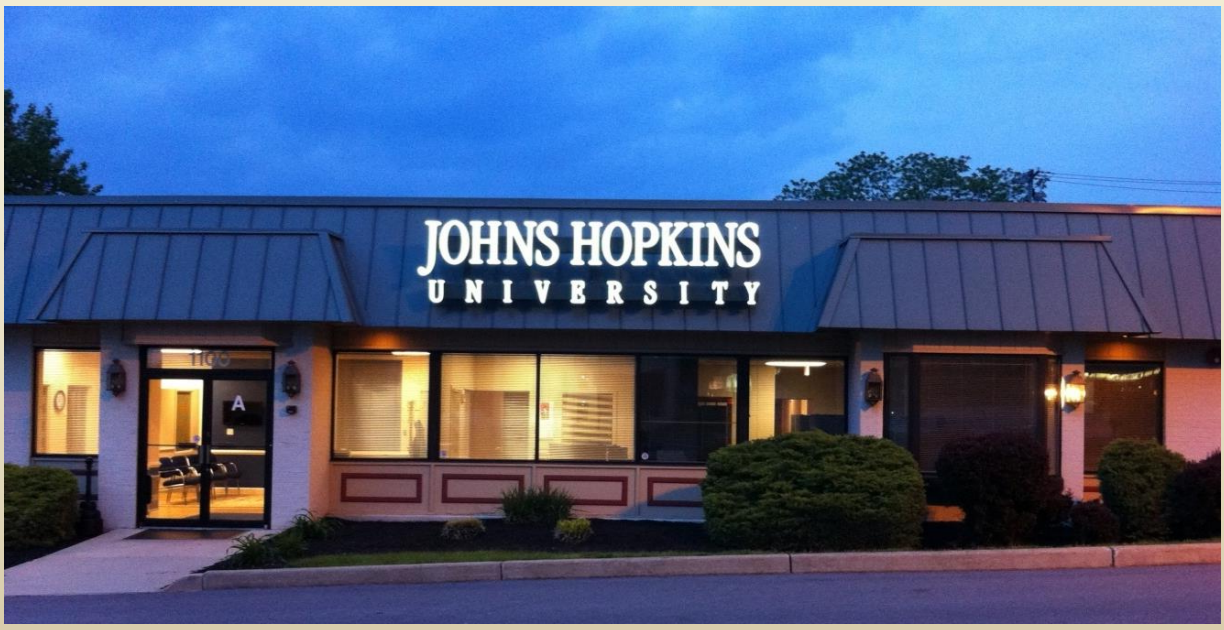
George W. Comstock Center for Public Health Research and Prevention

JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

1100 Dual Highway, Hagerstown, MD



For more information about the Comstock Center, visit our website: http://www.jhsph.edu/comstockcenter

The George W. Comstock Center for Public Health Research and Prevention
1100 Dual Highway, Suite A
Hagerstown, MD 21740
Phone: 301.791.1847, 301.733.8860, 301.797.3589
Fax: 301.791.3541

Center Director:
Josef Coresh, MD PhD
coresh@jhu.edu

Center Operations Director:
Melissa Minotti
mminott2@jhu.edu

In the Same Vein: Joe Coresh and the Comstock Professorship [YouTube Video]

Message from the Director

The George W. Comstock Center for Public Health Research and Prevention connects scientists, students, and staff at Johns Hopkins University with participants from Washington County, Maryland, to improve the evidence base for prevention efforts. The science aims to leave a lasting legacy of data and knowledge which will improve health and prevent disease in Washington County, nationally and internationally.

We benefit from nearly a century of innovation and collaboration between scientists and the community. New studies benefit from the data, experience and wisdom accumulated in previous studies.

Our research facility on 1100 Dual Highway realized the vision of sharing expertise across the full range of research activities, from large mail surveys and specimen bank studies to in-depth clinical research studies. Our strengths in clinic-based studies of heart disease, obesity, diabetes, aging, cognition, hearing, and sleep disorders will enhance our leading studies of cancer etiology as they require more in-depth molecular characterization. Equipment is shared across existing studies and welcomes new leading science.

Our staff, led by Ms. Melissa Minotti collect the highest quality data through an in-depth knowledge of the community and a commitment to respecting the participants' VIP status as the people who donate their time and experience.

We completed ARIC visit 6 with excellent retention and large neurocognitive and home heart rate monitoring ancillary studies. New and older cancer studies are doing well and we are launching new studies correction of hearing loss, healthy aging, and prevention of falls. We are proud to have over 35 outstanding staff in Hagerstown.

Faculty based at Johns Hopkins University are committed to designing the best possible studies and obtaining the funding to make them happen. I strongly believe that **data are the gift that keeps on giving** and thank everyone for their help in allowing us to advance prevention now and in the future.

Josef Coresh

Mission

To collect the highest quality data with the goal of advancing disease prevention by bringing together participants, staff, students and scientists in a partnership between Johns Hopkins University and Washington County, Maryland.

Core Values

- Participant respect as the source and ultimate beneficiary of prevention research
- Data quality, integrity and privacy
- Science in the service of people: Win some victories for humanity, big or small

Goals

- Complete ongoing studies' data collection
- Publish key results from ARIC visit 6 and its ancillaries (NCS, PET, MRI, Hearing) and obtain funding for visits eight to eleven.
- Complete new clinical trials: STURDY (Vitamin D and Falls Risk) and ACHIEVE (Aging and Cognitive Health Evaluation in Elders)
- Develop new studies in public health priority areas: pilot studies for a large community based study with remote data collection (i.e. mobile phones, accelerometers).
- Enhance partnerships with community health leaders: expand collaborative data research with Meritus Health; assist studies of the opioid epidemic
- Continue to expand the network of active investigators writing grants and high impact publications
- Use the George Comstock Professorship funds for innovative pilot studies and pursue center grants

CORE FACULTY

Lawrence Appel, MD, MPH (Medicine)
Josef Coresh, MD, PhD (Epidemiology)
Michelle Carlson, PhD (Mental Hygiene)
Jennifer Deal, PhD, MHS (Epidemiology)
Rebecca Gottesman, MD, PhD (Neurology)
Morgan Grams, MD, PhD (Nephrology)
Corinne E. Joshu, PhD, MPH (Epidemiology)
Frank Lin, MD, PhD (Otolaryngology)
Kunihiro Matsushita, MD, PhD (Epi.)
Erin Michos, MD, MHS (Cardiology)
Chiadi Ndumele, MD, MHS (Cardiology)
Elizabeth Platz, ScD, MPH (Epidemiology)
Naresh M. Punjabi, MD, PhD (Medicine)
Nicholas Reed, AUD (Otolaryngology)
Elizabeth Selvin, PhD, MPH (Epidemiology)
Jennifer Schrack, PhD (Epidemiology)
Kala Visvanathan, MBBS, MHS (Epi.)
Bruce Wasserman, MD (Radiology)

ASSOCIATES

Dan Arking, PhD (Human Genetics)
Alden Gross, PhD, MHS (Epidemiology)
Anna Kottgen, MD, DrMed (Epidemiology)
Mariana Lazo, MD, PhD, ScM (Medicine)
Wendy Post, MD, MS (Cardiology)
Tariq Shafi, MBBS, MHS (Nephrology)
Adrienne Tin, PhD (Epidemiology)

AFFILIATED FACULTY AT JOHNS HOPKINS

Marilyn Albert, MD (Neurology)
Shoshana Ballew, PhD (Epidemiology)
Terri Beaty, PhD (Epidemiology)
Karen Bandeen-Roche, MS, PhD (Biostatistics)
Kathryn Carson, ScM (Epidemiology)
David Celentano, ScD, MHS (Epidemiology)
Aravinda Chakravarti, PhD (Human Genetics)
Jeanne Clark, MD, MPH (Medicine)
Ciprian Crainiceanu, PhD (Biostatistics)

