Implementation of Genomic Medicine:

A Public Health Approach

Muin J. Khoury MD, PhD

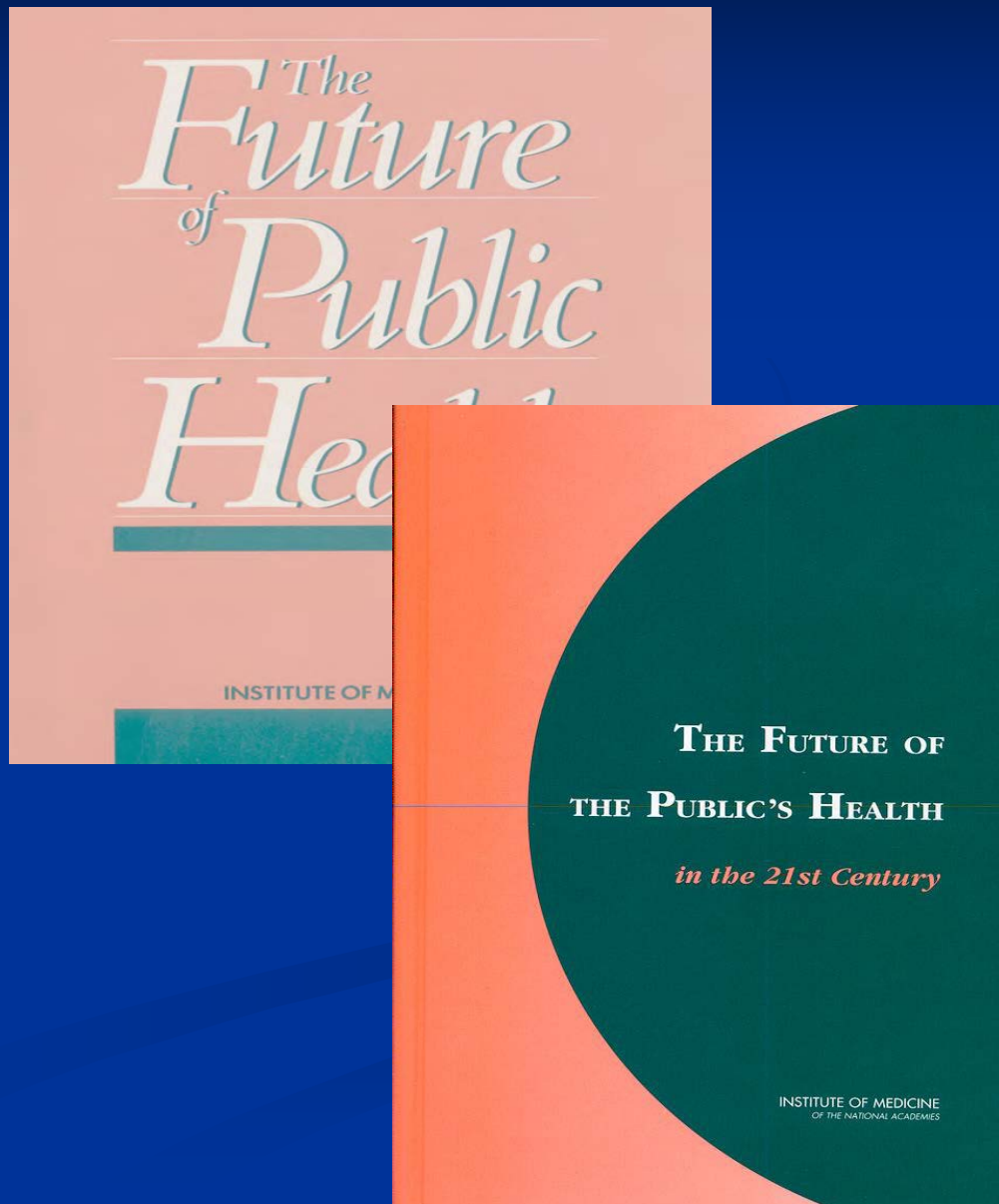
Office of Public Health Genomics, CDC

Outline

- What's public health got to do with genomic medicine?
- Public health genomics: 15 years on
- What are the priorities for public health genomics, 2012-2017?

What is Public Health?

- "An effort organized by society to protect, promote, and restore the people's health"
- 3 Essential Functions
  - Assessment
  - Policy Development
  - Assurance



CDC Priorities

- **Improving health security at home and around the world**
- **Better preventing the leading causes of illness, injury, disability, and death**
- **Strengthening public health – health care collaboration**

CDC "Winnable Battles": 6 key areas where public health can have a substantial impact

Tobacco

Motor Vehicle Injuries

Obesity, Nutrition, Physical Activity and Food Safety

Teen and Unintended Pregnancy

Healthcare-Associated Infections

HIV

Public Health Assessment Function

What Gets Measured Gets Done: Genomics, Surveillance Indicators and Healthy People 2020

Categories: genomics

September 13th, 2012 3:00 pm ET - Muin J Khoury, Director, Office of Public Health Genomics, Centers for Disease Control and Prevention
Katherine Kolor, Office of Public Health Genomics, Centers for Disease Control and Prevention

Public health surveillance indicators, such as those developed for the Healthy People initiative are useful for monitoring the development of genomic medicine in the United States. For several decades, Healthy People has established health benchmarks that are considered important metrics for tracking progress in health and healthcare in the United States.

The Healthy People objectives adopted in 2010 (HP 2020) introduced a new topic area to address the use of genomic testing in clinical and public health practice. HP 2020 includes two objectives related to genetic counseling and testing for hereditary cancer syndromes.

"The single most important thing that Public Health can do is to increase the degree to which decisions are made using good data" Tom Frieden, Jan 1, 2010

Public Health Assurance Function

CDC puts research into practice to advance public health, save lives

REBLOG From the CDC Foundation Blog

By Charles Stokes

May 13, 2013

"The best research will not save lives if it's not used…we have to invest in programs"
Tom Frieden, CDC Director, May 2013

