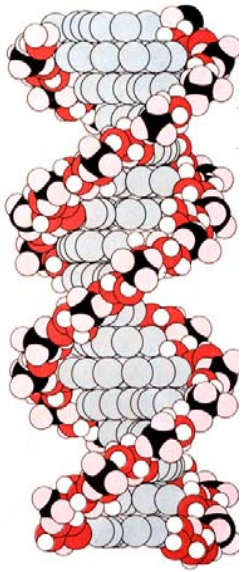
Cancer Prevention and Control in Maryland: Perspective from the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

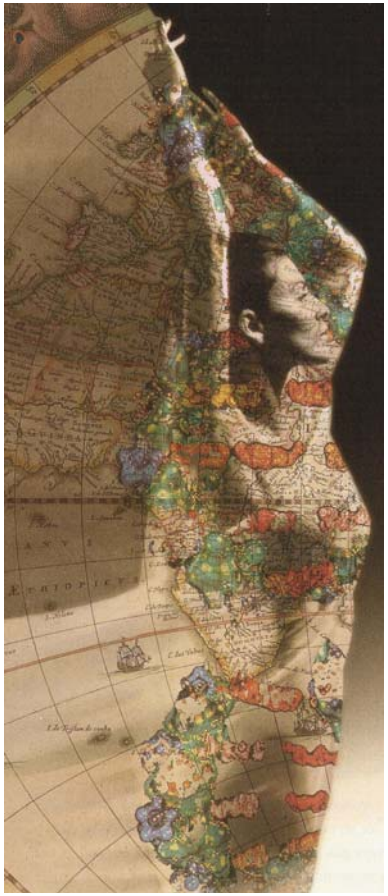
William G. Nelson, M.D., Ph.D.
Marion I. Knott Director

- **Human Genome Technologies and Cancer Prevention and Control**
- **Preventing Common Cancers: Prostate Cancer as an Example**
- **Translational Research and Cancer Prevention and Control**
- **Cancer Clinical Trials and Health Disparities**



Mapping/Sequencing of the Human Genome

- Milestone in molecular biology
- Revolutionized cancer genetics and epidemiology
- New technologies for molecular profiling of cancer cells
- Unprecendented opportunities for the discovery of new approaches to cancer treatment and prevention
- Greatly augmented public expectations



Transformation of Medicine by Translational Research*

20th century medicine	*21st century medicine*	*implications*
treat disease when symptoms arise and normal function is compromised	**intervene before symptoms appear and preserve normal function**	**prevention of disease and preservation of health**
morphological understanding of disease state	**cellular/molecular understanding of evolving disease process**	**prediction of disease risk permitting less toxic and more effective intervention**
high financial and disability costs	**opportunity for improved efficacy and efficiency**	**personalization of risks and treatments**

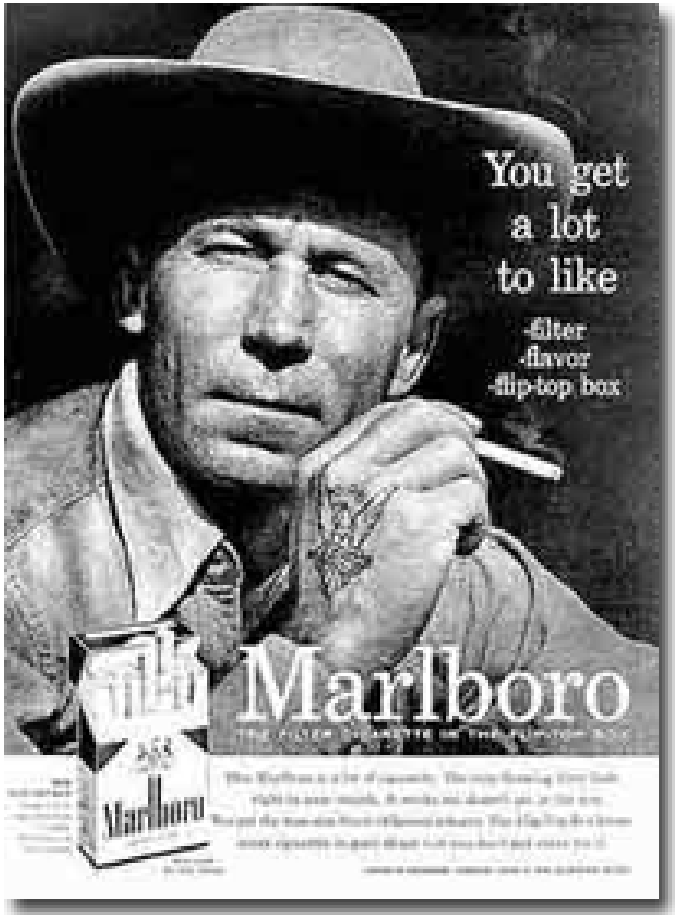
***adapted from Hood L, von Eschenbach A, and Zerhouni E (2005-6)**

Etiologies of the World's Leading Cancers*

Cancer site	Infection	Inflammation	Exposure
Lung/Bronchus		probably	smoking
Breast			estrogens, diet
Colon/Rectum		definitely	diet
Stomach	*H. pylori*	definitely	diet
Liver	Hep. viruses	definitely	diet (aflatoxin B_1)
Prostate	XMRV?	probably	diet
Uterine Cervix	HPV	probably	smoking
Esophagus		maybe	smoking, diet
Bladder	*S. haematobium*	maybe	smoking
All sites (excluding skin)	often	almost always	almost always

*Ordered by incidence as reported by the World Health Organization International Agency for Research on Cancer (IARC); see www.iarc.fr

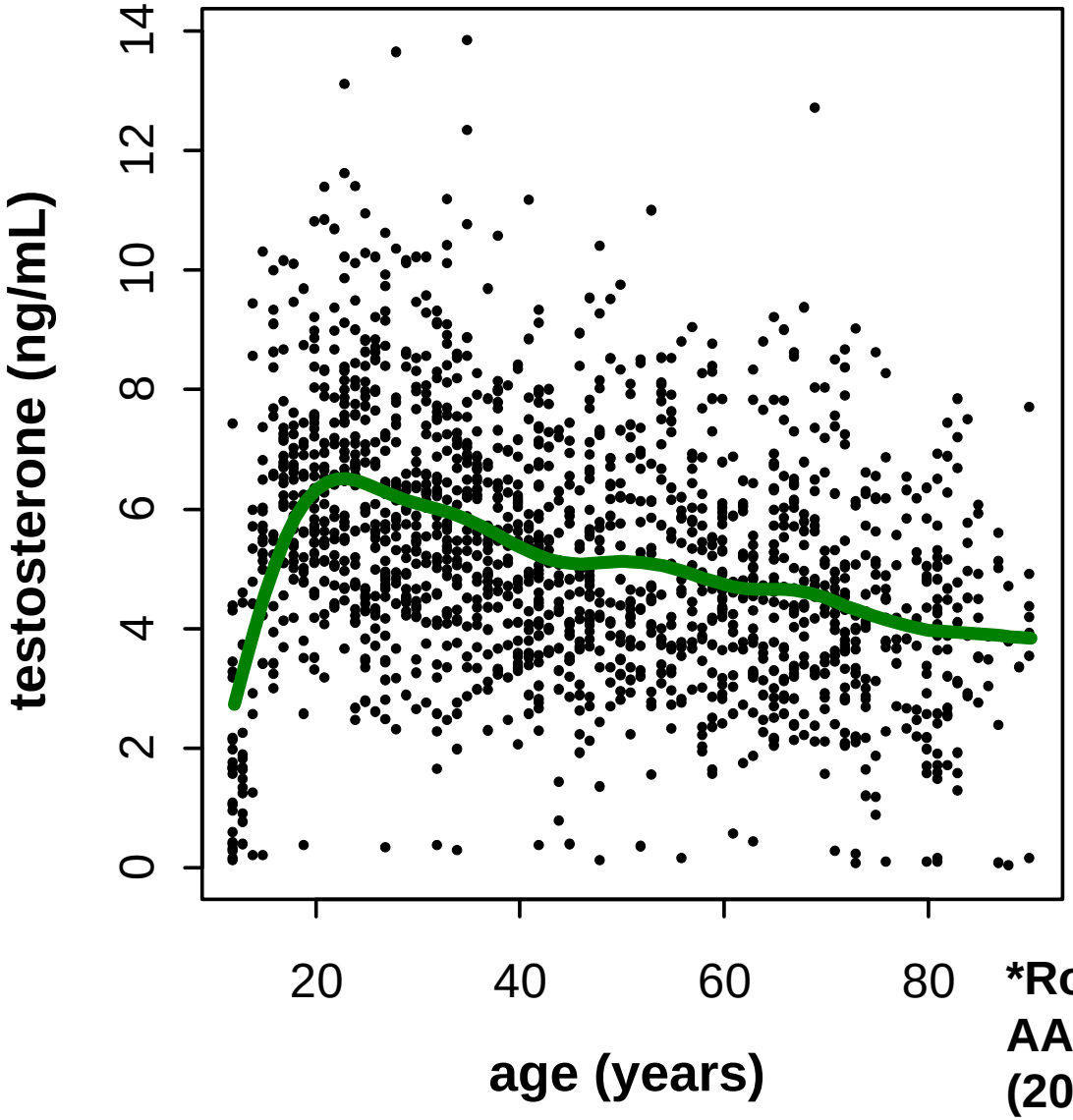
more than 70% of all cancer cases can be prevented


