

WHAT IS NEW AT THE NCI?

- NEW LEADERSHIP

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Doug Lowy
Deputy



Jim Doroshow
Deputy



John Czajkowski
Executive Officer



Barry Kramer
Prevention



Barbara Wold
Cancer Genomics



Ted Trimble
Global Health

WHAT IS NEW AT THE NCI?

- NEW LEADERSHIP
- DIMINISHING BUDGETS

BUT LOTS TO DO AND LOTS THAT CAN BE DONE

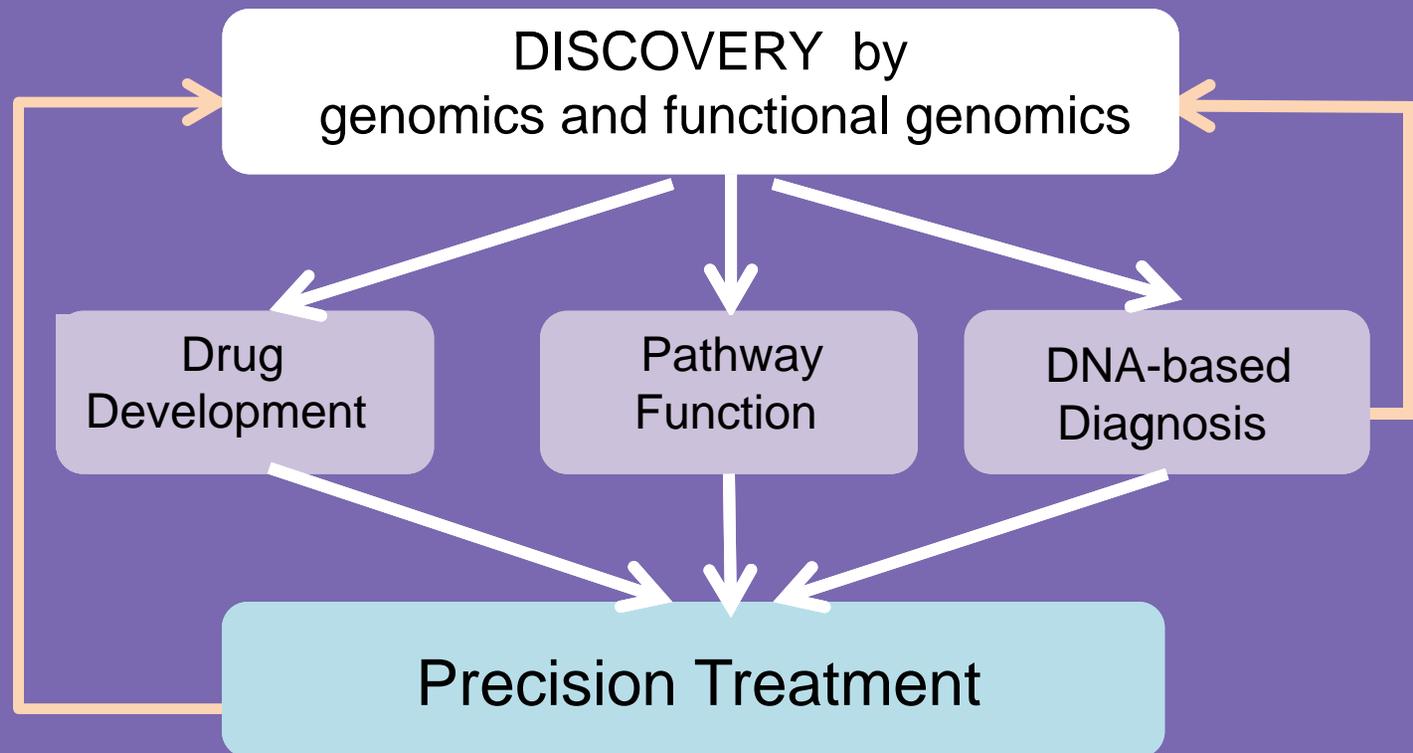
WHAT IS NEW AT THE NCI?

- NEW LEADERSHIP
- DIMINISHING BUDGETS
- EXPANSIONS/REARRANGEMENTS OF THE MANDATORY:
 - CENTER FOR CANCER GENOMICS

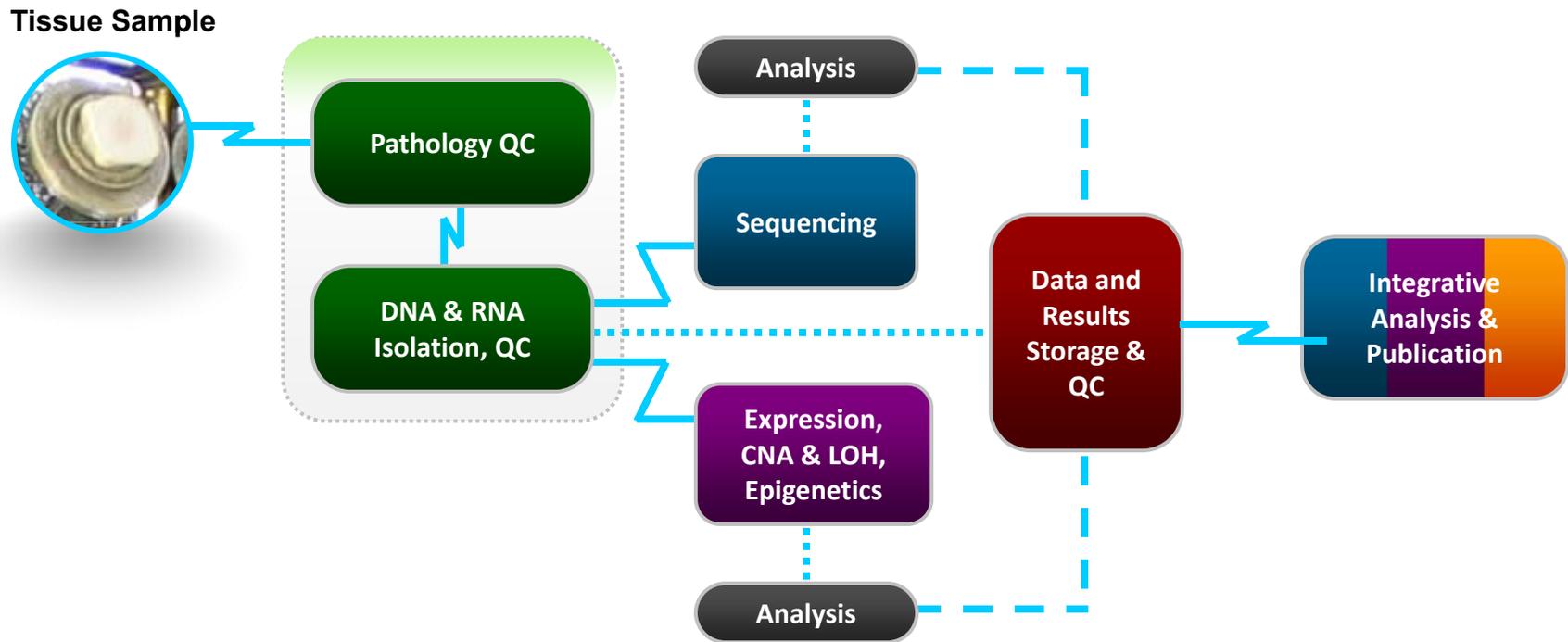


NCI Center for Cancer Genomics

Develop and apply
genome science
to better treat cancer patients



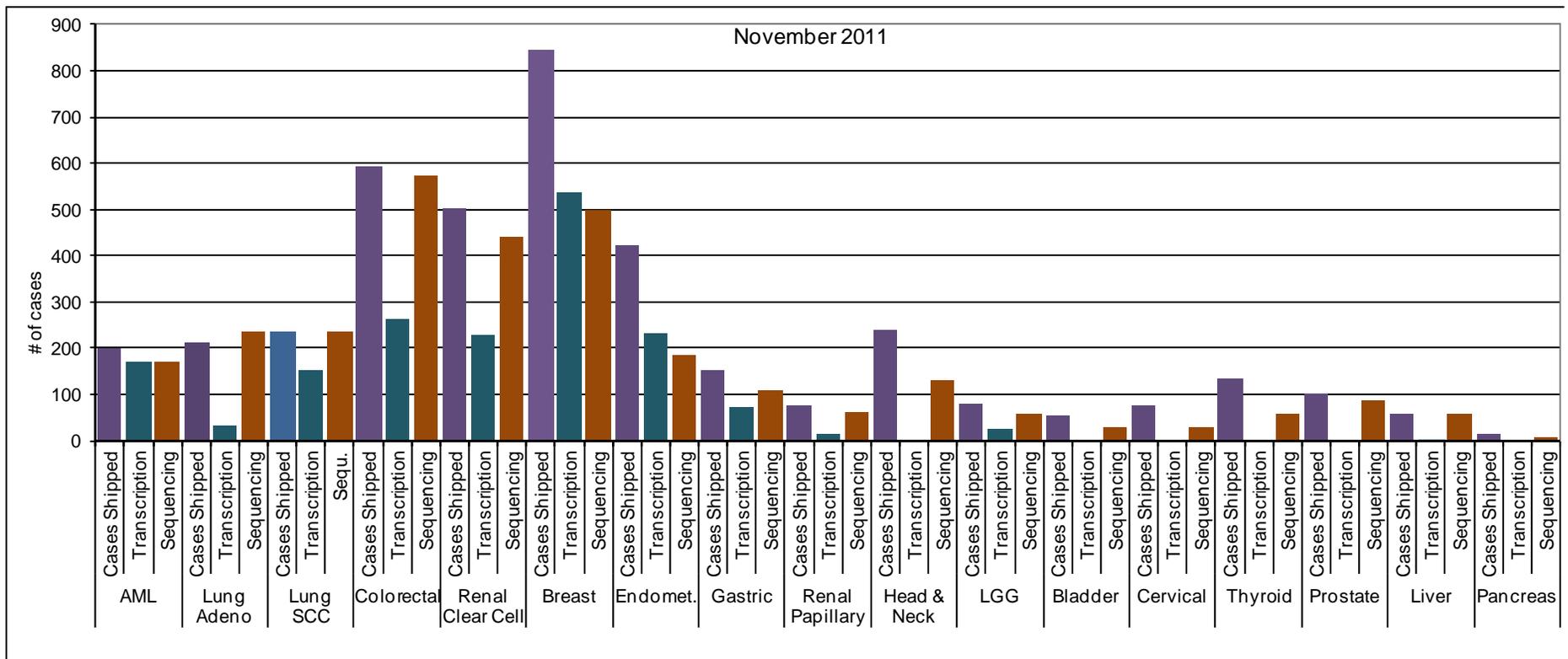
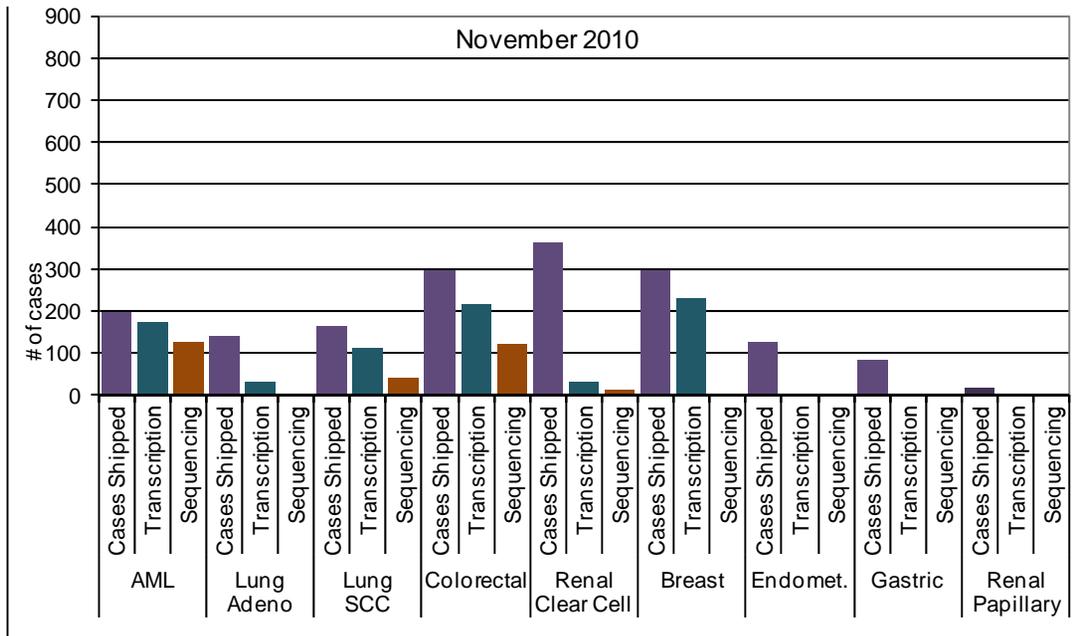
Inventing a Pipeline for Comprehensive Characterization



