

But How Do We Translate New Genetic Knowledge into Practice?

Closing the Gap between Human Genome Discoveries and Population Health: Session 6

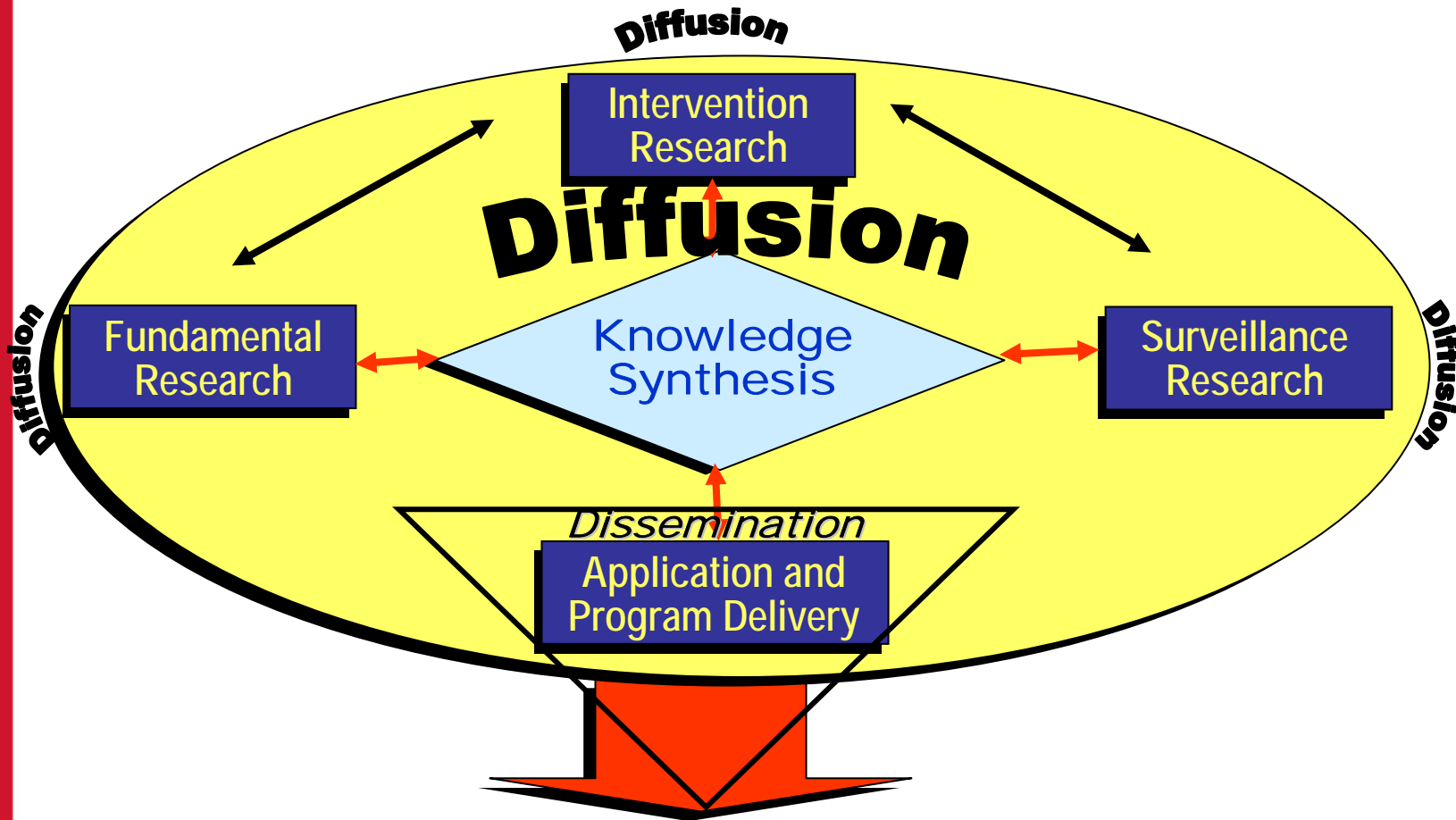
Jon F. Kerner, Ph.D.

Deputy Director for Research Dissemination & Diffusion
Division of Cancer Control & Population Sciences

Presentation Outline

- Diffusion, Dissemination, Implementation
 - Translation & Integration or Confusion & Consternation?
- Challenges of Translating Research into Public Health and Clinical (Primary Care and Disease Specialty) Practice
- Where Do We Go from Here?

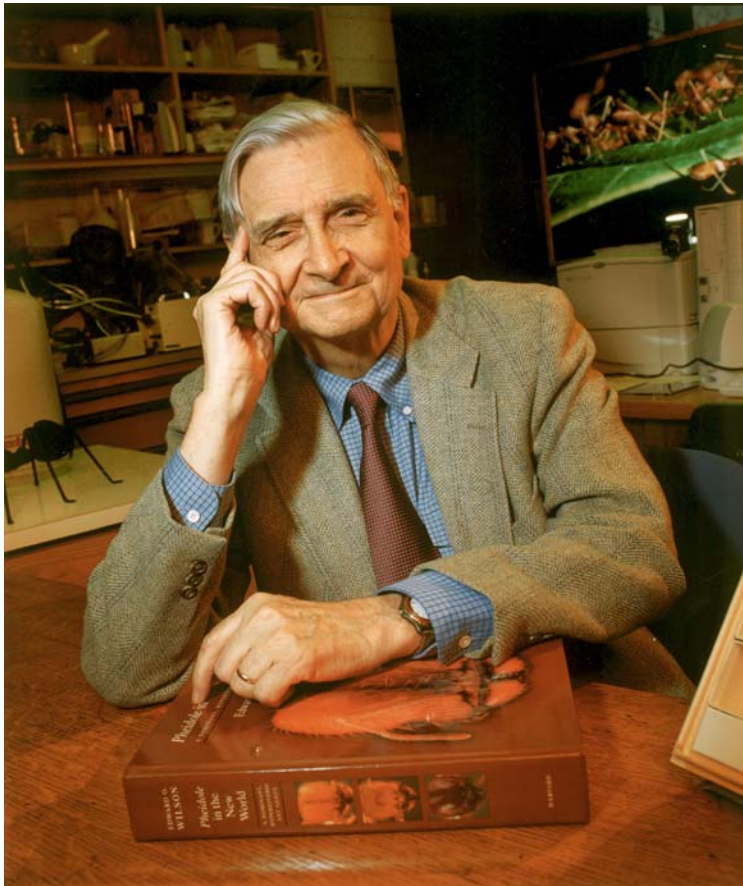
Dynamic Model of Cancer Research & Diffusion and Dissemination



Reducing the cancer burden

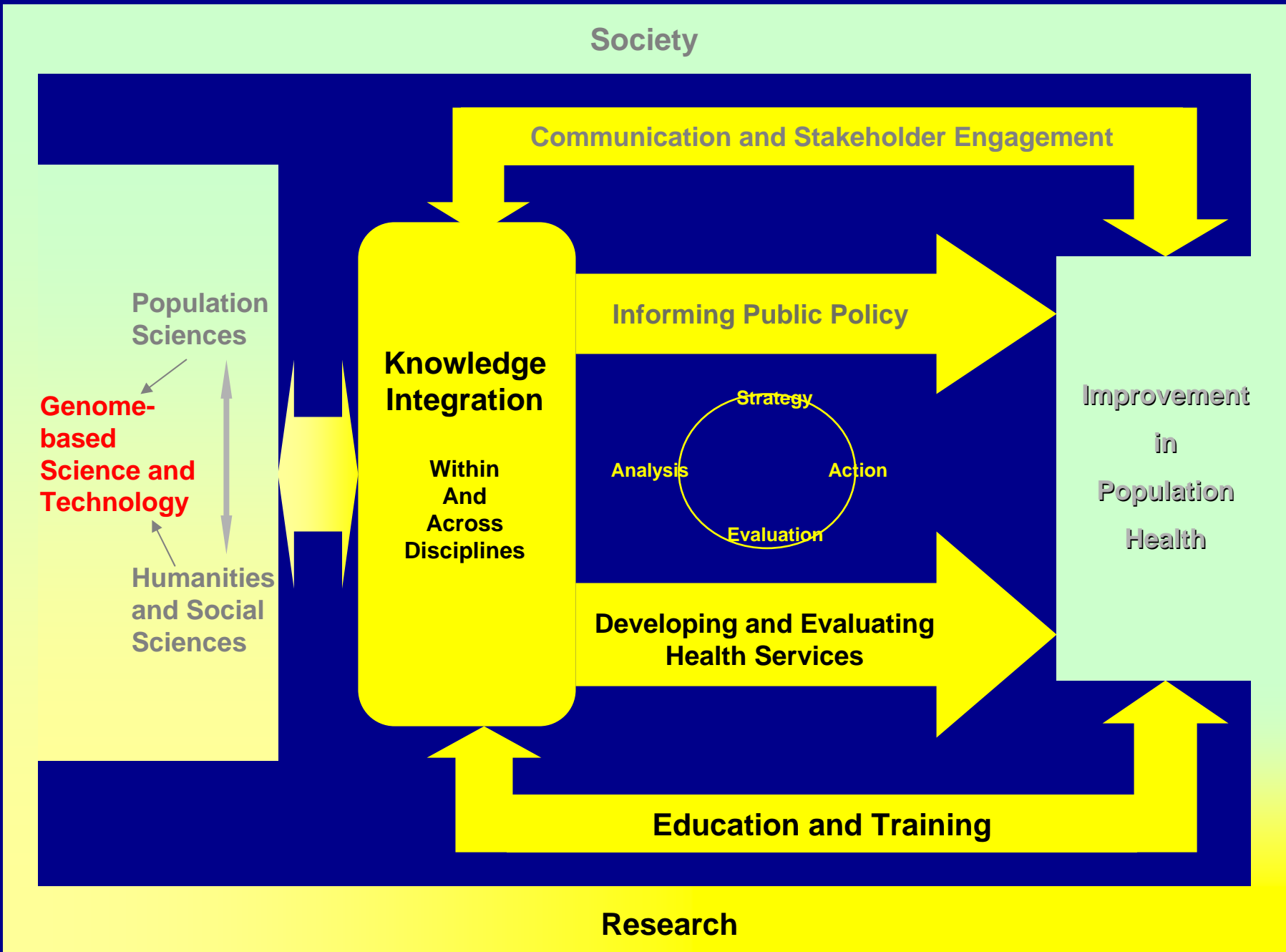
Adapted from the Advisory Committee on Cancer Control, National Cancer Institute of Canada, 1994.