You get
a lot
to like
-filter
-flavor
-flip-top box
Marlboro

CAMEL
Genuine Taste
CASINO

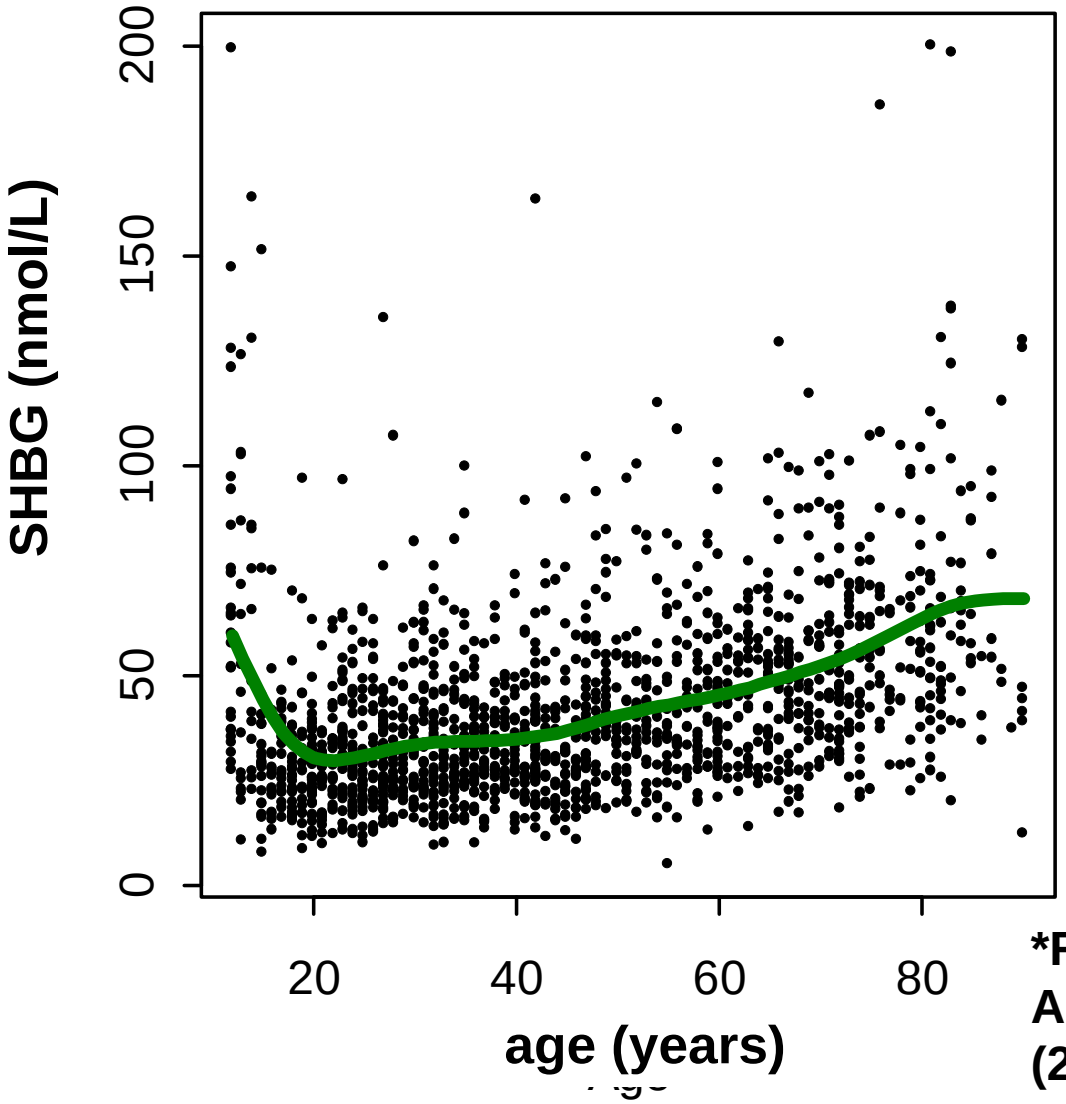
Marlboro
SALEM
CAMEL
FILTERS
ton

Change in Serum Testosterone with Age (n = 1,575 men in NHANES III)*



*Rohrman S *et al.* AACR Annual Meeting (2006)