THE CANCER GENOME ATLAS

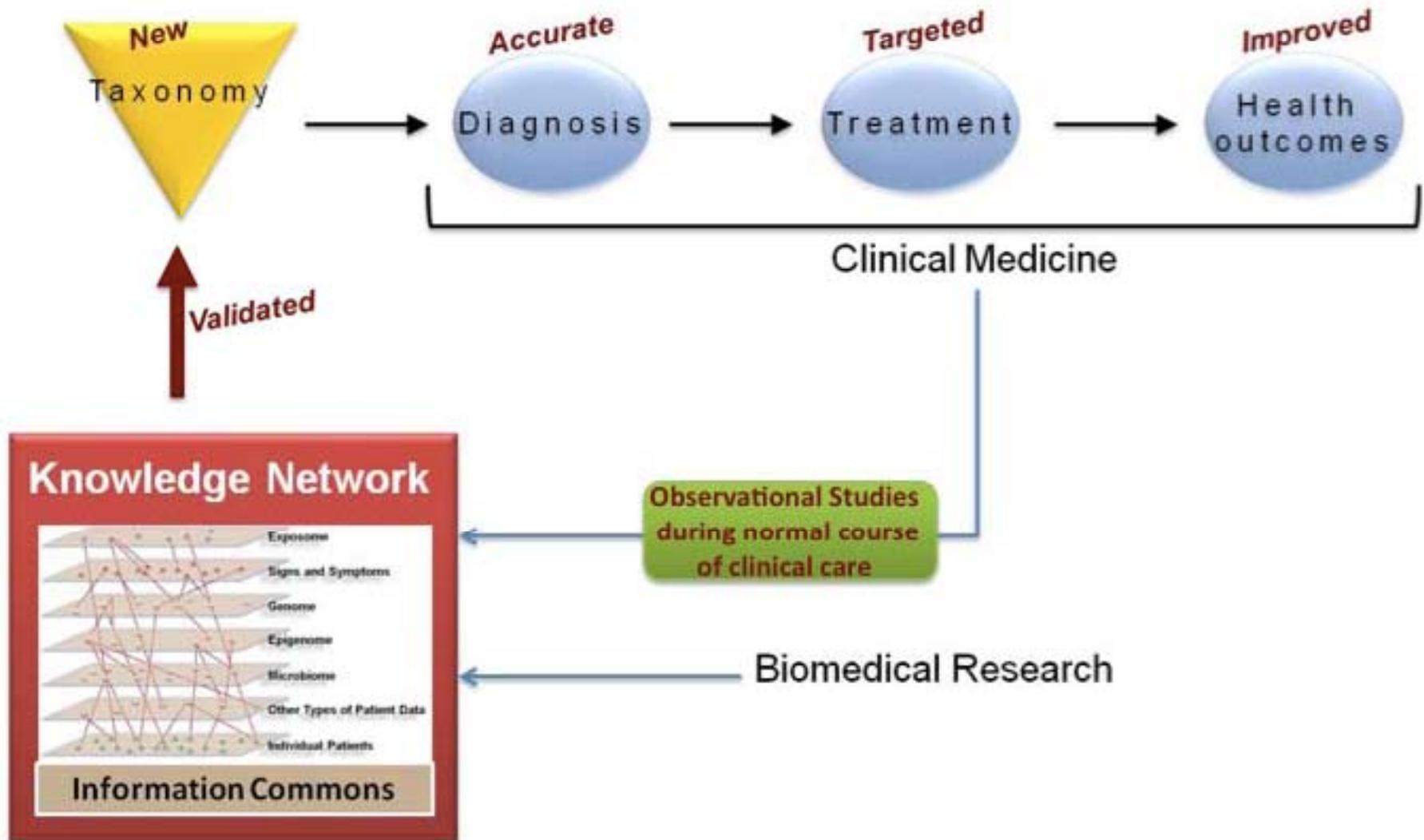
TCGA Project: Current Status

Nov 2010 Status
Vs.
Nov 2011 Status

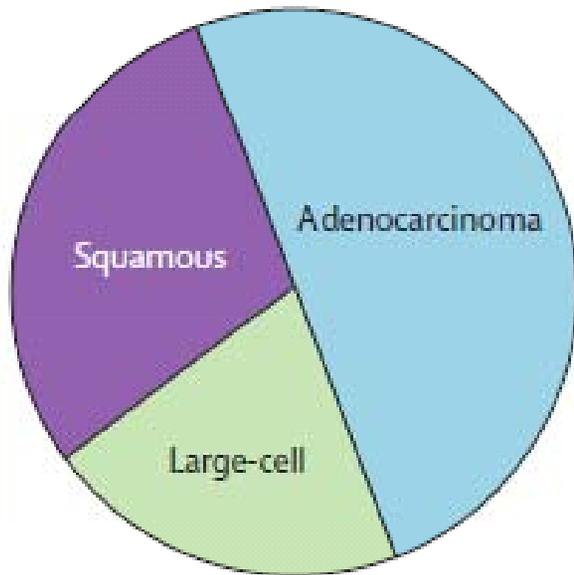


TOWARDS PRECISION MEDICINE

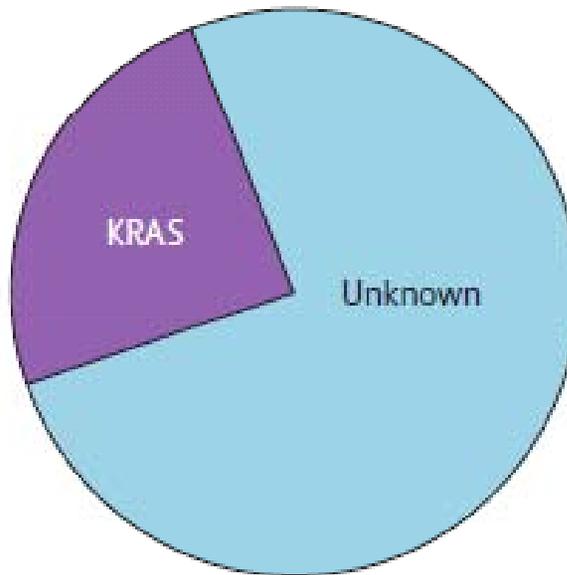
(NRC REPORT, NOVEMBER 2011)



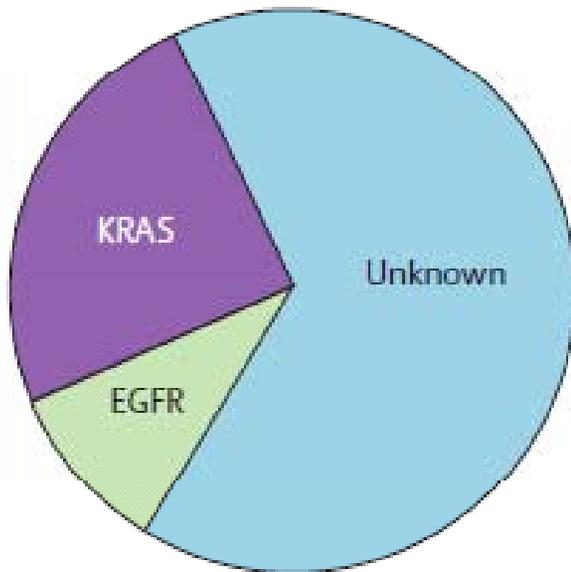
Traditional view



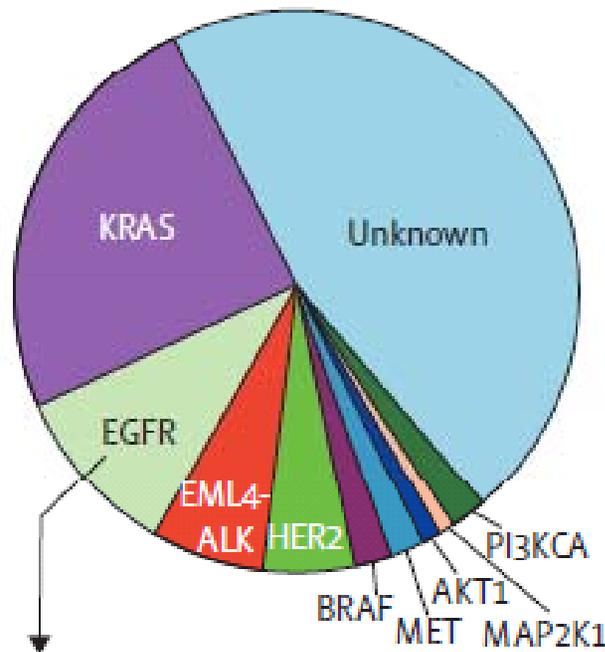
1987



2004



2009

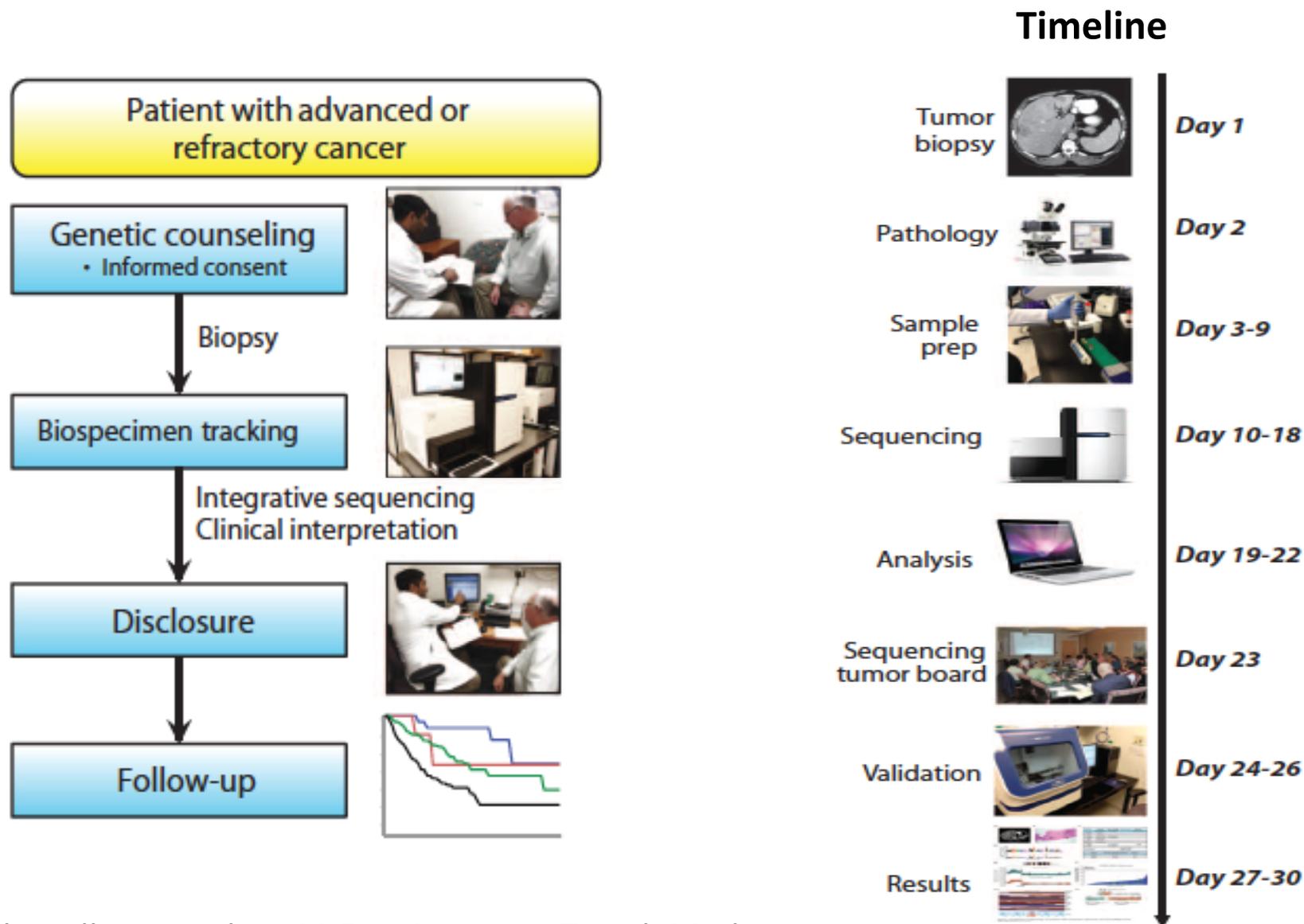


From microscopes
to DNA sequence:

How cancer genomics
is beginning to
confer precision
on treatment
for lung cancers

Path forward to Clinical Sequencing

Arul Chinnaiyan and colleagues: Dec 1, 2011



Achieving Completeness: *Clinical data should drive more and deeper discovery*

Global Cancer Alliance

Shared knowledge base to which patients can choose to contribute their genomic data, clinical data



Many challenges, but essential

WHAT IS NEW AT THE NCI?