Can We Achieve Consilience?



A “jumping together” of knowledge by the linking of facts and fact-based theory across disciplines to create a common groundwork of explanation.

- Edward O. Wilson
Consilience: The Unity of Knowledge



The path from genome-based research to population health

- As with other emerging technologies, the pressing challenge is to devise an efficient strategy to distinguish innovative advances from false leads.
- Genetic testing will have its greatest public health value when it identifies individuals who would benefit from specific interventions based on their risk.
 - This paradigm is the basis for newborn screening, and for the use of a small number of genetic tests, such as *BRCA* testing, which have become a part of clinical practice.

Which Populations - Whose Health?

Courtesy of Dr. Muin Khoury

Genomics and Health Disparities (W Foege, 2005)

- “The challenge to genomics is to overcome inequitable allocation of benefits, the tragedy that would befall us if we made the promise of genetics only for those who could afford it and not for all society”

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

The Central Goals of Healthy People 2010*

- Increase quality and years of healthy life
- Eliminate health disparities

* USDHHS Healthy People 2010. Washington D.C. January 2000.
Volume #1: page 2

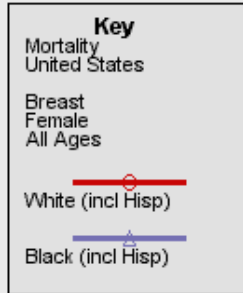
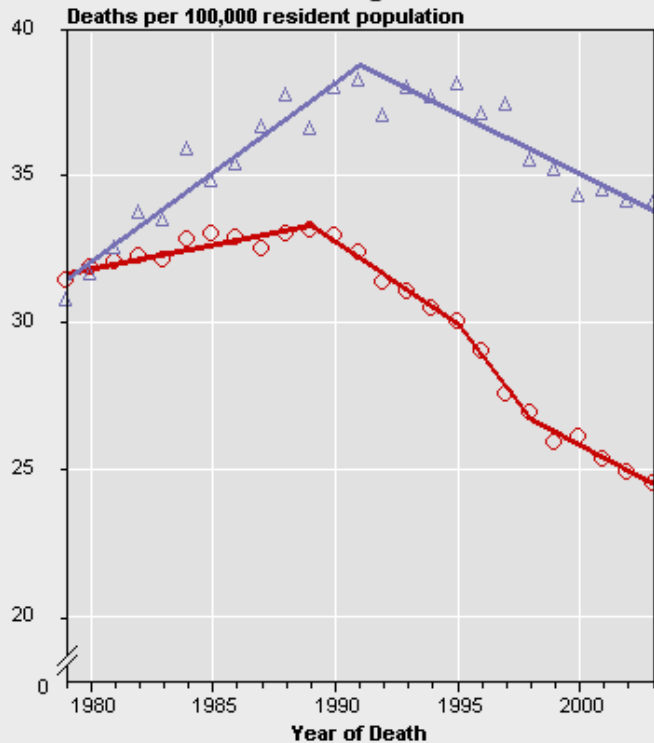
Public Health Challenge: Close the Gap Between Discovery and Delivery

- There is a critical disconnect between research discovery and program delivery and this disconnect is, in and of itself, a key determinant of the unequal burden of cancer in our society.
- *Barriers that prevent the benefits of research from reaching all populations, particularly those who bear the greatest disease burden, must be identified and removed. – Harold Freeman, MD*

Breast Cancer in U.S. White and Black Women

Historical Trends (1979-2003)

Mortality, United States Breast, Female All Ages

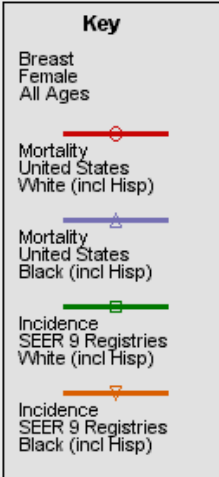
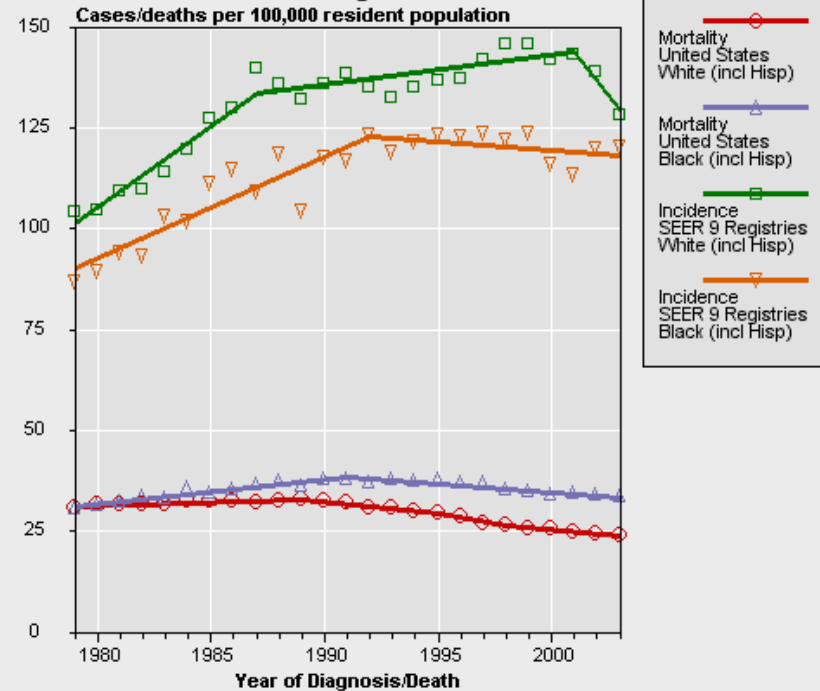


Created by statecancerprofiles.cancer.gov on 07/20/2007 7:27 pm.
Regression lines calculated using the [Joinpoint Regression Program](#).

Source: Death data provided by the [National Vital Statistics System](#) public use data file. Death rates calculated by the National Cancer Institute using [SEER*Stat](#). Death rates (deaths per 100,000 population per year) are age-adjusted to the [2000 US standard population](#) (19 age groups: <1, 1-4, 5-9, ..., 80-84, 85+). Population counts for denominators are based on Census populations as [modified](#) by NCI.

Historical Trends (1979-2003)

Breast, Female All Ages

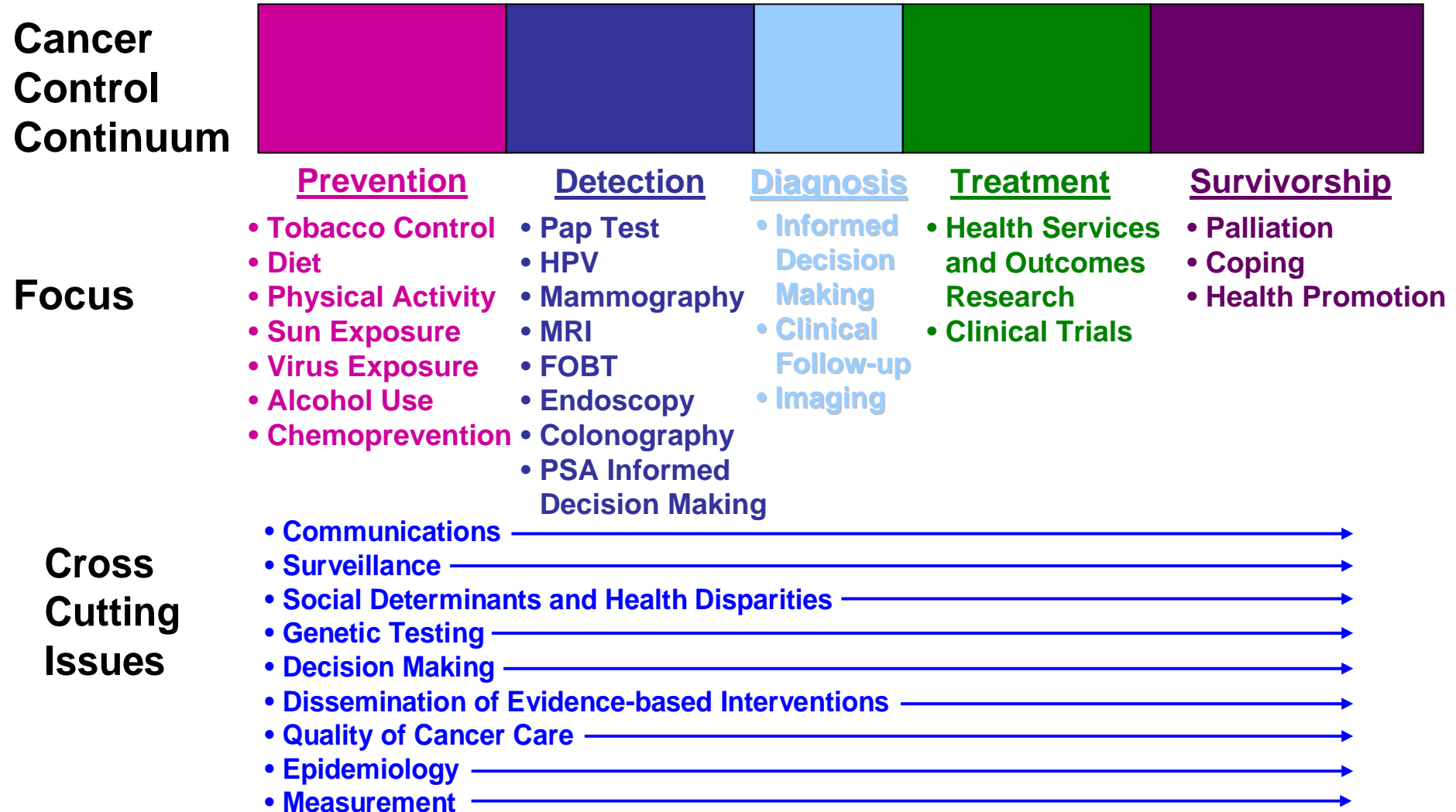


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Regression lines calculated using the [Joinpoint Regression Program](#).