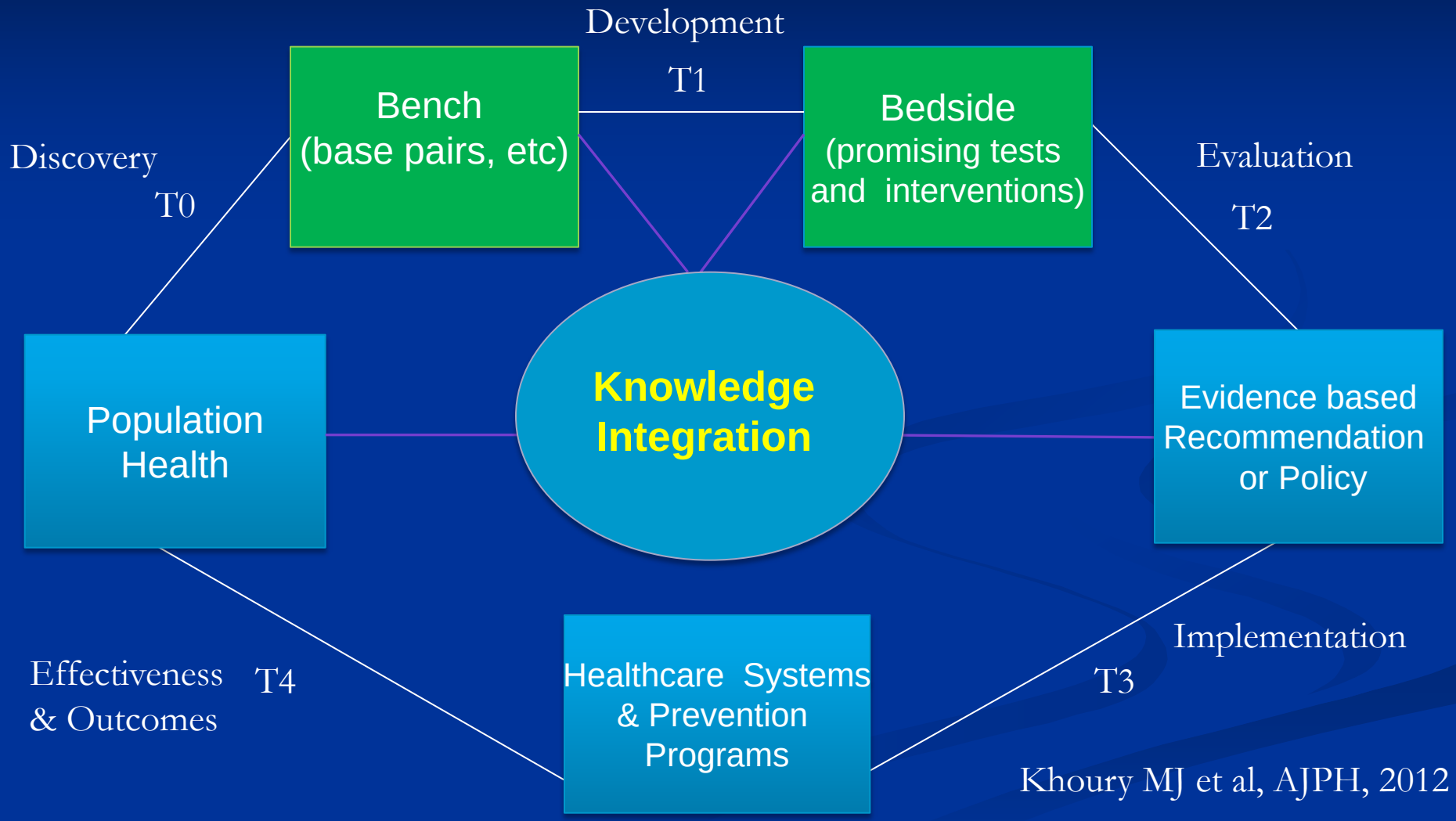
Outline

- What's public health got to do with genomic medicine?
- Public health genomics 15 years on
- What are the priorities for public health genomics, 2012-2017?

CDC Public Health Genomics Movement

- 1997- Office of Public Health Genomics
- 1998- First National Conference
- 2000- Genomic Competencies for Public Health
- 2001- “Model” State Public Health Programs
- 2002- Family History Public Health Initiative
- 2003- NHANES Genomics initiative
- 2005- EGAPP Initiative
- 2006- GRaPHInt global public health genomics
- 2008- Model Translation Research and Programs
- 2009- GAPPNet collaboration
- 2010- Fourth National Conference
- 2011- A New Beginning

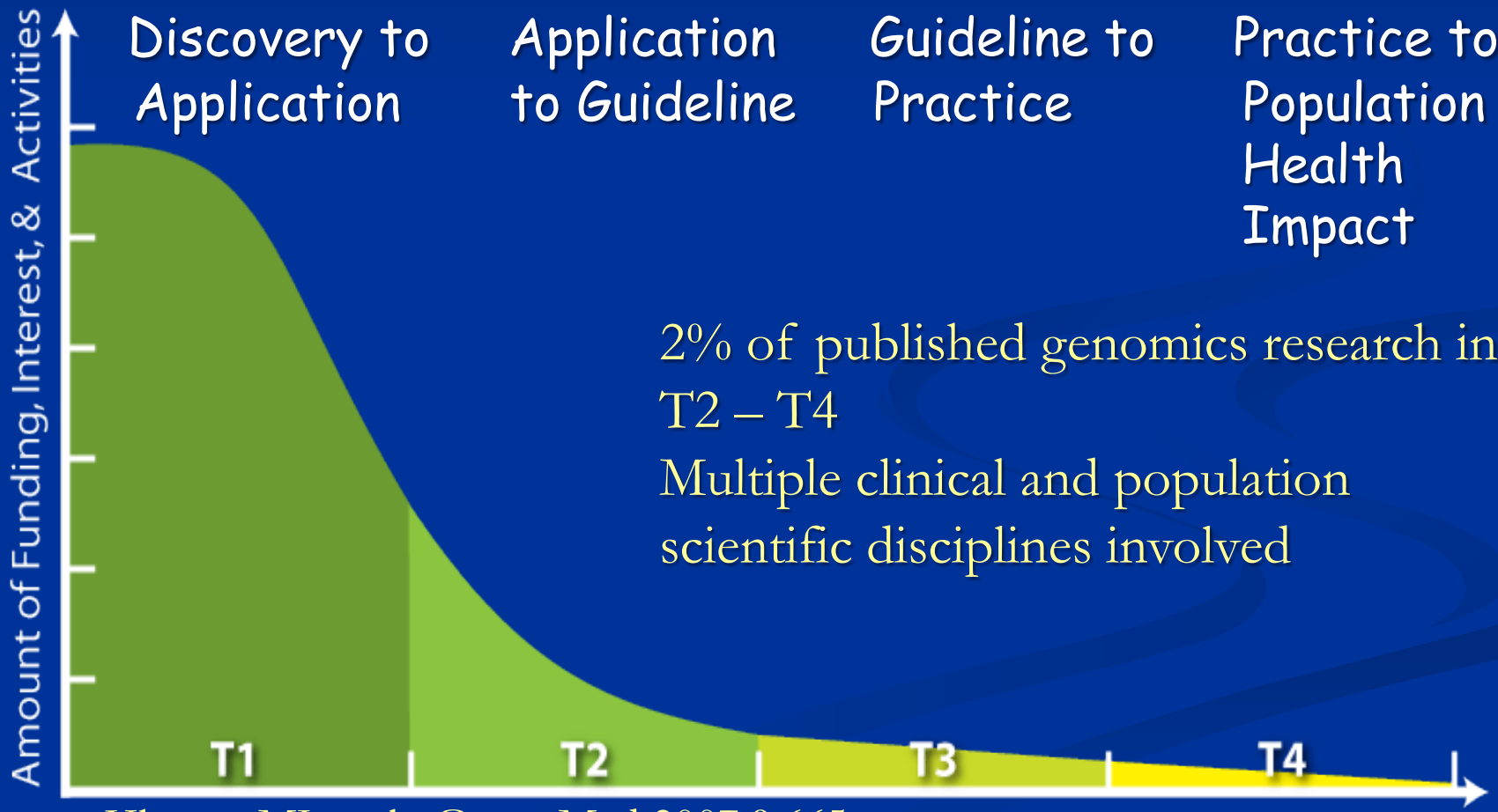
The Public Health Genomics Model for Genomics Implementation



