Biomedical Research... from fundamental discovery to clinical effectiveness and patient outcomes research.

Ann Bonham, PhD
Chief Scientific Officer
October 2013
• The National Landscape

• The Research Ecosystem

• Biomedical Research – from fundamental discovery to comparative effectiveness to patient outcomes research
Affordable Care Act

One Hundred Eleventh Congress of the United States of America
AT THE SECOND SESSION
Begun and held in the City of Washington on Tuesday, the fifth day of January, two thousand and ten

In Act
Enacted the Patient Protection and Affordable Care Act.
Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE—This Act may be cited as the "Patient Protection and Affordable Care Act.

As used in this Act—The purposes of this Act in its entirety:

TITLE I—QUALITY, AFFORDABLE HEALTH CARE FOR ALL AMERICANS
Subtitle A. Improvements in Health Care Coverage for All Americans Sec. 201, Amendment

The Changing Face of America

<table>
<thead>
<tr>
<th>Year</th>
<th>White</th>
<th>Black</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>65%</td>
<td>13%</td>
<td>16%</td>
</tr>
<tr>
<td>2030</td>
<td>56%</td>
<td>3%</td>
<td>23%</td>
</tr>
<tr>
<td>2050</td>
<td>47%</td>
<td>13%</td>
<td>29%</td>
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</tbody>
</table>

Democratization of data

Increasing calls for accountability for research $
The Emerging Research Ecosystem

Increased use of Registries

Increased voice of patients and vulnerable groups

Fundamental Science Breakthroughs Continue:

12 Cancer Types
- Leukemia
- Breast
- Kidney
- Lung Squamous
- Colon
- Glialblastoma
- Bladder
- Rectum
- Ovarian
- Lung Adenocarcinoma
- Head and Neck
- Endometrial

$1000 Genome

NIH National Institutes of Health
Turning Discovery Into Health

Fact sheet: Impact of Sequestration on the National Institutes of Health

Genetic Alliance

Big Data

Increased use of Registries
Convergence around CER/PCOR

Building national infrastructure to conduct CER

IOM CTSA Recommendations

FDASIA 2012 “a turning point for patients”

National Minority Quality Forum
Getting there....but we’re not there yet...

Remaining Challenges
1. Cost

Cost effectiveness in clinical care: Yes!

Cost effectiveness in PCORI CER: NO!
2. Making effective use of EHR

In Search of a Data-in-One, Electronic Health Record-Linked, Multicenter Registry — How Far We Have Come and How Far We Still Have to Go

Keith Marolo
Cincinnati Children's Hospital Medical Center, keith.marolo@chmc.org

Caveats for the Use of Operational Electronic Health Record Data in Comparative Effectiveness Research

William R. Hersh, MD,* Mark G. Weiner, MD,† Peter J. Embi, MD, MS; Judith R. Logan, MD, MS; Philip O. Payne, PhD;† Einer V. Bernstam, MD, MSE; Harold P. Lehmann, MD, PhD; George Hripcsak, MD, MS; Timothy H. Hartzog, MD, MS; James J. Cinquina, MD,** and Joel H. Saltz, MD, PhD††

Abstract: The growing amount of data in operational electronic health record systems provides unprecedented opportunity for its reuse for many tasks, including comparative effectiveness research. However, there are many caveats to the use of such data. Electronic health record data from clinical settings may be inaccurate, incomplete, transformed in ways that undermine their meaning, unrecoverable for research, of unknown provenance, of insufficient granularity, and incompatible with research protocols. However, the quantity and real-world nature of these data provide impetus for their use, and we develop a list of caveats to inform would-be users of such data as well as provide an informatics roadmap that aims to assure this opportunity to augment comparative effectiveness research can be best leveraged.

Key Words: comparative effectiveness research, electronic health records, clinical data, codal (claims) data, biomedical informatics (Med Care 2013;51: S30-S37)
3. Disaggregating clinical risk and research risk

Aug 6, 2013
Office for Human Research Protections
Department of Health and Human Services
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

Submitted to www.regulations.gov

RE: Notice of a Department of Health and Human Services Public Meeting and Request for Comments on Matters Related to the Protection of Human Subjects and Research Studying Standard of Care Interventions, 78 FR 38343, Docket number HHS-OPHS-2013-0004

The Association of American Medical Colleges (AAMC) welcomes the opportunity to respond to the above-referenced notice and request for comments from the Department of Health and Human Services (HHS) and Office for Human Research Protections (OHRP) on matters related to research studying standard of care interventions. The AAMC is a not-for-profit association representing all 143 accredited U.S. and 17 accredited Canadian medical schools; nearly 400 major teaching hospitals and health systems, including 51 Department of Veterans Affairs medical centers; and 90 academic and scientific societies. Through these institutions and organizations, the AAMC represents 128,000 faculty members, 75,000 medical students, and 110,000 resident physicians.