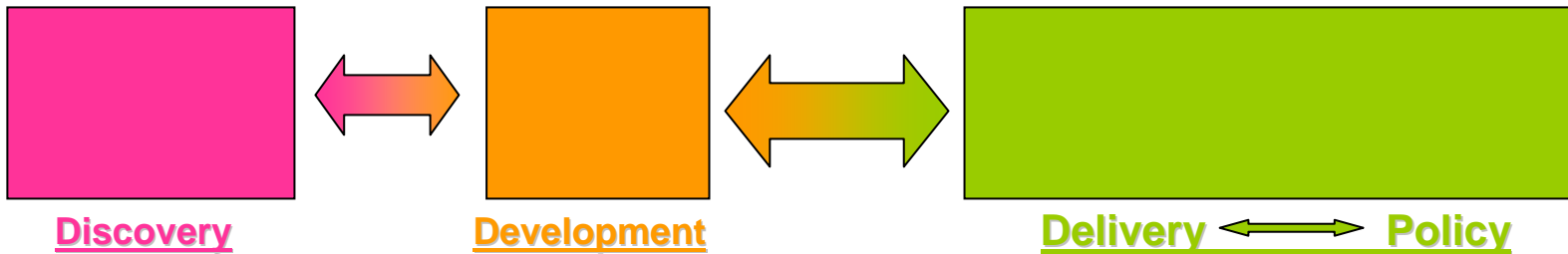
Source: Incidence data provided by the [SEER Program](#). Rates calculated by the National Cancer Institute using [SEER*Stat](#). Rates are age-adjusted to the [2000 US standard population](#) (19 age groups: <1, 1-4, 5-9, ..., 80-84, 85+). Rates are for invasive cancer only (except for bladder cancer which is invasive and in situ) or unless otherwise specified. Population counts for denominators are based on Census populations as [modified](#) by NCI.

Source: Death data provided by the [National Vital Statistics System](#) public use data file. Death rates calculated by the National Cancer Institute using [SEER*Stat](#). Death rates (deaths per 100,000 population per year) are age-adjusted to the [2000 US standard population](#) (19 age groups: <1, 1-4, 5-9, ..., 80-84, 85+). Population counts for denominators are based on Census populations as [modified](#) by NCI.

THE CANCER CONTROL CONTINUUM



THE DISCOVERY-DELIVERY CONTINUUM



Translational Research Research Translation

Industry



Context ↓ Counts



Public Health Practice

Primary Care Practice

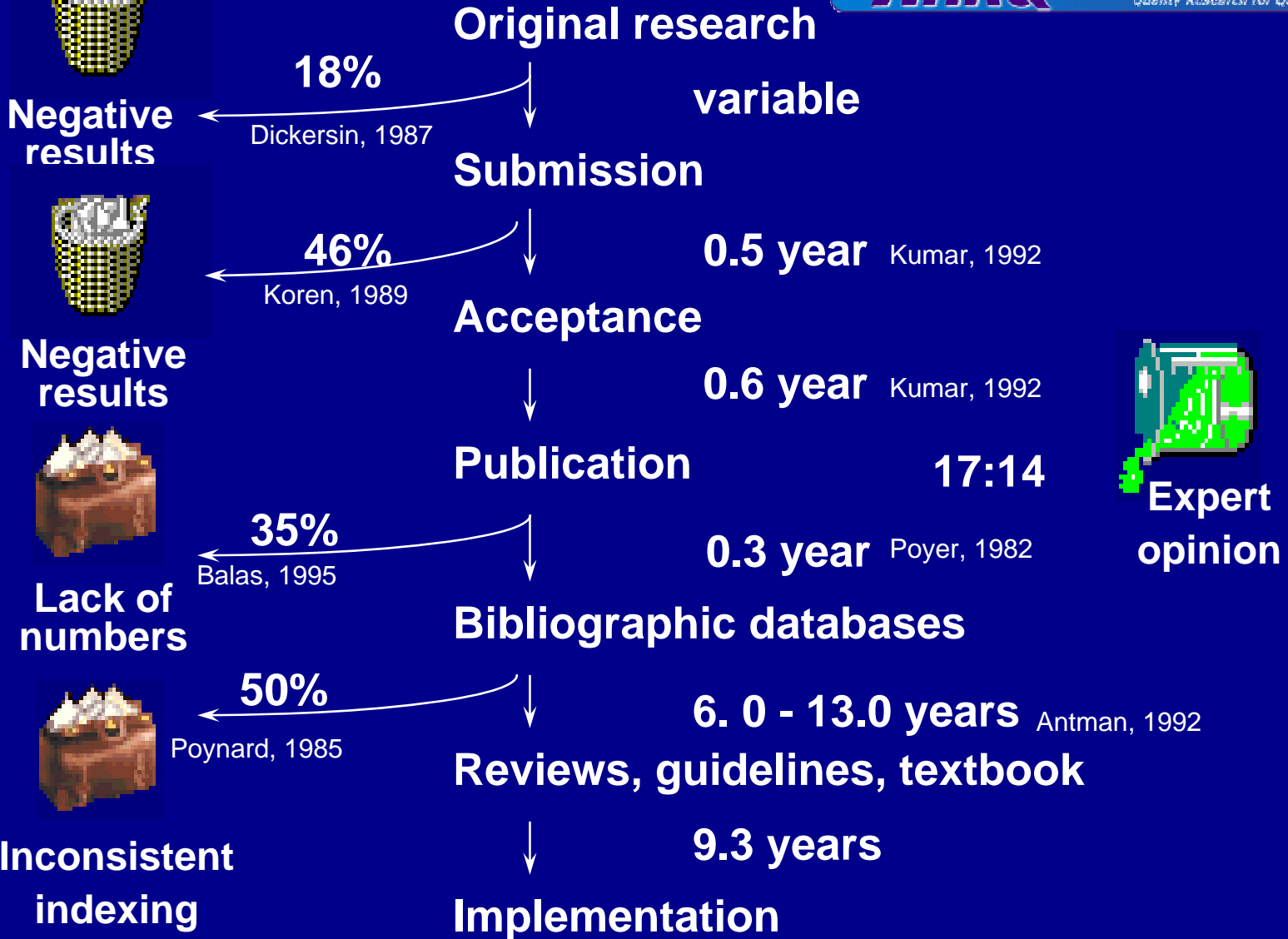
Disease Specialty Practice

The Public?



Diffusion

... the passive process by which a growing body of information about an intervention, product, or technology is initially absorbed and acted upon by a small body of highly motivated recipients (Lomas, 1993).



It takes 17 years to turn 14 per cent of original research to the benefit of patient care

Dissemination

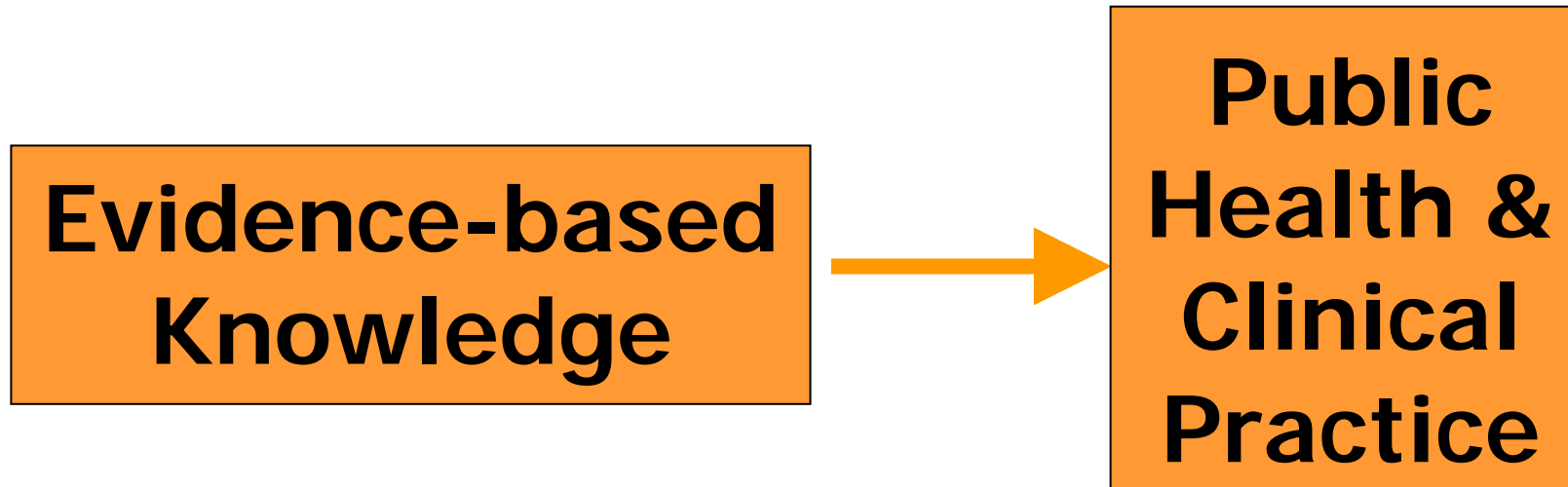
Active process through which target groups are made aware of, receive, accept and use information and other interventions.

Dissemination and Implementation

- **Dissemination** is “the targeted distribution of information and intervention materials to a specific public health or clinical practice audience.”
- **Implementation** is “the use of strategies to introduce or change evidence-based health interventions within specific settings.”

Adapted from Lomas (1993)

TRANSLATION



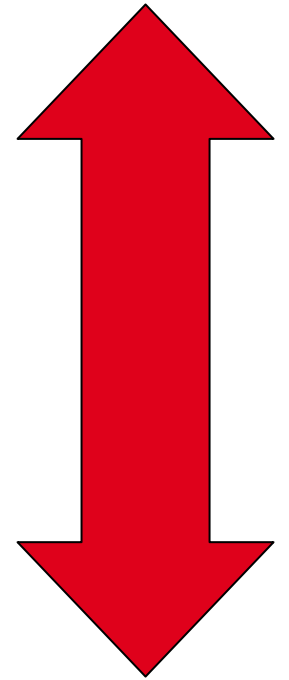
“The transfer of evidenced-based knowledge into routine or representative practice”

Glasgow, R SBM (2005) *26th Annual SBM Meeting, Symposium #22: Disseminating Behavioral Medicine Research: Making the Translational Leap.*

What is Evidence.....?

