DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
164th NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
February 8, 2013

Building 31C, Conference Room 10
National Institutes of Health
Bethesda, Maryland

NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
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The National Cancer Advisory Board (NCAB) convened for its 164th regular meeting on 8 February 2013, in Conference Room 10, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Friday, 8 February 2013, from 9:00 a.m. to 11:30 a.m. and from 12:50 p.m. to 1:44 p.m. The meeting was closed to the public from 11:30 a.m. to 12:30 p.m. The NCAB meeting was chaired by Dr. William R. Sellers, Vice President/Global Head of Oncology, Novartis Institutes for BioMedical Research, Inc., who presided as Chair *pro tem* during both the open and closed sessions in the absence of NCAB Chair, Dr. Tyler E. Jacks, Director, Koch Institute for Integrative Cancer Research, David H. Koch Professor of Biology, Massachusetts Institute of Technology, who participated by conference phone.

NCAB Members
Dr. Tyler E. Jacks (Chair) (by telephone)
Dr. Victoria L. Champion
Dr. David C. Christiani
Dr. Marcia R. Cruz-Correa
Dr. Kevin J. Cullen
Dr. Judy E. Garber (by telephone)
Mr. William H. Goodwin, Jr.
Dr. Waun Ki Hong
Dr. Elizabeth M. Jaffee
Dr. Beth Y. Karlan
Ms. Mary Vaughan Lester
Dr. H. Kim Lyerly
Dr. Olufunmilayo I. Olopade (absent)
Dr. Jennifer A. Pietenpol
Dr. Mack Roach III
Dr. Jonathan M. Samet
Dr. Charles L. Sawyers
Dr. William R. Sellers (Chair *pro tem*)

Alternate *Ex Officio* NCAB Members
Dr. Michael A. Babich, CPSC
Dr. Patricia Bray, OSHA/DOL (absent)
Dr. Vincent J. Cogliano, EPA
Dr. Michael Kelley, VA
Dr. Aubrey Miller, NIEHS
Dr. Richard Pazdur, FDA
Dr. Craig D. Shriver, DoD
Dr. Michael Stebbins, OSTP (absent)
Dr. Marie Sweeney, NIOSH (absent)
Dr. Lawrence Tabak, NIH (absent)
Dr. Sharlene Weatherwax, DOE (absent)

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. Harold Varmus, Director, National Cancer Institute
Dr. Jeff Abrams, Co-Director, Division of Cancer Treatment and Diagnosis
Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences
Mr. John Czajkowski, Deputy Director for Management and Executive Officer
Dr. James Doroshow, Deputy Director for Clinical and Translational Research
Dr. Daniela S. Gerhard, Director, Office of Cancer Genomics
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. Peter Greenwald, Associate Director for Prevention
Dr. Ed Harlow, Special Assistant for Science Planning
Dr. Lee Helman, Scientific Director for Clinical Research, Center for Cancer Research
Dr. George Komatsoulis, Acting Director, NCI Center for Bioinformatics and Information Technology
Dr. Barry Kramer, Director, Division of Cancer Prevention
Dr. Douglas R. Lowy, Deputy Director, National Cancer Institute
Dr. Alan Rabson, Deputy Director, National Cancer Institute
Dr. Dinah Singer, Director, Division of Cancer Biology
Dr. Sanya Springfield, Director, Center to Reduce Cancer Health Disparities
Dr. Joseph Tomaszewski, Co-Director, Division of Cancer Treatment and Diagnosis
Dr. Ted Trimble, Director, Center for Global Health
Dr. Margaret A. Tucker, Acting Director, Division of Cancer Epidemiology and Genetics
Mr. Michael Weingarten, Director, Small Business Innovation Research
Dr. Linda Weiss, Director, Office of Cancer Centers
Dr. Jonathan Wiest, Director, Center for Cancer Training
Dr. Robert Wiltrout, Director, Center for Cancer Research
Ms. Joy Wiszneauckas, Executive Secretary, Office of the Director
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy

Liaison Representatives

Ms. Carolyn Aldige, Cancer Research and Prevention Foundation
Dr. Jeff Allen, National Cancer Institute, Director's Consumer Liaison Group
Ms. Paula Bowen, Kidney Cancer Association
Mr. William Bro, Kidney Cancer Association
Dr. Carlton Brown, Oncology Nursing Society
Dr. Carol Brown, Society of Gynecologic Oncologists
Ms. Pamela K. Brown, Intercultural Cancer Council
Ms. Suanna Bruinooge, American Society of Clinical Oncology
Mr. George Dahlman, Leukemia and Lymphoma Society
Mr. Matthew Farber, Association of Community Cancer Centers
Dr. Margaret Foti, American Association for Cancer Research
Dr. Leo Giambarresi, American Urological Association
Dr. Francis Giardiello, American Gastroenterological Association
Ms. Christy M.P. Gilmour, American Academy of Orthopaedic Surgeons
Ms. Ruth Hoffman, Candlelighters Childhood Cancer Foundation
Dr. Gerald F. Joseph, Jr. American College of Obstetricians and Gynecologists
Ms. Rebecca A. Kirch, American Cancer Society
Dr. Steven Klein, National Science Foundation
Dr. W. Marston Linehan, Society of Urologic Oncology
Ms. Margo Michaels, Education Network to Advance Cancer Clinical Trials
Dr. Patricia Mullan, American Association for Cancer Education

Ms. Christy Schmidt, American Cancer Society
Ms. Susan Silver, National Coalition for Cancer Survivorship
Ms. Barbara Duffy Stewart, Association of American Cancer Institutes
Ms. Pamela Wilcox, American College of Radiology
COL (Ret.) James E. Williams, Jr., Intercultural Cancer Council

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I. CALL TO ORDER, OPENING REMARKS, AND CONSIDERATION OF 29 NOVEMBER 2012 MINUTES—DR. WILLIAM R. SELLERS

Dr. William R. Sellers called to order the 164th NCAB meeting. Dr. Sellers welcomed members of the Board, *ex officio* members of the Board, liaison representatives, staff, and guests. Members of the public were welcomed and invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI), in writing and within 10 days, any comments regarding items discussed during the meeting. He reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Motion. A motion to approve the minutes of the 29 November 2012 NCAB meeting was unanimously approved.

II. FUTURE BOARD MEETING DATES—DR. WILLIAM R. SELLERS

Dr. Sellers called Board members' attention to future meeting dates listed on the agenda.

III. NCI DIRECTOR'S REPORT—DR. HAROLD E. VARMUS

Dr. Harold E. Varmus, Director, NCI, welcomed members and thanked Dr. Sellers for serving as Chair *pro tem* in the absence of Dr. Jacks, who attended by telephone from Boston, MA. Dr. Varmus informed members about the departure of several scientific leaders appointed by the Administration: Drs. Subra Suresh, Director, National Science Foundation (NSF); Dr. Stephen Chu, Secretary, Department of Energy (DOE); Dr. Jane Lubchenco, Administrator, National Oceanic and Atmospheric Administration (NOAA); and Dr. Carolyn Clancy, Director, Agency for Healthcare Research and Quality (AHRQ). He also expressed sadness at the recent passing of Dr. David Cox, an imminent geneticist who worked in the field of oncology. Recruitment remains underway for NCI positions mentioned at the last meeting, and that Ms. Crystal Wolfrey has replaced Mr. Leo F. Buscher Jr., Director, Office of Grants Administration, who has retired after more than 50 years of service at the NCI.

NCI Budget and Legislative Concerns. Dr. Varmus reminded members that the NCI is operating under a Continuing Resolution (CR) until March 27, and facing budgetary effects of the looming sequestration. The fiscal year (FY) 2014 budget is being prepared, but no legislative hearings have been scheduled at this time. The Institute continues to make grant awards albeit at smaller amounts than in the past. Members were referred to the NCI website to review the success rates for FY 2012 awards. He informed members that changes in Congressional leadership following the recent elections include the Honorable Barbara Mikulski and Hal Rogers are the Chairs of the Senate and House Appropriations Committees, respectively. Chairs for the Appropriations Subcommittees for the NIH have not yet been assigned.

Dr. Varmus reported that the NCI has established working groups to address pancreatic ductal carcinoma and small-cell lung cancer research in response to the mandates of the Recalcitrant Cancer Research Act. The report of the Pancreatic Cancer Working Group, chaired by Dr. James L. Abbruzzese, The University of Texas MD Anderson Cancer Center, is in final preparation. The Small-Cell Lung Cancer Working Group is being formed and will be chaired by Dr. John Minna, University of Texas Southwestern.

NCI Special Activities. Dr. Varmus informed members that the NCI-Frederick Advisory Committee (NFAC), chaired by Dr. Zach Hall, recently met with scientists at the Lawrence Berkeley

National Laboratory, a Federally Funded Research and Development Center (FFRDC) in California, to gain an understanding of that organization's scope and work to help inform the direction and activities of the Frederick National Laboratory for Cancer Research (FNLCR). Dr. Varmus noted that he had co-chaired a workshop in San Francisco, CA, with Dr. Frank McCormick, Director, University of California, San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center, regarding mutant *Ras* genes, a topic that is the focus of a megaproject to be initiated at the FNLCR.

Dr. Varmus told members that Dr. Francis Collins, Director, NIH, had established a working group of Institute and Center (IC) Directors, chaired by Dr. Story Landis, to review information on data replication. He noted that the working group met in the fall of 2012, and had developed recommendations. He also noted that a recent workshop was held on the storage of genetic and other data from cancer studies. Members were told about an upcoming meeting of the NCI-designated Cancer Centers regarding funding issues related to new guidelines for the Centers.

Members were informed that the legal case against Myriad Genetics, which likely will be heard by the Supreme Court in mid-April 2013 to determine whether genes and genetic mutations can be patented, is of significant concern to the NCI. He noted that NCI and numerous other scientific organizations will submit testimony at the appropriate time and that an updated report will be given at a future Board meeting.

IV. ANNUAL REPORT TO THE NATION—DR. BRENDA EDWARDS

Dr. Brenda K. Edwards, Senior Advisor for Cancer Surveillance, Division of Cancer Control and Population Sciences (DCCPS), provided an update on the 15th Annual Report to the Nation. Dr. Edwards informed members that the report highlights human papilloma virus (HPV)-related cancers, vaccination coverage, and Papanicolaou (Pap) testing for cervical cancer. She next described the methodology, collection of data, and sources of data used in the report.

Key findings of the report include a continuing decrease in all-cancer mortality among men, women, and children; a decrease in the incidence of cancer in men, but no change in the incidence in women; and an increase in the incidence of childhood cancers. Trends in cancer incidence are determined from the population-based NCI Surveillance, Epidemiology, and End Results (SEER) Program and state-based registries funded by the U.S. Centers for Disease Control and Prevention (CDC). Geographic coverage of the SEER Program and the CDC registries account for 93 percent of the cancers diagnosed in the United States (U.S.) each year in the most recent five years. Coverage is 87% for the 2000-2009 trends; the 93% coverage refers to the 2005-2009 trends. Cancer mortality data are from the CDC National Center for Health Statistics and cover the entire U.S. Members were told about the methods used for developing trend data.

Highlights of cancer site data for mortality and incidence were reported by Dr. Edwards in some detail. Overall, mortality is increasing in men and women in the liver and pancreas. Increases in mortality also are occurring for melanoma and soft tissue (sarcoma) in men and uterine cancer for women. By cancer site, the leading cause of mortality and incidence in the U.S. is in the lung and bronchus. Lung cancer differs by racial/ethnic group, with African American men having the highest mortality and increasing trends observed for American Indian/Alaska Native women. After years of increasing mortality, lung cancer among white women has begun to decrease. Although overall mortality and incidence of colon and rectal cancer are decreasing, they continue to be higher among African American, American Indian and Alaska Native men and women. Breast cancer mortality continues to decline although incidence is stable. Mortality from breast cancer continues to be higher among African American women. For prostate cancer, mortality and incidence are substantially higher among African

American men than white men.

Pancreatic cancer, one of the designated recalcitrant cancers, is increasing for mortality and incidence. Liver cancer mortality and incidence are increasing with different patterns among racial/ethnic groups. For example, liver cancer incidence is highest among Asian American/Pacific Islanders, although the high death rate is decreasing in this group. Incidence in kidney and renal cancers continues to increase but mortality decreased, with the highest rates among Native Americans. Overdiagnosis may play a role in the increase in incidence, but one cause may be the increase in obesity. Data on corpus and uterine cancer indicate that mortality is much higher in African American women than in white women although incidence is lower except for some types of uterine cancer. Melanoma incidence is increasing among men and women, with a slight increase in mortality among men. It may be that the increase in incidence is due to overdiagnosis. The dramatic increase in thyroid cancer incidence is due to overdiagnosis, but may not explain the increase in mortality.

Questions and Answers

Dr. Charles Sawyers, Chairman, Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, Investigator, Howard Hughes Medical Institute, and Professor of Medicine, Weill-Cornell Medical College, asked about the strategy to track cancers in light of new molecular sub-classification and characterization methods as well as longitudinal data collection based on these subsets. Dr. Edwards responded that a system to track all cancers by molecular characterization is not in place, but data collection on some known prognostic factors such as biomarkers e.g., HER2 has begun. Dr. Sellers queried about the collection of stage information, as early diagnosis may be partly responsible for perceived overdiagnoses. Dr. Edwards reported that collection of stage information occurs but has been inconsistent among collection/reporting sources and is becoming more complicated. *In situ* data are collected, but the earlier biological conditions are challenging to capture.

Dr. Sellers observed that mortality attributed to renal cancer has decreased, whereas incidence has increased for each of the past 10 years; it would be helpful to understand this phenomenon and determine the relevance of the diagnoses for mortality rates.

Dr. Waun Ki Hong, Professor, Head, Division of Cancer Medicine, Department of Thoracic/Head & Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, asked about the exclusion of brain cancer incidence from the report as well as information about head and neck cancers. Dr. Edwards said that brain cancer is included in the report and was featured in the *Annual Report* several years prior and noted that nonmalignant brain tumors are now reportable. She added that data on head and neck cancers are collected, and examples will be discussed in the presentation on HPV-associated cancers.

Dr. Aubrey Miller, National Institute of Environmental Health Sciences (NIEHS), expressed interest in incidence changes seen in pediatric cancers. Dr. Edwards replied that the two main types of children's cancers, leukemia and brain cancer, vary by age and overall appear to be increasing in incidence or are stable, respectively.

HPV-Related Cancers. Dr. Douglas R. Lowy, Deputy Director, NCI, provided an update report about issues related to HPV-associated cancers based on data from the *Annual Report to the Nation*. Dr. Lowy said that, in males, approximately 60 percent of oropharyngeal and 90 percent of anal cancers are HPV positive. Among women, virtually all cervical cancers and approximately 60 percent of oropharyngeal cancers are HPV positive.

Dr. Lowy described cervical cancer screening tests and the approved vaccines for HPV. The HPV vaccines are approved for cervical and various other anogenital cancers, but not for oropharyngeal cancer. Data indicate that HPV vaccine uptake is higher in minority populations than among whites, and also is higher in populations with low socioeconomic status (SES) than in populations with high SES. The U.S. Food and Drug Administration (FDA) has approved two vaccines, produced by GlaxoSmithKline (GSK) and Merck, to protect against HPV-16 and -18 in females. One of the vaccines (Merck) also protects against HPV-6 and -11 and is approved for males. The target group is 11- and 12-year olds, and both vaccines are given in three intramuscular injections over 6 months. Safety studies of the HPV vaccines indicate they are safe, and there is long duration of viral protection. Data from Australia, which initiated a national vaccine program and since has experienced a higher rate of vaccine uptake than the United States, show a dramatic decrease (four-fold) in prevalence among vaccinated individuals. Unpublished data from a Costa Rican vaccine trial provide evidence that the HPV vaccine may protect against oropharyngeal cancer.

Dr. Lowy summarized data on the uptake of the HPV vaccine in the United States. HPV vaccination uptake is substantially less than that of other teenage vaccination, such as the meningococcal conjugate vaccine. Uptake has been approximately the same for children living above and below the poverty level, due partly to the efficacy of the Vaccines for Children (VFC) Program. Whites have a lower uptake of the HPV vaccine than African Americans or Hispanics. Regionally, there is lower uptake in the southern region of the United States and where there tends to be higher rates of cervical cancer.

Questions and Answers

Dr. Sellers asked whether there were any efforts to model the projected incidence rates for HPV-related cancer incidence in Australia compared to the United States to better direct prevention efforts in the United States. Dr. Lowy suggested that there will not be the same impact on herd immunity in the United States as experienced in Australia. Small studies from California and Ohio indicate a positive impact of HPV vaccination, but key concerns remain about what happens to those not vaccinated.

Dr. Jacks wondered how underlying differences in state health policies affect adoption rates of the HPV vaccine. Dr. Lowy commented that individual state policies may play a role in acceptance of vaccination. Dr. Barbara Rimer, Dean and Alumni Distinguished Professor, Gillings School of Global Public Health, The University of North Carolina at Chapel Hill, added that interesting differences exist among states, including pharmacy vaccinations, school programs, and reimbursement coverage, but no definitive analysis of the role of state policies has been completed.

Dr. Marcia R. Cruz-Correa, Associate Professor of Medicine and Biochemistry, University of Puerto Rico, Basic and Translational Science Director, University of Puerto Rico Comprehensive Cancer Center, encouraged anal cancer screening, which could be conducted at the same time people have colonoscopies. Dr. Lowy responded that there are proponents for this strategy in high-risk populations.

Ms. Mary Vaughan Lester, Board of Directors, University of California, San Francisco Foundation, asked if the same vaccine is used in men and women, as well as about differences in marketing. Dr. Lowy answered that, while the same vaccine is used in both sexes, marketing has been directed more toward women, and the early clinical trials were conducted only in women. He also indicated that the interval of time between transmission of HPV and diagnosis of an HPV-associated disease appears to be at least 20 years.

Dr. Sawyers observed that, in some high socioeconomic urban areas, physicians are not encouraging vaccination among their patients, and he wondered about current physician education and

outreach efforts. Dr. Lowy deferred the question to Dr. Rimer's presentation regarding the President's Cancer Panel (PCP, the Panel) activities.

Dr. H. Kim Lyerly, Vice President/Global Head of Oncology, George Barth Geller Professor of Cancer Research, Professor of Surgery, Duke University School of Medicine, asked about the utility and cost associated with conducting a global strategy for HPV vaccination. Dr. Lowy responded that such a strategy is greatly abetted by manufacturers' significant reductions in the cost of the vaccines, making them available in poorer areas of the world. He referred to Rwanda's vaccination program, which is supported by an appropriate infrastructure and has achieved high uptake rates, as a model for vaccination efforts in developing countries.

Dr. Beth Y. Karlan, Director, Women's Cancer Program, Samuel Oschin Comprehensive Cancer Institute, Director of Gynecologic Oncology, Department of Obstetrics & Gynecology, Cedar-Sinai Medical Center, Professor, Obstetrics and Gynecology, David Geffen School of Medicine, University of California, Los Angeles, asked about the duration of vaccine effectiveness given that many individuals do not receive more than one or two doses. Dr. Lowy said that data from the Costa Rica HPV vaccine trial indicate that one dose of the GSK vaccine confers 4 years of protection; however, data are not available about the Merck vaccine, which represents the majority of uptake in the United States.

V. PRESIDENT'S CANCER PANEL REPORT—DR. BARBARA RIMER

Dr. Barbara Rimer, Dean, Gillings School of Global Public Health, Alumni Distinguished Professor of Health Behavior and Health Education, The University of North Carolina at Chapel Hill, updated members on the 2012–2013 HPV workshop series held by the President's Cancer Panel (PCP, the Panel). Dr. Rimer reminded members of PCP's mission to monitor the development and execution of activities of the National Cancer Program and to report directly to the President about any delays in rapid execution of these activities. She announced that actor and author Hill Harper, J.D., a cancer survivor, lawyer, and actor, was appointed to the Panel as its third member, along with Dr. Owen Witte and herself.

HPV vaccination stands at the nexus of scientific, communication, political, global health, legal, and behavioral realms. The PCP scheduled four workshops, three of which had already taken place, as part of the HPV vaccination series. The first of these workshops was held in San Francisco, CA, in July 2012, co-chaired by Dr. Lowy and Dr. Cosette Wheeler, University of New Mexico, and titled "HPV Vaccination as a Model for Cancer Prevention." Topics encompassed the fundamental science and efficacy of HPV vaccines, surveillance and epidemiology of the global distribution of HPV-related cancers, high-priority populations for vaccination, and next-generation vaccines. Ideas that resulted from the workshop included a need for strategies to increase HPV vaccine uptake and a review of data from ongoing studies (e.g., Costa Rica) on efficacy and duration of protection. Reducing the number of recommended doses to less than three should be a priority because of the positive impact on uptake. Research gaps that were identified included the need to: define the natural history of oropharyngeal HPV infections; develop validated screening methods for non-cervical HPV-associated cancers; and create high-quality data systems to support vaccine monitoring and surveillance.

Dr. Rimer reviewed information from the second HPV-series workshop, held in Washington, DC, in September 2012. This workshop was co-chaired by Dr. Noel Brewer, Gillings School of Global Public Health, University of North Carolina, and Dr. Robert Croyle, Director, DCCPS. The workshop "Achieving Widespread HPV Vaccine Uptake" included discussions about barriers and behavioral factors that influence uptake; programmatic approaches, including policies, to increase uptake; financing, development, and implementation of large-scale HPV vaccine efforts; and lessons from countries with high vaccine uptake (e.g., Australia). Participants at the workshop recognized that HPV vaccination for prevention of several forms of cancer is a major global public health opportunity that requires a

substantial communication effort to educate physicians, health care providers, and the public. Suggested strategies for increasing uptake are to allow pharmacists to administer booster vaccines, consider vaccination as part of a broader adolescent health platform, possibly including school health professionals, and provide special attention to increasing vaccination rates in areas with low uptake. Participants also suggested that the emphasis in communication should be on the vaccine as a cancer prevention strategy. They also recommended a national cancer campaign for HPV vaccination in both males and females. Monitoring and surveillance should include the linkage of at least some vaccine registries with cancer registries.

Dr. Rimer reviewed information from the third HPV-series workshop, held in Chicago, IL, in November 2012. The co-chairs were Drs. Marcus Plescia and Mona Saraiya from CDC and Dr. Tamera Coyne-Beasley, University of North Carolina at Chapel Hill, a member of the CDC's Advisory Committee on Immunization Practices. The workshop was titled "Creating an Integrated HPV Vaccination and Screening Program." Topics included: population health and economic impacts of widespread HPV vaccination; tools and resources needed to support integrated approaches to HPV vaccination and screening; and venues in which vaccines can be provided and health professionals authorized to administer vaccinations. The workshop included a review of national cervical cancer screening guidelines from the American Cancer Society (ACS) and the U.S. Preventive Services Task Force (USPSTF), and the 2010 Vaccine Plan produced by the U.S. Department of Health and Human Services (HHS).

The fourth HPV-series workshop will be held April 23–24, 2013, in Miami, FL. The "Challenges of Global HPV Vaccination" workshop will be co-chaired by Dr. Anne Schuchat, CDC; Dr. Ted Trimble, NCI; and Dr. Funmi Olopade, University of Chicago. This workshop will encompass the topics of global epidemiology of HPV infection and HPV vaccination coverage; global HPV vaccine policy and financing; and global vaccine program development, implementation, monitoring, and evaluation.

Dr. Rimer noted that the final annual report from the previous members of the President's Cancer Panel titled "The Future of Cancer Research: Accelerating Scientific Innovation" would soon be available on the PCP website.

Questions and Answers

Dr. Jennifer A. Pietenpol, Director, Vanderbilt-Ingram Cancer Center, B.F. Byrd, Jr. Professor of Oncology, Vanderbilt University Medical Center, commented that the success of a communication effort depends on training the trainers. She also commended Drs. Rimer and Lowy for the efforts on HPV vaccination for cancer prevention. Dr. Elizabeth M. Jaffee, The Dana and Albert "Cubby" Broccoli Professor of Oncology, Co-Director of the Gastrointestinal Cancers Program, Associate Director for Translational Research, The Sidney Kimmel Comprehensive Cancer Center at The Johns Hopkins University, added that it is difficult to find information about this topic in the public domain. Dr. Rimer acknowledged that health professionals are becoming more interested in the topic and said that the national groups and organizations are communicating information about the HPV vaccine but are less visible than other immunization groups, such as those promoting the influenza vaccine.

Dr. Victoria L. Champion, Associate Dean for Research, Mary Margaret Walther Distinguished Professor of Nursing, Center for Research & Scholarship, Indiana University School of Nursing, asked about the age restrictions (e.g., 16–17 years) on vaccinations by pharmacists. Dr. Rimer responded that restrictions are state-specific and have to be dealt with on a state level. Dr. Karlan suggested that separating the vaccine program from cervical cancer screening would help remove the perception of a link with sexual activity. Dr. Rimer stressed that this underlies the efforts of the American Academy of

Pediatrics and other groups to frame HPV vaccination with an anti-cancer message.

Dr. Lyerly asked whether the decrease in male cancer risk with the HPV vaccine is based on evidence. Dr. Lowy confirmed that evidence from the Merck trials investigating anal infection and dysplasia shows a reduction in the incidence of HPV infection with the vaccine, but it is too early to determine changes in the incidence or mortality from cancer. Dr. Lyerly commented that the lack of data makes it difficult to develop a public health message that will convince consumers about the importance of the vaccination; a reduction of dysplasia is not understood by most consumers. Dr. Lowy observed that the FDA recognizes that dysplasia is an early part of the pathway leading to anogenital cancer. He added that prevention of dysplasia is recognized as a valid surrogate for later reductions in cancer, and that the basis of cervical cancer screening relies on the presence or absence of dysplasia. Moreover, this message has been communicated successfully.

Ms. Lester queried about administration of the vaccine at an earlier age, such as infancy. Dr. Rimer indicated that there is discussion of administering the vaccine at earlier ages, but currently it is approved only for children 9 years or older.

VI. OBESITY AND CANCER—DR. RACHEL BALLARD-BARBASH

Dr. Rachel Ballard-Barbash, Associate Director, Office of the Associate Director, Applied Research Program, DCCPS, provided an overview of body mass index (BMI) and cancer mortality and cancer outcomes. Dr. Ballard-Barbash summarized many years of observational epidemiologic research showing that cancer risk (incidence) increases as BMI increases, with the largest increase in relative risk found for endometrial cancer. A review article summarizing prior research comparing obese patients who either did or did not undergo bariatric surgery showed that there was little or no decrease in cancer incidence or mortality among men but significant decreases in both measures for women. A meta-analysis of observational epidemiologic research of breast cancer survival among obese patients suggests that there is a 20–40 percent increase in mortality among obese patients. One reason for this may be because until recently obese women with breast cancer were less likely to receive full kg based chemotherapy dosing as demonstrated in a study of adjuvant therapy for breast cancer among obese women that found they more often receive a reduced dose of chemotherapy drugs than non-obese women. Results from observational epidemiologic research also show that there is a risk of colorectal cancer, higher in men than in women, although data on cancer outcomes is equivocal for both cancers. Data on prostate cancer indicate no increased risk but a slight risk of being diagnosed with a higher grade cancer; there also may be a slight increase in the recurrence of prostate cancer.

Dr. Ballard-Barbash reviewed two recent journal articles that investigated BMI and all-cause mortality. Flegal, et. al. (*JAMA*, 2013) conducted a meta-analysis of results from more than 100 studies and found that BMI $\geq$ 35 kg/m^2 was associated with higher all-cause mortality; patients with a BMI 25-<30 kg/m^2 had a slight decrease in all-cause mortality. Berrington, et. al. (*NEJM*, 2010) conducted a pooled analysis of 19 studies in healthy, non-smoking non-Hispanic white men and women on the association of BMI and mortality. They concluded that overweight, obesity, and underweight are associated with increased all-cause mortality, increasing progression with higher and lower BMI. Additional analyses showed that smoking was a significant indicator of increased all-cause mortality, and that larger waist circumference and lower levels of physical activity were associated with higher risk.

Dr. Ballard-Barbash informed members about a report regarding the global health burden of obesity and the years of life lost and mortality outcomes versus disability outcomes. Using the years 1990–2010, the report details the decline in mortality from infectious and nutrient deficiency diseases and the increase in mortality from obesity-associated conditions, such as diabetes and ischemic heart disease.

Disability-related conditions that have obesity as a risk factor also have risen during this period. In looking at all risk factors attributable to the burden of disease, BMI is ranked as the sixth highest risk factor.

Dr. Ballard-Barbash summarized data on BMI-associated diseases and conditions that show BMI increases the incidence of hypertension, coronary heart disease in women, and the risk of postmenopausal breast cancer, endometrial cancer, and type 2 diabetes. As the population ages and people are living longer after a diagnosis of cancer, comorbidities have greater importance. Data on the prevalence of comorbidities by cancer type show that many are compounded by the presence of obesity, which can influence the survival of patients after a cancer diagnosis. This illustrates that a number of health behaviors, different obesity phenotypes, and health conditions may alter BMI and mortality associations, and that these associations may vary across racial/ethnic or immigrant populations. This is causing a shift in disease burden from mortality to morbidity, particularly in developed countries. Dr. Ballard-Barbash noted that obesity is a complex, multi-factorial health problem that is being explored with complex systems science approaches. The impact of obesity on disease burden in the United States is becoming significant on many levels and must be addressed at both scientific and policy levels.

Questions and Answers

Dr. Jonathan M. Samet, Professor and Flora L. Thornton Chair, Department of Preventive Medicine, Keck School of Medicine, Director, Institute for Global Health, University of Southern California, commented that all-cause mortality may be misleading because there are different patterns for different diseases, such as increases in mortality among those with sleep disorders as well as the relationship of obesity with cancer, respiratory conditions, and other diseases. Dr. Ballard-Barbash stated that the accelerometer data to be added to the National Health and Nutrition Examination Survey (NHANES) in 2014 will incorporate a sleep measure. Dr. Champion commented that obesity has been called the next "smoking gun" risk factor in some publications.

Dr. Sellers questioned the strength of the link between obesity and cancer, given that recent trends indicate a decrease in cancer mortality but an increase in obesity. Dr. Ballard-Barbash responded that, for many of these cancers, obesity is one of multiple risk factors and exerts varying influences depending on cancer site. Data suggest that the relationship likely is stronger with thyroid, liver, and esophageal cancers and less strong with breast cancer. Areas for future research include: the effect of *in utero* and early childhood obesity on cancer; and high birth weight and adult onset of cancer.

Dr. Cruz-Correa asked if the National Center for Health Statistics (NCHS) collects data on obesity and mortality. Dr. Ballard-Barbash responded that some data are available from both the NCHS and NHANES, but neither survey is of sufficient sample size to use for cancer cite-specific mortality in terms of obesity although they have been used related to mortality of very common conditions, such as heart disease. Dr. Miller said that the NIEHS has conducted research on the influences of early life exposure to endocrine disrupters and the advent of obesity and cancers in later life.

VII. ANNUAL DELEGATIONS OF AUTHORITY—DR. PETER J. WIRTH

Dr. Peter J. Wirth, DEA, requested concurrence by the NCAB on two Delegations of Authority to the Director of the NCI. He described the delegations and the provisions in the Statement of Understanding. Delegation A allows the Director to obtain the services of not more than 151 special experts or consultants who have scientific or professional qualifications. Dr. Wirth also said that Delegation B specifies that the NCAB delegates to the NCI Director can appoint advisory committees composed of private citizens and officials of Federal, state, and local governments to advise the Director.

The Statement of Understanding with NCI Staff on Operating Principles in Extramural Grants also falls within the Delegations of Authority to the Director, NCI. NCAB operations are conducted in accordance with management and review procedures described in the NIH Manual Issuance 4513. Concurrence of the NCAB with recommendations of initial review groups will be required, except for the following: (1) Training grants and fellowships and other non-research grant applications are not subject to NCAB review and approval, and without other concerns may be awarded without presentation to the NCAB for concurrence, with the exception of Ruth L. Kirschstein National Research Service Awards. (2) Applications over the 50th percentile will not have summary statements presented to the NCAB unless the Institute is considering an award of such an application or other special consideration is required, requested, or required by NCI or NIH policy or for special consideration by an appointed member of the Board. (3) For applications assigned raw scores that are not percentiled, the cutoff will be a priority impact score of 50 for all mechanisms except R41, R42, R43, and R44 awards; for the latter, all scored applications will be included. Expedited Concurrence and Special Council Review (SCR): (1) A process of expedited concurrence will be used for R01 and R21 applications with percentiled or raw scores that fall within the NCI paylines. (2) The Executive Secretary will alert Board members with responsibility for expedited concurrence when review outcomes for eligible applications are available on the Electronic Expedited Concurrence portion of the Electronic Council Book; and, (3) Applications from PIs who have more than $1 million dollars in direct costs from active NIH Research Grants must be given additional consideration by the Board. Administrative Adjustments: (1) Permission is delegated to the Director, NCI, to allow staff to negotiate appropriate adjustments in dollars or other terms and conditions of grant and cooperative agreement awards. (2) Administrative requests for increases in direct costs that are the result of marked expansion or significant change in scientific content of a program after formal peer review will be referred to the Board for advice and recommendation. (3) Actions not requiring Board review or advice, such as change of institution, change of principal investigator (PI), phase-out or interim support, or additional support, need not be reported to the Board. (4) NCI staff may restore requested time and support that were deleted by the initial review group when justified by the PI in an appeal letter or when restoration is in the best interest of the NCI and the project is of high NCI programmatic relevance.

Motion. A motion to approve the Annual Delegations of Authority was unanimously approved.

VIII. ONGOING AND NEW BUSINESS—DR. WILLIAM R. SELLERS

***Ad hoc* Subcommittee on Communications.** Dr. Champion, Subcommittee Chair, provided a brief report of the Subcommittee's meeting. Members were told that Dr. Lenora Johnson, Director, Office of Communications and Education (OCE), presented an overview of the structure and budget of the OCE to the Subcommittee. Dr. Champion said that the Subcommittee plans to meet via videoconference to develop objectives for the Subcommittee and also may have an in-person meeting before the next NCAB meeting. Progress by the Subcommittee would be shared with the Board at the June 2013 meeting.

Comments on The Cancer Genome Atlas (TCGA) Project. Dr. Varmus informed members that the impending closure of TCGA in 2014 is on track to achieve all of its goals and the focus now will be shifted to the Center for Cancer Genomics (CCG). Major programs within the CCG, in addition to TCGA, are the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) Program for pediatric cancer and a program for linking genomic analyses to therapeutic development. In addition, the CCG will address technology development in genomics. More detailed discussions will occur at the upcoming NCI-designated Cancer Centers meeting, and at the next joint Board of Scientific Advisors (BSA)/NCAB meeting.

Future Agenda Items. Dr. Sellers requested that members submit agenda topics for future meetings.

IX. BI-ENNIAL REVIEW OF INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH REPORT—DR. JEFF ABRAMS

Dr. Jeff Abrams, Co-Director, Division of Cancer Treatment and Diagnostics (DCTD), explained that the NIH policy on the inclusion of women and minorities in all clinical research studies, particularly Phase III clinical trials, was mandated by Congress in 1993 (P.L. 103-43), in espousal of the ethical principle of justice and of the importance of balancing research burdens and benefits. Dr. Abrams told members that the policy does not allow cost as an acceptable reason for exclusion. The NIH Revitalization Act of 1993 required the preparation of biennial reports that describe the NIH IC's compliance with this requirement. He described the process for preparing the biennial report and the role of the DEA in implementing the policy.

Dr. Abrams informed members of the NCI implementation procedures. During the pre-award phase of the grant application process, peer reviewers receive instructions and evaluate inclusion plans for all applications. Where concerns are noted, bars to award are put in place. NCI staff work with applicants to ensure appropriate revisions are made. Applications with bars are identified in a closed NCAB session, and a subsequent resolution is reported. In FY 2011, there were 16 bars to award compared to 11 in FY 2012. During the post-award phase, awardees report cumulative accrual annually, with Program Directors reviewing progress of studies and cumulative accruals. This information is entered into the NIH Population Tracking application. Staff provides oversight, advice, and assistance and work with awardees to disseminate findings and encourage new studies. The NCI is required to aggregate these data whether the clinical trial is a treatment or behavioral trial or an epidemiological observation trial, as well as subset analyses by race, ethnicity, and sex/gender for all Phase III clinical trials with initial funding after 1995. Inclusion of women and minorities sections must include subject selection criteria and rationale, rationale for any exclusions, enrollment dates (start and end), and outreach plans for recruitment. A Phase III clinical trial is defined as a broadly based prospective Phase III clinical investigation that usually involves several hundred or more human subjects to evaluate an experimental intervention or compare two or more existing treatments, often with the aim of providing scientific evidence that can result in a change in health policy or standard of care. The current report cycle covers data reported in FY 2011–2012, which represents subjects enrolled in FY 2010–2011.

Dr. Abrams described overall reporting data and provided data specifically for cancer treatment trials. The U.S. cancer incidence rates estimated for 2005–2009 by race indicate that rates are highest among blacks, with whites second followed by lesser rates for American Indians, Asian/Pacific Islanders, and Hispanics. Dr. Abrams also provided data on clinical trial enrollment by gender during 2011–2012 showing that there is an overall balance between males and females; if all-male and all-female trials are removed from the data, there still is relative gender equality in accrual. For Phase III enrollment by racial composition, data from 2011–2012 indicate a balance racially, although the data illustrated the complexity of racial composition, cancer incidence rates, and enrollment data for extramural and intramural research studies, ethnic categories, and sex/gender. Enrollment data for Cancer Therapy Evaluation Program treatment trials, predominantly through Cooperative Groups, show relative balance in accrual by gender and race. For the Division of Cancer Prevention (DCP), trial data indicate relative balance by gender but a slight under-representation of Hispanics and Asian Americans during 2011–2012.

Questions and Answers

Dr. Cruz-Correa asked if there were data on the accrual of children in clinical trials. Dr. Abrams answered that the NIH Population Tracking system currently does not collect age data, but the ability to collect this information is being pursued through the Office of Management and Budget (OMB).

Dr. Sellers wondered whether the current focus of clinical trials on breast cancer could account for the under-representation of Asian American women in trials. Dr. Abrams agreed, noting that breast cancer treatment trials have the greatest female accrual rates, especially in treatment trials.

Dr. Pietenpol referred to the data from NCI extramural and intramural research studies to ask if it is possible to have a breakdown of the data by therapeutic versus nontherapeutic studies. Dr. Abrams said that the data presented were intervention trials.

Dr. Richard Pazdur, Division Director, Division of Hematology and Oncology Products, U.S. Food and Drug Administration, asked if the clinical trial results are analyzed for efficacy and safety based on ethnic parameters. Dr. Abrams responded that, as required by legislation, data are analyzed for efficacy, safety, and toxicity. Dr. Pazdur commented that trial participants may become less representative of the U.S. population as more clinical trials are being conducted internationally. This could become a significant factor in the future for the design of trials and approval of treatments in the United States. Dr. Pietenpol queried about the extent to which Phase I trials are conducted in the United States but Phase II and III trials elsewhere, and Dr. Sellers indicated that this occurs frequently.

Motion. A motion to approve the Bi-ennial Review of Inclusion of Women and Minorities in Clinical Research Report was unanimously approved.

X. IMPACT OF THE IMPLEMENTATION OF THE OPERATIONAL EFFICIENCY WORKING GROUP (OEWG) REPORT ON THE CLINICAL TRIALS SYSTEM—DR. JEFF ABRAMS

Dr. Abrams informed members about efforts to improve the clinical trial system, now known as the NCI National Clinical Trials Network (NCTN). In 2010, the Operational Efficiency Working Group (OEWG) recommended that the NCI implement a new process to develop clinical trials in an interactive and collaborative fashion; target timelines were to be developed, and absolute timelines established for trial development. The NCI produced the implementation plans to achieve these targets and as of April 2010, all treatment trials have been monitored according to the new timelines. As of January 2011, all trials that do not achieve "absolute" deadlines will not proceed. Dr. Abrams said that when comparing historical data with the target and absolute deadlines for measuring progress, the median time in days before the new target deadlines was 830 days for Cooperative Group Phase III trials, with an OEWG target of 300 days and an absolute deadline of 730 days. For CTEP Early Phase trials, the median time in days was 550 days with an OEWG target of 210 days (240 days for groups and others) and an absolute deadline of 540 days. In April 2012, the NCI decreased the absolute deadline for CTEP Early Phase studies from 540 to 450 days, decreased Phase III studies from 730 to 540 days, and instituted a 6-month deadline for CTEP Cooperative Research and Development Agreements (CRADAs).