The AAMC is pleased that OHRP is engaging the broad research, clinical, and bioethics community to respond to the complex issues that arose in the context of the SUPPORT study.

We are concerned that the controversy significantly and unnecessarily damaged the public's trust in the commitment of physicians and scientists to protecting human research subjects, especially those in high-risk populations.

We underscore the critical need for empirical research to refine the "standard of care" and clarify the definition of reasonable foreseeable risk and provide informative and reasonable guidelines for disclosure of those risks. We urge HHS and OHRP to undertake a process for providing guidance that supports and facilitates comparative effectiveness research to determine safety. The OHRP actions and subsequent controversy in response to the SUPPORT study has created a chilling environment for clinical research, and may essentially discourage future clinician researchers from engaging in rigorous research to generate evidence for the best possible treatments for critically ill patients, leaving physicians in the difficult position of making clinical judgments on a case-by-case basis. This will be a disservice to future patients and to the public.
4. Addressing disparities

The Potential Impact Of Comparative Effectiveness Research On The Health Of Minority Populations

By C. Daniel Mullins, Eberechukwu Onukwugha, Jesse L. Cooke, Arif Hussain, and Claudia R. Baquet

ABSTRACT Minorities suffer more frequently and more severely from many diseases than do non-Hispanic whites, and they often receive lower-quality care, which leads to poorer health outcomes. Given the diversity of the US population, comparative effectiveness research should capture the health outcomes of racial and ethnic minority groups and investigate whether disparities reflect variations in care or different responses to treatment. We recommend a number of measures to ensure that this research addresses the needs of minorities, including greater attention to subgroup analysis. We also recommend the increased recruitment of minorities for clinical trials, and such measures as using community health workers to translate research results in ways that will increase their relevance to minority patients.

PUBLIC HEALTH

Confronting the Sorry State of U.S. Health

Ronald Bayer, Amy L. Fairchild, Kim Hopper, Constance A. Nathanson

In January 2013, the U.S. National Research Council (NRC) and Institute of Medicine (IOM) issued U.S. Health in International Perspective: Shorter Lives, Poorer Health, a stunning depiction of how, over the past four decades, the comparative health status of Americans has declined (1). The report applied a term, commonly used to describe the relative deprivation of social groups, to the nation as a whole: the “U.S. health disadvantage.” How can this be death or disability only as a result of personal misbehavior and environmental conditions?” The average American can either “change his personal bad habits or stop complaining. . . . Beneficent Government cannot—indeed, should not—do it for him.” (7)

As the individual-focused approach was pursued in the United States, studies from England gave new life to the more-than-century-old understanding of the relation between wealth and health. In a nation with
5. Workforce:

- Protected time
- Ability to work in teams
- Incentives and recognition
## CTSA Analysis of CER Needs: Implications for Workforce

### Table 1
Summary of 2009 Survey of 33 CTSA Institutions on CER Capacity and Needs

<table>
<thead>
<tr>
<th>Research Area/Competency</th>
<th>No to minimal research</th>
<th>Need large growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electronic health record (EHR) research</td>
<td>58%</td>
<td>53%</td>
</tr>
<tr>
<td>Registry (clinically-based) research</td>
<td>52%</td>
<td>50%</td>
</tr>
<tr>
<td>Economic analyses</td>
<td>46%</td>
<td>34%</td>
</tr>
<tr>
<td>Working with other research networks (HMO, CTRN, CCOP)</td>
<td>49%</td>
<td>25%</td>
</tr>
<tr>
<td>Stakeholder involvement in planning and implementing research</td>
<td>55%</td>
<td>19%</td>
</tr>
<tr>
<td>Practice-based research network research</td>
<td>39%</td>
<td>31%</td>
</tr>
<tr>
<td>Analysis of approaches for delivering and/or paying for care</td>
<td>46%</td>
<td>23%</td>
</tr>
<tr>
<td>Clinical trials (especially effectiveness)</td>
<td>30%</td>
<td>38%</td>
</tr>
<tr>
<td>Cohort studies, long-term observational</td>
<td>33%</td>
<td>34%</td>
</tr>
</tbody>
</table>
Physician shortage may mean fewer physician scientists

Projections prepared by the Lewin Group for the AAMC Center for Workforce Studies.
How can the AAMC help?
AAMC Guiding Principle: Improving Health through the Full Spectrum of Research

