ACC Events Bulletin

Penn Medicine

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ABRAMSON CANCER CENTER

March 19, 2018

Upcoming Events

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The Real Cost of the US Health Care System

High drug prices as well as the excessive use of imaging and surgical procedures, and excessive administrative burdens contribute the majority to America's health care overspending compared to Europe, argues policy expert Ezekiel J. Emanuel, MD, PhD, chair of the department of Medical Ethics and Health Policy at the Perelman School of Medicine at the University of Pennsylvania, and member of the Abramson Cancer Center, in an editorial in JAMA.

Americans average a whopping $9,403 per person in annual health care spending, which is much more than the per-capita health spending in other wealthy, aging countries—Germans and Dutch, for example, average $5,182 and $5,202 respectively. But while America's higher prices tend to get most of the attention in analyses of its health care overspending, there are also big differences in the volumes of health care purchases.

"There are twice as many caesarean deliveries per capita in the United States compared to the Netherlands, for example," Emanuel said. "That difference in volume clearly is a major contributor to the overall spending discrepancy—$62 per capita for caesareans in the US vs. $9 in the Netherlands."

In the editorial, Emanuel noted that administrative costs are another big contributor, accounting for $752 per-capita of Americans' annual health care spending, versus just $208 in the Netherlands, and $232 in Germany. He argued that health care policy in America should take aim at these major drivers of excessive spending, which could free up hundreds of billions of dollars for better social uses.

The editorial referenced a new analysis from other researchers in the same issue of JAMA which included a comparison of health care expenditures in the U.S. and ten other wealthy countries, most in Europe, and showed that on a per-capita basis, the U.S. spends roughly twice as much as these peer countries. Using the data from this analysis as well as from other sources, Emanuel highlighted several key drivers of this huge spending difference.

One consists of high-price, high-volume surgical procedures such as caesareans, knee and hip replacements, coronary artery bypasses, and angioplasties. Americans per-capita spend 2 to 6 times more on these procedures than their peer country counterparts. "Just the top 25 of these high-margin, high-volume procedures, with cost differences of $20-$40 per capita, explains approximately 20 percent of the per-capita healthcare spending difference between the U.S. and other high-income countries," Emanuel said.

Administrative bloat in the U.S. is a second major spending driver, with per-capita costs that are three to five times higher than costs in peer countries.

Medical imaging procedures, meaning mostly CT scans and MRIs, are a third major driver of spending differences, and also involve both high prices and high volumes. "CT scans alone account for $220 in annual per-capita spending in the U.S., compared to $23 per-capita in the Netherlands for example," he writes.

The fourth major driver, pharmaceuticals spending, is the only one where high prices are the dominant factor. Americans spend $1,443 per capita on pharmaceuticals, versus $566 for Swedes, for example, yet this huge excess is almost entirely due to higher U.S. prices, not higher volume.

Doctors, too, cost more in America; their average salary is higher than the averages in most peer countries. Yet Americans' net per-capita spending on doctors' salaries isn't much greater than in peer countries, because there are proportionately fewer doctors in the U.S. "There are just 2.6 physicians per 1,000 citizens in the U.S., whereas in Germany the ratio is 4.1 per 1,000 and in Sweden 4.2 per 1,000," Emanuel said. "The difference in per-capita spending on doctors' salaries accounts for only 4 percent of the overall health spending gap."

Emanuel emphasized that the four largest drivers of excess U.S. spending — high-price-high-volume

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The Real Cost of the US Health Care System

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procedures, administrative bloat, excessive medical imaging, and pharmaceutical spending — account for about two-thirds of the overall per-capita spending gap, and thus should be the prime targets of cost-reduction policies.

Such policies should include government regulation to force down drug prices; mandatory shared decision-making among doctors to reduce the overuse of expensive procedures and imaging; Medicare-style reference pricing to lower per-procedure costs; and automated/electronic record-keeping to reduce administrative costs.