- NEW LEADERSHIP
- DIMINISHING BUDGETS
- EXPANSIONS/REARRANGEMENTS:
 - CANCER GENOMICS
 - CLINICAL TRIALS GROUPS

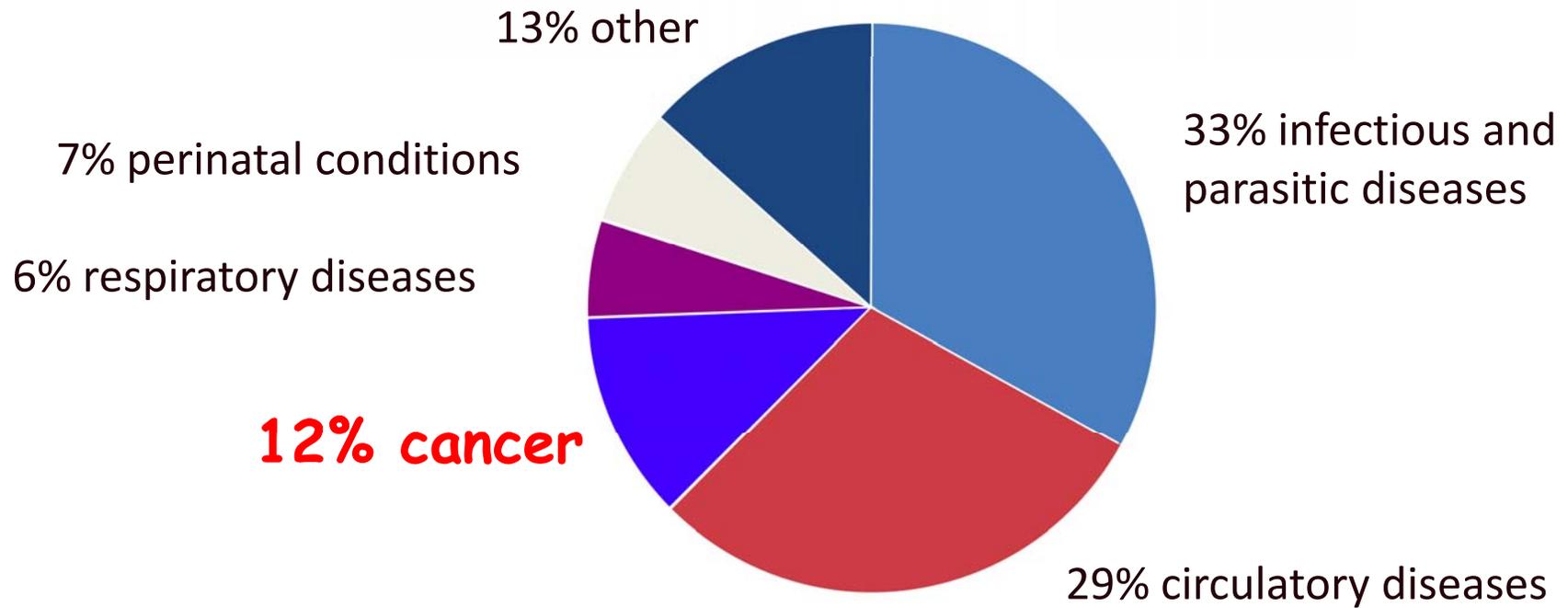
RE-ENGINEERING COOPERATIVE GROUPS

- CONSOLIDATE GROUPS AND IMPROVE EFFICIENCY
- STRENGTHEN DATA AND SPECIMEN COLLECTION
- INCORPORATE GENOMICS AND OTHER SCIENTIFIC ISSUES INTO TRIALS
- ENFORCE CONNECTIONS WITH CANCER CENTERS

WHAT IS NEW AT THE NCI?

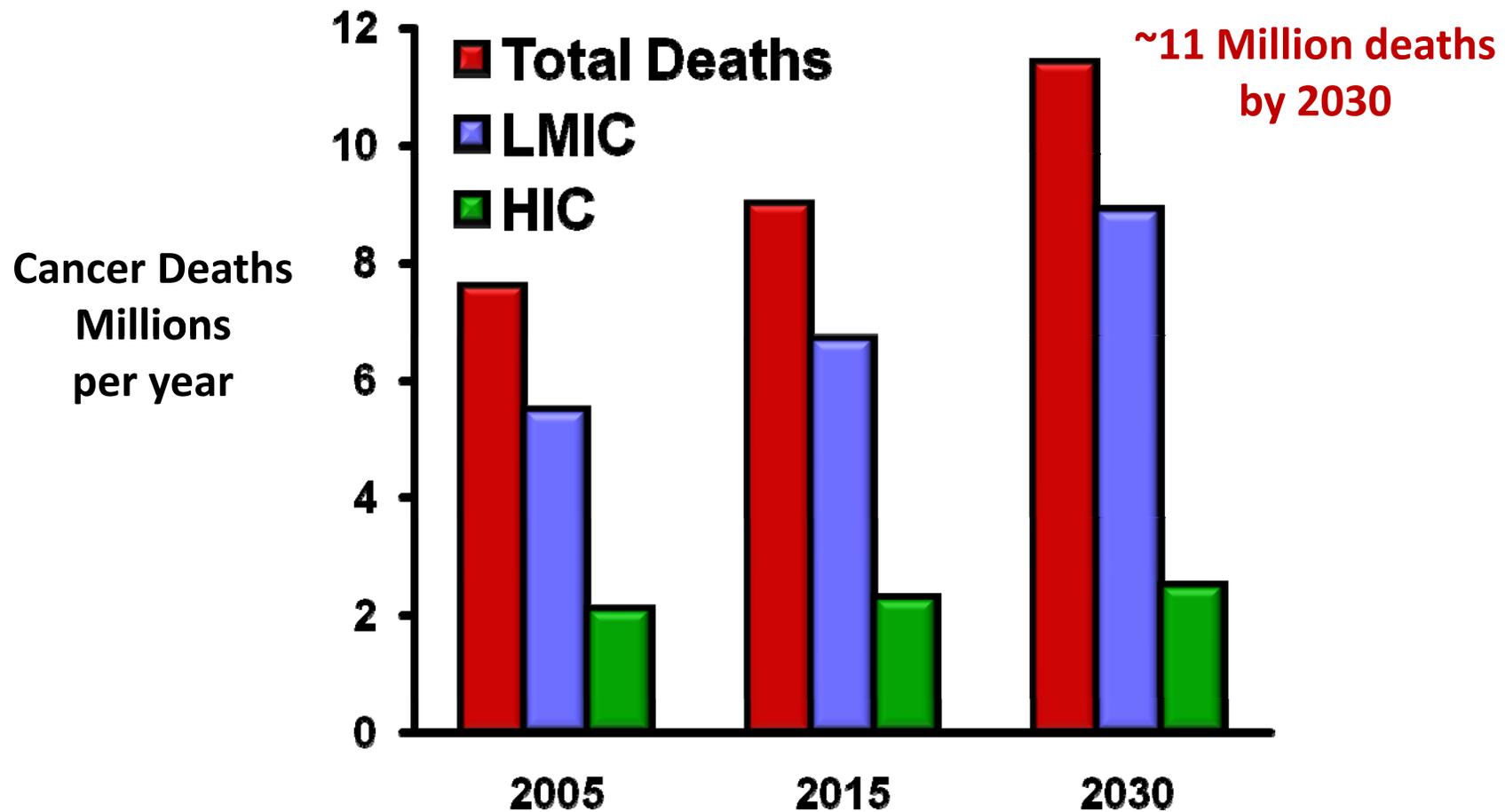
- NEW LEADERSHIP
- DIMINISHING BUDGETS
- EXPANSIONS/REARRANGEMENTS:
 - CANCER GENOMICS
 - CLINICAL TRIALS GROUPS
- NEW FOCUS ON THE LESS OBVIOUS:
 - CANCER AS PART OF GLOBAL HEALTH

GLOBAL CAUSES OF MORTALITY



Cancer Cases Are Rising Globally Especially in Less Developed Settings

Cancer currently accounts for ~12.5% of ~60 Million global deaths.



NCI'S NEW CENTER FOR GLOBAL HEALTH

- AMALGAMATE EXISTING INITIATIVES
- GUIDE DEVELOPMENT OF REGISTRIES AND NATIONAL CANCER PLANS
- CAPITALIZE ON ONCOGENIC INFECTIONS: NEW AND EXISTING VACCINES, ETC
- LINK TO TRANS-DISEASE PREVENTION: TOBACCO, OBESITY, ALCOHOL...
- PURSUE OPERATIONAL IMPROVEMENTS: SCREENING, ACCESS TO TREATMENT AND SYMPTOM CONTROL, SURGERY, HEALTH SYSTEMS...
- HARNESS ENTHUSIASM, FIND PARTNERS, AND BUILD CAPACITY