Dr. Abrams informed members of NCI's actions based on the OEWG recommendations beyond the timelines. The Institute hired Project Managers to closely track study timelines; developed a secure website to allow investigators, operations staff, and NCI staff to monitor timelines; and held routine conference calls between NCI reviewers and external investigators instituted at key points in the review process to quickly resolve issues and decrease the need for multiple document revisions. In addition, medical editors were hired to compile and edit Consensus Reviews and insert applicable revisions directly into an unofficial copy of the Protocol using document tracking software. Between April 2010 and September 2012, the NCI held 686 conference calls, with 247 calls regarding Letters-of-Intent (LOI), 156 calls regarding concept reviews, and 262 calls regarding protocols. Dr. Abrams noted that these calls have been effective in addressing questions and helping projects to meet the deadlines. He further described the steps in the approval process and the phases from LOI through concept review to protocol.

Dr. Abrams showed data comparing pre-OEWG deadlines and post-OEWG deadlines for protocol revisions. The data show that the average number of revisions has been reduced dramatically and that the number of protocols moving to activation after only one revision has more than doubled post-OEWG deadlines. Data on study development stages of Early Phase Trials from April 2010 to August 2012 show that the NCI has met the OEWG deadlines of 60 days for stage 2 (LOI approval to protocol submission), but did not meet the deadlines of either 60 days for stage 1 (LOI submission to LOI approval) or 90 days for stage 3 (protocol submission to protocol activation). The data indicate that the NCI is taking 78 days for stage 1 and 247 days for stage 3, which shows there still is much to be done to meet the OEWG deadlines, especially in stage 3. Kaplan-Meier analyses comparing pre-OEWG and post-OEWG recommendations show approximately a 30 percent improvement in reducing the number of days from LOI submission through protocol activation post-OEWG. In Phase III trials, there has been marked improvement and none have passed the absolute deadline.

Dr. Abram reviewed the overall progress in meeting the OEWG recommendations. Many factors have contributed to the improved timelines, including the established target and absolute deadlines, staffing additions, and improvements in the process and technology. Because of the progress since 2010, in April 2012 the NCI implemented more stringent absolute timelines of 15 months for Phase I and II trials and 18 months for Phase III trials, toward an eventual goal of moving the absolute deadlines to 7 months for Phase I and II trials and 10 months for Phase III trials.

Questions and Answers

Dr. Mack Roach III, Professor of Radiation Oncology and Urology, Chair, Department of Radiation Oncology, University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, asked how the NCI is balancing the deadlines with the time needed for new studies to obtain adequate input from multiple and international partners, who may be disinterested in the deadlines; in addition, the NCI might not be able to control the number of revisions needed for a protocol before beginning trial accrual. Dr. Abrams agreed that many factors must be considered, but the NCI's rigorous timelines are not unreasonable. Dr. Sellers encouraged more aggressive deadlines and a revision process that allowed only two revisions. Dr. Abrams acknowledged the recommendations and indicated that the NCI has made significant efforts to provide a balanced response to input from all interested parties regarding the deadlines.

Dr. Hong lauded the NCI's progress in stages 1 and 2 and asked about possible changes on the NCI institutional side to improve the stage 3 record. Dr. Abrams appreciated the idea and noted that some stage 2 components, such as contracts and the Institutional Review Board (IRB) process, could be improved. Dr. Kevin J. Cullen, Director, Marlene and Stewart Greenebaum Cancer Center, Professor of Medicine, University of Maryland, commended Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research, for his dedication to implementing the OEWG recommendations and asked whether the review of U10 applications by the central IRB would positively affect the stage 3 process. Dr. Abrams responded that applications using the central IRB review process now take approximately 2 weeks; further efficiencies are possible, but the growing complexity of the science over time may slow the review process.

Dr. Roach cautioned that requirements that are too restrictive, such as in limiting the number of revisions for a protocol, may result in unintended consequences by discouraging clinicians from submitting applications, and he suggested that alternate ways more relevant to the particular trial may be found to speed the process. Dr. Sellers commented that, although artificial deadlines can present challenges, it helps to set deadlines to make sure applicants understand the need to have the process move forward. Dr. Doroshow agreed, noting that companies that are committed to the trial find a way to meet the deadlines.

XI. CLOSED SESSION— DR. WILLIAM R. SELLERS

"This portion of the meeting was closed to the public in accordance with the provisions set forth in Sections 552b(c) (6), Title 5 U.S. code and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2)."

Members were instructed to exit the room if they deemed that their participation in the deliberation of any matter before the Board would be a real conflict or that it would represent the appearance of a conflict. Members were asked to sign a conflict-of-interest/confidentiality certification to this effect.

The NCAB *en bloc* vote for concurrence with IRG recommendations was unanimous. During the closed session, a total of 2,251 NCI applications requesting support of $663,508,870 and 26 FDA applications were reviewed.

XII. ADJOURNMENT— DR. WILLIAM R. SELLERS

Dr. Sellers thanked all of the Board members, as well as all of the visitors and observers, for attending.

There being no further business, the 164th regular meeting of the NCAB was adjourned at 1:44 p.m. on Friday, 8 February 2013.

_____ _____

Date William R. Sellers, M.D., Chair *pro tem*

_____ _____

Date Paulette S. Gray, Ph.D., Executive Secretary

National Cancer Institute

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Annual Report to the Nation on the Status of Cancer, 1975-2009

National Cancer Institute
Surveillance Research Program

NCAB Feb 8, 2013

Anne-Michelle Noone, MS
Kathy Cronin, PhD, MPH
Mark Schiffman, MD, MPH
Brenda K Edwards, PhD

Report to the Nation 1975-2009
Focus: Burden & Trends in HPV-Associated Cancers and HPV Vaccination Coverage Levels

- Journal of the National Cancer Institute
  - ePub: Jan 7, 2013 4 pm embargo; Print Issue 3, Feb 2013
- Special Feature (Dr. Lowy)
  - Trends of HPV associated cancers
  - Prevalence of HPV vaccination coverage & Pap testing
- Coordinated & shared responsibility since 1998
  - National Cancer Institute (NCI)
  - Centers for Disease Control & Prevention (CDC)
  - American Cancer Society (ACS)
  - North American Association of Central Cancer Registries (NAACCR)
- ACS (lead)
  - Also: Cancer Statistics, 2013 published in January

ACS
Cancer Facts & Figures
2013

- **1,660.290** estimated new cases in 2013
- **580,35**0 estimated deaths in 2013
- Long-term cancer mortality trends (1930-2009)
- Regional variation in cancer rates
- **Based on NCI SEER website:**
- *Probably of developing invasive cancers*
- *Stage at diagnosis*
- *5-year relative survival rates*
- *Cancer occurrence by race/ethnicity*

CA Cancer J Clin 2013;63:11-30. © 2013 American Cancer Society.

CA CANCER J CLIN 2013;63:11–30

Cancer Statistics, 2013

Rebecca Siegel, MPH[1]; Deepa Naishadham, MA, MS[2]; Ahmedin Jemal, DVM, PhD[3]

Each year, the American Cancer Society estimates the numbers of new cancer cases and deaths expected in the United States in the current year and compiles the most recent data on cancer incidence, mortality, and survival based on incidence data from the National Cancer Institute, the Centers for Disease Control and Prevention, and the North American Association of Central Cancer Registries and mortality data from the National Center for Health Statistics. A total of 1,660,290 new cancer cases and 580,350 cancer deaths are projected to occur in the United States in 2013. During the most recent 5 years for which there are data (2005-2009), delay-adjusted cancer incidence rates declined slightly in men (by 0.6% per year) and were stable in women, while cancer death rates decreased by 1.8% per year in men and by 1.5% per year in women. Overall, cancer death rates have declined 20% from their peak in 1991 (215.1 per 100,000 population) to 2009 (173.1 per 100,000 population). Death rates continue to decline for all 4 major cancer sites (lung, colorectum, breast, and prostate). Over the past 10 years of data (2000-2009), the largest annual declines in death rates were for chronic myeloid leukemia (8.4%), cancers of the stomach (3.1%) and colorectum (3.0%), and non-Hodgkin lymphoma (3.0%). The reduction in overall cancer death rates since 1990 in men and 1991 in women translates to the avoidance of approximately 1.18 million deaths from cancer, with 152,900 of these deaths averted in 2009 alone. Further progress can be accelerated by applying existing cancer control knowledge across all segments of the population, with an emphasis on those groups in the lowest socioeconomic bracket and other underserved populations. **CA Cancer J Clin 2013;63:11-30. © 2013 American Cancer Society.**

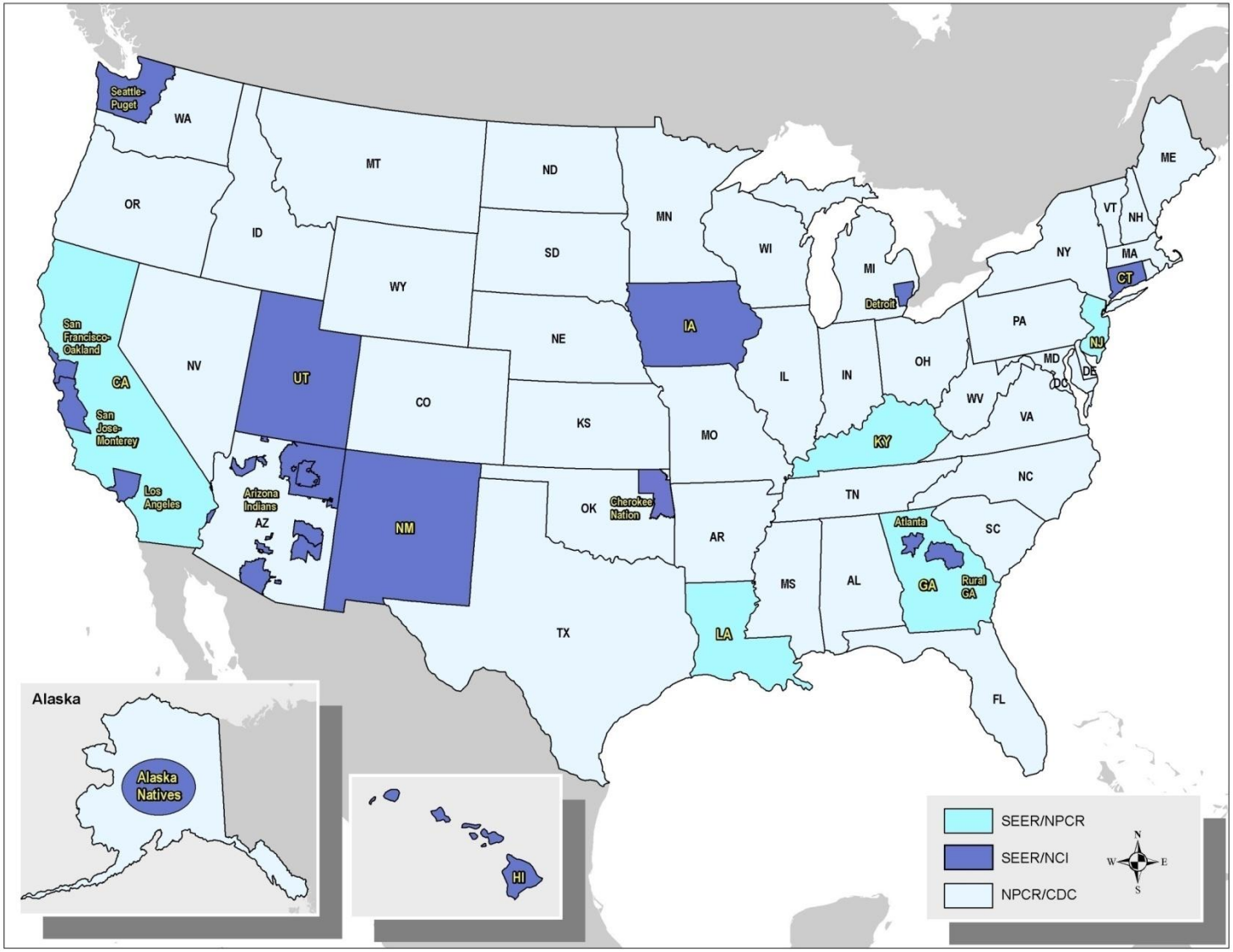
Selected Key Findings

- Decline in cancer mortality continues
- Decline in cancer incidence for men
- Cancer incidence stable for women
- Childhood cancer (age 0-14)
  - Incidence increased
  - Mortality decreased

- Dr. Lowy to present:
- 32% of girls aged 13-17 received three doses of HPV vaccine in 2010
  - 35% in 2011
  - Coverage lower among uninsured and some Southern states
- 87% of women aged 21-65 had a Pap test in last 3 years

- Incidence of HPV-related oropharyngeal cancer increased among white men and women
- Incidence of anal cancer increased among white and black men and women
- Incidence of cervical cancer generally declined among almost all women

Surveillance, Epidemiology and End Results (SEER) Program



Cancer Incidence & Mortality Statistics

- Cancer incidence
  - Long-term trends, 1992-2009
    - With and without delay adjustment
    - SEER areas, 14% coverage

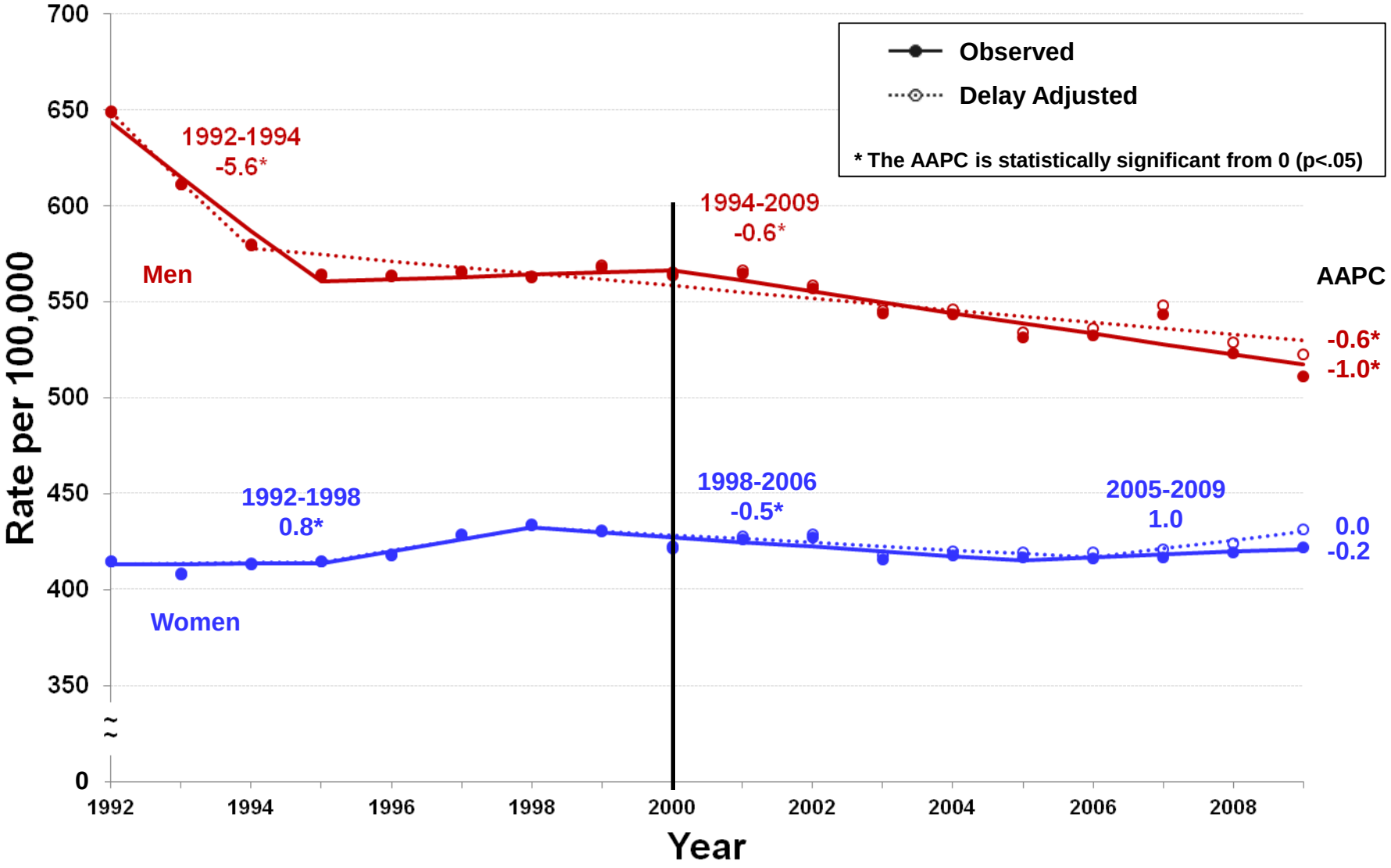
  - Short-term trends (2000-2009)
    - By race and ethnicity
    - SEER + NPCR, 87% coverage

  - Short-term rates (2005-2009)
    - By race and ethnicity
    - SEER + NPCR, 93% coverage

- Cancer mortality
  - Long-term trends, 1975-2009
  - Entire US (source: CDC's National Center for Health Statistics)

10 Year Average Annual Percent Change (AAPC) For Observed and Delay-Adjusted Incidence Rates

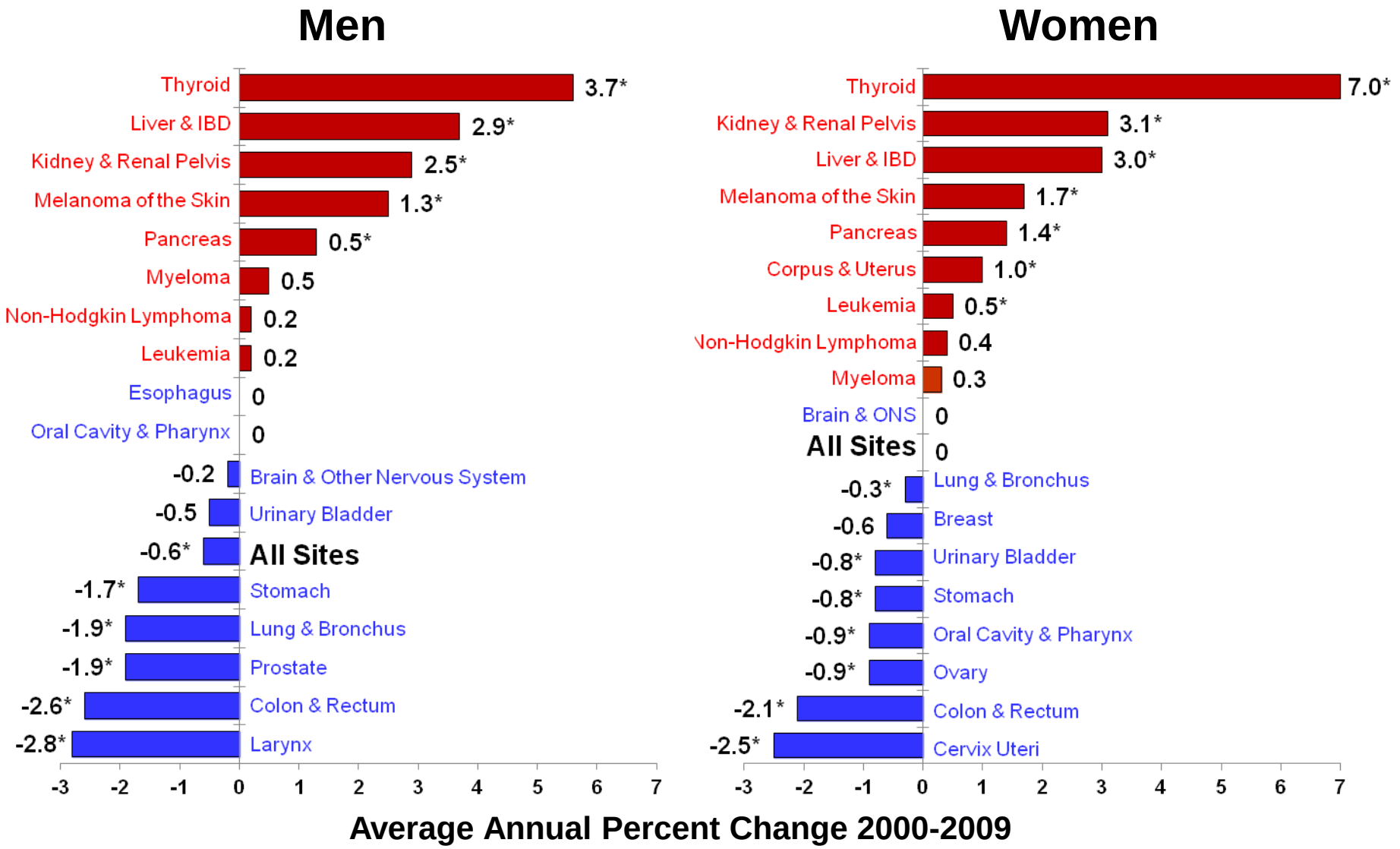
All Cancer Sites by Sex



Incidence data from SEER 13, 1992-2009

Recent Delay-adjusted SEER Incidence Trends with AAPC, 2000-2009

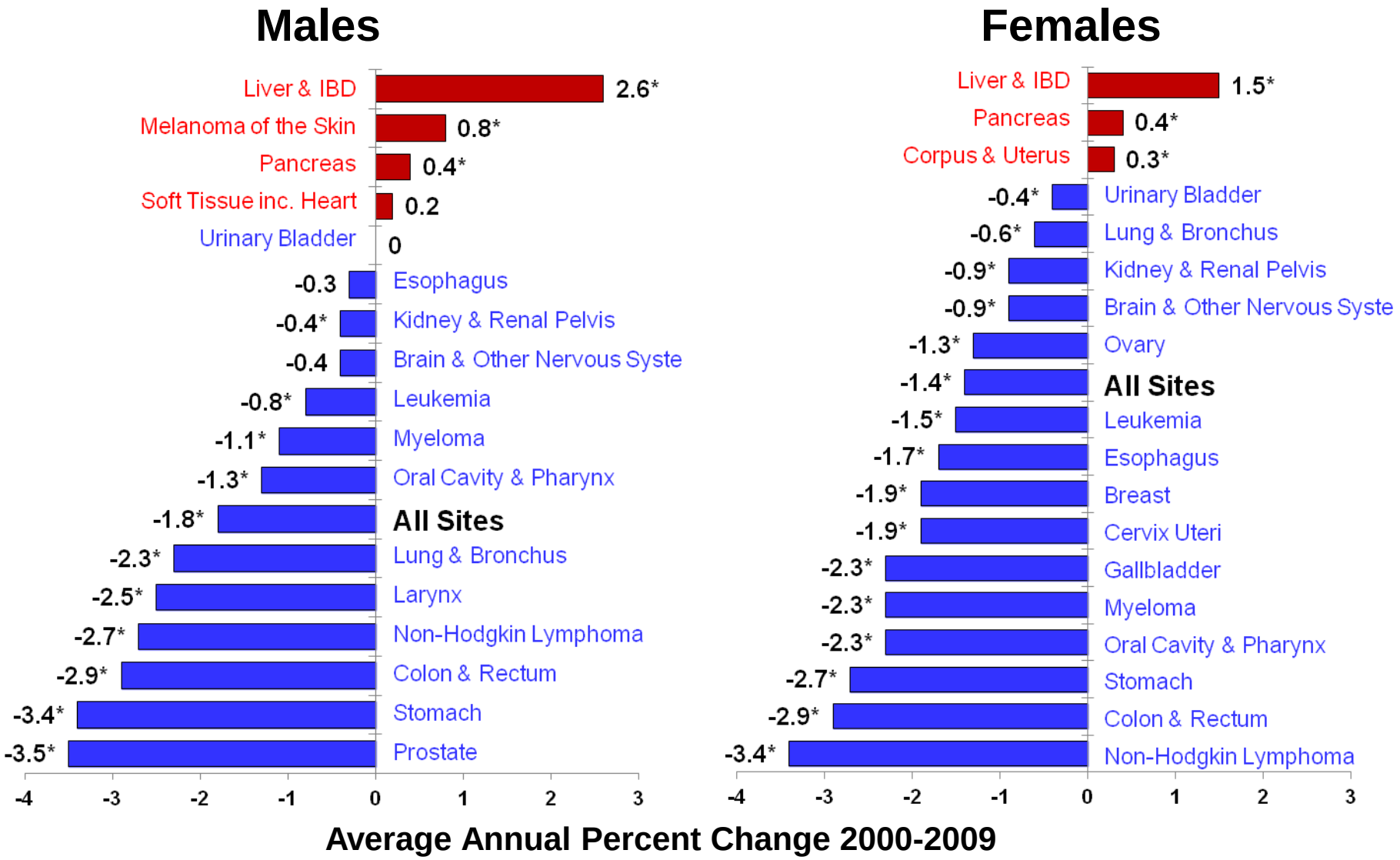
By Cancer Site*



* 10 year AAPC is statistically significant from 0 (p<.05) based on joinpoint model fit to SEER 13 delay adjusted rates from 1992-2009

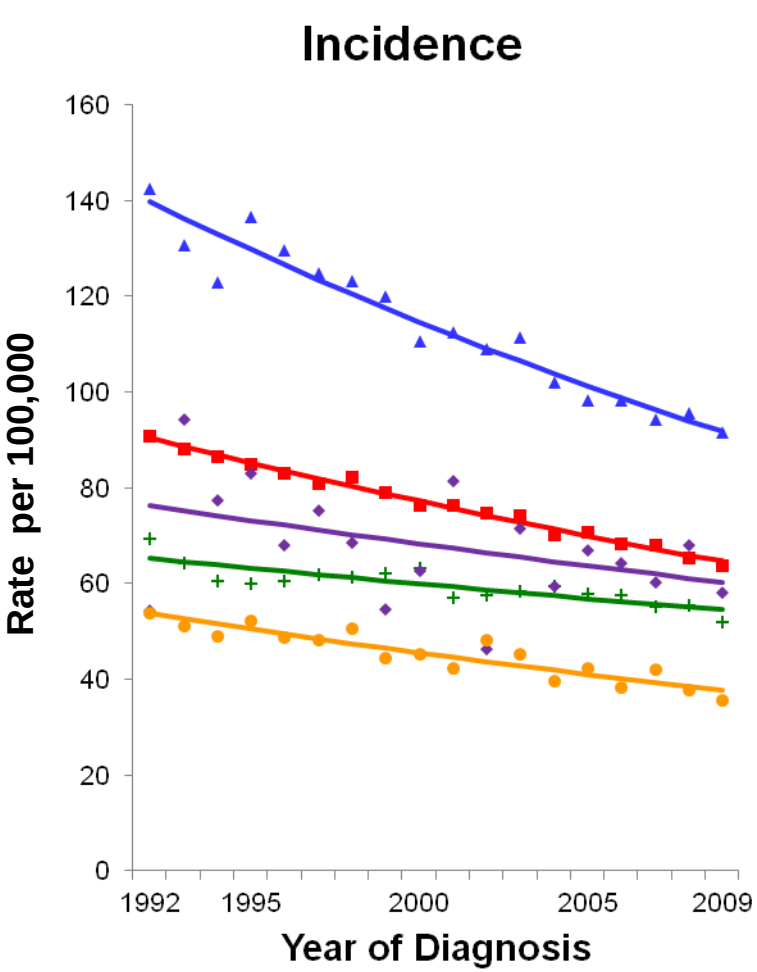
Long-Term US Mortality Trends with AAPC, 2000-2009

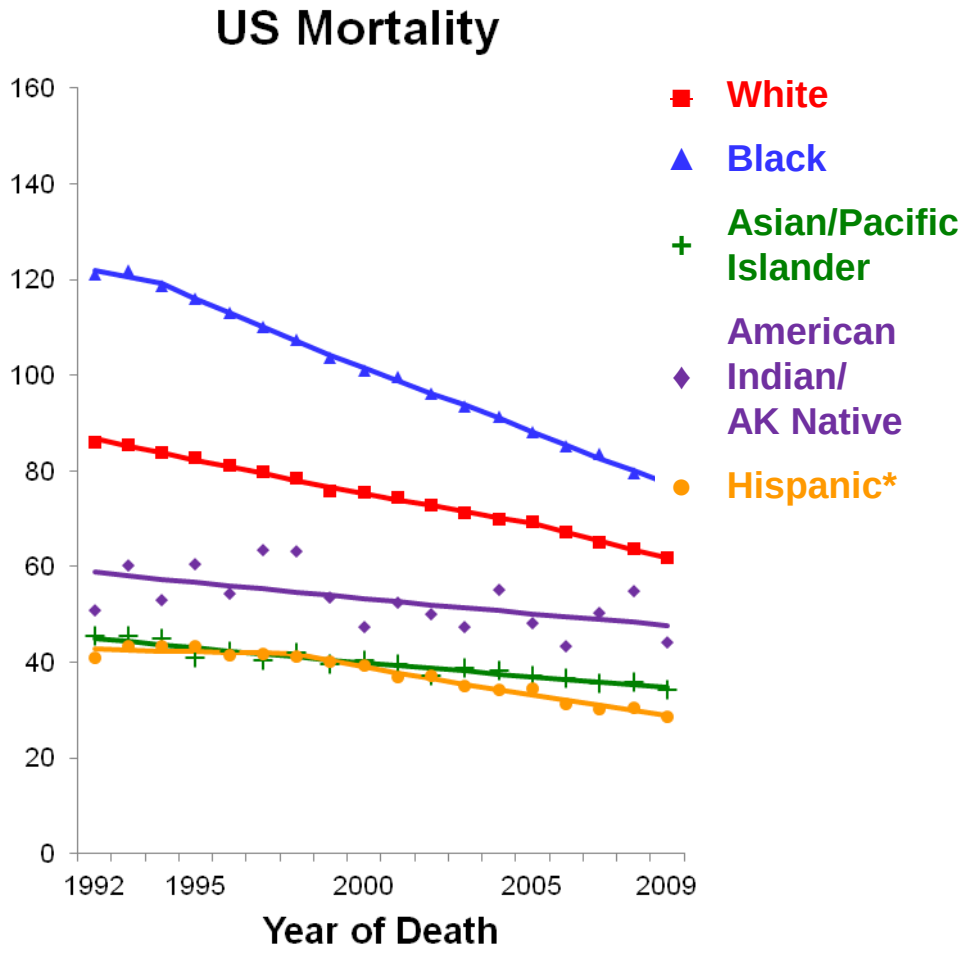
By Cancer Site*



* 10 year AAPC is statistically significant from 0 (p<.05) based on joinpoint model. Incidence data from SEER 13, mortality data from NCHS.

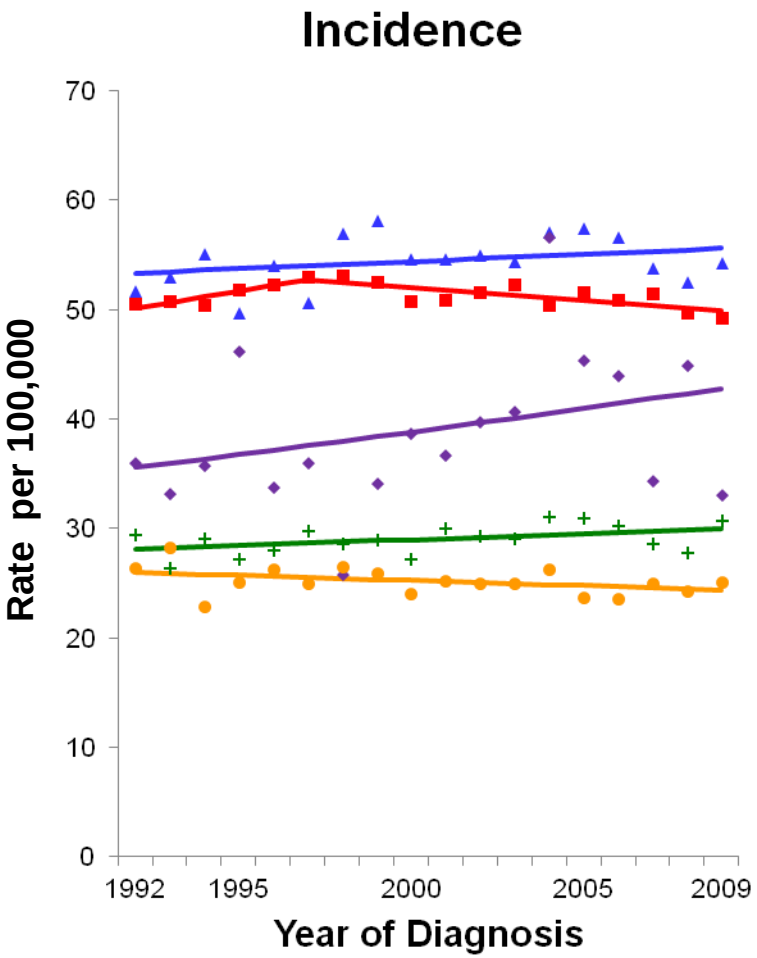
Lung & Bronchus: Men
Incidence and Mortality Age-Adjusted Trends

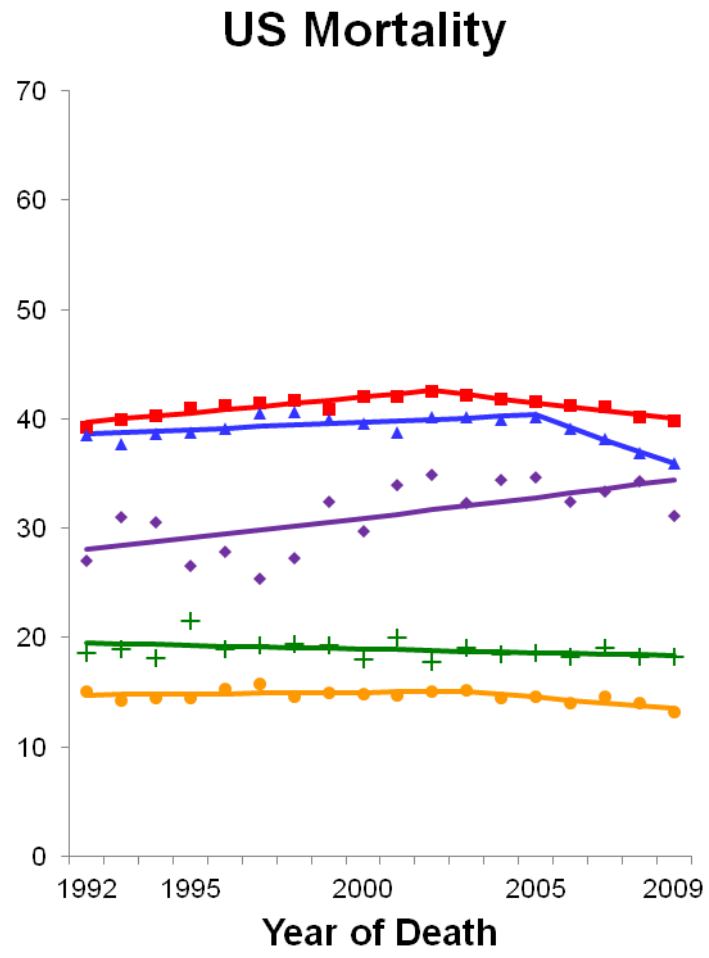




*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992-2009, Mortality data from NCHS

Lung & Bronchus: Women
Incidence and Mortality Age-Adjusted Trends

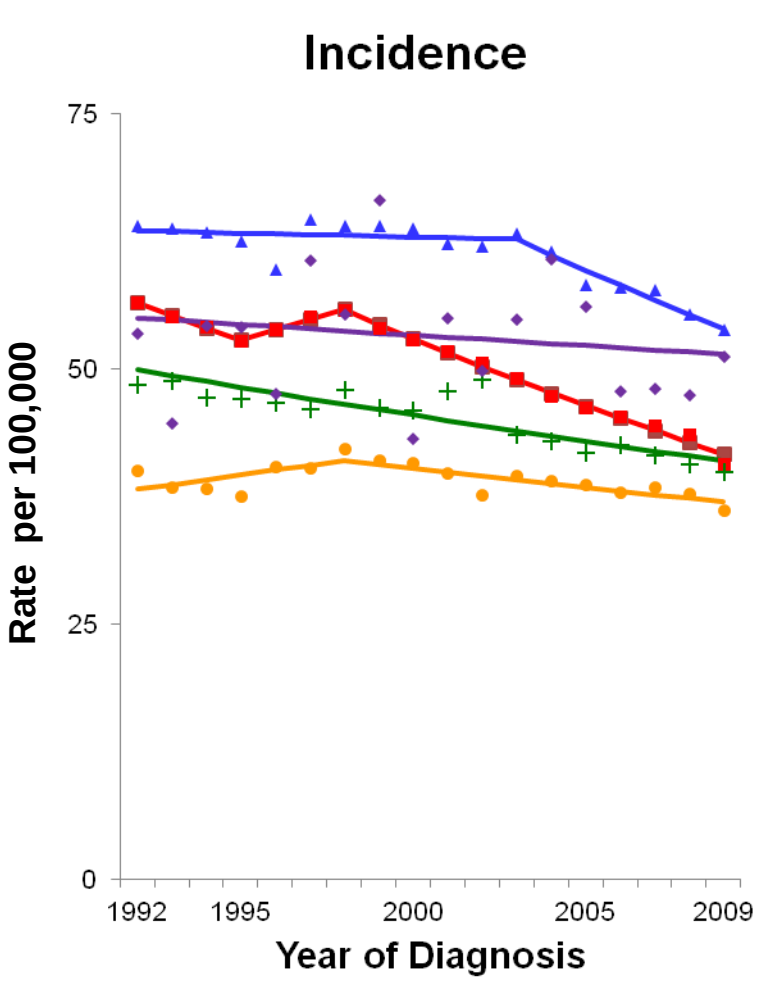


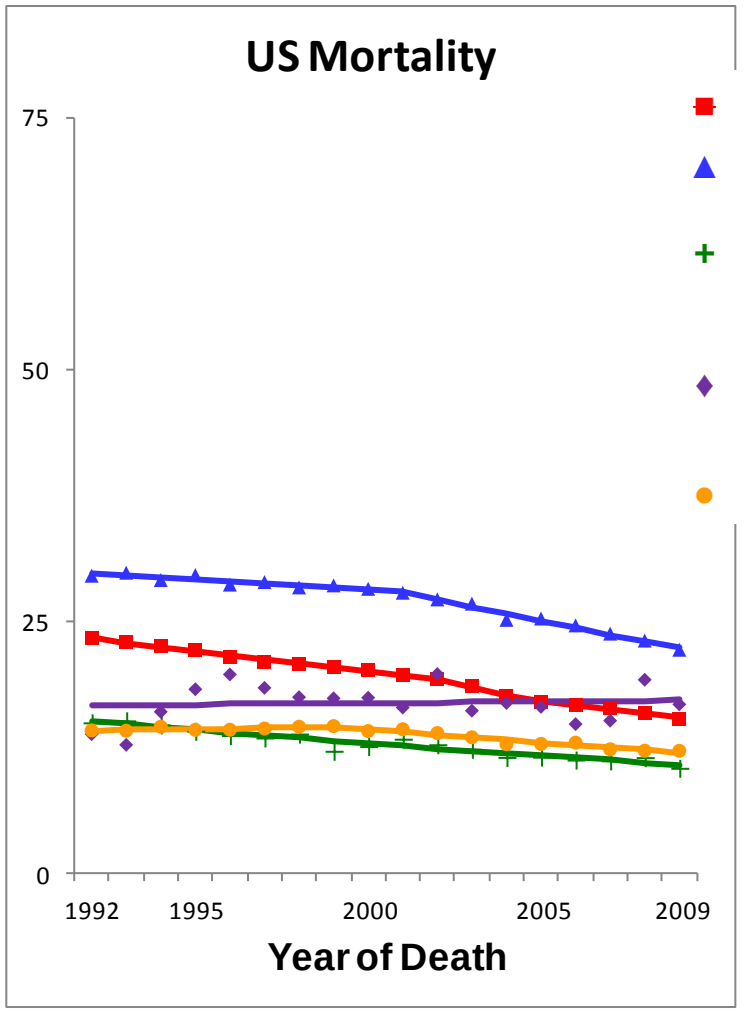


White
Black
Asian/Pacific Islander
American Indian/ AK Native
Hispanic*

*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992-2009, Mortality data from NCHS

