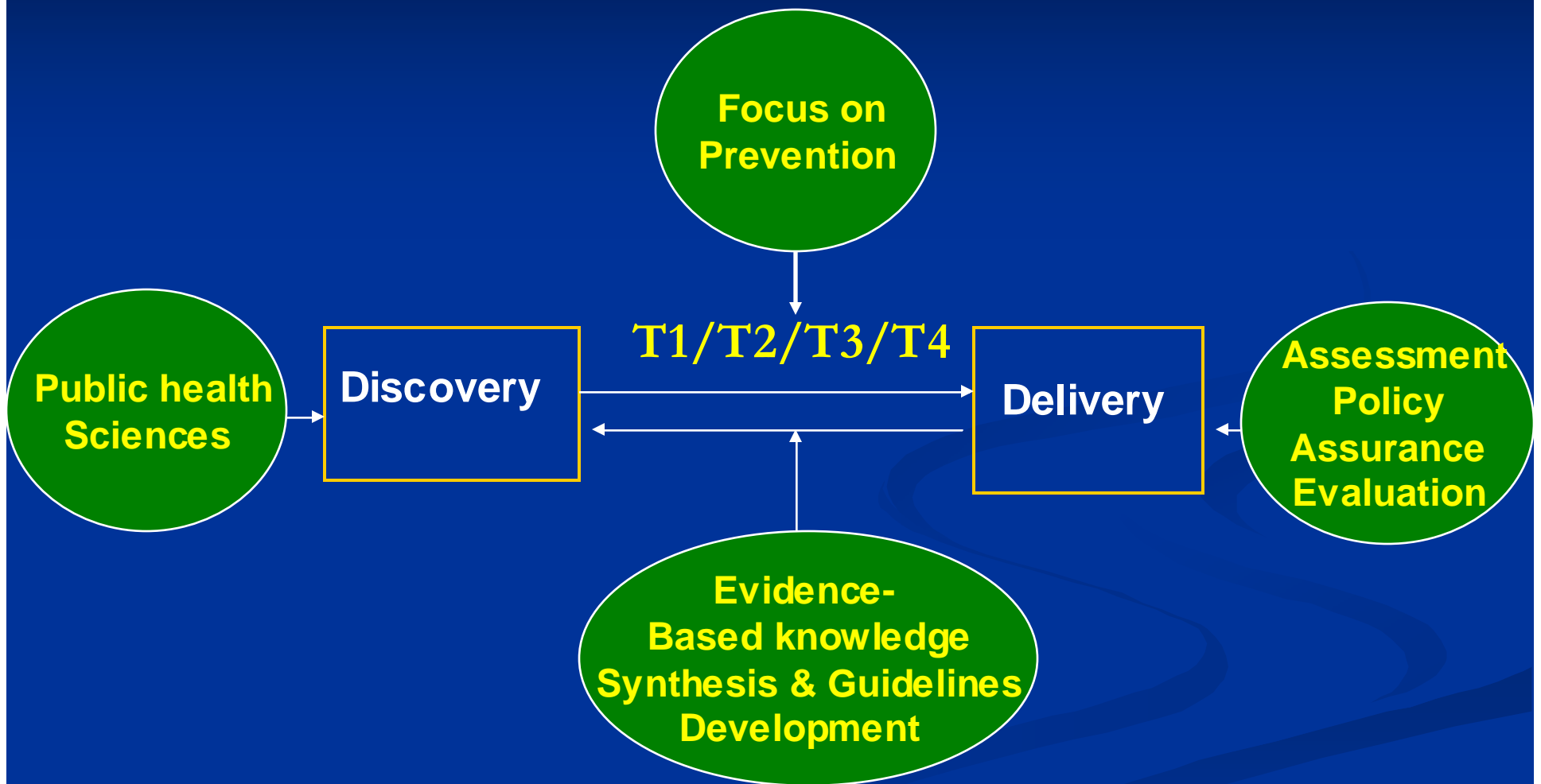


Figure 2. The Effects of Risk Genotypes of the *PPARG* P12A Poly-

Multiple Genetic Testing by PPARG and CAPN10 SNP 43/44 Does Not Improve the Prediction of Type 2 Diabetes by BMI and FPG