REGIONAL VARIATIONS IN CANCER

DATEC

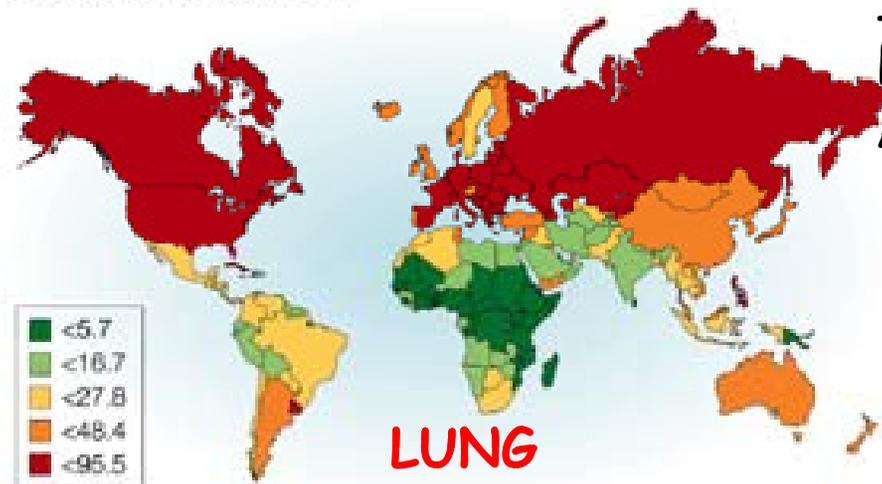
a Incidence of stomach cancer



b Incidence of cervical cancer

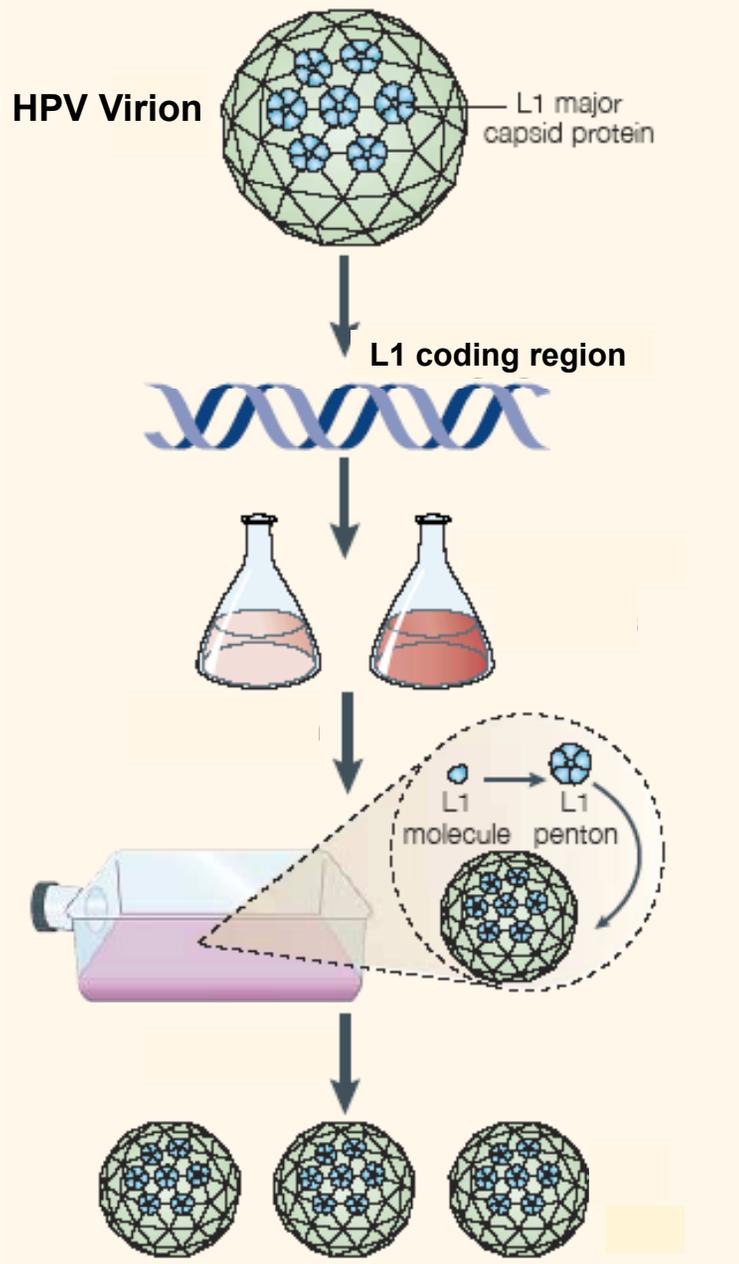


c Incidence of lung cancer



INFLUENCED
BY HPV INFECTION
AND SCREENING

Rastogi, T. et al. Opportunities for cancer epidemiology in developing countries. Nat Rev Cancer. 2004 Nov;4(11):909-17.



Prophylactic HPV Vaccines Are L1 Virus Like Particles (VLPs)

L1 Insertion in Baculovirus Expression Vector

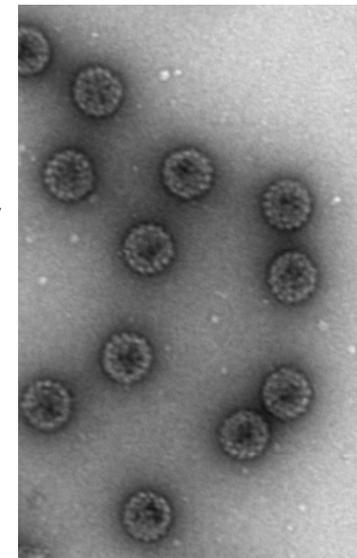
Production in Insect Cells

Spontaneous assembly of L1 into VLPs

Induce high titers of virion neutralizing antibodies

Non-infectious, Non-oncogenic

HPV16 L1 VLPs



Reinhard Kirnbauer et al. PNAS 1992

**IN RWANDA, FUNDS FROM GAVI,
AGREEMENT WITH MERCK, PLUS GOVERNMENT SUPPORT
HAVE MADE HPV VACCINATION MORE WIDESPREAD
THAN IN THE USA**



Some NCI-designated Cancer Centers active in Africa

- Fred Hutchinson Cancer Research Center: Uganda
- University of North Carolina: Malawi
- University of Maryland: Nigeria
- University of Michigan: Ghana
- Indiana University: Kenya



2011: FHCRC/UCI PROJECT



DENNIS
BURKITT

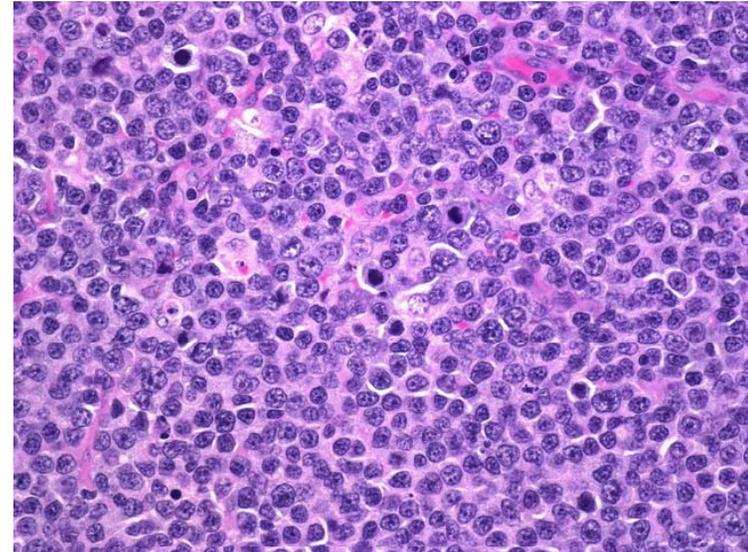
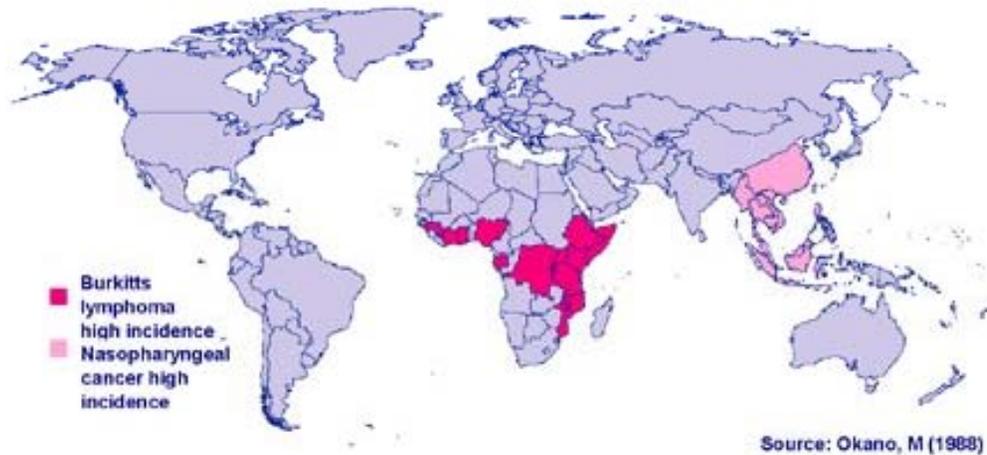
**50+ YEAR
HISTORY
OF THE
UGI**

BURKITT'S
LYMPHOMA



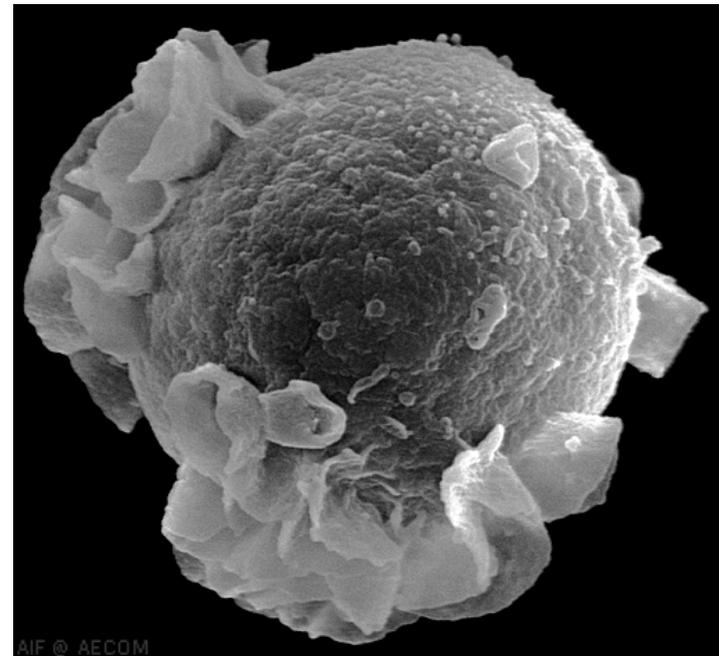
EBV AND BURKITT'S LYMPHOMA

Figure 4.2: Epstein-Barr virus-associated Burkitt lymphoma & nasopharyngeal carcinoma



UNRESOLVED ISSUES:

RELATIONSHIP TO MALARIA?
TARGETABLE MUTATIONS?
IMPROVED AFFORDABLE RX?
BETTER MONITORING
FOR RECURRENCE?
SCREENING? VACCINES?



Estimated new cases of EBV-associated cancers worldwide per year

<u>Cancer</u>	<u>Number of cases</u>	<u>Attributable to EBV</u>
Burkitt lymphoma		
Developed countries	400	100
Less-developed countries	7800	6600
Gastric carcinoma	933,900	84,050
Hodgkin lymphoma	62,400	28,600
Nasopharyngeal carcinoma	80,000	78,100
Total		197,450

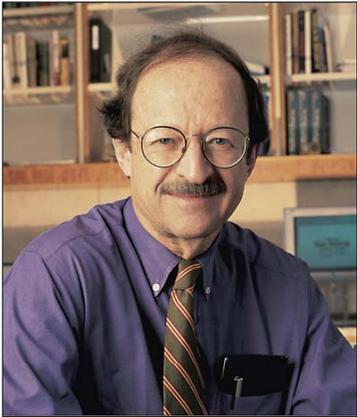
WHAT ARE THE PROSPECTS FOR AN EBV VACCINE?

A NEW PROJECT ON THE NON-OBVIOUS:

PROVOCATIVE QUESTIONS

What is the "Provocative Questions" Project?

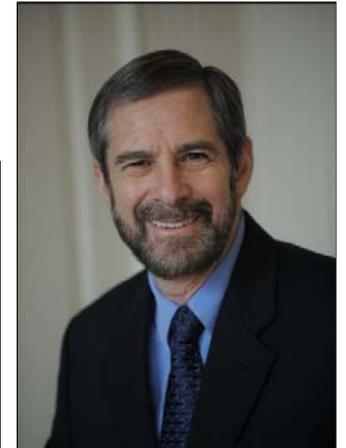
- Development of a list of **important but non-obvious** questions that will stimulate the NCI's research communities to use laboratory, clinical, and population sciences in especially effective and imaginative ways.
- The proposals should:
 - Build on specific advances** in our understanding of cancer and cancer control
 - Address broad issues** in the biology of cancer that have proven difficult to resolve
 - Take into consideration the **likelihood of progress** in the foreseeable future (e.g. 5 to 10 years)
 - Address **ways to overcome obstacles** to achieving long-term goals



Harold Varmus

<http://provocativequestions.nci.nih.gov/>

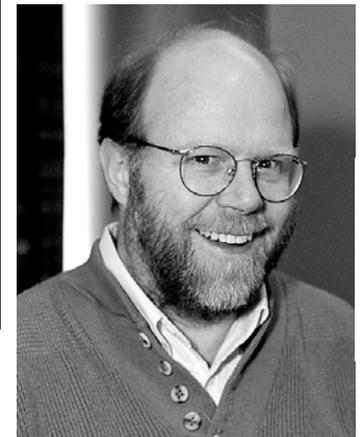
The screenshot shows the homepage of the National Cancer Institute's "Provocative Questions" project. The header features the NCI logo and the text "National Cancer Institute" and "U.S. National Institutes of Health | www.cancer.gov". The main heading is "Provocative Questions" in a large, bold font, followed by the subtitle "Identifying Perplexing Problems to Drive Progress Against Cancer". A search bar and navigation links for "News" and "Events" are visible. Below the header, there are links for "Home", "Proposed Provocative Questions", and "Workshops & Outcomes". The main content area is titled "What is the 'Provocative Questions' Project?" and contains a paragraph explaining the project's goal: to assemble a list of important but non-obvious questions that will stimulate the NCI's research communities. Below this, there are four bullet points listing the types of questions the project seeks: 1. Build on specific advances in our understanding of cancer and cancer control; 2. Address broad issues in the biology of cancer that have proven difficult to resolve; 3. Take into consideration the likelihood of progress in the foreseeable future (e.g. 5 to 10 years); and 4. Address ways to overcome obstacles to achieving long-term goals. The background of the text area features a silhouette of a person's head and a rack of test tubes.