Change in Serum SHBG with Age (n = 1,575 men in NHANES III)*

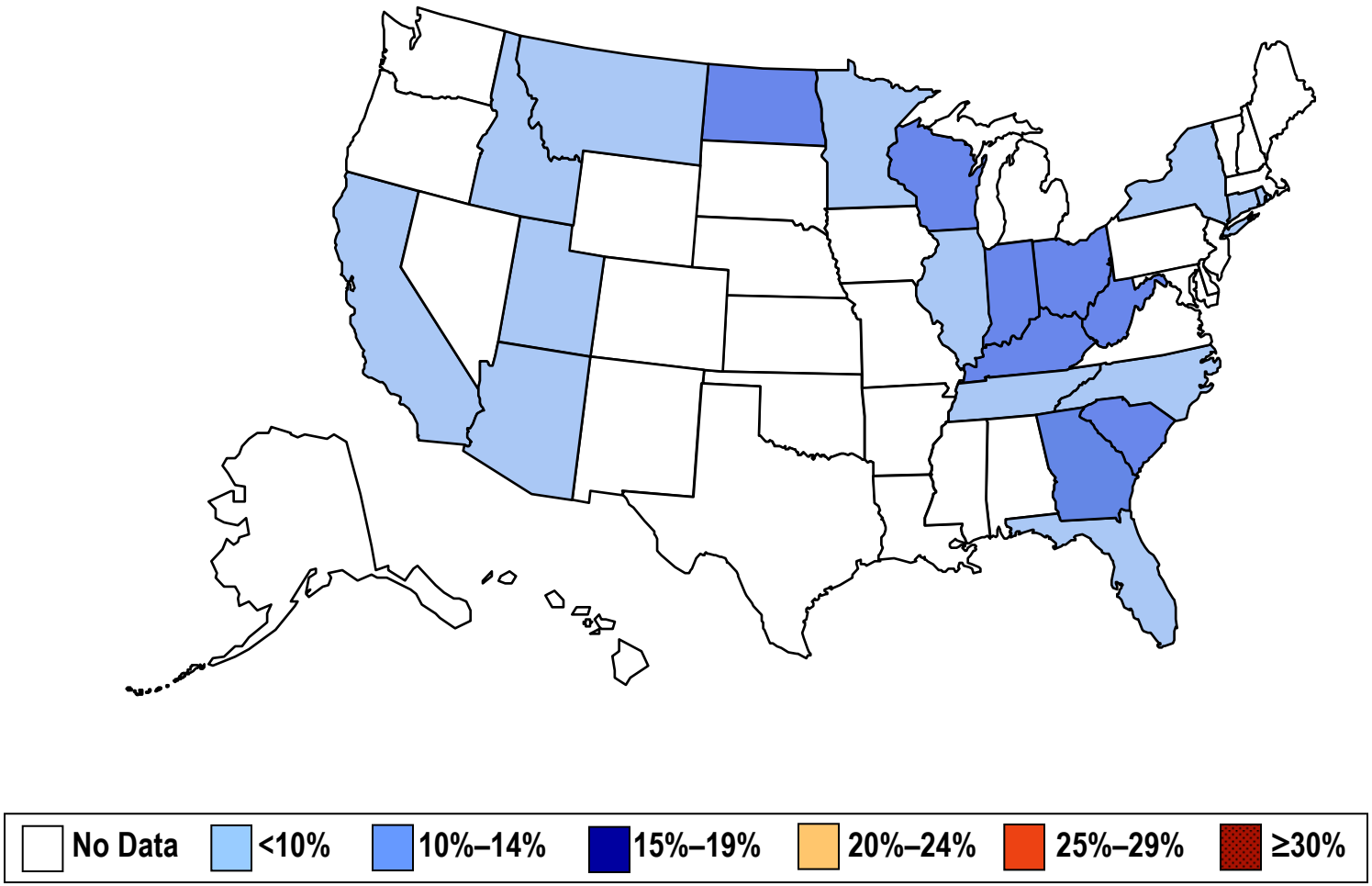


*Rohrman S *et al.* AACR Annual Meeting (2006)

Obesity Trends* Among U.S. Adults

1985

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” person)

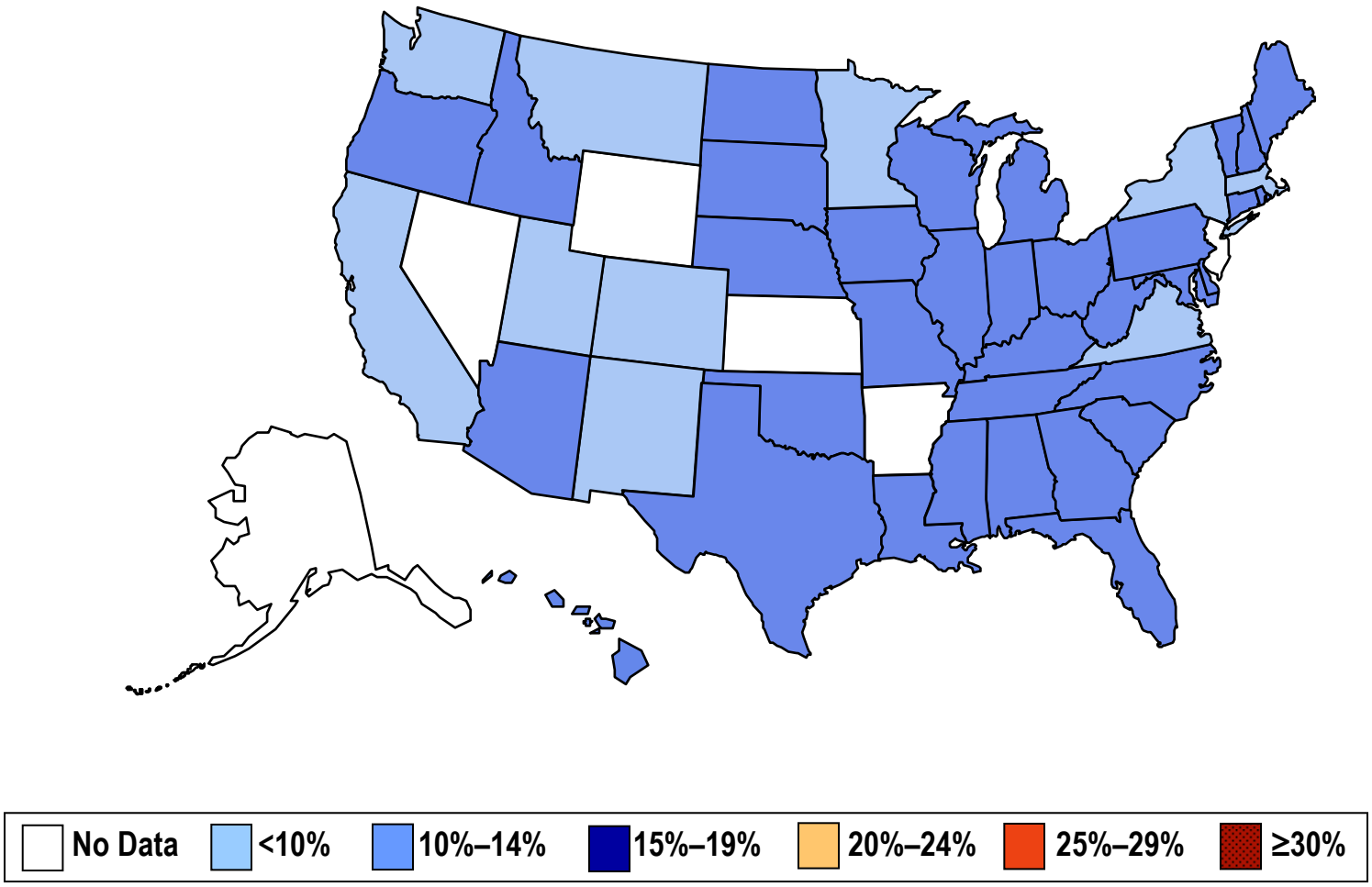


***Source: Behavioral Risk Factor Surveillance System, CDC**

Obesity Trends* Among U.S. Adults

1990

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” person)