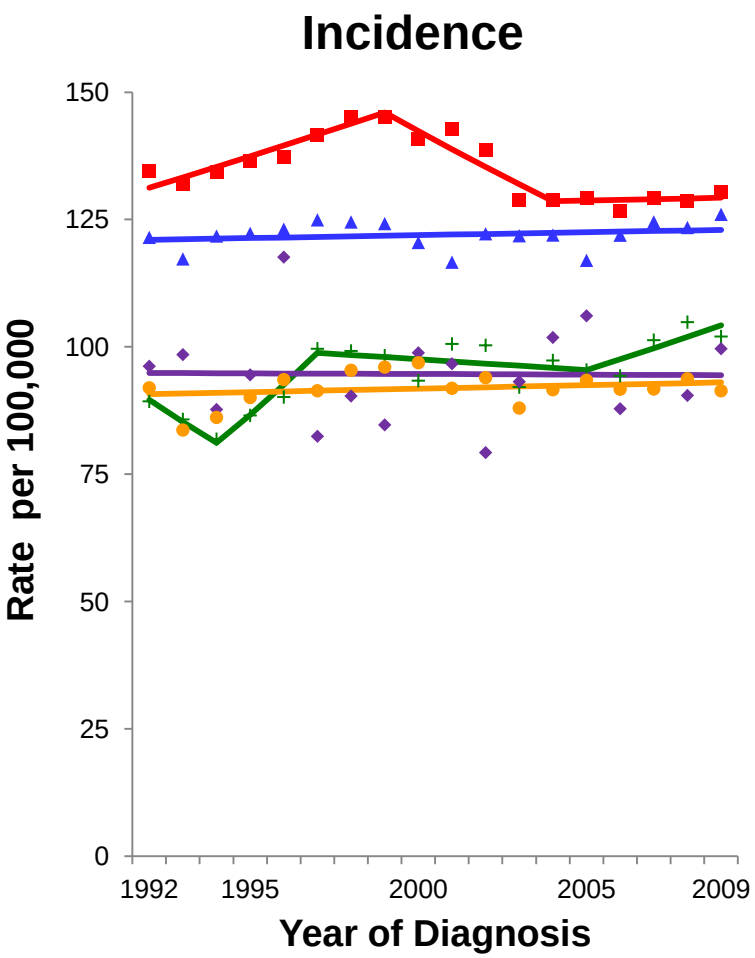
Colon & Rectum
Incidence and Mortality Age-Adjusted Trends

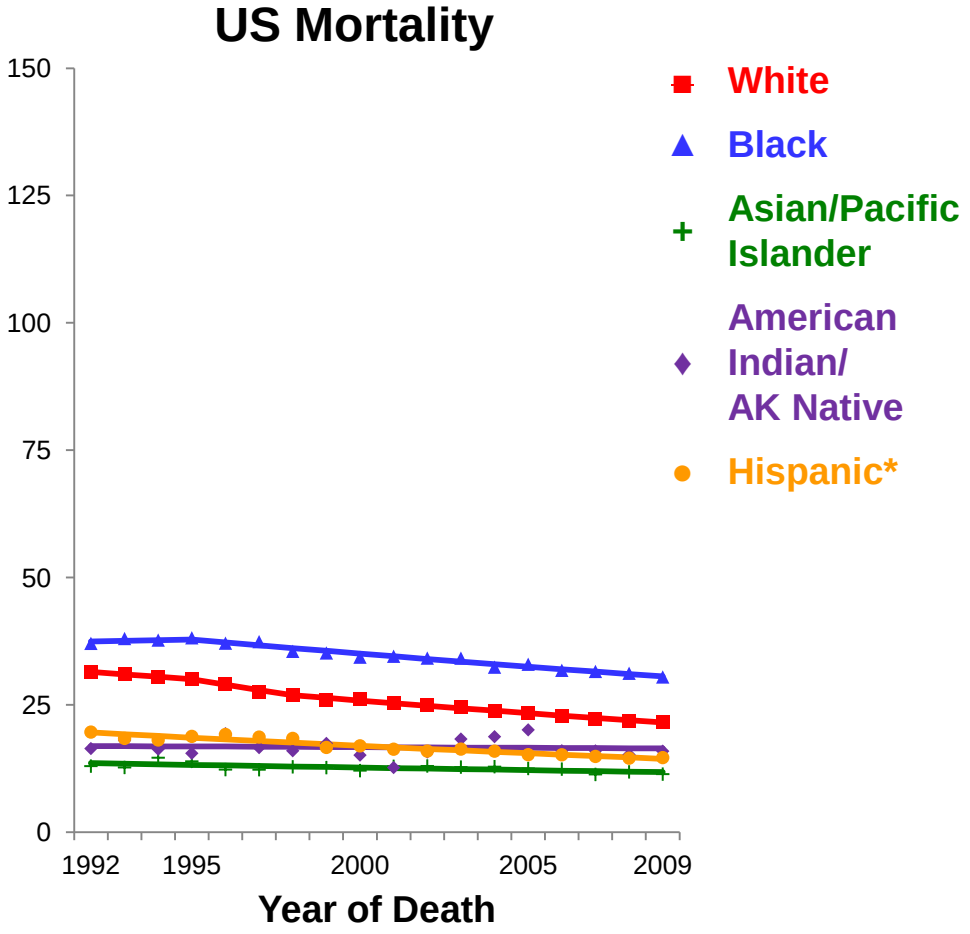




*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992-2009, Mortality data from NCHS

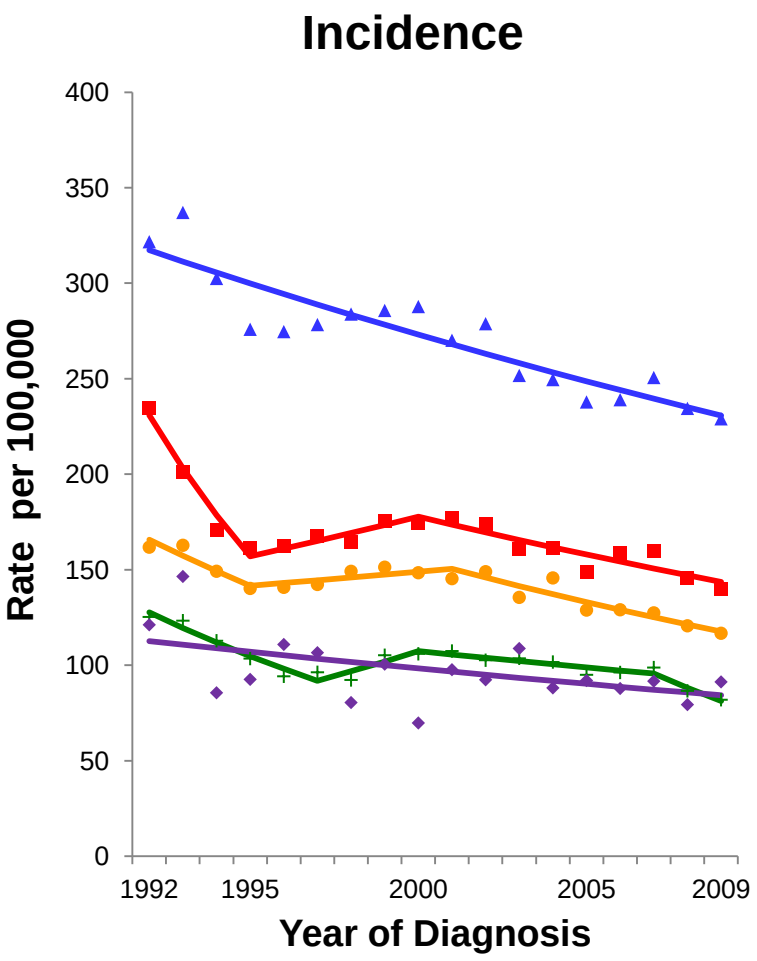
Breast (Women)
Incidence and Mortality Age-Adjusted Trends

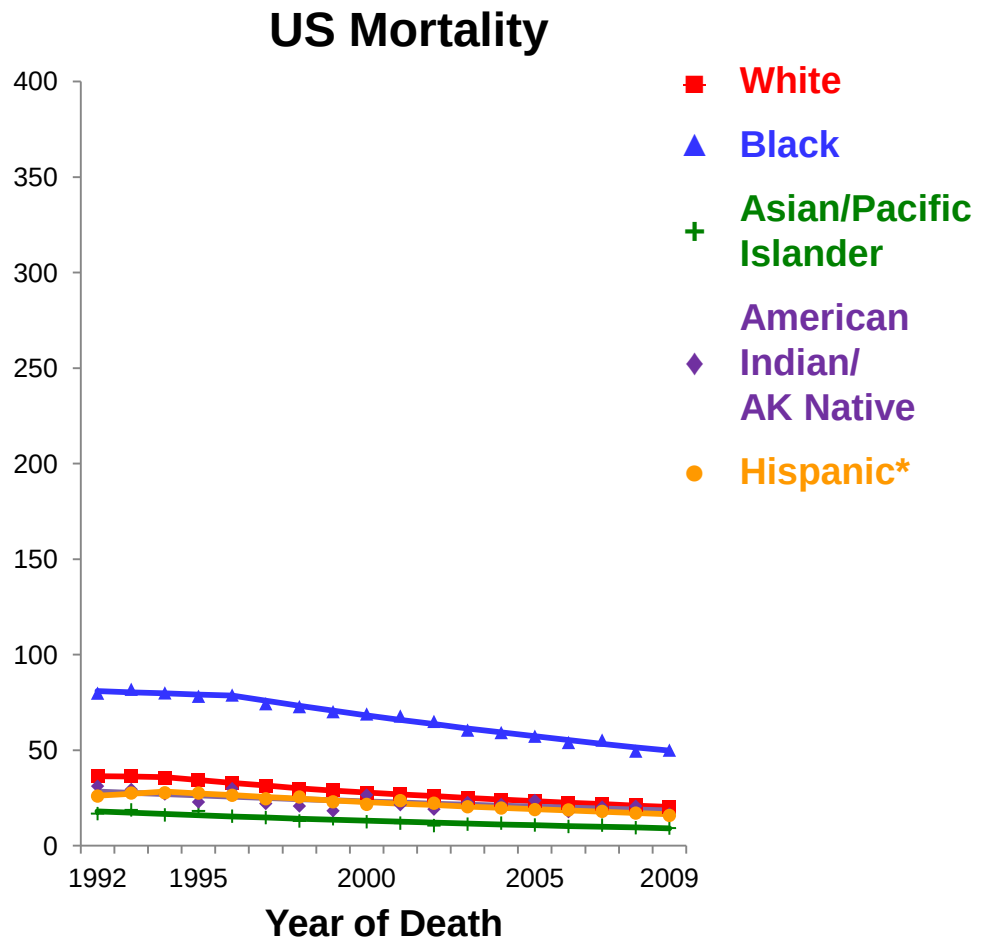




*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992-2009, Mortality data from NCHS

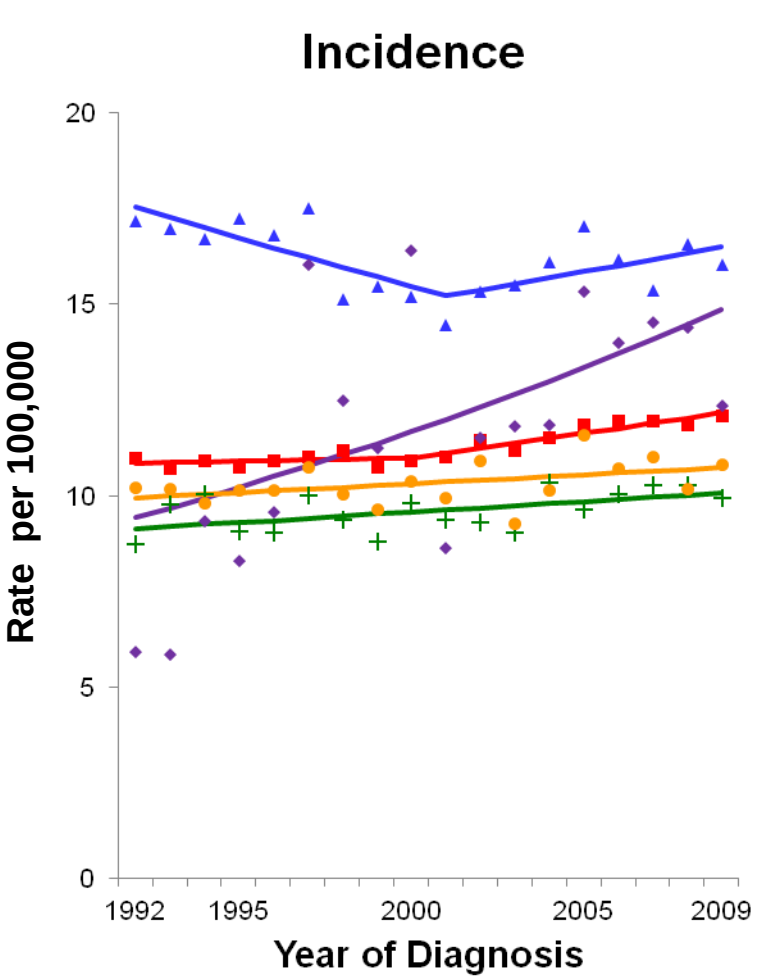
Prostate (Men)
Incidence and Mortality Age-Adjusted Trends

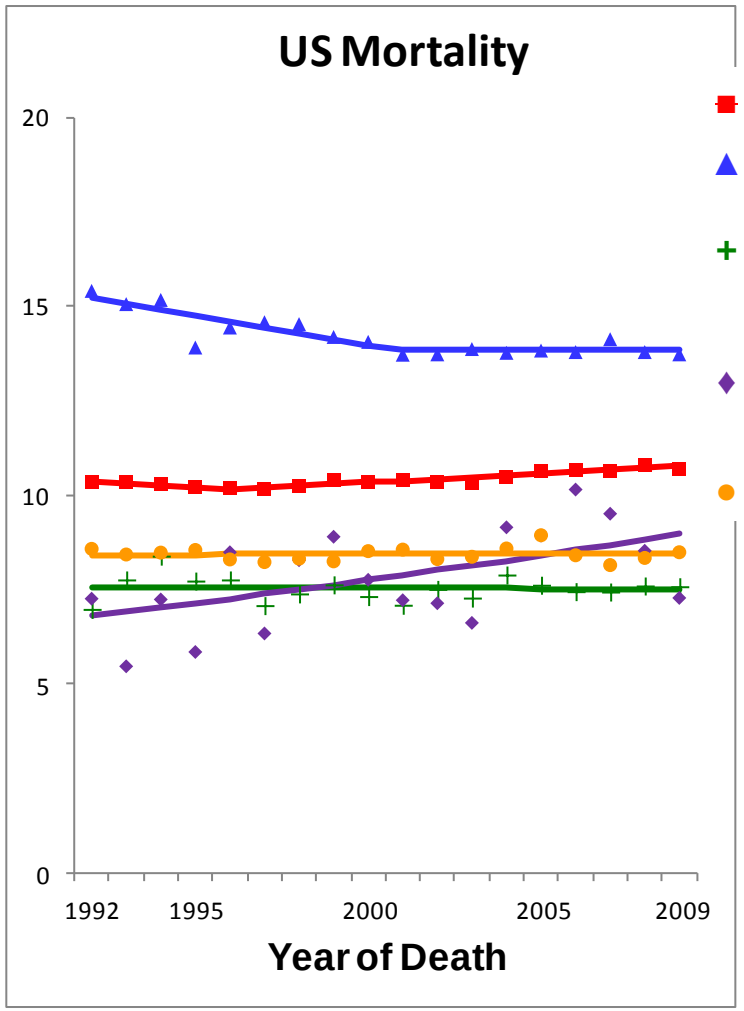




*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992-2009, Mortality data from NCHS

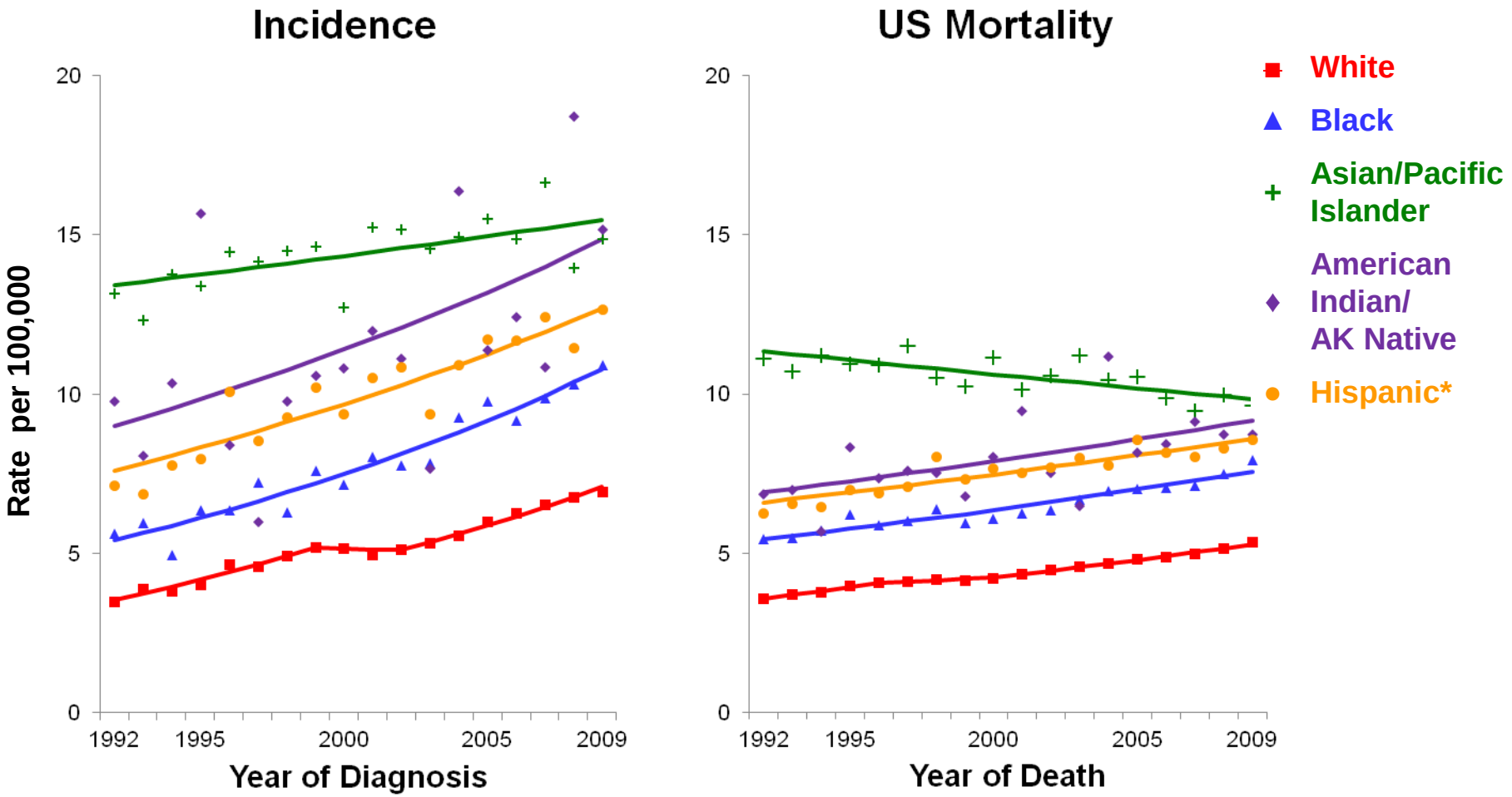
Pancreas
Incidence and Mortality Age-Adjusted Trends





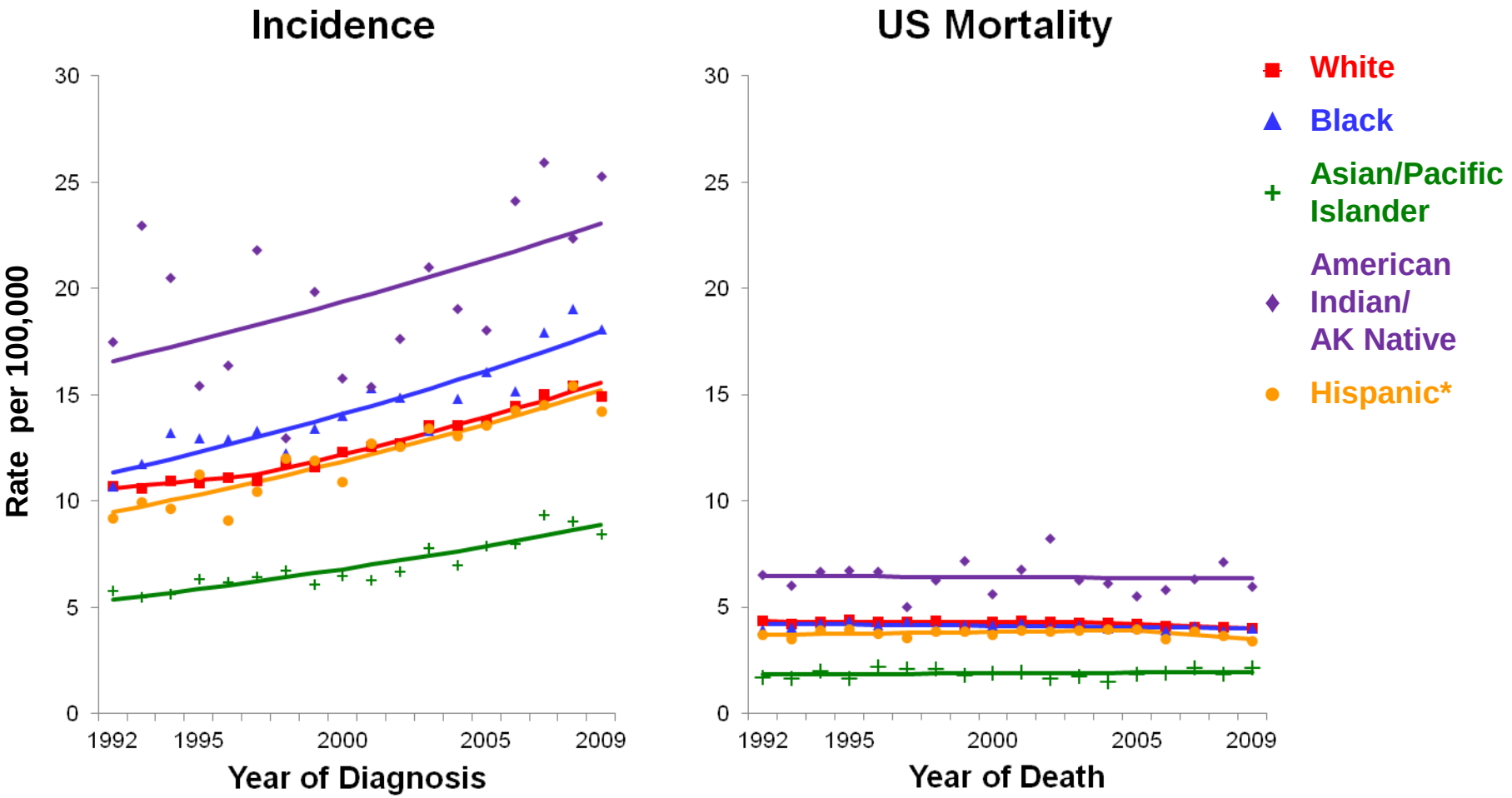
*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992-2009, Mortality data from NCHS

Liver & Intrahepatic Bile Duct
Incidence and Mortality Age-Adjusted Trends



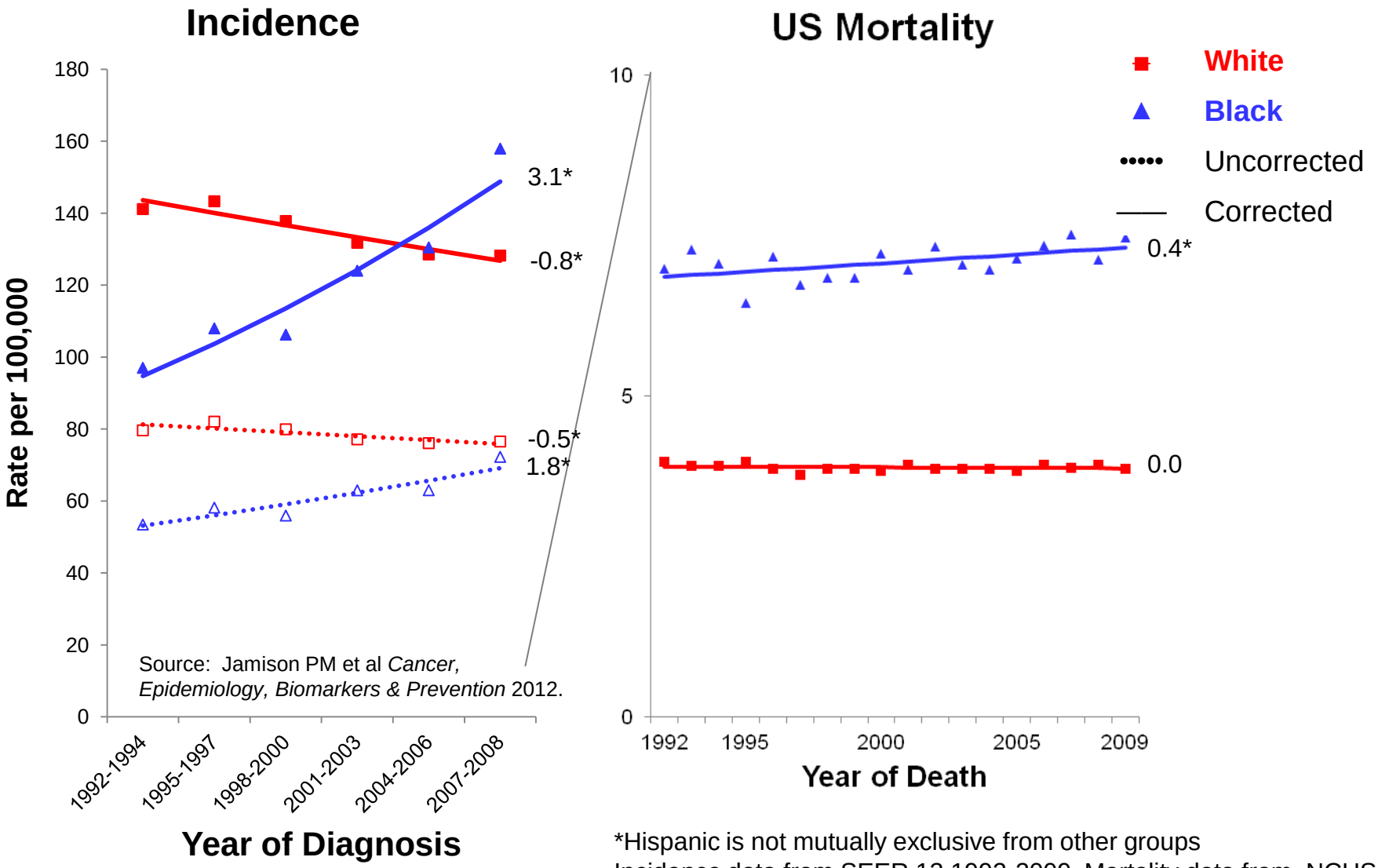
*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992-2009, Mortality data from NCHS

Kidney & Renal Pelvis
Incidence and Mortality Age-Adjusted Trends



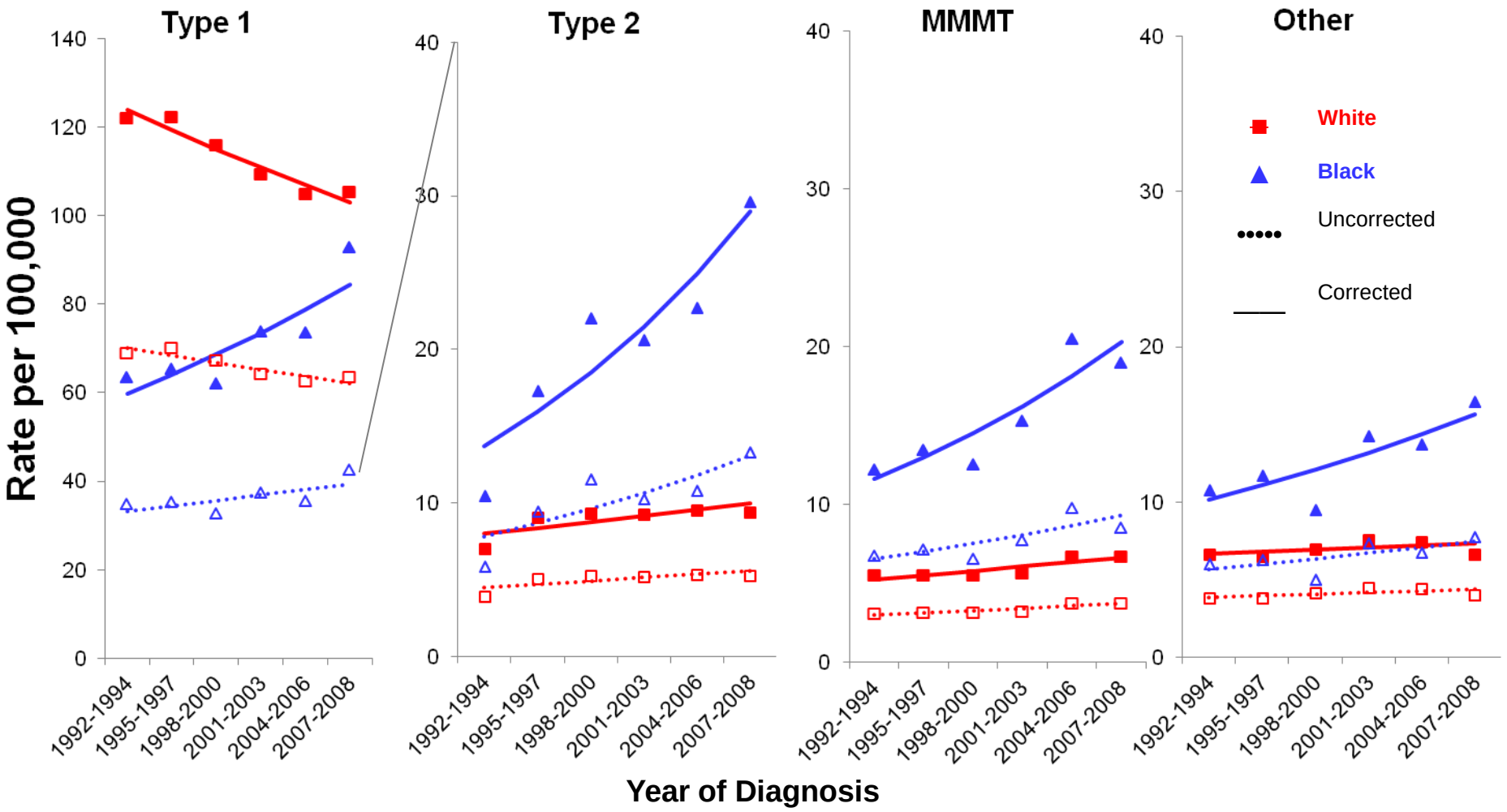
*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992-2009, Mortality data from NCHS

Corpus & Uterus, NOS
Incidence and Mortality Age-Adjusted Trends



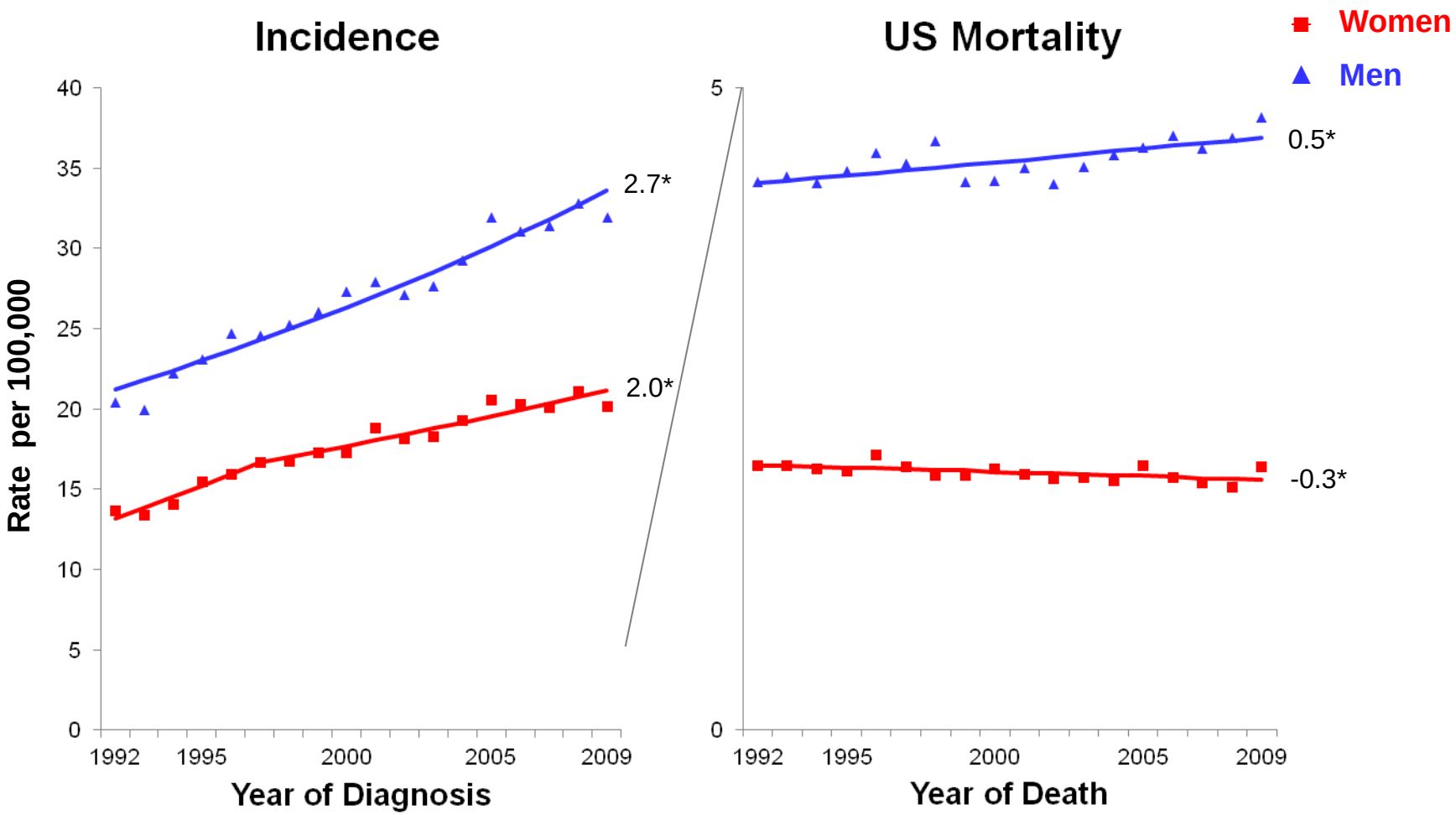
*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992-2009, Mortality data from NCHS

Corpus & Uterus, NOS by Type
Incidence Trends with Correction for Hysterectomy



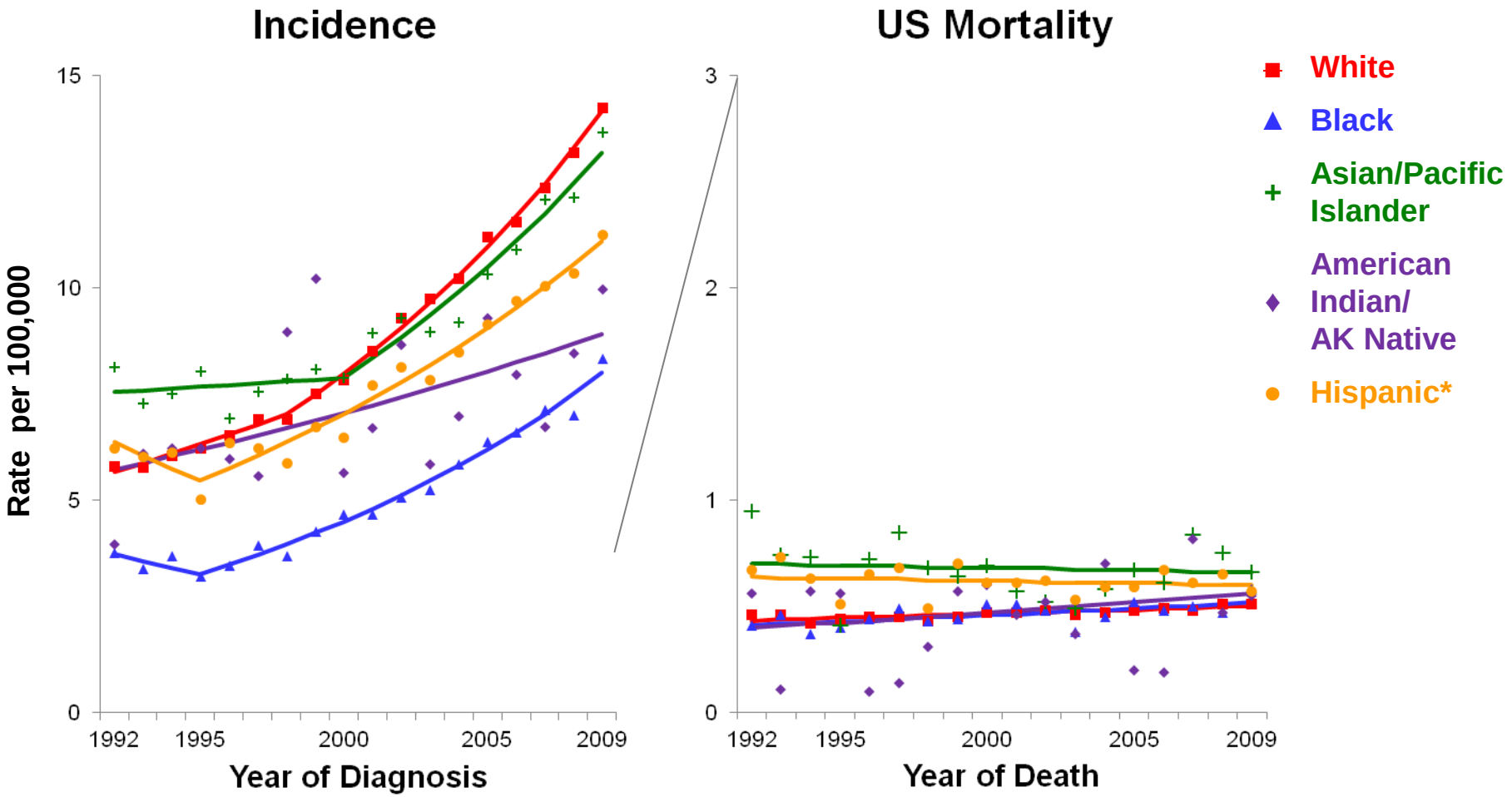
Source: Jamison PM et al. Trends in Endometrial Cancer Incidence by Rate and Histology with a Correction for the Prevalence of Hysterectomy, SEER 1992-2008. *Cancer, Epidemiology, Biomarkers & Prevention* 2012.

