MESA Project Officer Report

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MESA Project Officer
Division of Cardiovascular Sciences
National Heart, Lung, and Blood Institute

MESA Steering Committee

April 25, 2013

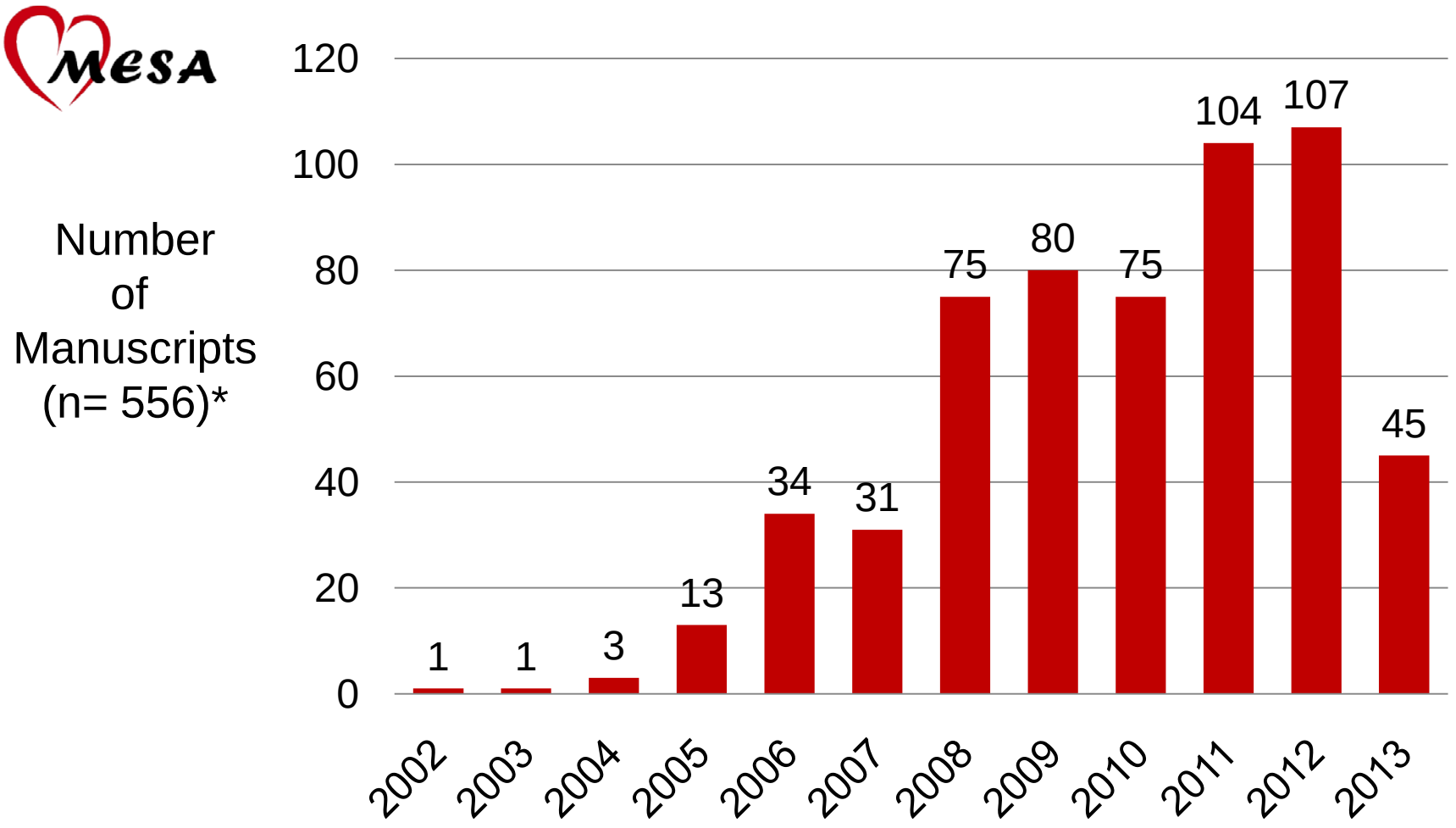
NIH National Heart, Lung, and Blood Institute

Items to cover

- Status report for MESA
  - Publications
  - Report to OSMB
- MESA renewal
- NIH and NHLBI
  - Budget
  - Other

Publications

MESA Publications



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* Published or in press as of April 18, 2013.

A few publication themes

- Connections among variables
- Extracting new variables from images
- Collaborations
- Potentially impactful findings
- Insights beyond CVD
- Amazing range of findings

Selected MESA findings

Peralta CA, Katz R, Bonventre JV, Sabbisetti V, Siscovick D, Sarnak M, Shlipak MG. Associations of Urinary Levels of Kidney Injury Molecule 1 (KIM-1) and Neutrophil Gelatinase-Associated Lipocalin (NGAL) With **Kidney Function Decline** in the Multi-Ethnic Study of Atherosclerosis (MESA). Am J Kidney Dis. 2012;60(6):904-911.