- Surveillance Data
- Systematic Reviews of Multiple Intervention Research Studies
- An Intervention Research Study
- Program Evaluation
- Word of Mouth/ Marketing
- Personal Experience

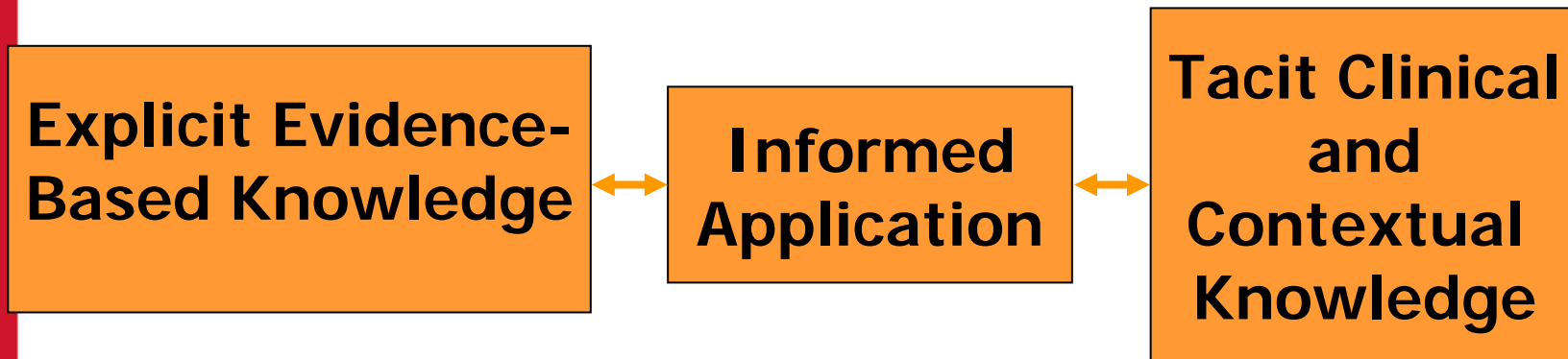
OBJECTIVE



SUBJECTIVE

...like beauty, it's in the eye of the beholder

INTEGRATION

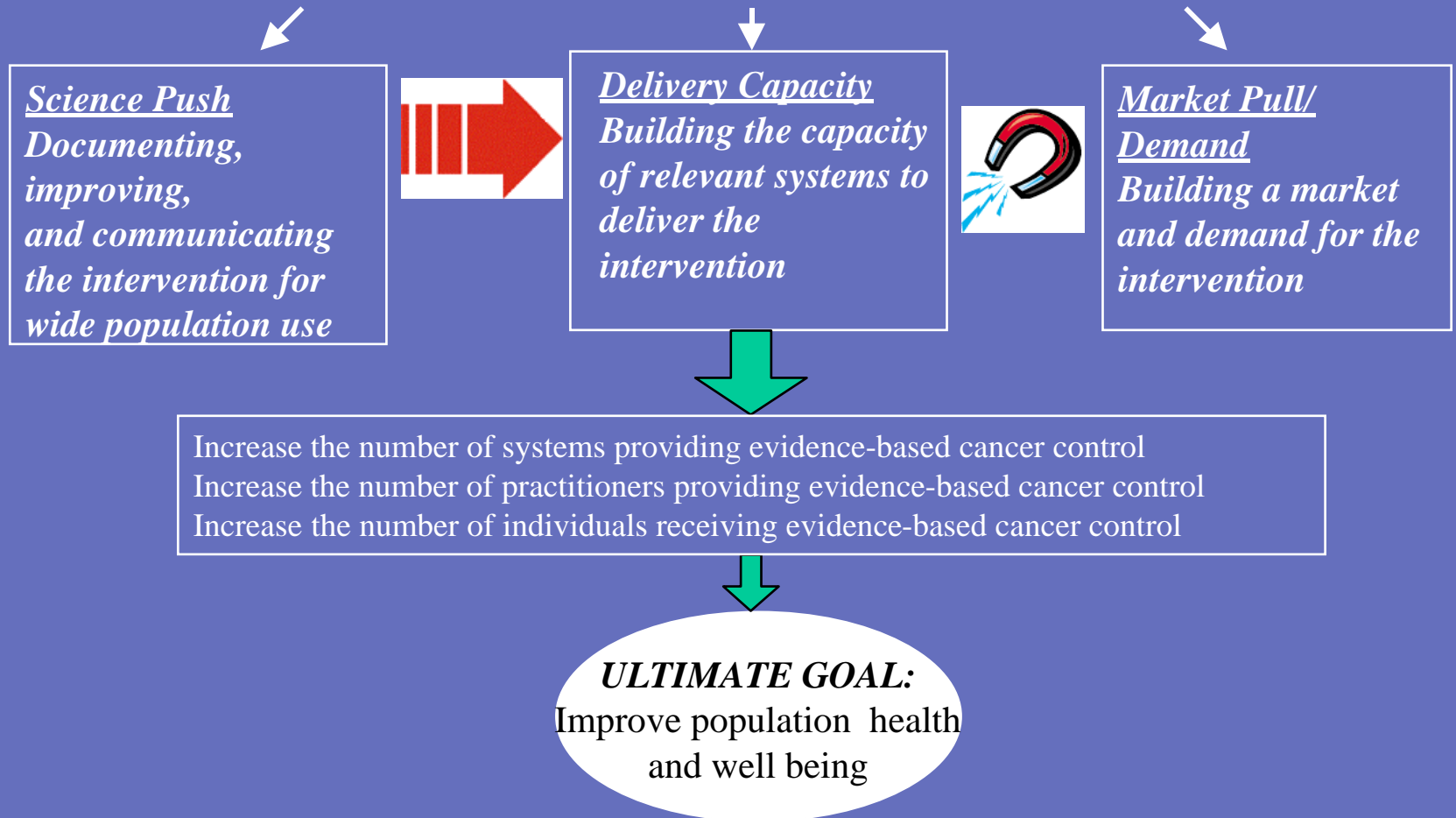


“The informed combination of evidence-based knowledge and local contextual knowledge into community applications.”

Bridging the Gap: A Synergistic Model

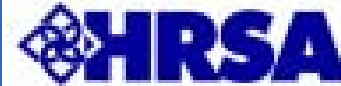
Getting Evidence-Based Cancer Control Interventions Into Practice

GOAL: To increase the adoption, reach and impact of evidence-based cancer control



Translating *R*esearch into *I*mproved *O*utcomes (*TRIO*)

- **Use and communicate cancer and behavioral surveillance data to identify needs, track progress and motivate action.**
- **Collaboratively develop tools for accessing, and promoting adoption of, evidence-based cancer control interventions.**



- **Support regional and local partnerships to develop models for identifying infrastructure barriers, expanding capacity and integrating science into comprehensive cancer control planning and implementation.**

The anatomy of tobacco's impact on the lung



Gary A. Giovino, Ph.D., M.S. Roswell Park Cancer Institute - Joseph W. Cullen Memorial Lecture 30th Annual Meeting of the American Society of Preventive Oncology Bethesda, Maryland - February 28, 2006

Oral Cancer in a 20 Year-Old Man Who Used Smokeless Tobacco

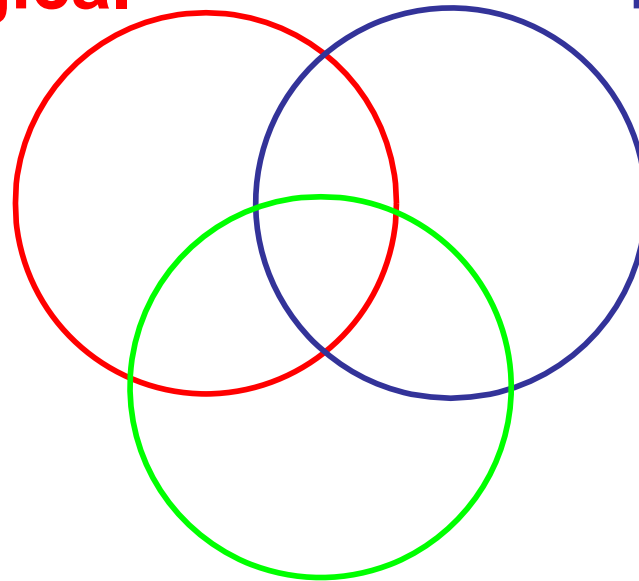


Gary A. Giovino, Ph.D., M.S. Roswell Park Cancer Institute - Joseph W. Cullen Memorial Lecture 30th Annual Meeting of the American Society of Preventive Oncology Bethesda, Maryland - February 28, 2006