Melanoma of the Skin among White Men & Women
Incidence and Mortality Age-Adjusted Trends



*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992-2009, Mortality data from NCHS

Thyroid
Incidence and Mortality Age-Adjusted Trends



*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992-2009, Mortality data from NCHS

2012 ARN Collaborators

- **ACS:** Ahmedin Jemal, Edgar Simard, Priti Bandi, Debbie Saslow
- **CDC:** Christina Dorell, Lauri Markowitz, Meg Watson, S. Jane Henley, Robert Anderson, David Yankey
- **NAACCR:** Betsy Kohler, Maria Schymura
- **NCI:** Anne-Michelle Noone, Kathy Cronin, Mark Schiffman, Brenda K. Edwards

ARTICLE

Annual Report to the Nation on the Status of Cancer, 1975–2009, Featuring the Burden and Trends in Human Papillomavirus (HPV)–Associated Cancers and HPV Vaccination Coverage Levels

Ahmedin Jemal, Edgar P. Simard, Christina Dorell, Anne-Michelle Noone, Lauri E. Markowitz, Betsy Kohler, Christie Eheman, Mona Saraiya, Priti Bandi, Debbie Saslow, Kathleen A. Cronin, Meg Watson, Mark Schiffman, S. Jane Henley, Maria J. Schymura, Robert N. Anderson, David Yankey, Brenda K. Edwards

Manuscript received August 15, 2012; revised October 18, 2012; accepted October 19, 2012.

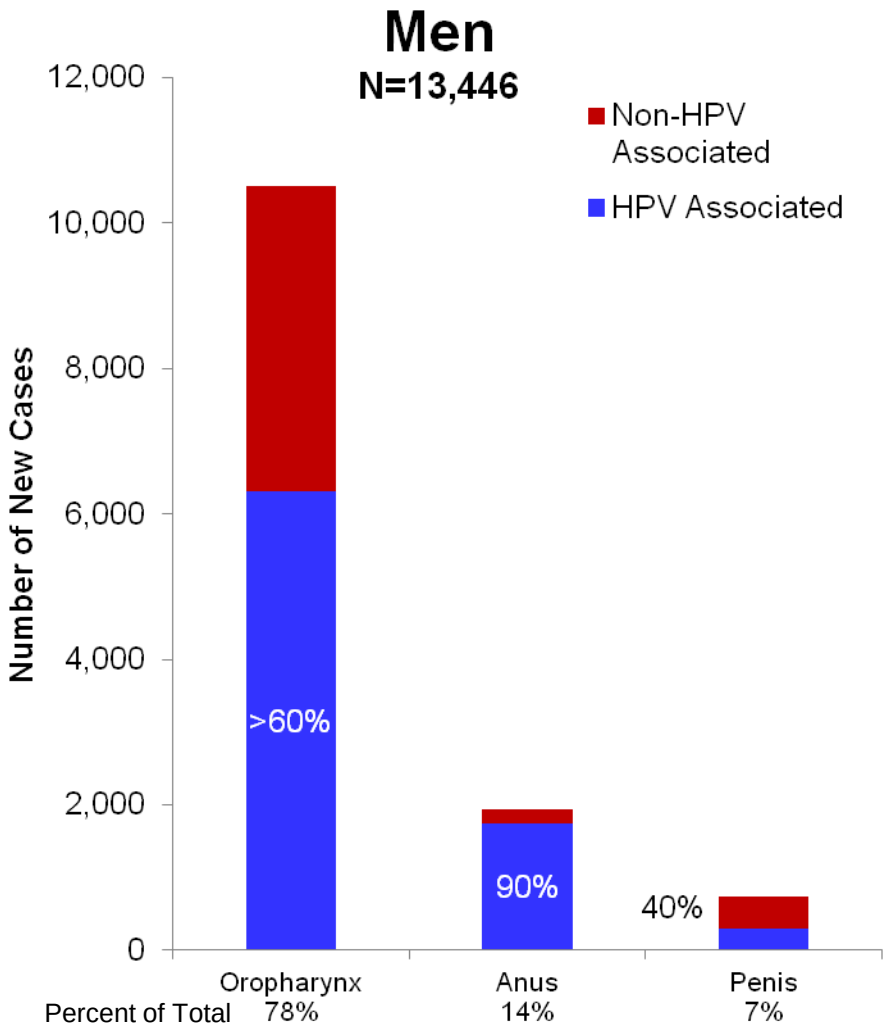
Correspondence to: Ahmedin Jemal, DVM, PhD, Surveillance Research Program, American Cancer Society, 250 Williams St NW, Atlanta, GA 30303 (e-mail: ajemal@cancer.org).

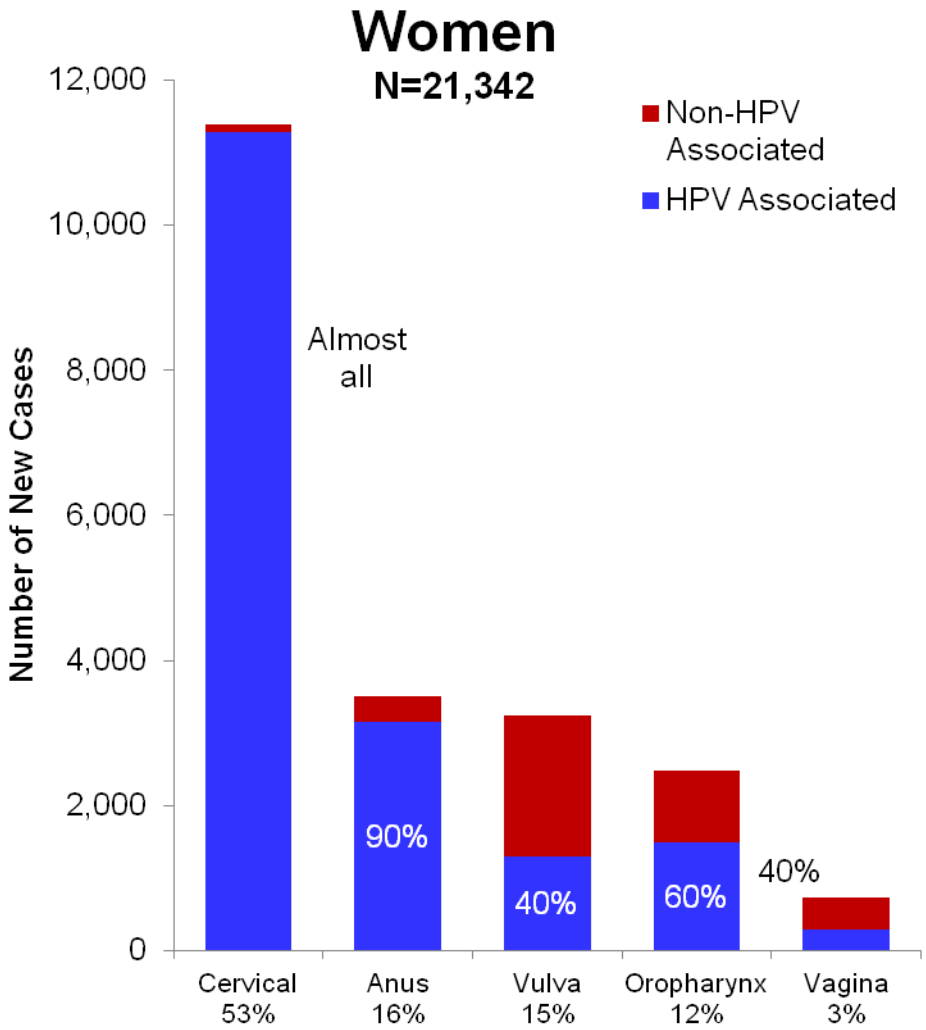
- Journal of the National Cancer Institute, ePub January 7, 2013; print: February, 2013 (issue 3)

Disclosure

- I am an inventor of NIH vaccine technology that has been licensed to Merck and GlaxoSmithKline, the two companies that manufacture the vaccine.

Number of New HPV-Associated Cancers 2009



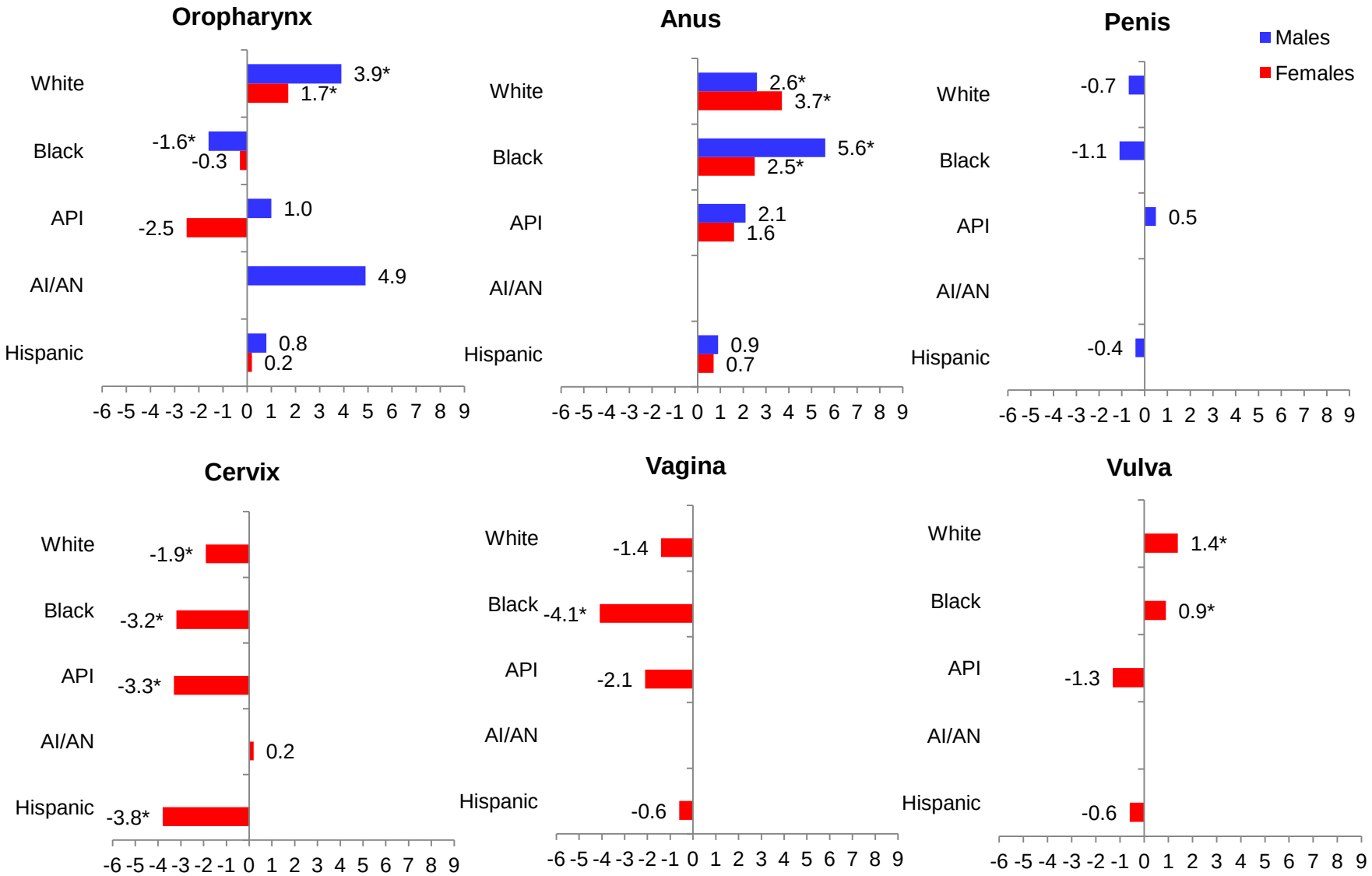


Data from SEER and National Program of Cancer Registries

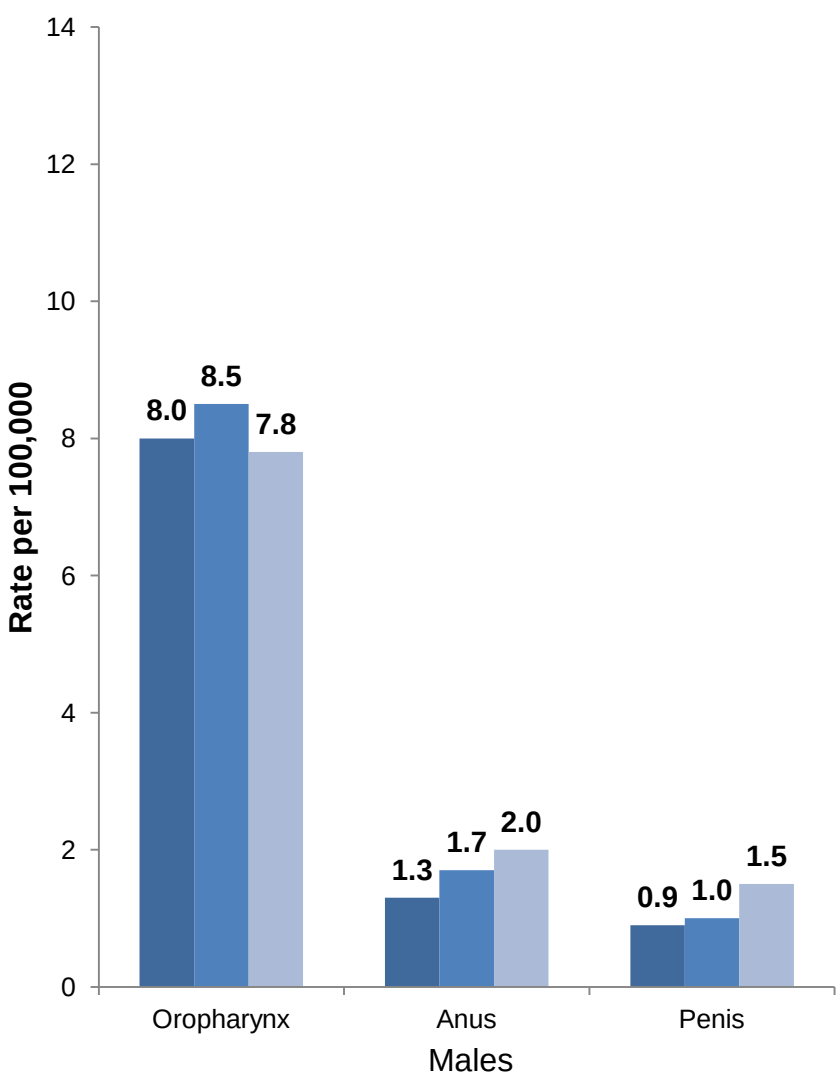
Public Health Interventions Against HPV-induced Disease

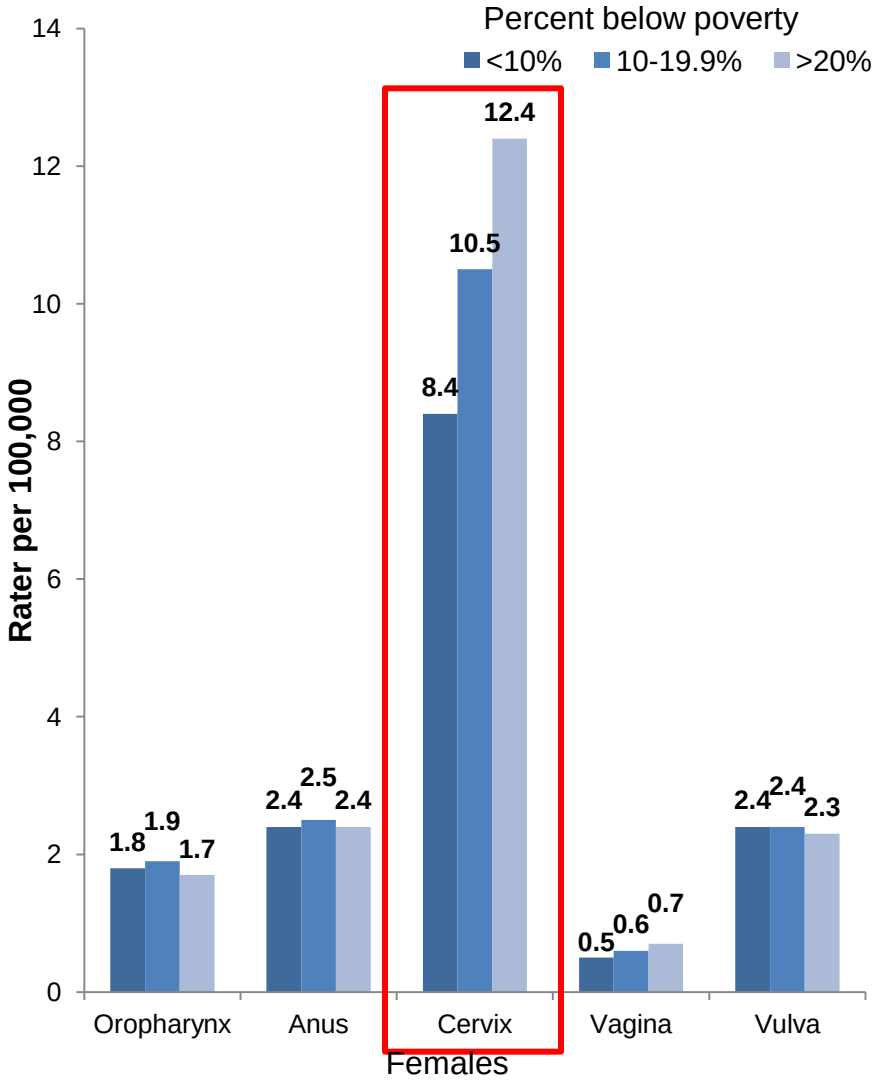
- Screening to identify pre-cancer (secondary prevention)
  - Approved for cervical cancer screening
  - Start at 21, stop at 65, can include HPV testing if over 30
- HPV vaccination (primary prevention)
  - Approved for prevention of cervical cancer, other anogenital cancers, and genital warts; plausible to be protective against cancer at other sites

Trends in HPV-Associated Cancer Incidence Rates in the US 2000–2009



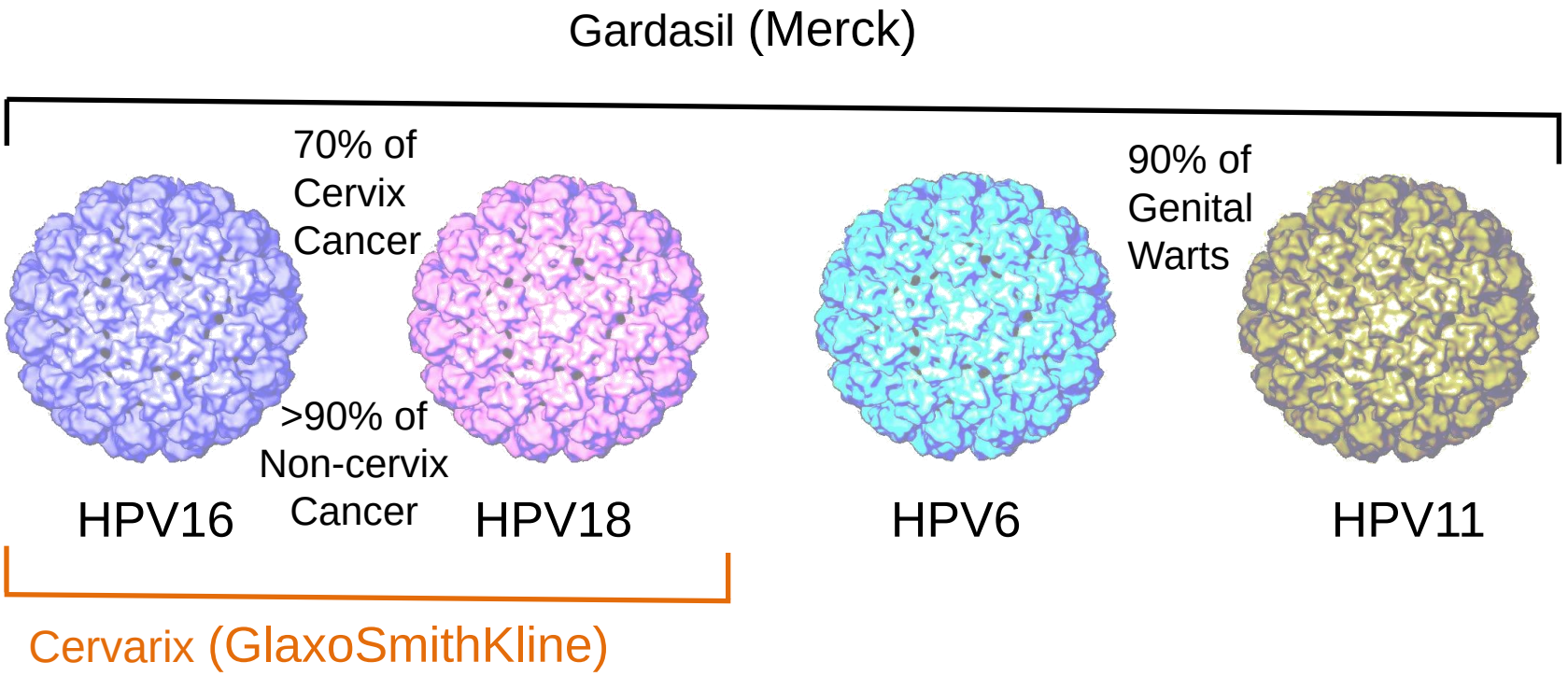
Age-Adjusted Incidence of HPV-Associated Cancers by SES 2005-2009





Data from SEER and National Program of Cancer Registries

The Commercial Vaccines Are Composed of Multiple Types of HPV L1 VLPs



- *Approved for females (both) and males (Merck)*
- *Target group: 11-12 year olds, catch-up to 26*
- *Three intramuscular injections over 6 months*

Vaccine 29 (2011) 8279–8284

Contents lists available at SciVerse ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Monitoring the safety of quadrivalent human papillomavirus vaccine: Findings from the Vaccine Safety Datalink☆

Julianne Gee[a,*], Allison Naleway[b], Irene Shui[c], James Baggs[a], Ruihua Yin[c], Rong Li[c], Martin Kulldorff[c], Edwin Lewis[d], Bruce Fireman[d], Matthew F. Daley[e], Nicola P. Klein[d], Eric S. Weintraub[a]

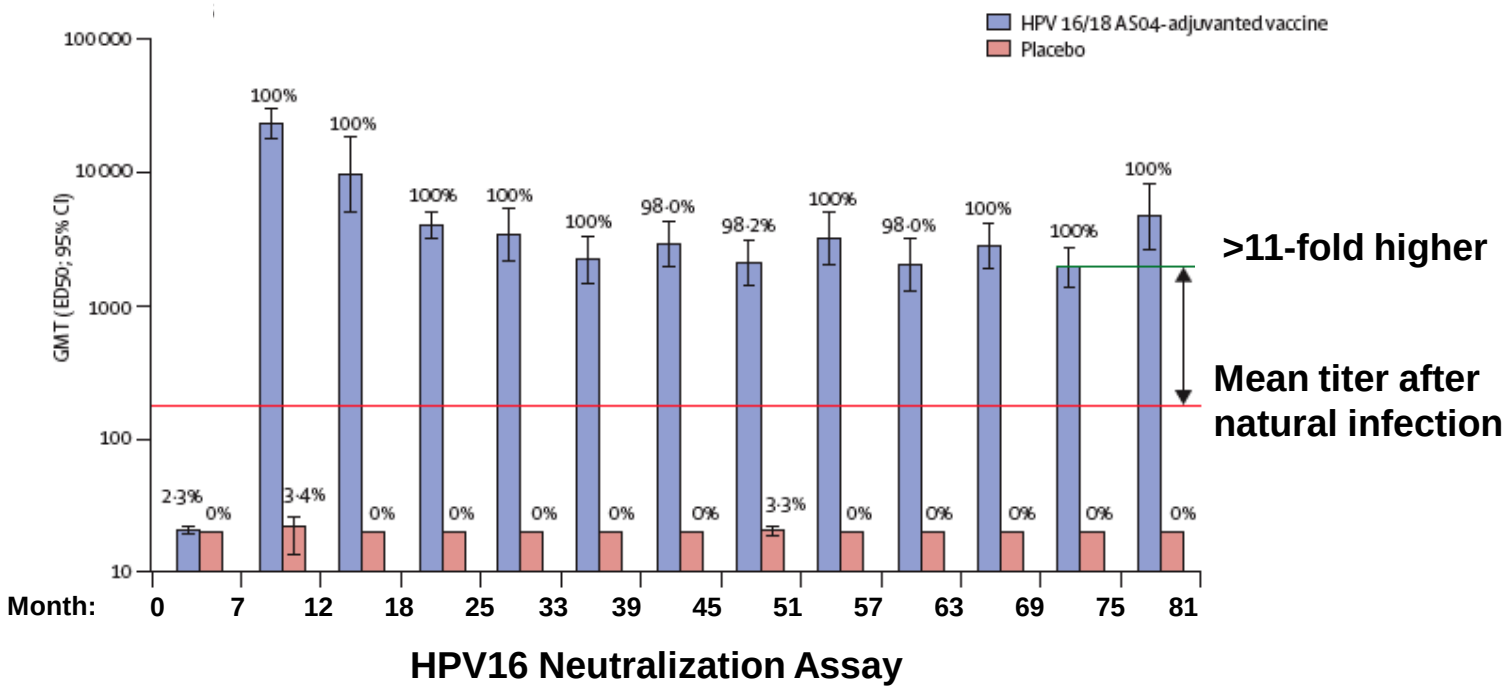
[a] Immunization Safety Office, Division of Healthcare Quality and Promotion, Centers for Disease Control and Prevention, 1600 Clifton Rd., Atlanta, GA 30333, USA
[b] Center for Health Research, Kaiser Permanente Northwest, Portland, OR, USA
[c] Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA, USA
[d] Vaccine Study Center, Northern California Kaiser Permanente, Oakland, CA, USA
[e] Institute for Health Research, Kaiser Permanente Colorado, Denver, CO, USA

- Prospective post-licensure assessment of 600,558 doses (Gardasil) from 7 managed care organizations
- No vaccine-related increased risk to prespecified outcomes: Guillan-Barré syndrome, stroke, venous thromboembolism, appendicitis, seizure, allergic reactions
  - Prespecified outcomes were derived from CDC analysis from VAERS [Vaccine Adverse Events Reporting System]: Slade et al, JAMA 2009
- Rate of anaphylaxis (1 case, 26 y.o.) similar to other vaccines
- Rate of fainting similar to that of other adolescent vaccines

Durability of Antibody Response to Cervarix

High level protection

Plateau phase



From The GSK Vaccine HPV-007 Study Group. Lancet 374:301-14, 2009

8.4 years sustained immunogenicity and efficacy: Roteli-Martins et al., Hum Vaccin Immunother 8: 390-7, 2012

Australia: Fall in HPV Prevalence After Initiating National Vaccine Program

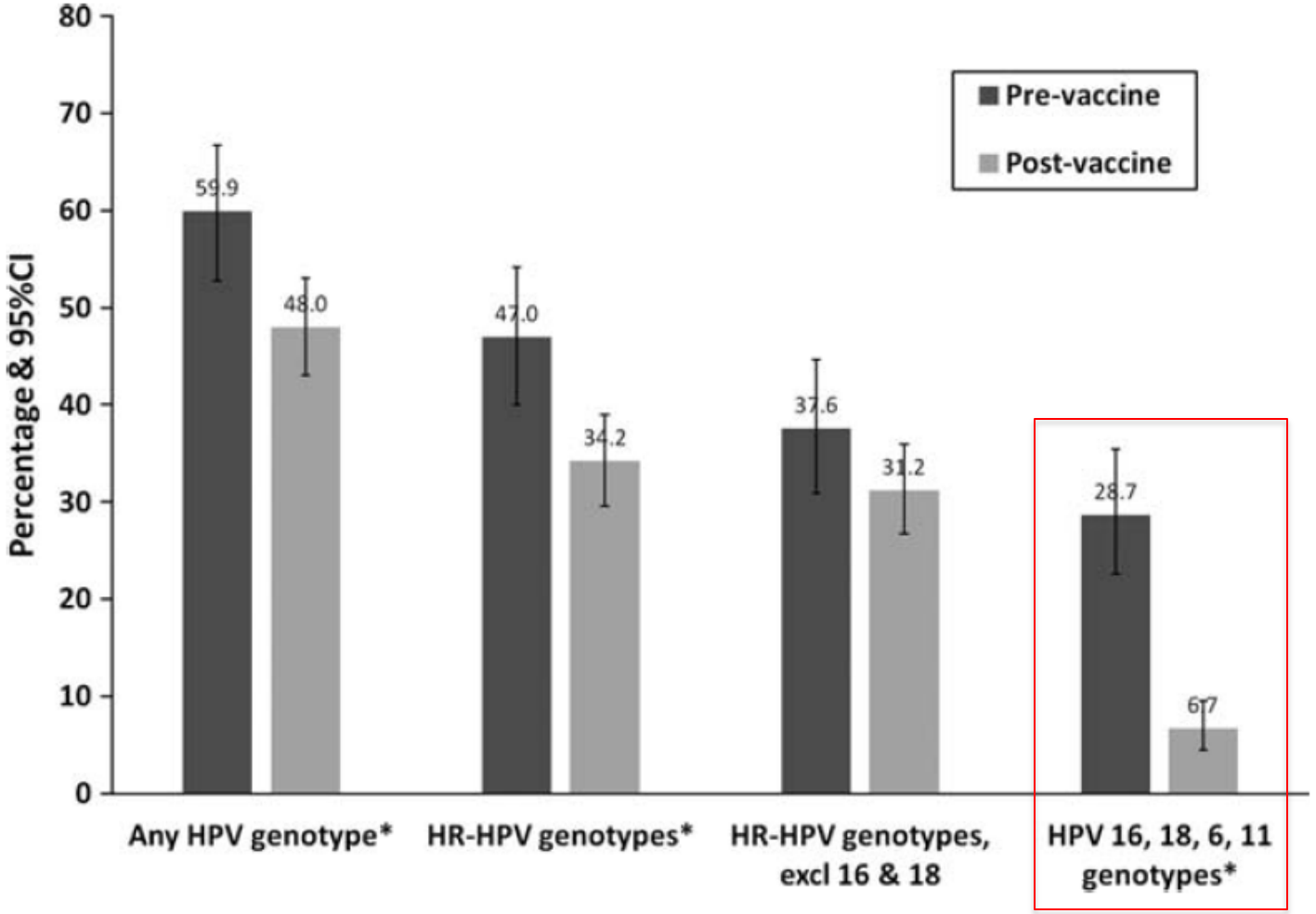


Figure 1. Differences in human papillomavirus (HPV) genoprevalence between prevaccine and postvaccine populations. *$P < .05$ for difference in percentages between groups. Abbreviations: CI, confidence interval; excl, excluding; HR-HPV, high-risk HPV.

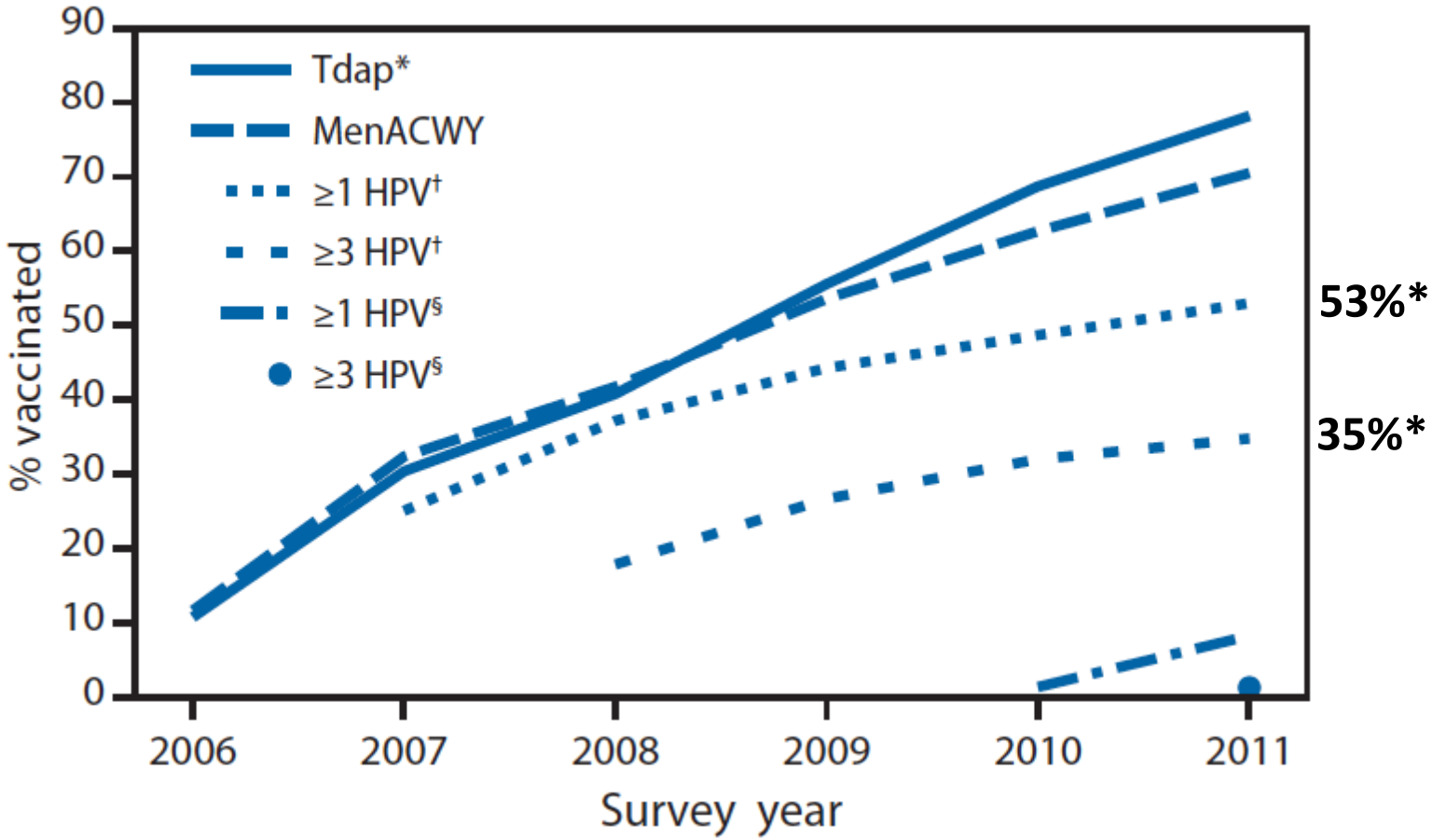
Tabrizi et al, J Infect Dis 206: 1645-51, 2012

NCI-Costa Rica Trial of GSK vaccine in 18-25 year old women: Vaccine Efficacy Against Oral Infection (End-point: HPV16/18 infection)

- 5840 **oral swabs at 4-year visit;** balanced between control and vaccine group
- **93% vaccine efficacy (1/16 infections in vaccine group)**
  - 12 HPV16 infections; 4 HPV18 infections
- **Suggestive evidence that HPV vaccination may protect against oropharyngeal cancer attributable to HPV infection**
- *Rolando Herrero, Allan Hildesheim, Aimee Kreimer and their colleagues, submitted*

Trends in U.S. Vaccination Rates: Ages 13-17 Yrs

MMWR Vol 61, #34, August 31, 2012



*** Females; adolescent male vaccination 8.3%**

Abbreviations: Tdap = tetanus, diphtheria, acellular pertussis vaccine; MenACWY = meningococcal conjugate vaccine; HPV-1 = human papillomavirus vaccine, ≥1 dose; HPV-3 = human papillomavirus, ≥3 doses.

* Tdap and MenACWY vaccination recommendations were published in March and October 2006, respectively.

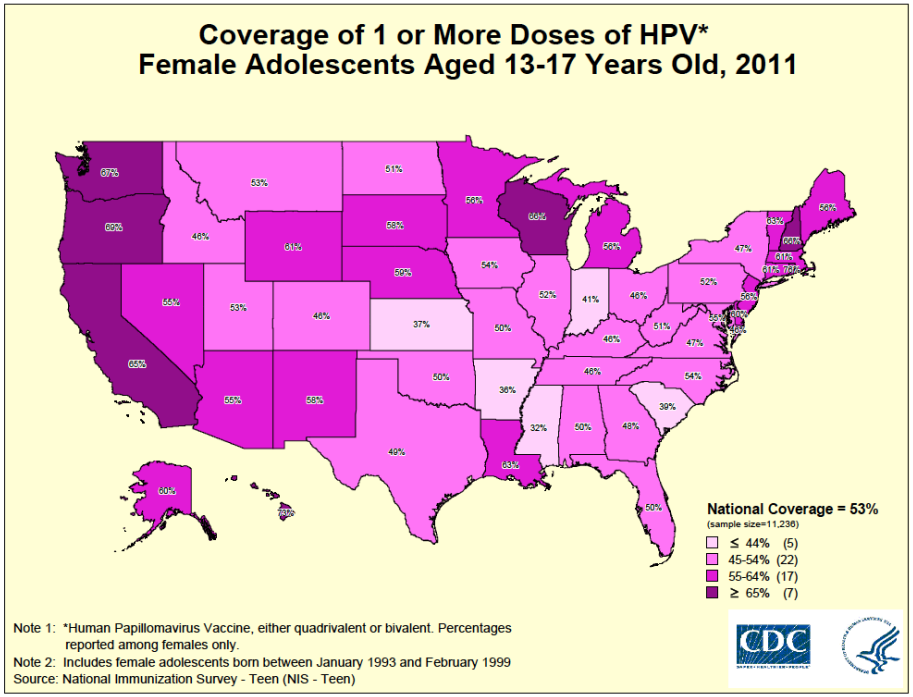
† HPV vaccination recommendations were published in March 2007.