Kawasaki R, Xie J, Cheung N, Lamoureux E, Klein R, Klein BE, Cotch MF, Sharrett AR, Shea S, Wong TY: for MESA. **Retinal Microvascular Signs** and Risk of **Stroke**: The Multi-Ethnic Study of Atherosclerosis (MESA). Stroke. 2012;43(12):3245-3251.

Yeboah J, Rodriguez CJ, Stacey B, Lima JA, Liu S, Carr JJ, Hundley WG, Herrington DM. **Prognosis** of Individuals with **Asymptomatic Left Ventricular Systolic Dysfunction** in the Multi-Ethnic Study of Atherosclerosis (MESA). Circulation. 2012;126(23):2713-2719.

Selected MESA findings

Vaidya D, Dobs A, Gapstur SM, Golden SH, Cushman M, Liu K, Ouyang P. Association of baseline sex **hormone levels** with baseline and longitudinal changes in **waist-to-hip ratio**: Multi-Ethnic Study of Atherosclerosis. Int J Obes (Lond). 2012;36(12):1578-1584.

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**. Age and association of kidney measures with mortality and end-stage renal disease. JAMA. 2012;308(22):2349-2360.

Harris B, Klein R, Jerosch-Herold M, Hoffman EA, Ahmed FS, Jacobs DR Jr, Klein BE, Wong TY, Lima JA, Cotch MF, Barr RG. The association of systemic **microvascular changes** with **lung function and lung density**: a cross-sectional study. PLoS One. 2012;7(12) Dec 20. [Epub ahead of print]

Nettleton JA, [TNTC]. Meta-analysis investigating associations between healthy diet and fasting glucose and insulin levels and modification by Loci associated with glucose homeostasis in data from **15 cohorts**. Am J Epidemiol. 2013;177(2):103-115.

Selected MESA findings

Champaneri S, Xu X, Carnethon MR, Bertoni AG, Seeman T, Desantis AS, Diez Roux A, Shrager S, Golden SH. **Diurnal salivary cortisol** is associated with body mass index and waist circumference: The multiethnic study of atherosclerosis. Obesity (Silver Spring). 2013;21(1):E56-63.

Carroll JE, Diez-Roux AV, Adler NE, Seeman TE. Socioeconomic factors and leukocyte **telomere length** in a multi-ethnic sample: Findings from the multi-ethnic study of atherosclerosis (MESA). Brain Behav Immun. 2013;28:108-114.

Duprez DA, Hearst MO, Lutsey PL, Herrington DM, Ouyang P, Barr RG, Bluemke DA, McAllister D, Carr JJ, Jacobs DR Jr. Associations among **lung function, arterial elasticity**, and circulating endothelial and inflammation markers: the multiethnic study of atherosclerosis. Hypertension. 2013;61(2):542-548.

Kanaya AM, Dobrosielski DA, Ganz P, Creasman J, Gupta R, Nelcanti V, Vogel-Claussen J, Herrington D. Glycemic associations with endothelial function and biomarkers among **5 ethnic groups**: the multi-ethnic study of atherosclerosis and the mediators of atherosclerosis in **South Asians** living in America studies. J Am Heart Assoc. 2013;2(1)e004283. doi: 10.1161/JAHA.112.004283.

Selected MESA findings

Budoff MJ, Young R, Lopez VA, Kronmal RA, Nasir K, Blumenthal RS, Detrano RC, Bild DE, Guerci AD, Liu K, Shea S, Szklo M, Post W, Lima J, Bertoni A, Wong ND. **Progression of Coronary Calcium** and Incident Coronary Heart Disease Events: The Multi-Ethnic Study of Atherosclerosis. J Am Coll Cardiol. 2013;61(12):1231-1239.

Polak JF, Szklo M, Kronmal RA, Burke GL, Shea S, Zavodni AE, O'Leary DH. The value of carotid artery **plaque** and **intima-media thickness** for incident cardiovascular disease: the multi-ethnic study of atherosclerosis. J Am Heart Assoc. 2013;2(2):e000087. doi: 10.1161/JAHA. 113.000087.

Li D, Mao SS, Khazai B, Hyder JA, Allison M, McClelland R, de Boer I, Carr JJ, Criqui MH, Gao Y, Budoff MJ. Noncontrast Cardiac Computed Tomography Image-Based Vertebral **Bone Mineral Density**: The Multi-Ethnic Study of Atherosclerosis (MESA). Acad Radiol. 2013;20(5):621-627.

