National Health and Nutrition Examination Survey (NHANES)

NHANES Genetic Program

Kathryn S. Porter, M.D., M.S.

Susan Lukacs, D.O., M.S.P.H.

Jody McLean, M.P.H.

Division of Health and Nutrition Examination Surveys

National Center for Health Statistics

Division of Health and Nutrition Examination Surveys

Overview

- **Introductions**
  - Geraldine McQuillan, PhD – Project officer, point of contact
  - Susan Lukacs, DO, MSPH – Science Advisor
  - Jody McLean, MPH - Geneticist

- **Where we are now**
- **HHS Ignites – winning innovation**
- **Summary of National Academy of Sciences Workshop**
- **NHANES Plan for reopening DNA bank**
- **Discussion**

Where we are now

RDC RESEARCH DATA CENTER
Confidential and Secure Access

NHANES DNA Bank

- n=26,000
- Collected 1991-2012
- Currently closed to researchers

Located at NCEH
Atlanta, Georgia

NHANES Genetic Data Repository

- Restricted microdata from NHANES DNA genetic studies
- 1999-present

Located at NCHS
Hyattsville, Maryland

Worth the effort?

HEALTH DIET/NUTRITION

Soda May Age You as Much as Smoking, Study Says

Mandy Oaklander
@mandyoaklander

Oct. 17, 2014

The link between soda and telomere length

Soda and Cell Aging: Associations Between Sugar-Sweetened Beverage Consumption and Leukocyte Telomere Length in Healthy Adults From the National Health and Nutrition Examination Surveys

Cindy W. Leung, ScD, Barbara A. Laraia, PhD, Belinda L. Needham, PhD, David H. Rehkopf, ScD, Nancy E. Adler, PhD, Jue Lin, PhD, Elizabeth H. Blackburn, PhD, and Elissa S. Epel, PhD

Objectives. We tested whether leukocyte telomere length maintenance, which underlies healthy cellular aging, provides a link between sugar-sweetened beverage (SSB) consumption and the risk of cardiometabolic disease.

Methods. We examined cross-sectional associations between the consumption of SSBs, diet soda, and fruit juice and telomere length in a nationally representative sample of healthy adults. The study population included 5309 US adults, aged 20 to 65 years, with no history of diabetes or cardiovascular disease, from the 1999 to 2002 National Health and Nutrition Examination Surveys. Leukocyte telomere length was assayed from DNA specimens. Diet was assessed using 24-hour dietary recalls. Associations were examined using multivariate linear regression for the outcome of log-transformed telomere length.

Results. After adjustment for sociodemographic and health-related charac-

Sugar-sweetened beverages (SSBs), including soft drinks or sodas, fruit-flavored drinks, sports drinks, and energy drinks, are the largest source of added sugar in the US diet.[1,2] Between 1999 and 2008, it was estimated that adults aged 20 to 34 years consumed an average of 333 to 421 calories per day, and adults aged 35 years or older consumed an average of 236 to 260 calories per day from SSBs.[3] Because of these strikingly high levels of consumption, SSBs have emerged as an important target of public health efforts and policies.[4,5]

Published online ahead of print October 16, 2014 | American Journal of Public Health