Even if such policies were to achieve proportionately only a modest amount of reduction, they would liberate very large sums, given the scale of the problem. "If we in the United States could lower the prices and per-capita volumes of our CT scans, MRIs, and just the top 25 high-volume-high-price surgical procedures to those of the Netherlands, for example, we would see savings of about $425 per capita, or a total of $137 billion," Emanuel said.

Of the many alternative uses that could be made of that much money, he added, probably none could be worse than its current wastage on unnecessary — and often risky — medical procedures.

Article: The Real Cost of the US Health Care System. Emanuel EJ. JAMA. 2018 Mar 13;319(10):983-985.

Source: Penn Medicine Communications

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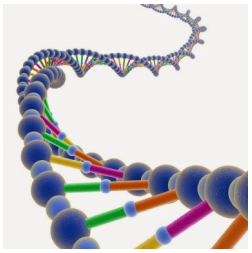

Epigenetics of the Aging Brain

Although certain genetic variants increase the risk of Alzheimer's disease (AD), age is the strongest known risk factor. But the way in which molecular processes of aging predispose people to AD, or become impaired in AD remains a mystery.

A team of researchers from PSOM, publishing in Nature Neuroscience, profiled the epigenomic landscape of AD brains, specifically in one of the regions affected early in AD, the lateral temporal lobe. They compared these to both younger and elderly cognitively normal control subjects. The team described the genome-wide enrichment of a chemical modification of histone proteins that regulates the compaction of chromosomes in the nucleus (called acetylation of lysine 16 on histone H4, or H4K16ac for short).

Changes to the way H4K16ac is modified along the genome in disease versus normal aging brains may signify places for future drug development. Because changes in H4K16ac govern how genes are expressed, the location and amount of epigenetic alterations is called the "epigenetic landscape."

"This is the first time that we have been able to look at these relationships in human tissue by using donated postmortem brain tissue from the Penn Brain Bank," said Shelley Berger, PhD, a professor of Cell and Developmental Biology in PSOM, a professor of Biology in the School of Arts and Sciences, and a member of the Abramson Cancer Center's Tumor Biology Program. "Our results establish the basis for an epigenetic link between aging and Alzheimer's disease."

Berger, also the director of the Penn Epigenetics Institute, Nancy Bonini, PhD, a professor of Biology, and Brad Johnson, MD, PhD, an associate professor of Pathology and Laboratory Medicine, are co-senior authors of the new study.

H4K16ac is a key modification in human health because it regulates cellular responses to stress and to DNA damage. The team found that, while normal aging leads to increasing H4K16ac in new positions along the genome and an increase in where it is already present, in great contrast, AD entails losses of H4K16ac in the proximity of genes linked to aging and AD. In addition, the team discovered an association between the location of H4K16ac changes and genetic variants identified in prior AD genome-wide association studies.

A three-way comparison of younger, older, and AD brain tissue revealed a specific class of H4K16ac changes in AD compared to normal age-established changes in the brain. This finding indicates that certain normal aging changes in the epigenome may actually protect against AD and when these goes awry, a person may become predisposed to AD.

"These analyses point to a new model of Alzheimer's disease. Specifically it appears that AD is not simply an advanced state of normal aging, but rather dysregulated aging that may induce disease-specific changes to the structure of chromatin – the combination of histone proteins and DNA." said first author Raffaella Nativio, PhD, a post-doctoral fellow in Berger's lab.

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Seminars and So Forth

Monday 3/19/18 **12:00 pm**
Genetics Distinguished Seminar
"Understanding and manipulating RNA-protein interactions in human disease." Gene Yeo, PhD, MBA, Professor of Cellular and Molecular Medicine, UC San Diego
BRB II/III Glen Gaulton Auditorium

Tuesday 3/20/18 **12:00 pm**
Distinguished Lecture in Cancer Research
"Mitochondria control cancer and immunity." Navdeep S. Chandel, PhD, David W. Cugell, MD, Professor, Professor of Medicine (Pulmonary and Critical Care) and Cell and Molecular Biology, Feinberg School of Medicine, Northwestern University
BRB II/III Glen Gaulton Auditorium