Cardiovascular Epidemiology Faculty and Students at American Heart Association

Cardiovascular Epidemiology Faculty and Students at Welch Center Seminar

Marie Diener-West, PhD (Biostatistics)
Adele Goman, PhD (Otolaryngology)
Eliseo Guallar, MD, DrPH (Epidemiology)
Sherita Hill Golden, MD, MHS (Medicine)
Stephen Juraschek, PhD, MD (Medicine)
Marc Halushka, MD, PhD (Pathology)
Felicia Hill-Briggs, PhD (Medicine)
Nisa Maruthur, MD, MHS (Medicine)
Seth Martin, MD, MHS (Cardiology)
Christine Mitchell, ScM (Epidemiology)
Mara M DeMarco, MHS, PhD (Epi.)
Edgar (Pete) Miller, MD, PhD (Medicine)
Noel Mueller, PhD (Epidemiology)
Casey Rebholz, PhD (Epidemiology)
Yingying Sang, MS (Epidemiology)
A. Richey Sharrett, MD, PhD (Epidemiology)
Paul T. Strickland, PhD (Environmental Health)
Moyses Szklo, MD, DrPH (Epidemiology)
Larisa Tereshchenko, MD, PhD (Cardiology)
David Thiemann, MD (Cardiology)
Mark Woodward, PhD (Epidemiology)
Hsin-Chieh (Jessica) Yeh, PhD (Medicine)

STUDENTS: Johns Hopkins Bloomberg School of Public Health, School of Medicine

Core faculty - Principal Investigators or supervisors of major projects at the Comstock Center in Hagerstown.
Associates - Principal Investigators or supervisors of major projects using Comstock Center data or staff where the main project is based outside Hagerstown.
Affiliated faculty - Investigators playing a major role in projects or papers using data generated at Comstock Center.

A Brief History of Health Research Collaboration in Washington County

In 1921, the Johns Hopkins University's Washington County Health Demonstration started. One of the first studies was the series of Hagerstown Morbidity Surveys, the first truly representative community health surveys. Other pioneering research studies were studies on child growth and dental caries in the 1930s.

In 1957, the National Cancer Institute established the Environmental Cancer Field Research Project in a building adjacent to the health department. However, when, after several years of data collection, none of the expected associations of cancers with geography developed, the National Cancer Institute decided to terminate the study and the building sat idle.

Former Location of Health Monitoring Unit

In 1962, the Johns Hopkins Training Center for Public Health Research was established. Early support of the Center came from a contract with the National Cancer Institute to conduct a private health census of the county to collect personal and housing information that would allow completion of the study of geographic and residential distribution of cancer cases. This 1963 census of ~90,000 residents was the basis for a series of health studies for many years and continues to be today. A large specimen bank study, Operation CLUE, was conducted in 1974 followed by a second county health census in 1975. The 1980s saw the launch of several large scale studies, including ARIC, CLUE II, and CHS. Following Dr. Comstock, the center was directed by Dr. Helzlsouer and since 2008 by Dr. Coresh. A new facility opened in 2011 at 1100 Dual Highway to merge all staff activities and expand the scope of research.

Former Location of Surveillance and Disease Prevention Unit

The Comstock Center collaborates with local health agencies including Washington County Health Department, Washington County Hospital (now called Meritus Medical Center), and Western Maryland Hospital Center. Washington County is an outstanding place to conduct health studies. It has a state-of-the-art hospital and medical community. Most importantly, the population has a high interest in health research and willingness to participate in projects that will benefit the advancement of medical knowledge in order to improve the health of future generations and society as a whole.

New Location of George W. Comstock Center in Hagerstown 1100 Dual Highway

Conducting Health Research in Washington County

Center staff based in Hagerstown, in the heart of Washington County, Maryland, have organized and collected data since 1921, accumulating a wealth of data that rivals or exceeds any other community in the world. Staff bring a wealth of experience and in depth knowledge of research methods and of the community.

Several leaders stand out for their contributions over the years. CLUE I data collection in 1974, was organized by Knud Helsing working closely with Drs. Cedric Garland, George Comstock and Abraham Lilienfeld. Sandra Clipp, MA, MPH led the staff operations during CLUE II, overseeing many studies from 1988 to 2010. Since 2010, Judith Hoffman-Bolton has managed existing and new CLUE studies, provided data analysis, and supervised CLUE staff. Joel Hill, MS played a key role in establishing the research center in downtown Hagerstown working closely with Drs. Comstock and Szklo. She hired, trained and supervised the staff in that unit for over a decade and subsequently established the staffing structure for the MESA study and, even after retirement, continued to teach on the Baltimore campus until her passing in 2014. Joel Hill mentored numerous staff, including Ms. Crowley, in the management of large epidemiologic studies. Patricia Crowley, MS has led the ARIC and CHS staff from 1999 to 2015. Since 2015, Ms. Melissa Minotti is the Center Operations Director in Hagerstown, coordinating activities of over 35 staff members. Over the decades the center's staff numbers have varied from over 100 during the active phase of the CLUE studies to less than a dozen. Dr. Comstock's observation that the center's staff are outstanding remains as true as ever.

Washington County Sociodemographic and Health Facts

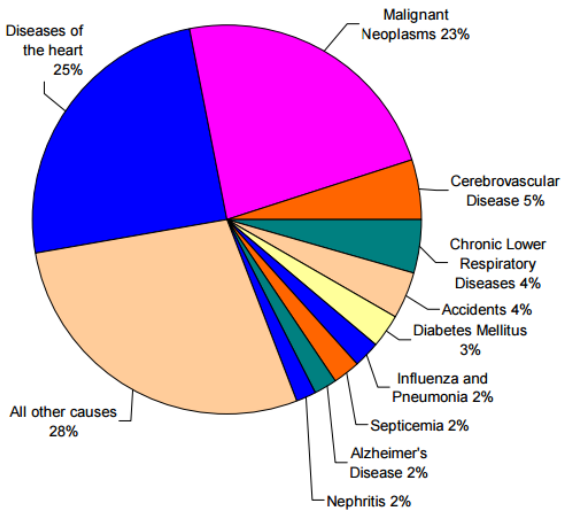
Total population: 149,588 in 2013
Racial distribution: 85% White,
11% Black, 4% Latino, Asian or other
Life expectancy: 78.1 years

Washington Monument, Washington Co, Md.
Built in 1827

Top 4 employment sectors:
(1) Services, (2) Retail trade, (3) Government,
(4) Manufacturing

Primary Causes of Death, 2009

Source: Maryland Vital Statistics



http://www.cscc.unc.edu/aric/

The Atherosclerosis Risk in Communities (ARIC) study recently celebrated its 30th anniversary. ARIC has emerged as a world leading study with enormous past contributions and tremendous potential for continued success over the next decades. Our web site features a video produced by the local TV station.

ARIC is a prospective epidemiologic study conducted in four U.S. communities, including Washington County, Maryland. Sponsored by the National Heart, Lung and Blood Institute, ARIC was originally designed to investigate the etiology and natural history of atherosclerosis, cardiovascular diseases, and its risk factors as well as medical care and disease by race, gender, location and date. ARIC data have also become an important resource for the study of all aging related diseases including dementia and cancer.

ARIC includes two components: cohort and community surveillance. The cohort component began in 1987. Each field center randomly selected and recruited approximately 4,000 individuals ages 45 to 64 from a defined population in their community. A total of 15,792 participants received an extensive examination, including medical, social and demographic data. These participants were reexamined every three years until 1996-98. Follow-up continued twice a year telephone to assess participants' health status, including hospitalization. A fifth follow-up visit was completed in 2011-2013 and future visits are underway (visit 6 2016-2017, visit 7 2018-2019).

The community surveillance component is designed to measure the community-wide occurrence of hospitalized cardiovascular disease. In 2015, routine community surveillance ended and a pilot study is rigorously evaluating automated record review's ability to validate medical diagnoses as a future form of surveillance.