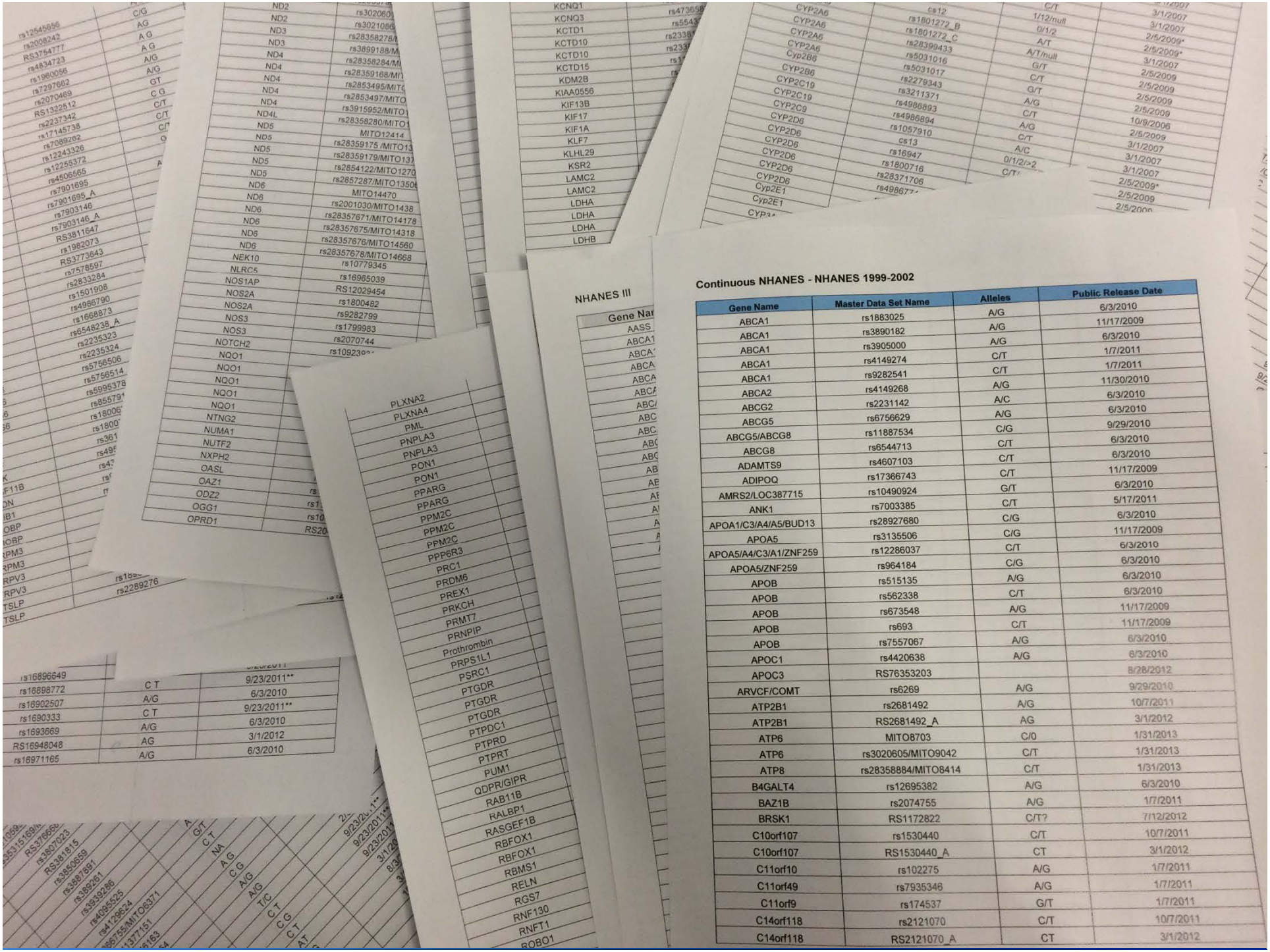
DHANES Innovation : HHS Ignite Winner

- 11 winner teams out of 76 applicants
- 3 months of support
- 3-day Innovation Boot Camp in DC
- On-the-job exposure to new methodologies and tools
- $5,000 to go towards the project idea