Mewton N, Opdahl A, Choi EY, Almeida AL, Kawel N, Wu CO, Burke GL, Liu S, Liu K, Bluemke DA, Lima JA**. Left ventricular global function index** by magnetic resonance imaging--a novel marker for assessment of cardiac performance for the prediction of cardiovascular events: the multi-ethnic study of atherosclerosis. Hypertension. 2013;61(4):770-778.

Selected MESA findings

Ventetuolo CE, Barr RG, Bluemke DA, Jain A, Delaney JA, Hundley WG, Lima JA, Kawut SM. **Selective Serotonin Reuptake Inhibitor Use** Is Associated with Right Ventricular Structure and Function: The MESA-Right Ventricle Study. PLoS One. 2012;7(2):30480. Epub 2012 Feb 17.

Manichaikul A, Palmas W, Rodriguez CJ, Peralta CA, Divers J, Guo X, Chen WM, Wong Q, Williams K, Kerr KF, Taylor KD, Tsai MY, Goodarzi MO, Sale MM, Diez-Roux AV, Rich SS, Rotter JI, Mychaleckyj JC. Population structure of **Hispanics** in the United States: the multi-ethnic study of atherosclerosis. PLoS Genet. 2012;8(4):e1002640. Epub 2012 Apr 12.

Vaidya D, et al. [TNTC] A genome-wide association meta-analysis of circulating sex hormone-binding globulin reveals multiple Loci implicated in **sex steroid hormone regulation**. PLoS Genet. 2012 Jul;8(7)e1002805.

Ebong IA, Goff DC Jr, Rodriguez CJ, Chen H, Bluemke DA, Szklo M, Bertoni AG. The relationship between measures of **obesity and incident heart failure**: The multi-ethnic study of atherosclerosis. Obesity (Silver Spring). 2013 Jan 2.

Selected MESA findings

McClelland RL, Jorgensen NW, Post WS, Szklo M, Kronmal RA. Methods for estimation of disparities in **medication use** in an observational cohort study: results from the Multi-Ethnic Study of Atherosclerosis. Pharmacoepidemiol Drug Saf. 2013 Feb 4.

Bosworth C, Sachs MC, Duprez D, Hoofnagle A, Ix JH, Jacobs DR Jr, Peralta CA, Siscovick, DS, Kestenbaum B, de Boer, IH. **Parathyroid hormone** and arterial dysfunction in the Multi-Ethnic Study of Atherosclerosis. Clin Endocrinol (Oxf). 2013 Feb 13.

Alonso A, Soliman EZ, Chen LY, Bluemke DA, Heckbert SR. Association of blood pressure and aortic distensibility with **P wave indices and PR interval**: The Multi-Ethnic Study of Atherosclerosis (MESA). J Electrocardiol. 2013 Feb 25.

Pan CW, Klein BE, Cotch MF, Shrager S, Klein R, Folsom A, Kronmal R, Shea SJ, Burke GL, Saw SM, Wong TY. Racial Variations in the Prevalence of **Refractive Errors** in the United States: The Multi-Ethnic Study of Atherosclerosis. Am J Ophthalmol. 2013 Feb 27.

Selected MESA findings

Desai CS, Ning H, Kang J, Folsom AR, Polak JF, Sibley CT, Tracy R, Lloyd-Jones DM. **Competing Cardiovascular Outcomes** Associated With Subclinical Atherosclerosis (from the Multi-Ethnic Study of Atherosclerosis). Am J Cardiol. 2013 Mar 14.

Allison MA, Ix JH, Morgan C, McClelland RL, Rifkin D, Shimbo D, Criqui MH. Higher **leptin** is associated with hypertension: the Multi-Ethnic Study of Atherosclerosis. J Hum Hypertens. 2013 Mar 28.

Foster T, Anania FA, Li D, Katz R, Budoff M. The Prevalence and Clinical Correlates of **Nonalcoholic Fatty Liver Disease** (NAFLD) in **African Americans**: The Multiethnic Study of Atherosclerosis (MESA). Dig Dis Sci. 2013 Apr 2.

Steffen BT, Steffen LM, Liang S, Tracy R, Jenny NS, Tsai MY**. n-3 and n-6 fatty acids** are independently associated with lipoprotein-associated phospholipase A2 in the Multi-Ethnic Study of Atherosclerosis. Br J Nutr. 2013 Apr 3: 1-8.