Khoury MJ et al, AJPH, 2012

Limited Translational Research in Genomics Beyond Bench to Bedside

T0 ↔ T1 ↔ T2 ↔ T3 ↔ T4



2% of published genomics research in T2 – T4

Multiple clinical and population scientific disciplines involved

Khoury MJ et al, Genet Med 2007;9:665

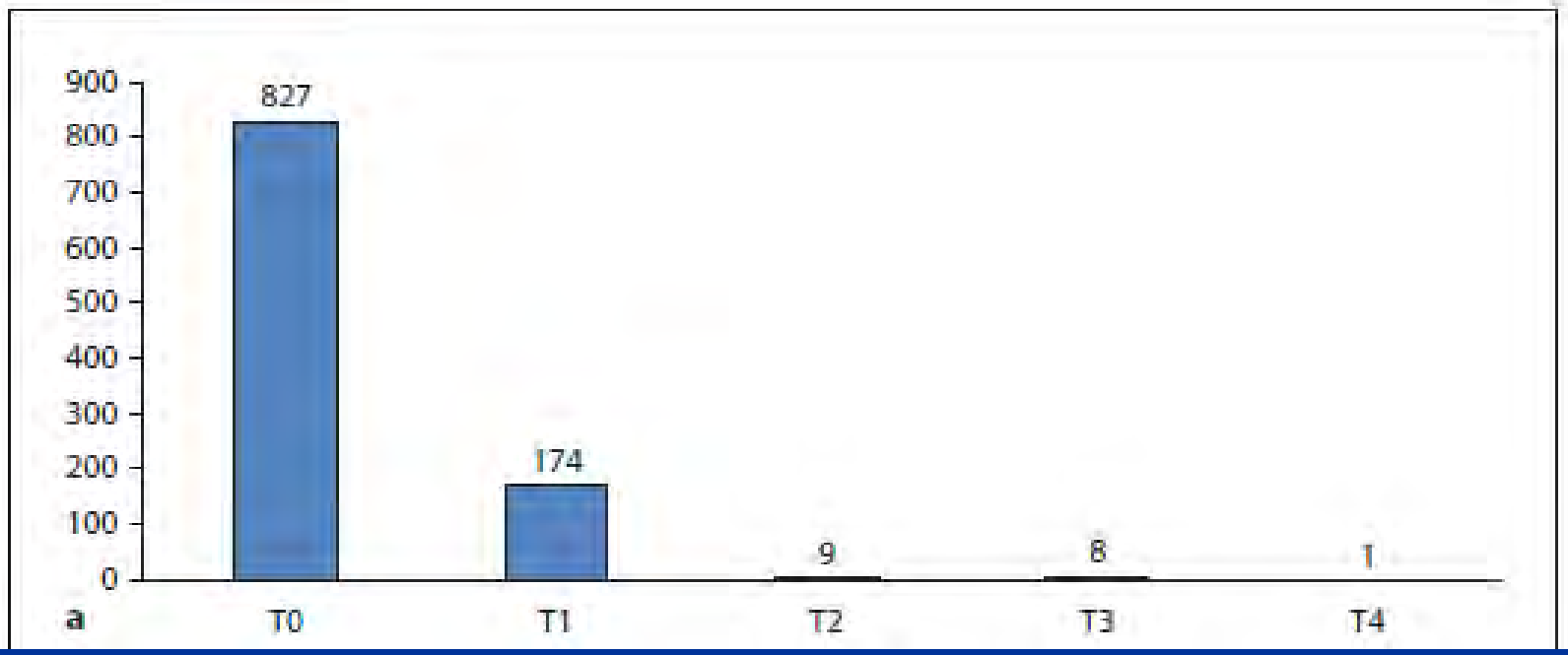
Genomics Research
The Road Less Traveled

Public Health Genomics 2010

Translational Research in Cancer Genetics: The Road Less Traveled

S.D. Schully[a] C.B. Benedicto[b] E.M. Gillanders[a] S.S. Wang[c] M.J. Khoury[a, d]

[a]Division of Cancer Control and Population Sciences and [b]Office of Workforce Development, National Cancer Institute, Bethesda, Md., [c]Division of Etiology, Department of Population Sciences, City of Hope, Duarte, Calif., and



Population Data Needed!

ORIGINAL RESEARCH ARTICLE | Genetics inMedicine

Utilization of epidermal growth factor receptor (*EGFR*) testing in the United States: a case study of T3 translational research

Julie A. Lynch, PhD, RN[1,3], Muin J. Khoury, MD, PhD[2], Ann Borzecki, MD, MPH[3], Jerry Cromwell, PhD[4], Laura L. Hayman, PhD, RN[5], Pat Reid Ponte, D.N.Sc., RN[6], Glenn A. Miller, PhD[7,8] and Christopher S. Lathan, MD, MPH[6]

Purpose: We examined hospital use of the epidermal growth factor receptor assay in patients with lung cancer in the United States. Our goal was to inform the development of a model to predict phase 3 translation of guideline-directed molecular diagnostic tests.

Methods: This was a retrospective observational study. Using logistic regression, we analyzed the association between hospitals' institutional and regional characteristics and the likelihood that an epidermal growth factor receptor assay would be ordered.

Results: Significant institutional predictors included affiliation with an academic medical center (odds ratio, 1.48; 95% confidence interval, 1.20–1.83), participation in a National Cancer Institute clinical research cooperative group (odds ratio, 2.06, 1.66–2.55), and availability of positron emission tomography scan (odds ratio, 1.44, 1.07–1.94) and cardiothoracic surgery (odds ratio, 1.90, 1.52–2.37) services. Significant regional predictors included metropolitan county (odds ratio, 2.08, 1.48–2.91), population with above-average education (odds ratio, 1.46, 1.09–1.96), and population with above-average income (odds ratio, 1.46, 1.04–2.05). Distance from a National Cancer Institute cancer center was a negative predictor (odds ratio, 0.996, 0.995–0.998), with a 34% decrease in likelihood for every 100 miles.

Conclusion: In 2010, only 12% of US acute-care hospitals ordered the epidermal growth factor receptor assay, suggesting that most patients with lung cancer did not have access to this test. This case study illustrated the need for: (i) increased dissemination and implementation research, and (ii) interventions to improve adoption of guideline-directed molecular diagnostic tests by community hospitals.

Genet Med advance online publication 28 February 2013

Key Words: dissemination and implementation; EGFR assay; equity in access; lung cancer genomics; T3 translation

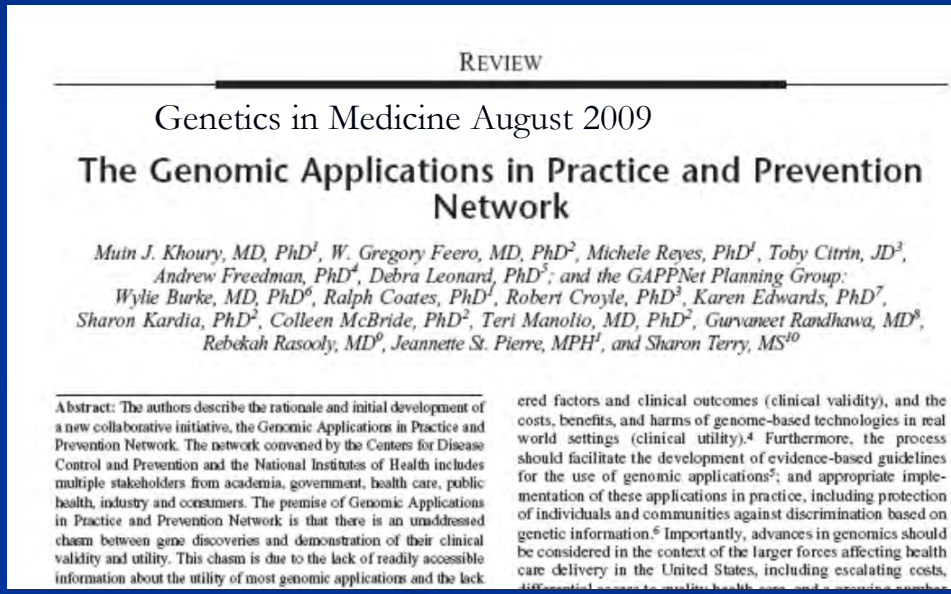
Predictors of Use: Affiliation with academic center, participation in NCI cooperative group, metropolitan county, education, income

Knowledge Integration: EGAPP Working Group

- Independent, multidisciplinary, non-federal panel established by CDC in 2004
- Established a systematic, evidence-based process to assess validity & utility of genomic tests & family health history applications.
  - New methods for evidence synthesis and modeling in 2013, including next generation sequencing and stratified screening
- Six recommendation statements to date:
  - Colorectal cancer, breast cancer, heart disease, clotting disorders, depression
- New recommendations in 2013
  - Prostate cancer, diabetes, and more
- Uncovering major knowledge gaps
  - Setting a translational research agenda

What is GAPPNet?