A “Population Health” Approach to Genomics Translation



Khoury MJ et al. Am J Prev Med 2007

Genomics and Public Health Functions (Khoury et al, 1996)

■ Public Health Functions

- Assessment
- Policy Development
- Assurance

The
Future
of
Public
Health

INSTITUTE OF MEDICINE

Public Health Policy Forum

From Genes to Public Health:
The Applications of Genetic
Technology in Disease Prevention

Muin J. Khoury, MD, PhD, and the Genetics Working Group

ABSTRACT

Objectives. With advances in the Human Genome Project, the implications of genetic technology in disease prevention should be assessed.

Methods. The paradigm suggested in *The Future of Public Health*—assessment, policy development, and assurance—was used to examine the continuum from genetic technology to public health practice.

Results. First, important public

Introduction

During the past decade, there have been tremendous advances in molecular genetic technology. These advances have led to the Human Genome Project, a long-term initiative to map and sequence the human genome. In the next decade, most if not all human genes will be mapped and sequenced.¹⁻³ Relatively simple technology such as the polymerase

Also, there are disease genes that account for a small fraction of the more common chronic diseases, such as α_1 -antitrypsin deficiency in pulmonary emphysema.¹⁴ Furthermore, genes play important roles in the etiology of most, if not all, human diseases ranging from cancer to coronary heart disease.¹⁵ The roles that genes play differ greatly, ranging from genes that completely determine the disease state (*i.e.*, disease genes) to genes that interact

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CDC Public Health Genomics Initiatives



CDC's National Office of Public Health Genomics

Vision

- To use genomic knowledge to improve the lives and health of all people

Mission

- To integrate genomics into public health research, policy, and programs

The screenshot shows the website for the CDC's National Office of Public Health Genomics. At the top, there is a navigation bar with links for 'CDC Home', 'Search', and 'Health Topics A-Z'. The main header features the CDC logo and the text 'National Office of Public Health Genomics'. Below this, there is a 'home' link and a 'SITE SEARCH' button. A featured article titled 'When is BRCA Genetic Testing for Breast and Ovarian Cancer Appropriate?' is prominently displayed, with a sub-headline 'Weekly Update Spotlight: October 4-10'. The article text states that the U.S. Preventive Services Task Force (USPSTF) recommends against routine referral for BRCA testing if a woman's family history does not... and includes links for 'Read more' and 'Subscribe to the Weekly Update'. On the left side, there is a vertical menu with items: Home, Weekly Update, Genomics & Your Health, Family History, Genomics in Practice, Population Research, Resources & Links, Frequently Asked Questions, Training, and Events. The main content area below the featured article has a 'Welcome to Public Health Genomics' section, followed by a paragraph describing the office's mission. Below this are sections for 'Focus Areas' and 'Highlights', each with a small image and a link to a 'Weekly Update'.

CDC Public Health Genomics Initiatives

Population Studies

US Genome Profile
Public Health Studies



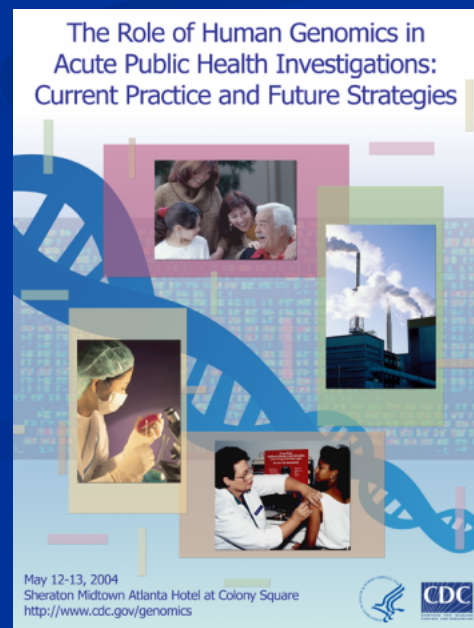
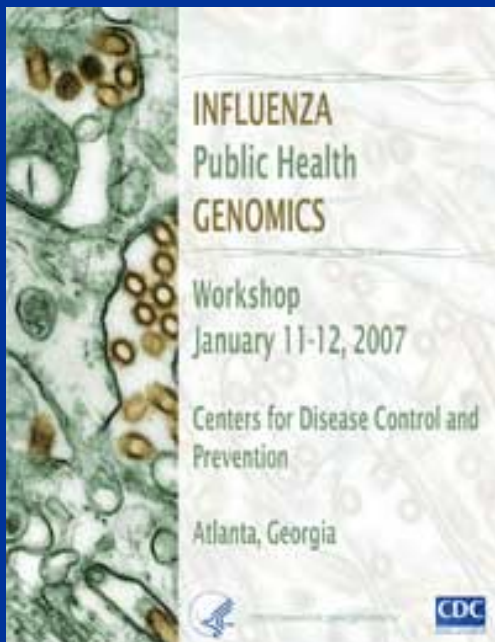
Gene
Discovery