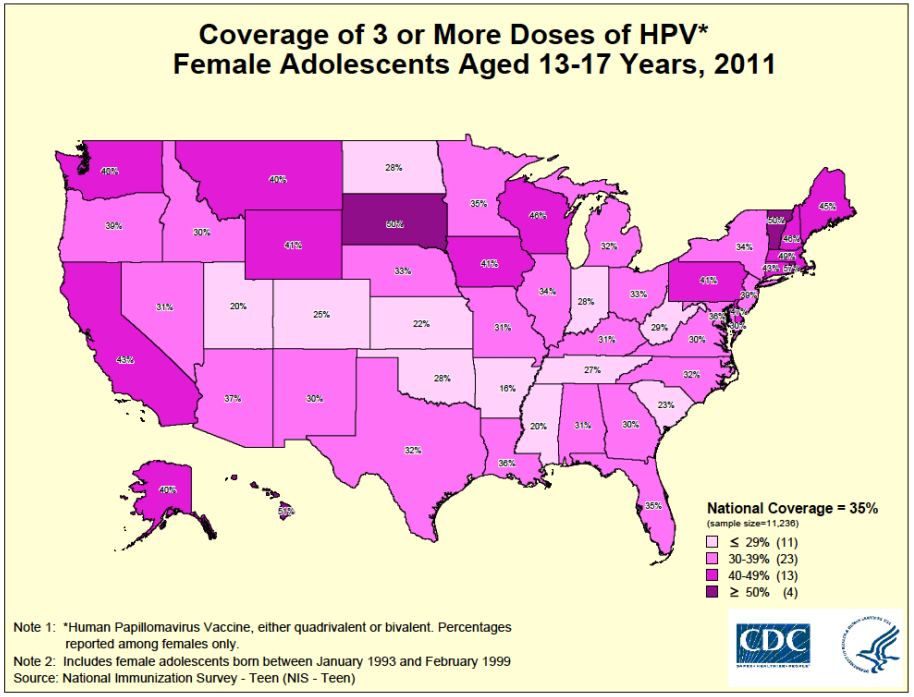
USA: 2011 HPV and Meningococcal Vaccination Rates for 13-17 year olds

	HPV vaccine 1 dose or more only girls	Meningococcal vaccine 1 dose or more
United States	53%	70%
Below poverty	62% (boys:14%)	69%
Above poverty	50% (boys: 7%)	71%
Hispanics	65%	75%
Blacks	56%	72%
Whites	48%	68%

From MMWR August 31, 2012

HPV vaccine uptake: 2011

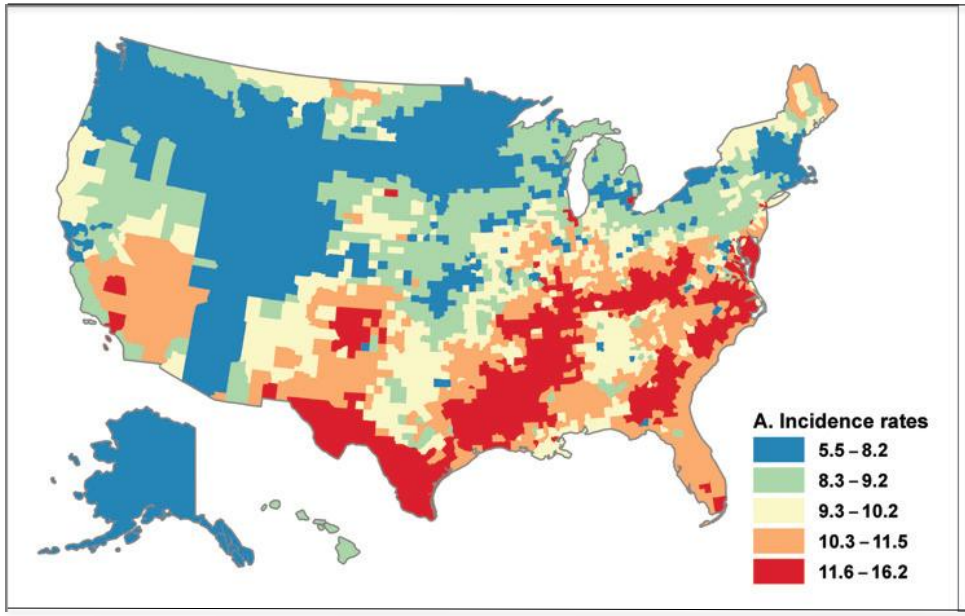




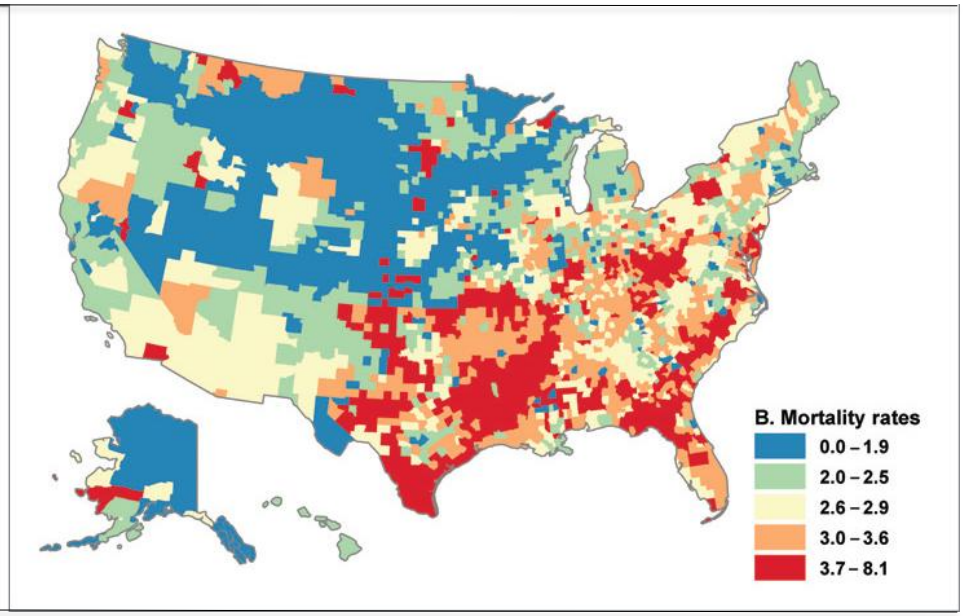
- Vaccination uptake rates vary widely among states: from 32% to 76% for 1 dose, from 16% to 57% for 3 doses

USA: Wide Regional Differences in Cervical Cancer Incidence and Mortality Rates

Incidence Rates



Mortality Rates

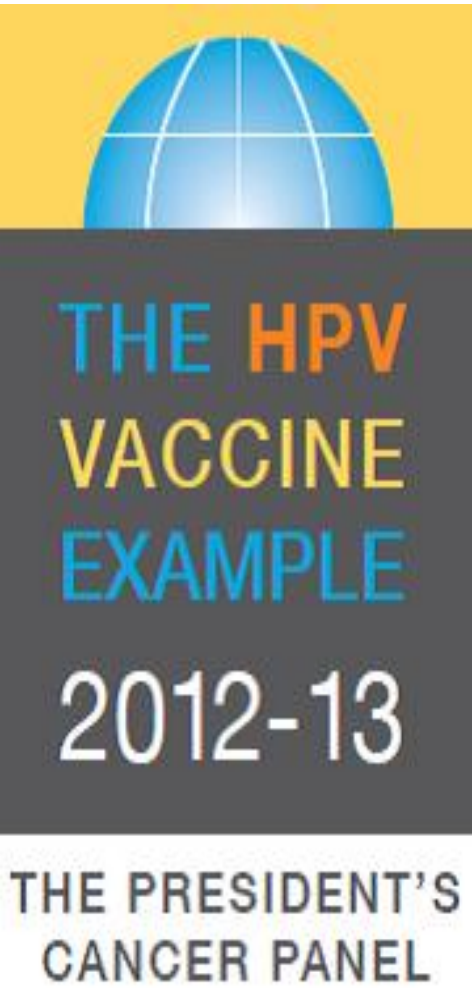


Horner et al, Cancer Epidemiol Biomarkers Prev 20: 591-9, 2011

Suggested Reading

- Jemal et al, Annual Report to the Nation on the Status of Cancer, 1975–2009, Featuring the Burden and Trends in Human Papillomavirus (HPV)–Associated Cancers and HPV. J Natl Cancer Inst ePub Jan 7, 2013; print Feb, 2013
- Siegel et al, Cancer Statistics 2013. Ca Cancer J Clin 63: 11-30, 2013
- Moscicki et al, Updating the natural history of human papillomavirus and anogenital cancers. Vaccine Suppl 5: F24-33, 2012
- Zandberg et al, The role of human papillomavirus in nongenital cancers. Ca Cancer J Clin 63: 57-81, 2013

Thank you!



PRESIDENT'S CANCER PANEL UPDATE

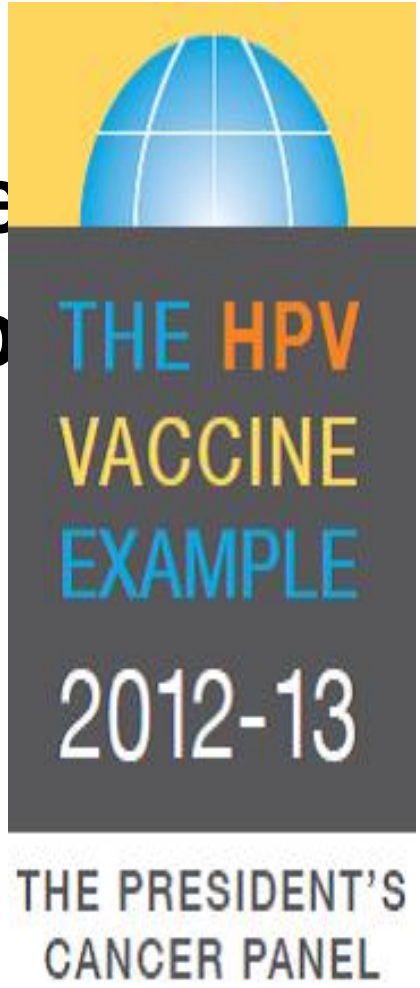
NATIONAL CANCER ADVISORY BOARD MEETING

2/8/2013

Barbara K. Rimer, DrPH

Overview

- Update: HPV Vaccine Serie
- Release of 2010-2011 repo



PCP Mission

- **The Panel shall monitor the development and execution of the activities of the National Cancer Program, and shall report directly to the President.**
- **Any delays or blockages in rapid execution of the Program shall immediately be brought to the attention of the President.**

Authority: 42 U.S.C. 285a-4; Sec. 415 of the Public Service Act, as amended.

PCP Members

- **Barbara K. Rimer, DrPH,** *Univ. of North Carolina at Chapel Hill (Chair)*
- **Owen N. Witte, MD,** *University of California Los Angeles (Member)*
- **Hill Harper, JD,** *Cancer Survivor, Actor and Best-Selling Author, Los Angeles, CA (Member)*


HILL HARPER

Accelerating Progress in Cancer Prevention: The HPV Vaccine Example

Four Workshops *(3/4 completed)*

1. **HPV Vaccination as a Model for Cancer Prevention**
2. **Achieving Widespread HPV Vaccine Uptake**
3. **Creating an Integrated HPV Vaccination and Screening Program**
4. **Challenges of Global HPV Vaccination**

HPV Vaccination as a Model for Cancer Prevention (San Francisco, 7/2012)

Workshop Co-Chairs

- **Doug Lowy, MD** *(NCI)*
- **Cosette Wheeler, PhD** *(University of New Mexico)*

HPV Vaccination as a Model for Cancer Prevention

Workshop Focus

- Fundamental science and efficacy of HPV vaccines
- Global distribution of HPV-related cancers—surveillance and epidemiology
- High priority populations for vaccination
- Next-generation vaccines

HPV Vaccination as a Model for Cancer Prevention

Key Points

- **Increasing HPV vaccine uptake, especially among males, should be a high priority.**
- **Data from ongoing studies on the efficacy/duration of protection from <3 vaccine doses may influence changes in vaccination recommendations and policies** *(e.g., number of doses required).*

HPV Vaccination as a Model for Cancer Prevention

Key Points

- **Research is needed to define natural history of oropharyngeal HPV infections.**
- **Validated screening methods should be developed for non-cervical** *(e.g. oral)* **HPV-associated cancers**
- **High quality data systems are essential to support vaccine monitoring and surveillance.**

Achieving Widespread HPV Vaccine Uptake (Washington, DC, 9/2012)

Workshop Co-Chairs

- **Noel Brewer, PhD** *(Gillings School of Global Public Health at UNC)*
- **Robert Croyle, PhD** *(NCI, Div. of Cancer Control and Population Sciences)*

Achieving Widespread HPV Vaccine Uptake

Workshop Focus

- Barriers and behavioral factors influencing uptake
- Programmatic approaches, including policies, to increase vaccine uptake and dissemination
- Financing, development, and implementation of large-scale HPV vaccine efforts
- Lessons from countries with high vaccine

Achieving Widespread HPV Vaccine Uptake

Key Points

- **Major opportunity to increase vaccine uptake and realize goal of cancer prevention**
- **Endorse Healthy People 2020 HPV goals; encourage adding male vaccination goal.**
- **HPV vaccine is an anticancer vaccine that prevents several forms of cancer; most effective when given to adolescent males**

Achieving Widespread HPV Vaccine Uptake

Key Points: Health Providers

- **Educate physicians/providers about cancer prevention benefits and efficacy of HPV vaccine.**
- **Efforts are needed to overcome vaccine hesitancy.**
- **Vaccine uptake could be improved by allowing pharmacists (and other providers?) to administer booster**

Achieving Widespread HPV Vaccine Uptake

Key Points

- **Consider HPV vaccination as part of broader adolescent health platform.**
- **Give special attention to increasing vaccination rates in areas with low uptake.**
- **Monitoring and surveillance depend upon EHRs and vaccine registries, integrated with reminder systems, and linked to**

Creating an Integrated HPV Vaccination and Screening Program (Chicago, 11/2012)

Workshop Co-Chairs

- **Marcus Plescia, MD, MPH** *(CDC)*
- **Tamera Coyne-Beasley, MD, MPH** *(UNC-Chapel Hill; ACIP)*
- **Mona Saraiya, MD, MPH** *(CDC)*

Creating an Integrated HPV Vaccination and Screening Program

Workshop Focus

- **Potential population health and economic impacts of widespread HPV vaccination—esp. on cervical cancer screening**
- **Tools and resources to support integrated approaches to HPV vaccination and screening, e.g., EHRs, linked vaccine and cancer registries**
- **Health professionals authorized to**

Creating an Integrated HPV Vaccination and Screening Program

Key Points

- **Widespread uptake of HPV vaccines will shift balance of screening risks and benefits—may enable reductions in screening *(initiation & interval)* and provide rationale for primary HPV testing.**

- **Physicians need tools to facilitate adherence to guidelines and communication with patients about evidence-based screening practices in the HPV era.**

Creating an Integrated HPV Vaccination and Screening Program

Key Points

- **Effective consumer education/information campaign, using social media and other strategies, is needed.**
- **Electronic health records and vaccine registries linked to cancer registries are critical for monitoring, surveillance and evaluating impact of HPV vaccination.**

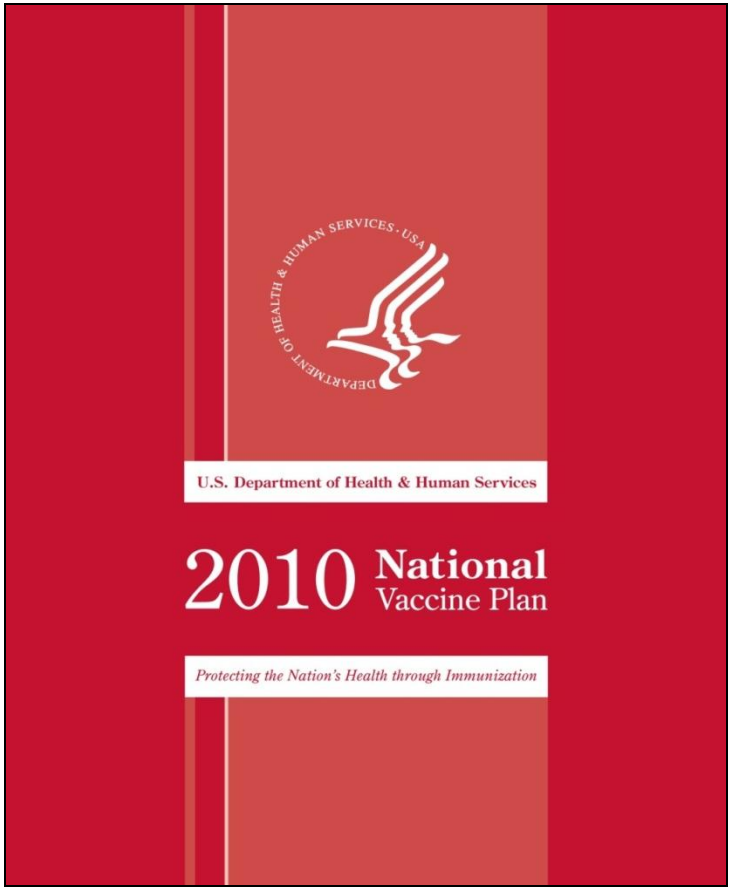
New Cervical Cancer Screening Guidelines (ACS, 2012; USPSTF, 2012)

- **Cervical cancer screening should begin at age 21.**
- **Women aged 21-29 should have Pap tests every 3 years**. HPV testing should *not* be used in this age group unless needed after an abnormal Pap test result.
- **Women aged 30-65 should have Pap tests + HPV tests ("co-testing") every 5 years.** It is also OK to have Pap tests alone every 3 years. (**ACS)**
- **USPSTF: Women aged 21-65 should have Pap smears every 3 years or, for women aged 30-65, option of Pap tests and HPV testing every 5**

New Cervical Cancer Screening Guidelines (ACS, 2012)

- **Women over age 65 who've had regular cervical cancer testing with normal results should *not* be tested.**
- **A woman who had her uterus removed (also cervix)** for reasons not related to cervical cancer and who has no history of cervical cancer or serious pre-cancer **should *not* be tested.**
- **A woman who has been vaccinated against HPV should still follow the screening recommendations for her age group.**

DHHS 2010 National Vaccine Plan



1. **Develop new and improved vaccines.**
2. **Enhance the vaccine safety system.**
3. **Support communications to enhance informed vaccine decision-making.**
4. **Ensure a stable supply of recommended vaccines and achieve better use of existing vaccines to prevent disease, disability and death in the United States.**

http://www.hhs.gov/nvpo/vacc_plan/

Slide from Bruce Gellin, Deputy Asst Sec for

Challenges of Global HPV Vaccination (Miami, 4/23 - 24, 2013)

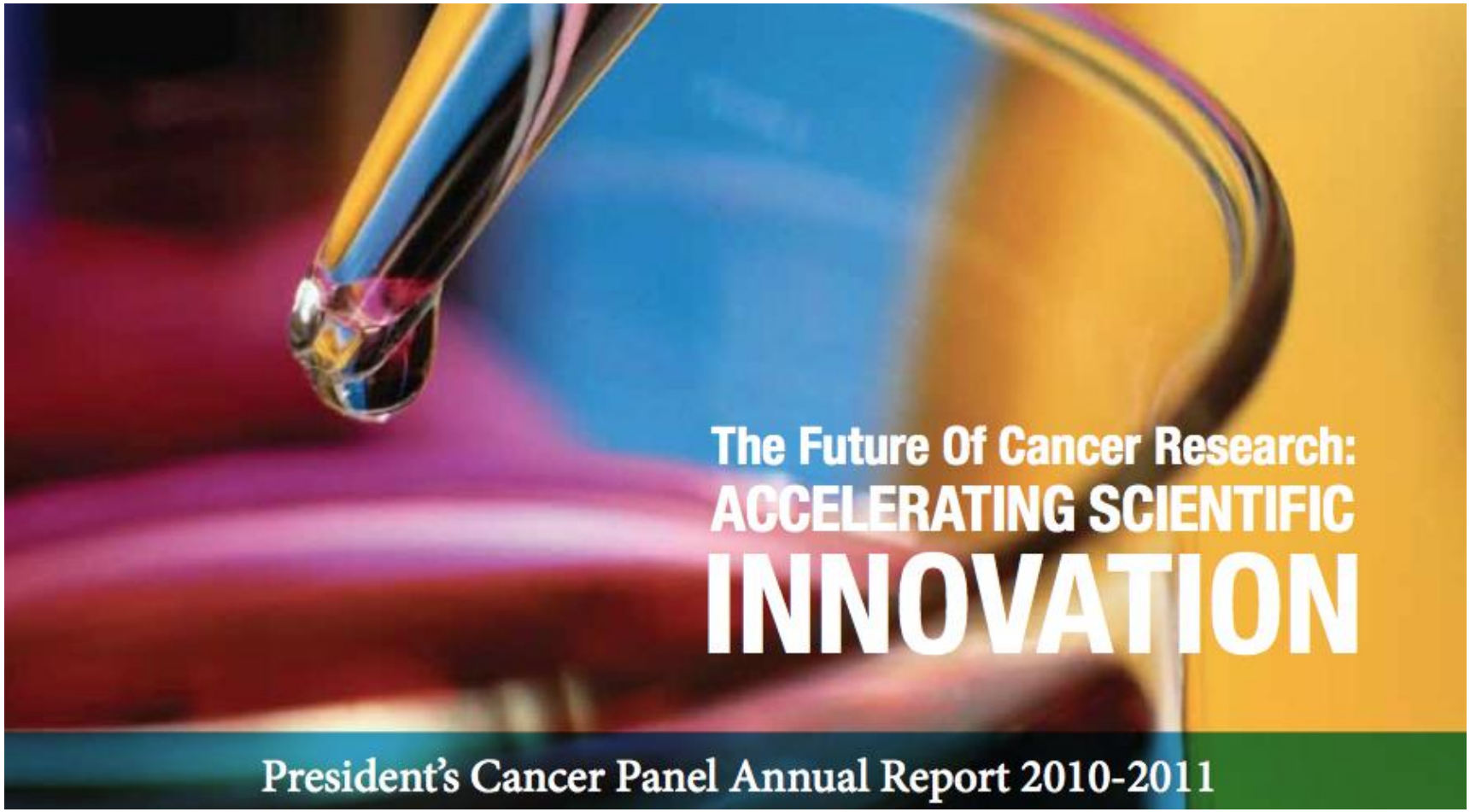
Workshop Co-Chairs

- Anne Schuchat, MD (CDC)
- Ted Trimble, MD, MPH (NCI)
- Funmi Olopade, MD, FACP (University of Chicago)

Workshop Focus

- Global epidemiology of HPV infection and HPV vaccination coverage
- Global HPV vaccine policy and financing
- Global vaccine program development,

Report of the Previous Panel



The Future of Cancer Research: Accelerating Scientific Innovation

- **Final report of the previous Panel**
- **Full report will be available at http://pcp.cancer.gov**

Contact Information:

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Bethesda, MD 20892

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BMI and Mortality: Do conflicting results alter interpretation of BMI and cancer outcomes research?

Rachel Ballard-Barbash, MD, MPH

Applied Research Program (ARP)
Division of Cancer Control and Population Sciences (DCCPS)
National Cancer Institute (NCI)

NCI NCAB

February 2013

Outline/Purpose

- Overview of BMI and cancer outcomes
  - Incidence and Mortality in Cancer Patients
- Overview results in two papers on BMI and all cause mortality that were asking very different questions and used different methods
  - Flegal et al, JAMA 2013
  - Berrington et al NEJM 2010
- Discuss how question being addressed and methods influence interpretation and implications of results
- Global Burden of Disease 2010 - increased contribution of morbidity to disease burden
- If time – highlights of research on physical activity and mortality

Obesity and Cancer Risk
Bulk of Evidence is on Cancer Incidence

Type of cancer	Relative risk[a] with BMI of 25–30 kg/m²	Relative risk[a] with BMI of ≥30 kg/m²
Colorectal (men)	1.5	2.0
Colorectal (women)	1.2	1.5
Female breast (post-menopausal)	1.3	1.5
Endometrial	2.0	3.5
Kidney (renal cell)	1.5	2.5
Esophageal (adeno-carcinoma)	2.0	3.0
Pancreatic	1.3	1.7
Liver	ND	1.5–4.0
Gallbladder	1.5	2.0
Gastric cardia (adeno-carcinoma)	1.5	2.0

Fair AM, Montgomery K. Methods Mol Biol. 2009;472:57-88.

Cancer Incidence (I) and Mortality (M) Rates Between Bariatric Surgical and Nonsurgical Obese Groups

Men

Author	N	Surgical Obese Cancer Rate	Nonsurgical Obese Cancer Rate	Reduction in Cancer RR
Adams, 2009	942	I = 4.14% M = 1.06%	I = 4.14% M = 1.53%	I = No change M = 30%
McCawley, 2009	Effect on Cancer Outcomes Not Reported			
Sjostrom, 2009	590	I = 6.4%	I = 6.6%	I = 3%

Women

Author	N	Surgical Obese Cancer Rate	Nonsurgical Obese Cancer Rate	Reduction in Cancer RR
Adams, 2009	5654	I = 3.8% M = 0.55%	I = 5.23% M = 1.05%	I = 27.3% ($p<0.05$) M = 47.6% ($p<0.05$)
McCawley, 2009	1482	I = 3.6%	I = 5.8%	I = 38% ($p<0.05$)
Sjostrom, 2009	1447	I = 5.56%	I = 8.98%	I = 38% ($p<0.05$)

Ashrafian et al, Cancer 2011

Obesity and Survival in Breast Cancer Patients

Meta-Analysis

43 studies published 1963-2005 • comparison of obese vs. non-obese subjects

Subgroup	No. of estimates	Pooled HR (95% CI)		P-value
Survival measure				
All-cause	36	**1.33 (1.21-1.47)**		0.91
Breast cancer specific	19	**1.33 (1.19-1.50)**		
Obesity measure				
BMI	55	**1.33 (1.23-1.44)**		0.95
WHR	6	**1.31 (1.14-1.50)**		
Study design				
Observational cohort	48	**1.36 (1.23-1.49)**		0.53
Treatment cohort	7	**1.22 (1.14-1.31)**		
Menopausal status				
Pre-menopausal	16	**1.47 (1.19-1.83)**		0.25
Post-menopausal	12	**1.22 (0.95-1.57)**		
Both	36	**1.33 (1.23-1.43)**		
Year of diagnosis				
Pre-1995	30	**1.31 (1.16-1.46)**		0.17
Post-1995	11	**1.49 (1.31-1.68)**		

Protani M et al. BCRT 2010: 123:627-635

BMI and Quality of Dosing for Breast Cancer Adjuvant Chemotherapy

Table 4. Multivariate Analysis of Initial Chemotherapy Dose < 85% of Standard (N = 737)

Characteristic	Odds Ratio	95% CI		*P*
Age, years	1.01	0.98 to 1.05	.49	
CCI ≥ 1	1.16	0.60 to 2.25	.67	
BMI				
Normal	1.00			
Overweight	1.18	0.74 to 1.87	.65	**.0004**
Obese	**2.47**	**1.36 to 4.51**	**.003**	
Severely obese	**4.04**	**1.46 to 11.19**	**.007**	
Median household income, $ (in thousands)	1.02	0.85 to 1.22	.81	
Education less than high school	**3.07**	**1.57 to 5.99**	**.001**	
Non-white race	1.30	0.49 to 3.47	.60	
Region				
Northeast	1.00			
Central	1.67	0.43 to 6.44	.46	**< .0001**
West coast	0.90	0.26 to 3.18	.87	
South	**5.58**	**2.20 to 14.14**	**.0003**	

Griggs JJ, et al. JCO 2007; 25:3

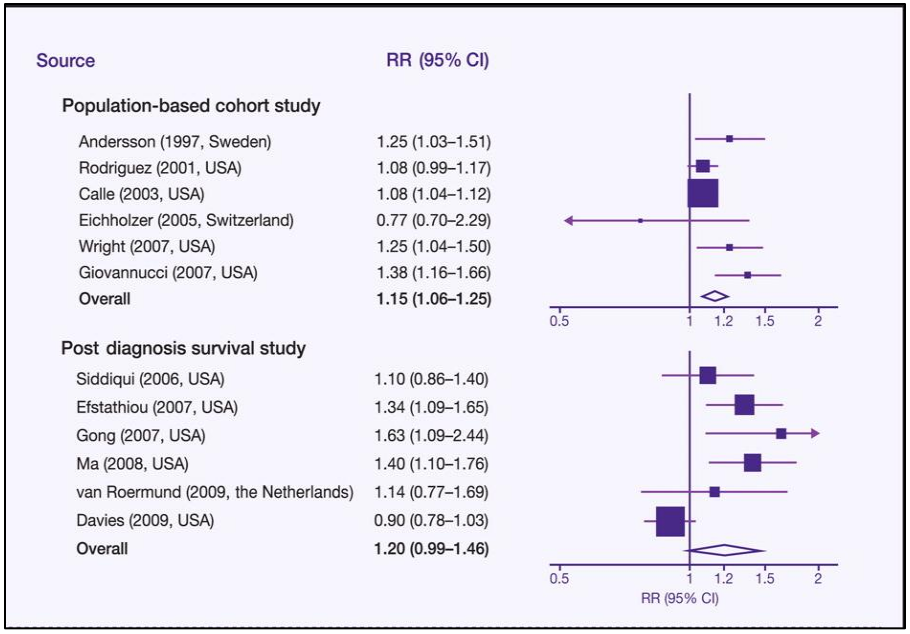
BMI and Colorectal Cancer Outcomes

Author	Stage	HR or P
Tartter 1984	Colon – B1, C1, C2 (n=279)	Recurrence: p=0.03 (weight > vs. < median)
Meyerhardt 2003	Colon – B2, B3, C (n=3759)	DFS: HR 1.11 (0.94-1.30) OS: HR 1.11 (0.96-1.29) (BMI kg/m^2 ≥ 30 vs. < 30 kg/m^2)
Meyerhardt 2004	Rectal – I, II (n=1792)	DFS: HR 1.10 (0.91-1.32) OS: HR 1.09 (0.90-1.33) Local: HR 1.31 (0.91-1.88) (BMI kg/m^2 ≥ 30 vs. < 30 kg/m^2)
Dignam 2006	Colon – B, C (n=4288)	DFS: HR 1.27 (1.05-1.53) Events: HR 1.38 (1.10-1.73) (BMI ≥ 35 kg/m^2 vs. < 30 kg/m^2)
Meyerhardt 2008	Colon – III (n=1053)	DFS: HR 1.24 (0.83-1.83) RFS: HR 1.27 (0.85-1.89) OS: HR 0.87 (0.54-1.42) (BMI ≥ 35 kg/m^2 vs. < 30 kg/m^2)

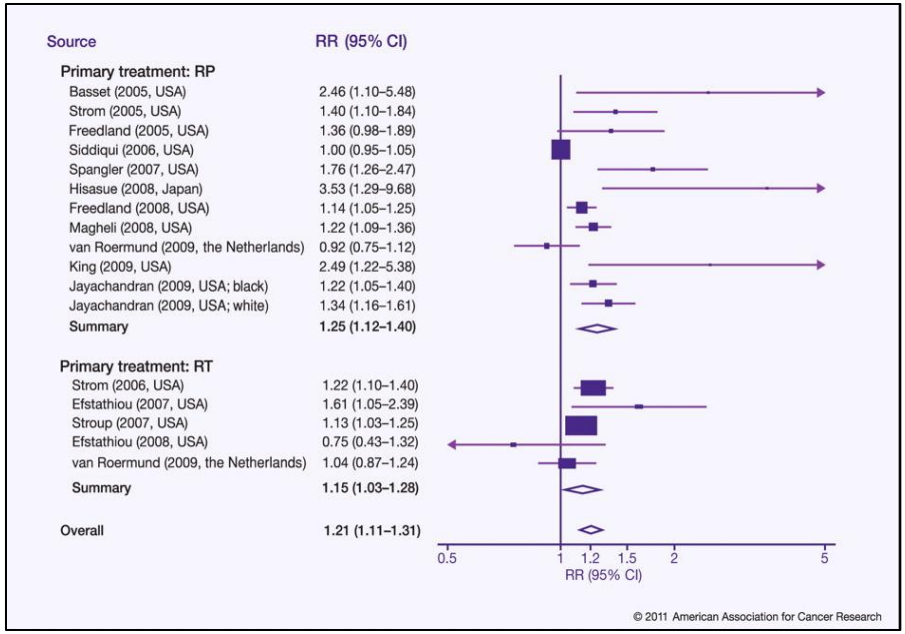
Meyerhardt JA, J Clin Oncol;2010;28:4066-4073

BMI and Prostate Cancer Specific Mortality

RRs per 5 kg/m^2 increase in BMI and prostate cancer–specific mortality



RRs per 5 kg/m^2 increase in BMI and biochemical recurrence after treatment

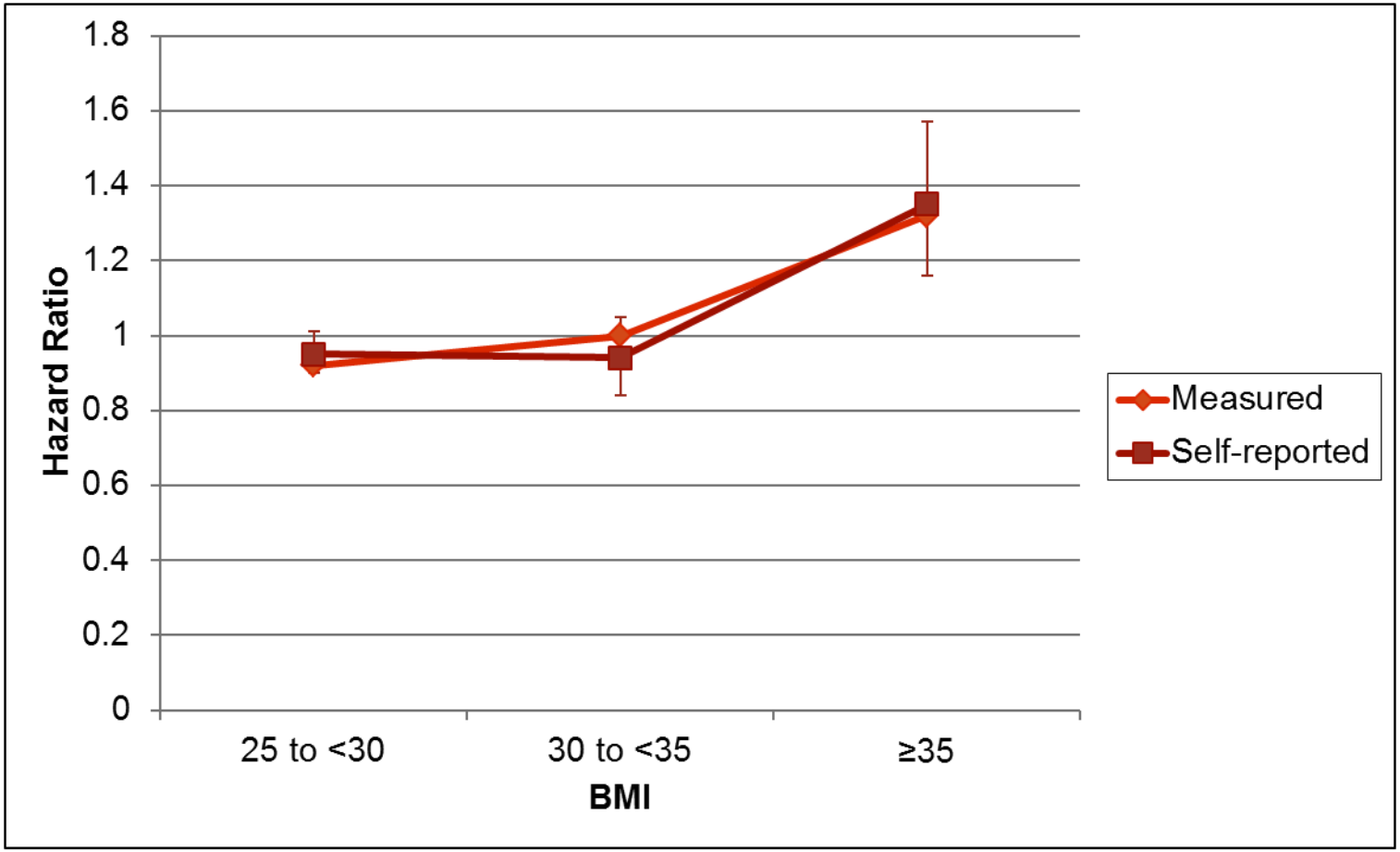


Cao Y, Ma J, Cancer Prev Res;2011;4:486-501

Two Studies
Different Questions, Methods and Results

- Flegal et al JAMA 2013: All-Cause Mortality, Overweight and Obesity
  - Research Question: How are the standard BMI categories associated with mortality in published literature?
  - Methods: Meta-analysis of 97 studies with standardized measures of overweight (25 - <30), obesity (>30), grade 1 (30-<35), grade 2,3 (>35); sample of 2.88M people with 270,000 deaths
  - Included adults of all ages, and populations covered in existing studies, with FU of 5 to 42 years
  - Conclusion: Relative to normal weight (BMI <25),
    - Overall obesity (>30), and higher grade (2,3) obesity (>35) are associated with higher all-cause mortality (21% and 34% respectively)
    - Grade 1 obesity (30-<35) is not associated
    - Overweight (25-<30) is associated with modest decreased mortality (6%)

Risk of All Cause Mortality for Overweight and Obesity Relative to Normal Weight for All Ages

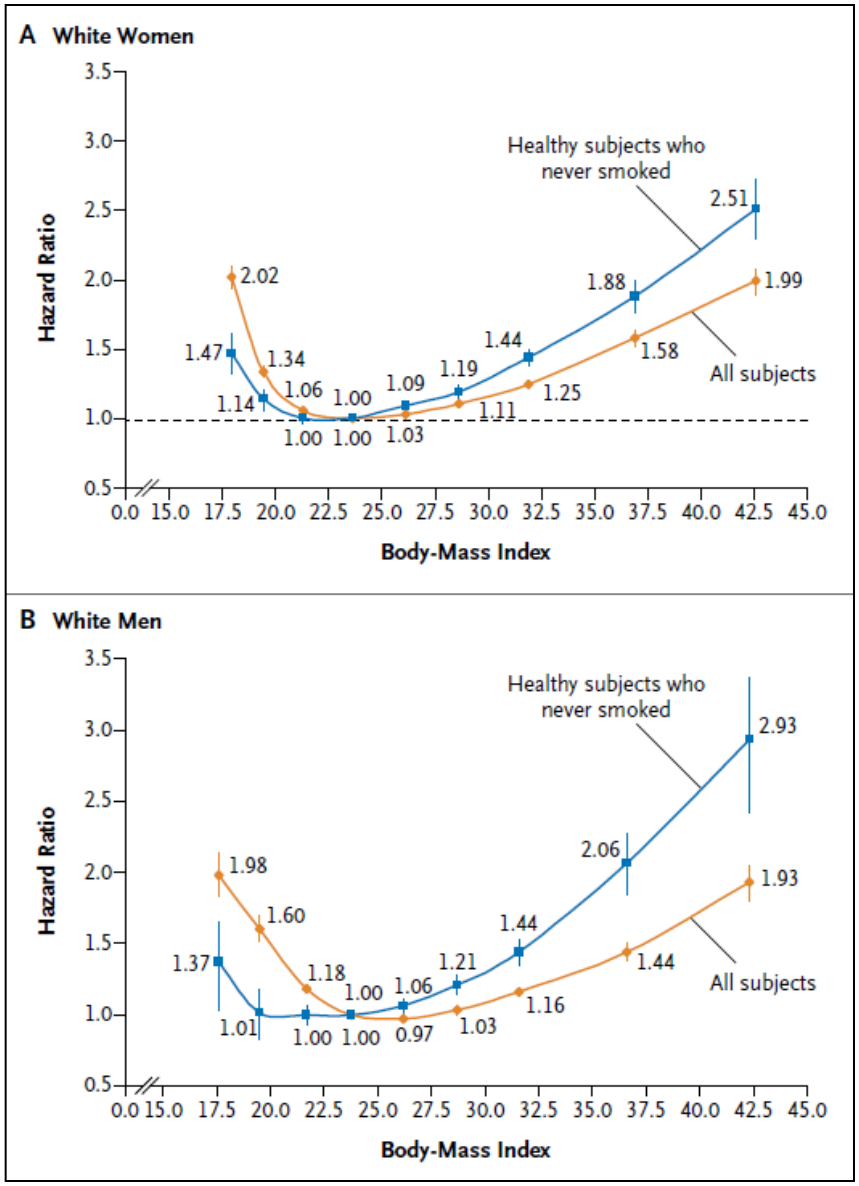


Flegal KM, et al. JAMA 2013;309:71-82

Two Studies with Different Questions, Methods and Results

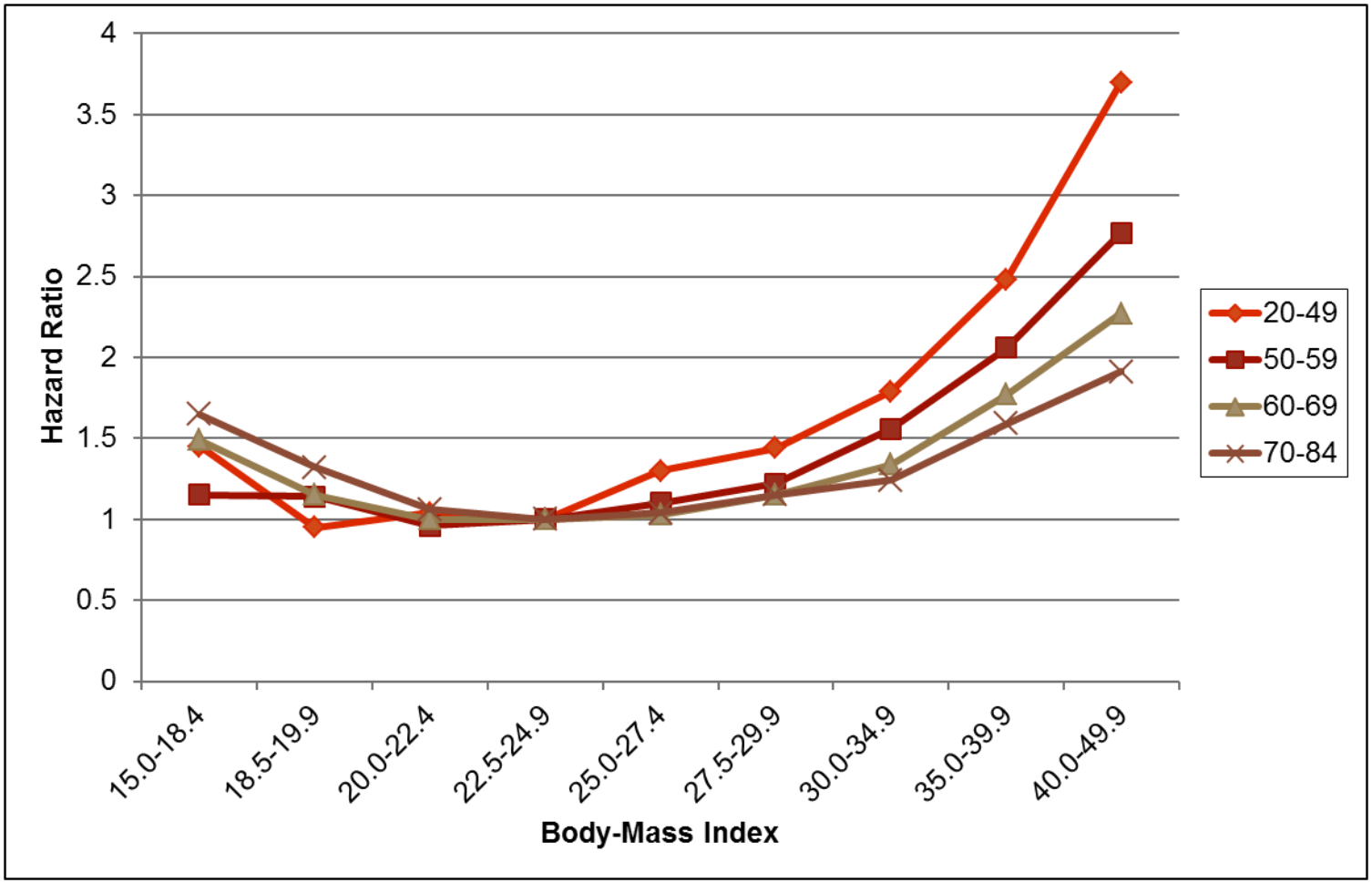
- Berrington et al, NEJM 2010: BMI and Mortality
  - Research Question: What is the independent effect of BMI on mortality in healthy non-smoking, white adults?
  - Methods: Pooled analysis of 19 studies with 1.49 M people; in examining the effect of BMI on mortality in healthy non-smokers used 560,000 health people among the 670,000 never smokers
  - Included healthy, non-smoking non-Hispanic white adults 19 to 84 years of age with BMI range of 15-49.9; studies with at least 5 yrs of FU and >1000 deaths in NHW adults, baseline year 1970
  - Conclusions:
    - In non-Hispanic white adults, overweight and obesity and underweight are associated with increased all-cause mortality.
    - All-cause mortality in healthy, non-smoking non-Hispanic white adults is lowest among the group with a BMI of 20.0-24.9