- Fundamental Discovery Research
- Comparative Effectiveness
- Patient Outcomes Research
- Implementation & Quality Improvement Research
- Health Care Delivery Research
- Community & Population Research
- Health Equity
- Diverse Workforce
Implementation and Dissemination Research: Translating research to practice and health

National Institutes of Health Approaches to Dissemination and Implementation Science: Current and Future Directions

Russell E. Glasgow, PhD, Cynthia Vinson, MPA, David Chambers, DPhil, Muin J. Khoury, MD, PhD, Robert M. Kaplan, PhD, and Christine Hunter, PhD

To address the vast gap between current knowledge and practice in the area of dissemination and implementation research, we address terminology, provide examples of successful applications of this research, discuss key sources of support, and highlight directions and opportunities for future advances. There is a need for research testing approaches to scaling up and sustaining effective interventions, and we propose that further advances in the field will be achieved by focusing dissemination and implementation research on 6 core values: rigor and relevance, efficiency, collaboration, improved capacity, and cumulative knowledge. (Am J Public Health. 2012;102:1274–1281. doi:10.2105/AJPH.2012.300755)

Despite the demonstrable benefits of many new medical discoveries, we have done a surprisingly poor job of putting research findings into practice. The ultimate goal of new discoveries is to enhance human health, yet most discoveries are slow to or never fulfill this promise. The challenge of moving health research innovations from discovery to practice is complex and multifaceted. Only about 65% of individuals older than 65 years have received the pneumococal vaccine despite evidence that it offers life-extending protection for the elderly.

BALANCING DISCOVERY WITH IMPLEMENTATION

As argued by Woolf and Johnson, the return on investment for dissemination and implementation research dwarfs the return on investment for new discovery. In the current federal research model, basic biomedical and behavioral research accounts for the lion’s share of funding. To close the gap between research and practice, we must build a robust system for disseminating and implementing research findings.
ADVOCACY: New messaging, new partnerships, new venues
Call on Congress: Stop Sequestration Cuts to NIH

The letters were signed by nearly 200 leaders of medical schools and teaching hospitals

What is worse is that these cuts come at a time when the loss of clinical revenue and the potential for further cuts in federal funding to teaching hospitals will severely limit the ability of our medical schools and teaching hospitals to invest in their research mission and to train the next generation of physicians and scientists.

Enacted and proposed cuts in NIH funding threaten current and emerging basic research opportunities across the country, as well as the clinical studies that are essential to bring scientific discoveries from the bench to the bedside. Further, these cuts also will discourage young people from careers in medical research, risking the loss of the next generation of innovators and their ideas.

We recognize the enormous challenges facing our nation’s economy and acknowledge the difficult decisions that must be made to restore our country’s fiscal health. Nevertheless, we strongly believe that NIH is an essential element in ensuring the health and well-being of the American people and remaining competitive in today’s global information and innovation-based economy.

We urge Congress and the Administration to work together on a solution that avoids sequestration and the devastating impact these continued across-the-board cuts to NIH and academic medicine will have on the millions of Americans depending on the lifesaving research conducted at the nation’s medical schools and teaching hospitals.

Sincerely,
Graduate, MD-PhD students, and postdocs support funding for NIH

1135 individual responses as of 10/25/13
September-October 2013 Newsletter

PCORI & Patient- and Population-Centered Research

As I See It

Sequestration and budgetary uncertainties weigh heavily on the minds of all of us in academic medicine and on the minds of all those committed to improving health through research. Amidst this environment of severely constrained resources and understandable angst, some encouraging trends in the research community endure. There is a palpable convergence of energy, attention and resources towards engaging persons in the community and patients as part of the research community. This convergence is playing out:

- via funding mechanisms, such as the new PCORI-funded clinical

Ann Bonham, Ph.D.
Chief Scientific Officer
AAMC
PCORI Webinar - August 26, 2013
Discussion on the Patient-Centered Outcomes Research Institute (PCORI) peer review process for the PCORI Cooperative Agreement Funding Announcement: National Patient Centered Clinical Research Network Clinical Data Research Networks (CDRN).

View the slides PDF

Watch the webinar ▶

Webinar Q&A PDF

Now available on the AAMC website at https://www.aamc.org/initiatives/rocc/webinars/
AAMC Research on Care Community (ROCC)

Goal
To improve quality, safety, health equity & efficiency by integrating effectiveness and implementation research into clinical practice.

