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™

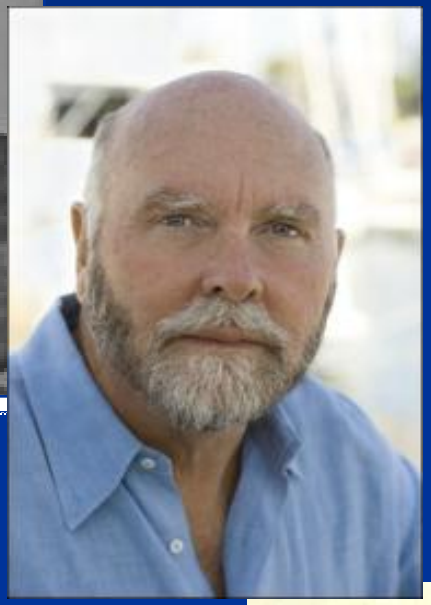
Outline

- 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

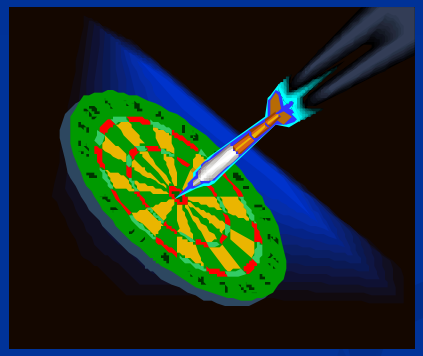
GWAS

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

Sciencexpress Report

A Common Allele on Chromosome 9 Associated with Coronary Heart Disease

Ruth McPherson,[1*†] Alexander Pertsemlidis,[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,[5] Aaron R. Folsom,[6] Eric Boerwinkle,[7] Helen H. Hobbs,[2,8] Jonathan C. Cohen[2,8†]

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

Science May 3, 2007

Sciencexpress Report

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

Anna Helgadottir,[1*] Gudmar Thorleifsson,[1*] Andrei Manolescu,[1*] Solveig Gretarsdottir,[1] Thorarinn Blondal,[1] Aslaug Jonasdottir,[1] Adalbjorg Jonasdottir,[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 Matthiasdottir,[1] Thorbjorg Jonsdottir,[1] Stefan Palsson,[1] Helga Einarsdottir,[1] Steinunn Gunnarsdottir,[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 Thorsteinsdottir,[1] Augustine Kong,[1†] Kari Stefansson[1†]

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

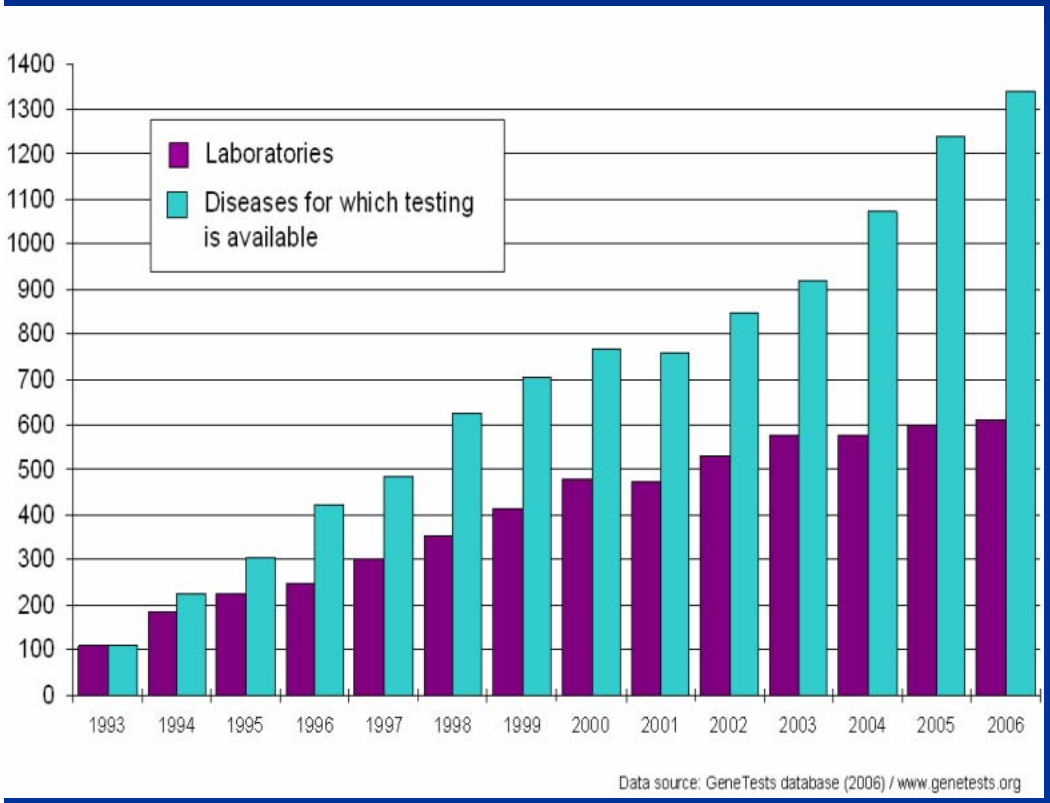
The global endemic of cardiovascular diseases calls for chance (fig. S1). Hence, we further explored the SNPs that

- '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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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

International Journal of Epidemiology
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