- Collaboration of individuals and organizations interested in validating and translating genome-based applications into practice and prevention
- Vision: to realize the promise of genomics in treating and preventing disease, improving health and reducing health disparities



REVIEW

Genetics in Medicine August 2009

The Genomic Applications in Practice and Prevention Network

Muin J. Khoury, MD, PhD[1], W. Gregory Feero, MD, PhD[2], Michele Reyes, PhD[1], Toby Citrin, JD[3], Andrew Freedman, PhD[4], Debra Leonard, PhD[5]; and the GAPPNet Planning Group: Wylie Burke, MD, PhD[6], Ralph Coates, PhD[1], Robert Croyle, PhD[3], Karen Edwards, PhD[7], Sharon Kardia, PhD[2], Colleen McBride, PhD[2], Teri Manolio, MD, PhD[2], Gurvaneet Randhawa, MD[8], Rebekah Rasooly, MD[9], Jeannette St. Pierre, MPH[1], and Sharon Terry, MS[10]

Abstract: The authors describe the rationale and initial development of a new collaborative initiative, the Genomic Applications in Practice and Prevention Network. The network convened by the Centers for Disease Control and Prevention and the National Institutes of Health includes multiple stakeholders from academia, government, health care, public health, industry and consumers. The premise of Genomic Applications in Practice and Prevention Network is that there is an unaddressed chasm between gene discoveries and demonstration of their clinical validity and utility. This chasm is due to the lack of readily accessible information about the utility of most genomic applications and the lack ered factors and clinical outcomes (clinical validity), and the costs, benefits, and harms of genome-based technologies in real world settings (clinical utility).[4] Furthermore, the process should facilitate the development of evidence-based guidelines for the use of genomic applications[5]; and appropriate implementation of these applications in practice, including protection of individuals and communities against discrimination based on genetic information.[6] Importantly, advances in genomics should be considered in the context of the larger forces affecting health care delivery in the United States, including escalating costs,

GAPPNet

CDC SAFER·HEALTHIER·PEOPLE™

GAPPNet Meeting
October 29-30, 2009 - Ann Arbor, Michigan

GAPPNet

CDC
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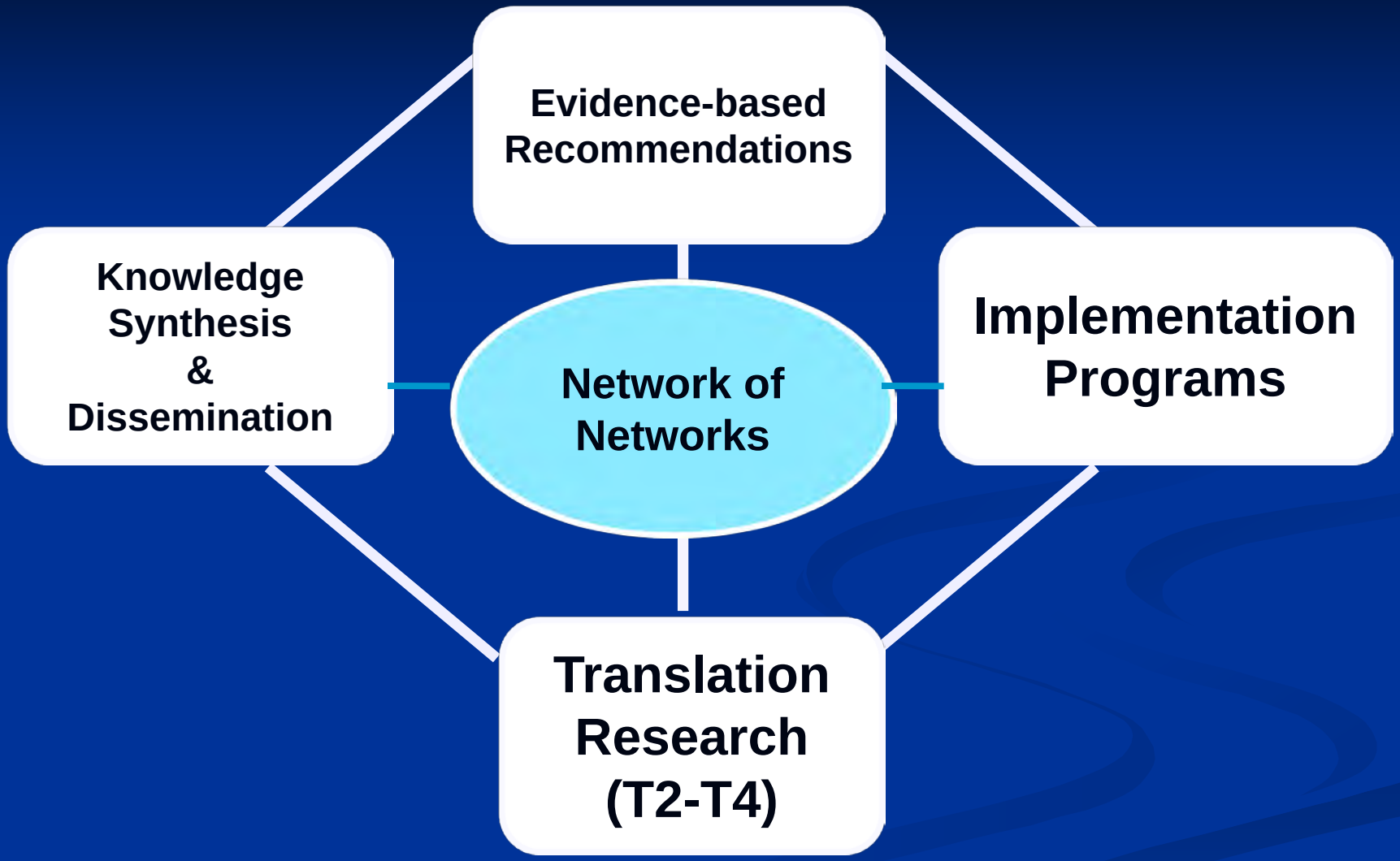
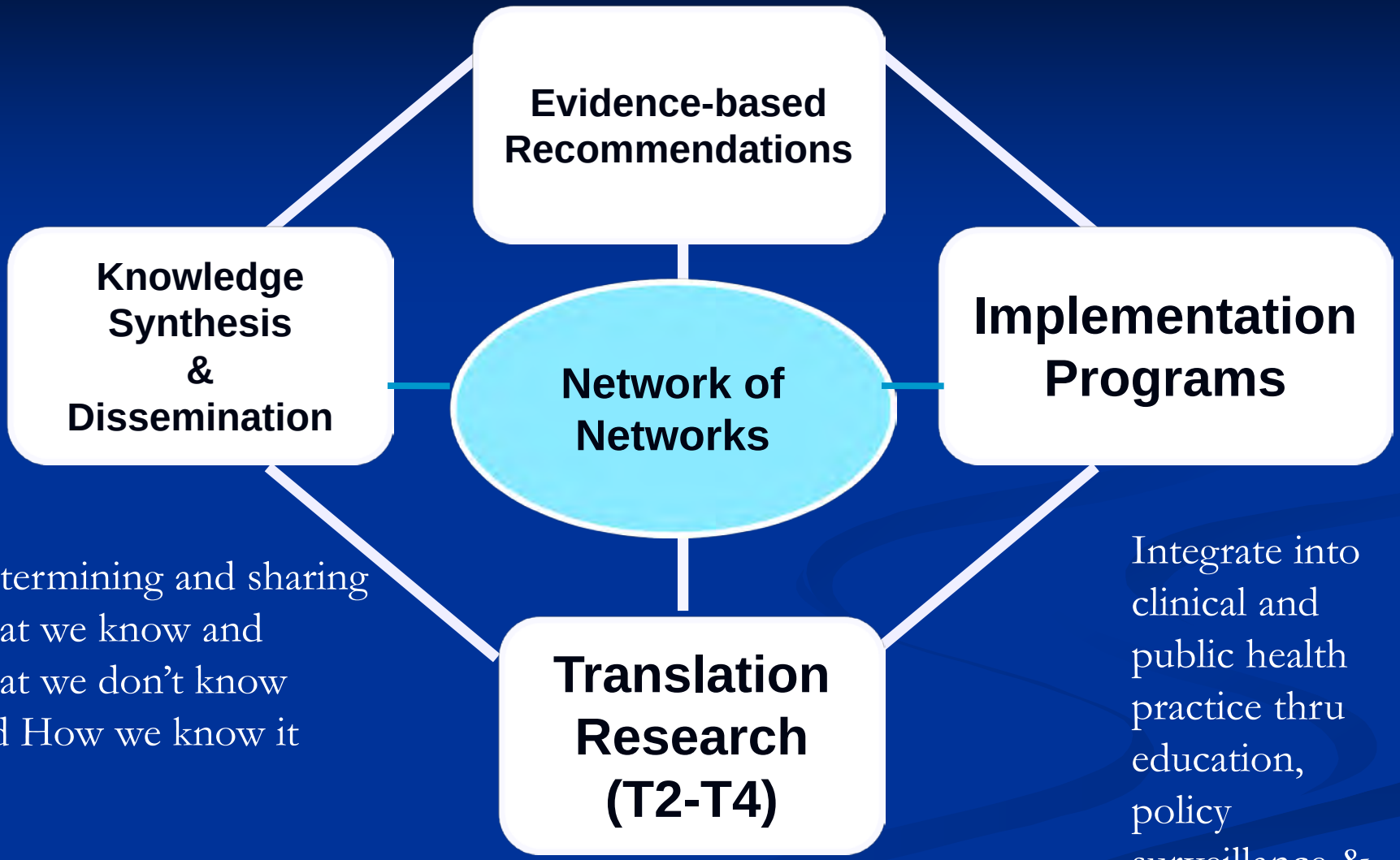
4 Domains of GAPPNet