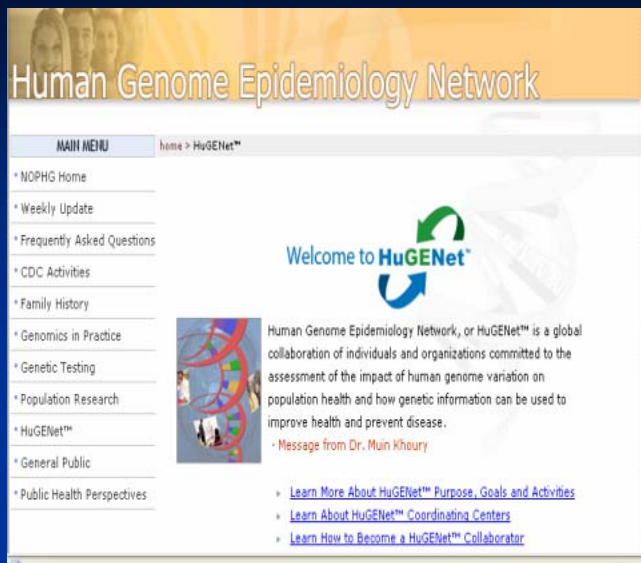
Closing the Gap



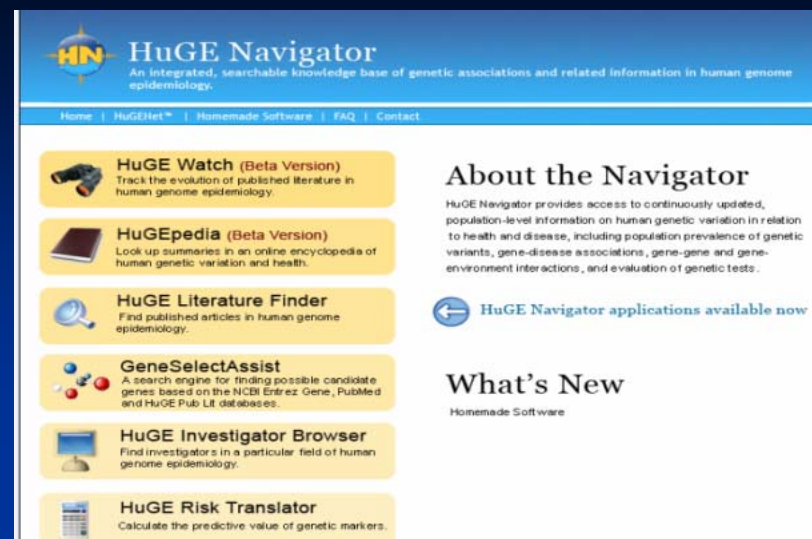
Population
Health



CDC Public Health Genomics Initiatives



HuGENet
Human
Genome
Epidemiology
Network



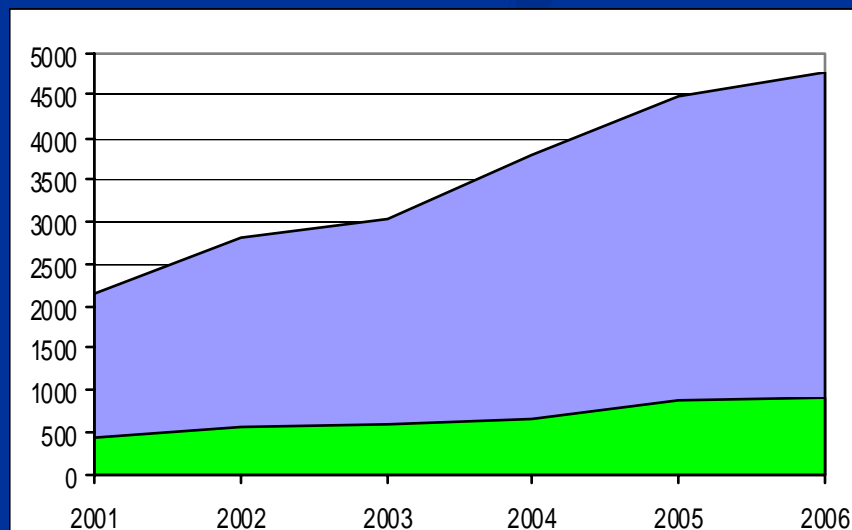
Gene
Discovery



Closing the Gap



Population
Health



CDC Public Health Genomics Initiatives

Independent nonfederal panel
Commissions evidence based evaluations
Makes recommendations

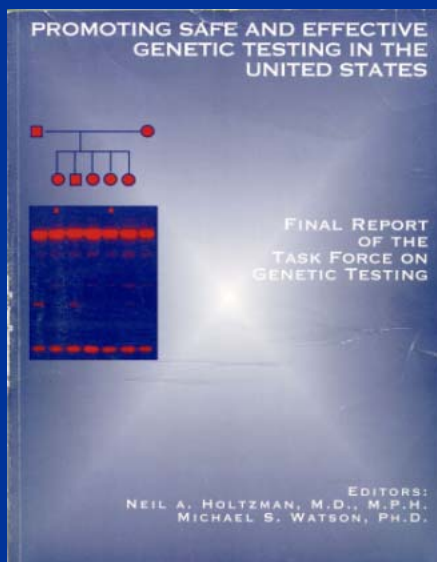
Gene
Discovery



Closing the Gap



Population
Health



EGAPP

Evaluation of
Genomic
Applications in
Practice &
Prevention



EGAPP Topics 2007

- Proteomic tests for ovarian cancer detection and management
- Hereditary nonpolyposis colorectal cancer (HNPCC) screening
- Cyp450 Polymorphisms testing in adults with depression
- UGT1A1 testing in colorectal cancer patients treated with Irinotecan
- Impact of gene expression profiles on breast cancer outcomes
- Use of genomic profiling to assess cardiovascular risk and identify individualized prevention strategies
- Cyp450 testing to predict response to pain Management with codeine

CDC Public Health Genomics Initiatives

Population Studies

US Genome Profile
Public Health Studies

HuGENet

Human
Genome
Epidemiology
Network

Gene
Discovery



Closing the Gap



Population Health

EGAPP

Evaluation of
Genomic
Applications in
Practice &
Prevention

Practice

Family history
State Capacity
Genomics Centers
Website/Reports/
Competencies

Centers for Genomics and Public Health

Provide bridge between genomics research and practice

- Provide public sector access to specialized expertise
- Create networked partnership spanning academic and public sectors and multiple levels of government

UNIVERSITY OF WASHINGTON
Center for Genomics and Public Health

INTRANET • CALENDAR • FORUMS

ABOUT US • CENTER GOALS • WORKING GROUPS • CONTACT

NEWSLETTERS
Spotlight's March issue on Colorectal Cancer and Screening
Spotlight, November issue: "Family History Matters!"
NCHPE's Genetic Family History in Practice (Winter 2006 issue in Spanish)

ANNOUNCEMENTS
Surgeon General's Office: New Family Health History Projects Focus on Alaska Native, Appalachian Communities, 11/14/2006 in U.S.

DID YOU KNOW?
Genetic testing for colorectal cancer, ovarian cancer, and depression is being evaluated as part of a new project supported by the Centers for Disease Control and Prevention (CDC).