American Journal of
EPIDEMIOLOGY

Volume 161
Number 9
May 1, 2005

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

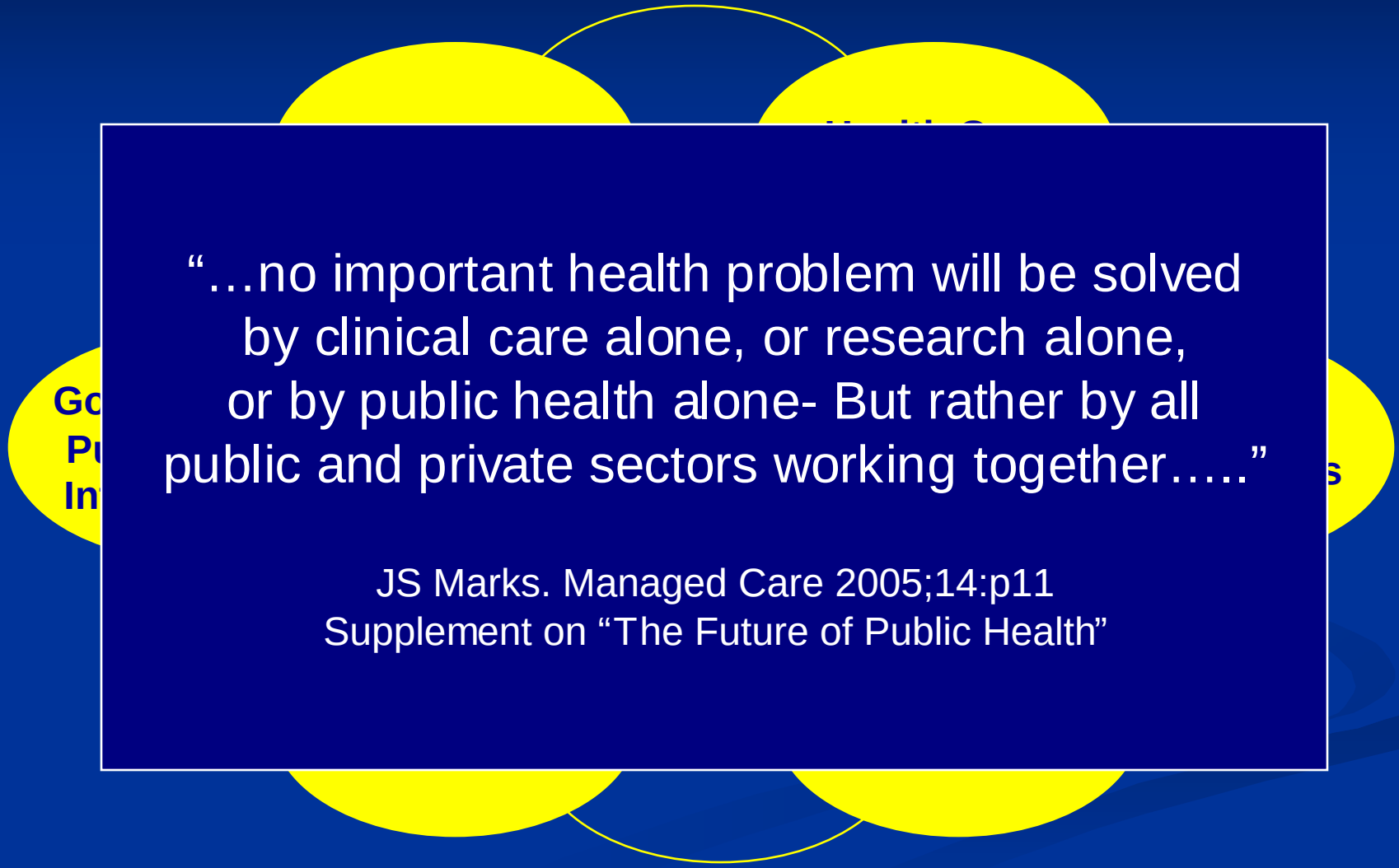
Khoury MJ et al. Am J Prev Med 2007

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"