Linking evidence to practice
In a credible and transparent way



Determining and sharing what we know and what we don't know and How we know it

Integrate into clinical and public health practice thru education, policy surveillance & evaluation

Research to fill gaps and how to implement

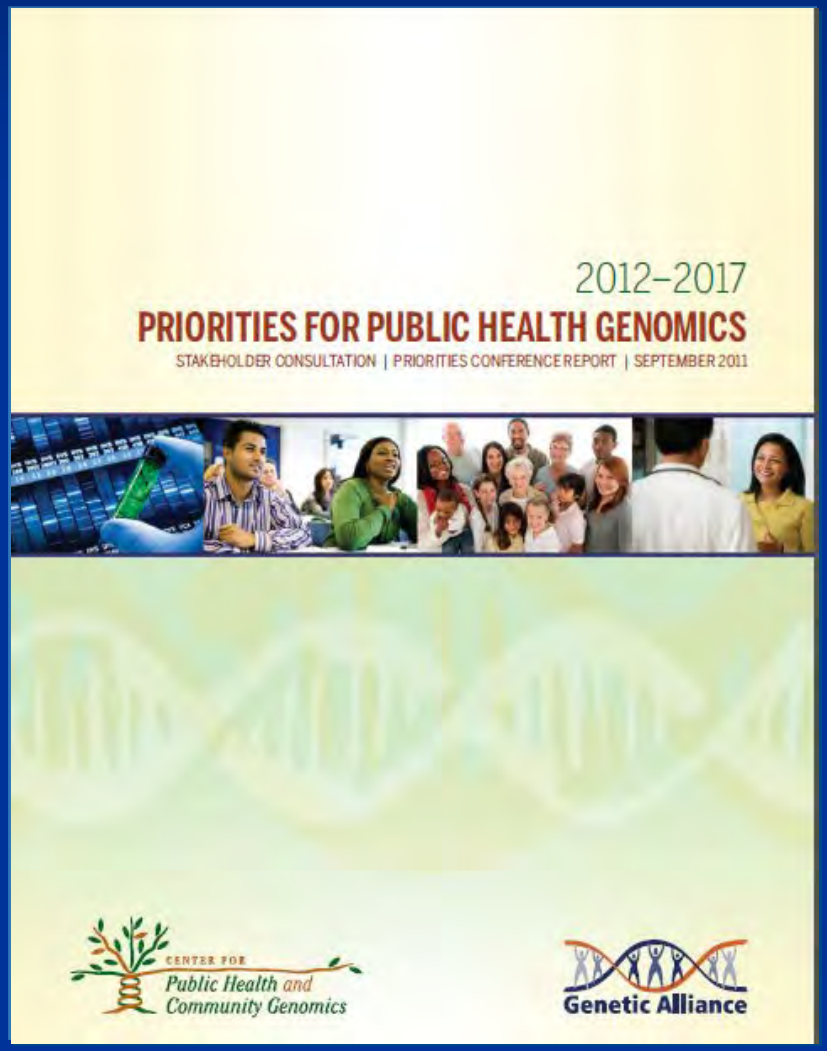
GAPPNet

Outline

- What's public health got to do with genomic medicine?
- Public health genomics 15 years on
- What are the priorities for public health genomics, 2012-2017?