Doug Lowy



Tyler Jacks



Ed Harlow

PROCESS

MULTI-DISCIPLINARY WORKSHOPS
AT THE NIH AND AROUND THE U.S.

PQ WEBSITE FOR POSTING, READING, AND
RESPONDING TO QUESTIONS

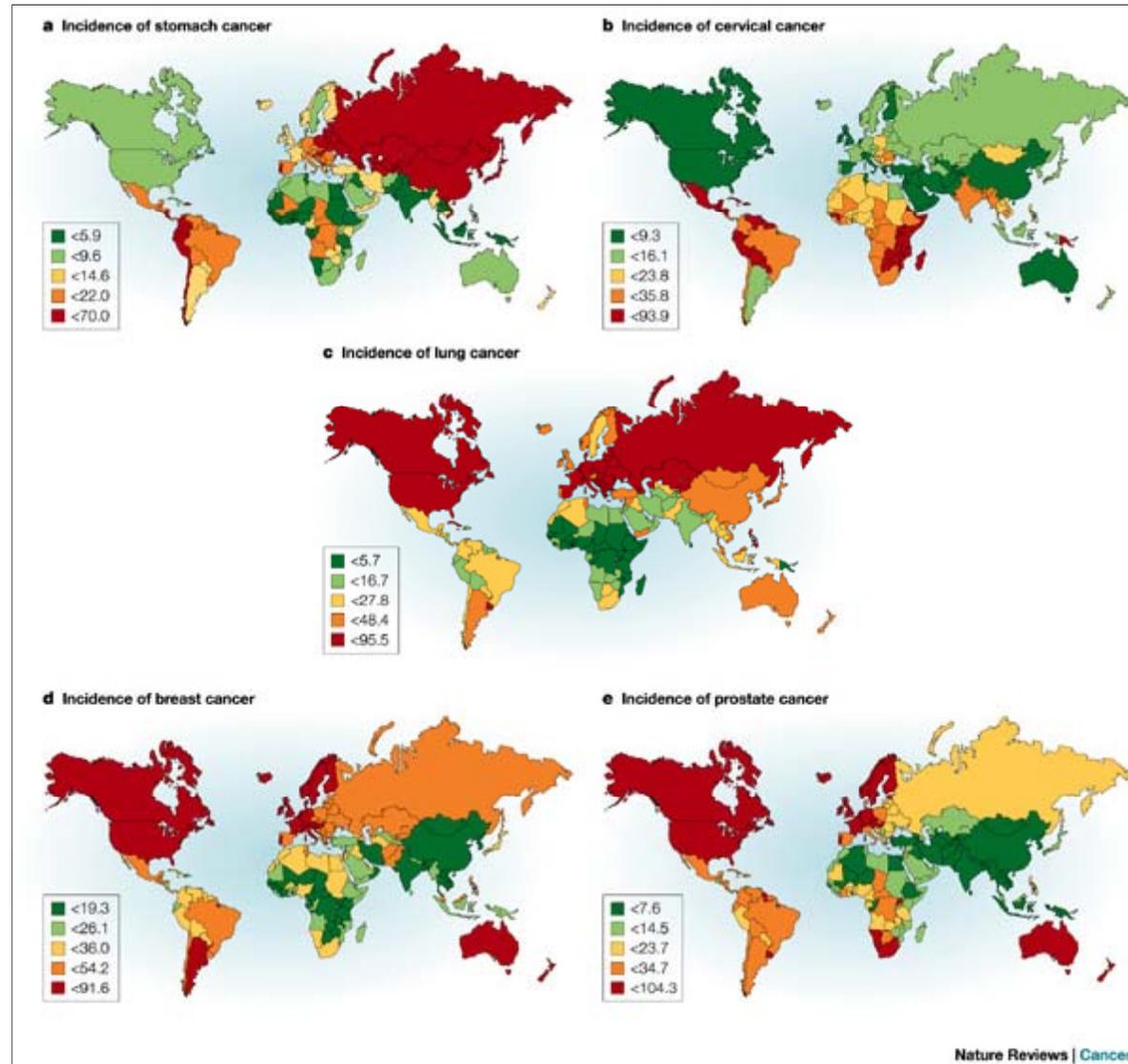
REQUEST FOR PROPOSALS TO ANSWER 24 PQ'S
APPROVED BY BSA FOR RO1'S/R21'S (\$15M)

752 APPLICATIONS, SOME FOR EACH PQ

BEING REVIEWED BY NCI SEP'S

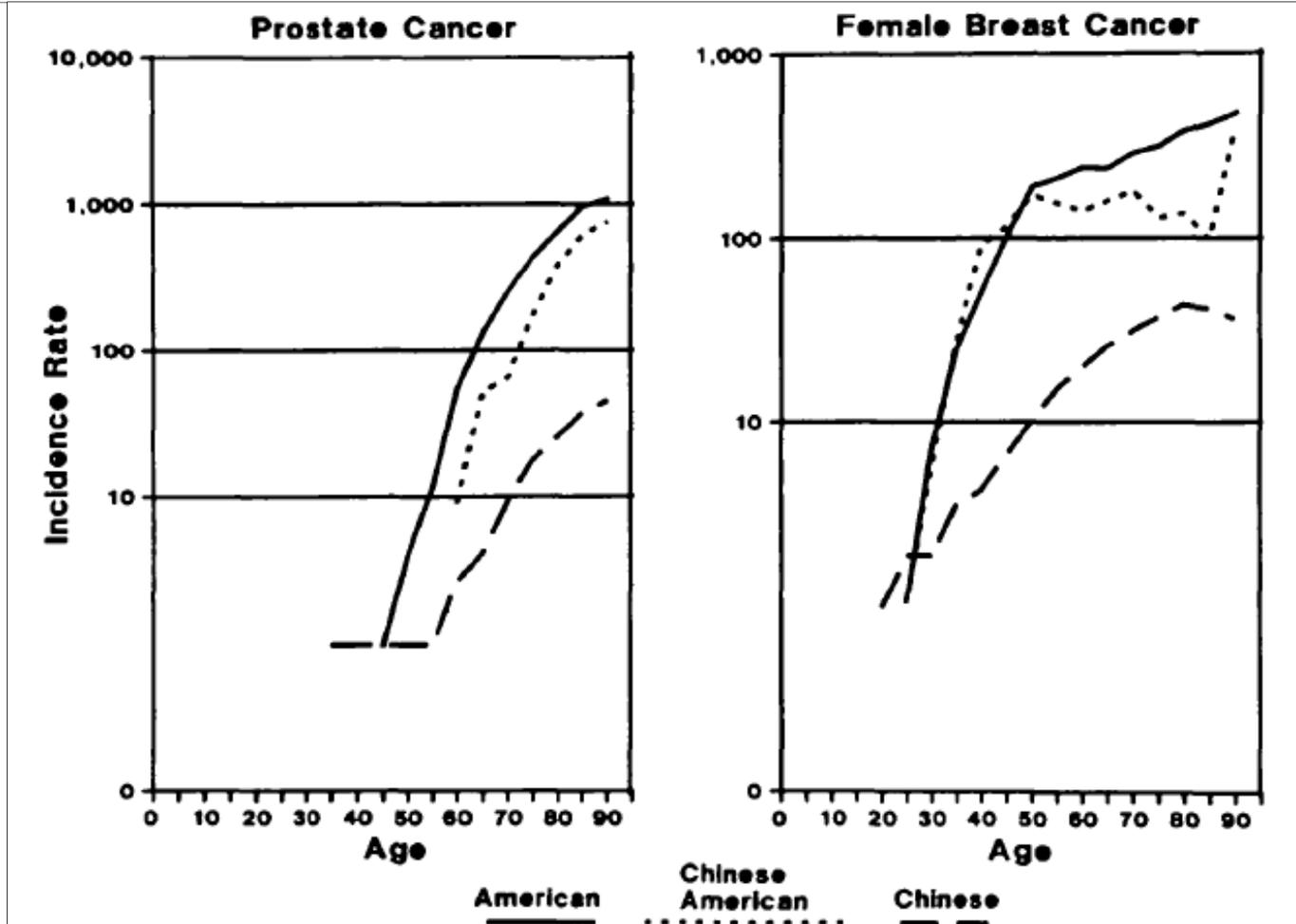
EPIDEMIOLGY

WHY ARE THERE REGIONAL VARIATIONS IN CANCER RATES?



Rastogi, T. et al. Opportunities for cancer epidemiology in developing countries. *Nat Rev Cancer*. 2004 Nov;4(11):909-17.

WHAT ENVIRONMENTAL FACTORS CHANGE THE RISKS OF VARIOUS CANCERS WHEN PEOPLE MOVE FROM ONE GEOGRAPHIC REGION TO ANOTHER?



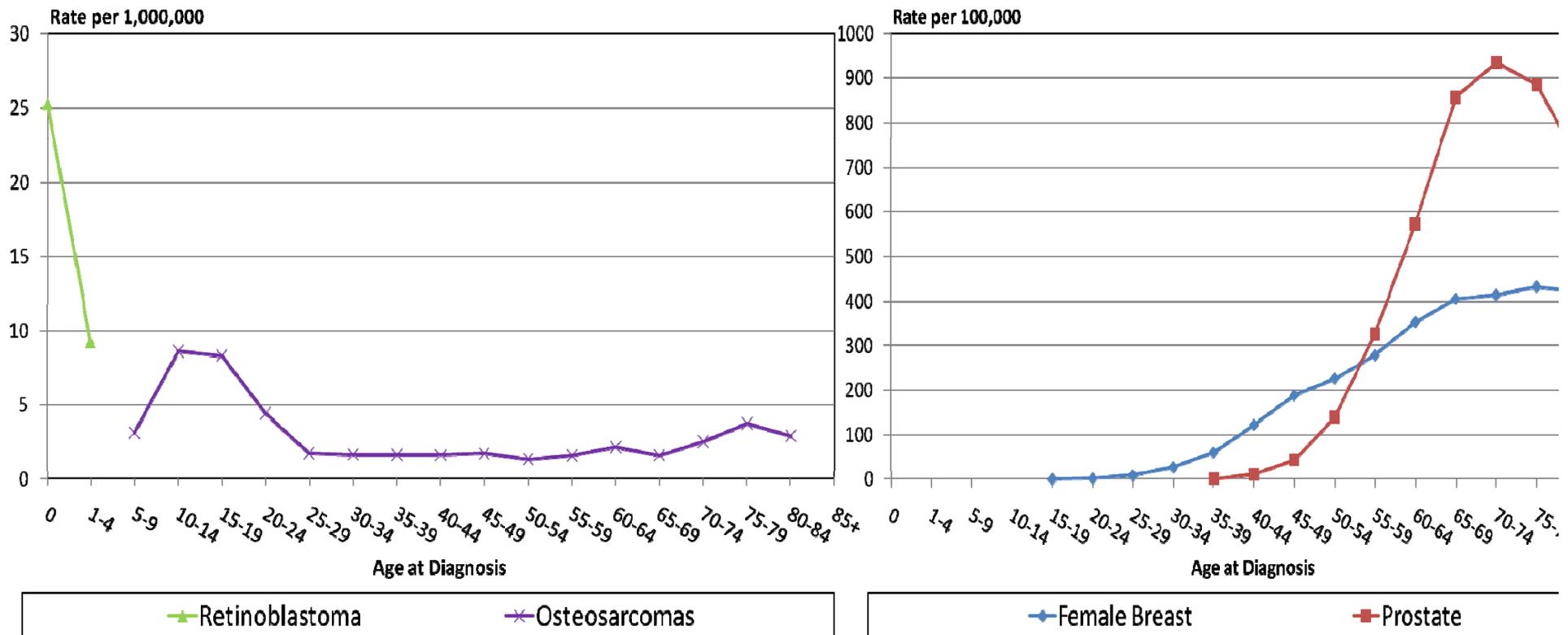
Yu H., et al. Comparative epidemiology of cancers of the colon, rectum, prostate and breast in Shanghai, China versus the United States. *International Journal of Epidemiology* 1991, 20: 76-81.