Liu A, Kronmal R, Zhou X, Ma S. Determination of **proportionality in two-part models** and analysis of Multi-Ethnic Study of Atherosclerosis (MESA). Statistics and Its Interface. (In press)

Selected MESA findings

Albrecht SS, Diez Roux AV, Kandula NR, Osypuk TL, Ni H, Shrager S. **Immigration assimilation** and BMI and waist size: a longitudinal examination among Hispanic and Chinese participants in the Multi-Ethnic Study of Atherosclerosis. Obesity. (In press)

Nguyen HT, Bertoni AG, Nettleton JA, Bluemke DA, Levitan EB, Burke GL. **DASH Eating Pattern** Is Associated with Favorable Left Ventricular Function in the Multi-Ethnic Study of Atherosclerosis. Journal of the American College of Nutrition. (In press)

Hirsch JA, Moore KA, Evenson KR, Rodriguez DA, Diez Roux AV. Associations of **Walk Score®** and **Transit Score®** with Walking in the Multi-Ethnic Study of Atherosclerosis. American Journal of Preventive Medicine. (In press)

Nettleton JA, et al. [TNTC]. Genome-wide meta-analysis of observational studies reveals common **genetic variants associated with macronutrient intake**. American Journal of Clinical Nutrition. (In press)

Report to OSMB, February 2013

- Endorsed continuation of MESA → OK
- Suggested adding a pulmonary expert to the OSMB → no action yet
- Requested further information on lower retention at Exam 5 for two Field Centers (JHU and UCLA) →
  - Reviewed history at these sites
  - Reviewed participants' expressed reasons
  - Reviewed suggested actions

Report to OSMB, February 2013, cont.

- Requested data on retention by age and ethnicity and plans for retaining those with cognitive impairment →
  - Provided retention data by ethnicity
  - Outlined how contact information and proxies are obtained
  - Further consideration by PRC promised
- Unexpected findings on CT and MRI →
  - Outlined procedures for handling

Report to OSMB in January 2013

Baseline age group	Gender	Retention (%)
45-54	M	81.2
	F	82.0
55-64	M	81.4
	F	79.0
65-74	M	74.3
	F	71.9
75-84	M	62.7
	F	53.0

Report to OSMB, February 2013, cont.

- Requested information about use of MESA data by non-MESA investigators →
  - Outlined how this is encouraged – for example, of 130 ancillary studies, 53 have PI's who are "outside investigators"
  - 123 data sets had been downloaded from dbGaP
  - MESA data sets have been provided to 78 non-MESA investigators
  - 103 requests filled for data repository data
  - Among 512 publications, ~90 different institutions represented

MESA Renewal

- Proposal for a renewal presented to the NHLBI Idea Forum in January
- Proposal discussed by Institute leadership in March
- Proposal discussed by Board of External Experts in April
- Proposal will be discussed in open session of NHLB Advisory Council on June 19

MESA Renewal

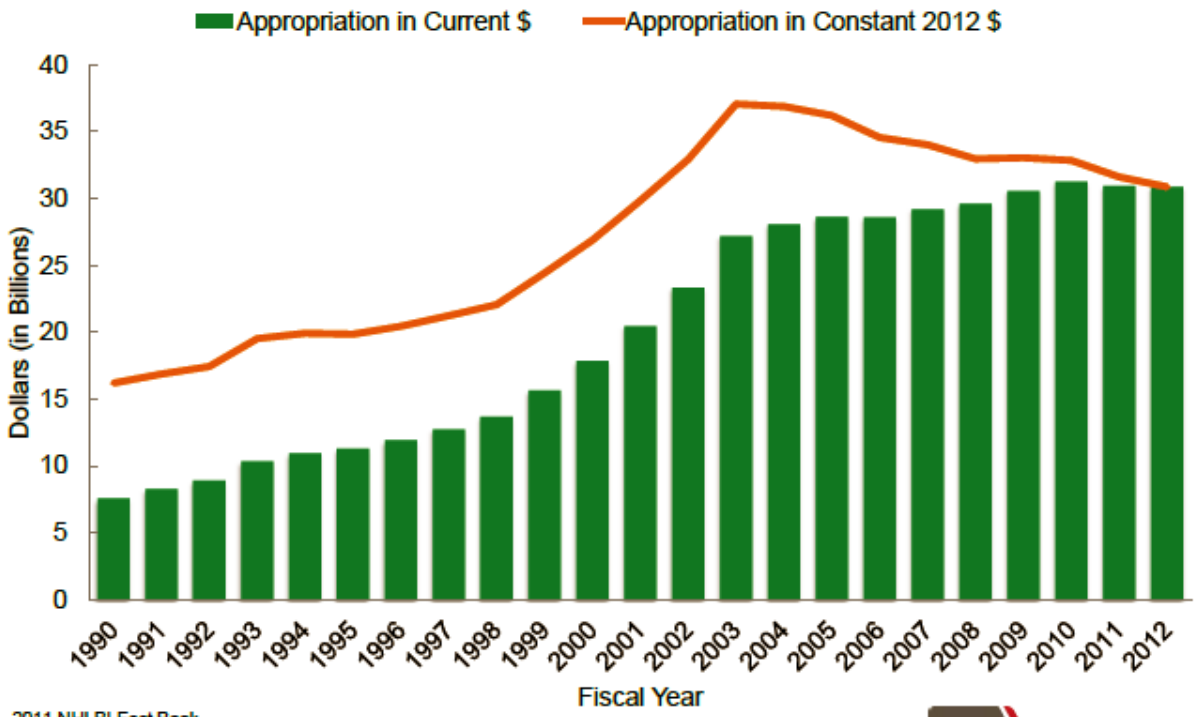
Timeline

- Original contracts awarded in January 1999
- Renewal contracts awarded in August 2008
- Current (renewal) contracts end in August 2015