Individual Tobacco Dependency

Physiological

Psychological



Social



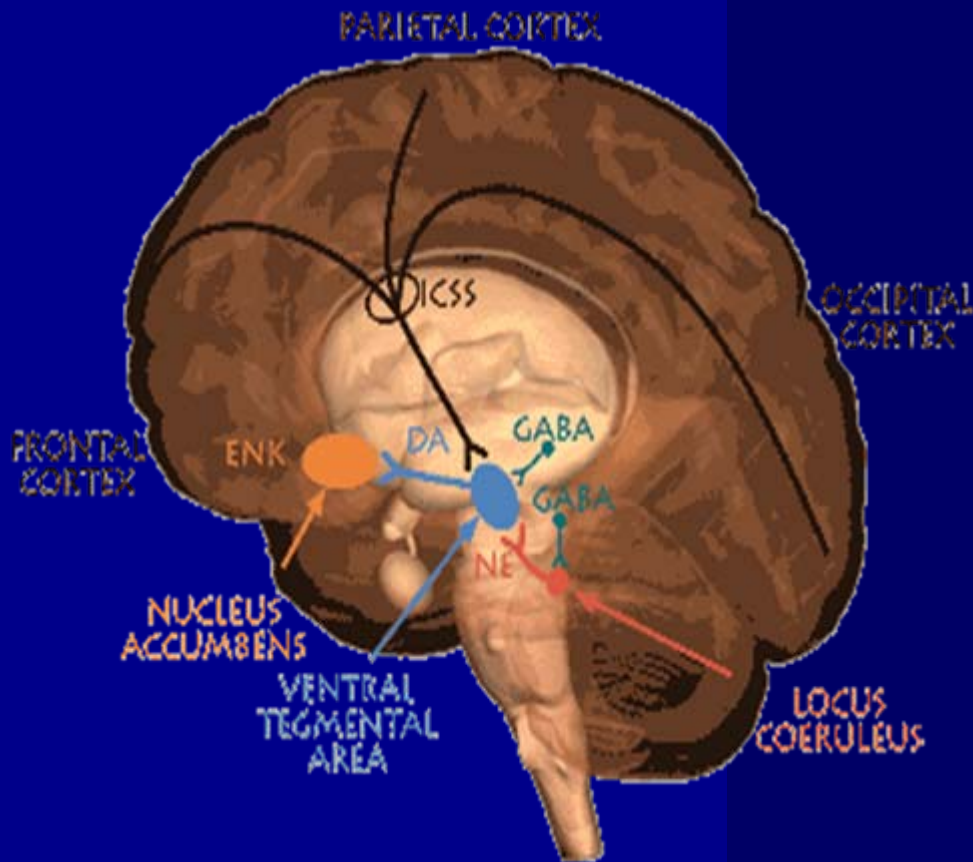
Nicotine Dependence Treatment

- **FDA-approved medications, NRT, bupropion, and varenicline are effective for only a fraction of smokers. As many as 80% of smokers respond poorly or not at all to these therapies.**
- **There is a need to develop new treatment models that can be readily translated to the clinical setting to maximize the effectiveness of nicotine dependence treatment.**

Courtesy of Dr. Caryn Lerman

Pharmacogenetics and ND Treatment

Identify Biological Targets



Predict Efficacy and Safety of Treatment



Courtesy of Dr. Caryn Lerman

Translational and Transdisciplinary Pharmacogenetic Research Model

Animal Models

- Mouse genetic models
- Mouse behavioral models
- Neurobiology

Field Studies

- Translation to practice
- Bioethics
- Health policy

Human Lab Models

- Nicotine reward
- Abstinence effects
 - Psychological
 - Hormonal
 - Neurocognitive/fMRI

Clinical Trials

- Pharmacogenetics
- Behavioral Tx

Which Populations - Who Benefits?

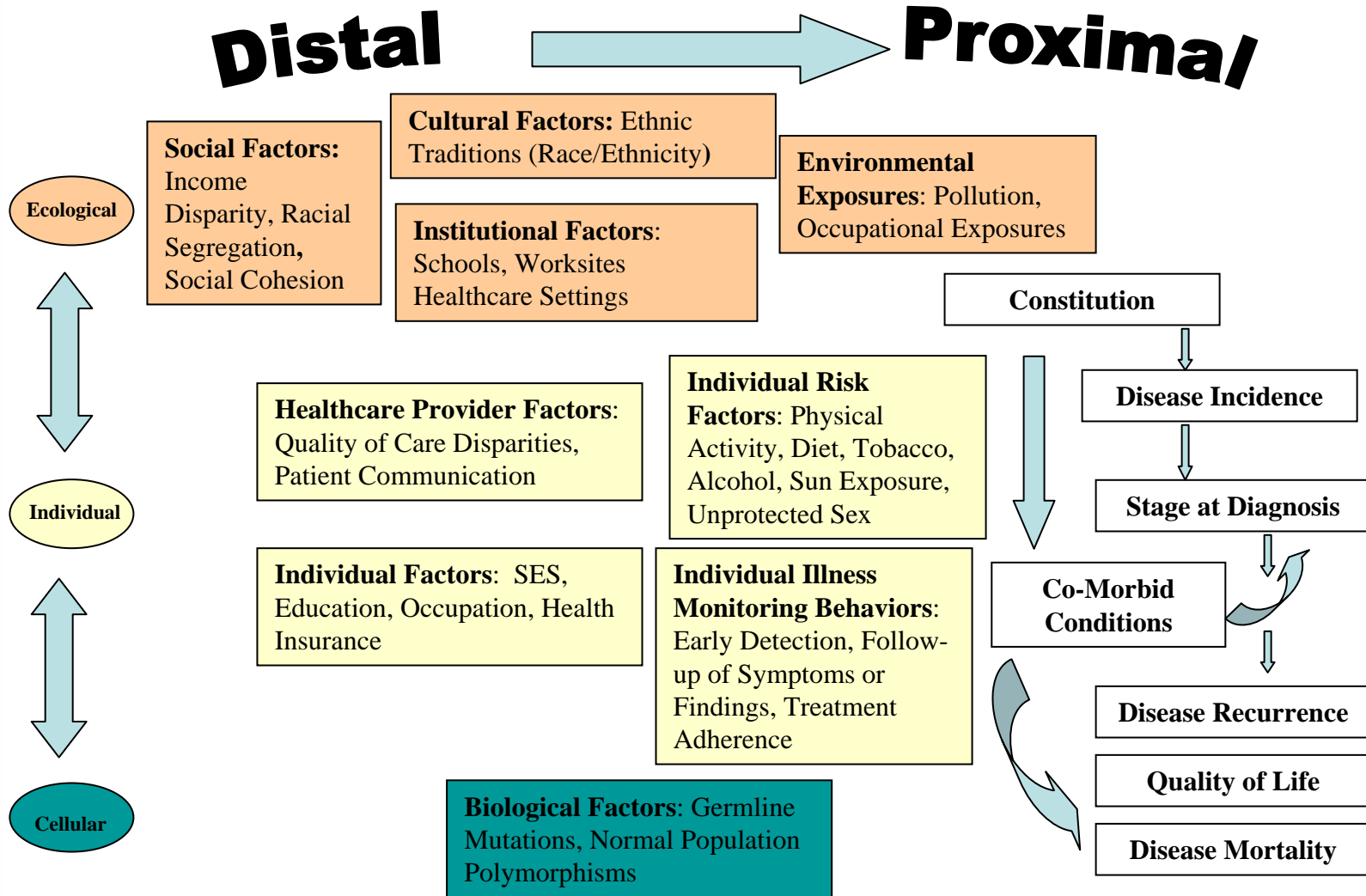
Discovery ----- **Development** ----- **Delivery**

Examples of Physician Perceived Benefits of & Barriers to Genetic Testing to Tailor Smoking Treatment*

- Destigmatize addiction
- Select and direct individual treatment
- Increase motivation
- Enhance prevention strategies
- Immediate treatment matching vs. cycling through treatments based on patient preference
- Overemphasizing biological factors would undermine importance of psychological and behavioral determinants
- Integrating genetic testing would add to time pressures; provoke patient anxiety while waiting for results
- Positive test results could lead to insurance and employment discrimination
- Worried about telemarketers and cigarette industry getting information for targeted marketing

*Park ER, Kleimann S, Shields AE, Pelan JA. Anticipating clinical integration of genetically tailored tobacco dependence treatment: perspectives of primary care physicians. *Nicotine & Tobacco Research*, 9(2): 271-279.