WHY ARE INCIDENCE RATES FOR MANY CANCERS HIGHER IN MEN THAN WOMEN?

Estimated New Cancer Cases and Deaths by Sex, US, 2010				
Type	New Cases		Deaths	
	Male	Female	Male	Female
All Sites	789,620	739,940	299,200	270,290
Oral cavity and pharynx	25,420	11,120	5,430	2,450
Esophagus	13,130	3,510	11,650	2,850
Liver and intrahepatic bile duct	17,430	6,690	12,720	6,190
Larynx	10,110	2,610	2,870	730
Urinary bladder	52,760	17,770	10,410	4,270
Thyroid	10,740	33,930	730	960

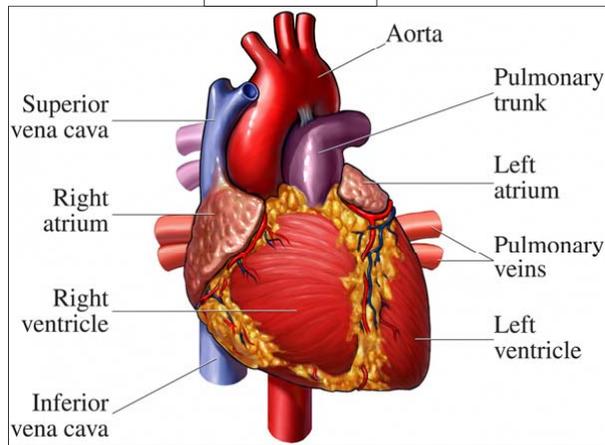
**American Cancer Society
Cancer Facts and Figures, 2010**

Not all cancers increase with age; age; what determines kinetics?

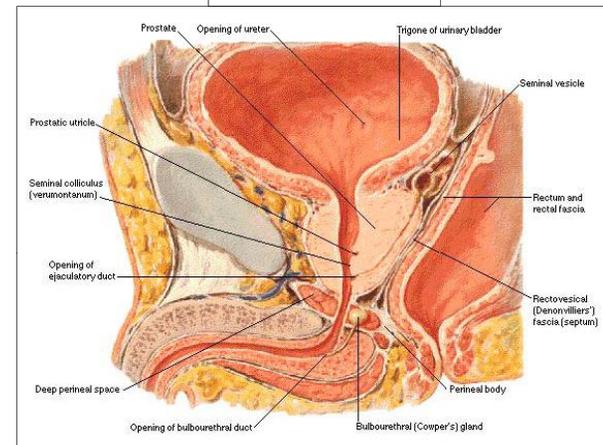


Why are different tissues so dramatically different in their tendency to develop cancers?

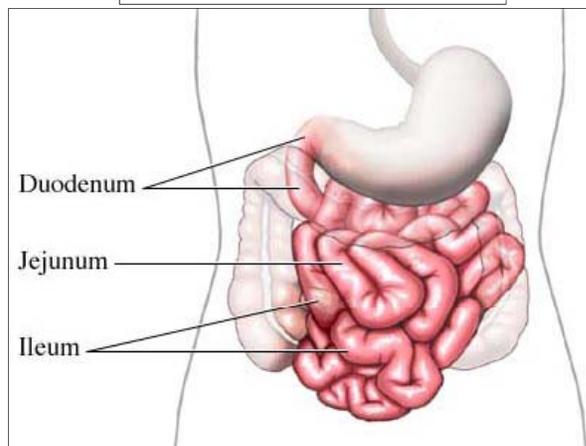
Heart



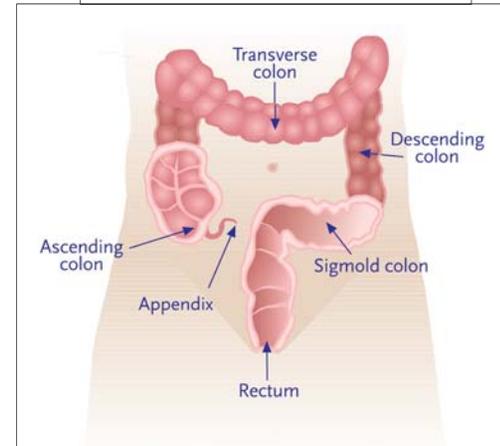
Prostate



Small Intestine



Large Intestine



Why are different animals with different sizes and different

life spans so different with respect to cancer incidence?

Turtles

Mice



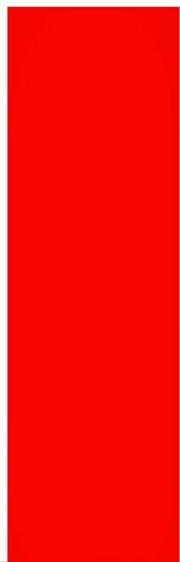
Sharks



Whales....except belugas
from the SLE!

WHY ARE PATIENTS WITH CERTAIN NEURODEGENERATIVE DISEASES (PD, HD, AD, FRAGILE X) AT LOWER RISK OF MOST CANCERS?

Alzheimer's Disease protects against cancer



Cases of cancer in people without AD



Cases of cancer in people with AD

Cancer protects against Alzheimer's Disease



Cases of AD in people without cancer



Cases of AD in people with cancer

Vascular dementia does not protect against cancer



Cases of cancer in people without VD



Cases of cancer in people with VD

Roe CM, et al. Cancer linked to Alzheimer's disease but not vascular dementia. *Neurology* 2010; 74:106-112.

RISK MODIFICATION



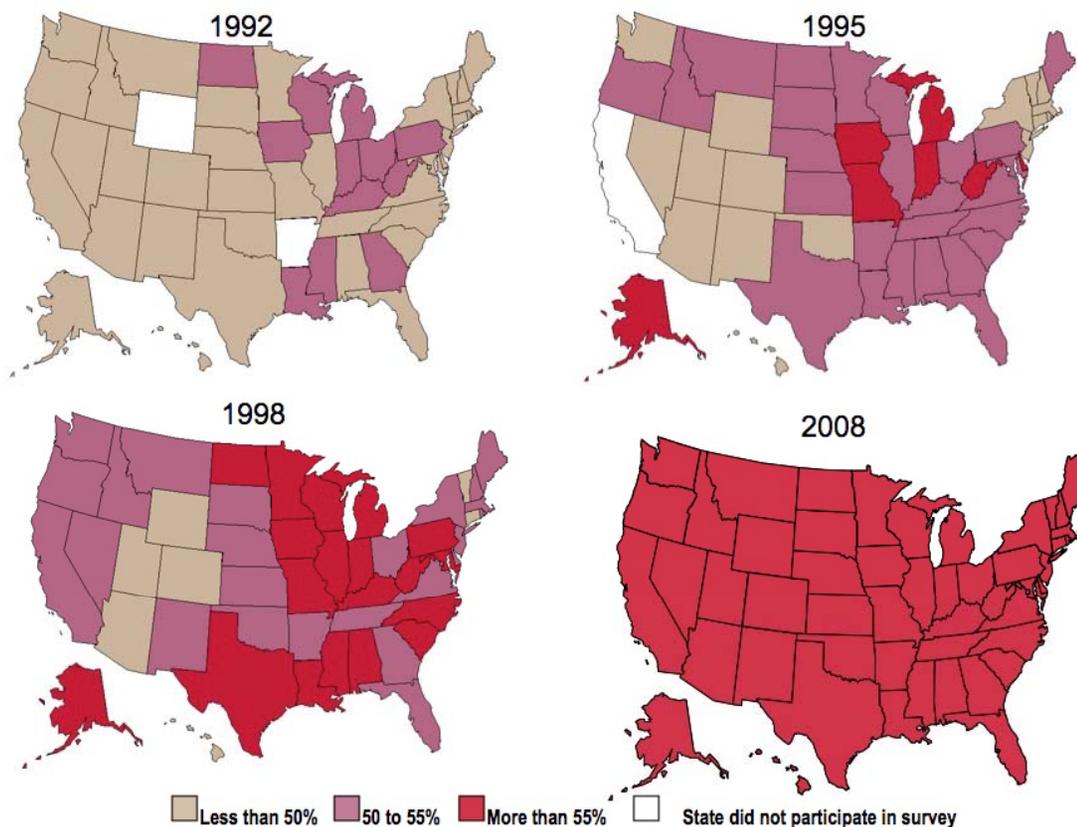
WHY DON'T MORE PEOPLE ALTER BEHAVIORS KNOWN TO INCREASE THE RISK OF CANCERS?

- The message itself is not optimally designed
- The message is not effectively delivered
- The interventions to facilitate behavior change are not optimal



HOW DOES OBESITY CONTRIBUTE TO CANCER RISK?

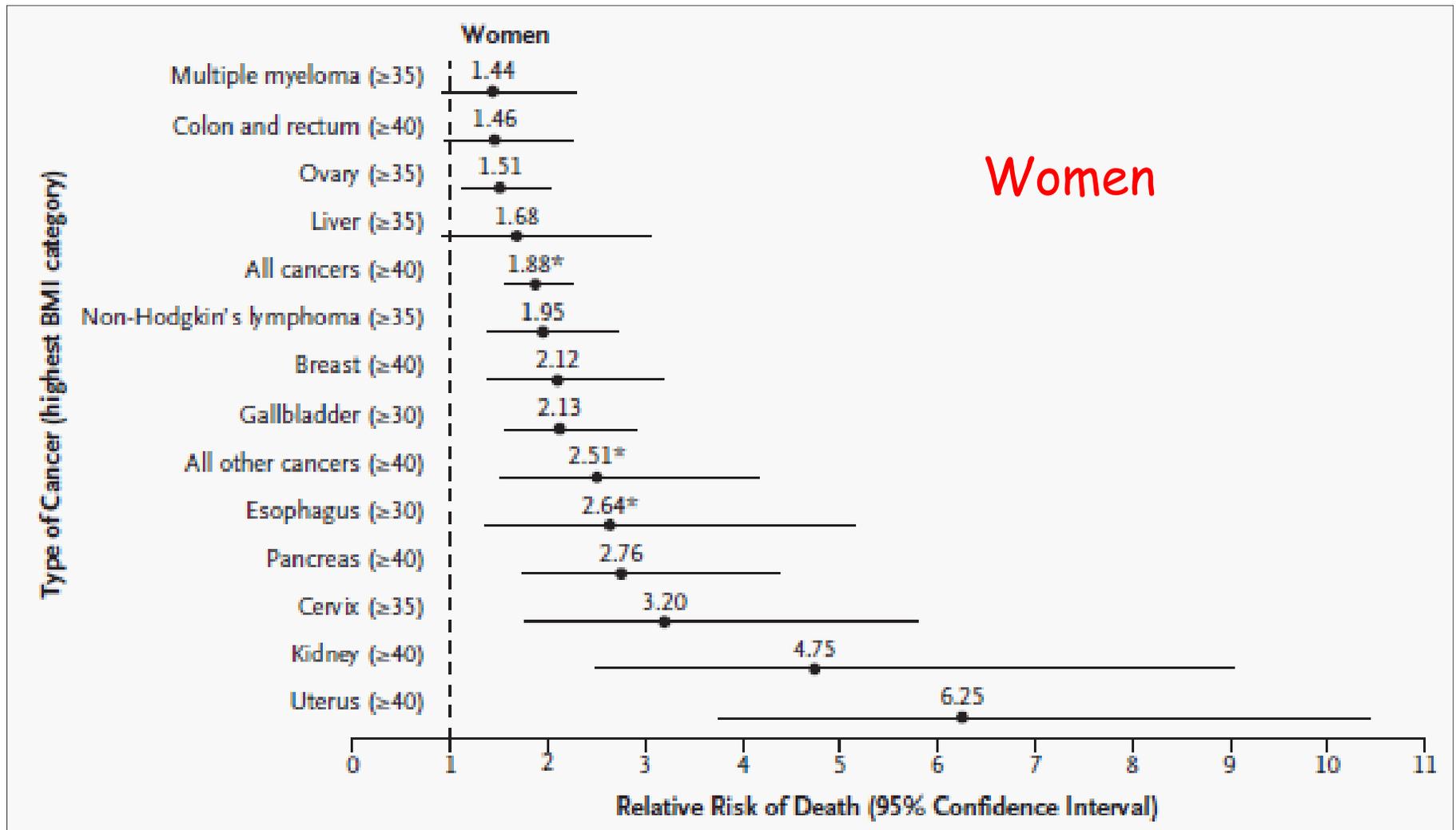
Trends in Overweight* Prevalence (%), Adults 18 and Older,
US, 1992-2008



*Body mass index of 25.0 kg/m² or greater. Source: Behavioral Risk Factor Surveillance System, CD-ROM (1984-1995, 1998) and Public Use Data Tape (2004-2008), National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 1997, 2000, 2005, 2007, 2008, 2009.