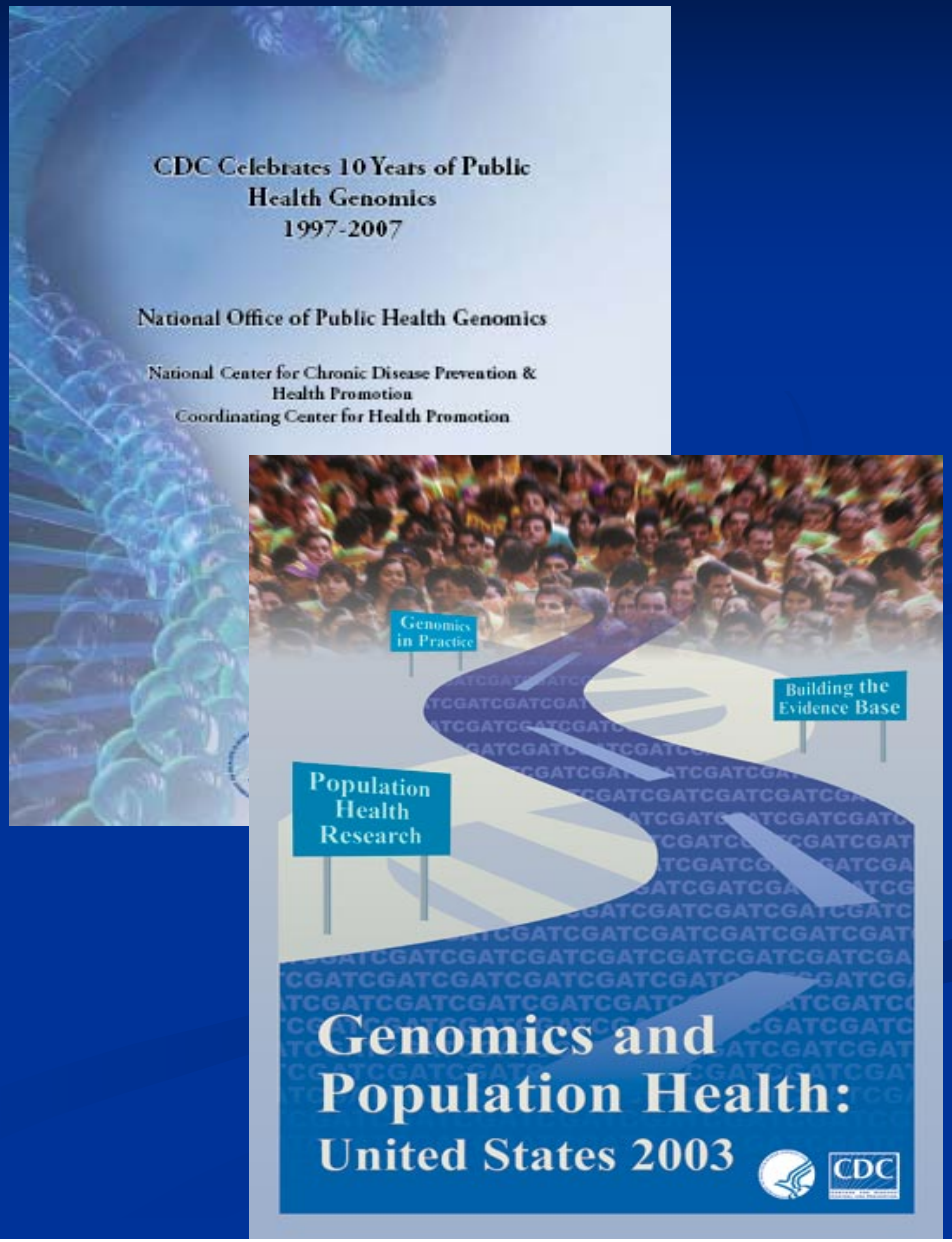
The Emergence of Public Health Genomics

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



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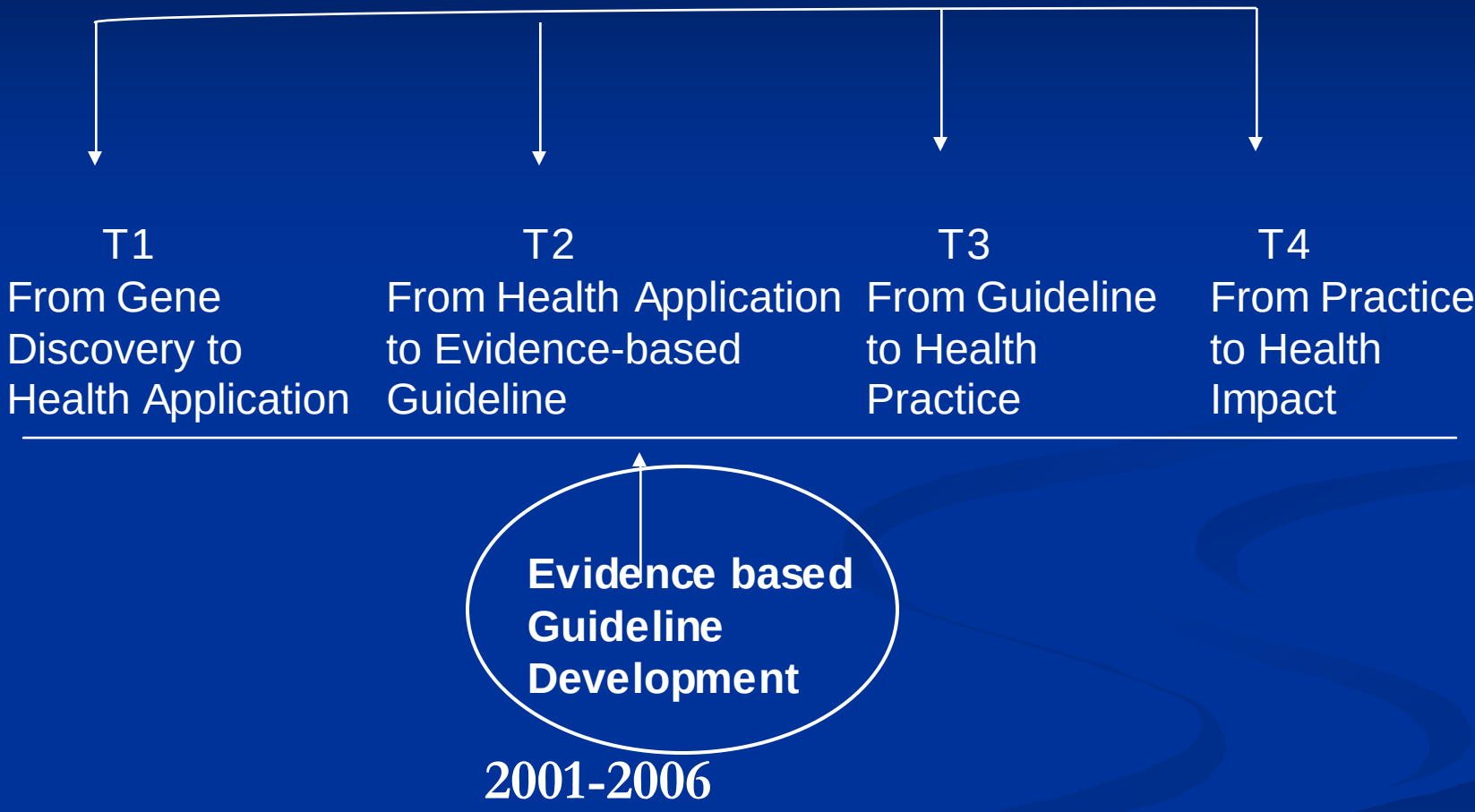
The Four Phases of Translation For Genomic Applications in Population Health