NIH and NHLBI news

From NHLBI Director's report to NHLBAC, February 11, 2013

Nimble Adaptation with Enduring Principles: Wise Stewardship Amid Fiscal Challenges



2011 NHLBI Fact Book

NIH National Heart, Lung, and Blood Institute

7

From NHLBI Director's report to NHLBAC, February 11, 2013

Budget Update: Current Status

- We are operating under a continuing resolution (CR) through March 27, 2013
- The American Taxpayer Relief Act passed Jan. 1, 2013
  - The immediate threat of a 8.2 percent cut in NIH spending for FY 2013 was averted
  - If no resolution is achieved, a new sequester will be ordered by the President on March 1; implemented on March 27
  - The potential reduction for FY 2013 NIH spending would be approximately 6.4 percent
- *Bottom Line*:
  - Operate cautiously, judiciously and conservatively by limiting commitments until there is greater fiscal clarity under the CR.
  - Continue to fund non-competing grants in FY 2013 at 90% of the approved level, as we have always done under a CR.

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8

Letter from Sally Rockey, Deputy Director for Extramural Research, NIH

March 4, 2013

Dear NIH Signing Official,

As you are likely aware, in accordance with the Budget Control Act of 2011, a series of spending cuts, called sequestration, will cancel approximately $85 billion in budgetary resources across the Federal government for the remainder of the Federal fiscal year. As a partner with you in accomplishing the NIH mission, we are writing to provide you with information about what this reduction means for the funds provided to your organization.

At this time, the Department of Health and Human Services and NIH are taking every step to mitigate the effects of these cuts, but based on our initial analysis, it is possible that your grants or cooperative agreement awards may be affected. Examples of this impact could include: not issuing continuation awards, or negotiating a reduction in the scope of your awards to meet the constraints imposed by sequestration. Additionally, plans for new grants or cooperative agreements may be re-scoped, delayed, or canceled depending on the nature of the work and the availability of resources.

To the extent that fiscal year 2013 funds for your grants or cooperative agreement are affected due to these budget cuts, you will be contacted by the appropriate Grant Management Officer with additional details at a later point. Please note that these budget cuts do not affect grant or cooperative agreement awards made with fiscal year 2012 resources.

Letter from Diane Frasier, Head of Contracting Activity, NIH

Sent: Monday, March 04, 2013 12:19 PM
To: 'NIH-CONTRACTORS@list.nih.gov'
Subject: National Institutes of Health (NIH) Sequestration Notice to Contractors
Importance: High

To All NIH Contractors:

As you are likely aware, in accordance with the Budget Control Act of 2011, a series of spending cuts, called sequestration, will cancel approximately $85 billion in budgetary resources across the Federal government for the remainder of the Federal fiscal year. As a partner with you in accomplishing the National Institutes of Health's (NIH) mission, I am writing to provide you with information about what this reduction means for the contract(s) with your organization.