To date, the ARIC project and ancillary studies have led to more than 2000 articles in peer-reviewed journals, and numerous abstracts and other summary reports of ARIC data at various national and international scientific conferences and meetings. ARIC is also participating in global consortia including the Emerging Risk Factor Collaboration, The Chronic Kidney Disease Prognosis Consortium (CKD-PC, led by Coresh at Hopkins) and the CHARGE genetics consortium.

The dedication of staff and participants has led to an annual follow-up rate of over 90% more than 30 years after recruitment. Follow-up will be valuable to 2030 and beyond.

Major Ancillaries

ARIC Neurocognitive Study (ARIC-NCS)

This study focuses on vascular disease, as a potentially preventable basis for cognitive decline and dementia. The study added extensive neurocognitive testing (~6,000 participants) and brain MRI imaging (~2,000 participants) to the 25-year follow-up visit of the ARIC cohort (Visit 5, 2011-2013) and again at 30-years (Visit 6, 2016-2017) and planned for 32 years (Visit 7, 2018-2019) across its four field centers. ARIC-NCS will be one of the largest studies in the world able to examine long term cognitive decline since ARIC participants completed three cognitive tests during visits 2 and 4 (1992-1995 and 1997-1999). Results will inform dementia prevention strategies by identifying vascular therapeutic targets, optimal timing for interventions and useful intermediate outcomes. The study will also clarify ethnic disparities in dementia burden. Dr. Coresh is the study principal investigator at Hopkins working closely with a large team of experts including Drs. Sharrett, Gottesman, and Albert.

ARIC PET Imaging Study

A brain PET scan with 18F-AV-45 had made it possible to identify accumulation of β-amyloid in the brain, thought to be the hallmark of Alzheimer's Disease. By imaging 300 ARIC participants in three field centers and continuing their follow-up cognitive evaluation, the study will determine: 1) whether vascular risk factors and markers, especially from midlife, are associated with increased β-amyloid binding, which would indicate that vascular disease directly contributes to Alzheimer's Disease changes in the brain, and 2) whether β-amyloid deposits in the brain *in combination* with vascular risk factors and markers contribute to cognitive impairments and development of dementia. The study was selected by the US President's office as one of the most meritorious and recently published its results in the prestigious JAMA. Dr. Gottesman is the principal investigator.

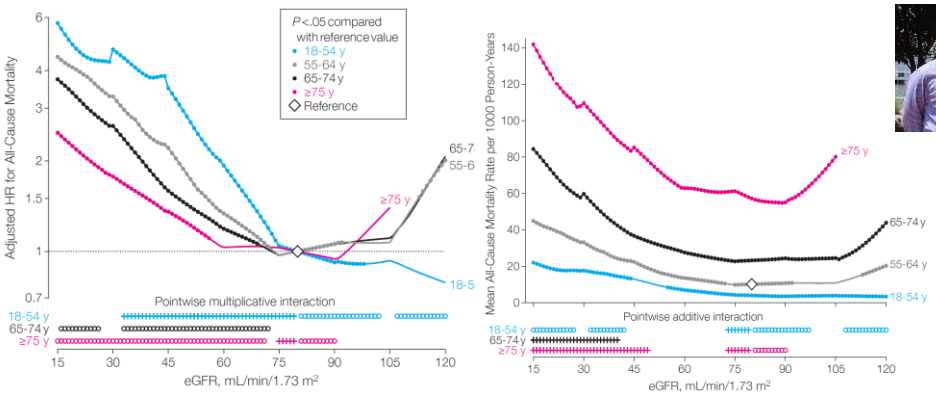
ARIC MRI Study

Using advanced image processing the MRI brain images in the ARIC-NCS study are used to directly quantify atherosclerosis in the brain to study its risk factors and consequences. Dr. Wasserman is the principal investigator.

Age and Association of Kidney Measures With Mortality and End-stage Renal Disease

Hallan SI ◆ Matsushita K ◆ Sang Y ◆ Mahmoodi BK ◆ Black C ◆ Ishani A ◆ Kleefstra N ◆ Naimark D ◆ Roderick P ◆ Tonelli M ◆ Wetzels JF ◆ Astor BC ◆ Gansevoort RT ◆ Levin A ◆ Wen CP ◆ Coresh J ◆ Chronic Kidney Disease Prognosis Consortium.

Context Chronic kidney disease (CKD) is prevalent in older individuals, but the risk implications of low estimated glomerular filtration rate (eGFR) and high albuminuria across the full age range are controversial. **Objective** To evaluate possible effect modification (interaction) by age of the association of eGFR and albuminuria with clinical risk, examining both relative and absolute risks. **Design, Setting, and Participants** Individual-level meta-analysis including 2 051 244 participants from 33 general population or high-risk (of vascular disease) cohorts and 13 CKD cohorts from Asia, Australasia, Europe, and North/South America, conducted in 1972-2011 with a mean follow-up time of 5.8 years (range, 0-31 years). **Main Outcome Measures** Hazard ratios (HRs) of mortality and end-stage renal disease (ESRD) according to eGFR and albuminuria were meta-analyzed across age categories after adjusting for sex, race, cardiovascular disease, diabetes, systolic blood pressure, cholesterol, body mass index, and smoking. Absolute risks were estimated using HRs and average incidence rates. **Results** Mortality (112 325 deaths) and ESRD (8411 events) risks were higher at lower eGFR and higher albuminuria in every age category. In general and high-risk cohorts, relative mortality risk for reduced eGFR decreased with increasing age; eg, adjusted HRs at an eGFR of 45 mL/min/1.73 m2 vs 80 mL/min/1.73 m2 were 3.50 (95% CI, 2.55-4.81), 2.21 (95% CI, 2.02-2.41), 1.59 (95% CI, 1.42-1.77), and 1.35 (95% CI, 1.23-1.48) in age categories 18-54, 55-64, 65-74, and75 years, respectively (*P*.05 for age interaction). Absolute risk differences for the same comparisons were higher at older age (9.0 [95% CI, 6.0-12.8], 12.2 [95% CI, 10.3-14.3], 13.3 [95% CI, 9.0-18.6], and 27.2 [95% CI, 13.5-45.5] excess deaths per 1000 person-years, respectively). For increased albuminuria, reduction of relative risk with increasing age was less evident, while differences in absolute risk were higher in older age categories (7.5 [95% CI, 4.3-11.9], 12.2 [95% CI, 7.9-17.6], 22.7 [95% CI, 15.3-31.6], and 34.3 [95% CI, 19.5-52.4] excess deaths per 1000 person-years, respectively by age category, at an albumin-creatinine ratio of 300 mg/g vs 10 mg/g). In CKD cohorts, adjusted relative hazards of mortality did not decrease with age. In all cohorts, ESRD relative risks and absolute risk differences at lower eGFR or higher albuminuria were comparable across age categories. **Conclusions** Both low eGFR and high albuminuria were independently associated with mortality and ESRD regardless of age across a wide range of populations. Mortality showed lower relative risk but higher absolute risk differences at older age.