Public Health Genomics Priorities 2012-2017

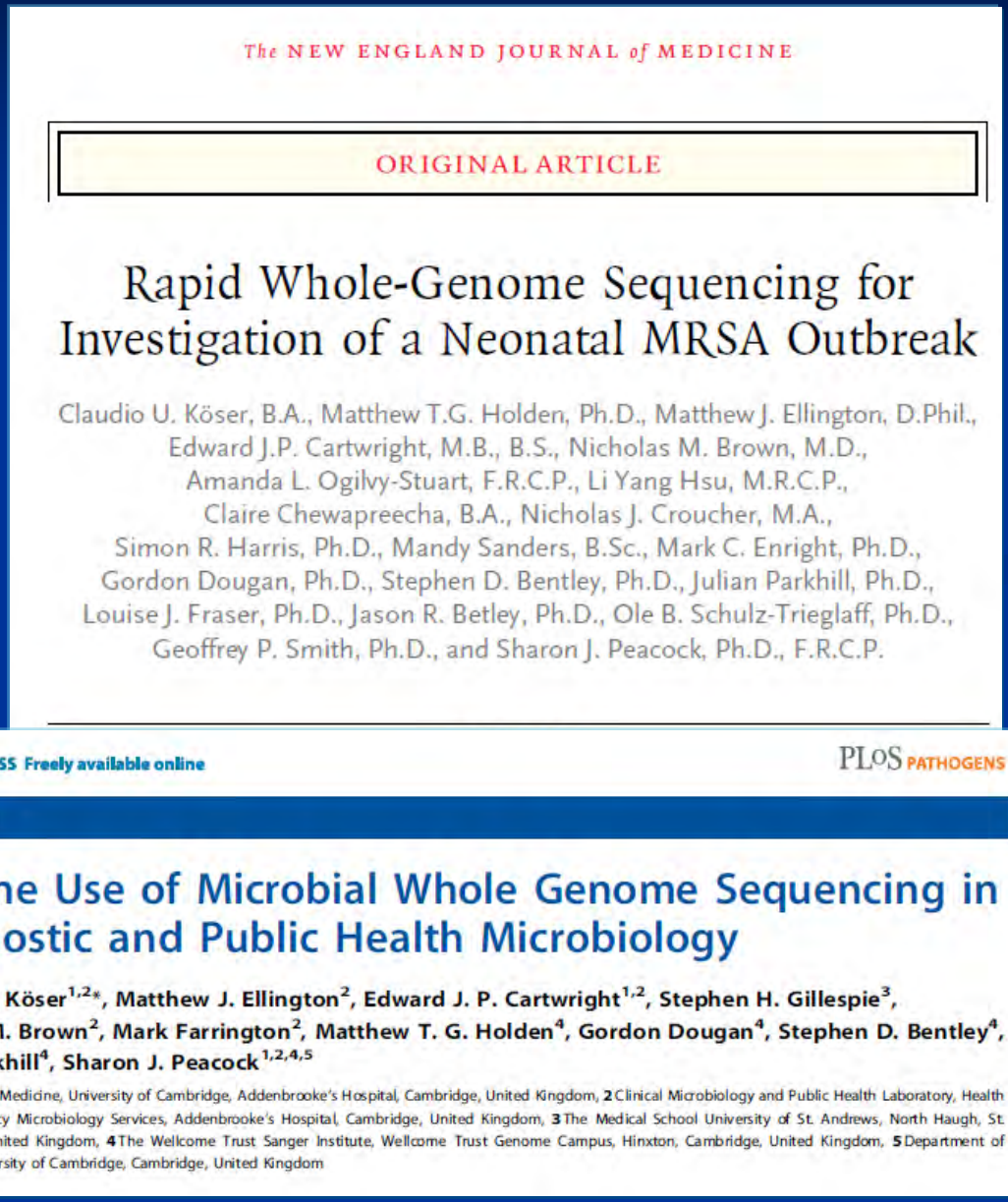
2011



2012

CDC Advanced Molecular Detection Initiative

- Improve pathogen identification &detection
- Adapt new diagnostics to meet public health needs
- Help states meet future reference testing needs
- Implement enhanced & integrated lab information systems
- Develop prediction, modeling, and better surveillance tools



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rapid Whole-Genome Sequencing for Investigation of a Neonatal MRSA Outbreak

Claudio U. Köser, B.A., Matthew T.G. Holden, Ph.D., Matthew J. Ellington, D.Phil., Edward J.P. Cartwright, M.B., B.S., Nicholas M. Brown, M.D., Amanda L. Ogilvy-Stuart, F.R.C.P., Li Yang Hsu, M.R.C.P., Claire Chewapreecha, B.A., Nicholas J. Croucher, M.A., Simon R. Harris, Ph.D., Mandy Sanders, B.Sc., Mark C. Enright, Ph.D., Gordon Dougan, Ph.D., Stephen D. Bentley, Ph.D., Julian Parkhill, Ph.D., Louise J. Fraser, Ph.D., Jason R. Betley, Ph.D., Ole B. Schulz-Trieglaff, Ph.D., Geoffrey P. Smith, Ph.D., and Sharon J. Peacock, Ph.D., F.R.C.P.

OPEN ACCESS Freely available online

PLoS PATHOGENS

Opinion

Routine Use of Microbial Whole Genome Sequencing in Diagnostic and Public Health Microbiology

Claudio U. Köser[1,2*], Matthew J. Ellington[2], Edward J. P. Cartwright[1,2], Stephen H. Gillespie[3], Nicholas M. Brown[2], Mark Farrington[2], Matthew T. G. Holden[4], Gordon Dougan[4], Stephen D. Bentley[4], Julian Parkhill[4], Sharon J. Peacock[1,2,4,5]

1 Department of Medicine, University of Cambridge, Addenbrooke's Hospital, Cambridge, United Kingdom, 2 Clinical Microbiology and Public Health Laboratory, Health Protection Agency Microbiology Services, Addenbrooke's Hospital, Cambridge, United Kingdom, 3 The Medical School University of St. Andrews, North Haugh, St Andrews Fife, United Kingdom, 4 The Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, United Kingdom, 5 Department of Pathology, University of Cambridge, Cambridge, United Kingdom

CDC Evidence-based Classification of Genomic Tests and Family History to Inform Policy and Practice

Tier 1: Recommended for clinical use by evidence-based panels, based on systematic review of evidence of validity and utility.

Tier 2: May be useful for informed decision making, based on demonstrated validity, and promising utility.

Tier 3: Not ready for clinical use, due to validity or utility not demonstrated, or systematic assessment finding harms outweigh benefits.

Healthy People 2020

http://www.cdc.gov/genomics/gtesting/tier.htm

Genomic Applications in Research and Practice, by Tier of Evidence

Genomic Applications	Tier 1	Tier 2	Tier 3
Definition	Established validity utility +evidence Rx	Established Validity + promising utility	Unclear Validity & Utility
Examples	Lynch, BRCA, FH, Newborn Screening	FDA pharmaco-genomic drug labels;	Whole Genome Sequence, personal genomic tests
Actions	Implement in general practice	Informed decision making in practice	Do not implement in general practice
Research	Implementation & outcomes research (T3-T4)	Comp Effectiveness Res, Patient-centered OR, Trials (T2-T4)	Validity & efficacy research (T1-T2)
Potential for disparities	High for disparities in implementation	High for both research & implementation	High for research disparities

Selected Emerging Tier 1 Genomic Applications

- Hereditary Breast and Ovarian Cancer (BRCA)
- Hereditary Nonpolyposis Colorectal Cancer (Lynch Syndrome)
- Familial Hypercholesterolemia

Selected Tier 1 Genomic Applications: What's in Common?

- Genetic autosomal dominant disorders with adult onset
- Relatively common (collectively 2 million people in the USA)
- Most not ascertained or managed by health care system
- Effective interventions that reduce morbidity and mortality
- Evidence based recommendations
- Involves family history and cascading interventions
- Can be integrated into public health programs (Cancer and Heart Disease Programs)
- Could serve as models for similar genomic applications
- Only the tip of the iceberg

Underutilization of *BRCA1/2* testing to guide breast cancer treatment: Black and Hispanic women particularly at risk

Douglas E. Levy, PhD[1,2,3], Stacey D. Byfield, PhD, MPH[4], Catherine B. Comstock, MPH,[5] Judy E. Garber, MD, MPH[3,6], Sapna Syngal, MD, MPH[3,6,7], William H. Crown, PhD[4], and Alexandra E. Shields, PhD[1,2,3]

Purpose: Women with early-onset (age ≤40 years) breast cancer are at high risk of carrying deleterious mutations in the *BRCA1/2* genes; genetic assessment is thus recommended. Knowledge of *BRCA1/2* mutation status is useful in guiding treatment decisions. To date, there has been no national study of *BRCA1/2* testing among newly diagnosed women. **Methods:** We used administrative data (2004–2007) from a national sample of 14.4 million commercially insured patients to identify newly diagnosed, early-onset breast cancer cases among women aged 20–40 years (n = 1474). Cox models assessed *BRCA1/2* testing, adjusting for covariates and differential lengths of follow-up. **Results:** Overall, 30% of women aged 40 years or younger received *BRCA1/2* testing. In adjusted analyses, women of Jewish ethnicity were significantly more likely to be tested (hazard ratio = 2.83, 95% confidence

to assess risk of hereditary breast and ovarian cancer (HBOC) is among the most established genetic tests in clinical use.[1–3] Guidelines and commercial testing for *BRCA1/2* mutations have been available for more than a decade,[4] and most health insurers now reimburse at least partially for these tests in individuals at high risk for mutations.[5] National guidelines recommend that women diagnosed with early-onset breast cancer receive *BRCA1/2* testing to guide treatment decisions.[6] Among patients newly diagnosed with cancer, a positive test result will often prompt more aggressive surgical treatment (e.g., bilateral salpingo oophorectomy or prophylactic contralateral mastectomy) with the goal of minimizing the potential for second primary cancers.[3,7,8] A positive test result may also prompt consideration

Genetics in Medicine 2011

Public Health Approach to BRCA

Public Health Genomics

Public Health Genomics
DOI: 10.1159/000334267

Received: September 2, 2011
Accepted: October 6, 2011
Published online: December 20, 2011

Using Core Public Health Functions to Promote *BRCA* Best Practices among Health Plans

D. Duquette[a] K. Lewis[b] J. McLosky[a] J. Bach[a]

[a]Division of Genomics, Perinatal Health and Chronic Disease Epidemiology, Michigan Department of Comm
Health, Lansing, Mich., and [b]Priority Health, Grand Rapids, Mich., USA

Key Words
BRCA · Cancer · Education · Genetic counseling · Genomics · Health plan · Policy · Public health · Surveillance

Conclusions: MDCH has imple
tive approach to promote canc
through health plan policies tha
eral and state agencies.