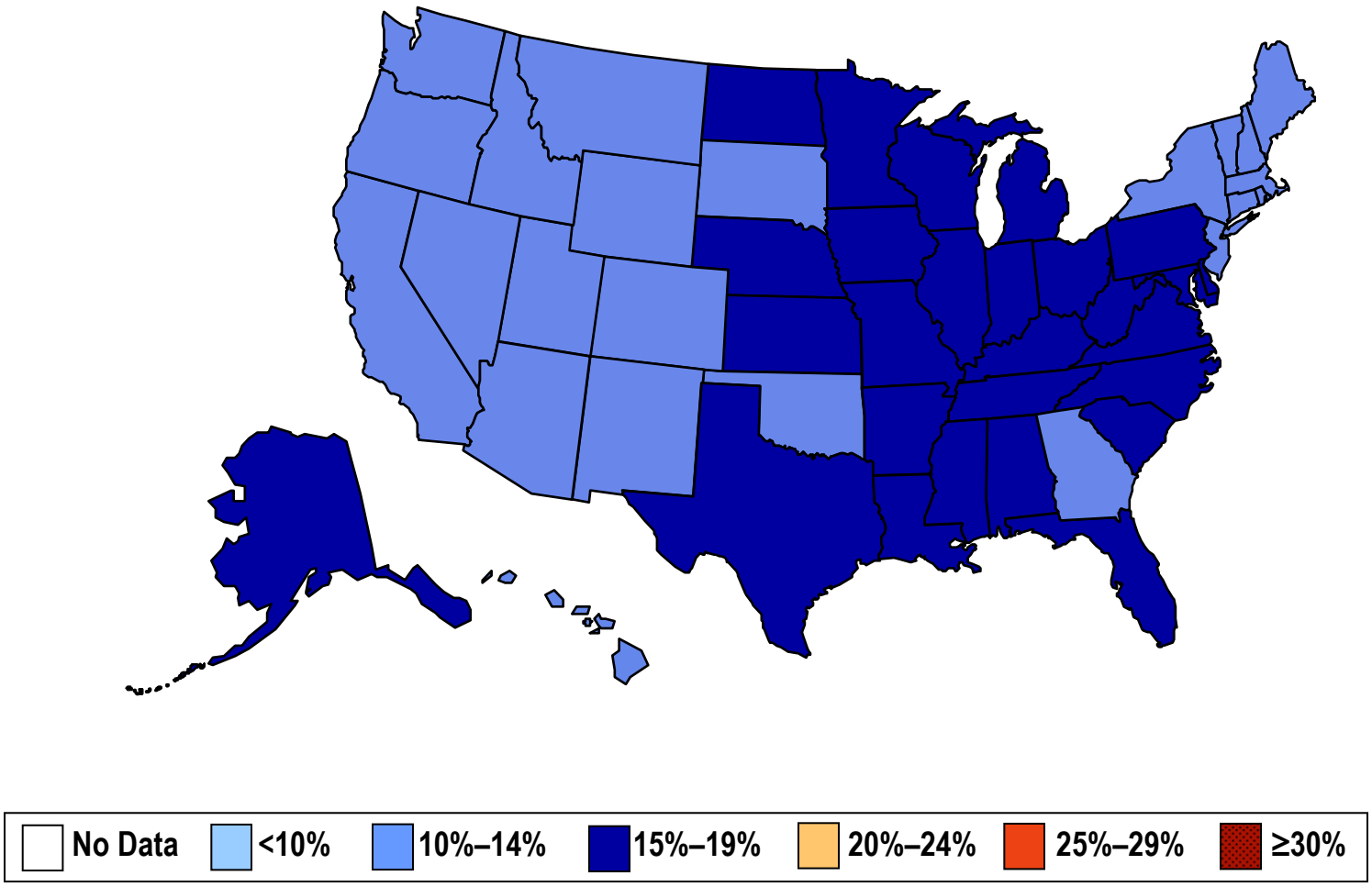


***Source: Behavioral Risk Factor Surveillance System, CDC**

Obesity Trends* Among U.S. Adults

1995

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” person)



***Source: Behavioral Risk Factor Surveillance System, CDC**

Obesity Trends* Among U.S. Adults

2000

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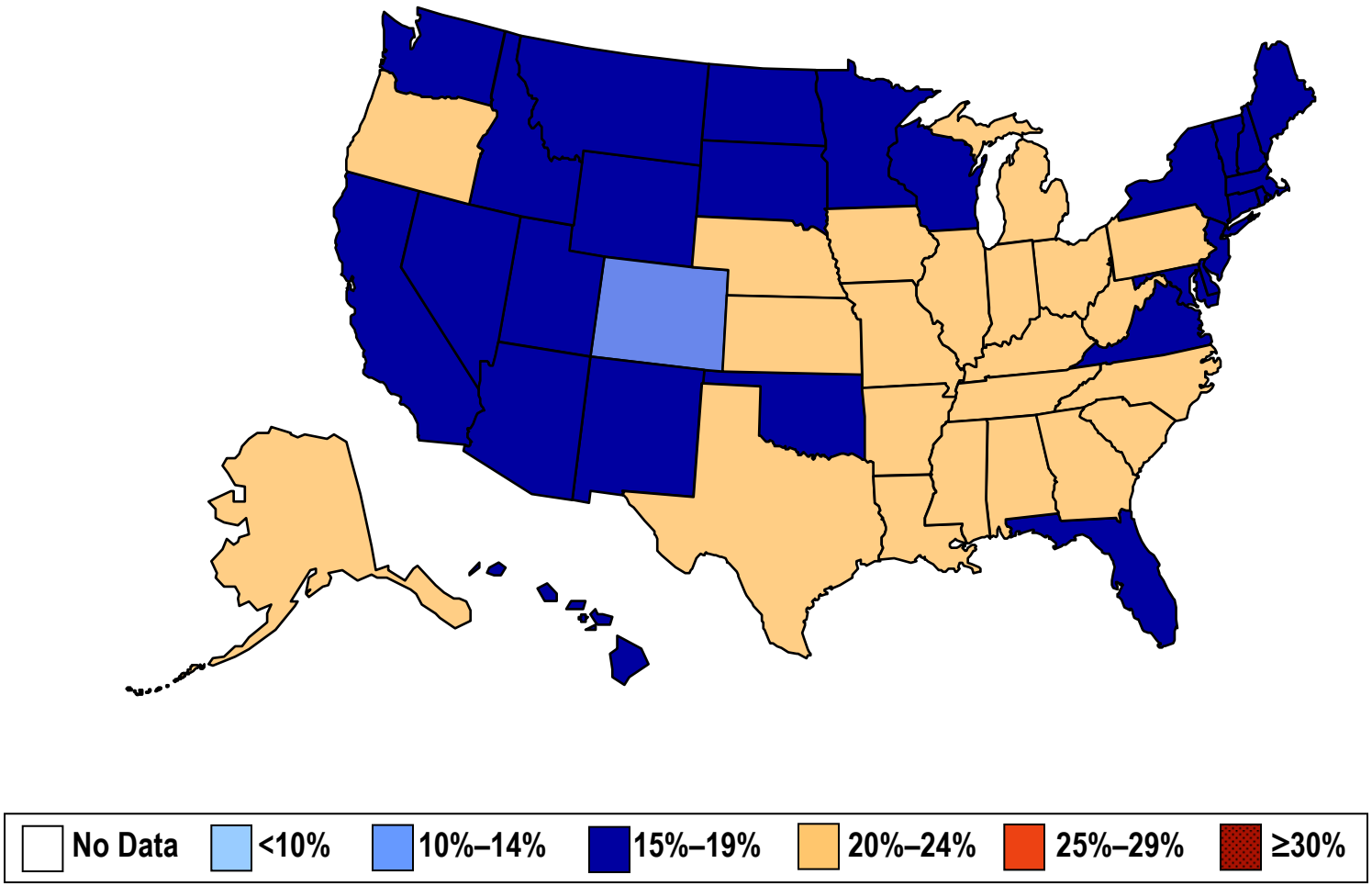
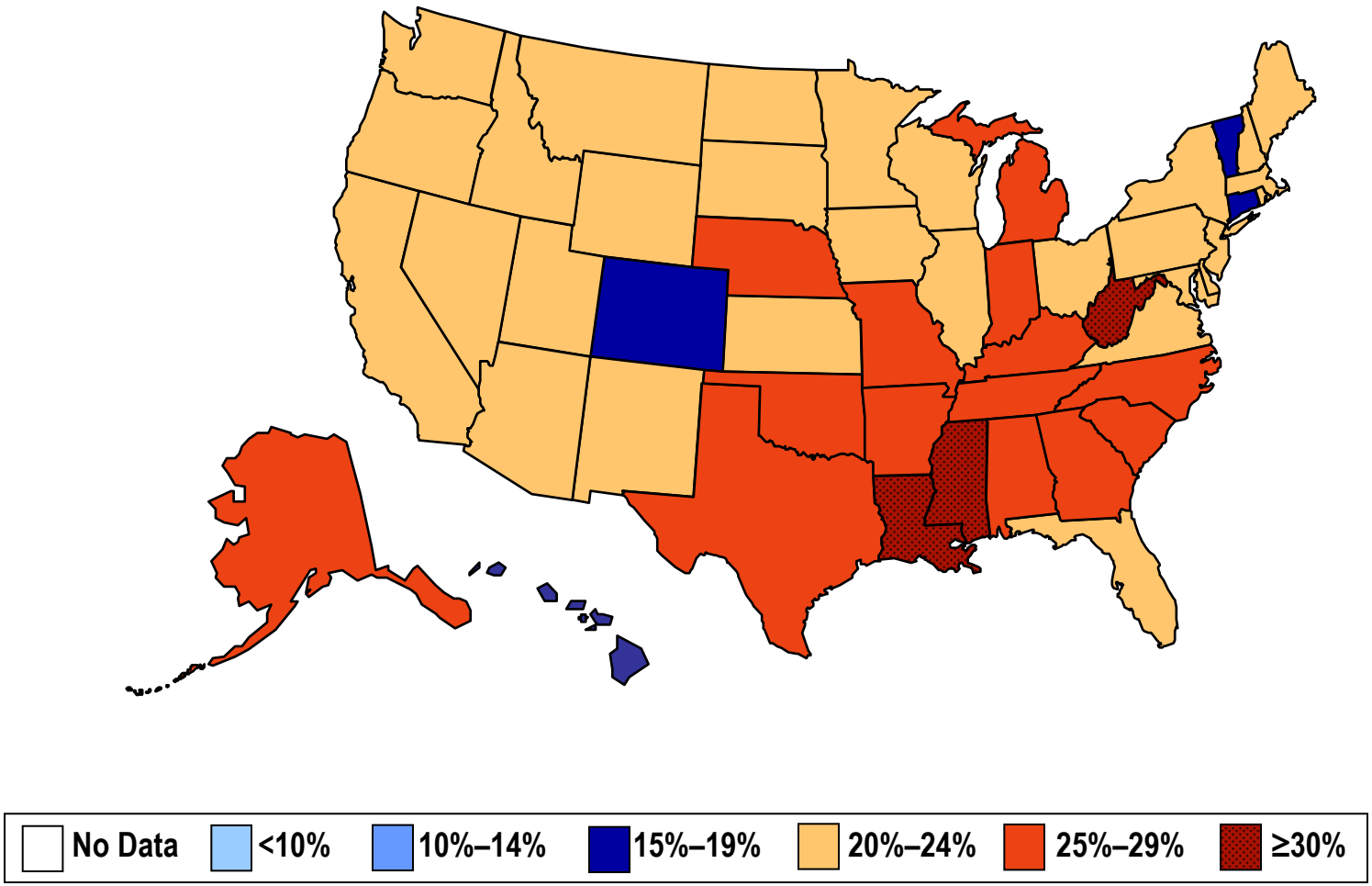