All Cause Mortality Increases with Progressively Higher and Lower BMIs



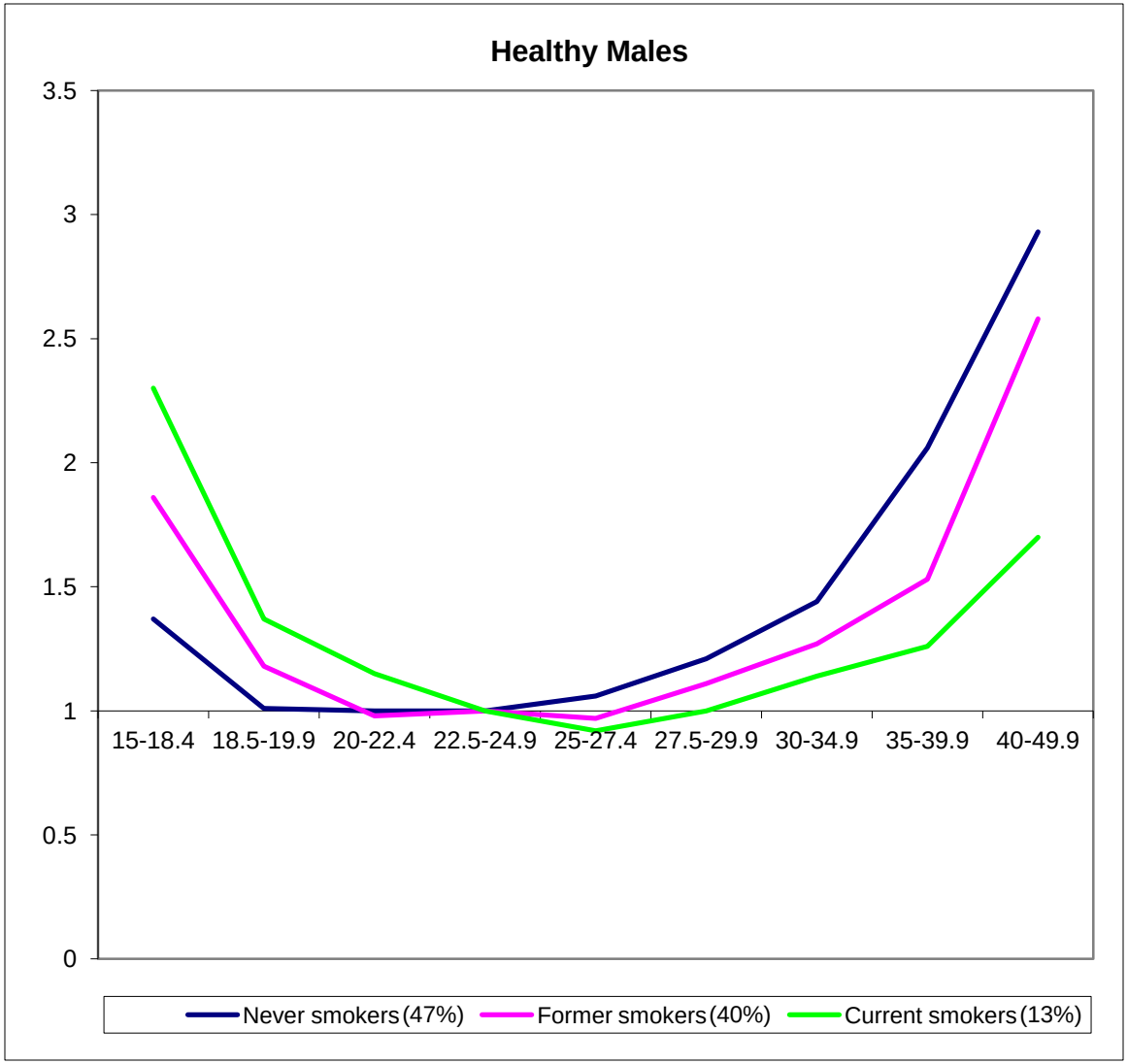
Berrington A, NEJM 2010; 363; 23: 2211-2219

BMI and Mortality Stratified by Age



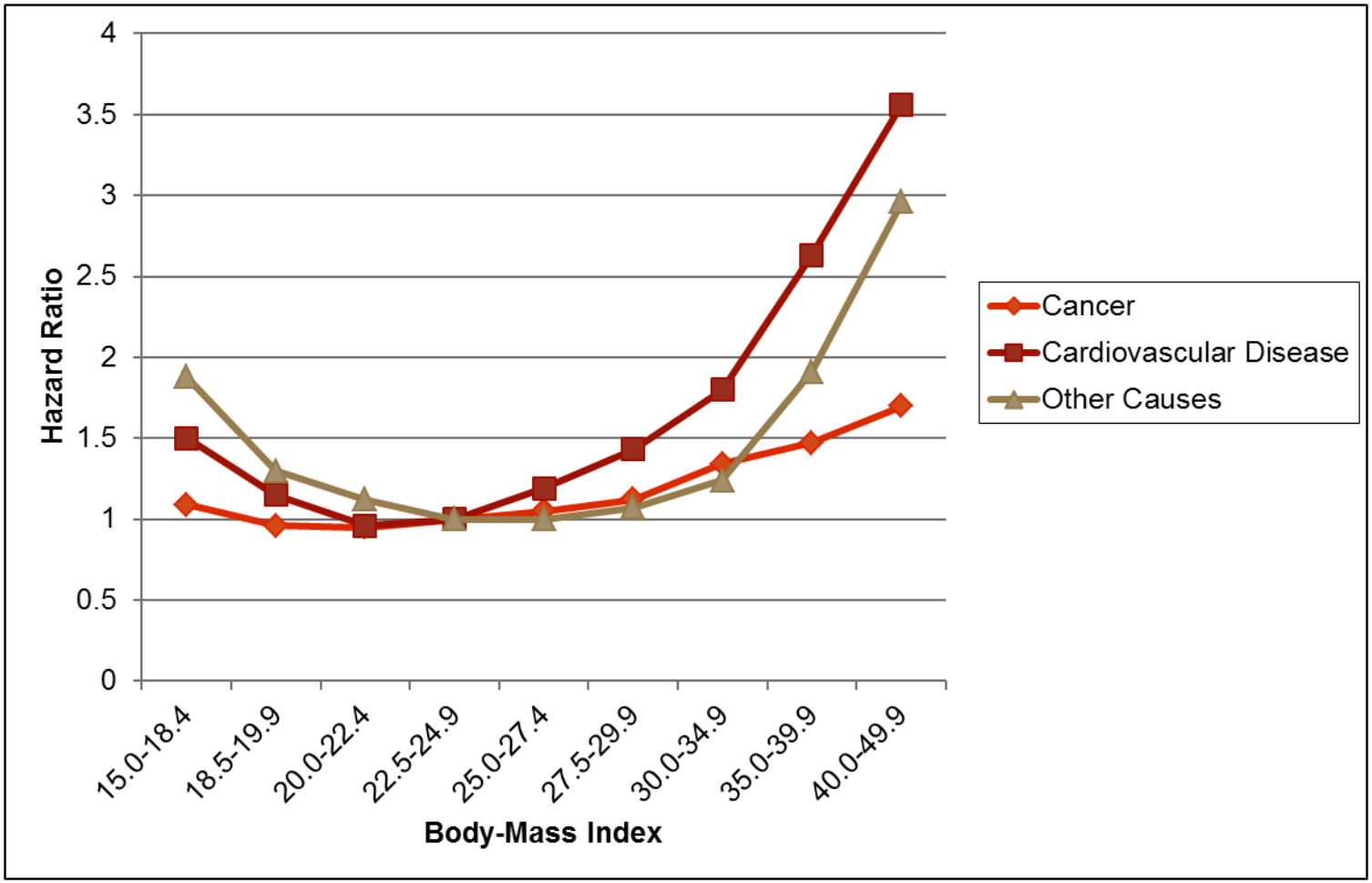
Berrington A, NEJM 2010; 363; 23: 2211-2219

BMI and Mortality by Smoking Status – Men without Cancer or CVD at Baseline



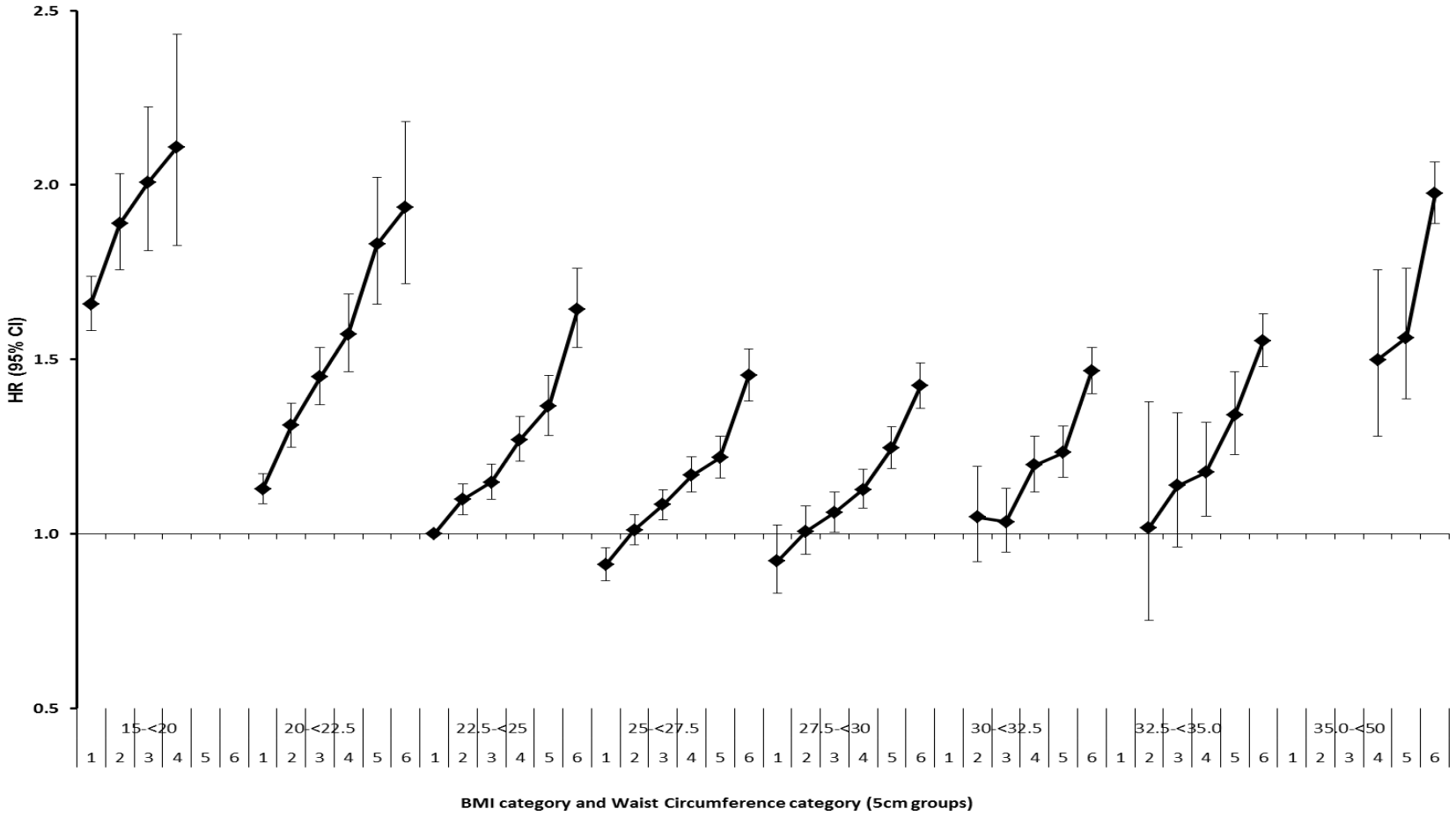
Berrington A, NEJM 2010; 363; 23: 2211-2219

BMI and Cause Specific Mortality among Healthy Never Smokers



Berrington A, NEJM 2010; 363; 23: 2211-2219

Waist Circumference and Mortality by BMI

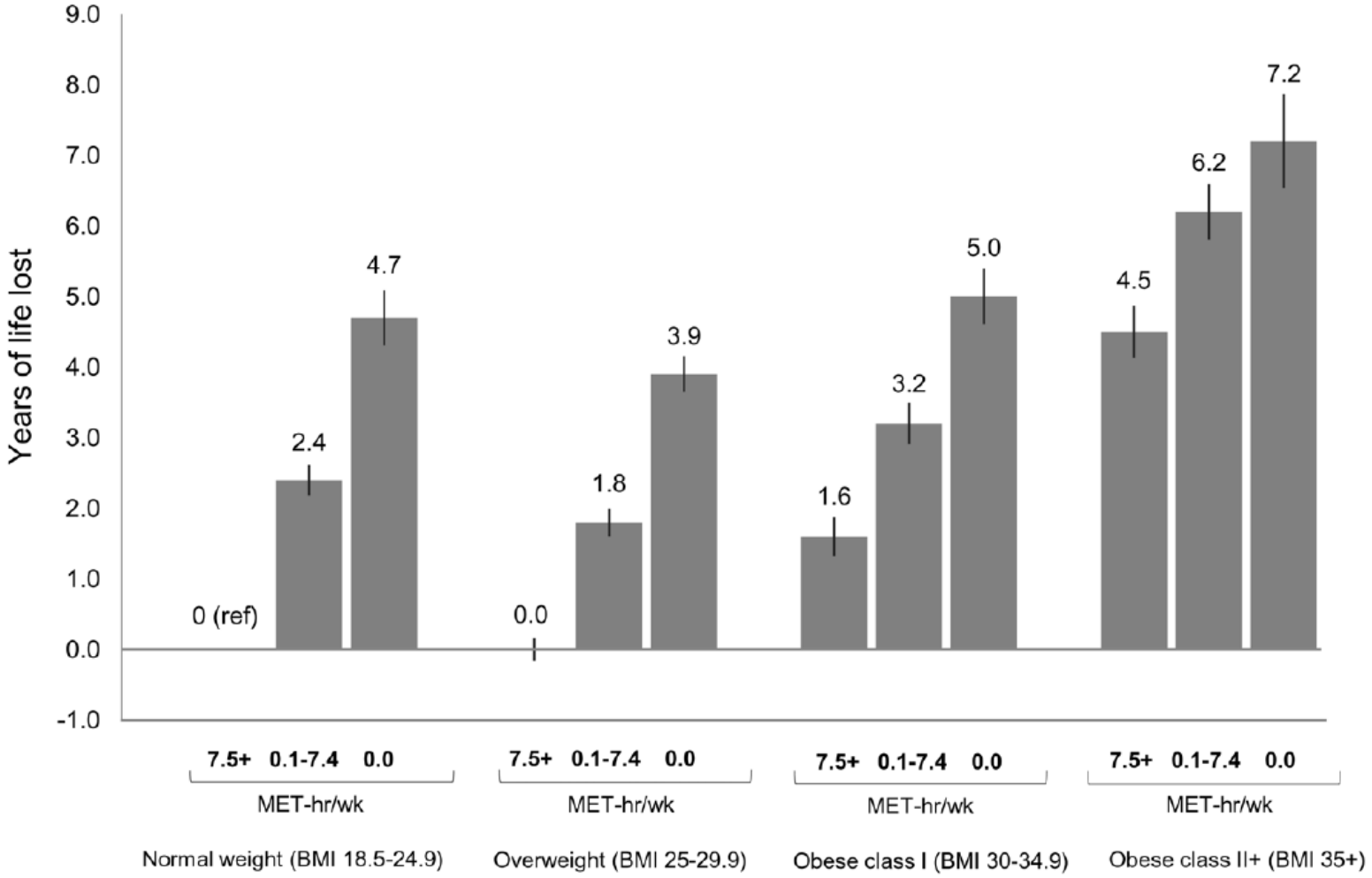


WC cutpoints (cm) for men: <90.0, 90.0-94.9, 95.0-99.9, 100.0-104.9, 105.0-109.9, 110.0+

WC cutpoints (cm) for women: <70.0, 70.0-74.9, 75.0-79.9, 80.0-84.9, 85.0-89.9, 90.0+.

Cerhan JR, et al. Submitted 2013

Years of Life Lost with Physical Inactivity across BMI Categories

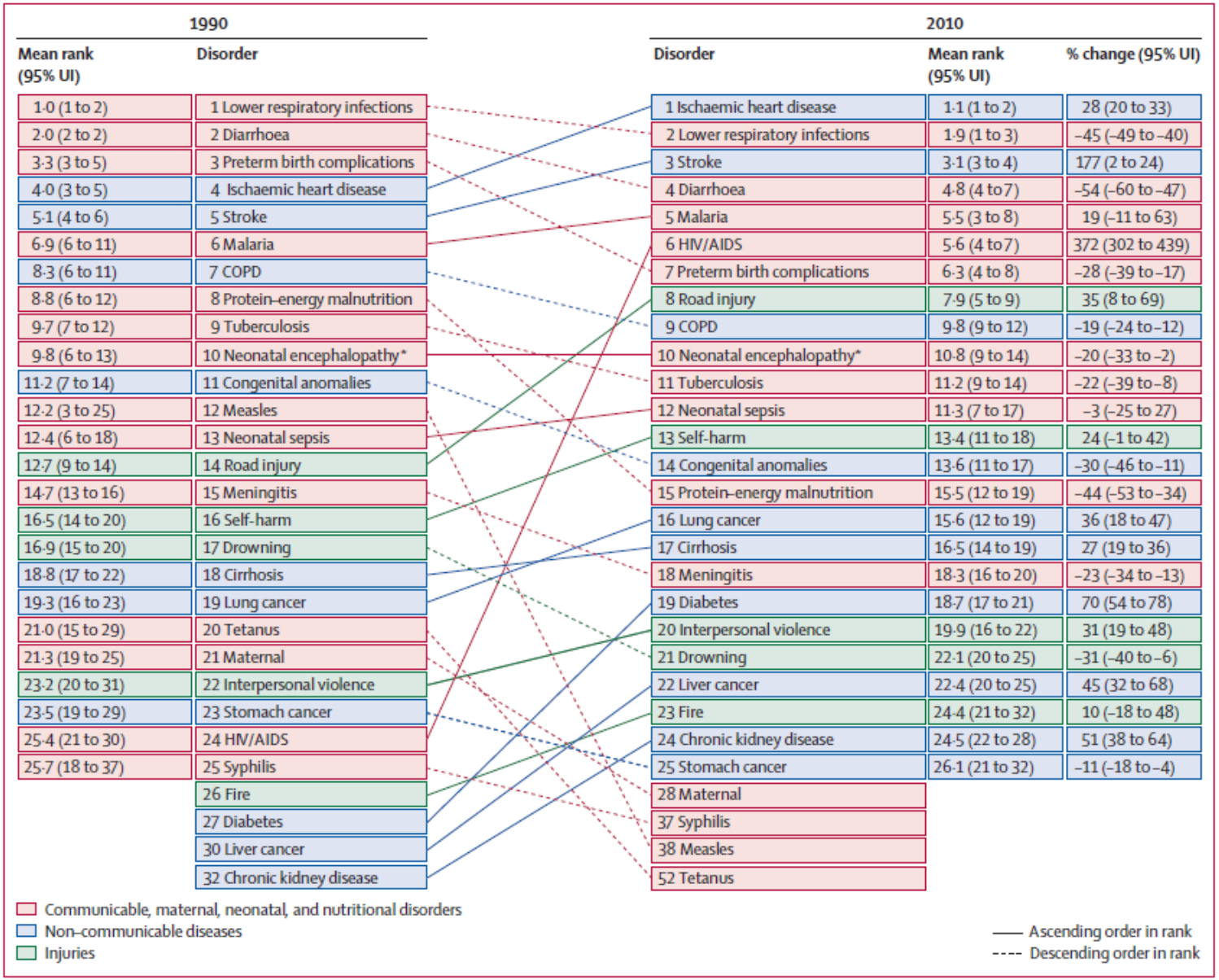


Moore SC, et al. PLoS Med 2012;9(11)

Issues in Interpretation

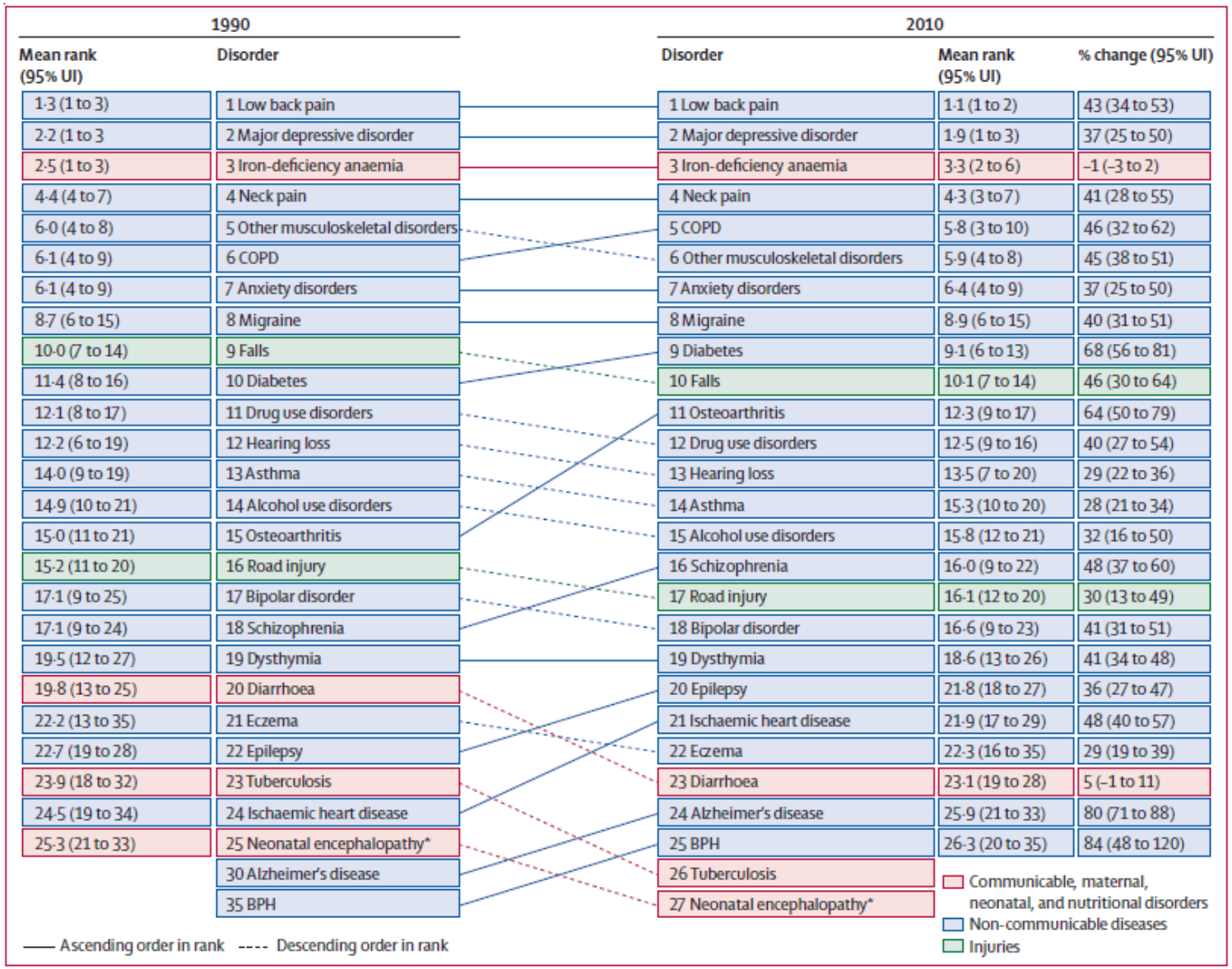
- Critical to consider the question being addressed
- BMI correlates with obesity but is not a precise measure of metabolically active fat mass
- Epidemiologic analysis of independent effect of BMI is addressed by analyses of healthy, non-smokers
  - Removes bias from two strong predictors of mortality
  - But difficult to extrapolate to other patient groups
- BMI/mortality and cause-specific mortality may differ by
  - Age at time BMI is assessed
  - Smoking status
  - Gender and racial/ethnic population mix
  - Elimination of people with comorbid disease at baseline
  - Body fat distribution
  - Other risk factors for overweight/obesity – PA, Diet, Alcohol

Global Years of Life Lost Ranks for the Top 25 Causes, 1990 and 2010



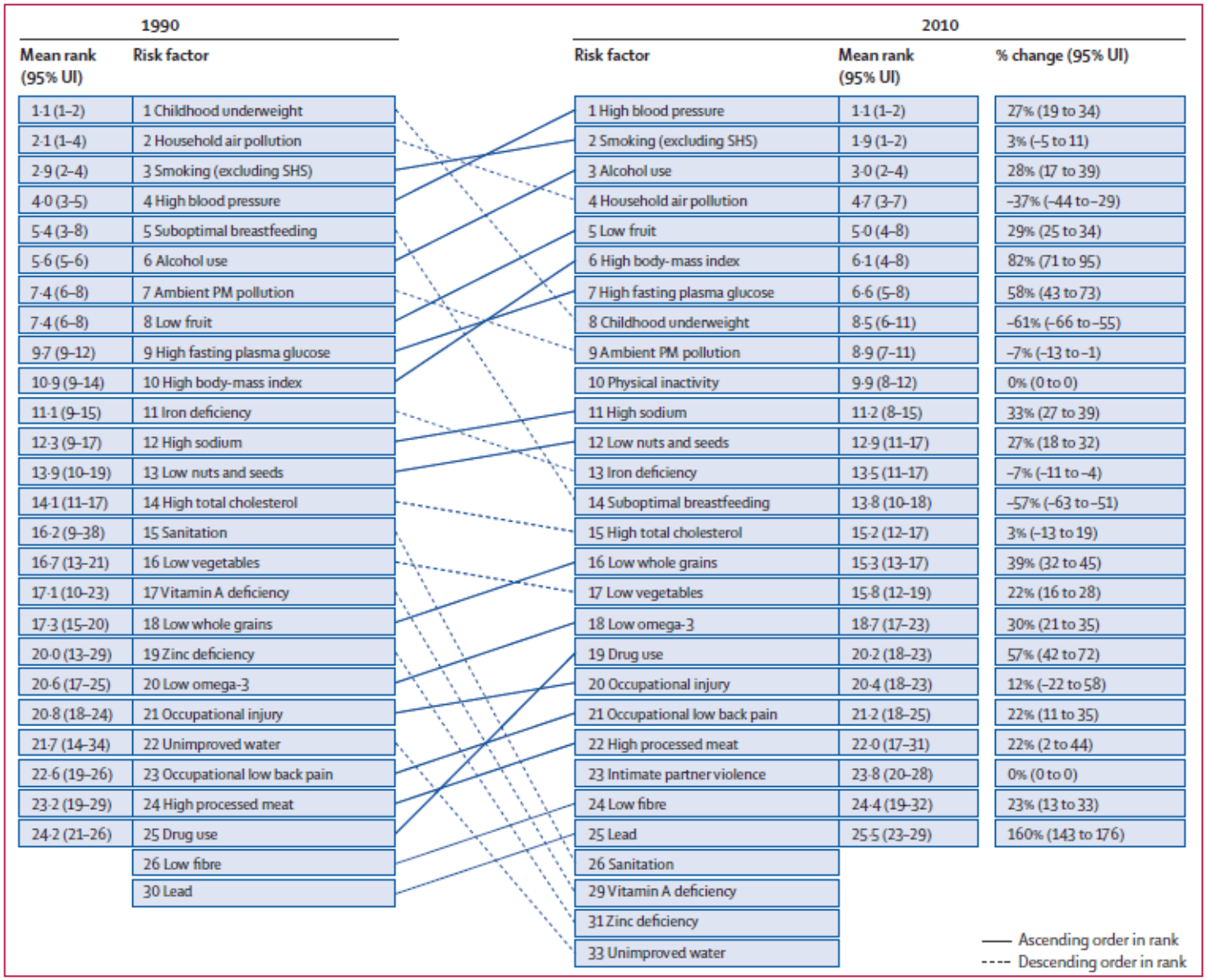
Lozano R, et al. Lancet 2012; 380: 2095-128

Global Years Lived with Disability Ranks for the 25 Most Common Causes, 1990 and 2010



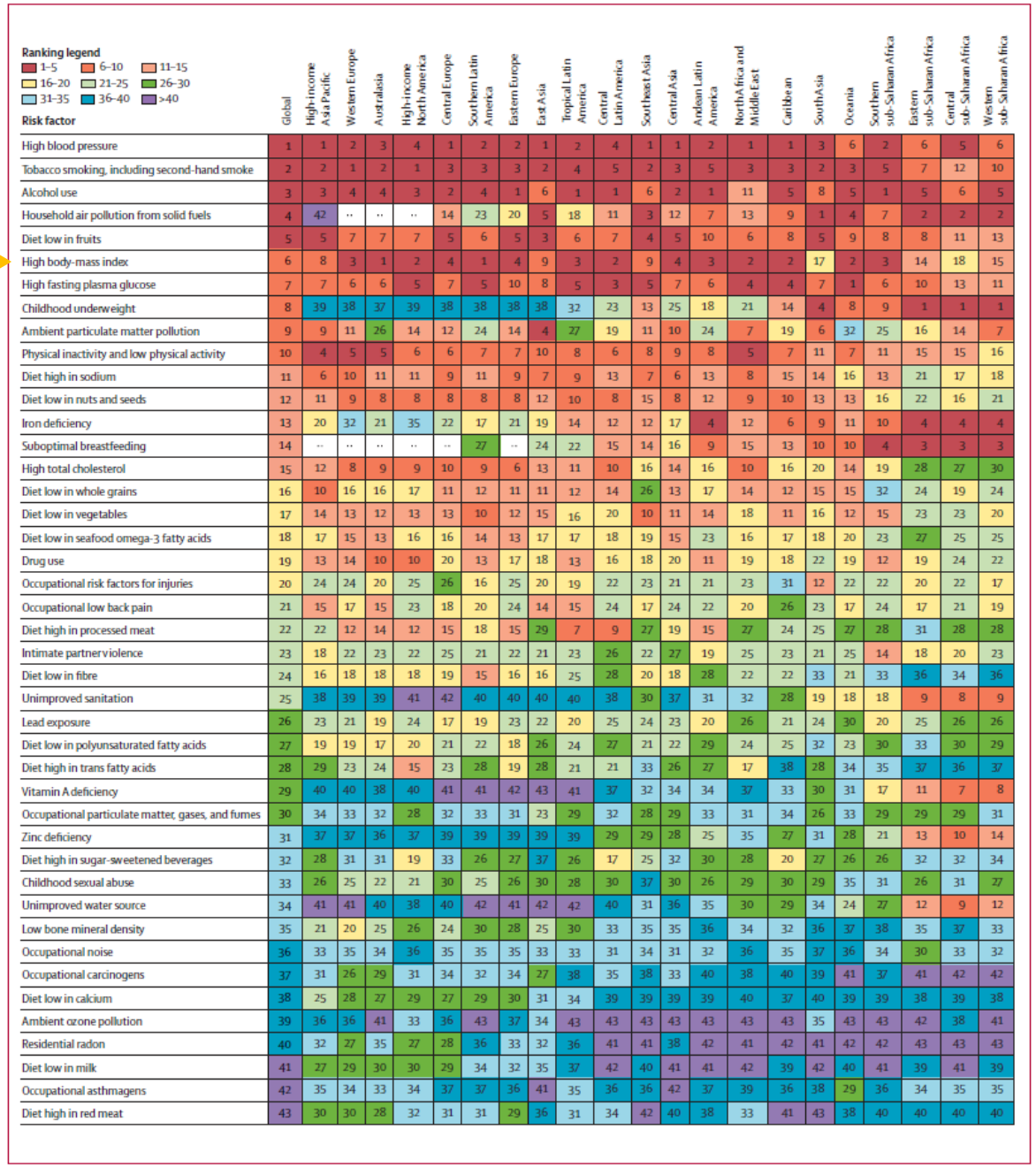
Vos T, et al. Lancet 2012; 380: 2163-96

Global Risk Factor Ranks for All Ages and Sexes Combined, 1990 and 2010



Lim SS, et al. Lancet 2012; 380: 2224-60

Risk Factors Ranked by Attributable Burden of Disease, 2010

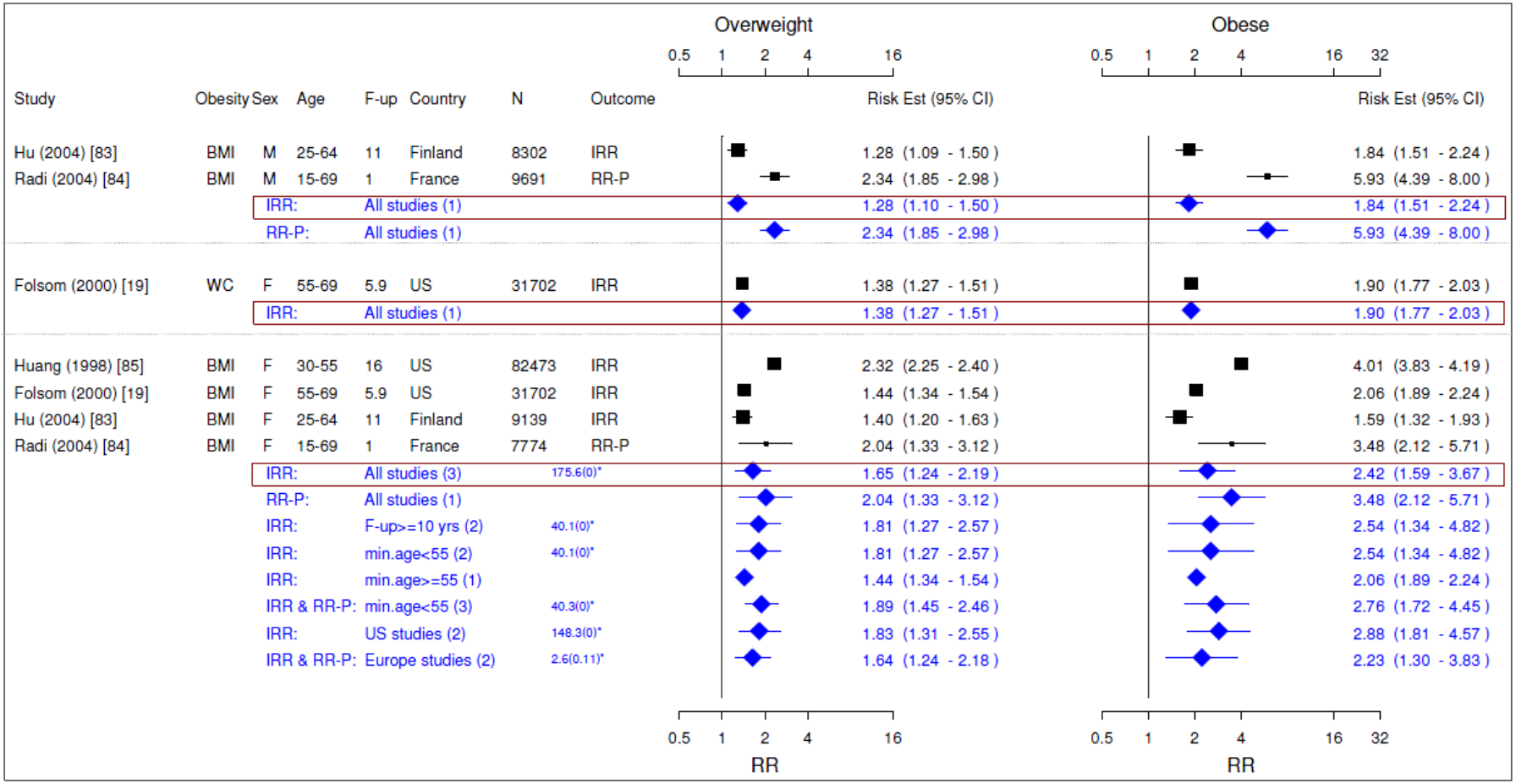


Ranking legend
1–5 | 6–10 | 11–15 | 16–20 | 21–25 | 26–30 | 31–35 | 36–40 | >40

Risk factor	Global	High-income Asia Pacific	Western Europe	Australasia	High-income North America	Central Europe	Southern Latin America	Eastern Europe	East Asia	Tropical Latin America	Central Latin America	Southeast Asia	Central Asia	Andean Latin America	North Africa and Middle East	Caribbean	South Asia	Oceania	Southern sub-Saharan Africa	Eastern sub-Saharan Africa	Central sub-Saharan Africa	Western sub-Saharan Africa
High blood pressure	1	1	2	3	4	1	2	2	1	2	4	1	1	2	1	1	3	6	2	6	5	6
Tobacco smoking, including second-hand smoke	2	2	1	2	1	3	3	3	2	4	5	2	3	5	3	3	2	3	5	7	12	10
Alcohol use	3	3	4	4	3	2	4	1	6	1	1	6	2	1	11	5	8	5	1	5	6	5
Household air pollution from solid fuels	4	42	..	..	..	14	23	20	5	18	11	3	12	7	13	9	1	4	7	2	2	2
Diet low in fruits	5	5	7	7	7	5	6	5	3	6	7	4	5	10	6	8	5	9	8	8	11	13
High body-mass index	6	8	3	1	2	4	1	4	9	3	2	9	4	3	2	2	17	2	3	14	18	15
High fasting plasma glucose	7	7	6	6	5	7	5	10	8	5	3	5	7	6	4	4	7	1	6	10	13	11
Childhood underweight	8	39	38	37	39	38	38	38	38	32	23	13	25	18	21	14	4	8	9	1	1	1
Ambient particulate matter pollution	9	9	11	26	14	12	24	14	4	27	19	11	10	24	7	19	6	32	25	16	14	7
Physical inactivity and low physical activity	10	4	5	5	6	6	7	7	10	8	6	8	9	8	5	7	11	7	11	15	15	16
Diet high in sodium	11	6	10	11	11	9	11	9	7	9	13	7	6	13	8	15	14	16	13	21	17	18
Diet low in nuts and seeds	12	11	9	8	8	8	8	8	12	10	8	15	8	12	9	10	13	13	16	22	16	21
Iron deficiency	13	20	32	21	35	22	17	21	19	14	12	12	17	4	12	6	9	11	10	4	4	4
Suboptimal breastfeeding	14	..	..	..	..	..	27	..	24	22	15	14	16	9	15	13	10	10	4	3	3	3
High total cholesterol	15	12	8	9	9	10	9	6	13	11	10	16	14	16	10	16	20	14	19	28	27	30
Diet low in whole grains	16	10	16	16	17	11	12	11	11	12	14	26	13	17	14	12	15	15	32	24	19	24
Diet low in vegetables	17	14	13	12	13	13	10	12	15	16	20	10	11	14	18	11	16	12	15	23	23	20
Diet low in seafood omega-3 fatty acids	18	17	15	13	16	16	14	13	17	17	18	19	15	23	16	17	18	20	23	27	25	25
Drug use	19	13	14	10	10	20	13	17	18	13	16	18	20	11	19	18	22	19	12	19	24	22
Occupational risk factors for injuries	20	24	24	20	25	26	16	25	20	19	22	23	21	21	23	31	12	22	22	20	22	17
Occupational low back pain	21	15	17	15	23	18	20	24	14	15	24	17	24	22	20	26	23	17	24	17	21	19
Diet high in processed meat	22	22	12	14	12	15	18	15	29	7	9	27	19	15	27	24	25	27	28	31	28	28
Intimate partner violence	23	18	22	23	22	25	21	22	21	23	26	22	27	19	25	23	21	25	14	18	20	23
Diet low in fibre	24	16	18	18	18	19	15	16	16	25	28	20	18	28	22	22	33	21	33	36	34	36
Unimproved sanitation	25	38	39	39	41	42	40	40	40	40	38	30	37	31	32	28	19	18	18	9	8	9
Lead exposure	26	23	21	19	24	17	19	23	22	20	25	24	23	20	26	21	24	30	20	25	26	26
Diet low in polyunsaturated fatty acids	27	19	19	17	20	21	22	18	26	24	27	21	22	29	24	25	32	23	30	33	30	29
Diet high in trans fatty acids	28	29	23	24	15	23	28	19	28	21	21	33	26	27	17	38	28	34	35	37	36	37
Vitamin A deficiency	29	40	40	38	40	41	41	42	43	41	37	32	34	34	37	33	30	31	17	11	7	8
Occupational particulate matter, gases, and fumes	30	34	33	32	28	32	33	31	23	29	32	28	29	33	31	34	26	33	29	29	29	31
Zinc deficiency	31	37	37	36	37	39	39	39	39	39	29	29	28	25	35	27	31	28	21	13	10	14
Diet high in sugar-sweetened beverages	32	28	31	31	19	33	26	27	37	26	17	25	32	30	28	20	27	26	26	32	32	34
Childhood sexual abuse	33	26	25	22	21	30	25	26	30	28	30	37	30	26	29	30	29	35	31	26	31	27
Unimproved water source	34	41	41	40	38	40	42	41	42	42	40	31	36	35	30	29	34	24	27	12	9	12
Low bone mineral density	35	21	20	25	26	24	30	28	25	30	33	35	35	36	34	32	36	37	38	35	37	33
Occupational noise	36	33	35	34	36	35	35	35	33	33	31	34	31	32	36	35	37	36	34	30	33	32
Occupational carcinogens	37	31	26	29	31	34	32	34	27	38	35	38	33	40	38	40	39	41	37	41	42	42
Diet low in calcium	38	25	28	27	29	27	29	30	31	34	39	39	39	39	40	37	40	39	39	38	39	38
Ambient ozone pollution	39	36	36	41	33	36	43	37	34	43	43	43	43	43	43	43	35	43	43	42	38	41
Residential radon	40	32	27	35	27	28	36	33	32	36	41	41	38	42	41	42	41	42	42	43	43	43
Diet low in milk	41	27	29	30	30	29	34	32	35	37	42	40	41	41	42	39	42	40	41	39	41	39
Occupational asthmagens	42	35	34	33	34	37	37	36	41	35	36	36	42	37	39	36	38	29	36	34	35	35
Diet high in red meat	43	30	30	28	32	31	31	29	36	31	34	42	40	38	33	41	43	38	40	40	40	40