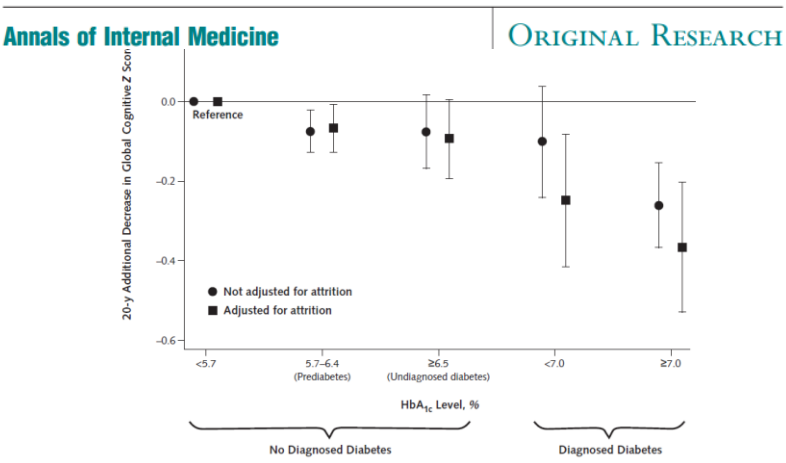
CKD Prognosis Data Coordinating Center (60 cohorts Including ARIC)
Kunihiro Matsushita, MD, PhD
Yejin Mok, MPH
Yingying Sang, MS
Morgan Grams, MD, PhD, MHS
Shoshana Ballew, PhD
Josef Coresh, MD, PhD

ORIGINAL CONTRIBUTION *Published in JAMA, 2012 Dec; 308(22): 2349-60. Epub 2012 Nov 01*

Diabetes in Midlife and Cognitive Change Over 20 Years: A Cohort Study

Rawlings AM ◆ Sharrett AR ◆ Schneider AL ◆ Coresh J ◆ Albert M ◆ Couper D ◆ Griswold M ◆ Gottesman RF ◆ Wagenknecht LE ◆ Windham BG ◆ Selvin E

Background: Type 2 diabetes is associated with dementia risk, but evidence is limited for possible associations of diabetes and prediabetes with cognitive decline.
Objective: To determine whether diabetes in midlife is associated with 20-year cognitive decline and to characterize long-term cognitive decline across clinical categories of hemoglobin A1c (HbA1c) levels.
Design: Prospective cohort study.
Setting: The community-based ARIC (Atherosclerosis Risk in Communities) study.
Participants: 13 351 black and white adults aged 48 to 67 years at baseline (1990 to 1992).
Measurements: Diabetes was defined by self-reported physician diagnosis or medication use or HbA1c level of 6.5% or greater. Undiagnosed diabetes, prediabetes, and glucose control in persons with diagnosed diabetes were defined by clinical categories of HbA1c level. Delayed word recall, digit symbol substitution, and word fluency tests were used to assess cognitive performance and were summarized with a global *Z* score.
Results: Diabetes in midlife was associated with a 19% greater cognitive decline over 20 years (adjusted global *Z*-score difference, 0.15 [95% CI, 0.22 to 0.08]) compared with no diabetes. Cognitive decline was significantly greater among persons with prediabetes (HbA1c level of 5.7% to 6.4%) than among those with an HbA1c level less than 5.7%. Participants with poorly controlled diabetes (HbA1c level 7.0%) had greater decline than those whose diabetes was controlled (adjusted global *Z*-score difference, 0.16; *P* 0.071). Longer-duration diabetes was also associated with greater late-life cognitive decline (*P* for trend 0.001). Rates of decline did not differ significantly between white and black persons (*P* for interaction 0.44).
Limitation: Single HbA1c measurement at baseline, 1 test per cognitive domain, and potential geographic confounding of race comparisons.
Conclusion: Diabetes prevention and glucose control in midlife may protect against late-life cognitive decline.




Andreea Rawlings, MS


A. Richey Sharrett, MD, PhD


Andrea Schneider, PhD


Josef Coresh, MD, PhD


Rebecca Gottesman, MD, PhD


Elizabeth Selvin, PhD, MPH

Annals of Internal Medicine. 2014, Dec;161(11):785-93. Epub 2014 Dec 2

Association Between Midlife Vascular Risk Factors and Estimated Brain Amyloid Deposition

Gottesman RF ◆ Schneider AL ◆ Zhou Y ◆ Coresh J ◆ Green E ◆ Gupta N ◆ Knopman DS ◆ Mintz A ◆ Rahmim A ◆ Sharrett AR ◆ Selvin E ◆ Wagenknecht LE ◆ Wong DF ◆ Mosley TH

Background: Midlife vascular risk factors have been associated with late-life dementia. Whether these risk factors directly contribute to brain amyloid deposition is less well understood.

Objective: To determine if midlife vascular risk factors are associated with late-life brain amyloid deposition, measured using florbetapir positron emission tomography (PET).

Design: Prospective cohort study.

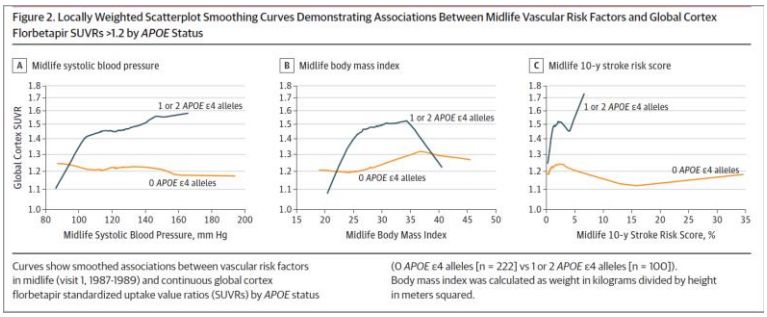
Setting: The community-based ARIC (Atherosclerosis Risk in Communities) PET Amyloid Imaging Study.

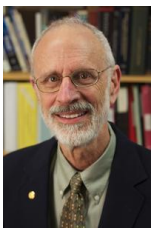
Participants: 346 participants without dementia in 3 US communities (Washington County, Maryland; Forsyth County, North Carolina; and Jackson, Mississippi) who have been evaluated for vascular risk factors and markers since 1987-1989 with florbetapir PET scans in 2011-2013. Positron emission tomography image analysis was completed in 2015.

Measurements: Standardized uptake value ratios (SUVRs)were calculated from PET scans and a mean global cortical SUVR was calculated. Elevated florbetapir (defined as a SUVR >1.2) was the dependent variable.

Results: Among 322 participants without dementia and with nonmissing midlife vascular risk factors at baseline (mean age, 52 years; 58%female; 43%black), the SUVR (elevated in 164 [50.9%] participants) was measured more than 20 years later (median follow-up, 23.5 years; interquartile range, 23.0-24.3 years) when participants were between 67 and 88 (mean, 76) years old. Elevated body mass index in midlife was associated with elevated SUVR (odds ratio [OR], 2.06; 95%CI, 1.16-3.65). At baseline, 65 participants had no vascular risk factors, 123 had 1, and 134 had 2 or more; a higher number of midlife risk factors was associated with elevated amyloid SUVR at follow-up (30.8%[n = 20], 50.4%[n = 62], and 61.2%[n = 82], respectively). In adjusted models, compared with 0 midlife vascular risk factors, the OR for elevated SUVR associated with 1 vascular risk factor was 1.88 (95%CI, 0.95-3.72) and for 2 or more vascular risk factors was 2.88 (95%CI, 1.46-5.69). No significant race × risk factor interactions were found. Late-life vascular risk factors were not associated with late-life brain amyloid deposition (for2 late-life vascular risk factors vs 0: OR, 1.66; 95%CI, 0.75-3.69).

Conclusion: An increasing number of midlife vascular risk factors was significantly associated with elevated amyloid SUVR; this association was not significant for late-life risk factors. These findings are consistent with a role of vascular disease in the development of Alzheimer disease.





A. Richey Sharrett, MD, DrPH

Yun Zhou, PhD

Andrea Schneider, PhD

Josef Coresh, MD, PhD

Rebecca Gottesman, MD, PhD

Elizabeth Selvin, PhD, MPH

Journal of the American Medical Association. 2017, April;317(14):1443-50. Epub 2017 May 9

ARIC Cancer Ancillary (ARIC-Ca)

This study creates an infrastructure in ARIC for population-based research on cancer incidence, mortality, recurrence, progression, and case-fatality.

ARIC was originally designed to investigate the etiology and natural history of atherosclerosis, and over the years, the focus has expanded to other major chronic diseases. In those efforts, repeated anthropometric, lifestyle, medical data, blood samples and biomarkers have been collected.