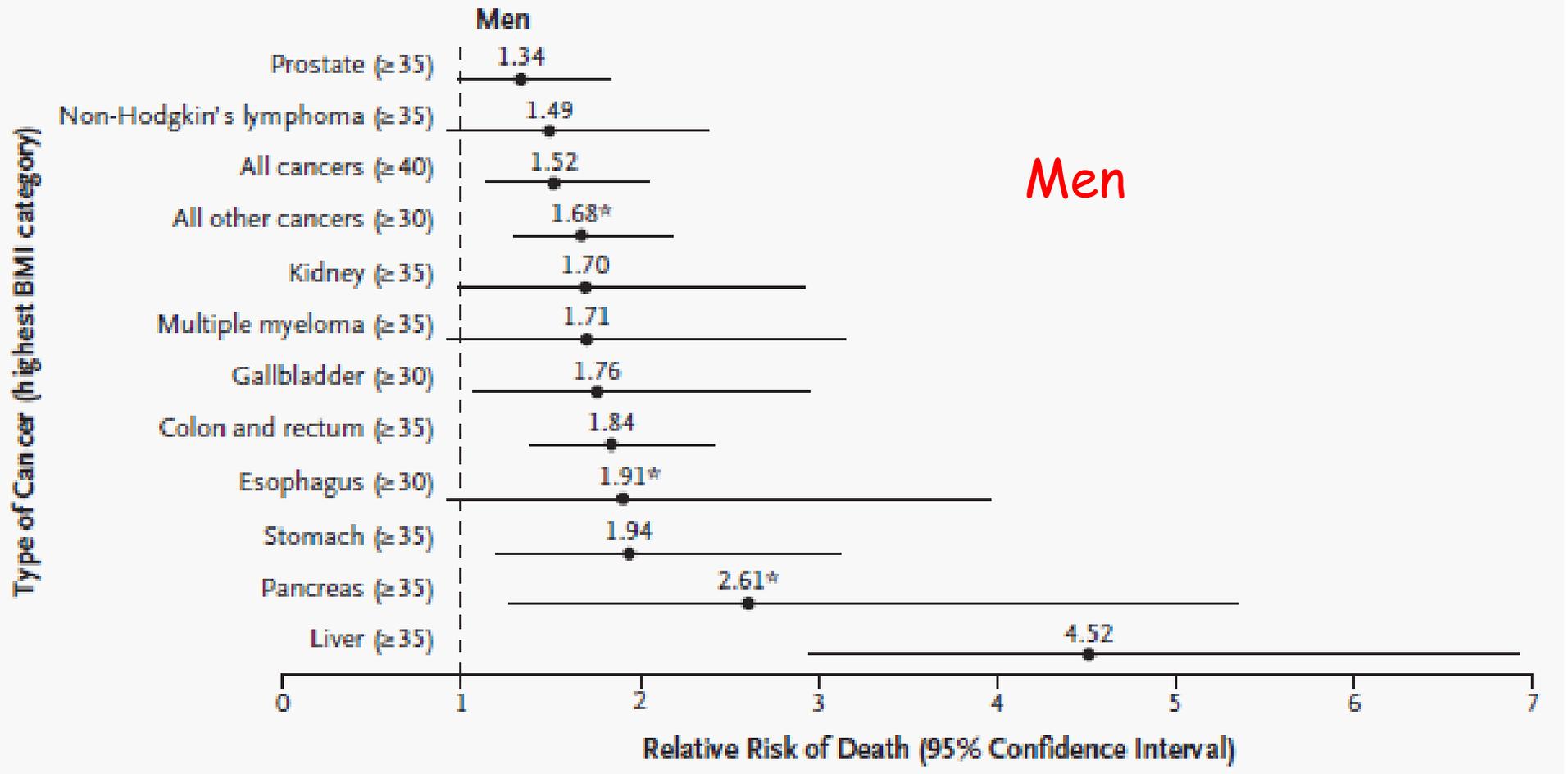
American Cancer Society, Cancer Facts and Figures, 2010.

HOW DOES OBESITY CONTRIBUTE TO CANCER RISK?



Calle, EE et al., Overweight, Obesity, and Mortality from Cancer in a Prospectively Studied Cohort of U.S. Adults. *N Engl J Med* 2003;348:1625-38.

HOW DOES OBESITY CONTRIBUTE TO CANCER RISK?



Calle, EE et al., Overweight, Obesity, and Mortality from Cancer in a Prospectively Studied Cohort of U.S. Adults. N Engl J Med 2003;348:1625-38.

Long-Term Mortality after Gastric Bypass Surgery

Distribution of Deaths and Death Rates per 10,000 Person-Years*				
End Point	Matched Subjects			
	Surgery Group (N=7925)		Control Group (N=7925)	
	no.	no./10,000 person-yr	no.	no./10,000 person-yr
All causes of death	213	37.6	321	57.1
Cardiovascular disease	55	9.7	104	18.5
Diabetes	2	0.4	19	3.4
Cancer	31	5.5	73	13.3
Other diseases	62	11.0	89	15.5
All non-disease causes	63	11.1	36	6.4

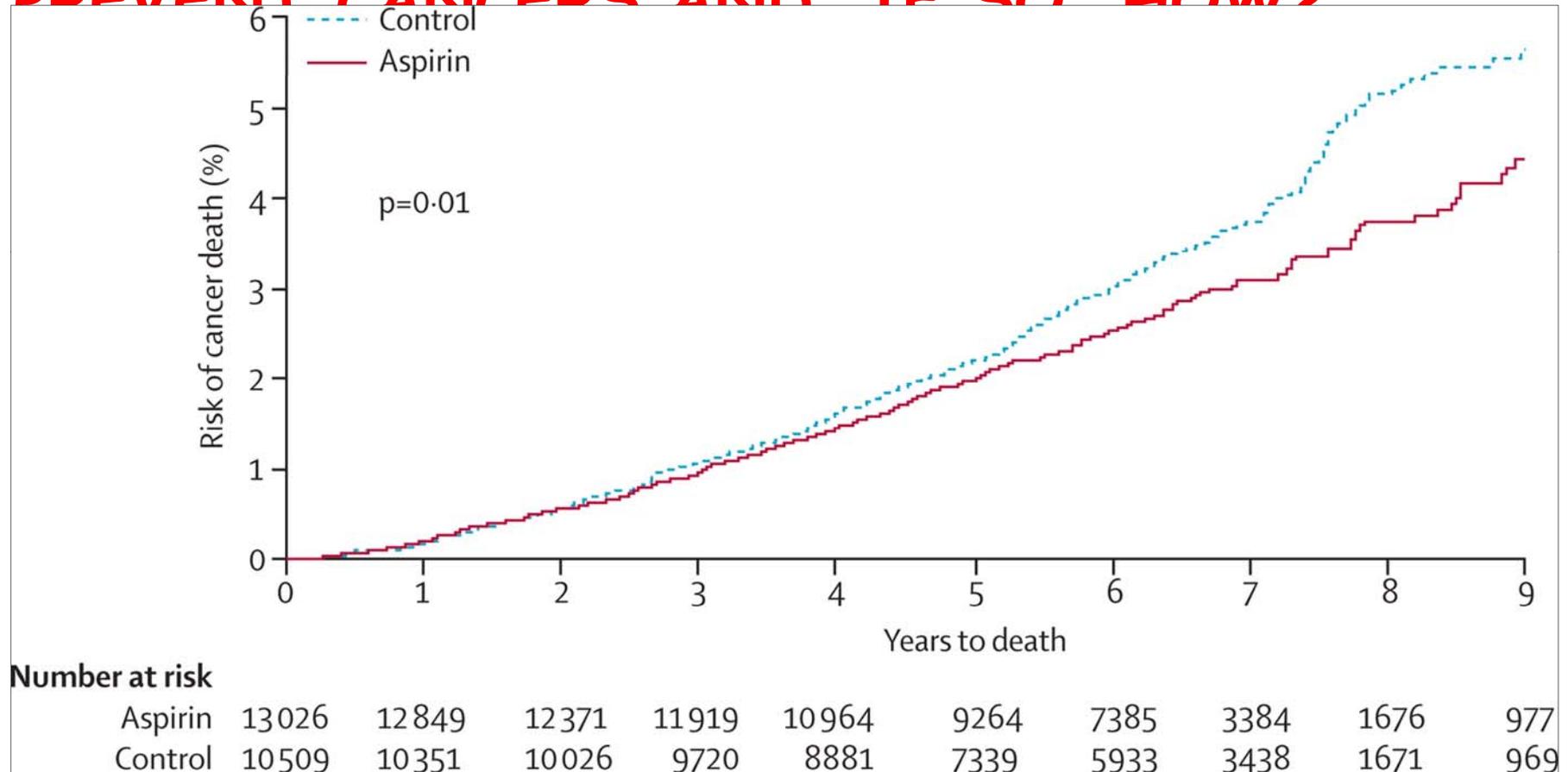
*Deaths that were caused by disease include all deaths minus those caused by accidents unrelated to drugs, poisonings of undetermined intent, suicides, and other non-disease deaths.

Adams, TD et al., Long-term mortality after gastric bypass surgery. N Engl J Med 2007; 357:753-61.

PREVENTION

DO DRUGS THAT ARE COMMONLY AND CHRONICALLY USED FOR OTHER INDICATIONS

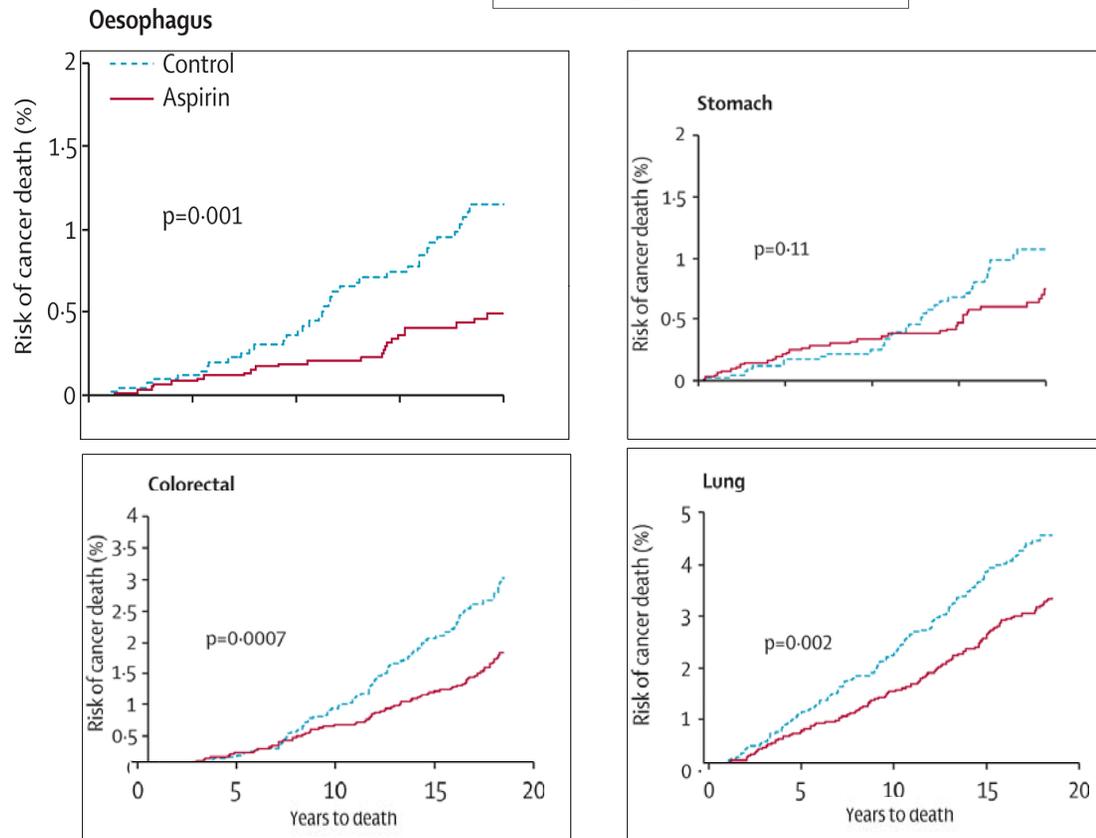
PREVENT CANCERS AND IF SO HOW?