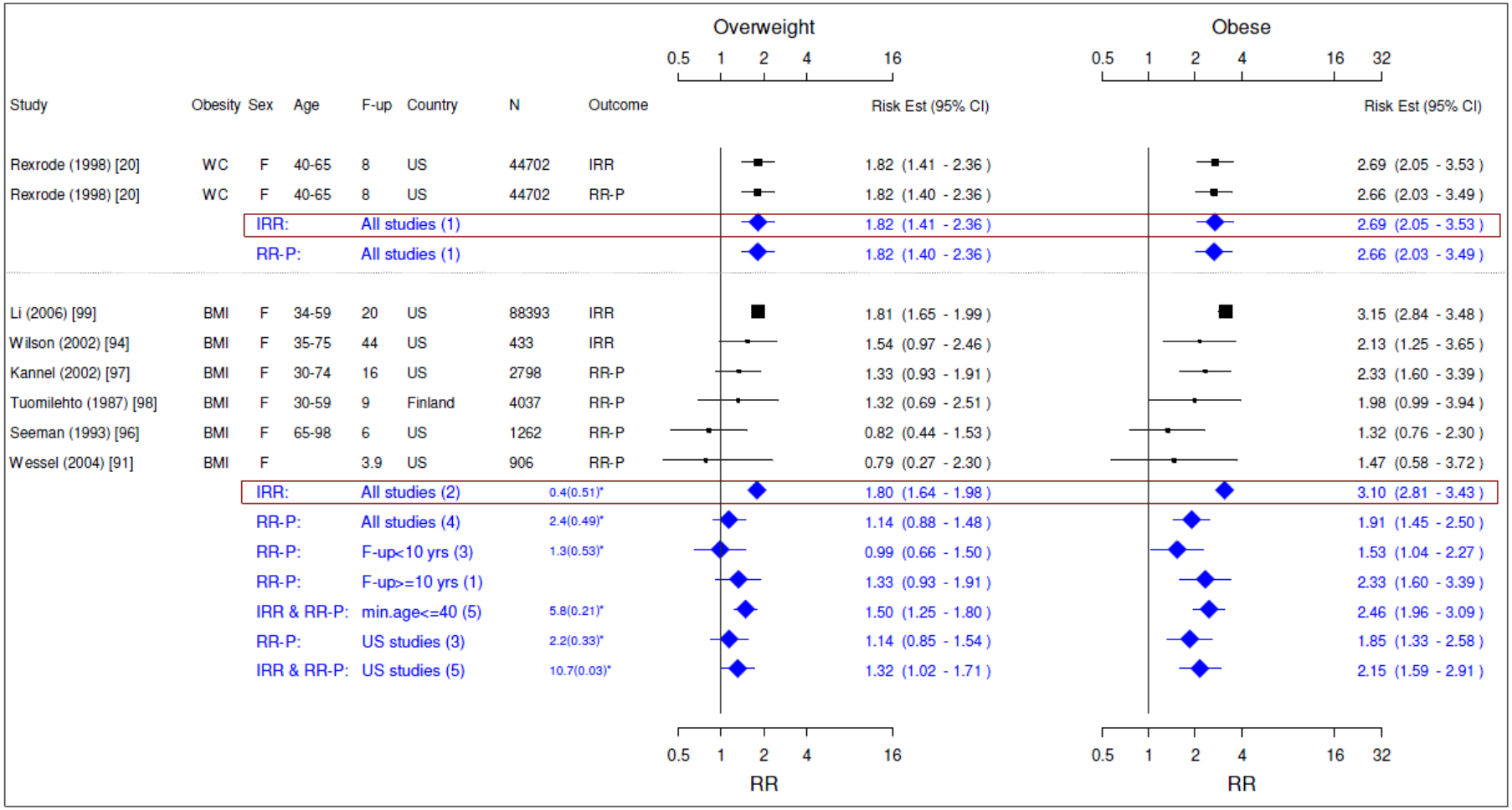
Lim SS, et al. Lancet 2012; 380: 2224-60

BMI and Hypertension Incidence



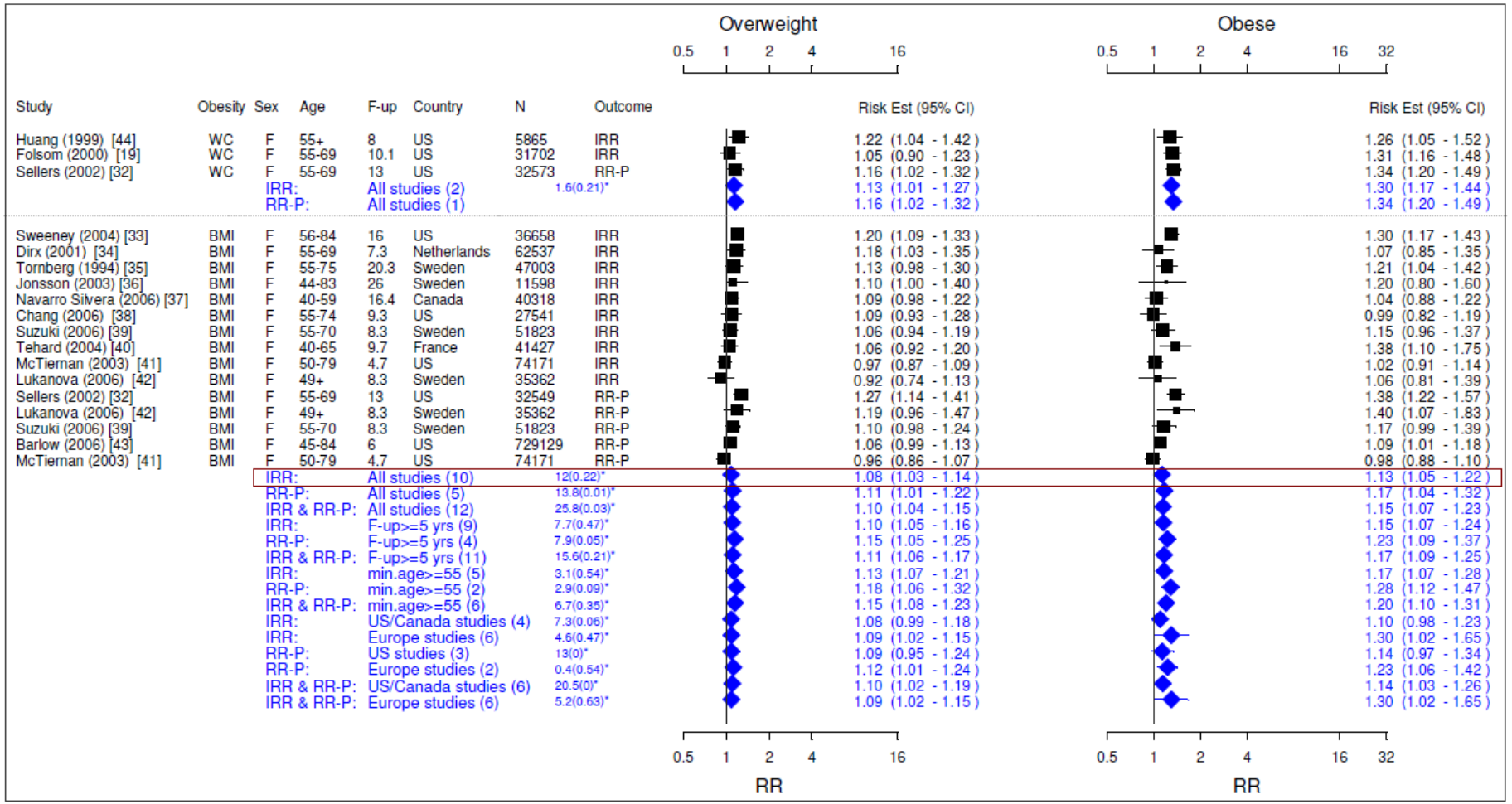
Guh DP, et al. BMC Public Health 2009; 9:88

BMI and CHD Incidence in Women



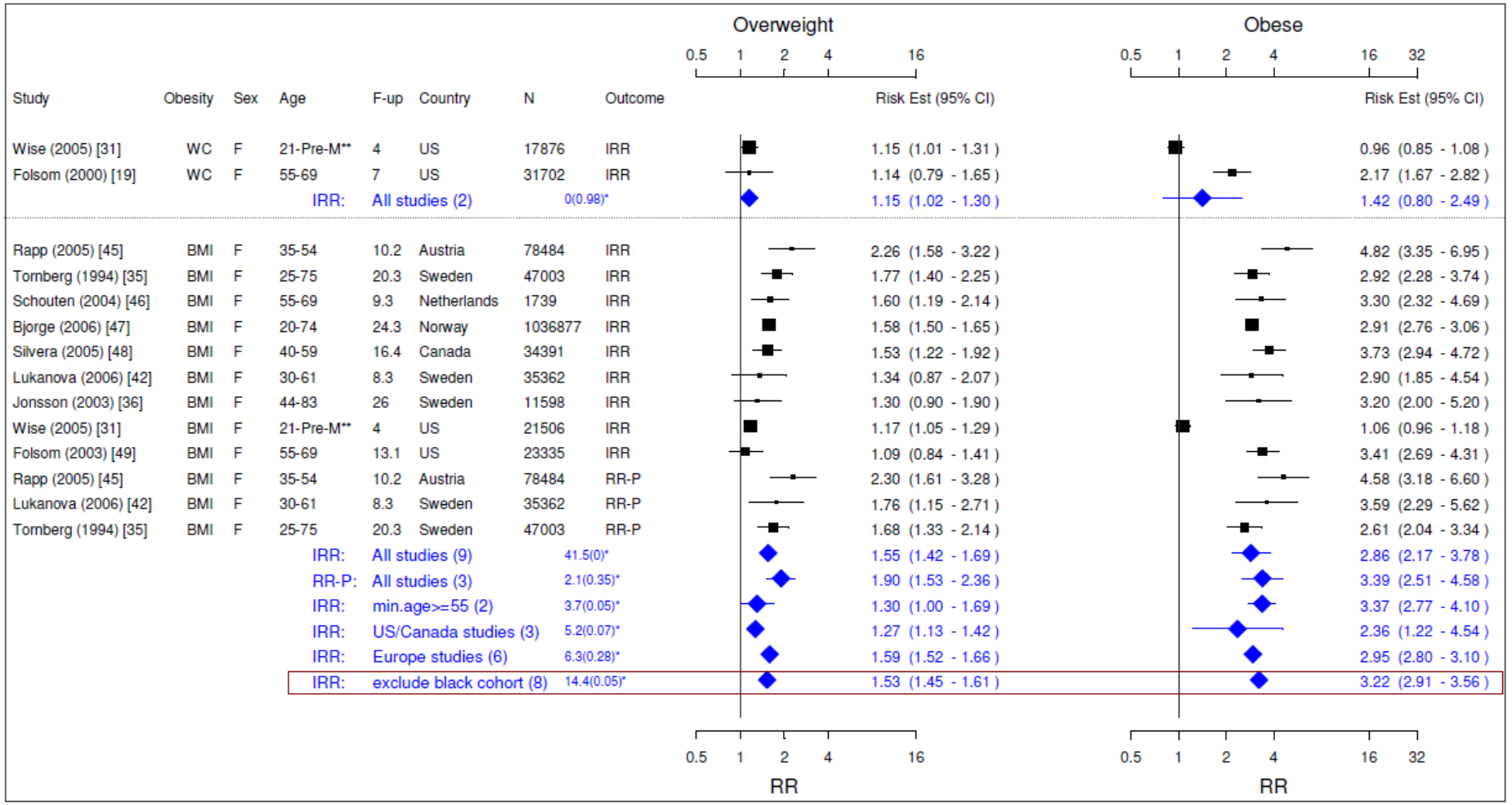
Guh DP, et al. BMC Public Health 2009; 9:88

BMI and Post Menopausal Breast Cancer Risk



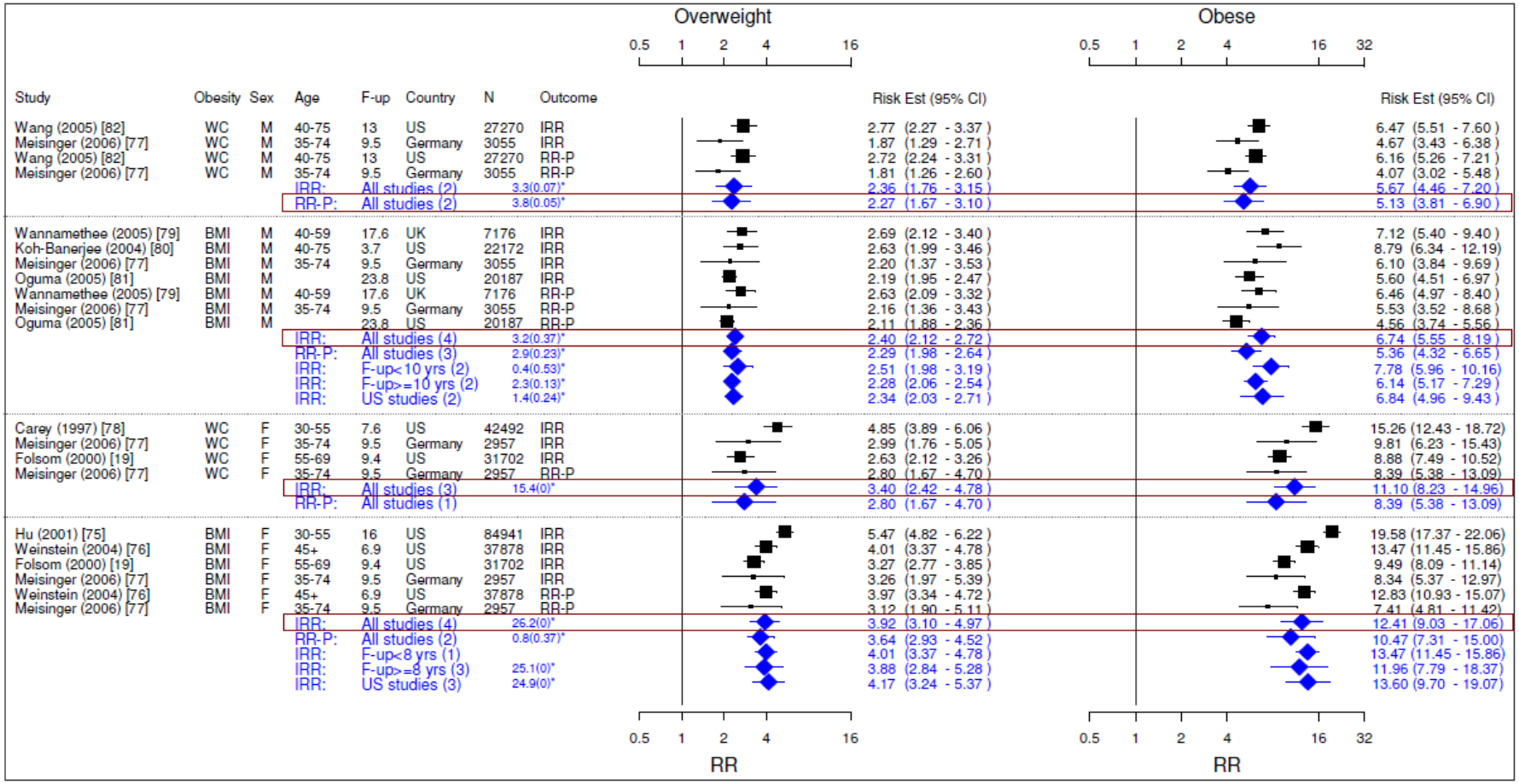
Guh DP, et al. BMC Public Health 2009; 9:88

BMI and Endometrial Cancer Risk



Guh DP, et al. BMC Public Health 2009; 9:88

BMI and Type 2 Diabetes Risk



Guh DP, et al. BMC Public Health 2009; 9:88

Prevalence of Common Comorbidities among Patients with the Three Most Common Cancers

Condition	All claims (%)			
	Breast	Prostate	Colorectal-female	Colorectal-male
Chronic pulmonary disease	7.2	16.2	4.7	4.8
Diabetes	10.2	17.4	6.4	5.4
Congestive heart failure	5.7	9.8	5.1	3.6
Cerebrovascular disease	3.6	7.4	2.4	2.2
Peripheral vascular disease	2.1	4.6	1.5	1.5
Old myocardial infarction	0.8	2.9	0.5	1.0

Klabunde CN, et al. Ann Epidemiol 2007;17:584–590. Medicare data from 1992-1996.

Risk of Death Varies by Comorbidity for Patients with the Three Most Common Cancers

Condition	Hazard Ratios (HRs)		
	Breast n=13,247 (841 non-CA deaths)	**Prostate** n=26,766 (2,122 non-CA deaths)	**Colorectal** n=16,829 (1,756 non-CA deaths)
Mod./severe renal disease	3.28	1.97	2.63
Congestive heart failure	2.33	2.40	2.16
Dementia	3.29	2.17	1.92
Chronic pulmonary disease	1.60	2.06	1.40
Cerebrovascular disease	2.04	1.30	1.41
Paralysis	1.23	1.48	1.65
Diabetes	1.57	1.27	0.99

Klabunde CN, et al. Ann Epidemiol 2007;17:584–590. Medicare data from 1992-1996.

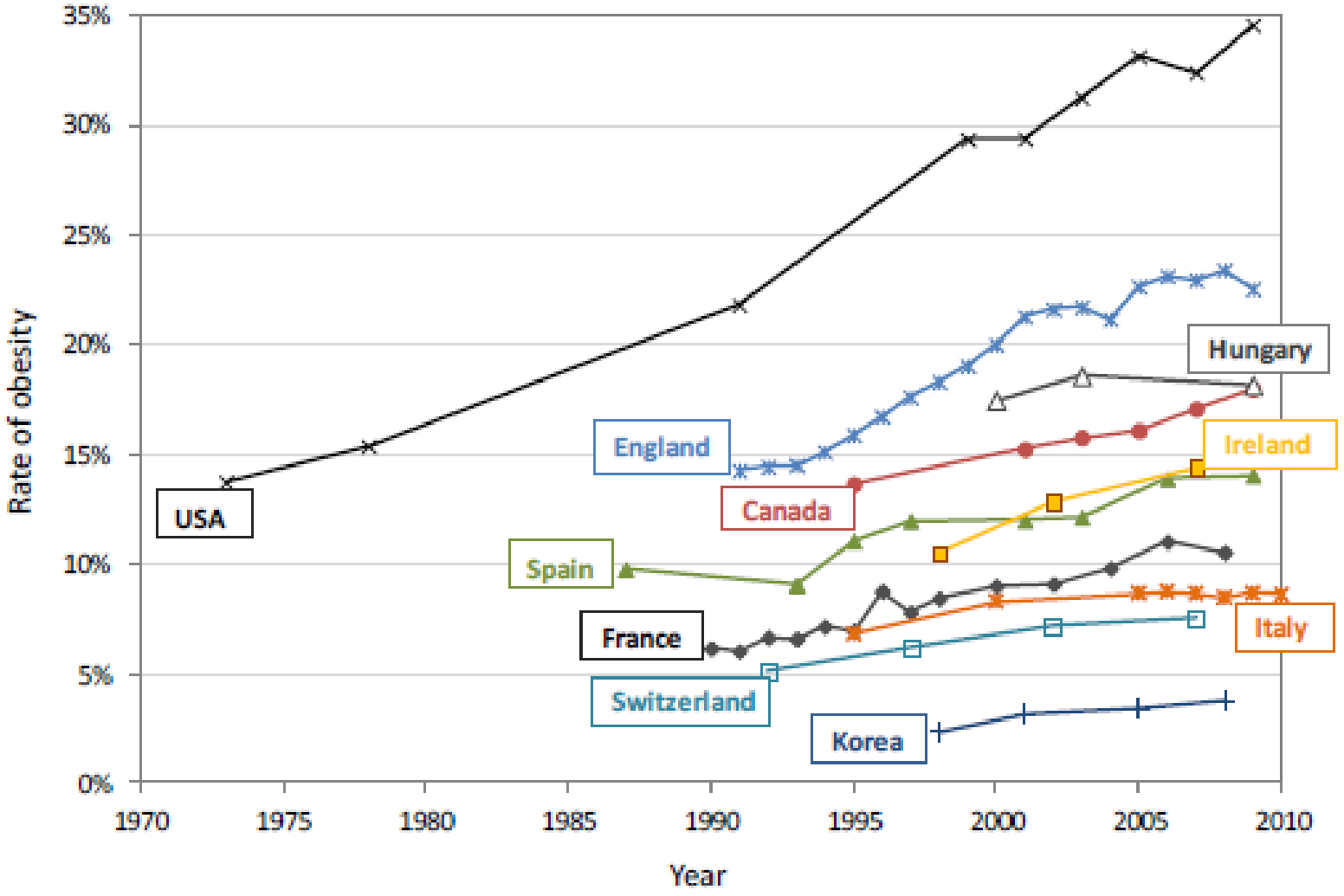
Conclusion

- A number of health behaviors, different obesity phenotypes, and health conditions may alter BMI and mortality association
- Associations may vary across racial/ethnic or immigrant populations but this may vary in US vs country of origin
- Disease burden is shifting from mortality to morbidity, particularly in developed countries – estimated to be 50% for the US in 2010
- This change in disease burden suggests a need for a shift from a focus on mortality as a predominant measure of disease burden
- Obesity is a complex multi-factorial health problem that is being explored with complex systems science approaches

Complex Adaptive Systems: Challenges for Science and Policy

- Features (nonlinearity, interdependence, spatial and dynamic complexity, heterogeneity) make system behavior difficult to capture fully using traditional scientific tools or analyses
- "Mental models" and intuition can be very limiting, misleading
- Policy Resistance
  - Policies that do not take complexity into account may have unanticipated consequences… or even backfire
  - Interventions that are successful in one area alone may be offset by response elsewhere in system
  - Heterogeneity means policy solutions may not be "one size fits all"
- Multiple levels of scale (neurons to nations) necessitate interdisciplinary communication, make policy focus challenging
- The best policies may be subtle, novel, unconventional; may leverage hidden synergies; and may need to use "systems" approach

US Continues to Lead the World in Obesity Rates

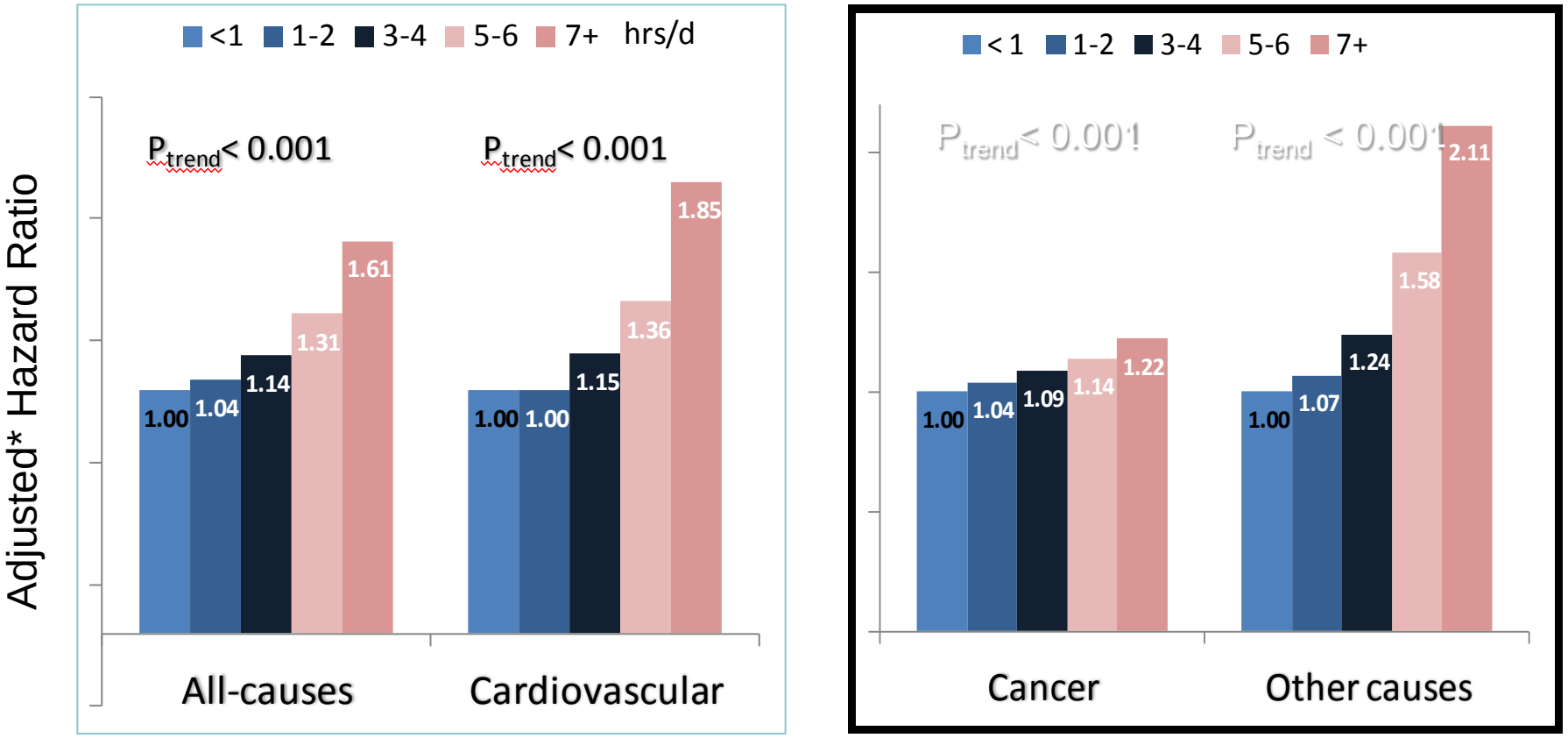


OECD Obesity Update 2012

Questions?

Highlights on Physical Activity and Cancer

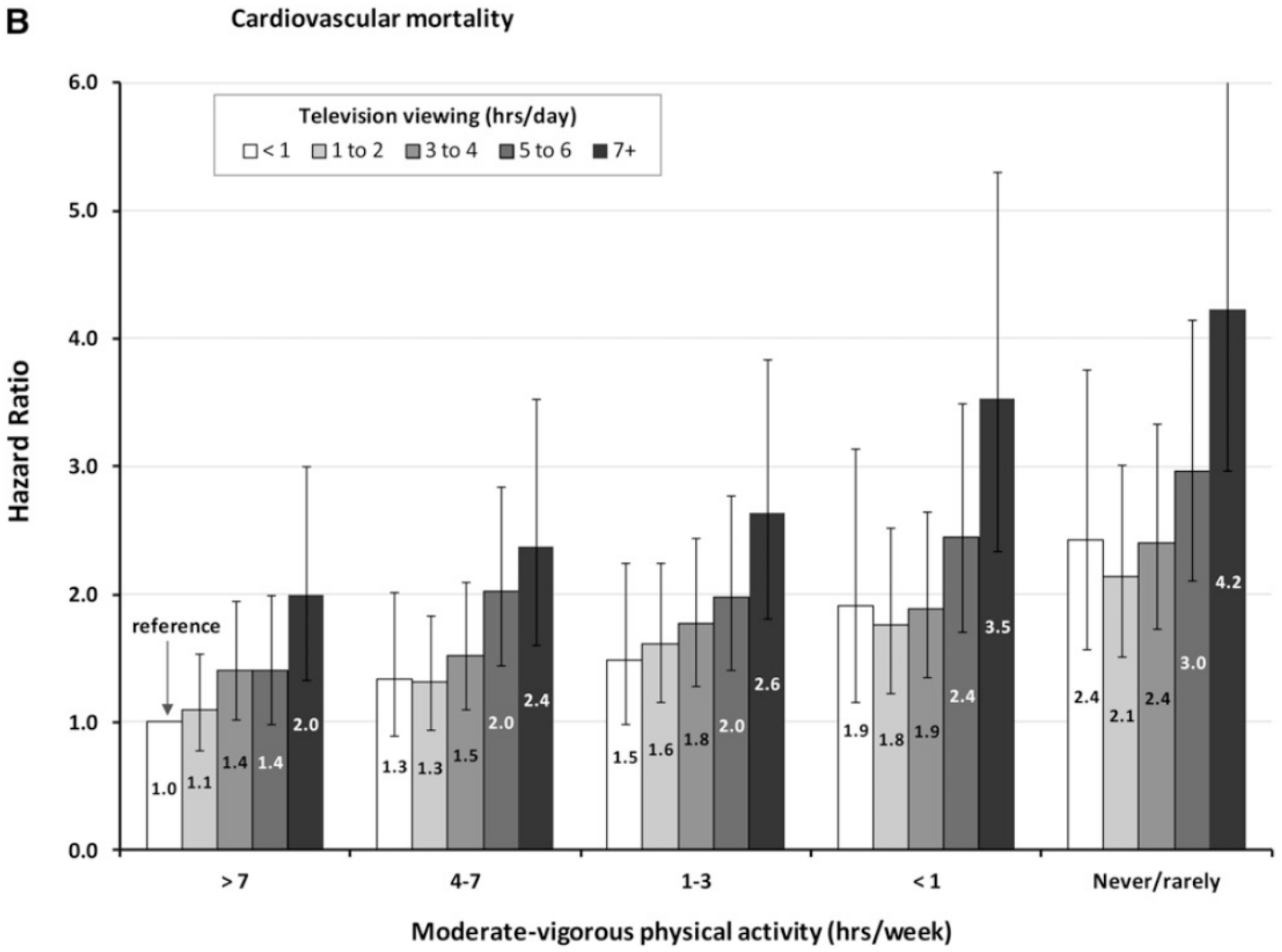
Television viewing and mortality



*Age, sex, education, race, smoking, diet quality, and moderate-vigorous physical activity

Matthews CE, George SM, et al. AJCN 2012;95:437–45.

Joint-effects of television viewing and physical activity on cardiovascular mortality



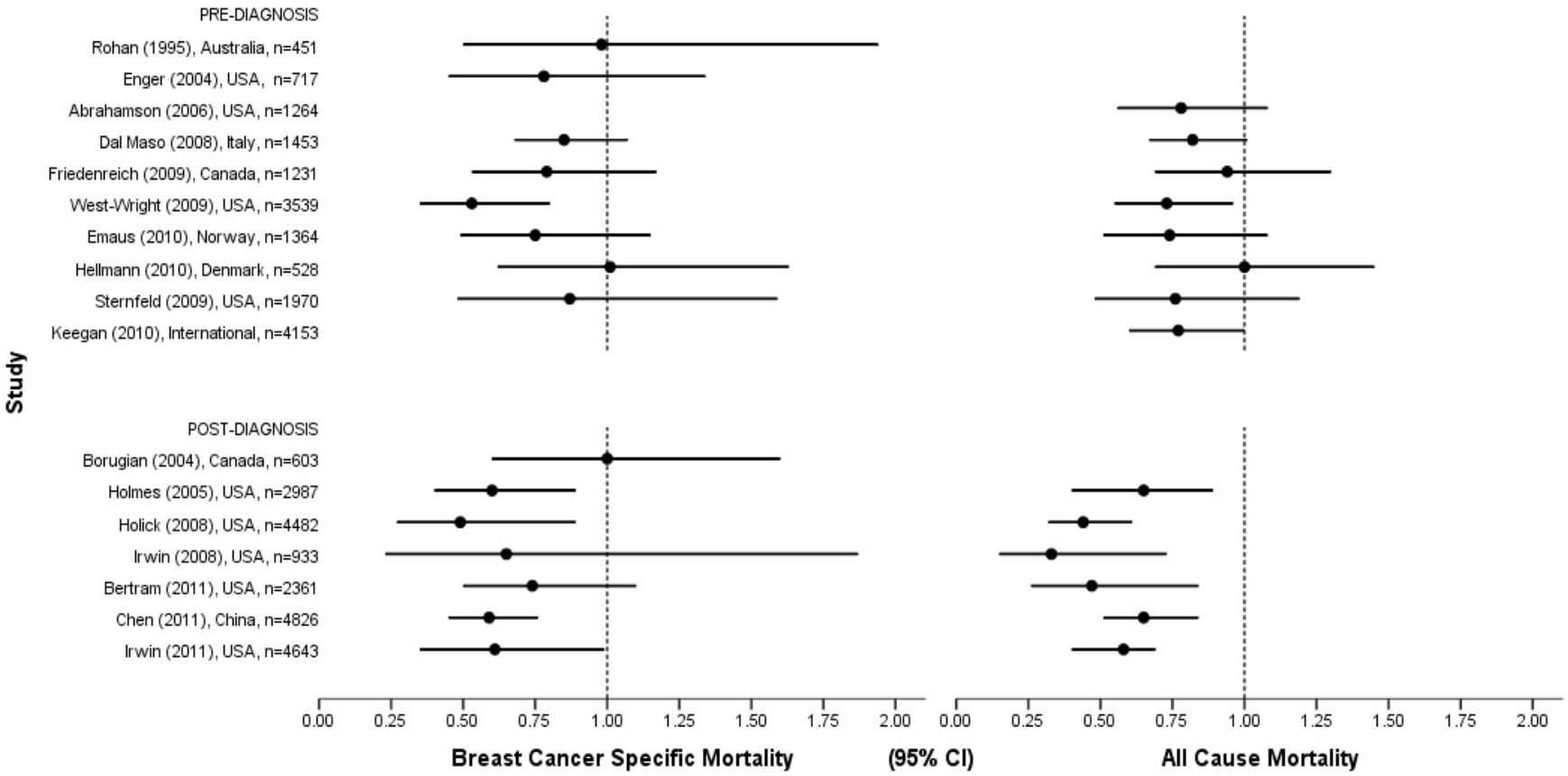
Matthews, C.E. George, S.M, et al. AJCN 2012;95:437–45.

Physical Activity & Cancer Prognosis

Cancer	Number of Studies	Decrease Risk of Cancer Death	Decrease Risk of All Cause Death
Breast	17	Yes	Yes
Colorectal	6	Yes	Yes
Prostate	1	Too few studies to reach conclusion on the effect	
Ovarian	2		
Brain	1		

Ballard-Barbash R et al, JNCI 2011

HRs for Physical Activity and Mortality Outcomes in Women with Breast Cancer



Ballard-Barbash R et al. JNCI 2012

National Cancer Institute

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Advisory Board

Biennial Review of Inclusion of Women and Minorities in Clinical Research

February 2013

NIH Policy on Inclusion of Women and Minorities in Clinical Research

Why does NIH have this policy?

- Mandated by Congress in 1993, Public Law 103-43.
- Ethical principle of justice and importance of balancing research burdens and benefits.

Public Law PL 103-43

- Women and minorities must be included in all clinical research studies.
- Women and minorities must be included in Phase III clinical trials, and the trial must be designed to permit valid analysis.
  - For the purpose of this policy, Valid Analysis means an unbiased assessment that does not require high statistical power and should be conducted for both large and small studies.

Public Law PL 103-43

- Cost is not allowed as an acceptable reason for exclusion.

- NIH supports outreach efforts to recruit and retain women, minorities, and their subpopulations in clinical studies.

NIH Revitalization Act of 1993

"The Advisory Council of each National Institute shall prepare biennial reports describing the manner in which the institute has complied with this section."

- Reported in odd-numbered years.

NIH Report Approach

A summary report is prepared centrally by the NIH Office of Extramural Research and includes a statement that the NCAB reviews.

- NCI procedures for implementation of the NIH policy for inclusion of women and minorities in clinical studies.
- The results of that implementation.
- NCI compliance.

NCI Coordination
Division of Extramural Activities

Implements Inclusion Policy at NCI

- Institute-wide coordination and communication
- Accrual Working Group –Division Reps
- Information, Training, Problem Solving

NCI Procedures for Implementation of NIH Policy

POLICY DISSEMINATION

- ESAs work with applicants to disseminate requirements *(NIH Guide and NCI and NIH Websites).*

- NCI extramural staff are kept up-to-date via trans-NIH education programs and desktop distribution of policies and procedures.