Framework for Understanding Multi-Level Determinants of Health & Illness

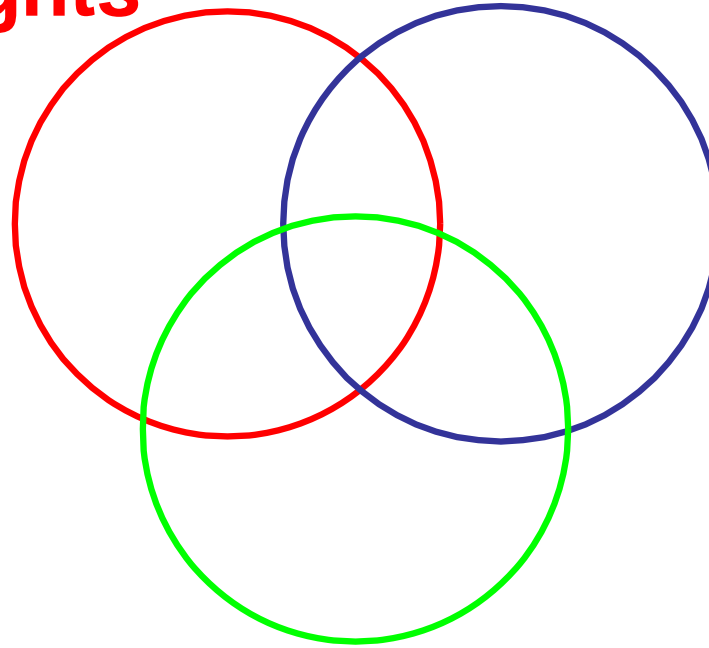


Potential Predictors of Health & Illness

Organizational & Institutional Dependency on Tobacco Dollars

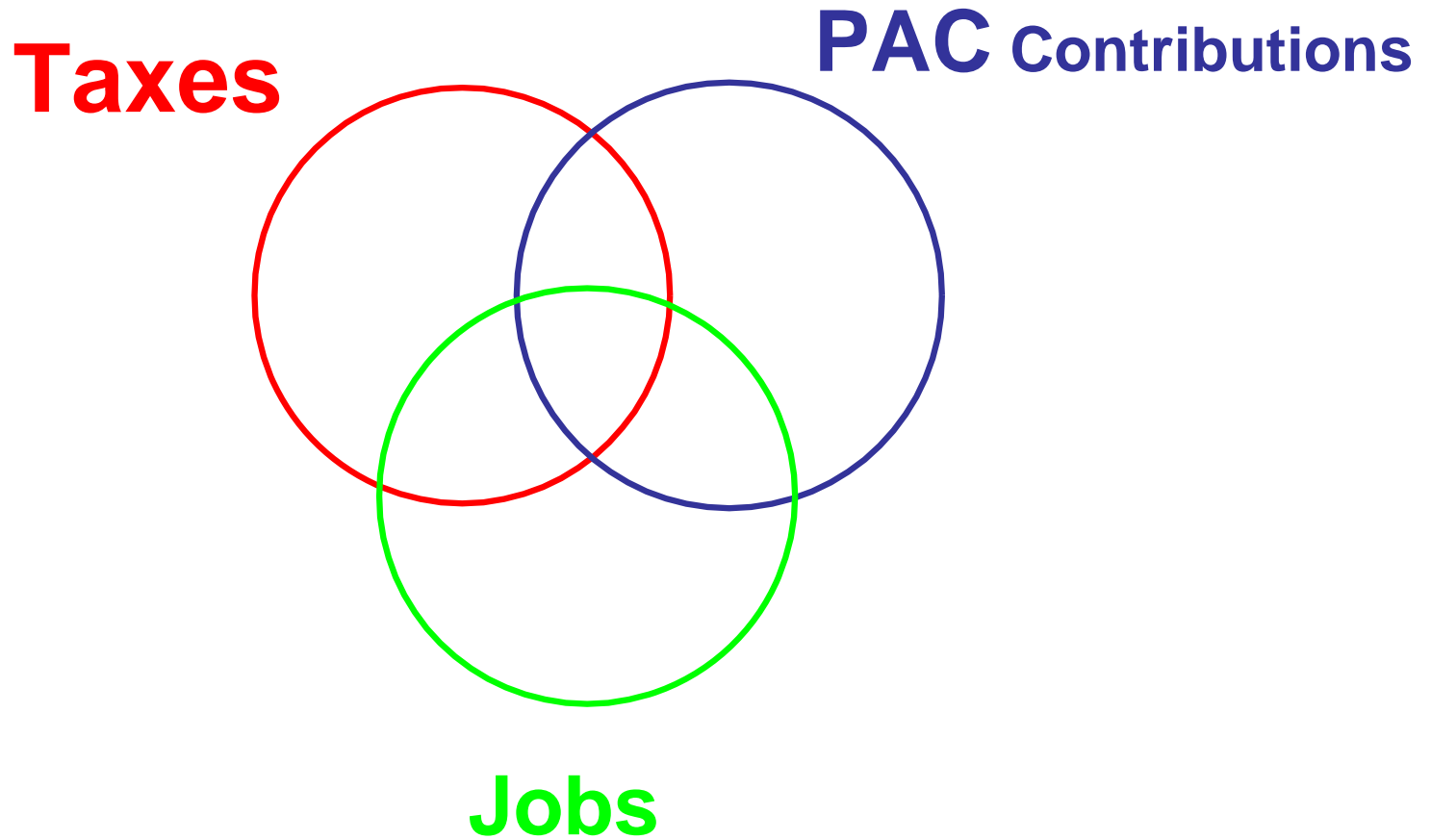
Civil Rights

Educational



Community-Based

State & National Dependency on Tobacco Dollars





Rotate Clockwise

STATE CIGARETTE EXCISE TAX RATES & RANKINGS

Overall All States' Average: \$1.073 per pack
 Major Tobacco States' Average: 33.5 cents per pack
 Other States' Average: \$1.171 per pack

State	Tax	Rank
Alabama	\$0.425	42nd
Alaska	\$2.00	4th
Arizona	\$2.00	4th
Arkansas	\$0.59	38th
California	\$0.87	29th
Colorado	\$0.84	30th
Connecticut	\$2.00	4th
Delaware ¹	\$1.15	21st
DC	\$1.00	24th
Florida	\$0.339	46th
Georgia	\$0.37	43rd
Hawaii ²	\$1.80	9th
Idaho	\$0.57	39th
Illinois	\$0.98	27th
Indiana	\$0.995	26th
Iowa	\$1.36	17th
Kansas	\$0.79	32nd
Kentucky	\$0.30	47th

State	Tax	Rank
Louisiana	\$0.36	44th
Maine	\$2.00	4th
Maryland	\$1.00	24th
Massachusetts	\$1.51	13th
Michigan	\$2.00	4th
Minnesota ³	\$1.493	15th
Mississippi	\$0.18	49th
Missouri	\$0.17	50th
Montana	\$1.70	11th
Nebraska	\$0.64	35th
Nevada	\$0.80	31st
New Hampshire	\$1.08	22nd
New Jersey	\$2.58	1st
New Mexico	\$0.91	28th
New York	\$1.50	14th
North Carolina	\$0.35	45th
North Dakota	\$0.44	41st
Ohio	\$1.25	19th

State	Tax	Rank
Oklahoma	\$1.03	23rd
Oregon	\$1.18	20th
Pennsylvania	\$1.35	18th
Rhode Island	\$2.46	2nd
South Carolina	\$0.07	51st
South Dakota	\$1.53	12th
Tennessee	\$0.62	36th
Texas	\$1.41	16th
Utah	\$0.695	34th
Vermont	\$1.79	10th
Virginia	\$0.30	47th
Washington	\$2.025	3rd
West Virginia	\$0.55	40th
Wisconsin	\$0.77	33rd
Wyoming	\$0.60	37th
Puerto Rico	\$1.23	NA
Guam	\$1.00	NA
Northern Marianas	\$1.75	NA

¹ Effective 7/31/07.

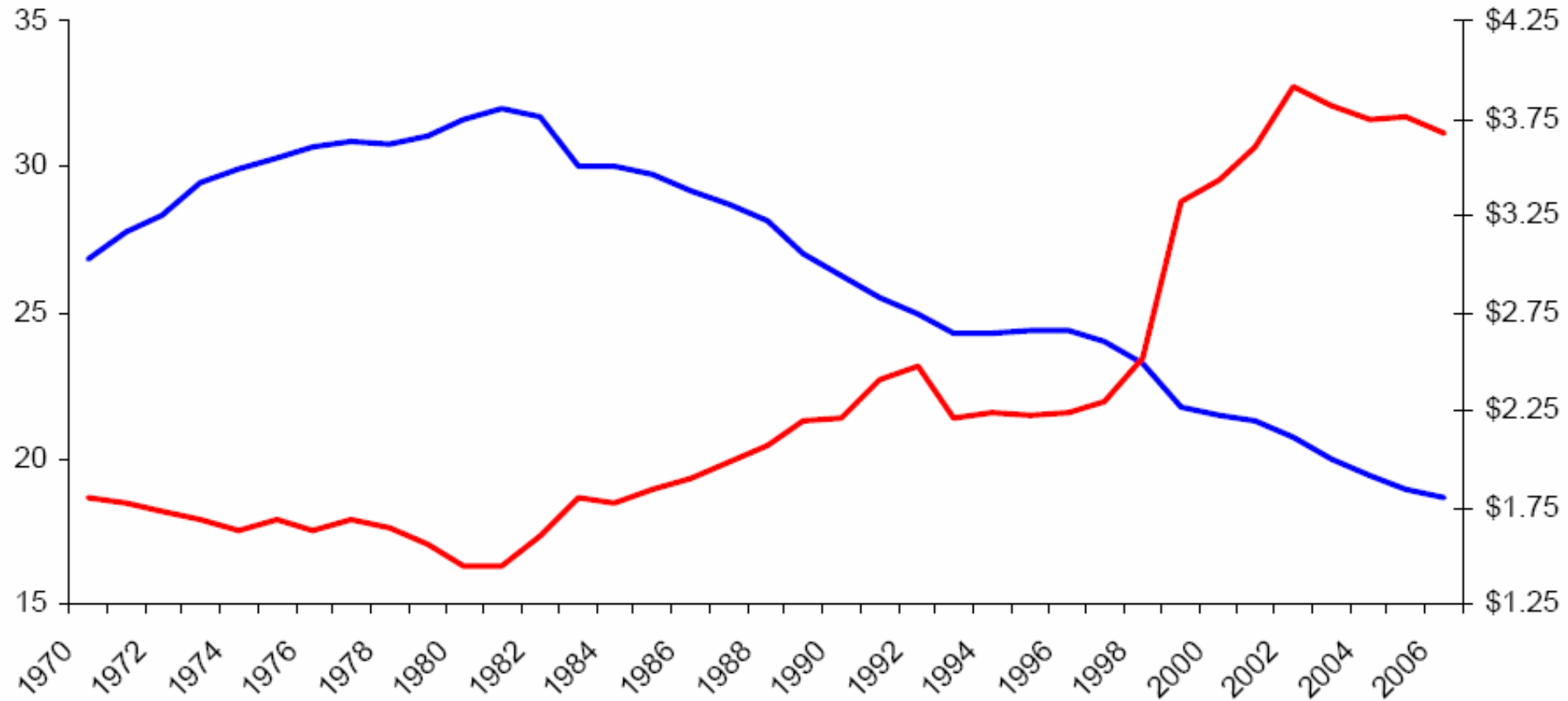
² Effective 9/30/07.

³ Includes 75¢ health impact fee & 26.3¢ wholesale sales tax (all part of tax stamp).

Table shows all cigarette taxes already passed into law that will go into effect in the 2007 calendar year. Since 2002,

U.S. Cigarette Prices vs. Consumption 1970-2006

— Cigarette Consumption (billions of packs) — Avg. Retail Price Per Pack (in current dollars)



Architectures of Genetic Medicine: Comparing Genetic Testing for Breast Cancer in the US & the UK*

- As innovators determine how to build genomic technologies, they choose among a finite set of possibilities that are framed by existing national laws, traditions, and institutional structures for the provision of biomedical services.
- They make choices among these possibilities based on their own interests, as well as their vision of what might be easiest to develop successfully.

Where lies the path of least resistance?