Tuesday 3/20/18 **4:00 pm**
Immunology Colloquium
"Using single-cell transcriptional approaches to elucidate the ontogeny of T cell memory." John Chang, MD, PhD, Associate Professor of Medicine, UC San Diego School of Medicine
CRB Austrian Auditorium

Tuesday 3/20/18 **4:00 pm**
CHOP CCCR Oncology Seminar Series
"Restoration of spermatogenesis after chemotherapy-induced infertility." Sandra W. Ryeom, PhD, Associate Professor, Cancer Biology, PSOM
CTRB 1200B (CHOP)

Wednesday 3/21/18 **12:00 pm**
CT3N Seminar
"Polymeric Nanomaterials for Therapeutic Delivery and Regenerative Engineering" Hai-Quan Mao, PhD, Professor of Materials Science and Engineering, Johns Hopkins University
SCTR 10-146AB

Wednesday 3/21/18 **12:00 pm**
Berkman Lectureship in Palliative Care
"Palliative Care Futurist: Matching Care to Our Patients' Needs." Diane Meier, MD, FACP, Director of the Center to Advance Palliative Care; Vice Chair for Public Policy and Professor of Geriatrics and Palliative Medicine, Icahn School of Medicine at Mount Sinai
JMEC Law Auditorium

Thursday 3/22/18 **12:00 pm**
Gastroenterology Seminar Series
"Epithelial differentiation and immune function in the gastrointestinal mucosa." Ezra Burstein, MD, PhD, Division Chief, Professor of Internal Medicine, UT Southwestern Medical Center
901 BRB II/III

Thursday 3/22/18 **12:00 pm**
Radiation Oncology Seminar Series
"Individualized Decision Making Through Treatment Response in Esophageal Cancer." Steven H. Lin, MD, Associate Professor, Radiation Oncology, MD Anderson Cancer Center
SCTR 8-146AB

Monday 3/26/18 **12:00 pm**
Pathology & Laboratory Medicine Grand Rounds
"The Nicholas Gonatas Memorial Lecture." John P.A. Ioannidis, MD, C.F. Rehnborg Chair in Disease Prevention Professor of Medicine, Professor of Health Research and Policy, Professor (by courtesy) of Statistics and Biomedical Data Science, Stanford University School of Medicine
CRB Austrian Auditorium

Monday 3/26/18 **1:00 pm**
CHOP Normal and Malignant Hematopoiesis
RAG Seminar Series
"Leukemia Stem Cells: To Seek and Destroy." Monica Guzman, PhD, Associate Professor of Pharmacology in Medicine, Weill Cornell Medicine
CTRB 1100B (CHOP)

Monday 3/26/18 **3:00 pm**
SPATT Annual Carl F. Schmidt Lecture
"Blood from a Petri Dish." George Q. Daley, MD, PhD, Dean, Harvard Medical School; Caroline Shields Walker Professor of Medicine and Professor of Biological Chemistry and Molecular Pharmacology, Harvard Medical School
BRB II/III Glen Gaulton Auditorium

Tuesday 3/27/18 **12:00 pm**
Distinguished Lecture in Cancer Research
"Population and tumor heterogeneity in the context of cancer genomics and precision medicine." John D. Carpten, PhD, Professor and Chair of Translational Genomics, Keck School of Medicine, University of Southern California
Caplan Auditorium, 37th & Spruce Sts. (Wistar)

Wednesday 3/28/18 **8:00 am**
Abramson Cancer Center Grand Rounds
"Tissue Regeneration In Mice: From Phenotype to Genes to Small Molecules." Ellen Herber-Katz, PhD, Resident Faculty Professor, Lankenau Institute for Medical Research
SCTR Rubenstein Auditorium

Thursday 3/29/18 **12:00 pm**
Gastroenterology Seminar Series
TBA. Marcia Cruz-Correa, MD, PhD, Professor of Medicine & Biochemistry, University of Puerto Rico Comprehensive Cancer Center
901 BRB II/III

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Philanthropy & Development Corner

Fuel the ImmunoRevolution

Penn's ImmunoRevolution began over 20 years ago. At the time, there were limited funding opportunities for novel ideas, and researchers relied on philanthropy to fuel innovation.