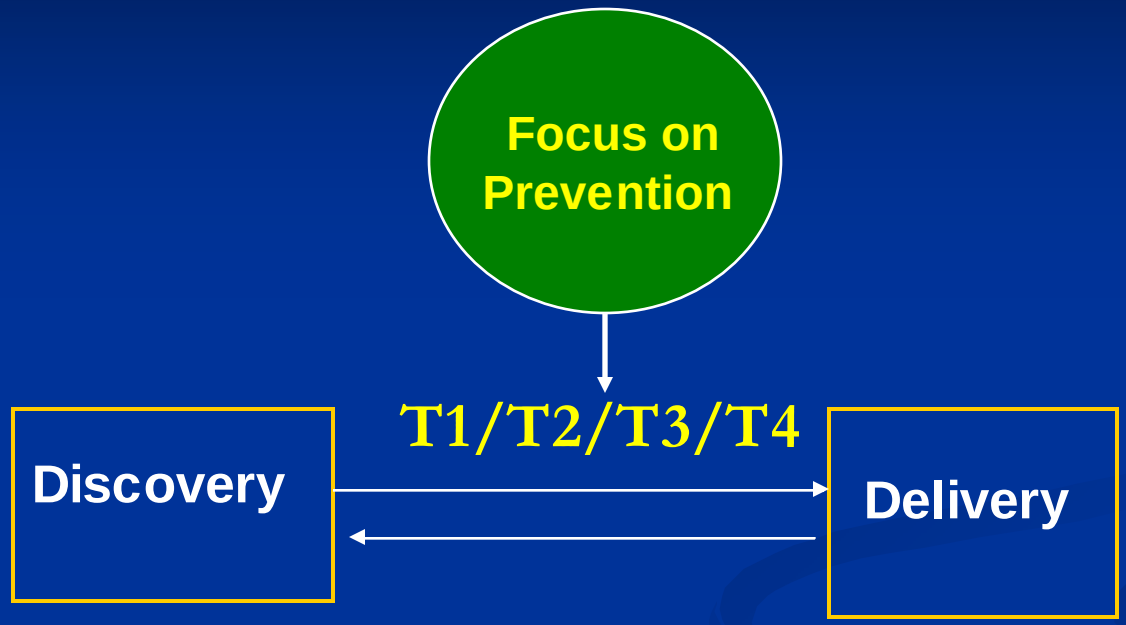


Less than 3% of published genomics research is T2 and beyond

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…

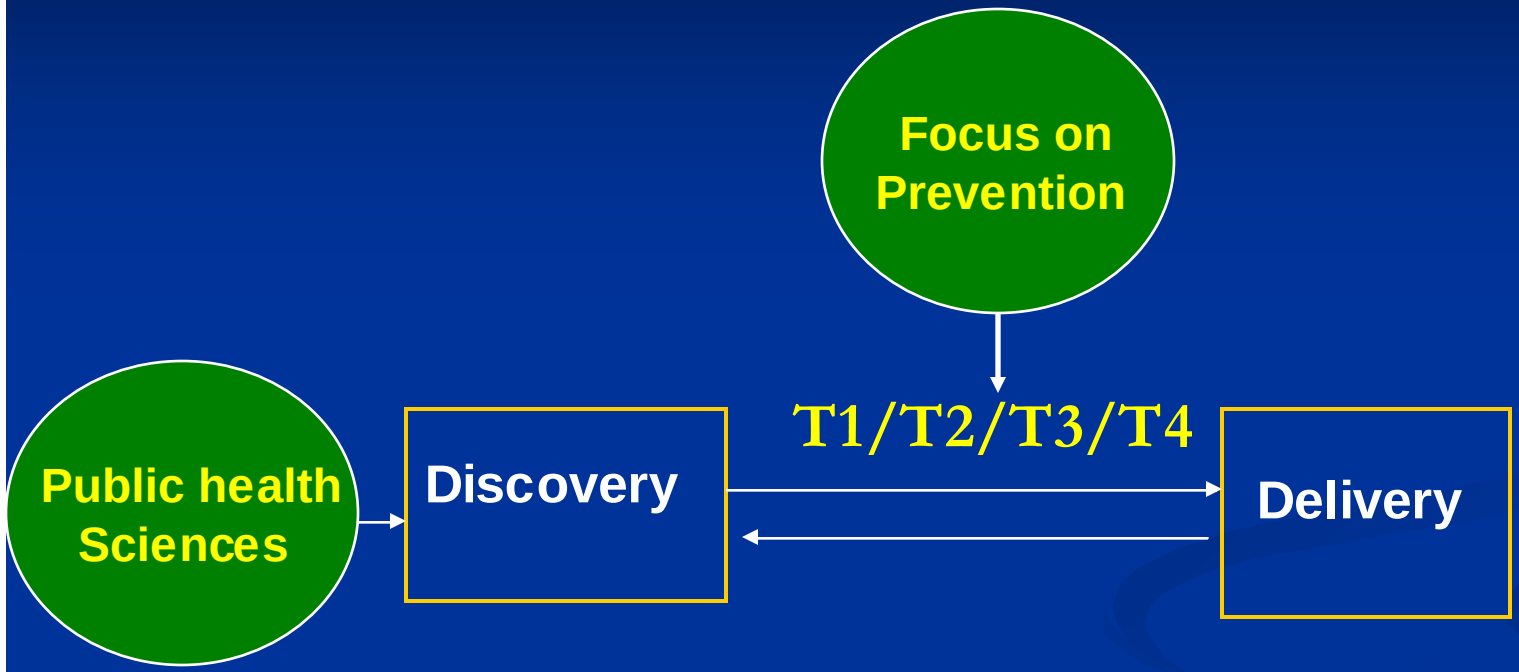
Condition	Genes	RR	Lifetime
Prostate Ca	HPC1, 2, 3	0.5	7%
Alzheimer's	APOE,FAD3,XAD	0.3	10%
Heart disease	APOB,CETP	2.5	70%
Colon Cancer	FCC4,APC	4.0	23%
Lung Cancer	NAT2	6.0	40%