NCI Procedures for Implementation of NIH Policy

PRE-AWARD ACTIVITIES

- Peer reviewers receive instruction on policies and evaluate inclusion plans.
- Where concerns are noted, bars to award are put in place. NCI staff work with applicants to ensure appropriate revisions are made.
- Applications with bars are identified in a closed NCAB session, and a subsequent resolution is reported.

NCI Procedures for Implementation of NIH Policy

POST-AWARD MONITORING

- Awardees report cumulative accrual annually.
- Progress of studies and cumulative accruals are reviewed by Program Directors.
- Target and enrollment numbers are entered into the NIH Population Tracking application.
- Staff provide oversight, advice, and assistance and work with awardees to disseminate findings and encourage new studies.

NCI Procedures for Implementation of NIH Policy

AGGREGATE REPORTING

- NIH requires a format that aggregates all clinical trials whether treatment, behavioral, or epidemiologic observation.
  - Individual clinical trials vary considerably.
  - Large population-based screening trials dominate aggregate data.

Instructions in PHS 398

Inclusion of women and minorities sections must include:

- Subject selection criteria and rationale.
- Rationale for any exclusions.
- Enrollment dates (start and end).
- Outreach plans for recruitment.
- Proposed composition using tables.

Accrual to NCI Clinical Trials

- Data include epidemiological, population-based interventions and therapeutic trials according to the NIH definition of clinical research.
- Subset analyses by race, ethnicity, and sex/gender are required of all Phase III clinical trials with initial funding after 1995.
- Current reporting cycle covers data reported in FY2011 and 2012, which represents subjects enrolled in FY2010 and 2011.

Requirements for NIH-Defined Phase III Clinical Trials

Definition: Broadly based prospective Phase III clinical investigation,

- usually involving several hundred or more human subjects,
- for the purpose of evaluating an experimental intervention or comparing two or more existing treatments.
- Often the aim of such investigation is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care.

US Cancer Incidence for All Cancers 2005-2009

	White	Black	Asian/ PI	American Indian	Total (All Races/ Sexes)	Hispanic **
Incidence Rate per 100,000	471.7	489.5	315.0	328.9	465.2	353.7
Number of Incidence Cases	1,577,573	194,295	111,376	7,255	1,922,239	175,955
Estimated Percent of Total*	82.1%	10.1%	5.8%	0.4%	100%	9.2%

*US Cancer Percent estimated from SEER Number of Incidence Cases for 2005-2009.

**Hispanic incidence included in other categories.

NCI Enrollment for FY 2011 and 2012 Extramural Research Studies by Sex/Gender

2011
2,392 Studies

Sex/Gender	Enrolled	Percent	US Cancer Incidence*
Female	4,279,066	70.5%	48.4%
Male	1,758,184	29.0%	51.6%
Unknown	28,225	0.5%	
Total	6,065,475	100%	100%

2012
2,169 Studies

Sex/Gender	Enrolled	Percent	US Cancer Incidence*
Female	3,359,328	53.9%	48.4%
Male	2,858,916	45.8%	51.6%
Unknown	19,620	0.3%	
Total	6,237,864	100%	100%

*US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009

NCI Sex/Gender Enrollments FY 2011 and 2012 excluding All Male and All Female Studies

2011 -1,695 Studies

Sex/ Gender	Enrollment	Percent of Total	US Cancer Incidence*
Female	693,041	50.3%	48.4%
Male	655,652	47.6%	51.6%
Other/Unknown	28,225	2.1%	
Total	1,376,918	100%	100%

2012 -1,561 Studies

Sex/ Gender	Enrollment	Percent of Total	US Cancer Incidence*
Female	2,109,101	52.9%	48.4%
Male	1,859,443	46.6%	51.6%
Other/Unknown	19,620	0.5%	
Total	3,988,164	100%	100%

Subset of studies reported for 2011 and 2012; Studies include both Males and Females.

*US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009.

NCI Extramural Research Studies

FY 2011 – 2,392 Studies FY 2012 – 2,169 Studies

Race/Ethnicity	2011 Count	2011 Percent	2012 Count	2012 Percent	US Cancer Incidence**
White	4,123,883	68.0%	3,772,476	60.5%	82.1%
Asian	817,196	13.5%	591,279	9.5%	5.8%
Unknown/Not Reported	545,393	9.0%	1,237,091	19.8%	
Black or African American	452,198	7.5%	537,974	8.6%	10.1%
Hispanic or Latino*	(391,220)	(6.5%)	(549,827)	(8.8%)	(9.2%)
American Indian/ Alaska Native	49,849	0.8%	24,502	0.4%	0.4%
More Than One Race	58,375	1.0%	45,994	0.7%	
Native Hawaiian/ Pacific Islander	18,581	0.3%	28,548	0.5%	
Total	6,065,475	100%	6,237,864	100%	100%

*Hispanic or Latino counts are not exclusive and may be included in other categories.

**US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009.

FY 2011 and 2012 NCI Enrollment Extramural Phase III Research Studies by Sex/Gender

FY 2011
306 Trials

Sex/Gender	Count	Percent of Total	US Cancer Incidence*
Female	86,317	58.3%	48.4%
Male	61,718	41.7%	51.6%
Unknown	50	0.03%	
Total	148,085	100%	100%

FY 2012
267 Trials

Sex/Gender	Count	Percent of Total	US Cancer Incidence*
Female	67,312	58.1%	48.4%
Male	48,312	41.7%	51.6%
Unknown	159	0.1%	
Total	115,783	100%	100%

*US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009.

NCI Extramural Phase III Research Studies

FY 2011 – 306 Studies FY 2012 – 267 Studies

Race/Ethnicity	2011 Count	2011 Percent	2012 Count	2012 Percent	US Cancer Incidence**
White	118,896	80.2%	87,661	75.7%	82.1%
Asian	11,311	7.6%	9,490	8.1%	5.8%
Black or African American	11,103	7.5%	12,761	11.0%	10.1%
Hispanic or Latino*	(9,261)	(6.3%)	(7,381)	(6.4%)	(9.2%)
Unknown/Not Reported	5,465	3.7%	4,569	3.9%	
Amer. Indian/Alaska Native	623	0.4%	516	0.4%	0.4%
Hawaiian/Pacific Islander	359	0.2%	270	0.2%	
More Than One Race	328	0.2%	516	0.4%	
Total	148,085	100%	115,783	100%	100%

*Hispanic or Latino counts are not exclusive and may be included in other categories.

**US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009.

NCI Intramural Research Studies

FY 2011– 522 Studies FY 2012 – 565 Studies

Race/Ethnicity	2011 Count	2011 Percent	2012 Count	2012 Percent	US Cancer Incidence**
White	1,543,245	69.4%	1,653,693	45.6%	82.1%
Unknown/Not Reported	262,438	11.8%	1,510,138	41.6%	
Black or African American	212,682	9.6%	243,094	6.7%	10.1%
Asian	195,464	8.8%	205,930	5.7%	5.8%
Hispanic or Latino*	(78,129)	(3.5%)	(110,638)	(3.1%)	(9.2%)
American Indian/ Alaska Native	6,339	0.3%	7,018	0.2%	0.4%
More Than One Race	1,582	0.1%	4,102	0.1%	
Hawaiian/Pacific Islander	1,096	0.1%	2,083	0.1%	
Total	2,222,846	100%	3,626,058	100%	100%

*Hispanic or Latino counts are not exclusive and may be included in other categories.

**US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009.

CTEP Treatment Trials Enrollment

FY 2011 – 596 Studies FY 2012 – 541 Studies

Race/Ethnicity	2011 Count	2011 Percent	2012 Count	2012 Percent	US Cancer Incidence**
White	19,020	81.1%	19,663	81.8%	82.1%
Black or African American	2,217	9.5%	2,157	8.9%	10.1%
Hispanic or Latino*	(1,844)	(7.9%)	(1,920)	(8.0%)	(9.2%)
Unknown/ Not Reported	1,092	4.7%	1,066	4.4%	
Asian	852	3.6%	887	3.0%	5.8%
American Indian/ Alaska Native	114	0.5%	124	0.5%	0.4%
Native Hawaiian/ Pacific Islander	81	0.3%	78	0.3%	
More Than One Race	53	0.2%	59	0.2%	
Total	23,429	100%	24,034	100%	100%

*Hispanic or Latino counts are not exclusive and may be included in other categories.

**US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009.

CTEP Treatment Trials Enrollment by Gender

FY 2011

596 Studies

Sex/Gender	Count	Percent of Total	US Cancer Incidence*
Female	14,103	60.2%	48.4%
Male	9,303	39.7%	51.6%
Unknown	23	0.1%	
Total	23,429	100%	100%

FY 2012

541 Studies

Sex/Gender	Count	Percent of Total	US Cancer Incidence*
Female	14,321	59.6%	48.4%
Male	9,696	40.3%	51.6%
Unknown	17	0.1%	
Total	24,034	100%	100%

*US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009.

CTEP Treatment Trials Enrollment by Gender
(excluding Gender Specific Trials)

FY 2011

459 Studies

Sex/Gender	2011 Count	Percent of Total	US Cancer Incidence*
Female	7,551	48.7%	48.4%
Male	7,928	51.1%	51.6%
Unknown	23	0.2%	
Total	15,502	100%	100%

FY 2012

406 Studies

Sex/Gender	2012 Count	Percent of Total	US Cancer Incidence*
Female	7,819	48.8%	48.4%
Male	8,184	51.1%	51.6%
Unknown	17	0.1%	
Total	16,020	100%	100%

Subset of studies reported for 2011 and 2012; Studies include both Males and Females.

* US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009.

DCP Trials Enrollment

2011 – 63 Studies 2012 – 70 Studies

Race/Ethnicity	2011 Count	2011 Percent	2012 Count	2012 Percent	US Cancer Incidence*
White	5,503	83.3%	8,514	85.2%	82.1%
Black or African American	664	10.1%	939	9.4%	10.1%
Hispanic or Latino*	(350)	(5.3%)	(454)	(4.5%)	(9.2%)
Asian	196	2.8%	246	2.5%	5.8%
Unknown/ Not Reported	165	2.6%	198	2.0%	
American Indian/ Alaska Native	52	0.8%	62	0.6%	0.4%
Native Hawaiian/ Pacific Islander	17	0.3%	14	0.1%	
More Than One Race	8	0.1%	21	0.2%	
Total	6,605	100%	9,994	100%	100%

*Hispanic or Latino counts are not exclusive and may be included in other categories.

** US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009.

DCP Trials Enrollment by Gender

FY 2011

63 Studies

Sex/Gender	Count	Percent of Total	US Cancer Incidence*
Female	4,553	68.9%	48.4%
Male	2,019	30.6%	51.6%
Unknown	33	0.5%	
Total	6,605	100%	100%

FY 2012

70 Studies

Sex/Gender	Count	Percent of Total	US Cancer Incidence*
Female	6,036	60.4%	48.4%
Male	3,938	39.4%	51.6%
Unknown	20	0.2%	
Total	9,994	100%	100%

* US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009.

DCP Trials Enrollment by Gender
(excluding Gender Specific Trials)

FY 2011

45 Studies

Sex/Gender	Count	Percent of Total	US Cancer Incidence*
Female	2,784	58.1%	48.4%
Male	1,971	41.2%	51.6%
Unknown	33	0.7%	
Total	4,788	100%	100%

FY 2012

44 Studies

Sex/Gender	Count	Percent of Total	US Cancer Incidence*
Female	3,068	44.8%	48.4%
Male	3,761	54.9%	51.6%
Unknown	20	0.3%	
Total	6,849	100%	100%

Subset of studies reported for 2011 and 2012; Studies include both Males and Females.

* US Cancer Incidence estimated from SEER Number of Incidence Cases for 2005-2009.

NCI Population Tracking Accrual Working Group

- Division of Extramural Activities
  - Gail Pitts, Chair
  - Clarissa Douglas
- Division of Cancer Biology
  - Jennifer Strasburger
- Division of Cancer Control and Population Sciences
  - Mark Alexander
- Division of Cancer Prevention
  - Cynthia Whitman
- Division of Cancer Treatment and Diagnosis
  - Rolanda Wade-Ricks
  - Kim Witherspoon
  - Peter Ujhazy
- Office of Centers, Training, and Resources
  - Martha Hare

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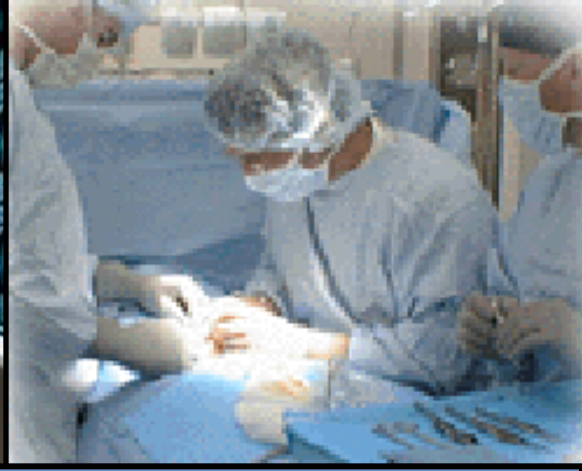

Impact of the Implementation of the Operational Efficiency Working Group (OEWG) Report on the Clinical Trials System

NCAB Meeting

February 8, 2013

Jeff Abrams, MD

Acting Director for Clinical Research

Division of Cancer Treatment and Diagnosis

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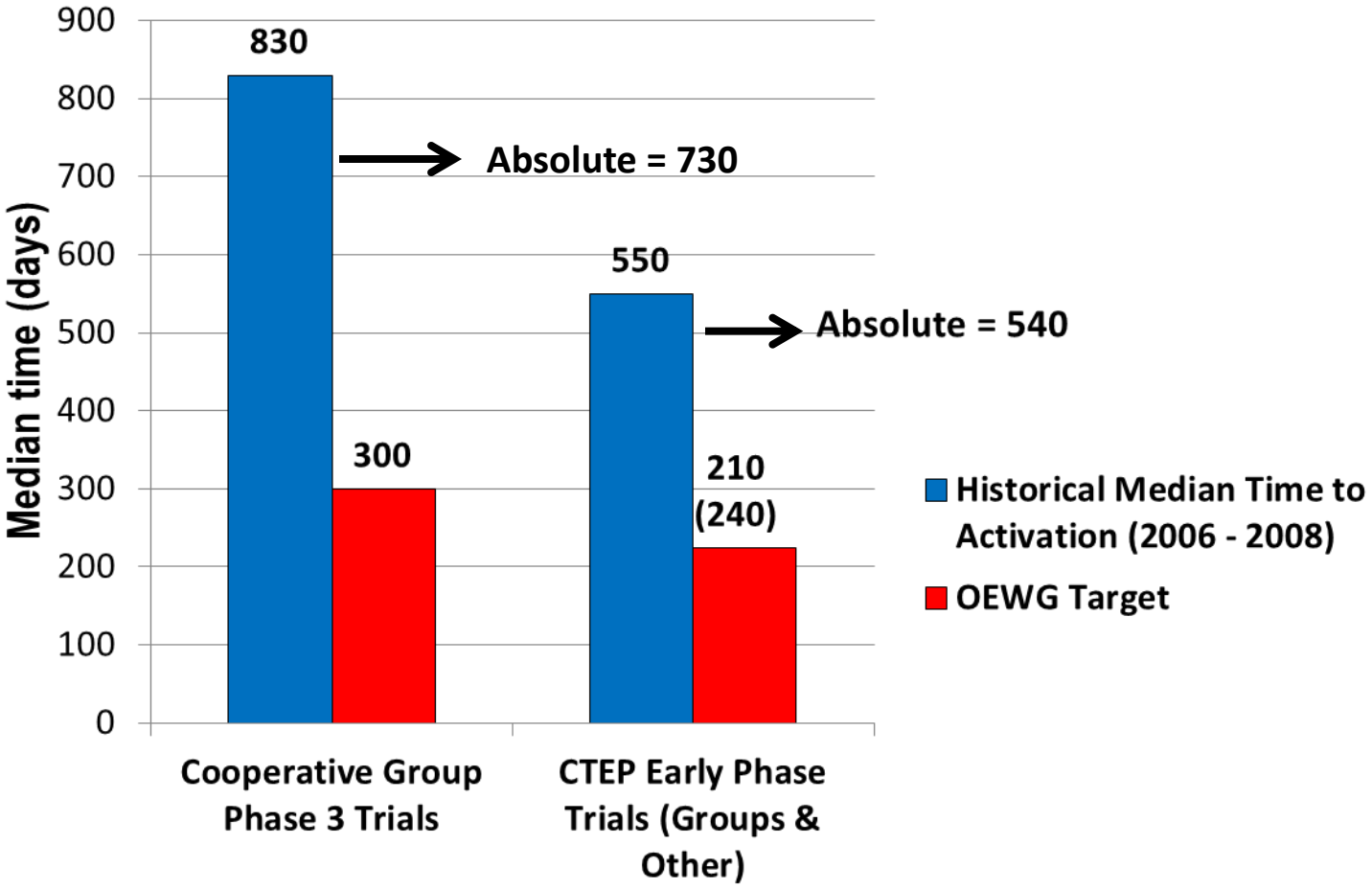
Operational Efficiency Working Group

Overview of Recommendations & Implementation

- New process to develop trials in interactive & collaborative fashion
- Timelines for target and absolute timelines for trial development (review of proposal to activation)
- Developed implementation plans to achieve targets
  - **As of Apr 2010:** All treatment trials monitored per new timelines
  - **As of Jan 2011:** All trials that do not achieve "absolute" deadlines do not go forward

Historical *vs* OEWG
Target & Absolute Timelines



Protocol terminated if absolute timelines not achieved

Revision of Timelines in April 2012

- **New Absolute Deadlines Based on Initial Assessment of Improvement in Timelines**
  - Decrease for Early Phase Studies (including larger Phase 2 Concepts) from 540 to 450 days
  - Decrease for Phase 3 Studies from 730 to 540 days
  - Implementation in April 2012

- **Institution of 6 Month Deadline for CTEP Cooperative Research & Development (CRADA) Agreements**

Update on Implementation

- **In March 2010, the OEWG provided recommendations to the NCI on strategies to decrease the time required to activate NCI-sponsored clinical trials**

- **A major component of the recommendations was the creation of target timelines and absolute deadlines for studies to go from Concept/LOI submission to activation (activation defined as study open to patient enrollment) with revision of absolute deadlines in April 2012**

  - **Phase 1 and 2 Studies:**
    - **Target Timeline – 210 days (7 months)**
    - **Absolute Deadline – ~~540 days~~ Now 450 days (15 months)**

  - **Phase 3 Studies:**
    - **Target Timeline – 300 days (10 months)**
    - **Absolute Deadline – ~~730 days~~ Now 540 days (18 months)**

NCI/DCTD/CTEP Response

- Project Managers were hired to closely track study timelines
- Secure website developed to allow investigators, operations staff, and NCI staff to monitor timelines
- Routine conference calls between NCI reviewers and external investigators instituted at key points in the review process to quickly resolve issues and decrease the need for multiple document revisions
- Medical Editors were hired with responsibilities including compiling and editing Consensus Reviews and inserting applicable revisions directly into an unofficial copy of the Protocol using Track Changes®, thus saving investigators valuable time

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OEWG Conference Call Process

- **Calls between study team & NCI to clarify/discuss Consensus Review to prevent review iterations that may slow the approval process**
- **Conference calls occur at several key points:**
  - **LOI's: on-hold, approved pending drug company review, or approved**
  - **Concepts: pending response to Steering Cmte evaluation or approved**
  - **Protocols: pending response to Consensus Review**
  - **Ad Hoc: as special issues arise during study development**
- **Approximately 686 conference calls between April 2010 – Sept 2012:**
  - **247 calls for LOI's**
  - **156 calls for Concepts**
  - **262 calls for Protocols**

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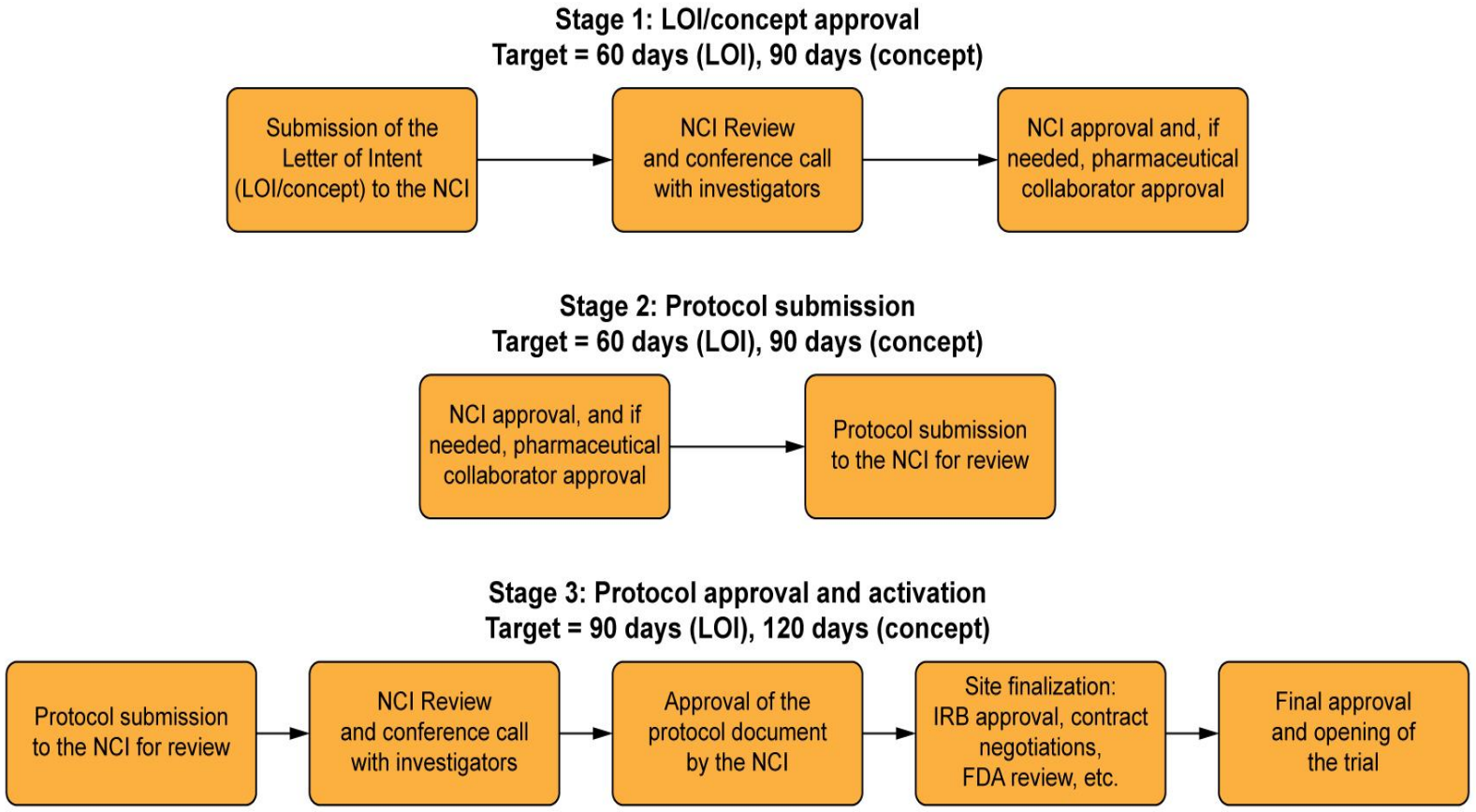
Stages of LOI/Concept Review & Protocol Development



Target for opening trial to entrollment is 210 (LOI)/300 (concept) days

Absolute deadline for opening trial to enrollment is 540 (LOI)/730 (concept) days

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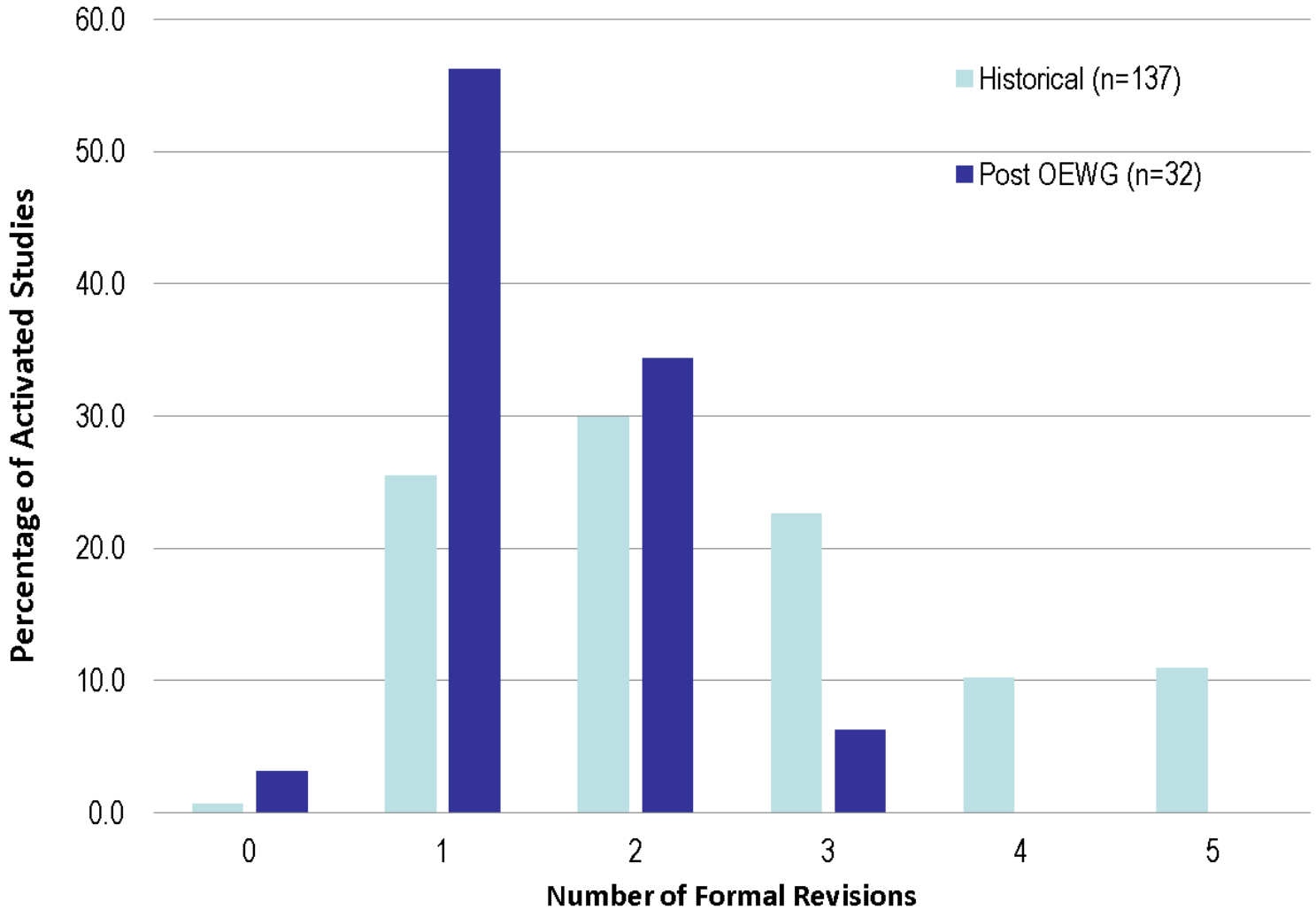
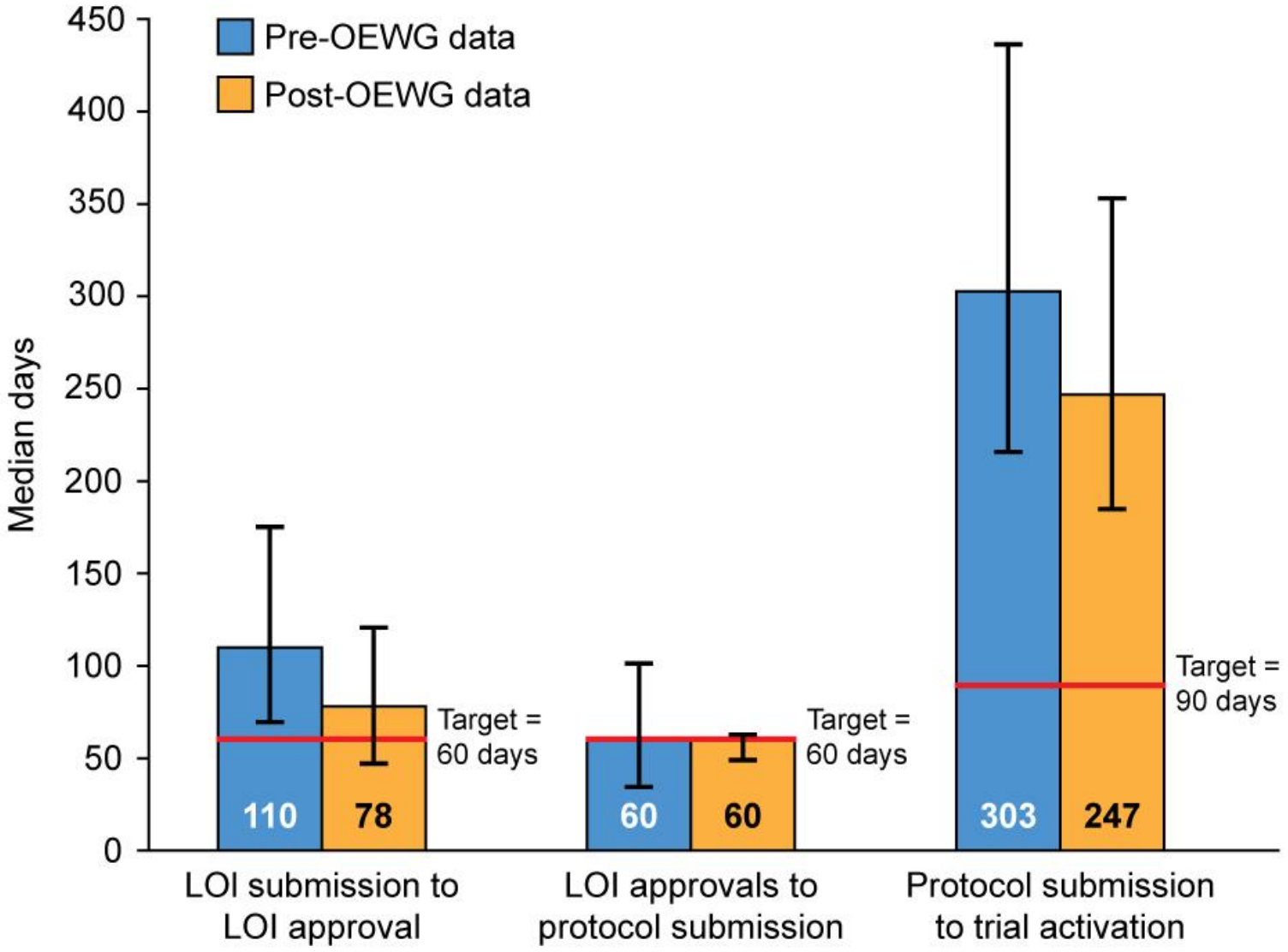
Comparison of Number of Protocol Revisions Prior to Activation

Post OEWG Group Studies (All Phases) vs Historical Studies
As of December 2011



Breakdown of the study development stages

Early Phase Studies



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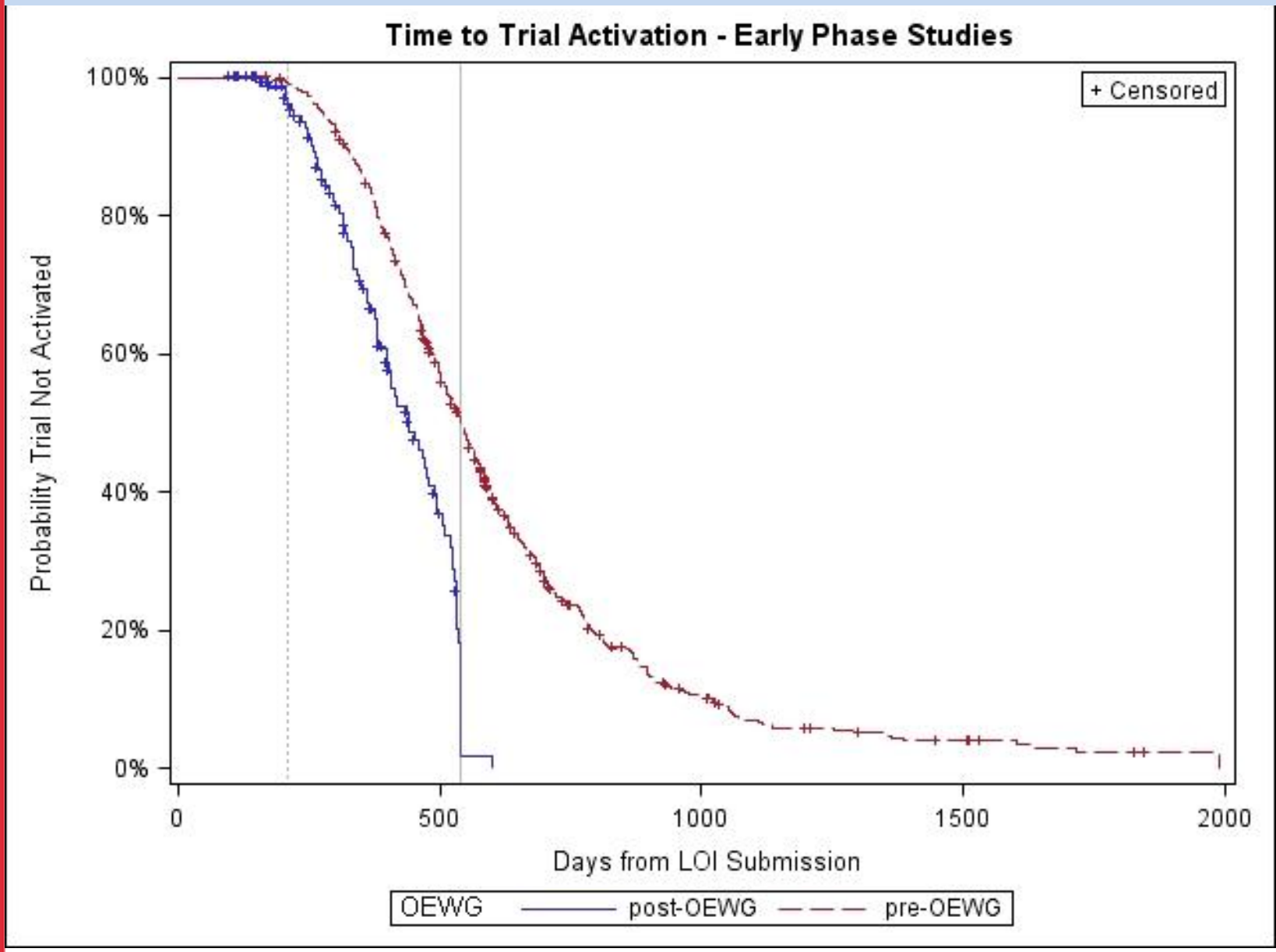
Timeline Comparison of Study Activation-Early Phase Trials: Historical vs. Post-OEWG (Apr 2010 – Aug 2012)



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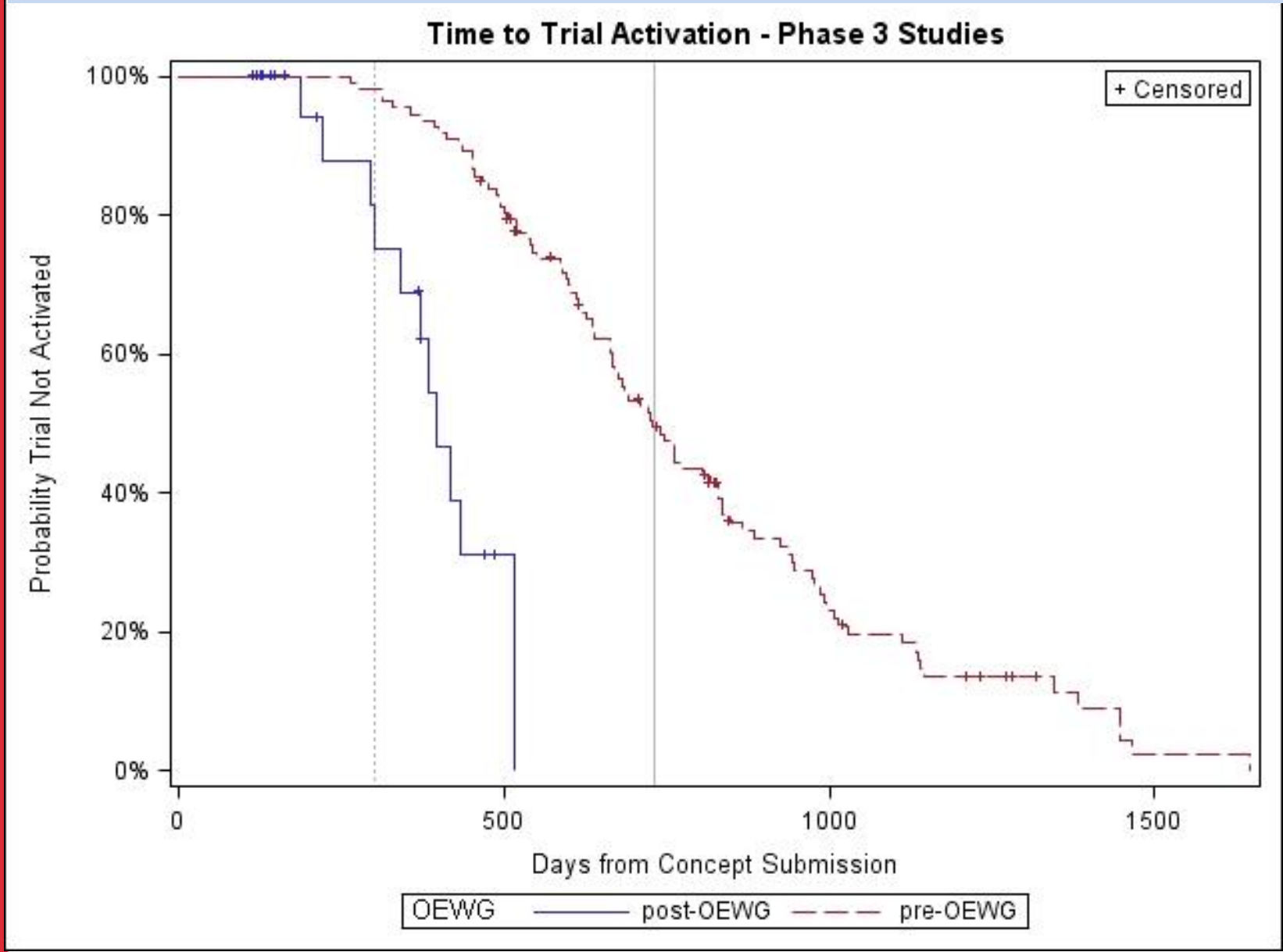
Timeline Comparison of Study Activation for Phase 3 Trials: Historical vs. Post-OEWG (Apr 2010 – Aug 2012)



Comprehensive Changes Undertaken to Improve Trial Initiation Timelines

	Change	Implementation
Target Timeline	**An ideal goal, achievable if all partners function optimally**	**7 months for phase 1-2 trials and 10 months for phase 3 trials**
Absolute Deadline	**An immoveable date by which the trial must be open to patient enrollment**	**18 months for phase 1-2 trials and 24 months for phase 3 trials***
Staffing Additions	**New positions created to manage protocol timelines and to assist physicians with protocol authorship, revisions, and editing**	
Process Improvement	**Implementation of uniform templates for protocol development and for reviewers' comments**	**Requirement for prompt teleconferences to resolve scientific and regulatory review issues at each step of review**
Information Technology	**Creation of a website to track all phases of protocol's life cycle**	

*The absolute timelines were revised in April 2012 to be more stringent – 15 months for phase 1-2 trials and 18 months for phase 3