Now, the breakthrough has arrived. But we still need more partners – more revolutionaries – to join the fight, so Penn's Abramson Cancer Center can design more treatments that put more patients' cancer into remission.

Share the video and story with your friends and family. And if you know of anyone that would be interested in learning more about the ImmunoRevolution and supporting this fundraising campaign, please be in touch with Tricia Bruning at tbruning@upenn.edu or 215-898-1033.

Funding Opportunities

RFA-CA-18-019/ RFA-CA-18-020 Research Answers to National Cancer Institute's (NCI) Provocative Questions (R01/R21)

LOI: 30 days prior to application date

Application Deadlines: 6/29/2018, 10/30/2018

The purpose of these FOAs is to support research projects designed to solve specific problems and paradoxes in cancer research identified by the National Cancer Institute (NCI) Provocative Questions initiative. These problems and paradoxes phrased as questions are not intended to represent the full range of NCI's priorities in cancer research. Rather, they are meant to challenge cancer researchers to think about and elucidate specific problems in key areas of cancer research that are deemed important but have not received sufficient attention.

R01: https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-18-019.html

R21: https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-18-020.html

PAR-18-704/PAR-18-703 Innovative Basic Research on Adducts in Cancer Risk Identification and Prevention (R01/R21)

LOI: 30 days prior to application date

Application Deadline: 7/11/2018

These FOAs encourage research projects focused on adducts to cellular macromolecules as indicators of exposures to cancer risk factors relevant to human populations. The priority is on projects that will focus on adductomic approaches, i.e., address some aspects of the totality of adducts. These projects should explore the basic aspects of adducts/adductomics that may have a potential utility in cancer detection, cancer prevention, and/or assessing cancer risks.

R01: https://grants.nih.gov/grants/guide/pa-files/PAR-18-704.html

R21: https://grants.nih.gov/grants/guide/pa-files/PAR-18-703.html

PA-18-713 Administrative Supplements for Research on Sexual and Gender Minority (SGM) Populations

Application Deadline: 5/7/2018

The National Institutes of Health (NIH) Office of the Director announces the availability of administrative supplements to expand existing research to focus on Sexual and Gender Minority (SGM) health.

SGM populations include, but are not limited to, lesbian, gay, bisexual, and transgender people, and individuals with differences or disorders of sexual development (sometimes referred to as "intersex" or as specific diagnoses). This trans-NIH effort, which involves multiple Institutes, Centers and Offices from across NIH, is intended to encourage investigation in this growing, field of research. To increase our collective understanding of the broad range of research needed to address the unique health issues of SGM populations, the supplement will focus on areas of research interest, including, but not limited to: studies on increased disease risk; mental, behavioral and social health; approaches to personalized medicine; access to care; reproductive and sexual development; neurological and cognitive development; and resilience.

https://grants.nih.gov/grants/guide/pa-files/PA-18-713.html

KMT2D Mutations

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Accumulation of intercellular amyloid plaques and neurofibrillary tangles are the two hallmarks of AD that drive the death of neurons and the corresponding loss of cognitive abilities. However, expression of plaques and tangles is very late in the development of AD, while epigenome alterations might occur much earlier and represent targets to attack with medications.

The authors emphasized that this study does not suggest a cure for AD, but rather the possibility of finding ways to prevent nerve cell death and enhance the quality of aging. Their upcoming experiments aim to discover the physiological changes that cause the decrease of H4K16ac specifically in AD brains, but not in normal-aged brains.

Article: Dysregulation of the epigenetic landscape of normal aging in Alzheimer's disease. Nat Neurosci. 2018 Mar 5

Source: Penn Medicine Communications

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