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



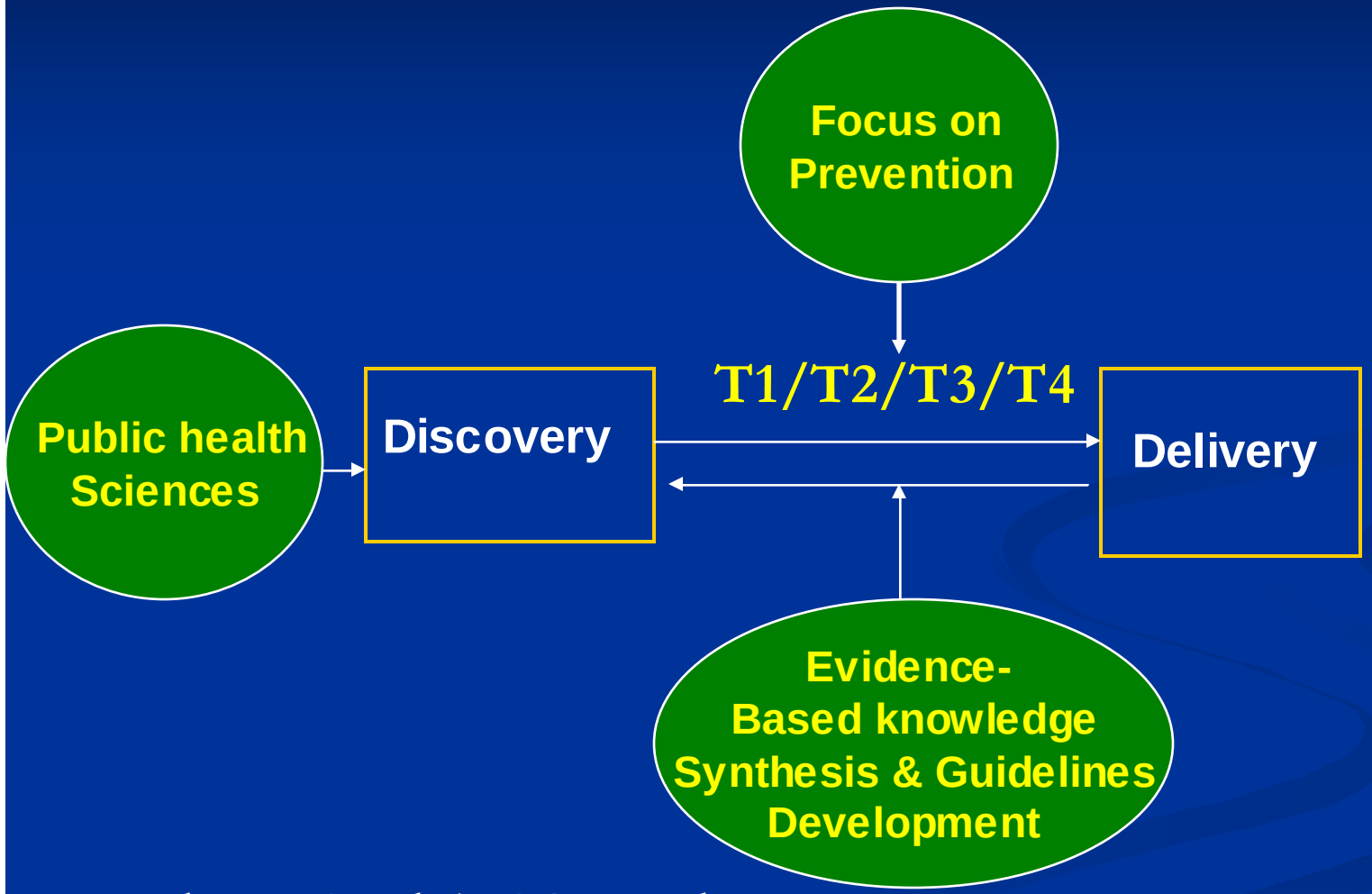
Khoury MJ et al. Am J Prev Med 2007

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

Open access, freely available online PLoS MEDICINE

Genetic Prediction of Future Type 2 Diabetes

Valeriya Lyssenko[1*], Peter Almgren[1], Dragi Anevski[1,2], Marju Orho-Melander[1], Marketa Sjögren[1], Carola Saloranta[3,4], Tiinamaija Tuomi[3,4], Leif Groop[1], 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
2 diabetes (T2D), Lyssenko and colleagues conclud
"genetic testing might become a future approach to
individuals at risk of developing T2D" [1]. One of th
most striking findings is an impressive 21.2-fold incr
risk for T2D in obese carriers of the *PPARG* PP and
SNP43/44 GG/TT genotypes with elevated fasting p
glucose (FPG).

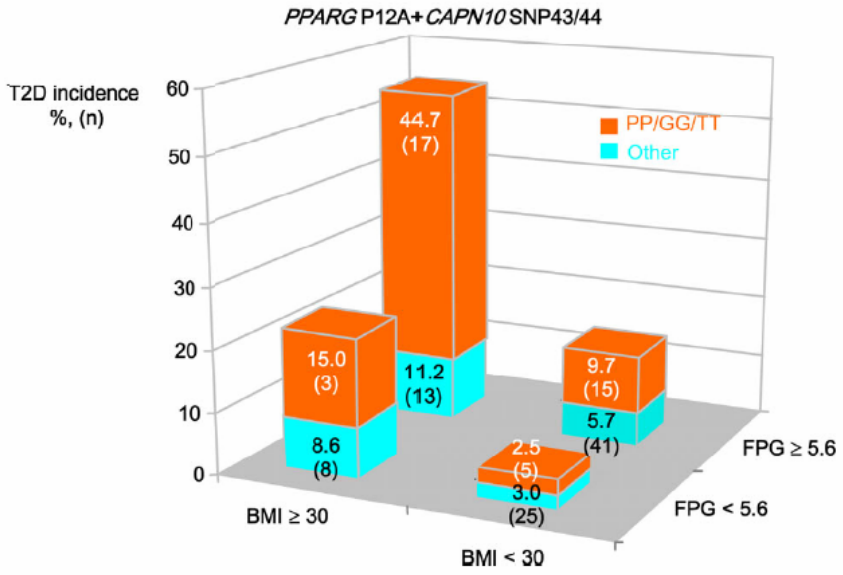
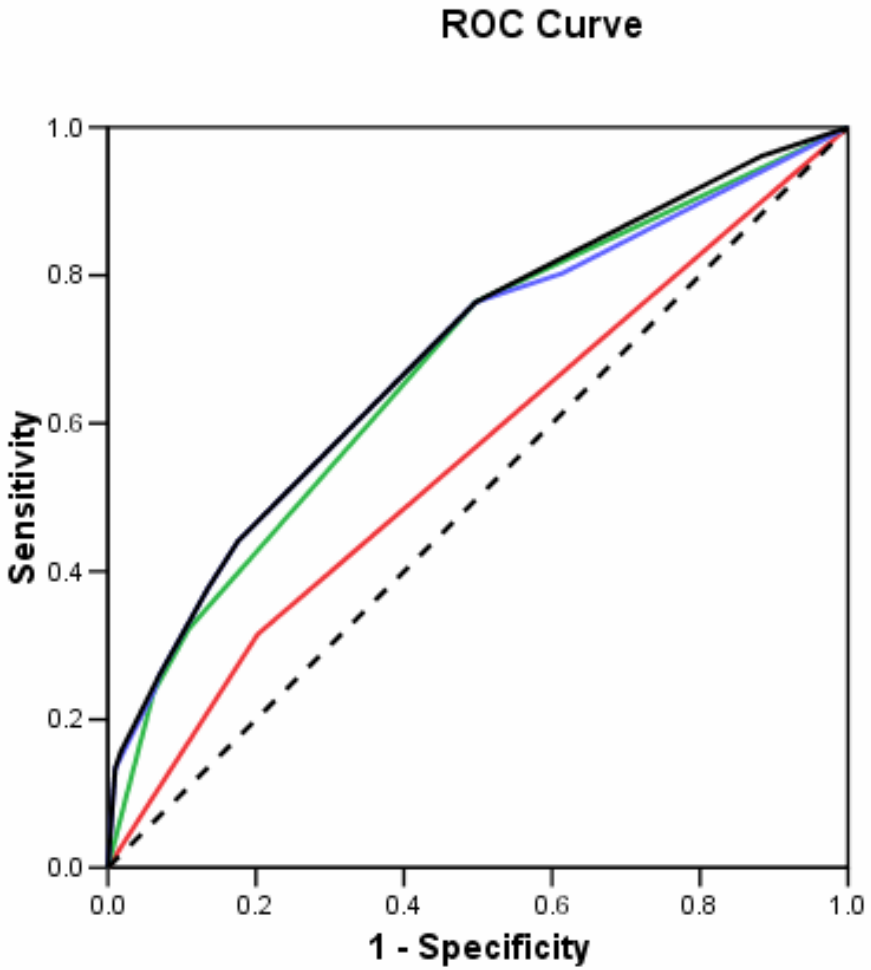
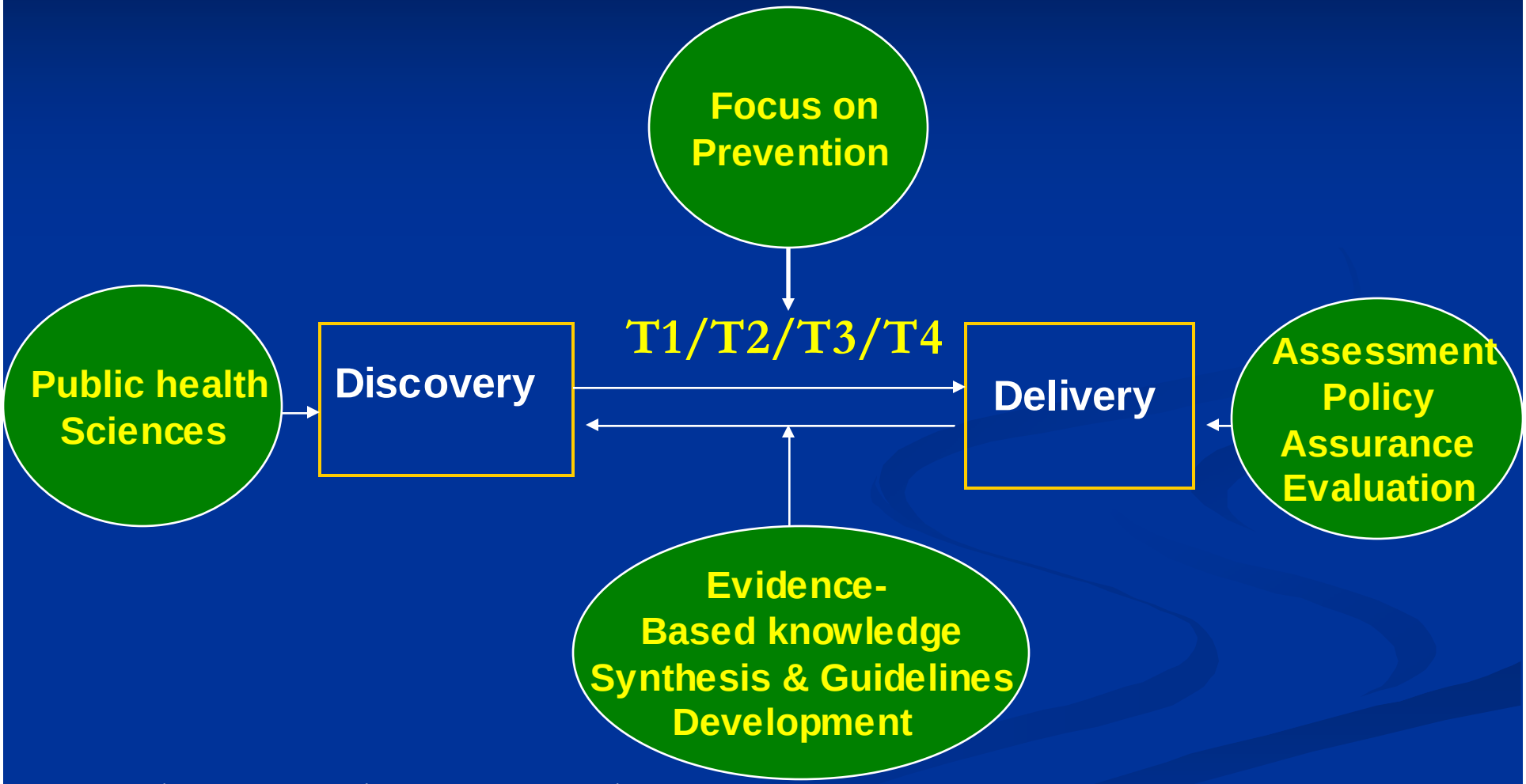