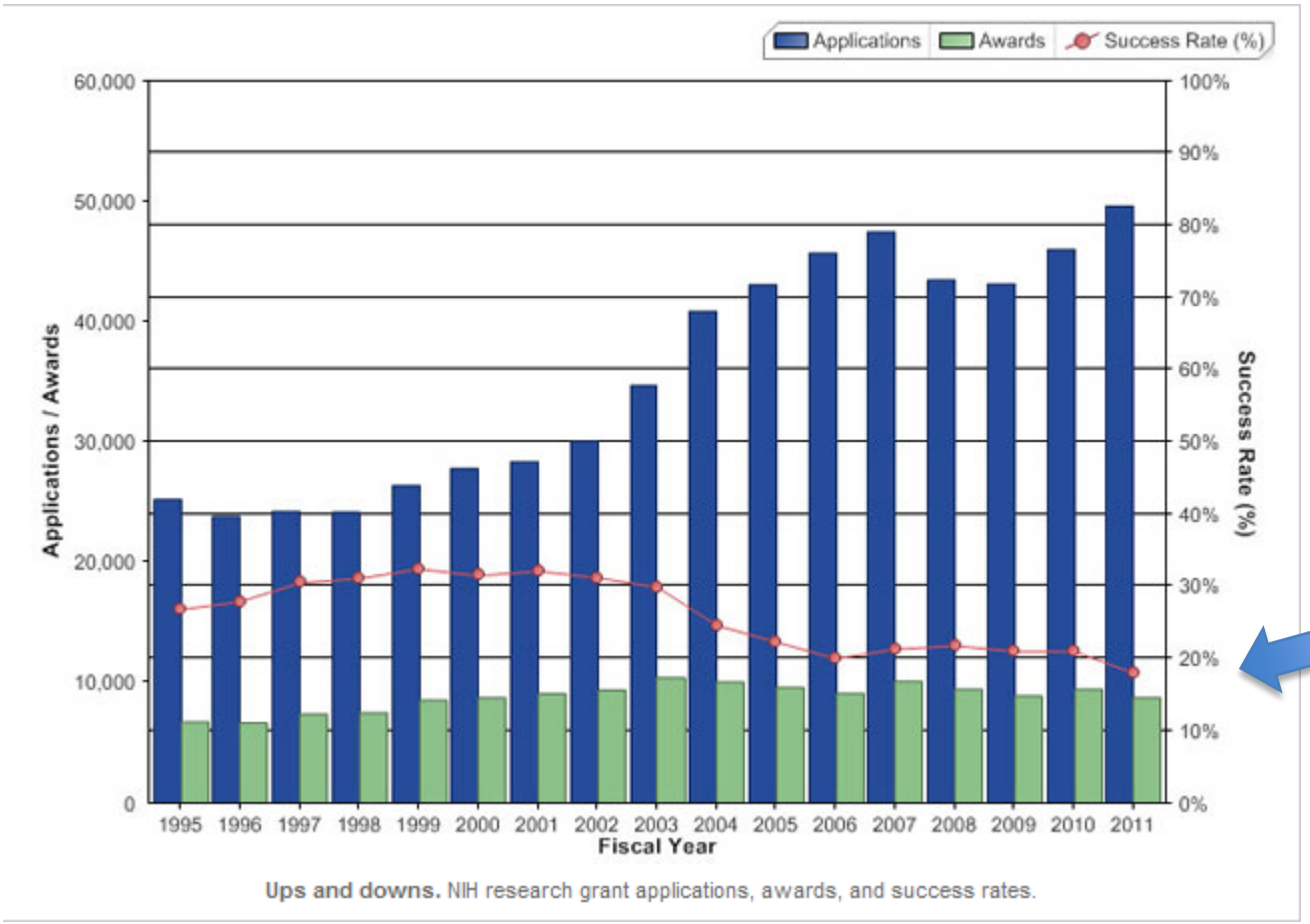
At this time, the Department of Health and Human Services and NIH are taking every step to mitigate the effects of these cuts, but based on our initial analysis, it is possible that your contract(s) may be affected. Examples of this impact could include: not exercising an option on your contract(s); or negotiating lower prices or other terms via a bilateral modification to meet the constraints imposed by sequestration. Additionally, plans for new contract(s) may be re-scoped, delayed, or canceled depending on the nature of the work and the availability of resources.

To the extent that fiscal year 2013 funds for your contract(s) are affected due to these budget cuts, you will be contacted by the appropriate Contracting Officer with additional details at a later point. Please note that these budget cuts do not affect contract awards made with fiscal year 2012 resources.

Thank you for your continued partnership with the Department of Health and Human Services and NIH, and for your cooperation as we work together to manage these circumstances.

Diane J. Frasier
Head of the Contracting Activity, and
Director of the Office of Acquisition and Logistics

NIH budget: Record low success rates



Ups and downs. NIH research grant applications, awards, and success rates.