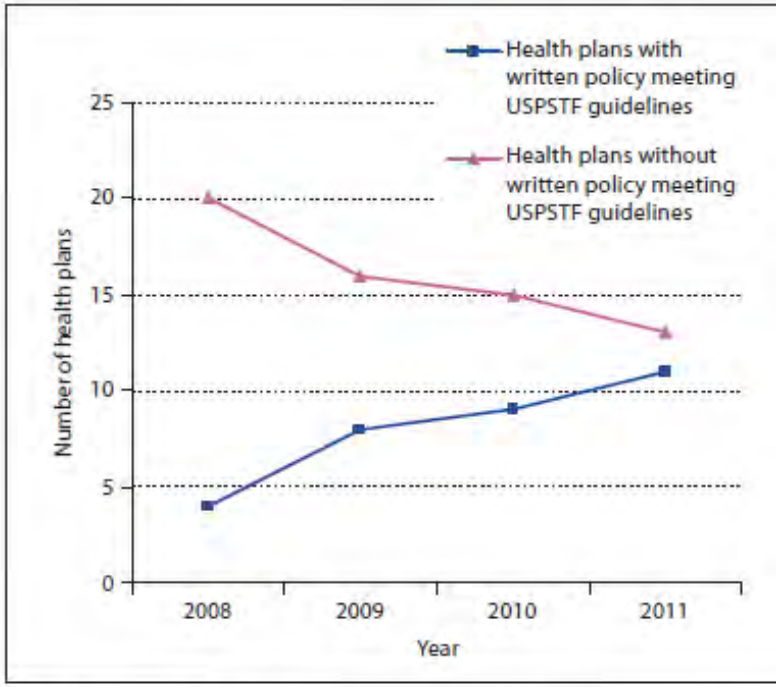


Fig. 2. Increase in number of health plans aligned with USPST
Grade B Recommendation.

Surveillance
Education
Policy

EGAPP Lynch Syndrome Recommendation
Genetics in Medicine Jan 2009

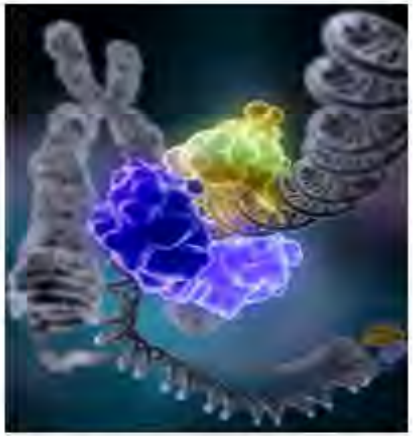
"The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group found sufficient evidence to recommend offering genetic testing for Lynch syndrome to individuals with newly diagnosed colorectal cancer (CRC) to reduce morbidity and mortality in relatives.

Lynch Syndrome Screening Implementation?

February 21, 2012 • Volume 9 / Number 4

Featured Article

Routine Lynch Syndrome Screening Varies at U.S. Cancer Centers



An enzyme encircles the double helix to repair a broken strand of DNA. Without molecules that can mend such breaks, cells can become cancerous. Mutations in genes that regulate this DNA repair system are a hallmark of

Screening practices for a condition called Lynch syndrome, which increases the risk of colorectal, endometrial, and other cancers, appear to vary substantially among different clinical centers in the United States, according to a new study.

Clinical guidelines developed by several different groups recommend routinely screening tumor samples from patients newly diagnosed with colorectal cancer for genetic markers of Lynch syndrome, although they differ with respect to exactly which patients should be screened (see Table). In the study—published online February 20 in the *Journal of Clinical Oncology*, and the first to attempt to assess current screening practices for the condition—only 42 percent of the responding centers reported that they conducted any routine screening for Lynch syndrome. Another 16 percent reported that they planned to do so.

NCI-designated comprehensive cancer centers—most of which are large academic medical centers that provide clinical cancer care and perform basic and clinical research—were far more likely than smaller hospitals and community cancer programs to perform this testing, the study showed.

In conducting the NCI-supported study, researchers from the City of Hope Cancer Center and Ohio State University Comprehensive Cancer Center surveyed all 39 NCI-designated comprehensive cancer centers that provide

Practice: Survey: Of 24 NCI-designated comprehensive cancer centers, 71 percent reported that they routinely screened tumor samples from colorectal cancer patients. Only 15 percent of smaller community-based cancer programs reported doing so.

Lynch Syndrome Screening Network

Genomics and Health Impact Blog

A blog devoted to discussing best practices and questions about the role of genomics in disease prevention, health promotion and healthcare.

Making Universal Screening for Lynch Syndrome a Reality: The Lynch Syndrome Screening Network

Categories: colorectal cancer, genomics

March 22nd, 2012 11:35 am ET - Guest Blogger

Deb Duquette, MS, CGC, Sarah Mange, MPH- Michigan Department of Community Health
Cecelia Bellcross, PhD, MS- Emory University
Heather Hampel, MS, CGC- The Ohio State University
Kory Jasperson, MS, CGC- Huntsman Cancer Institute

Authors are all from the Lynch Syndrome Screening Network (LSSN) Founding Board of Directors

Every day, about 400 people in the United States are diagnosed with colorectal cancer. Approximately twelve of them have Lynch syndrome, a hereditary condition that increases the risk of colorectal cancer and other cancers. Identifying people with Lynch syndrome could have substantial health

HHS Healthy People 2020 Genomics Objectives

G-1: Increase the proportion of women with a family history of breast and/or ovarian cancer who receive genetic counseling

➔ **U.S. Preventive Services Task Force Recommendation**

G-2: Increase the proportion of persons with newly diagnosed colorectal cancer who receive genetic testing to identify Lynch syndrome

➔ **Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group Recommendation**

Healthy People 2020

Realizing HP 2020 Objectives: State Genomics Programs

- Since 2008, CDC has supported state genomics programs in Michigan, Oregon, and more recently Georgia, to implement the evidence-based genomics recommendations underpinning the HP objectives.

States are:

- Identifying people targeted by the HP 2020 genomics objectives using cancer registries and educating health providers about evidence-based recommendations
- Implementing model payer policies to facilitate coverage consistent with the breast/ovarian cancer objective
- Developing and evaluating new data sources to measure progress toward these objectives

Healthy People 2020

Cancer Registries for Case Finding and Provider Education

Cancer registry bidirectional reporting

- Identify relevant breast, ovarian, colorectal and other cancer cases reported to state cancer registry
- Inform reporting institutions of relevant cancer cases with informational materials about hereditary breast and ovarian cancer and Lynch syndrome
- Michigan reported back over 15,000 cases of cancer relevant to HP 2020 objectives (2007-2008 data).
- Connecticut reported back over 5000 cases of cancer through a Healthy People 2020 Action Award (2008-2009 data).

Healthy People 2020

Current CDC OPHG Activities for Implementing Genomic Medicine

- **Public health Genomics Implementation Tool Kit**
- **Clickable State Map of Genomics Activities**
- **Population Level Surveillance Indicators**
- **Refining Tier 1-3 Evidence Classification**
- **Online Genomics & Health Impact Weekly Update**
- **Training and Technical Assistance**

Healthy People 2020

How about Whole Genome Sequencing?