***Source: Behavioral Risk Factor Surveillance System, CDC**

Obesity Trends* Among U.S. Adults

2005

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” person)

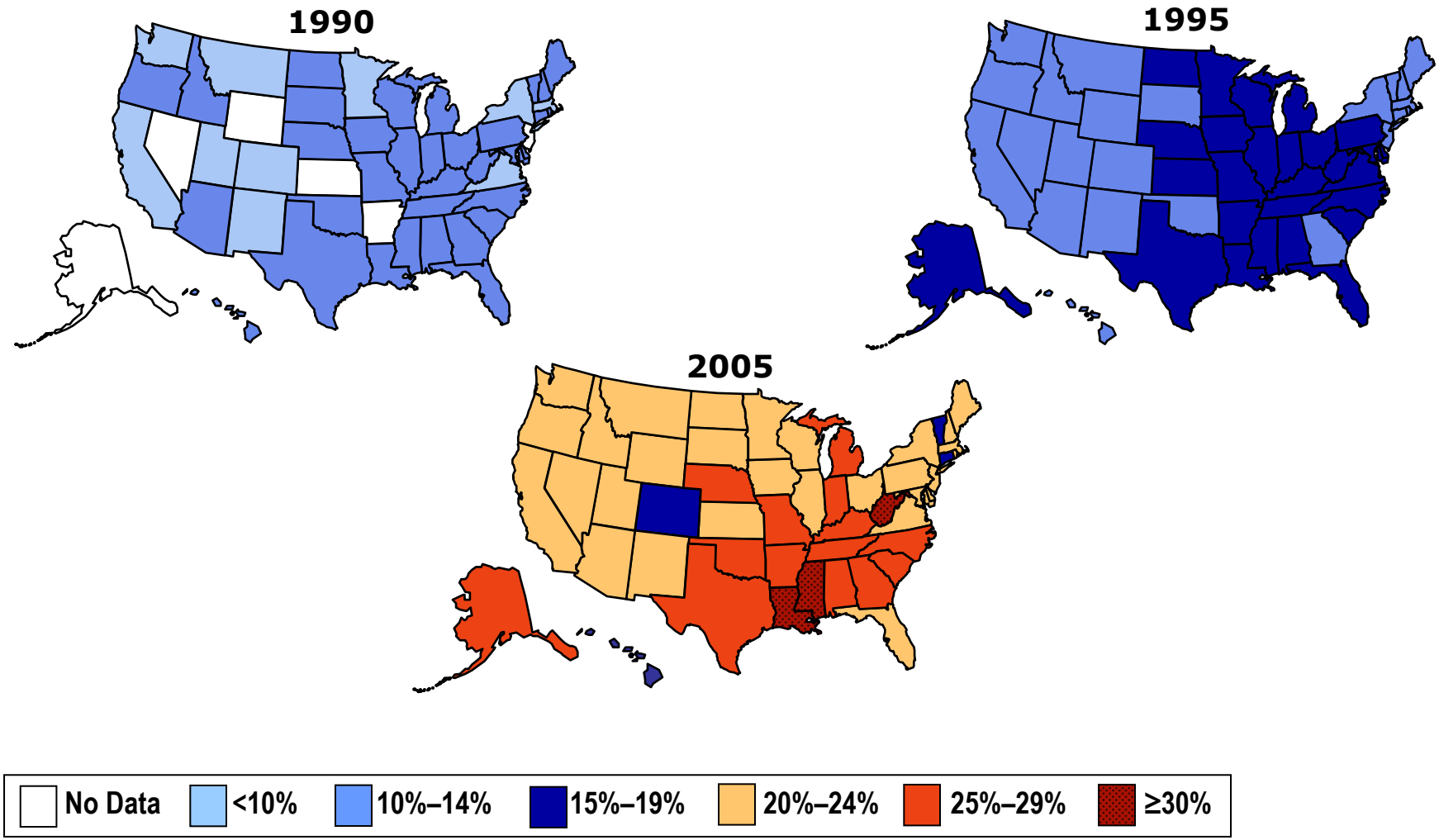


***Source: Behavioral Risk Factor Surveillance System, CDC**

Obesity Trends* Among U.S. Adults

1990, 1995, 2005

(*BMI ≥30, or about 30 lbs overweight for 5'4" person)



***Source: Behavioral Risk Factor Surveillance System, CDC**

The Diet and Cancer

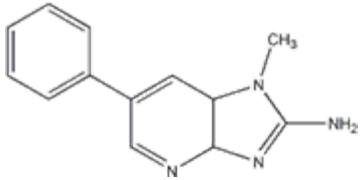
“Good”