Pilot projects
Peer-to-Peer site visits
Annual face-to-face meetings
Other forms of technical assistance
ROCC Members
Research On Care
Spotlight

Featuring: Catarina Kiefe, MD, PhD

Chair and Professor of Quantitative Health Sciences and Medicine, University of Massachusetts Medical Center

In addition to leading the University of Massachusetts’ Quantitative Health Sciences and Medicine Department, Dr. Kiefe also serves as an Adjunct Professor of Medicine and Biostatistics at the University of Alabama at Birmingham and chairs the Committee on Publications and Presentations within the CARDIA Study (or Coronary Artery Risk Development in Young Adults).

After earning her PhD in Mathematics from the State University of New York at Stony Brook on a Fulbright Scholarship, Dr. Kiefe went on to medical school at the University of California, San Francisco, beginning a lifelong blending of abstract and quantitative rigor with service in the medical community.

She was a resident in Internal Medicine at the University of Minnesota Hospitals and Clinics, and her research has advanced the field of clinical epidemiology, quality measurement and outcomes research, and health services to disadvantaged populations. Recently she has collaborated on a project funded by the NHLBI which focused on understanding the determinants and outcomes of transitions from hospital to community after serious coronary events. Concurrently she has been investigating health disparities in the Deep South due to lack of high quality colorectal and lung cancer care. In July she published a study on the risk of cognitive decline as a result of heart failure and possible cardiac treatments that would help prevent cognitive impairment. She also serves as Co-Editor-in-Chief of Medical Care, while editing and peer reviewing for many others.

Dr. Kiefe has been credited with leading UMMS’s Department of Quantitative Health Sciences to its rank in the top 25 research medical schools in the U.S. and achieving its goal of bridging basic research and clinical services because of her interdisciplinary background.

The AAMC would like to recognize Dr. Kiefe’s contribution to health disparities research and clinical epidemiology.
ROCC Grants

Deadline: October 30, 2013

Improved Outcomes for All

- Health Disparities
  - Challenge Awards
    - 6 awards

- Quality Improvement

- EHR
  - Development Pilots
    - 12 awards

Collaboration
Addressing Disparities
Health Equity Research and Policy

The AAMC recognizes that health inequities and disparities are deeply rooted in the conditions in which people are born, grow, live, work, and age. Achieving a state where all people have the same opportunity to attain their full health potential—a state of health equity—will require solutions discovered through the full spectrum of research and collaborative efforts from all sectors of society.

Read AAMC's Academic Medicine Perspective on Making Equity a Value in Value-Based Health Care

Challenge Award Announcement

AAMC is conducting the Learning Health System Challenge and Planning Awards to recognize programs within the AAMC membership that are building key aspects of learning health systems. Learn more about the Learning Health System Challenge and Planning Awards

Join us for a discussion on the awards>

Member Spotlight

Vanderbilt University’s Health Equity research draws on science from across the spectrum. From biorepositories, to cohort studies, to community-engaged research. Vanderbilt’s multi-pronged strategy holds promise for understanding and eliminating inequities in health.

Read the full profile>

News and Updates
Assessing Investment and Impact of Research

Cost of Research

Investment in Research

Outcomes of Research
Background

Medical research has vastly improved the health of average Americans and has bolstered both the length and quality of their lives. The statistics from federally funded research are compelling: the survival rate for children with the most common childhood leukemia is now 90 percent, the five-year breast cancer survival rate has increased from 75 percent in the mid 1970s to 90 percent in 2011, and chronic disability among American veterans has dropped nearly 30 percent since 1985, and the list goes on. Few would deny the social and economic benefits of medical advances made possible through research. After all, healthier Americans are more productive, and the academic research enterprise itself supports many jobs.

Nevertheless, recent trends call for the research community to revisit how we analyze and communicate the investment in and impact of research: new expectations and technologies such as social media platforms for advancing transparency, the national political and economic debate, and the engagement of patient advocacy groups in assessing research efficiency and impact.
AAMC Research Evaluation Initiative

New & Shifting Research Models Expert Panel
Health Equity Research Expert Panel
Foundational & Basic Science Research Expert Panel

Measuring research
A guide to research evaluation frameworks and tools

Susan Guthrie, Watu Wamae, Stephanie Diepeveen, Steven Wooding and Jonathan Grant

RAND EUROPE
AAMC Research Evaluation Initiative

The current political and economic climate is marked by downward pressures on government spending and rising calls for accountability. Federal investments in biomedical research have not escaped this trend, with policymakers and other stakeholders taking a hard look at returns on investment and seeking assurances that resources are being used efficiently. Pressures to communicate the quality, productivity and appropriateness of research investments are likely to intensify as budget pressures increase. In this environment, institutional leaders must be able to demonstrate the value of their research portfolio.