"With the arrival of the era in which we will have the ability to understand gene-

Connecting research, education, practice, & community

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Six Weeks to

MICHIGAN CENTER FOR GENOMICS & PUBLIC HEALTH

The Michigan Center for Genomics & Public Health seeks to integrate genomic

Integrating Genomics into State Public Health Programs

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Department of Community Health Michigan.gov

Printer Friendly | Text Version | Email Page | A- A+ Text Size

Public Health Genomics Program

Our Vision:

"Improved health outcomes and enhanced quality of life for the people of Michigan through appropriate use of genetic information, technology, and services"

Address: <http://egov.oregon.gov/DHS/ph/genetics/index.shtml>

Minnesota Department of Health
Protecting, maintaining and improving the health of all Minnesotans

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Search

Chronic Disease Genomics Project

Genomics Project

- Genomics Home
- About Us
- Resources & Research
- Genomics Interest Group (GIG)
- For The Public

"Genomics will be to the 21st century what infectious disease was to the 20th century.... Genomics should be considered in every facet of public health: infectious disease, chronic disease, occupational health, environmental health, in addition to maternal and child health." [Gerard et al.]

What is Genomics?

News and Hot Topics
[NEWS](#)

Genomics Weekly News Digest

HOT TOPICS

[NEW FACT SHEETS ON FAMILY HEALTH HISTORY AND](#)

[Breast Cancer](#)

Oregon Genetics Program

Department of Human Services

Departments | Divisions

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- Genetics Services
- Family Health History
- Genetic Privacy
- Data & Surveillance
- State Genetics Plan

What's New

- the Obesity Epidemic
- Family Health History
- Data & Surveillance
- Genetics in the News
- Publications & Talks

Colon Cancer
March is Colon Cancer Awareness Month

Genetic Privacy and Research

utah.gov Online Services Agency List Business

Utah Department of Health health.utah.gov | News | A to Z Index | Health Data | FAQs | Training | Local Health

Chronic Disease GENOMICS Program

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CURRENT PROJECTS

EDUCATION

FAMILY HISTORY

GENOMICS NEWS

RESOURCES

UPCOMING EVENTS

WORKGROUPS

Welcome!

The Chronic Disease Genomics Program wants to help you understand how **genomics, or the study of genes and their interaction with the environment**, will impact health. Genomics promises to revolutionize medicine and public health as we know it today.

As you explore our site you will discover how genomics can be applied to all areas of public health. Start by visiting our **Frequently Asked Questions** page for information on how genomics applies to you.

New!

GENOMICS AND YOU

Find out how genomics impacts health. Topics include:

Can genomics explain asthma disparities? New data reveal differences in asthma rates across Utah

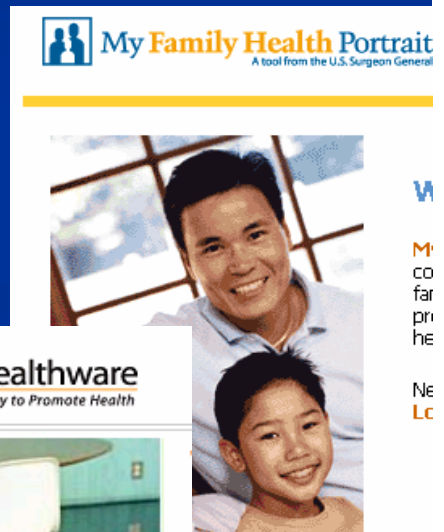
How far would you go to save your life?

A gene to cure

Family History Public Health Initiative

Benefit: Tools for Prevention

- Family history captures shared genes, behaviors, and environment
- Use to target screening, prevention
- CDC tool (6 diseases) & validation study in collaboration with NIH, academic centers
- Partnership with US Surgeon General