Figure 2. The Effects of Risk Genotypes of the *PPARG* P12A Poly-

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



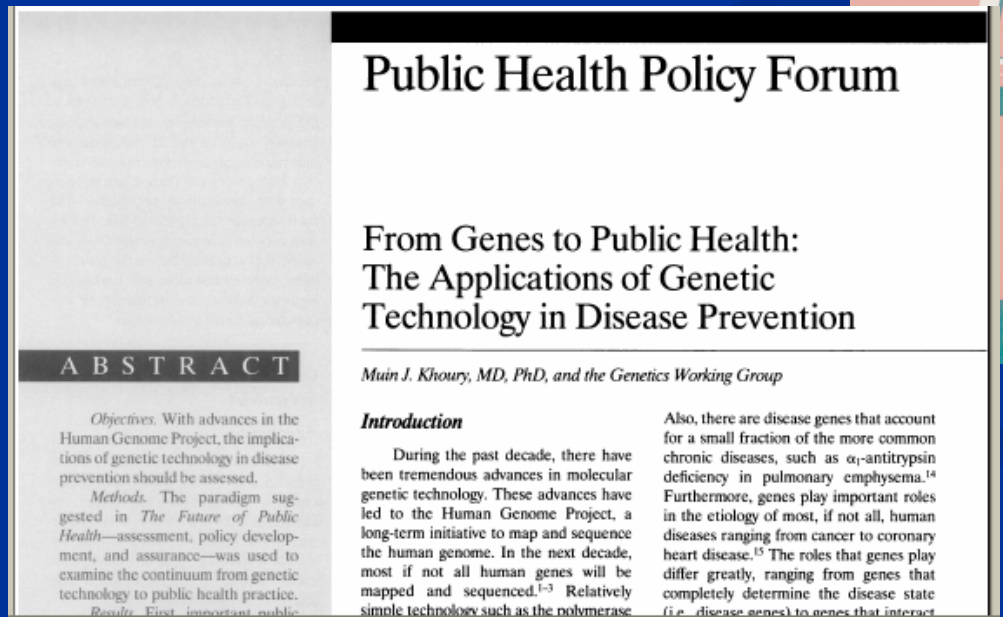
A "Population Health" Approach to Genomics Translation



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



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.