Final HHS Ignite talk

National Health and Nutrition Examination Surveys

Encourage research at the intersection of genetics and public health



Continuous NHANES - NHANES 1999-2002

Gene Name	Master Data Set Name	Alleles	Public Release Date
ABCA1	rs1883025	A/G	6/3/2010
ABCA1	rs3890182	A/G	11/17/2009
ABCA1	rs3905000	A/G	6/3/2010
ABCA1	rs4149274	C/T	1/7/2011
ABCA1	rs9282541	C/T	1/7/2011
ABCA2	rs4149268	A/G	11/30/2010
ABCG2	rs2231142	A/C	6/3/2010
ABCG5	rs6756629	A/G	6/3/2010
ABCG5/ABCG8	rs11887534	C/G	9/29/2010
ABCG8	rs6544713	C/T	6/3/2010
ADAMTS9	rs4607103	C/T	6/3/2010
ADIPOQ	rs17366743	C/T	11/17/2009
AMRS2/LOC387715	rs10490924	G/T	6/3/2010
ANK1	rs7003385	C/T	5/17/2011
APOA1/C3/A4/A5/BUD13	rs28927680	C/G	6/3/2010
APOA5	rs3135506	C/G	11/17/2009
APOA5/A4/C3/A1/ZNF259	rs12286037	C/T	6/3/2010
APOA5/ZNF259	rs964184	C/G	6/3/2010
APOB	rs515135	A/G	6/3/2010
APOB	rs562338	C/T	6/3/2010
APOB	rs673548	A/G	11/17/2009
APOB	rs693	C/T	11/17/2009
APOB	rs7557067	A/G	6/3/2010
APOC1	rs4420638	A/G	6/3/2010
APOC3	RS76353203		8/28/2012
ARVCF/COMT	rs6269	A/G	9/29/2010
ATP2B1	rs2681492	A/G	10/7/2011
ATP2B1	RS2681492_A	AG	3/1/2012
ATP6	MITO8703	C/0	1/31/2013
ATP6	rs3020605/MITO9042	C/T	1/31/2013
ATP8	rs28358884/MITO8414	C/T	1/31/2013
B4GALT4	rs12695382	A/G	6/3/2010
BAZ1B	rs2074755	A/G	1/7/2011
BRSK1	RS1172822	C/T?	7/12/2012
C10orf107	rs1530440	C/T	10/7/2011
C10orf107	RS1530440_A	CT	3/1/2012
C11orf10	rs102275	A/G	1/7/2011
C11orf49	rs7935346	A/G	1/7/2011
C11orf9	rs174537	G/T	1/7/2011
C14orf118	rs2121070	C/T	10/7/2011
C14orf118	RS2121070_A	CT	3/1/2012

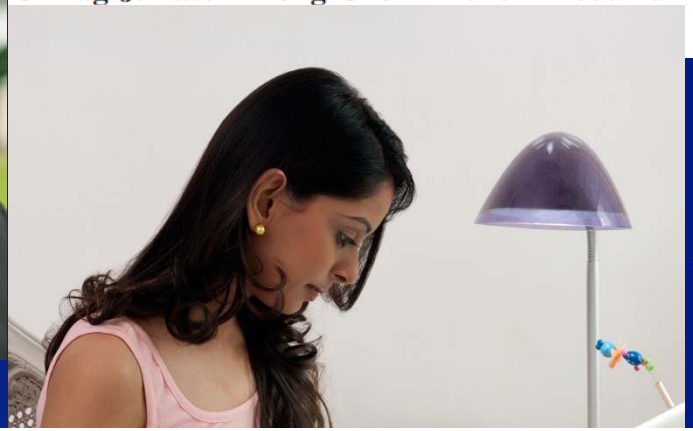
Users

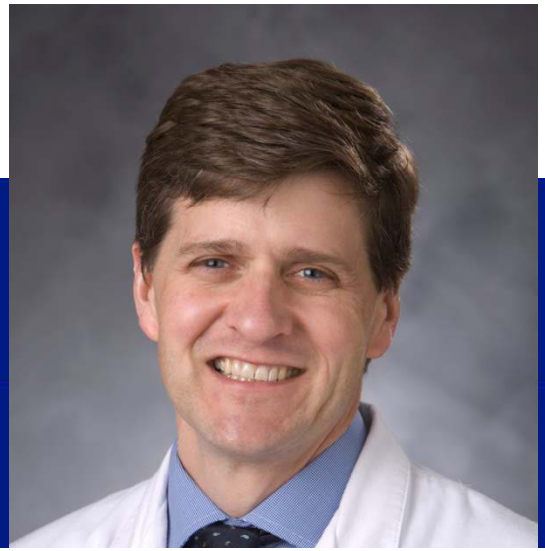
Warfarin pharmacogenetics: a single *VKORC1* polymorphism is predictive of dose across 3 racial groups

Nita A. Limdi,[1] Mia Wadelius,[2] Larisa Cavallari,[3] Niclas Eriksson,[4] Dana C. Crawford,[5] Ming-Ta M. Lee,[6] Chien-Hsiun Chen,[6]

Systematic identification of interaction effects between genome- and environment-wide associations in type 2 diabetes mellitus