A Systematic Approach to WGS

- Whole Genome Sequencing is now being applied in research and has begun to permeate clinical medicine
- Traditional models of test interpretation, reporting and patient counseling may be no longer feasible
- Given the large amount and heterogeneous nature of data with which we must deal, a categorical approach represents a promising way forward
- By categorizing genomic data within an *a priori* "binning" structure based upon current clinical knowledge and standards of care we can facilitate its use in practice

Proposal for "Binning" the Whole Genome Sequence (Berg et all, GIM 2011)

	Criteria:	*Clinical Utility*	*Clinical Validity*			*Unknown Clinical Implications*
Genes	Bins:	**Bin 1 Medically actionable incidental information**	**Bin 2A Low risk incidental information**	**Bin 2B Medium risk incidental information**	**Bin 2C High risk incidental information**	**Bin 3**
	Examples:	*BRCA1/2* *MLH1, MSH2* *FBN1* *NF1*	PGx variants and common risk SNPs	*APOE* Carrier status for recessive Mendelian disorders	Huntington Prion diseases ALS (SOD1)	**All other loci**
	Estimated number of genes/loci:	10s	10s (eventually 100s – 1000s)	1000s	10s	~20,000
Alleles that would be reportable (YES) or not reportable (NO) in a clinical context						
Variants	Known deleterious	YES	YES/NO [1]	YES/NO [1]	YES/NO [1]	N/A [2]
	Presumed deleterious	YES	N/A [3]	YES/NO [1]	YES/NO [1]	NO [4]
	VUS	NO	N/A [3]	NO	NO	NO [4]
	Presumed benign	NO	N/A [3]	NO	NO	NO
	Known benign	NO	NO	NO	NO	NO

Evidentiary and Ethical Issues around Return of Results in WGS Analysis

April, 2013

American College of Medical Genetics and Genomics

ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing

Robert C. Green, MD, MPH[1,2], Jonathan S. Berg, MD, PhD[3], Wayne W. Grody, MD, PhD[4-6], Sarah S. Kalia, ScM, CGC[1], Bruce R. Korf, MD, PhD[7], Christa L. Martin, PhD, FACMG[8], Amy McGuire, JD, PhD[9], Robert L. Nussbaum, MD[10], Julianne M. O'Daniel, MS, CGC[11], Kelly E. Ormond, MS, CGC[12], Heidi L. Rehm, PhD, FACMG[2,13], Michael S. Watson, MS, PhD, FACMG[14], Marc S. Williams, MD, FACMG[15], Leslie G. Biesecker, MD[16]

[1]Division of Genetics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA; [2]Partners Healthcare Center for Personalized Genetic Medicine, Boston, Massachusetts, USA; [3]Department of Genetics, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, USA; [4]Division of Medical Genetics, Department of Human Genetics, UCLA School of Medicine, Los Angeles, California, USA; [5]Division of Molecular Pathology, Department of Pathology & Laboratory Medicine, UCLA School of Medicine, Los Angeles, California, USA; [6]Division of Pediatric Genetics, Department of Pediatrics, UCLA School of Medicine, Los Angeles, California, USA; [7]Department of Genetics, University of Alabama, Birmingham, Alabama, USA; [8]Department of Human Genetics, Emory University School of Medicine, Atlanta, Georgia, USA; [9]Center for Medical Ethics and Health

Evidentiary and Ethical Issues around Return of Results in WGS Analysis: The Response to ACMG

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On Spinning Wheels and Genomes Revealed:

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March 28th, 201
Disease Control
Muin J Khou
Prevention

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In the classic Dis
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Incidental Findings from Genome Sequencing Nuances and Caveats

By Ricki Lewis | Scientific Am

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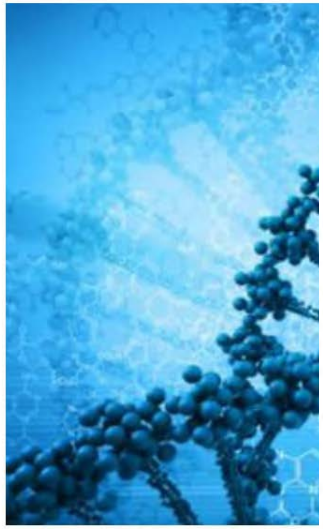

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By Christine Gorman | March 21, 2013 | 11

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Laboratories that sequence an individual's entire genome should limit the results they report to clinicians and their patients based on

Evidentiary and Ethical Issues around Return of Results in WGS Analysis: EGAPP Approach

ORIGINAL RESEARCH ARTICLE | Genetics inMedicine

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Description and pilot results from a novel method for evaluating return of incidental findings from next-generation sequencing technologies

Katrina A.B. Goddard, PhD[1], Evelyn P. Whitlock, MD, MPH[1], Jonathan S. Berg, MD, PhD[2], Marc S. Williams, MD[3], Elizabeth M. Webber, MS[1], Jennifer A. Webster, MS[1], Jennifer S. Lin, MD, MCR[1], Kasmintan A. Schrader, MBBS[4], Doug Campos-Outcalt, MD, MPA[5], Kenneth Offit, MD, MPH[4], Heather Spencer Feigelson, PhD[6] and Celine Hollombe, MPH[1]

Purpose: The aim of this study was to develop, operationalize, and pilot test a transparent, reproducible, and evidence-informed method to determine when to report incidental findings from next-generation sequencing technologies.

Methods: Using evidence-based principles, we proposed a three-stage process. Stage I "rules out" incidental findings below a minimal threshold of evidence and is evaluated using inter-rater agreement and comparison with an expert-based approach. Stage II documents criteria for clinical actionability using a standardized approach to allow experts to consistently consider and recommend whether results should be routinely reported (stage III). We used expert opinion to determine the face validity of stages II and III using three case studies. We evaluated the time and effort for stages I and II.

Results: For stage I, we assessed 99 conditions and found high inter-rater agreement (89%), and strong agreement with a separate expert-based method. Case studies for familial adenomatous polyposis, hereditary hemochromatosis, and α1-antitrypsin deficiency were all recommended for routine reporting as incidental findings. The method requires <3 days per topic.

Conclusion: We establish an operational definition of clinically actionable incidental findings and provide documentation and pilot testing of a feasible method that is scalable to the whole genome.

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Key Words: clinical actionability; population screening; secondary findings; whole-exome sequencing; whole-genome sequencing

A Public Health Approach to WGS?

COMMENTARY | Genetics inMedicine

We screen newborns, don't we?: realizing the promise of public health genomics

James P. Evans, MD, PhD[1], Jonathan S. Berg, MD, PhD[1], Andrew F. Olshan, PhD[2], Terry Magnuson, PhD[1] and Barbara K. Rimer, DrPH[3]

Genomics and public health have been uneasy bedfellows for some time. Most efforts to improve population health through genomic approaches have focused on the assessment of risks for common diseases, with the aim of tailoring interventions and screening.[1] However, the improvement of population health through such an approach has remained elusive.[2] Now, rapid progress in affordable, robust DNA sequencing offers a promising opportunity. By expanding the field's focus from common to rare diseases, it may be possible to realize the promise of public health genomics by identifying those millions of individuals who unknowingly carry mutations that confer a dramatic predisposition to preventable diseases.

In seeking to apply genomic technologies to public health, the traditional focus on common diseases is understandable. After all, even minor progress in risk reduction for disease population health risks;[4] medical interventions are usually most beneficial when identified disease risks and potential benefits are high. Finally, efforts that aim for genomic risk stratification often are justified by the hope that simply informing individuals of their genetic risks for disease will induce beneficial behavioral changes.[5] Thus far, this notion is largely contradicted by available evidence.[5,6] Although we already know how to lower risks for most common diseases, getting populations to eat properly, exercise, and give up unhealthy behaviors, especially without major policy changes, is challenging, and there is little evidence to suggest that genetic tweaking of risk will meaningfully augment these efforts.[7,8]

However, recent advances in sequencing technology provide a new opportunity to expand the focus of public health genomics in a way in which its promise can be realized. Millions of