ARIC-Ca is sponsored by the National Cancer Institute to leverage this wealth of data, the racial diversity of the cohort, and the cohort's long-term follow-up to enhance cancer epidemiology research. This work builds on initial studies by Dr. Aaron Folsom on cancer incidence in ARIC. By 2006, 3,145 participants have been diagnosed with an incident first primary cancer. Cancer cases diagnosed from 2006 to the present are currently being ascertained. For cancer cases diagnosed in the past, information on stage, grade and other tumor characteristics is being collected. With funding from the Maryland Cigarette Restitution Fund, the collection of archived tissue blocks for Washington County Field Center participants who were surgically treated is being piloted. By 2016, 4,900 fully annotated incident cancer cases are expected.

Dr. Elizabeth Platz is the principal investigator. She works closely with Dr. Corinne Joshu and The ARIC Cancer Working Group which is charged with developing protocols for adjudicating cancer endpoints and with prioritizing cancer research in ARIC. Initial data collection is proceeding well, the study is validating cancer events and being recognized as a leading cohort with enormous value for its well characterized biological risk factors.

Study To Understand Fall Reduction and Vitamin D in You (STURDY)

Scientists from the Comstock Center recently received a major new grant from the National Institute on Aging (NIA) to design and implement an important new trial with the goal of testing whether vitamin D supplements prevent falls in older-aged persons. This trial will be conducted at 2 sites – George W. Comstock Center (GWCC) in Hagerstown and ProHealth in West Baltimore. Comstock investigators include Drs. Appel (PI of the trial), Dr. Michos (PI of the trial at GWCC), Dr. Coresh, and Dr. Miller. Pat Crowley and Melissa Minotti have prominent leadership roles in implementing this study, which will begin enrollment in 2015. Below is a brief description of the trial.

The public health burden of falls in older persons is substantial. Several lines of evidence suggest that vitamin D supplements might reduce the risk of falls, potentially by 25% or more in persons with low serum 25-hydroxyvitamin D [25(OH)D] levels. However, existing evidence is inconsistent and insufficient to guide policy. The trial is a seamless two-stage, Bayesian response-adaptive, randomized dose-finding trial designed to select the best dose of vitamin D supplementation and to potentially confirm the efficacy of that dose for fall prevention and other related outcomes. Participants will be community-dwelling adults, aged 70+ (~40% black, ~60% women), with a baseline serum 25(OH)D level of 10-25 ng/ml, who are at high risk for falling.

Lawrence Appel, MD, MPH

Erin Michos, MD, MHS

Josef Coresh, MD, PhD

Pete Miller, MD, PhD

Melissa Minotti, MPH

ACHIEVE Clinical Trial

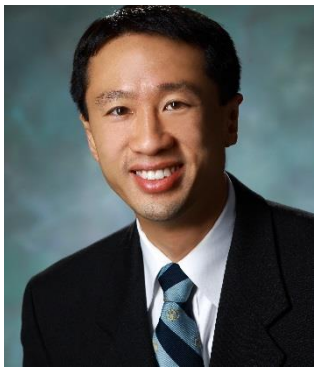
(Aging and Cognitive Health Evaluation in Elders Study)

Two-thirds of adults aged 70 and older have hearing loss and epidemiologic data now strongly suggest that age-related hearing loss is a risk factor for accelerated cognitive decline and incident dementia. Whether the use of hearing assistive technologies or other interventions could stem this decline is unknown.

Johns Hopkins University researchers Frank Lin, Josef Coresh and Jennifer Deal are leading efforts to answer this question through the Aging and Cognition Health Evaluation in Elders Study (ACHIEVE) Trial. The trial will randomize participants to either a best-practices hearing rehabilitation intervention designed by University of South Florida audiologists Terri Chisolm, Michelle Arnold, and Vicky Sanchez Williams and Johns Hopkins audiologist Nicholas Reed, or to an individualized successful aging intervention developed by University of Pittsburgh aging experts Nancy Glynn and Elizabeth Rodgers.

The ACHIEVE trial will be conducted at the four ARIC field sites, including Washington County, MD, and will enroll ~850 participants with mild to moderate hearing loss. Participants who are 70-84 years of age will be recruited from the existing ARIC cohort in addition to de novo participants from the surrounding communities. Study visits will include a baseline assessment, study intervention (hearing intervention or successful aging intervention), and a 6 months post-enrollment follow-ups for 3 years.

Funded by a National Institutes of Health Grant, the ACHIEVE trial will serve to definitively determine the effects of hearing rehabilitative treatment and a successful aging intervention on rates of cognitive decline in well-functioning and cognitively-normal older adults with hearing loss.



Frank Lin, MD, PhD

Josef Coresh, MD, PhD

Jennifer Deal, MHS, PhD

http://www.chs-nhlbi.org/

The Cardiovascular Health Study (CHS) is an observational study of risk factors for cardiovascular disease in adults 65 years or older that is funded by the National Heart, Lung and Blood Institute. The study is conducted four field centers, including Washington County, Maryland.

Starting in 1989, and continuing through 1999, participants underwent annual extensive clinical examinations. Measurements included traditional risk factors such as blood pressure and lipids as well as measures of subclinical disease, including echocardiography, carotid ultrasound, and cranial magnetic-resonance imaging (MRI).

At six-month intervals between clinic visits, and once clinic visits ended, participants were contacted by phone to ascertain hospitalizations and health status. The main outcomes are coronary heart disease, angina, heart failure, stroke, transient ischemic attack, claudication, and mortality. Participants continue to be followed for these events.

In 2006, surviving members of the cohort were invited to the clinic to participate in the "CHS All Stars" Study which examined physical and cognition function.

To date, more than 1500 research papers from CHS have been published and more than 120 ancillary studies are ongoing or complete. Participants, now 90-100+ years, delight the staff with their willingness to be interviewed over the telephone semi-annually so that we can learn about the health and hospitalizations of this older population.

Long-term function in an Older Cohort—The Cardiovascular Health Study All Stars Study

AB Newman ◆ AM Arnold ◆ MC Sachs ◆ DG Ives ◆ M Cushman ◆ ES Strotmeyer J Ding ◆ SB Kritchevsky ◆ PH Chaves ◆ LP Fried ◆ J Robbins

Objectives: To evaluate shared and unique risk factors for maintaining physical and cognitive function into the ninth decade and beyond. **Participants:** One thousand six hundred seventy-seven participants in the Cardiovascular Health Study All Stars Study, assessed in 2005/06. Median age was 85 (range 77-102), 66.5% were women, and 16.6% were black.

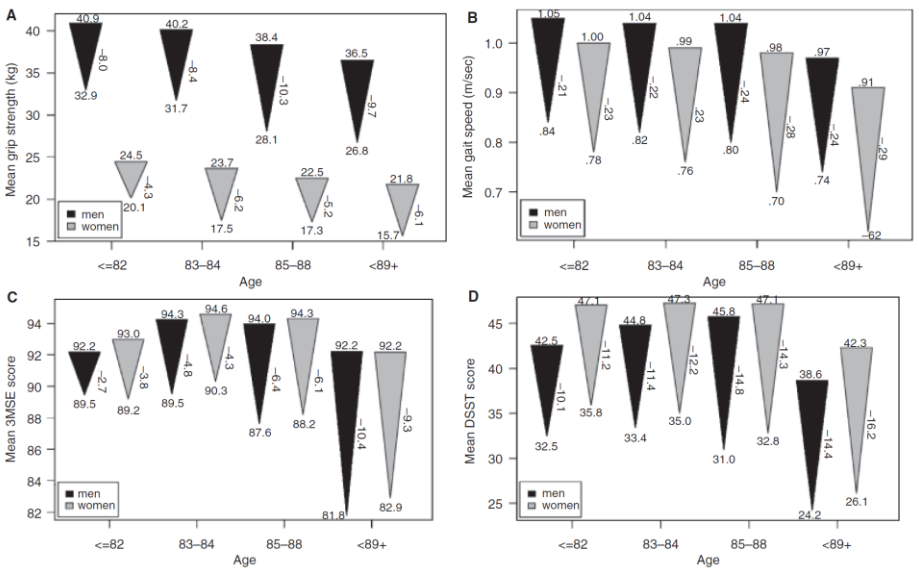
Measurements: Intact function was defined as no difficulty with any activities of daily living and a score of 80 or higher on the Modified Mini-Mental State Examination. **Results:** Of the 1,677 participants evaluated in both domains, 891 (53%) were functionally intact. Continuous measures of function, including the Digit Symbol Substitution Test and gait speed, showed that all groups, including the most functional, had declined over time. The functional group had less decline but also tended to have higher starting values and a higher baseline health profile. Women and individuals with greater weight had higher rates of physical impairment but not cognitive impairment. Risk factors common to both types of impairment included cardiovascular disease and hypertension.