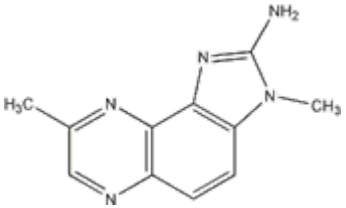
“Bad”

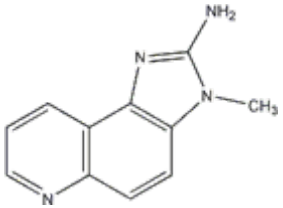
Overcooking and Charbroiling of Meats Creates Carcinogens

Heterocyclic amines

formed by heat-catalyzed reaction between creatinine and amino acids (*eg.* phenylalanine)

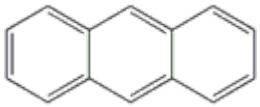


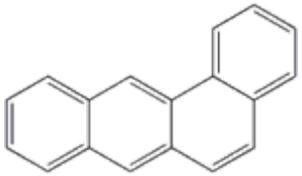


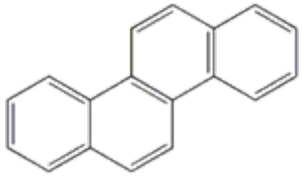


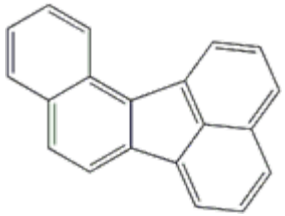
Polycyclic aromatic hydrocarbons

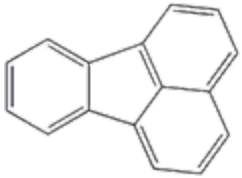
formed by incomplete combustion of meats

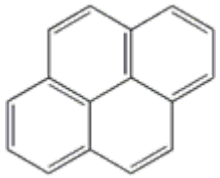












Heterocyclic Amine Carcinogens in Cooked Foods from Various Restaurants*

sample	"doneness"	heterocyclic amine content (ng/g)		
		MeIQx	PhIP	DiMeIQx
top loin steak	well-done	0.12	0.86	n.d.
top loin steak (different day)	well-done	1.3	7.7	0.77
flank steak	well-done	1.9	10	0.6
prime rib	well-done	n.d	n.d.	n.d.
beef fajitas	not specified	0.93	1.7	0.06
pork chop	not specified	0.4	2.4	n.d.
chicken fajitas	not specified	2.4	33.4	1.7
grilled chicken sandwich	not specified	0.74	4.1	0.64
fish tacos	not specified	n.d.	n.d.	n.d.

26 ng/kg body weight intake/day in US

*Pais P *et al.* J Agric Food Chem, *48:* 1721-6 (2000);
Layton *et al.* Carcinogenesis, *16:* 39-52 (1995)

Polycyclic Aromatic Hydrocarbon Carcinogens in Cooked Foods*

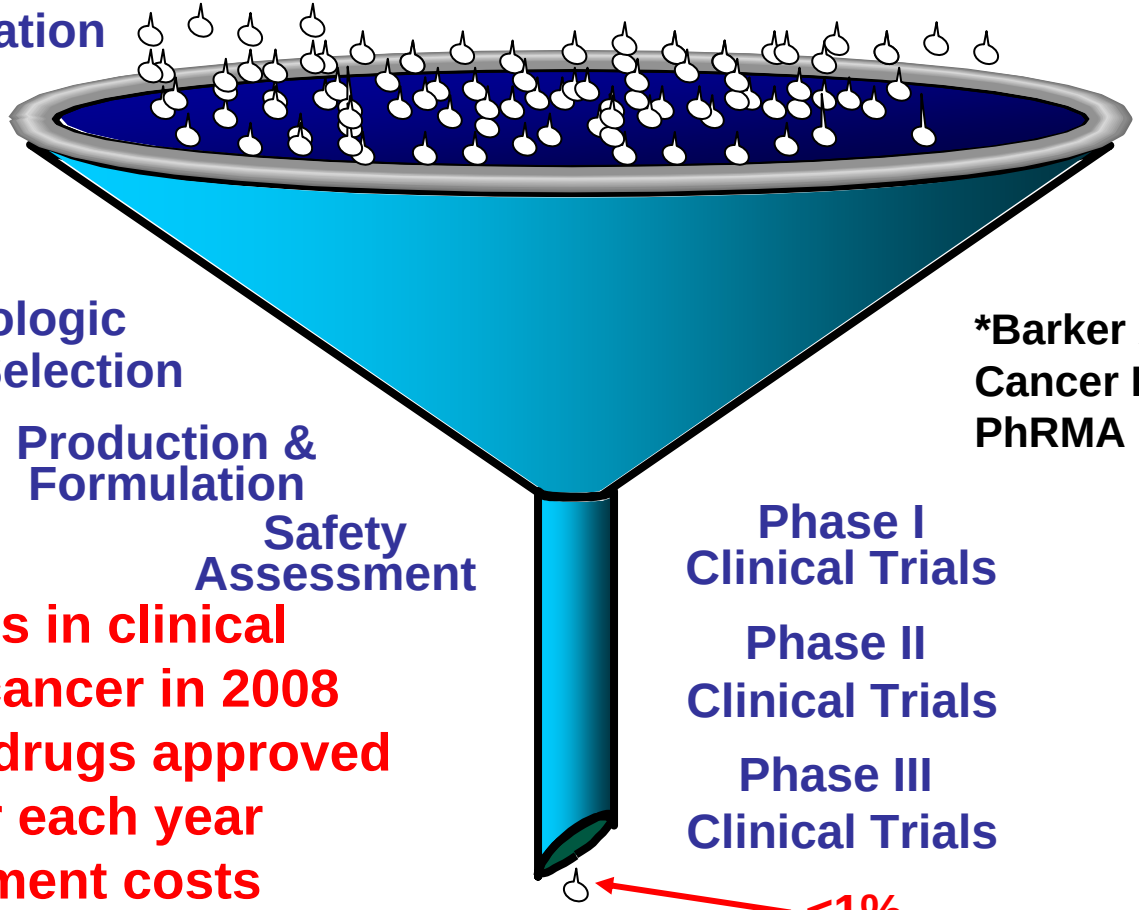
sample	cooking technique	"doneness"	benzo[*a*]pyrene (ng/g)
hamburger	oven broiled	very well	0.01
	pan-fried	very well	0.01
	grilled/barbecued	well	0.56
	grilled/barbecued	very well	1.52
steak	grilled/barbecued	medium	4.15
	grilled/barbecued	well	4.75
	grilled/barbecued	very well	4.86
chicken	oven broiled	well	0.08
(with skin)	pan-fried	well	0.12
	grilled/barbecued	well	4.57
chicken	grilled/barbecued	well	0.39
(w/o skin)	grilled/barbecued	very well	0.40
perch	grilled/barbecued	very well	0.24

40 ng/kg body weight intake/day in US

*Kazerouni N *et al.* Food Chem Toxicol, *39:* 423-36 (2001); Phillips DH Mutation Res, *443:* 139-47 (1999)

Current Challenges of Drug Discovery and Development

Flow of Approved Products*



- 750 drugs in clinical trials for cancer in 2008
- 1-2 new drugs approved for cancer each year
- development costs approach >$1B/drug

*Barker A, National Cancer Institute; PhRMA (www.phrma.org)