Technology Architecture – Medical Testing

- Direct individuals to testing
- Assess their eligibility
- Inform them about potential risks, benefits, and implications of the test
- Extract material or information for testing by a technical apparatus
- Report the results

BRCA testing in the US

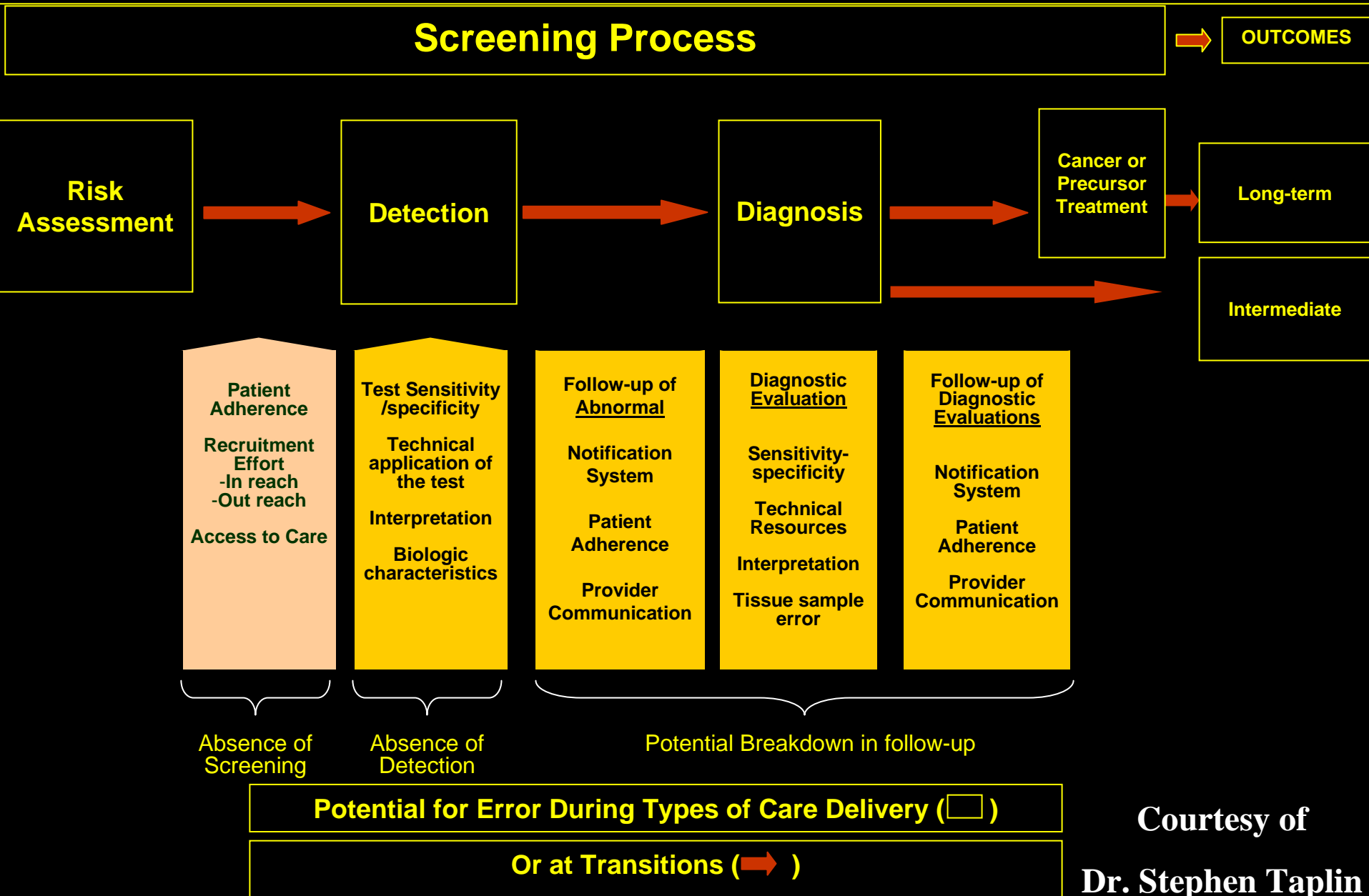
- University of Pennsylvania Genetic Diagnostic Laboratory (1995) ➤ \$700 - \$1,500
- OncorMed (1994) ➤ \$500 - \$2,100
- Genetics and In Vitro Fertilization Institute (1996) ➤ \$295
- Myriad Genetics, Inc.(1996) ➤ \$250 - \$4,000

By 1999, Who's Left?

BRCA Testing in the UK

- Mid-1990's UK National Health Service began to develop services to test for BRCA mutations
- Delivered through 20 already existing regional NHS genetic clinics
- Package of standard counseling but variable laboratory analysis connected to specialist and primary care physicians through hierarchical referral network
- Regional clinics initially varied in how they managed demand
- Subsequently NHS adopted Mackay & Zimmern low, moderate and high risk (using family history) triage system to manage demand

Screening Is a Process



System Differences for BRCA testing US vs. UK

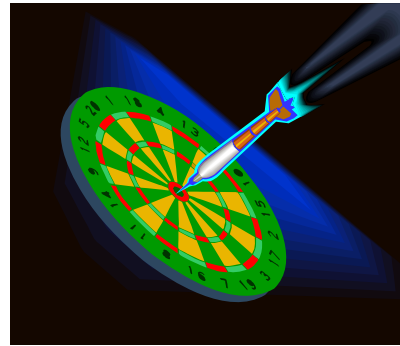
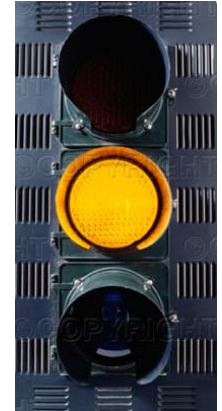
US

- Access to findings restricted for fear of insurance/employment discrimination
- Level of testing based on ability to pay
- Counseling not required
- Physicians facilitators to increase demand
- Individuals viewed as empowered to make own decisions but also assumed to be informed consumers of testing

Individual vs. Population?

UK

- Universal access to health care mitigates confidentiality concerns
- Level of testing restricted by fixed allotments
- Standard counseling provided
- Physicians gatekeepers to manage demand
- Individuals viewed as representing patient groups (low, moderate & high risk) whose access to testing should be managed by health care professionals

Vision for the Transformation of 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" (Zerhouni, 2006)

For Whom? From Where?

Courtesy of Dr. Muin Khoury

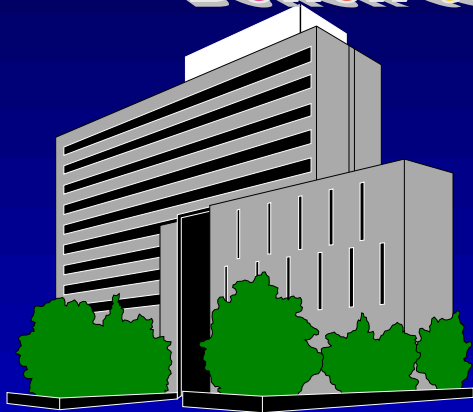
Translational Research vs. Research Translation

"Cutting-Edge"

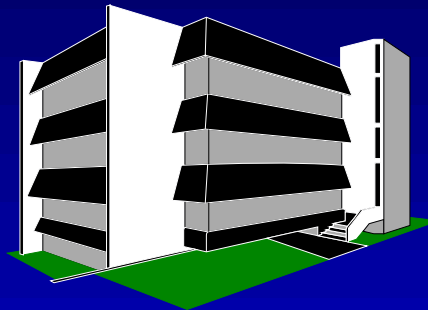
"State-Of-The-Art"

"Resource-Limited"

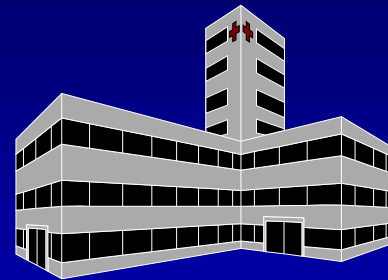
Bench to Bedside



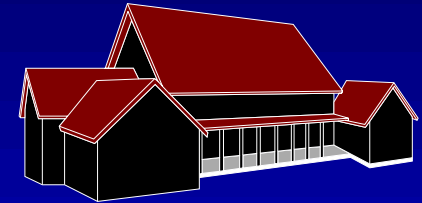
Academic Cancer
& Medical Centers



CCOPs & ACoS
Approved Cancer
Programs



Municipal & Rural
Hospitals & Clinics



Bench to Trench

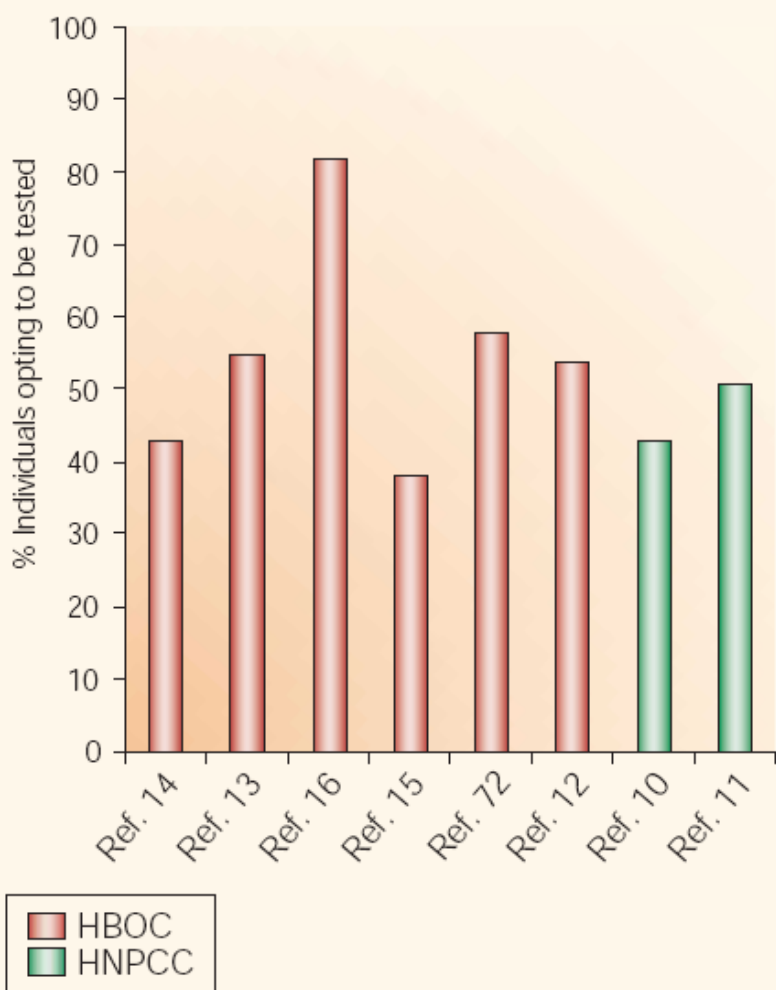


Figure 3 | **Comparing uptake rates of genetic testing in families with hereditary breast and ovarian cancer or hereditary non-polyposis colon cancer.** Numerous studies have been