Conclusion: Intact function was found in only approximately half of these older adults in the ninth decade and beyond. High baseline function and low vascular disease risk characterized functional aging.

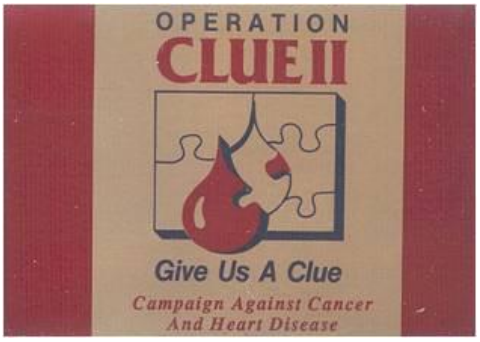
Michelle Carlson, PhD

Paulo Chaves, MD, PhD

Linda Fried, MD, MPH



Published in J Am Geriatr Soc. 2009 Mar;57(3):432-40. Epub 2009 Jan 29



http://www.jhsph.edu/comstockcenter/clue_research_activities.html

The CLUE studies were conducted in 1974 and 1989, under the direction of Dr. George Comstock with funding from the National Cancer Institute (NCI). The names of the cohorts were adopted from the campaign slogans *Give Us a Clue to Cancer and Heart Disease*. CLUE follow-up for cancer events and scientific productivity has been uninterrupted for nearly 40 years.

Volunteer participants were recruited across the county and surrounding communities. In 1974, approximately 26,000 participants enrolled from May to November. Blood samples were processed and stored as serum. In 1989, approximately 33,000 individuals participated in CLUE II which was conducted under the leadership of Drs. Helzlsouer and Comstock. Plasma and buffy coat were stored from the blood samples, and toenail samples and dietary questionnaires were also collected. In 1996, the CLUE II cohort began active follow-up with periodic mailing of health questionnaires. A recent pilot study examined the feasibility of collecting survey data via phone and web in addition to mailings.

More than 9,100 of the participants in CLUE I also participated in CLUE II, with 8,400 forming the Odyssey Cohort.

The CLUE studies have contributed to the understanding of cancer as well as other chronic diseases and are an integral member of the Cohort Consortium of the National Cancer Institute. Drs. Helzlsouer and Gallicchio lead work on vitamin D and rare cancers. Dr. Alberg leads studies of skin cancer. Dr. Visvanathan directs the study. Clue staff continues to meticulously steward the datasets, update approvals, conduct cancer surveillance and maintain the large specimen bank (>30 freezers and renovated lab), which is housed at Western Maryland Hospital Center.

A peripheral circulating TH1 cytokine profile is inversely associated with prostate cancer risk in CLUE II.

Nrupen A. Bhavsar ◆ Jay H. Bream ◆ Alan K. Meeker ◆ Charles G. Drake ◆ Sarah B. Peskoe ◆ Djeneba Dabitao ◆ Angelo M. De Marzo ◆ William B. Isaacs ◆ Elizabeth A. Platz

Background: TH1 cytokines, such as IFNg and TNFa, and potentially innate cytokines, such as IL6, can potentiate the immune response to tumor. Cytokines, such as IL1b, IL8, and IL10, may suppress anticancer immunity. Thus, we prospectively evaluated the association between peripheral-cytokine concentrations and prostate cancer.

Methods: We conducted an age-race matched case–control study (268 pairs) of incident prostate cancer in CLUE-II. We measured plasma IFNg, IL10, IL12p70, IL1b, IL6, IL8, and TNFa concentrations using an ultrasensitive multiplex kit. ORs and 95% confidence intervals (CI) were calculated using conditional logistic regression.

Results: The OR of prostate cancer decreased across quartiles of IFNg (highest vs. lowest quartiles: OR, 0.49; 95% CI, 0.30–0.81; Ptrend ¼ 0.006), TNFa (OR, 0.56; 95% CI, 0.33–0.96; Ptrend ¼ 0.01), and IL6 (OR, 0.46; 95% CI, 0.26–0.79; Ptrend ¼ 0.007). Higher TNFa (OR, 0.28; 95% CI, 0.09–0.85; Ptrend ¼ 0.01) and IL6 (OR, 0.20; 95% CI, 0.06–0.67; Ptrend ¼ 0.003) concentrations were associated with lower Gleason sum 7 disease risk. Other cytokines were not as clearly associated with risk.

Conclusions: Men with a prediagnostic circulating TH1 profile and higher IL6 may have a lower risk of prostate cancer, including aggressive disease. Whether this profile reflects (i) an intraprostatic immune environment in benign tissue that protects against prostate cancer, (ii) the immune milieu in response to a prostate adenocarcinoma that inhibits tumor growth and detectability, and/or (iii) a systemic immune profile that mediates the influence of modifiable factors on risk, warrants additional study.

Impact: Identifying specific inflammatory cytokines associated with prostate cancer may lead to improve prevention and treatment strategies.

Cancer Epidemiol Biomarkers Prev; 23(11); 2561–7. 2014 AACR.

Nrupen A. Bhavsar PhD, MPH

Elizabeth Platz, ScD, MPH

Table 3. Geometric mean concentration (pg/mL) of cytokines in prostate cancer cases and controls, CLUE II

Cytokine	Case (n = 268)	Control (n = 268)	P
IFNγ	0.72 (0.64–0.82)	0.92 (0.83–1.03)	0.004
IL10	2.53 (2.18–2.94)	2.59 (2.20–3.06)	0.82
IL12p70	2.64 (2.17–3.21)	2.72 (2.20–3.36)	0.84
IL1β	0.28 (0.24–0.32)	0.29 (0.25–0.34)	0.74
IL6	1.32 (1.23–1.43)	1.45 (1.33–1.58)	0.13
IL8	20.4 (18.0–23.2)	20.8 (18.3–23.7)	0.84
TNFα	7.50 (7.05–7.98)	8.27 (7.73–8.86)	0.04

DNA Repair Gene Variants in Relation to Overall Cancer Risk: A Population-based Study

AJ Alberg ◆ TJ Jorgenson ◆ I Rusczinski ◆ L Wheless ◆ YY Shugart ◆ Y Berthier-Schaad ◆ B Kessing ◆ J Hoffman-Bolton ◆ KJ Helzlsouer ◆ WH Kao ◆ L Francis ◆ RM Alani ◆ MW Smith ◆ PT Strickland

Abstract: The hypothesis that germ-line polymorphisms in DNA repair genes influence cancer risk has previously been tested primarily on a cancer site-specific basis. The purpose of this study was to test the hypothesis that DNA repair gene allelic variants contribute to globally elevated cancer risk by measuring associations with risk of all cancers that occurred within a population-based cohort. In the CLUE II cohort study established in 1989 in Washington County, MD, this study was comprised of all 3619 cancer cases ascertained through 2007 compared with a sample of 2296 with no cancer. Associations were measured between 759 DNA repair gene single nucleotide polymorphisms (SNPs) and risk of all cancers. A SNP was significantly associated with overall cancer risk. The association between rs2296675 and cancer risk was stronger among those aged ≤54 years old than those who were ≥55 years at baseline . OR were in the direction of increased risk for all 15 categories of malignancies studied, ranging from 1.22 for ovarian cancer to 2.01 for urinary tract cancers; the smallest P-value was for breast cancer. The results indicate that the minor allele of MGMT SNP rs2296675, a common genetic marker with 37% carriers, was significantly associated with increased risk of cancer across multiple tissues. Replication is needed to more definitively determine the scientific and public health significance of this observed association. ***Carcinogenesis (2012) doi: 10.1093***