National Cancer Institute
Translational Research Working Group

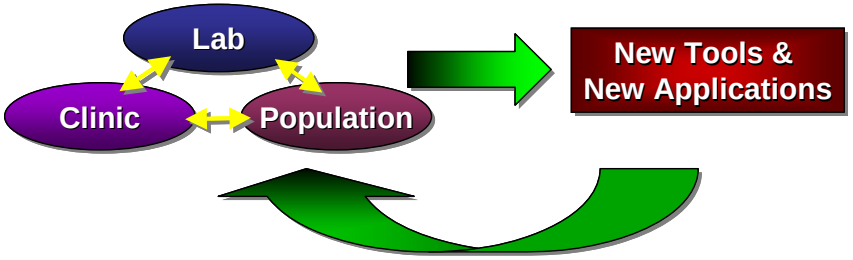
Co-Chairs: Ernest Hawk, MD, MPH, Lynn Matrisian, PhD, and William Nelson, MD, PhD

Membership: 60 cancer research leaders from diverse fields, institutions, backgrounds, perspectives

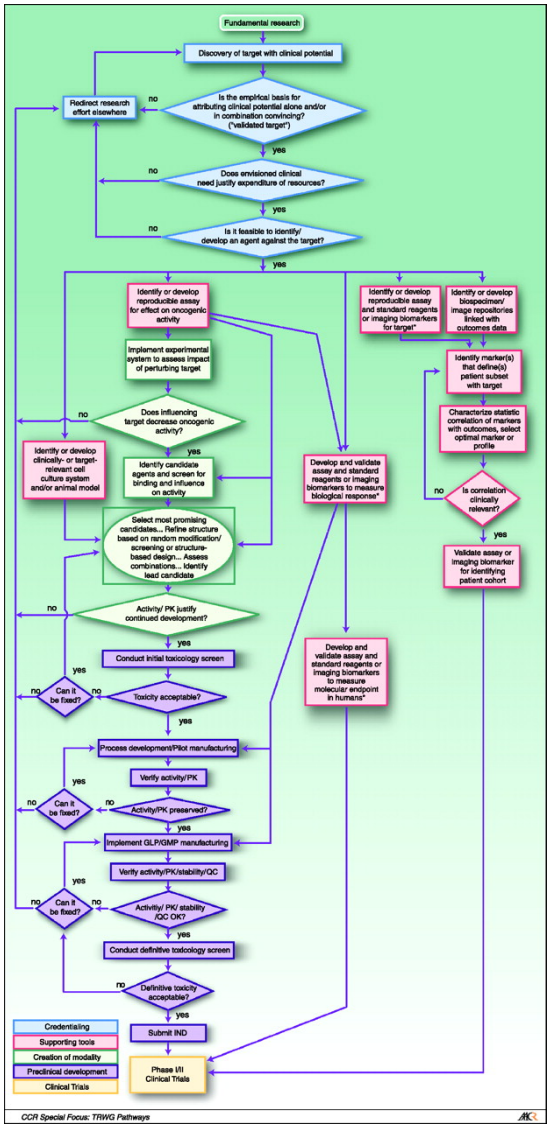
Process: face-to-face meetings, targeted roundtable conferences, on-line public comment

Report (June 2007): portfolio analysis, process analysis, pathways to clinical goals, consensus recommendations, implementation plan

translational research: "…research that transforms scientific discoveries …into new clinical tools … that reduce cancer incidence, morbidity and mortality…"



The Discovery and Development of Drugs to Treat and Prevent Cancer: Role of "Translational Research"*



target/pathway discovery

↓

target "credentialing"

↓

drug discovery
(identification of leads;
iterative process of synthesis/analysis)

↓

preclinical drug development
(safety/toxicity;
manufacturing)

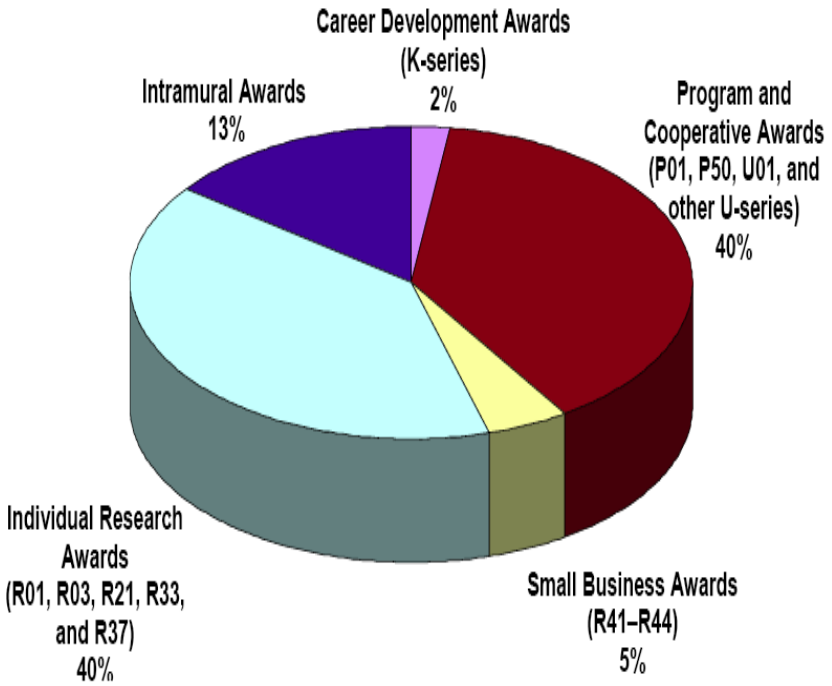
↓

Investigational New Drug (IND)
application filed with Food and Drug
Administration

***Schilsky RL *et al.* Clin Cancer Res. *14:* 5685-91 (2008)**

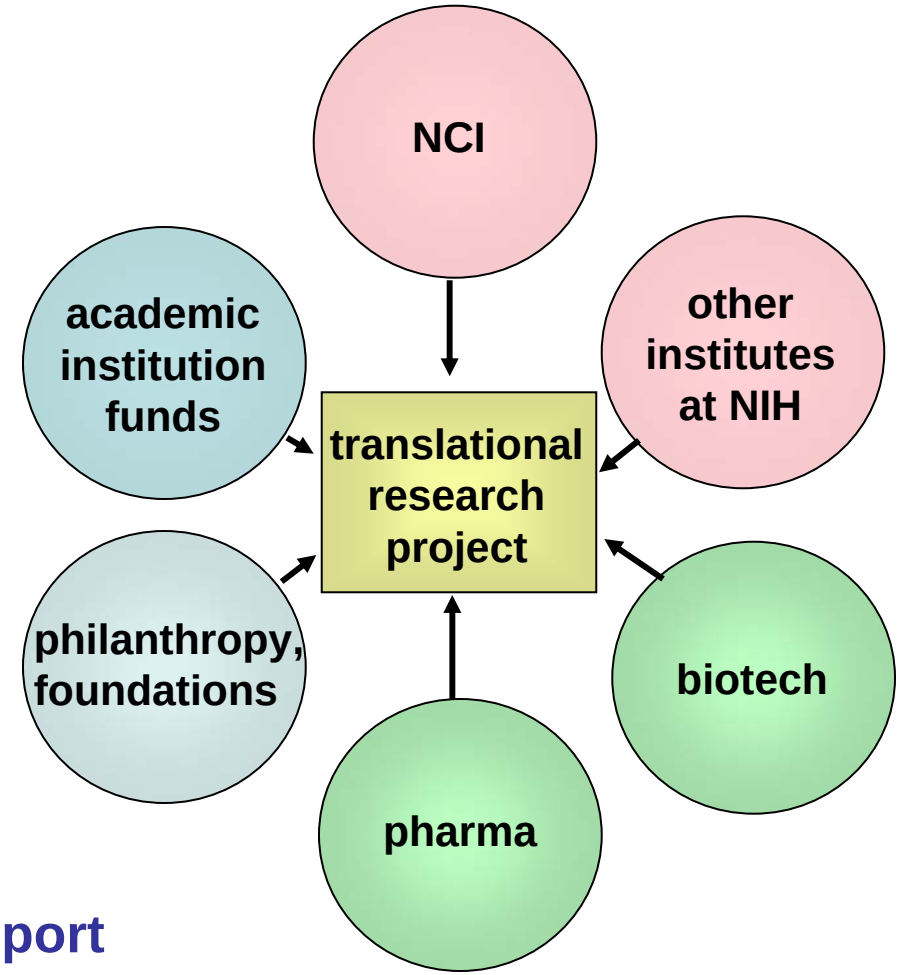
Translational Research NCI Portfolio Analysis