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

Gene Discovery ⇢ **Closing the Gap** ⇢ **Population Health**

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

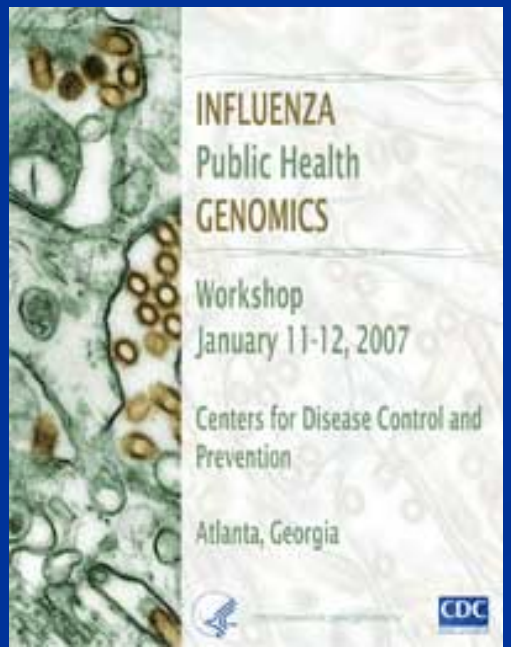
CDC Public Health Genomics Initiatives

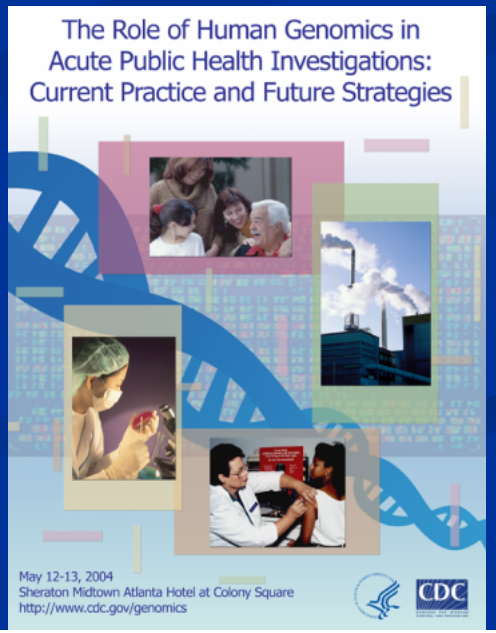
Population Studies

US Genome Profile

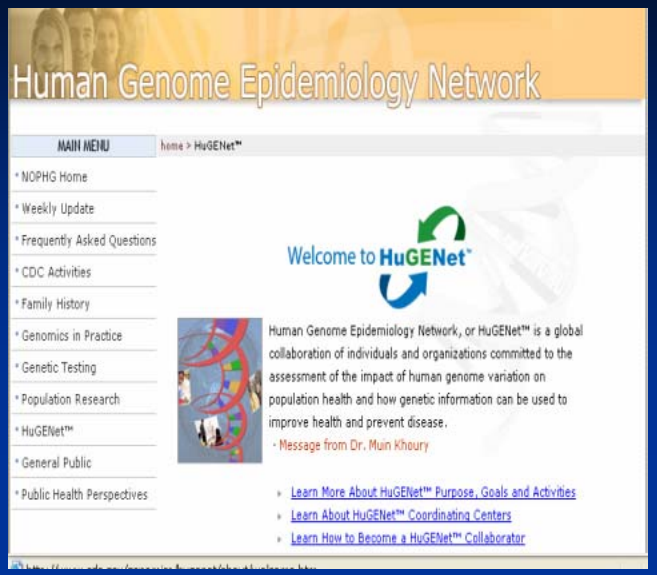
Public Health Studies

Gene Discovery ⇢ **Closing the Gap** ⇢ **Population Health**





CDC Public Health Genomics Initiatives



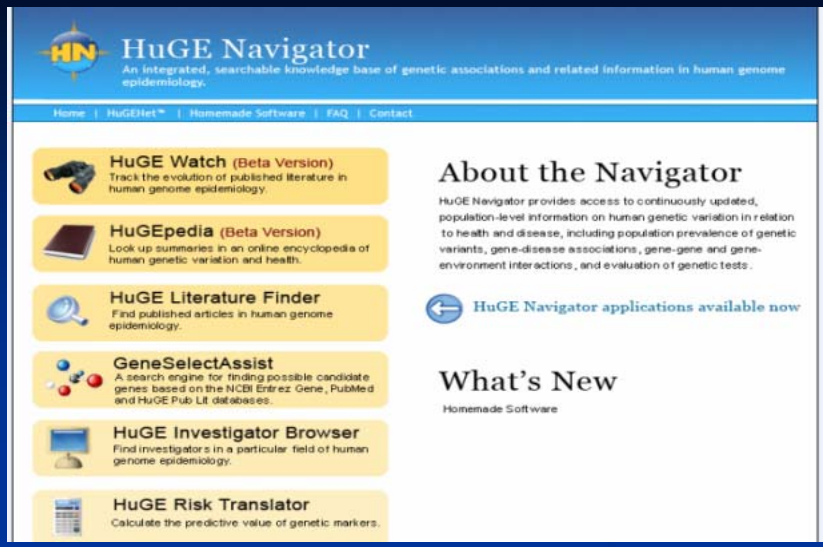
HuGENet

Human

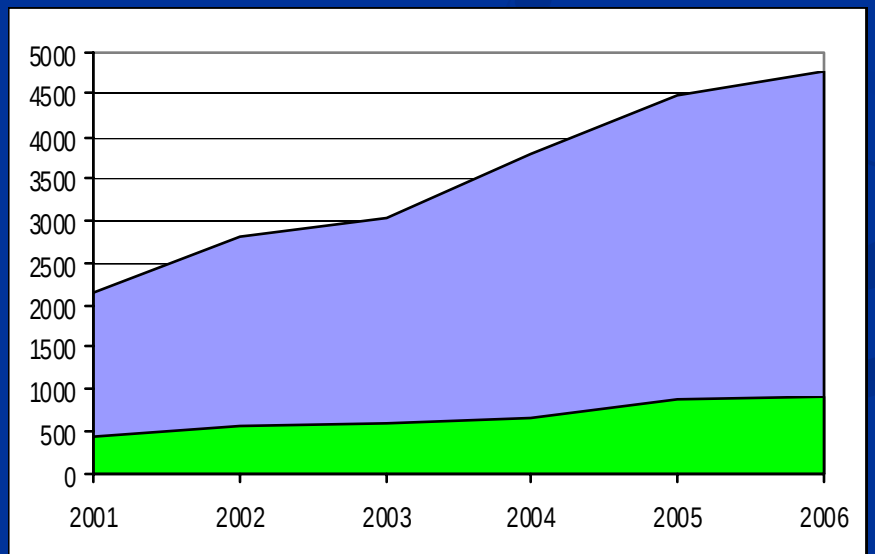
Genome

Epidemiology

Network



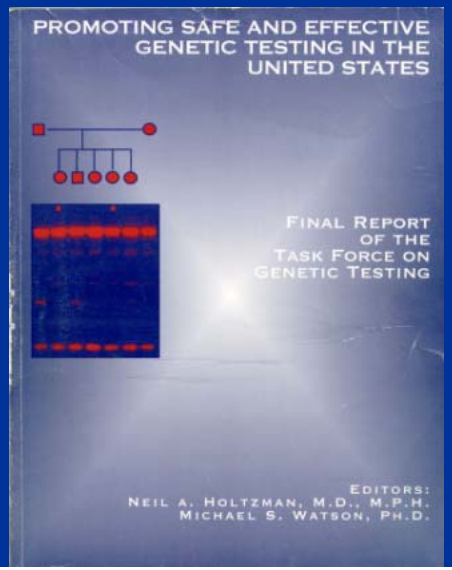
Gene Discovery ⋯▶ **Closing the Gap** ⋯▶ **Population Health**