Chirag J. Patel · Rong Chen · Keiichi Kodama ·





Racial/Ethnic Variation in the Association of Lipid-Related Genetic Variants With Blood Lipids in the US Adult Population

Man-huei Chang, Renée M. Ned, Yuling Hong, Ajay Yesupriya, Quanhe Yang, Tiebin Liu, A. Cecile J.W. Janssens and Nicole F. Dowling

Meet Tara

Web Demonstration

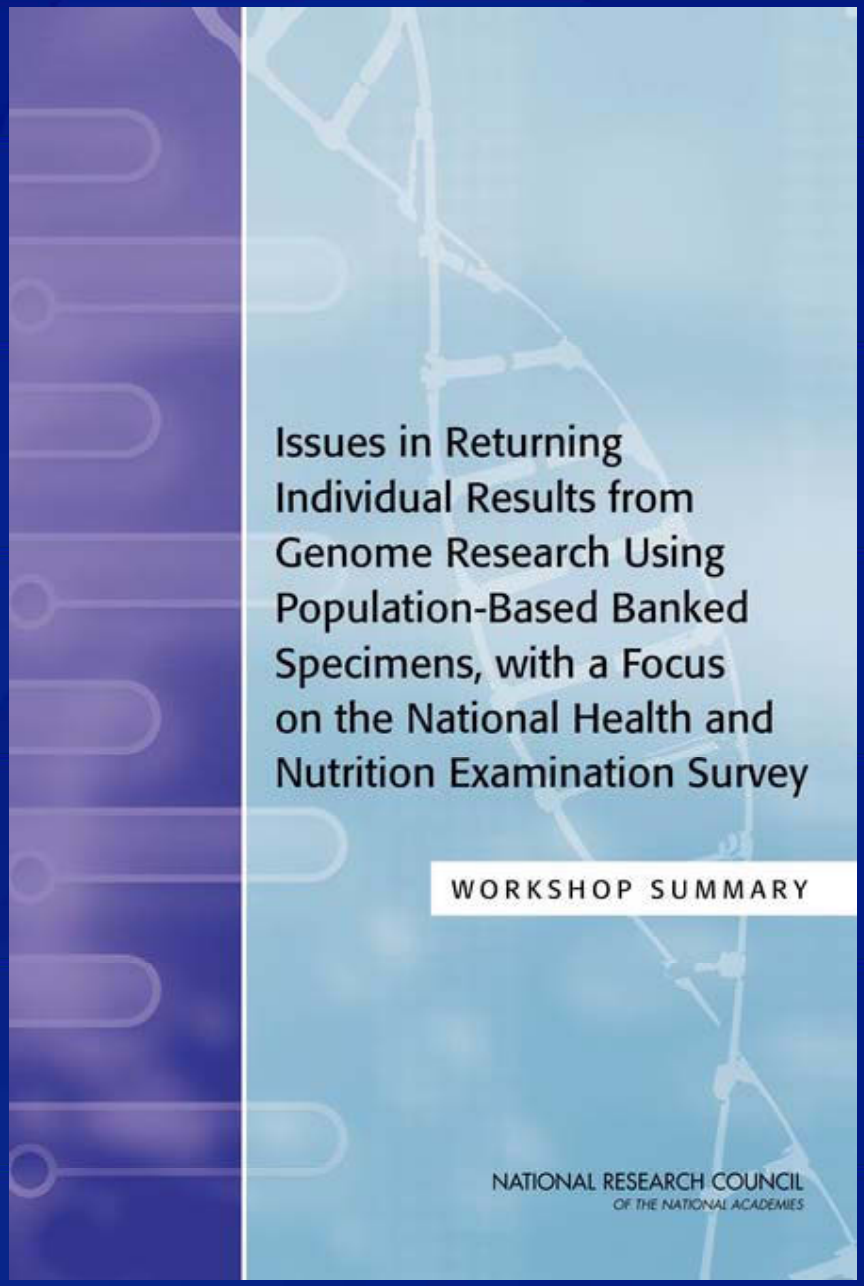
What did we learn?

- User interviews are invaluable
- Content over interface
- Reduced time

What's next?