Anthony Alberg, PhD, MPH

Kala Visvanathan, FRACPMBBS,MHS

Kathy Helzlsouer, MD, MHS

DNA Repair Gene Variants Associated with Benign Breast Disease in High Cancer Risk Women

TJ Jorgenson ◆ KJ Helzlsouer ◆ S Clipp ◆ J Hoffman-Bolton ◆ R Crum ◆ K Visvanathan

Abstract: Benign breast disease (BBD) is a risk factor for breast cancer and may have a heritable component. Deficient DNA repair has been implicated in breast cancer etiology and may exert its effect before BBD, a known precursor. The association between allelic variants in DNA repair genes and BBD was examined in a cohort of women in Washington County, Maryland. BBD was defined by two criteria: *(a)* a physician diagnosis of BBD or fibrocystic disease and/or *(b)* a benign breast biopsy. 3,212 women without BBD at baseline were genotyped for 12 candidate single nucleotide polymorphisms in seven DNA repair genes. Of these women, 482 subsequently reported a diagnosis of BBD. The Cox model was used to calculate hazard ratios (HR). Variant alleles of XRCC1 $Arg^{194}Trp$ (rs1799782) and ERCC4 $Arg^{415}Gln$ (rs1800067) were significantly associated with BBD [HR, 1.36; 95% confidence interval (95% CI), 1.06-1.74 and HR, 1.39; 95% CI, 1.09-1.76, respectively]. Similar estimates were also observed for each of the BBD criterion used. The BBD association for ERCC4 was even stronger among women with a family history of breast cancer (HR, 2.68; 95% CI, 1.52-4.66; $P_{interaction}$ = 0.02). This study suggests that variant alleles in DNA repair genes may modify BBD risk, a potential intermediate marker of breast cancer risk, particularly among high-risk subgroups. **Cancer Epidemiol Biomarkers Prev 2009;18(1):346–50**

Wen Hong (Linda) Kao, PhD, MHS

Judith Hoffman-Bolton

The BARI-Heart Study
Johns Hopkins University

The BARI-Heart study: The Effects of Intentional Weight Loss on Myocardial Injury, Structure and Function

The BARI-Heart study is a prospective, longitudinal cohort study of approximately 100 obese patients undergoing bariatric surgery, designed to evaluate the effects of weight loss on measures of myocardial injury, structure and function. It is being performed under the guidance of Principal Investigator Dr. Chiadi Ndumele, a cardiologist at the Johns Hopkins Ciccarone Center for Prevention of Heart Disease. BARI-Heart participants are currently being recruited from the population of patients who are intending to undergo bariatric surgery at the Meritus Weight Loss Center in Hagerstown, Maryland. Participants will be examined at two time points prior to bariatric surgery and at six months and twelve months post-bariatric surgery.

BARI-Heart participants will undergo various study procedures, including blood pressure measurement, electrocardiogram, overnight oximetry, physical activity monitoring, vascular assessment, and blood tests. The key testing component to the BARI-Heart study is the transthoracic echocardiogram, which will assess myocardial structure and function, including LV (left ventricular) ejection fraction, LV diastolic function, pulmonary arterial pressures, LV regional wall motion, LV strain, and RV systolic function. Additionally, the BARI-Heart study will measure pre and post surgery blood troponin levels with a high-sensitivity assay (hs-cTnT) to assess the relationship between weight loss and subclinical myocardial injury among individuals with baseline obesity.

Chiadi Ndumele, MD, MHS

Under the leadership of Dr. Naresh Punjabi, through funding from the National Heart, Lung and Blood Institute, a series of studies are being conducted to examine the relationship between sleep apnea, chronic disease and health outcomes. Methodological innovations are pursued in collaborations with biostatisticians Swihart, Crainiceanu and Caffo.

The following studies have been completed, and publications are ongoing:

- **GlycOSA study**, a multicenter randomized controlled trial to assess the effectiveness of continuous positive airway pressure in improving glycemic control in type 2 diabetic patients with newly diagnosed obstructive sleep apnea.
- **The Sleep Heart Health Study (SHHS)**, a multicenter cohort study to determine cardiovascular and other consequences of sleep-disordered breathing. Results have demonstrated associations with hypertension, stroke, heart disease and mortality.
- The Heart Biomarker Evaluation in Apnea Treatment (**HeartBEAT**) study, a multicenter randomized controlled trial to compare the effects of nocturnal supplemental oxygen and positive airway pressure versus optimized medical management on biomarkers of cardiovascular risk.
- **SOMNOS** (Sleep, Obesity and Metabolism in Normal and Overweight Subjects), a study to determine how moderate sleep apnea affects glucose metabolism.
- **HYPNOS** (Hyperglycemic Profiles in Obstructive Sleep Apnea: Effects of PAP Therapy), a study to determine how moderate sleep apnea affects glucose metabolism in diabetics.

HYPNOS is currently recruiting participants to examine the relationship between abnormalities in sleep due to a sleep apnea and diabetes, and how use of positive airway pressure (PAP) affects diabetes control.

Sleep-Disordered Breathing and Mortality: A Prospective Cohort Study

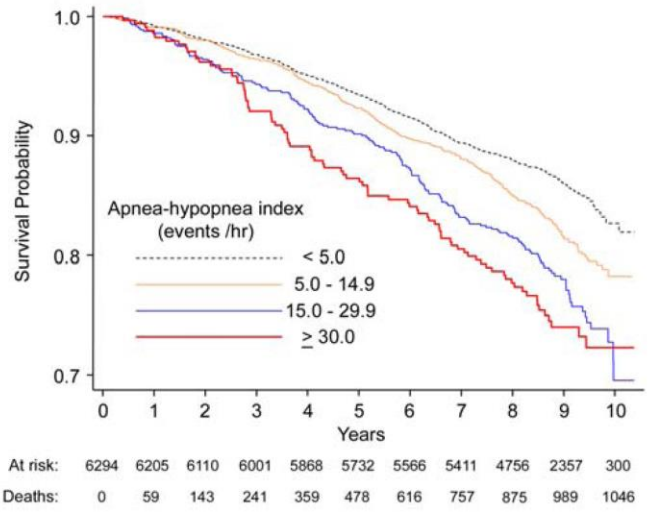
NM Punjabi ◆ BS Caffo ◆ JL Goodwin ◆ DJ Gottlieb
AB Newman ◆ GT O'Connor ◆ DM Rapoport ◆ S Redline
HE Resnick ◆ JA Robbins ◆ E Shahar ◆ ML Unruh ◆ JM Samet

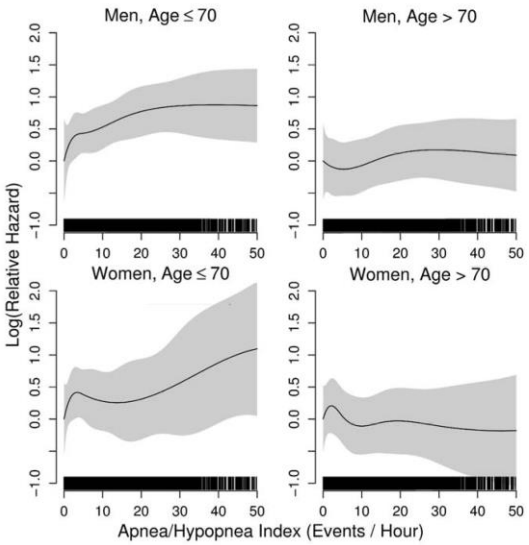
Naresh Punjabi, MD, PhD

Background: Sleep-disordered breathing is a common condition associated with adverse health outcomes including hypertension and cardiovascular disease.