SCIENCE AND SOCIETY

Genetic testing for cancer susceptibility: the promise and the pitfalls

Caryn Lerman and Alexandra E. Shields

Nature Review/ Cancer
Volume 4/March 2004
Pages 235 - 241

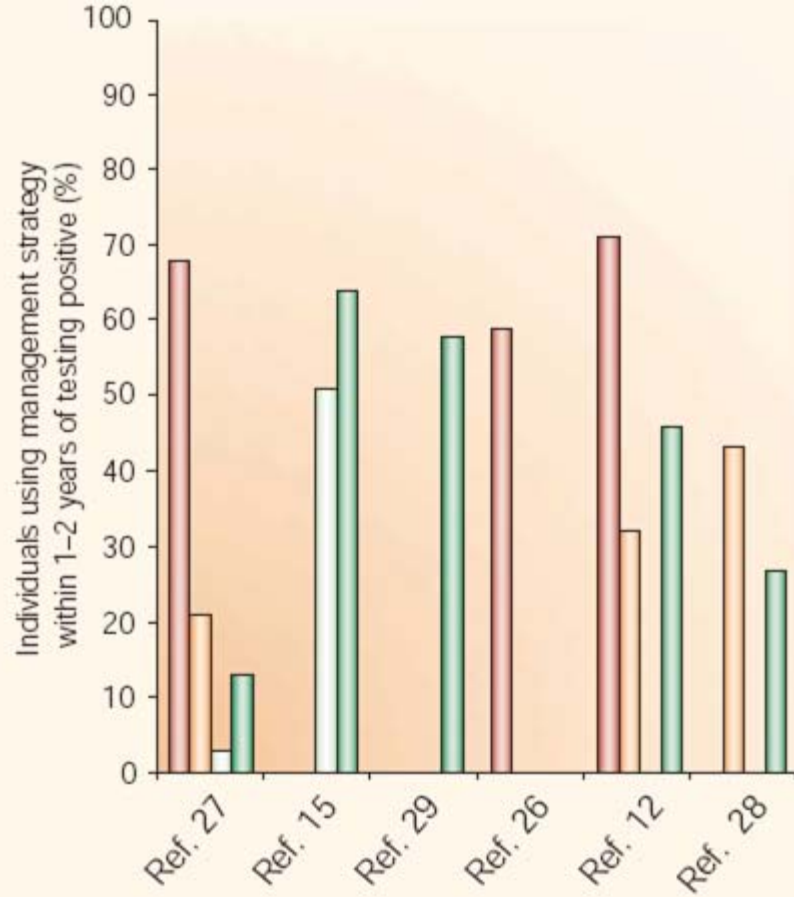


Figure 4 | **Use of medical-management strategies by patients who tested positive for hereditary breast and ovarian cancer mutations.** Breast screening, ovarian screening, prophylactic mastectomy, and prophylactic oophorectomy

Figure 4 | **Use of medical-management strategies by patients who tested positive for hereditary breast and ovarian cancer mutations.** Breast screening, ovarian screening, prophylactic mastectomy, and prophylactic oophorectomy

Lessons for Research & Practice

- If research should influence practice then practice should influence research to ensure that new interventions being developed and tested through research are informed by the wealth of tacit and contextual knowledge gained from practice experience.
- It may prove useful in continuing education of health professionals to focus more on bringing researchers and practitioners together to review and learn how best to integrate the lessons learned from research with the lessons learned from practice than standard CME approaches.
- We may need to accept that changing practitioner behavior has less to do with expanding practitioner knowledge of the evidence, and more to do with their being convinced that applying specific research evidence will benefit a particular patient when the opportunity arises in a particular office or clinic visit.*

* Majumdar SR, McAlister FA, Furberg CD. From knowledge to practice in chronic cardiovascular disease: A long and winding road. *J Am College Card.* 2004; 43(10):1738-42.

Where Do We Go From Here?

**Genome-
based
Science and
Technology**

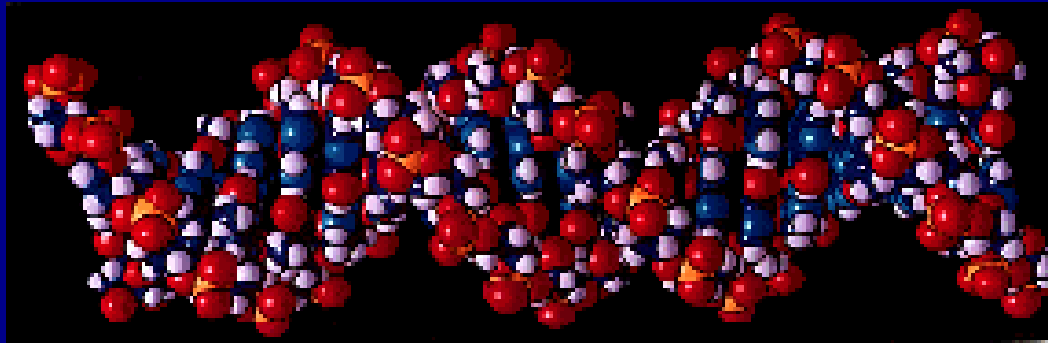


**Improvement
in
Population
Health**

**Closing the Gap Between Human
Genome Discoveries and Population Health**

Courtesy of Dr. Muin Khoury

Carcinogenesis as a Multi-stage Process*



Cancer Control as a Multi-Stage Process



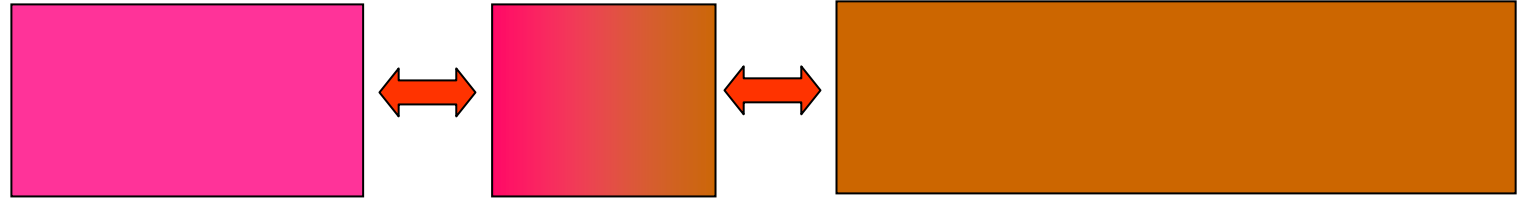
*Adapted from Shields PG, Harris CG. Principles of Carcinogenesis: Chemical.
In: Devita VT, Hellman S, Rosenberg SA. Cancer Principles & Practice of Oncology.
J.B. Lippencott Co. Philadelphia :1993.

Assumptions About Scientific Development

- Stage 1: Basic Research
- Stage 2: Treatment Development
- Stage 3: Efficacy
- Stage 4: Effectiveness
- Stage 5: Adaptation to Real World

Stage 5 assumed to be beyond research...

WHERE DO GENETIC INTERVENTIONS FIT?



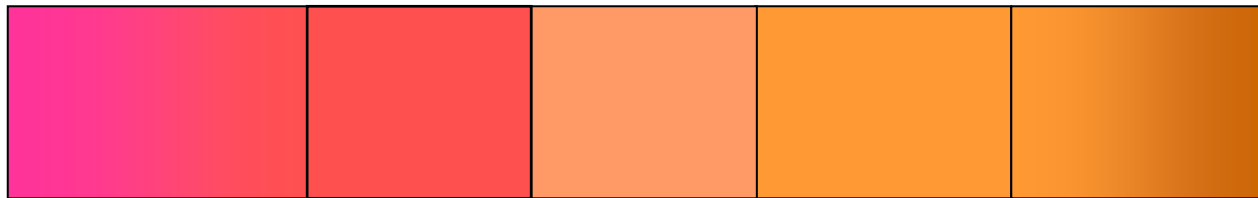
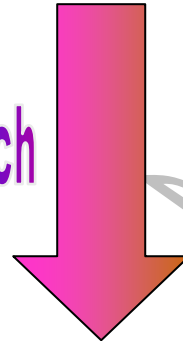
Discovery

Development

Delivery

Efficacy-Replication Research

D&I Research



Diffusion

Replication

Knowledge
Synthesis

Dissemination

Implementation

Genetic Interventions?

[Cancer Control and Population Sciences Home](#)

"Knowing is not enough, we must apply. Willing is not enough, we must do!" Goethe



Need Help?

Contact us by phone,
Web, and e-mail
1-800-4-CANCER

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What's New

[NIH Conference on Building the Science of Dissemination and Implementation in the Service of Public Health, September 10-11, 2007](#)

[Video Cast of Dissemination and Implementation Research: Technical Assistance Meeting Monday March 26, 2007](#)

[Effective February 5, 2007: Important Changes to the Grant Application Process for: Dissemination and Implementation Research in Health \(R03\) PAR-06-520, \(R21\) PAR-06-521, and \(R01\), PAR-07-086](#)

[Dissemination and Implementation Research in Health \(R03\), PAR-06-520](#)
Expiration date: October 2, 2009

[Dissemination and Implementation Research in Health \(R21\), PAR-06-521](#)
Expiration date: October 2, 2009

[Dissemination and Implementation Research in Health \(R01\), PAR-07-086](#)
Expiration date: September 2, 2009

[Cancer Prevention and Control Research Network](#)

Key Initiatives

[Cancer Control P.L.A.N.E.T. Dissemination and Diffusion of Evidence-based Cancer Control Interventions](#)

[Dialogue for Dissemination Meetings](#)

[Dissemination and Diffusion Supplements](#)

<http://cancercontrol.cancer.gov/d4d>

First Annual Trans-NIH Dissemination & Implementation State of the Science Meeting

NIH Conference on:

Building the Science of Dissemination and Implementation in the Service of Public Health

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September 10-11, 2007



Natcher Conference Center, NIH Campus
Bethesda, Maryland



Our goal is to turn knowledge into applications that benefit people.



“To him who devotes his life to science, nothing can give more happiness than increasing the number of discoveries, but his cup of joy is full when the results of his studies immediately find practical applications.”
~Louis Pasteur