18%

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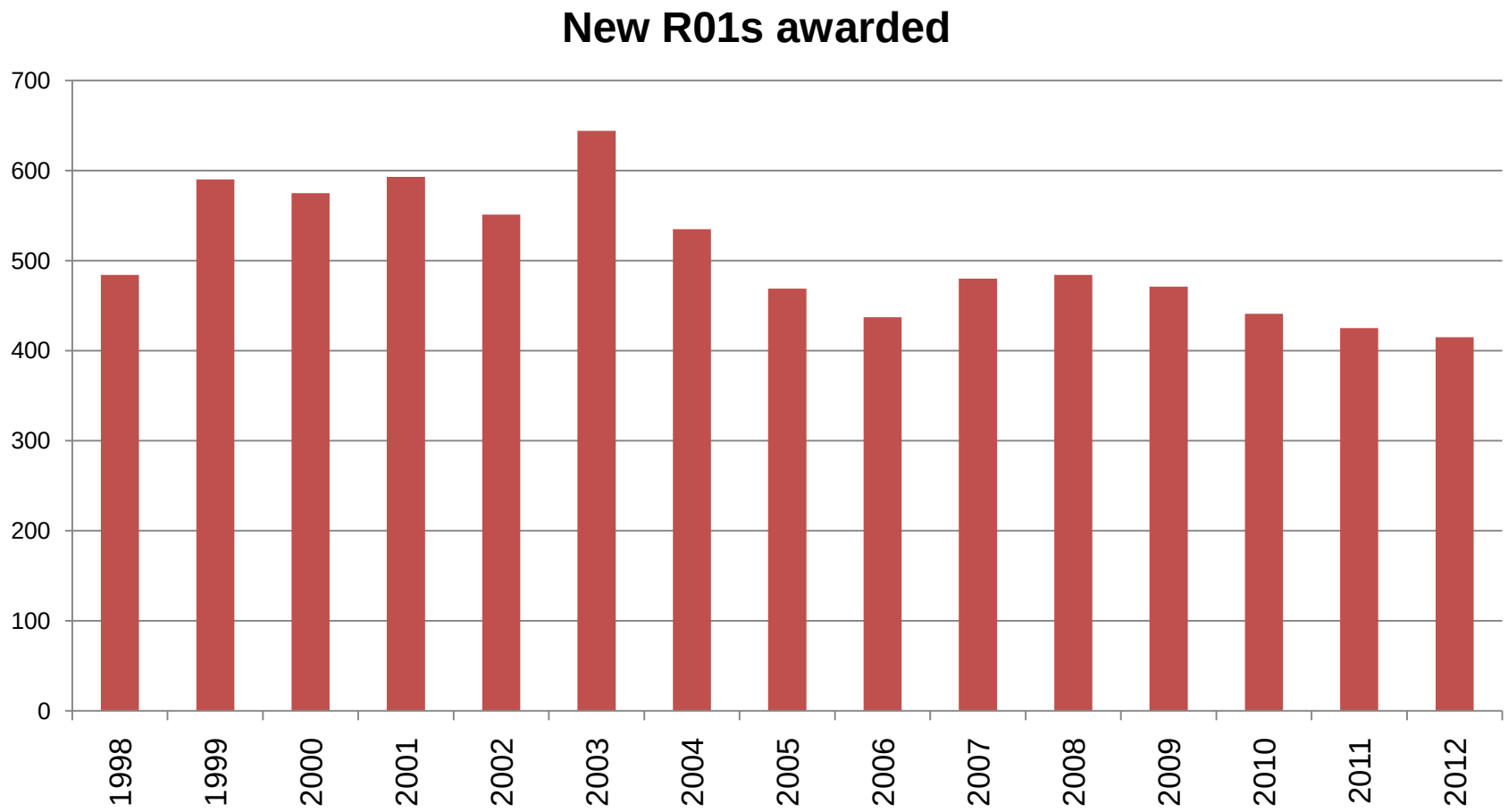
http://news.sciencemag.org/scienceinsider/2012/01/nih-examines-what-drove-its-grant.html

Data from NHLBI from NIH Reporter



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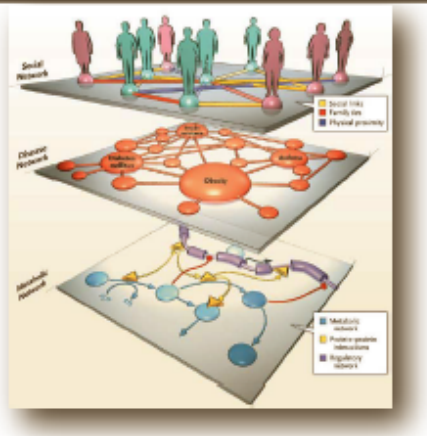
Thanks to Jeannie Olson

NHLBI Director's report, continued

A Systems Approach to the NHLBI Portfolio: Tapping the 'Collective Intelligence' of the Scientific Commons



- **"Scientific Commons"**
- Diverse Cohort Study Datasets
  Genome / Exposome
- Clinical Research
  Registry-Biobanks
- Phenomics:
  Ontologies
- Bioinformatic Tools;
  Computer Modeling
- **Open 'Omic' Data Repositories**

Schadt EE. Nature 2009;461:218-23; Barbabasi A. NEJM 2007;357:404-7

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NHLBI Director's report, continued

'Big Data' and Networking Health Systems: Catalyzing Genomic Medicine Connectivity

Cardiovascular Research Network Centers

- **Genomic Medicine Knowledge Networks**
- Health Systems Networks
- **Diverse Cohort Study Networks**
- Clinical Phenomics/Informatics
- EMR/Biorepositories
- System Biology Networks
- **Diverse, Cross-Disciplinary Trainees**

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40

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Current discussions about epidemiology

EDITORIAL

Editorials represent the opinions of the authors and *JAMA* and not those of the American Medical Association.