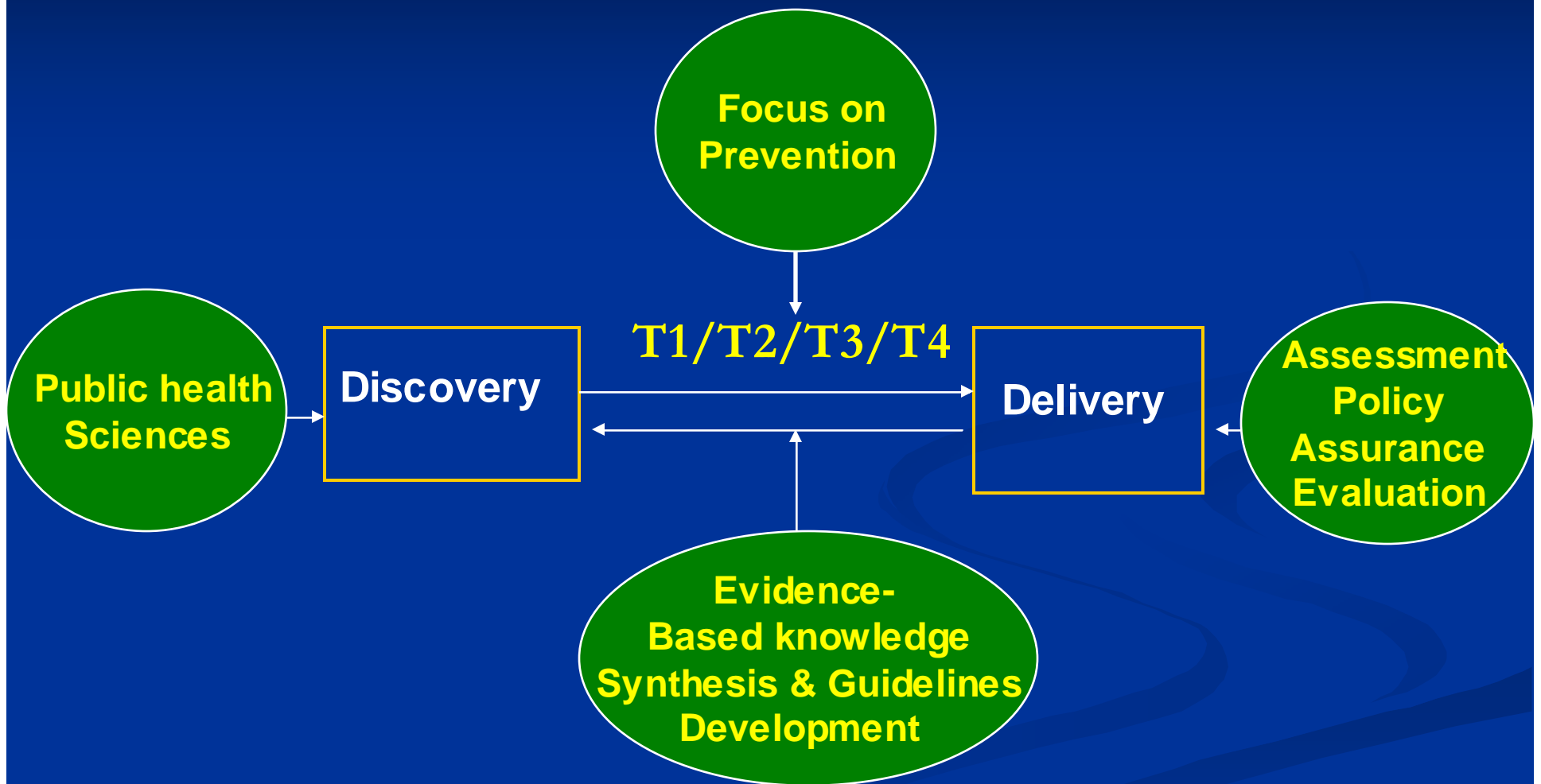


Public Health Surveillance of DTC Genetic Tests, 2006

	Oregon	Michigan	Utah	National
Total Sample Size	1867	5499	2441	5250
Awareness of DTC Tests (% Yes, CI)	24.4% [22.2%,26.7%]	7.6% [6.8%,8.4%]	19.7% [17.7%,22%]	14% [12.7%,14.6%]
Use of DTC Tests (% Yes, CI)	0.3%	0.9%	-	0.6% [0.4% - 0.8%]

Goddard K et al. Genetics in Medicine 2006

A “Population Health” Approach to Genomics Translation



Khoury MJ et al. Am J Prev Med 2007