To support our member institutions as they consider how to respond, the AAMC commissioned a team of experts at RAND Europe to conduct a systematic review of existing approaches to research evaluation. This report, “Measuring Research: A Guide to Research Evaluation Frameworks and Tools,” summarizes current conceptual models for how biomedical research translates into academic, health, social and economic impacts, and profiles 14 robust research evaluation initiatives already in use. The report also includes a detailed and critical review of a host of tested and documented assessment tools, which can be used for various purposes—whether for advocacy, accountability, analysis or internal allocation decision-making. A related research brief is also available.

We hope this report will serve as a starting point for considering a breadth of measures to capture the full value of research and ultimately account for investments in the medical research enterprise.

Research Evaluation Expert Panels
AAMC COST Initiative

RATIONAL

• Defending our investment with data
• Bringing attention to shifting costs to our members
• Creating shared definitions
• Providing an educational tool for faculty and other stakeholders
• Making the investment – value case
Data inputs from the AAMC Cost of Research Initiative

Revenues

- Sponsored program revenue
- Sponsored program F&A Recovery
- Other research funding sources

Expenditures

- Sponsored program direct expenditures
- Institutional cost sharing of direct expenditures
- Institutionally funded direct expenditures

Subsidies

- F&A cost covered by institutional funds
- SSF and recharge center subsidies

Research P&L Model Output

- Research revenues by external and internal funding sources
- Direct and indirect expenditures by external and internal funding source
- Calculation of research organization net performance

- Additional key research metrics and KPIs can be calculated from the P&L such as the Institutional Research Subsidy (% of institutional funds expended to support externally funded research):

Net Income (Loss)

Direct Research Revenues

Cost Sharing ($)
Institutional Research Investment (%)
In the End.....
All persons and populations should benefit from the way we conduct, view, value, and participate in medical research.
THANK YOU
Planning for the Future
Registries and CER?

The randomized trial is one of the most powerful tools clinical researchers possess, a tool that enables them to evaluate the effectiveness of new (or established) therapies while accounting for the effects of unmeasured confounders and selection bias by indication. Randomized trials, especially large, multinational, have transformed medical practice. Thanks to randomized trials, we no longer, for example, treat acute myocardial infarction with lidocaine and nitrates. Instead we use panels, as well as inadequate representativeness. What good are trials if the results aren’t applicable to real-world patients and if, because of excessive expense, they can be used to answer only a tiny fraction of our important clinical questions? One possible solution is to use registries and CER. The randomized trial is one of the most powerful tools clinical researchers possess, a tool that enables them to evaluate the effectiveness of new (or established) therapies while accounting for the effects of unmeasured confounders and selection bias by indication. Randomized trials, especially large, multinational, have transformed medical practice. Thanks to randomized trials, we no longer, for example, treat acute myocardial infarction with lidocaine and nitrates. Instead we use panels, as well as inadequate representativeness. What good are trials if the results aren’t applicable to real-world patients and if, because of excessive expense, they can be used to answer only a tiny fraction of our important clinical questions? One possible solution is to use registries and CER.

Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction

Ole Frotter, M.D., Ph.D., Bo Lagerqvist, M.D., Ph.D., Goran K. Olvecrona, M.D., Ph.D., Elmir Omerovic, M.D., Ph.D., Thorarinn Gudnason, M.D., Ph.D., Michael Maeng, M.D., Ph.D., Mikael Aasa, M.D., Ph.D., Oskar Anger, M.D., Fredrik Calais, M.D., Mikael Danielewicz, M.D., David Erlinge, M.D., Ph.D., Lars Hellsten, M.D., Ulf Jensen, M.D., Ph.D., Agneta C. Johansson, M.D., Anna Kåre, M.D., Johan Nilsson, M.D., Ph.D., Lotta Robertson, M.D., Lennart Sandhäll, M.D., Ivar Sjögren, M.D., Ollie Ostlund, Ph.D., Jan Harne, M.D., Ph.D., and Stefan K. James, M.D., Ph.D.

ABSTRACT

BACKGROUND
The clinical effect of routine intracoronary thrombus aspiration before primary percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI) is uncertain. We aimed to evaluate whether thrombus aspiration reduces mortality.

METHODS
We conducted a multicenter, prospective, randomized, controlled, open-label clinical trial, with enrollment of patients from the national comprehensive Swedish Coronary Angiography and Angioplasty Registry (SCAAR) and endpoints evaluated through national registries. A total of 7244 patients with STEMI undergoing PCI were randomly assigned to manual thrombus aspiration followed by PCI or to PCI only. The primary end point was all-cause mortality at 30 days.