Time for a Creative Transformation of Epidemiology in the United States

Michael S. Lauer, MD

THE LATE US SENATOR (D, KY) AND VICE PRESIDENT Alben Barkley enjoyed telling the story of his encounter with a disgruntled constituent. "'I recalled how I had helped get an access road built to his farm, how I had visited him in a military hospital . . . , how I had assisted in securing him veteran benefits, . . . how I had got him a disaster loan. . . . Surely you remember all these things I have done for you?' 'Yeah,' the fellow said, 'I remember.

disease; in regression models, these higher rates were largely accounted for by the risk factors. The REGARDS findings are consistent with other reports of persistent health disparities[7] and highlight the likely important role of risk factors, some of which are reversible, among some racial/ethnic groups.

In another report in this issue of *JAMA*, Daviglus and colleagues[8] describe the prevalence of cardiovascular risk factors in a large, diverse population-based cohort of US Hispanic and Latino individuals, including more than 15 000 participants of Cuban, Dominican, Mexican, Puerto Rican, Cen-

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Lauer MS. JAMA. November 2012

Current discussions about epidemiology

Cancer Epidemiology, Biomarkers & Prevention

Hypothesis/Commentary

Cancer Epidemiology in the 21st Century

Transforming Epidemiology for 21st Century Medicine and Public Health

Muin J. Khoury[1,5], Tram Kim Lam[1], John P.A. Ioannidis[6], Patricia Hartge[2], Margaret R. Spitz[7], Julie E. Buring[8], Stephen J. Chanock[2], Robert T. Croyle[1], Katrina A. Goddard[12], Geoffrey S. Ginsburg[13], Zdenko Herceg[14], Robert A. Hiatt[15], Robert N. Hoover[2], David J. Hunter[10], Barnet S. Kramer[3], Michael S. Lauer[4], Jeffrey A. Meyerhardt[9], Olufunmilayo I. Olopade[16], Julie R. Palmer[11], Thomas A. Sellers[17], Daniela Seminara[1], David F. Ransohoff[18], Timothy R. Rebbeck[19], Georgia Tourassi[20], Deborah M. Winn[1], Ann Zauber[21], and Sheri D. Schully[1]

Abstract

In 2012, the National Cancer Institute (NCI) engaged the scientific community to provide a vision for cancer epidemiology in the 21st century. Eight overarching thematic recommendations, with proposed corresponding actions for consideration by funding agencies, professional societies, and the research community emerged from the collective intellectual discourse. The themes are (i) extending the reach of epidemiology beyond discovery and etiologic research to include multilevel analysis, intervention evaluation, implementation, and outcomes research; (ii) transforming the practice of epidemiology by moving toward more access and sharing

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Khoury MJ, et al. Cancer Epidemiol Biomarkers Prev 2013;22

NHLBI Epidemiology “Blog” continues!

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Home » Information for Researchers » A Digital Forum: Challenges in Cardiovascular Epidemiology

Monday, April 22, 2013

Forum Home

- Background
- Contributors
- Comment Policy
- Contact Us

A Digital Forum: Challenges in Cardiovascular Epidemiology

A Conversation about the Future

The goal of this digital Epidemiology Forum is to facilitate an active and highly engaged discussion of the future of epidemiology in general and as it relates to the study of cardiovascular diseases in particular. The conversation is not an empty exercise, but will influence future program directions at the National Heart, Lung, and Blood Institute.

Four key broad challenges have been identified in a commentary in the American Journal of Epidemiology.

1) How can we avoid wasting resources on studies that provide little incremental knowledge?

2) How can we assure that we direct as economically as possible our resources towards innovative science?

3) How can we be nimble, responding quickly to new opportunities?

4) How can we identify prospectively the most meritorious research questions?

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http://www.nhlbi.nih.gov/resources/epidemiology-forum/

Epidemiology blog most recent discussion

U.S. Department of Health & Human Services | NIH National Institutes of Health

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A DIGITAL FORUM: CHALLENGES IN CARDIOVASCULAR EPIDEMIOLOGY

eCohorts and the future of epidemiology

MARCH 29, 2013

by nhlbistaff

Reporter Ron Winslow posted an **article** in the March 18, 2013 issue of *The Wall Street Journal* about a privately-funded University of California, San Francisco (UCSF) effort to track heart disease risk in over 1 million adults using mobile technology.

The project, called **"Health eHeart"** is described by Dr. Jeffrey Olgin, UCSF's chief of cardiology, as "a large-scale digital version of the **Framingham Heart Study**." The researchers plan to engage participants by encouraging them to enter their own data (e.g., brief surveys), be available for digital follow-up, and to use digital apps and sensors to record certain biological measures like blood pressure.

Questions for consideration:

1. Are "eCohorts" the wave of the future for epidemiology? For what types of research questions are they best suited?

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RECENT POSTS (ALL OPEN FOR COMMENTS)

- eCohorts and the future of epidemiology

Many, many thanks to you all!

- Hardworking staff
- Effective subcommittees
- Excellent Coordinating Center
- Productive and creative investigators

National Heart, Lung,
and Blood Institute