Rothwell et al., Effect of daily aspirin on long-term risk of death due to cancer: analysis of individual patient data from randomised trials. Lancet. 2011 Jan 1;377(9759):31-41. Epub 2010 Dec 6.

DO DRUGS THAT ARE COMMONLY AND CHRONICALLY USED FOR OTHER INDICATIONS PREVENT CANCERS AND, IF SO, HOW?

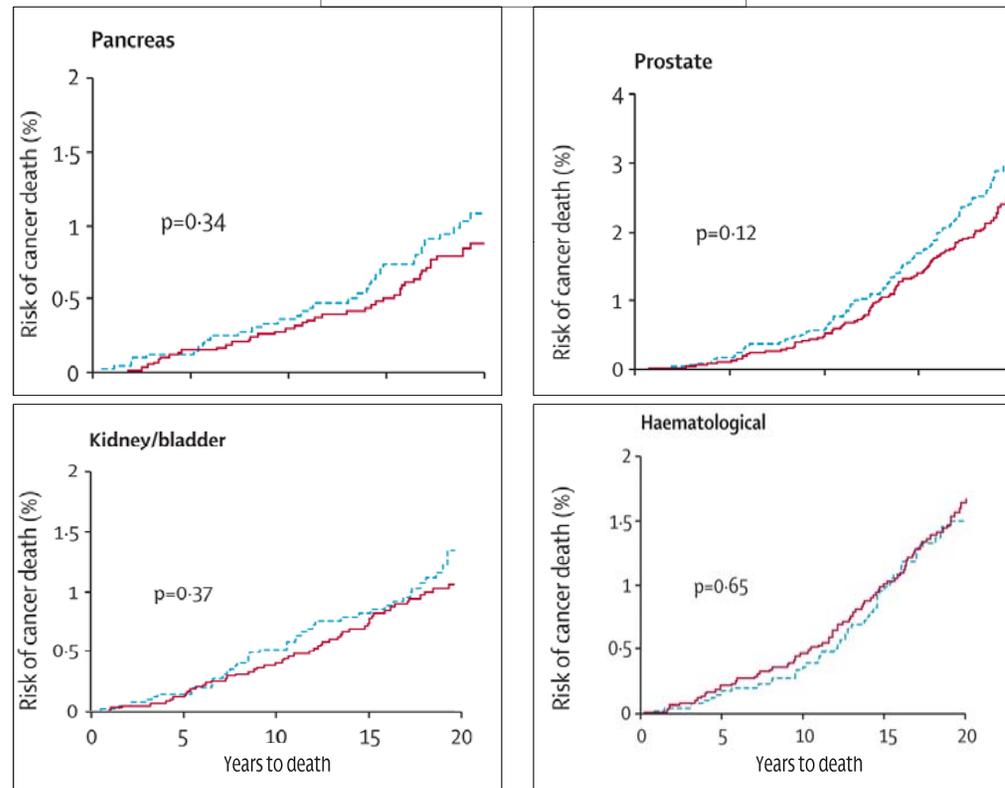
Strong Effects



Rothwell et al., Effect of daily aspirin on long-term risk of death due to cancer: analysis of individual patient data from randomised trials. *Lancet*. 2011 Jan 1;377(9759):31-41. Epub 2010 Dec 6.

DO DRUGS THAT ARE COMMONLY AND CHRONICALLY USED FOR OTHER INDICATIONS PREVENT CANCERS AND, IF SO, HOW?

Weak or No Effect

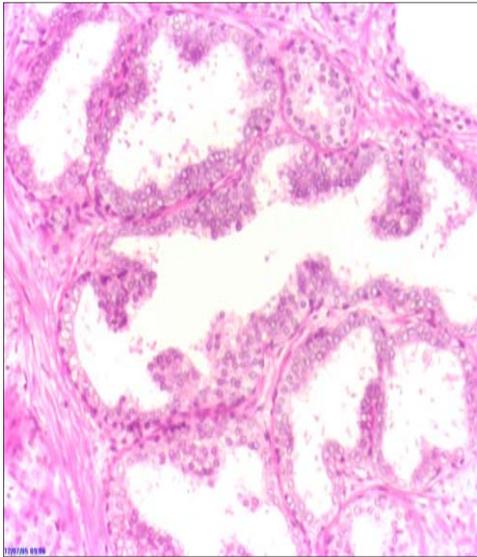


Rothwell et al., Effect of daily aspirin on long-term risk of death due to cancer: analysis of individual patient data from randomised trials. Lancet. 2011 Jan 1;377(9759):31-41. Epub 2010 Dec 6.

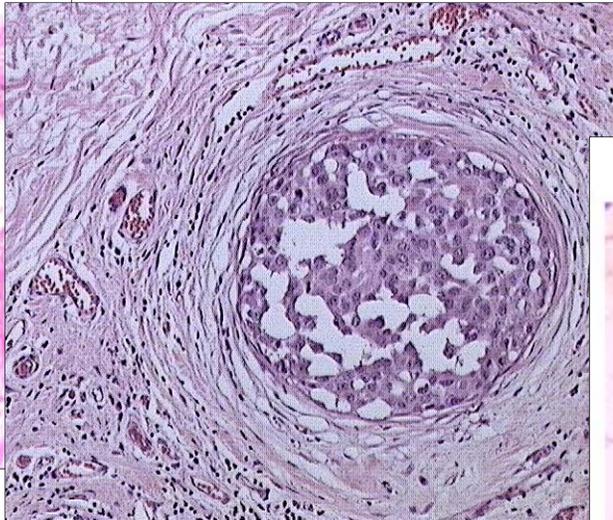
DIAGNOSTICS

WHAT PROPERTIES OF NON-MALIGNANT LESIONS (IN SITU CA'S) PREDICT THE LIKELIHOOD OF INVASIVE DISEASE?

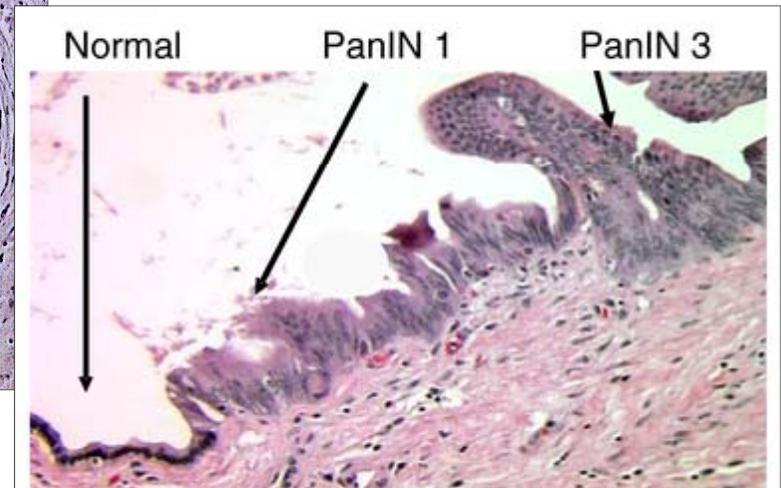
Prostatic
Intraepithelial
Neoplasia (PIN)



Ductal Carcinoma
In Situ (DCIS)

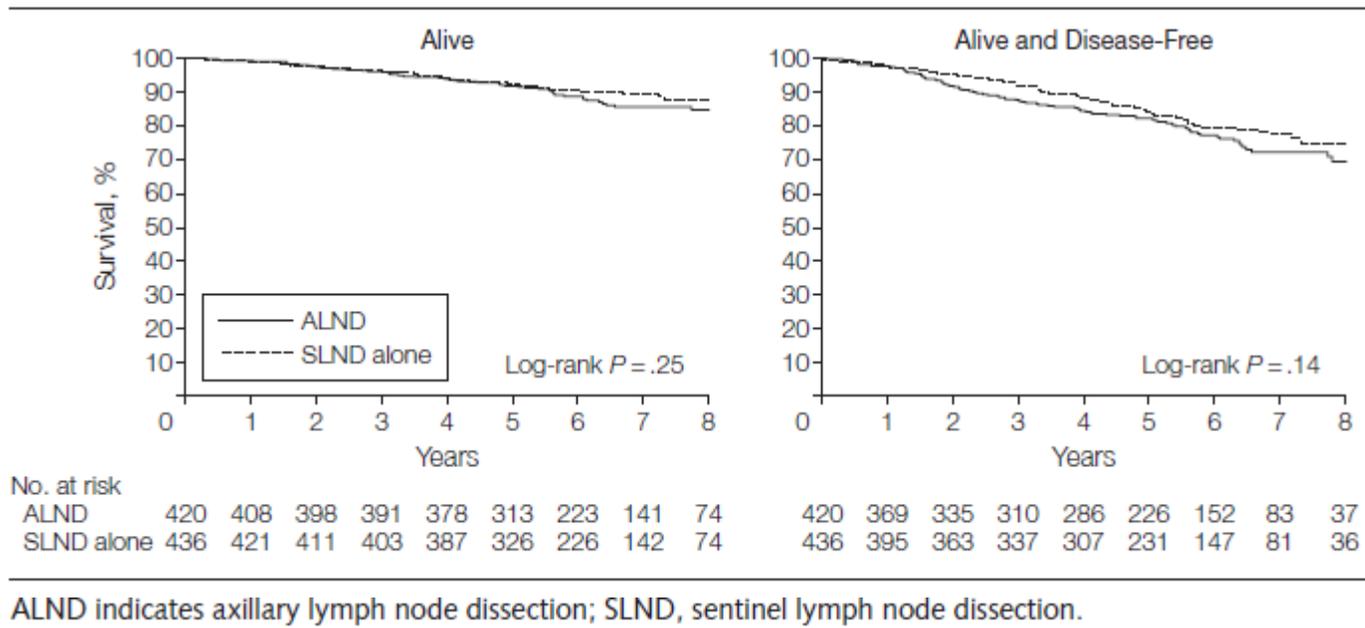


Pancreatic Intraepithelial
Neoplasia (PanIN)



(conversely) WHAT IS THE CLINICAL SIGNIFICANCE OF FINDING CELLS FROM A PRIMARY TUMOR AT ANOTHER SITE?

Figure 2. Survival of the ALND Group Compared With SLND-Alone Group



Giuliano, AE et al., Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis. JAMA, 2011. 305, 569-575.

THERAPEUTICS

TRADITIONAL CANCER TREATMENTS



SURGERY



CHEMOTHERAPY



RADIOTHERAPY

WHY ARE SOME DISSEMINATED CANCERS CURED BY CHEMOTHERAPY ALONE?



RÉPUBLIQUE FRANÇAISE



CONTRE LE
CANCER

CENTRE RÉGIONAL ANTI-CANCÉREUX
HOSPICE DE LA GRAVE . TOULOUSE . CONSULTATIONS
LUNDI . MERCREDI . VENDREDI . A 8 HEURES ET DEMIE

IMP. BARUTEL - TOULOUSE