- Send prototype
- Post the searchable database
- Add additional variables in 2015

Questions?


Issues in Returning Individual Results from Genome Research Using Population-Based Banked Specimens, with a Focus on the National Health and Nutrition Examination Survey
WORKSHOP SUMMARY
NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

National Health and Nutrition Examination Survey – Genetics Program

Board of Scientific Counselors meeting
October 29, 2014

Susan L. Lukacs D.O., M.S.P.H.
Science Advisor
Division of Health and Nutrition Examination Surveys
National Center for Health Statistics, CDC

National Academy of Science (NAS) Committee on National Statistics

- Two-day workshop
  - *Guidelines for Returning Individual Results from Genome Research Using Population-Based Banked Specimens*
- Workshop purpose
  - To determine if and how NHANES and other population surveys with banked DNA specimens should return results from genetic studies

NAS Workshop – February 10-11, 2014

- Onsite and remote attendance by ~ 100 persons
- Participants
  - Research Scientists
  - Bioethicists
  - Lawyers
  - Epidemiologists
  - Clinical Geneticists

Perspectives on returning results cautious vs. broad

- Cautious approach
  - Findings have important health implications
  - Risks established, substantial, and actionable
  - Test analytically valid
  - Disclosure plan complies with laws
  - Participant opted to receive results
- No results returned ethically and legally permissible

Perspectives on returning results cautious vs. broad

- Broad approach
- Maintain public trust by
  - Involving public in setting policy
  - Understanding what public thinks is valuable
- NHANES returns non-genetic results in live survey

Ethical frameworks

- Reasons to report
  - Beneficence
  - Duty to rescue or warn
  - Reciprocity
- Reasons against reporting
  - Benefits of research for generalizable knowledge not individual benefit
  - Risk of conflating research and clinical care
  - Resource limitations
- Presidential Commission for Study Bioethical Issues
  - No duty to look for secondary findings

Issues for return of results clinical vs. research

Clinical	Research
Optimize health care of individual	Production of general knowledge
Provide care in best interest of patient	Protect participant from harm Preserve integrity of study
Patient has right to access all clinical information	No consensus or legal requirement that participants have access to information
Treatment takes place in context of provider-patient relationship	Provider patient relationship is not created through participation in research study

Source; ADAPTED FROM Williams (2014) presented at the workshop *Guidelines for Returning Individual Results from Genome Research Using Population-Based Banked Specimens, February 10-11, National Research Council, Washington, DC.*

Other population studies

- Do not return results
  - National Longitudinal Study of Adolescent Health
  - Health and Retirement Study
  - National Social Life, Health and Aging Project
  - Wisconsin Longitudinal Study
- Plan to return clinically significant and actionable results
  - National Children's Study - no results returned yet

NHANES

- Scientific value
  - Environmental exposures, infectious diseases, mental health, nutrition, and risky behaviors
  - Unique opportunity to study gene-environment interactions
- Genetic data essential to NHANES primary mission
- NHANES needs to make genetic data more readily available to researchers

Consideration of whole genome sequencing

- Report discrete set of results
- Inform participants of what to expect
  - Web videos to explain concepts
- Engage participants
  - Understand trade-off between confidentiality and utility
  - Engagement can tell researchers about governance – what research, consents participants think valuable

NHANES - Should results be returned to participants?

- Ethically acceptable ***not*** to report results under no return of result consent
- Data not extracted under standard practice
  - Non-CLIA laboratory and non-CLIA procedures
  - Do not meet standard expected validity to return results
- Short-term obligation versus long-term research agreement

Return of results for retrospective specimens

- Three layered argument for no return
  - No-return consent sufficient
  - Do not meet standard practice
  - NHANES policy not to permit studies that are likely to develop clinically actionable findings

Prospective collecting of DNA

- Consider expectations and values of participants
  - Community advisory board
- Change consent form to return results
  - Careful process to define criteria for return (very high threshold)
  - Rely on genetic groups to determine what is returnable
  - “Return of results board”

Thank you

Plan for reopening NHANES DNA bank

How the workshop influenced our thinking

- For NHANES DNA specimens already collected, the consent language is determinative
- NHANES genetic studies are research
- DNA analyzed in non-CLIA labs using non-CLIA procedures