- $1.3B of $4.4B (~30%) NCI budget in 2004 identified as translational research (may be overestimated by 20-40%)
- 56% of funds go to institutes with NCI-designated cancer centers
- distributed across funding mechanisms
- 1161 of 4450 R01 grants (26.1% for $447M)
- 107 of 207 P01 grants (51.7% for $215M)
- 122 0f 209 U01 awards (58.4% for $98.6M)
- all SPOREs (58 for $131.7M), EDRNs (28 for $21.8M), ICMICs (7 for $15.8M)
- many other types of grants/awards



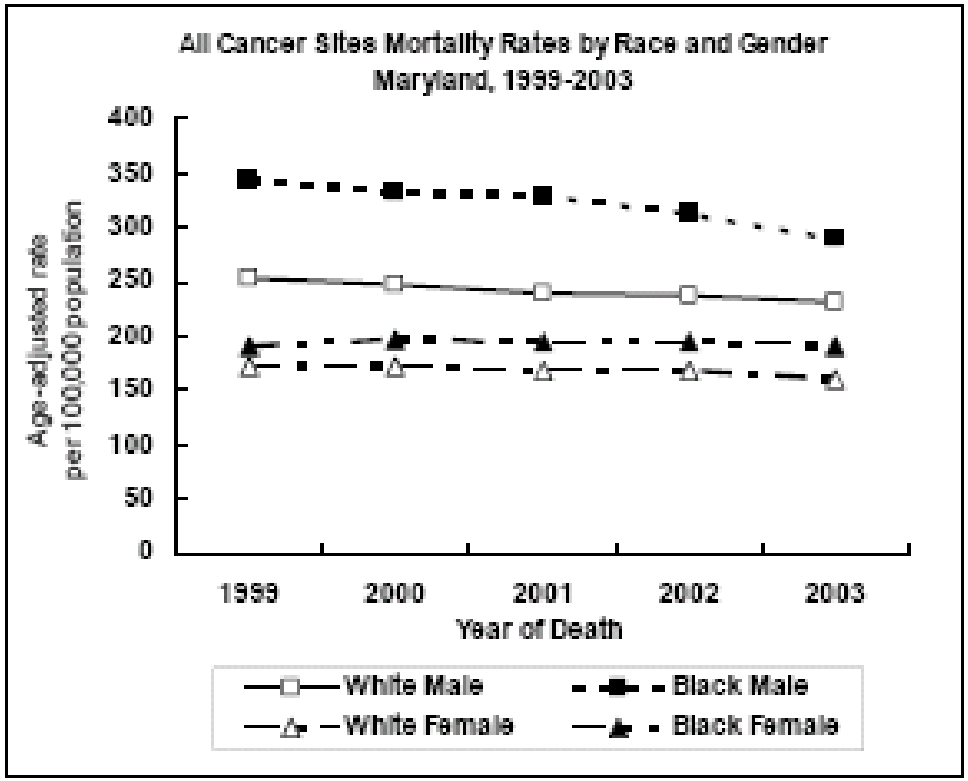
Translational Research Process Analysis

- 20 examples of translational research successes from all Developmental Pathways
- funding came from a wide variety of sources and mechanisms
- major challenges included: prioritization, management to milestones, recognition of productive failure, other inefficiencies



no one "formula" for support of translational reseach

Cancer Health Disparities in Maryland*



Rates are age-adjusted to 2000 U.S. standard population
Maryland Division of Health Statistics, 1999-2001
NCHS Compressed Mortality File in CDC WONDER, 2002, 2003

***Maryland Cigarette Restitution Fund Report for 2008**

Cancer Care and Clinical Trial Participation at the Sidney Kimmel Comprehensive Cancer Center: An Analysis of 2004 Data*

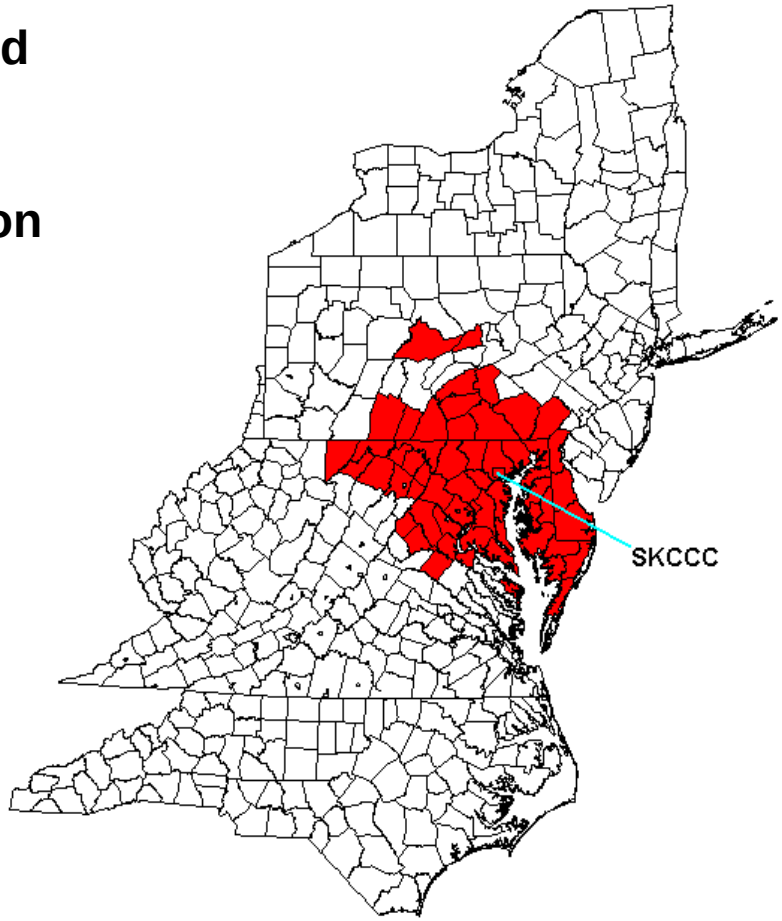
Rigorous examination of accrual and catchment data in an attempt to better define disparities in cancer clinical trial participation and cancer care at SKCCC

Geographic area covered

- **46 counties (MD, DE, DC, VA, WV)**
- **Baltimore City is 15% of catchment area**

Racial/ethnic diversity (N = 4,217)

- **Black 16%**
- **White 80%**
- **Other 3% (1% Hispanic)**



***Kanarek N, Piantadosi S *et al.* (2005)**

Participation Rates* in Therapeutic Clinical Trials at SKCCC by Race/Ethnicity and Geography**

	White	Black	Other
Baltimore City alone	15%	7%	15%
Remainder of the Catchment Area	18%	19%	18%
Entire Catchment Area	18%	13%	18%

•frequency of trial participation by persons *(i)* from different geographic regions within the catchment area and *(ii)* of different race/ethnicity

**Kanarek N, Piantadosi S *et al.* (2005)