Methods and Findings: We prospectively examined whether sleep-disordered breathing was associated with an increased risk of death from any cause in 6,441 men and women participating in the Sleep Heart Health Study. The average follow-up period for the cohort was 8.2 years during which 1,047 participants (587 men and 460 women) died. Compared to those without sleep-disordered breathing, the fully adjusted hazard ratios for all-cause mortality in those with mild, moderate, and severe sleep-disordered breathing were 0.93 (95% CI: 0.80–1.08), 1.17 (95% CI: 0.97–1.42), and 1.46 (95% CI: 1.14-1.86),respectively. Stratified analyses by sex and age showed that the increased risk of death associated with severe sleep-disordered breathing was statistically significant in men aged 40–70 y (hazard ratio: 2.09; 95% CI: 1.31–3.33). Measures of sleep-related intermittent hypoxemia, but not sleep fragmentation, were independently associated with all-cause mortality. Coronary artery disease–related mortality associated with sleep disordered breathing showed a pattern of association similar to all-cause mortality.

Conclusions: Sleep-disordered breathing is associated with all-cause mortality and specifically that due to coronary artery disease, particularly in men aged 40–70 years with severe sleep-disordered breathing.





Spline models: the apnea-hypopnea index to the log relative hazard for all-cause mortality

GEORGE W. COMSTOCK PROFESSORSHIP
IN EPIDEMIOLOGY ENDOWED 2012
TO SUPPORT CENTER ACTIVITIES
INAUGURAL PROFESSOR JOSEF CORESH, MD, PHD, MHS
Johns Hopkins Bloomberg School of Public Health

2015 YouTube Video
In the Same Vein:
Joe Coresh and the
Comstock Professorship

W.H. Linda Kao Memorial Fund Established 2015

January 12, 1972 — June 15, 2014

Dr. Kao was known as a brilliant scientist, generous mentor, as well as a caring and thoughtful friend and family member. In the Comstock Center, she was a co-Director of the CLUE Study and led genetic investigations in the ARIC study. Her seminal scientific discoveries were in the genetics of chronic kidney disease (CKD), but the depth and breadth of her too-brief career included over 200 published articles and reviews (cited over 8,000 times) spanning genetic and non-genetic risk factors for cardiovascular diseases.

First and foremost, Dr. Kao was a rigorous epidemiologist who could often be heard talking about the importance of "the science," regardless of the paper's outcome. She received numerous accolades, including the Award for Scientific Achievement by the Maryland National Kidney Foundation (2014) and a Top 10 Clinical Research Achievement in 2013 by the Clinical Research Forum. As a mentor, she won the prestigious AMTRA mentoring award (2006). In the weeks before she passed away, Dr. Kao continued to meet with and correspond with mentees. In all areas of her life, Dr. Kao was caring, selfless, practical, and efficient. She prioritized relationships with her colleagues, friends, and family above all else.

W.H. LINDA KAO MEMORIAL FUND

Linda's family and friends have established an endowed fund at the Bloomberg School of Public Health and the Department of Epidemiology. Annual distributions from this fund shall be used to support the research and academic activities of faculty or trainees who embody the following qualities:

- Excellence in research or teaching
- Selfless assistance to others
- Inner strength in the face of adversity

Inaugural W.H. Linda Kao Scholar: Nisa Maruthur, MD, MHS

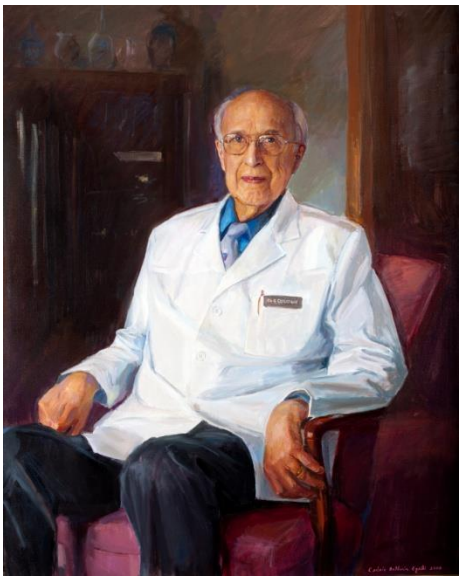
W.H. Linda Kao Collaboration Award: Adrienne Tin, PhD, MS

George Wills Comstock MD DrPH

(1915–2007) was a world-renowned public health physician, epidemiologist and educator. He obtained his medical degree from Harvard in 1941, joined the U.S. Public Health Service in 1942, and during 21 years of service conducted seminal community-based research into tuberculosis control. In 1962, Dr. Comstock founded the Johns Hopkins Training Center for Public Health Research and Prevention in Washington County, Maryland.

For the next 42 years, Comstock led research studies on numerous public health problems, primarily cancer and heart disease. Dr. Comstock also served as editor-in-chief of the American Journal of Epidemiology from 1979 to 1988 and was on faculty of the Johns Hopkins Bloomberg School of Public Health for 50 years.

In 2005, the Hopkins center in Hagerstown was renamed The George W. Comstock Center for Public Health Research and Prevention. Dr. Comstock frequently quoted these words from Horace Mann: "**I beseech you to treasure up in your hearts these my parting words: Be ashamed to die until you have won some victory for humanity.**" This struck him as the main purpose of living; as Comstock said, "**Most of us aren't going to win any big victories, but we can win little ones every day, and they mount up.**" In 2018, the center has two large clinical trials and expanded to the entire building at Dual Highway.




JOHNS HOPKINS
UNIVERSITY
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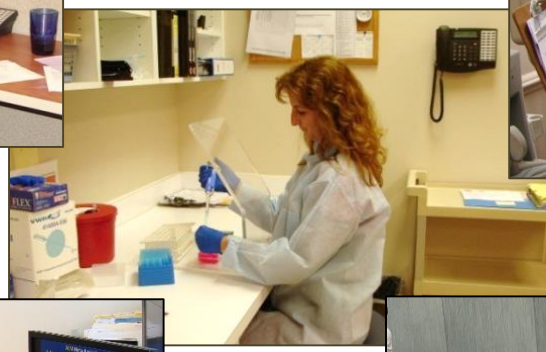

Comstock Center Organizational Chart

Director: Josef Coresh
Operations Director: Melissa Minotti
~37 staff members & ~12 core faculty

Main Research Studies

ARIC
Coresh
ARIC Cancer
Platz/Joshu
CAC
Matsushita
EyeDOC
Abraham
PET & Sleep
Spira & Gottesman

ACHIEVE
Lin & Coresh

STURDY
Appel

CHS
Carlson

SOMNOS
Punjabi

CLUE Studies
Kala Visvanathan
Supervisor:
Judith Hoffman-Bolton

Training & Public Health Activities
Director:
Moyses Szklo

Research Clinic Staff

Clinical Staff
8 staff members

Cardiac Evaluation
Echocardiography
Cardio Ankle Vascular Index
Blood Pressure

Cognitive Assessment
4-8 interviewers

Telephone Interviewing
6-8 interviewers

Medical Records Abstraction
4-6 abstractors

Data & Administration
Admin Coordinator
Data Manage
IT Support:
Automated Equipment Inc.

Affiliated Organizations

Study Specific Operations Committees have authority within each study (e.g. CLUE Serology Committee)

JHSPH Epidemiology Dept. Administration, Financial and Human Resouces Support & Staff

Community Advisors:
Earl Stoner (Wash. Co. Health Dept.)
Allen Twigg (Meritus Med Center)
Affiliated Faculty:
Principal Investigators
Public Health Leaders