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

SACGT

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

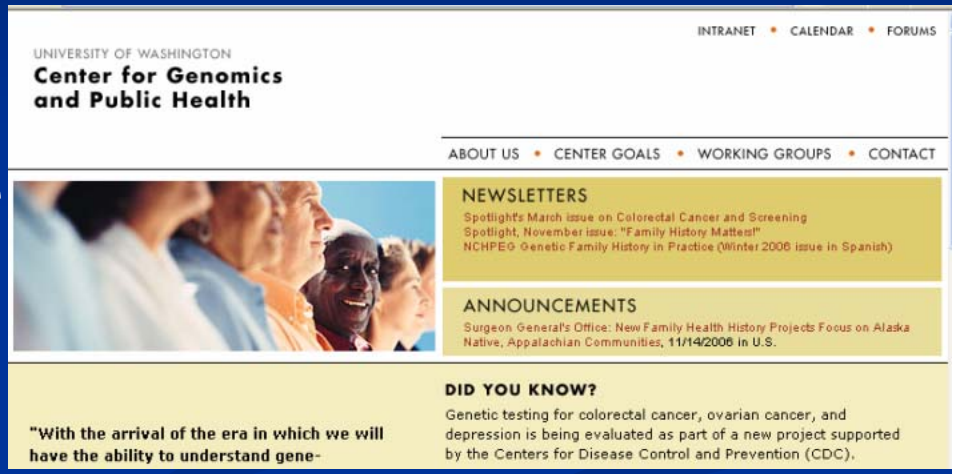
Website/Reports/

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



Integrating Genomics into State Public Health Programs

Family History Public Health Initiative

Benefit: Tools for Prevention

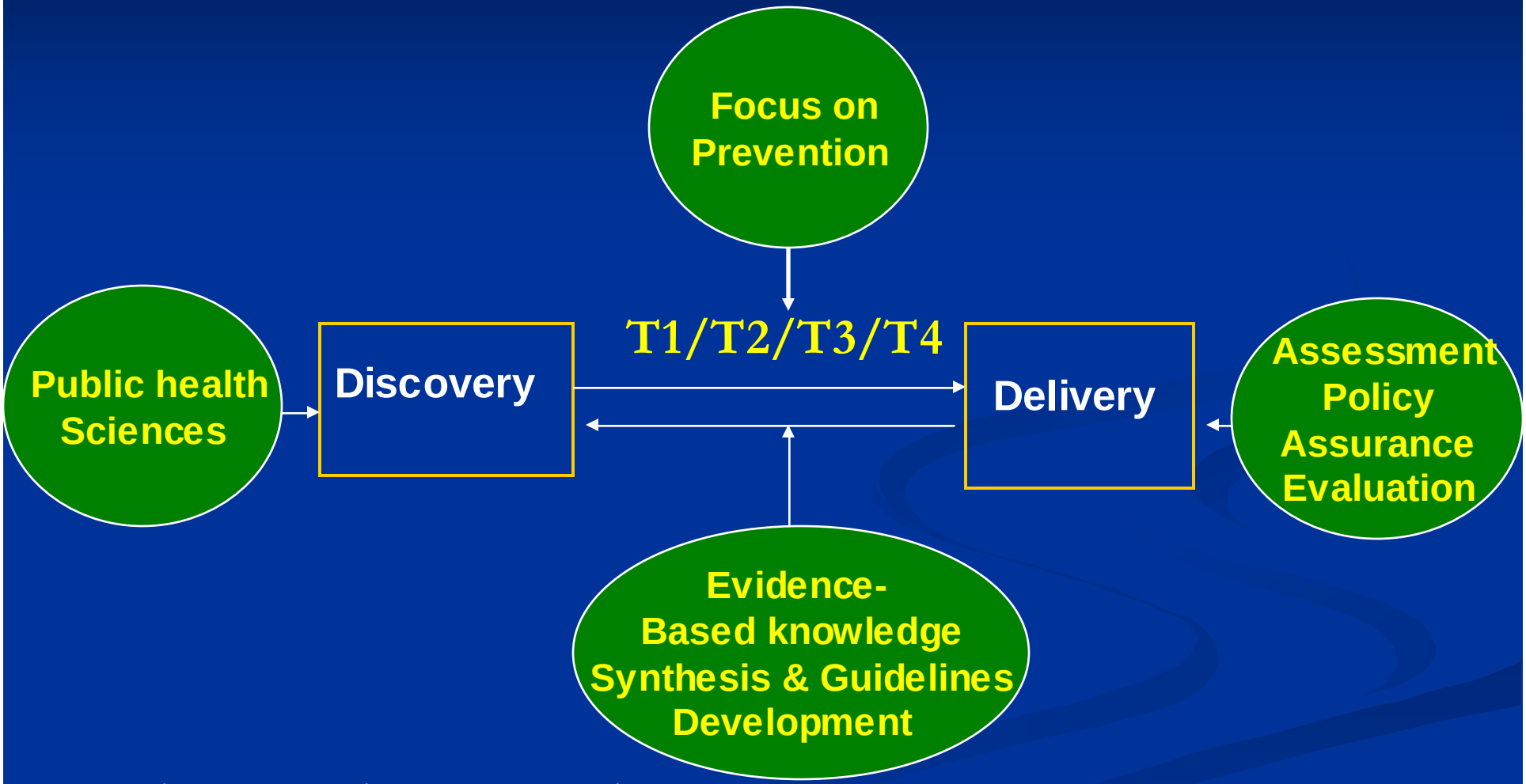
- Family history captures shared genes, behaviors, and environment
- Use to target screening, prevention
- CDC tool (6 diseases) & validation study in collaboration with NIH, academic centers
- Partnership with US Surgeon General

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