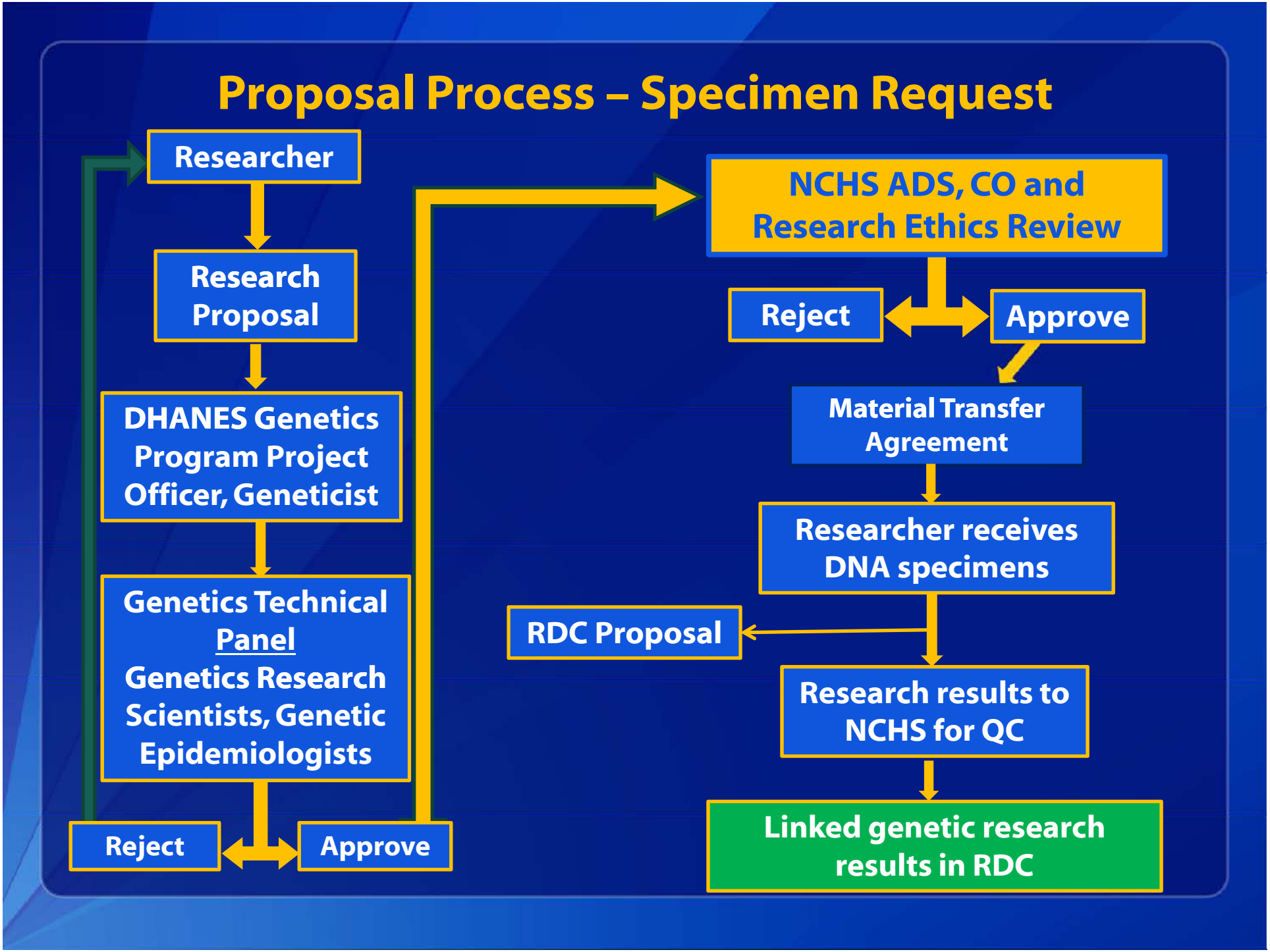
Plan for making NHANES DNA available to researchers

- Plan is basically the same as 1999-2012
- Individual results from genetic studies will not be returned to participants
- Use consensus recommendations to determine whether a result is reportable (clinically actionable)
- Only proposals that test for variants that are *not* clinically actionable may be submitted

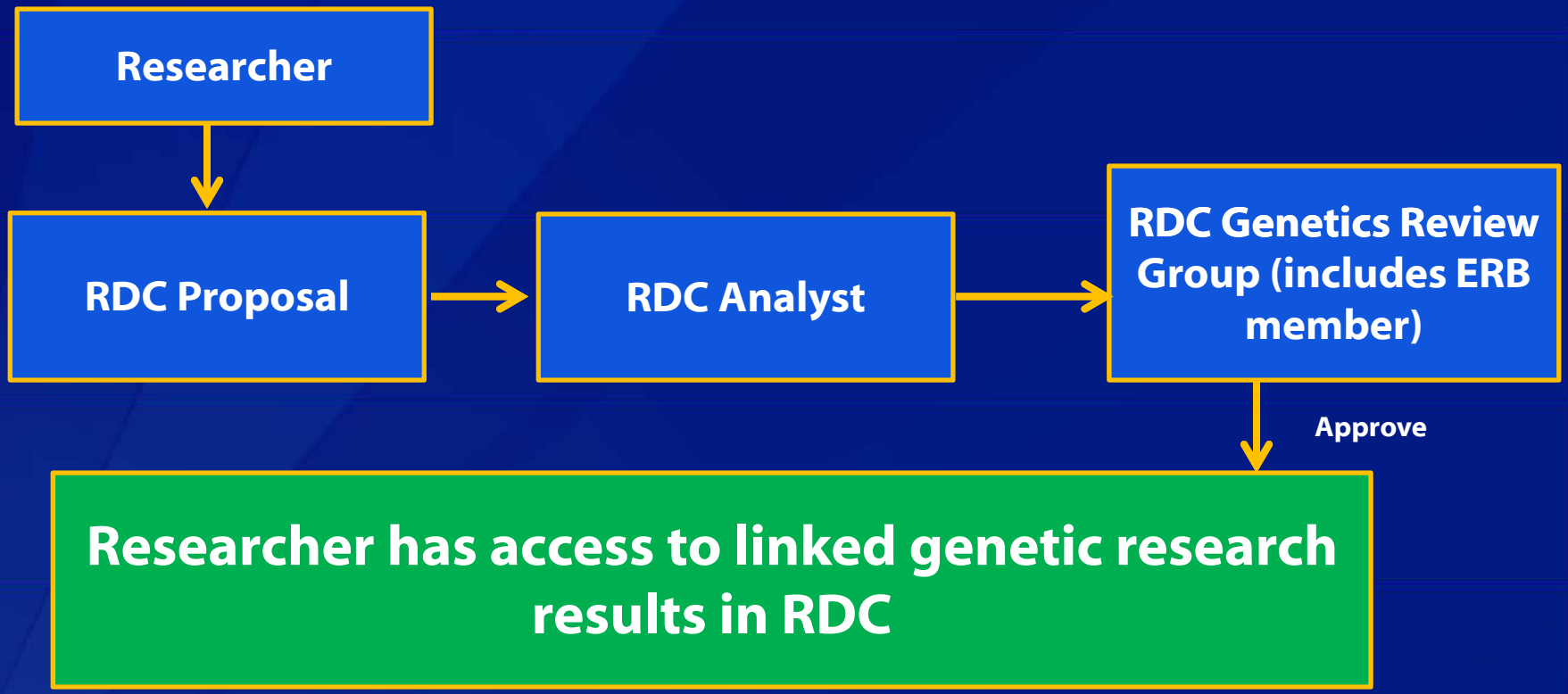
Defining "clinically actionable"

- American College of Medical Genetics and Genomics (ACMG)
- List of 56 genes – clinical variants of these genes should be reported to patients
- Found in: "ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing" published July 2013

Proposal Process – Specimen Request



The NCHS RDC Proposal Process



Manuscripts resulting from genetic research are reviewed by RDC prior to publication

Next steps

- **Seek endorsement from NCHS BSC**
- **Submit for review and approval**
  - NCHS Associate Director for Science
  - NCHS Confidentiality Officer
  - NCHS Research Ethics Review Board
- **Open DNA bank to researchers**