

**The Biomarkers Consortium**

**Metabolic Disorders Steering Committee**

**Sarcopenia Consensus Definition Project**

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**March 28, 2014: PRO Measure Development in Sarcopenia  
Bethesda, MD**



**FNIH**

Foundation for the  
National Institutes of Health

# FNIH Overview

- Sole organization authorized by the U.S. Congress to support the mission of the NIH by creating and managing public-private partnerships
- 501(c)(3) non-profit organization
  - Raised >\$560 million to support >400 projects
  - 100 currently active programs
- Non-governmental
  - Independent Board of Directors
  - NIH Director/FDA Commissioner *ex-officio* FNIH Board Members
- 94 cents of every \$ directly supports research programs
- Consistently rated highly on Charity Navigator

# The Role and Function of FNIH

- Create innovative public-private biomedical partnerships that complement NIH priorities and advance the public health
- Partner with corporations, foundations, academia, federal agencies, and philanthropic individuals
- Serve as “honest broker”, providing a neutral forum able to engage all partners
- Enable efficient, effective collaboration
- Structure flexible donor relationships
- Manage grants, contracts, and projects efficiently

## Foundation for the National Institutes of Health

The FNIH is an independent non-profit organization that facilitates groundbreaking research at the NIH and worldwide.

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#### Current Campaigns



**Diet Coke Launches 2011 Campaign in Support of The Heart Truth®** [↗](#)

Diet Coke partners with FNIH in support of *The Heart Truth*®. [Click here >>](#)

**The Heart Truth Red Dress Collection 2011 a Success**

*The Heart Truth* opened Mercedes-Benz Fashion Week with the Red Dress Collection. [Click here >>](#)

#### Contribute

**Learn how you can fund or donate to Alzheimer's research >>**

**FNIH Seeks Funding for COPD Program >>**

**Learn how you can support The Edmond J. Safra Family Lodge >>**

**Support research at the National Cancer Institute by donating to the Stephen J. Solarz Memorial Fund >>↗**

#### News

**Watch the PBS segment featuring I-SPY2**

**Stakeholder Interaction Results in Key Decisions for Microbiome Research**

**2011 mHealth Summit Announced**

**FNIH Awarded 4-star Charity Rating for 5th year in a row!**

**FNIH Biomarker Consortium & I-SPY2 featured in recent FDA article**

#### Upcoming Events

**2011 mHealth Summit: December 5-7, 2011**

Bringing together leaders from across the mHealth ecosystem to advance collaboration in the use of wireless technology to improve health outcomes. [Learn more >>](#)

# Major FNIH Research Partnerships

## **Gates Foundation Projects**

**\$300M**

Partner: Bill & Melinda Gates Foundation

*(6 grants in global health, AIDS, tuberculosis and malnutrition)*

## **Alzheimer's Disease Neuroimaging Initiative (ADNI & ADNI 2)**

**\$50M**

Partners: NIA/NIBIB & 19 companies/2 non-profits

## **Genetic Association Information Network (GAIN)**

**\$26M**

Partners: NHGRI, NLM & Pfizer, Affymetrix, Broad Institute, Perlegen Sciences

## **The Biomarkers Consortium**

**\$65M**

Partners: NIH, FDA, CMS, BIO, PhRMA, biopharmaceutical industry, non-profits

## **Accelerating Medicines Partnership (AMP)**

**\$120M**

Partners: NIH OD, NIA, NIDDK, NIAMS, NIAID, NHGRI, Abbott, Biogen Idec, BMS, Eli Lilly, GSK, JNJ, Merck, Pfizer, Sanofi

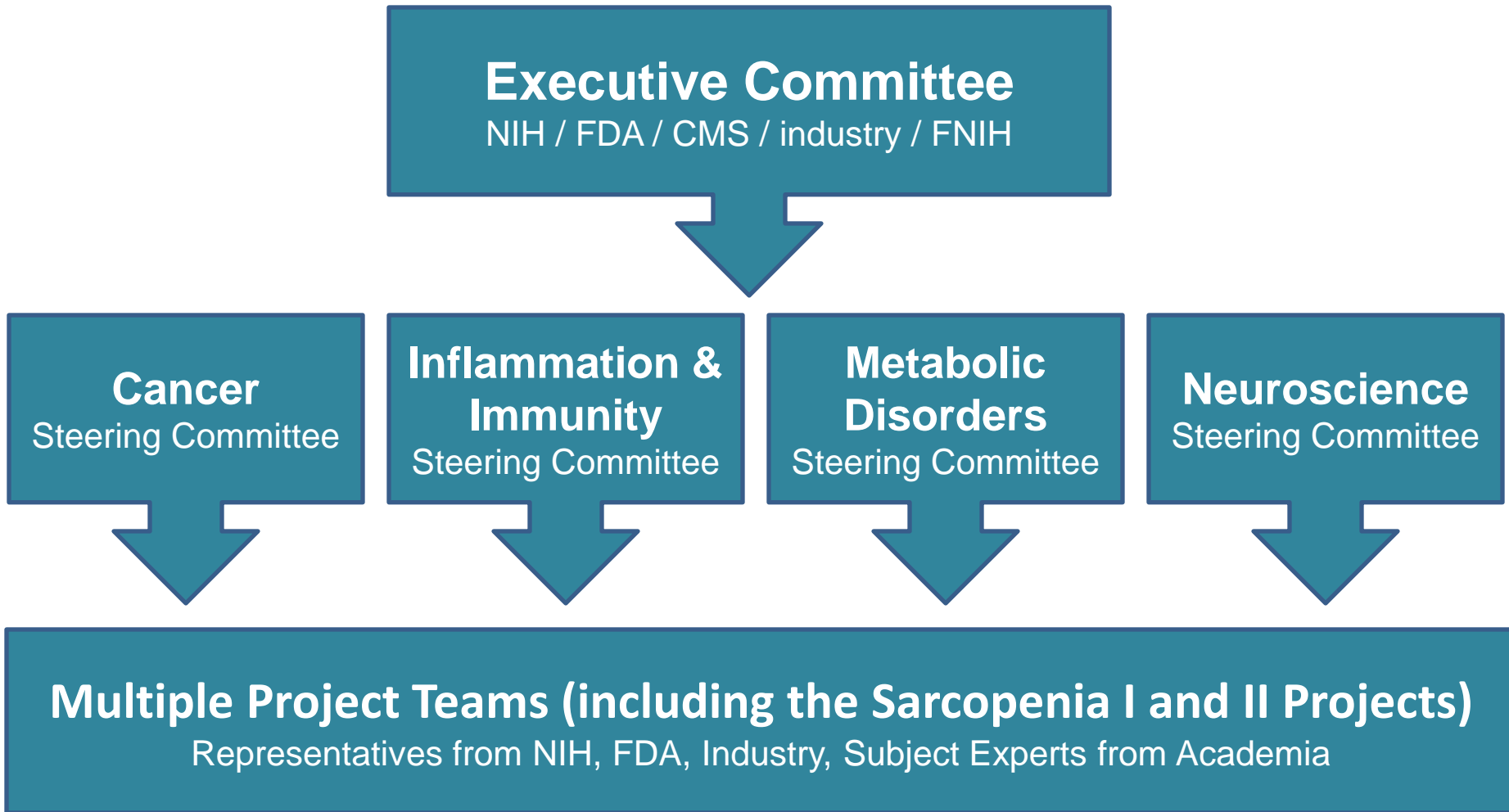


# The Biomarkers Consortium

## **Fosters the exchange of knowledge and expertise among industry, academic and government leaders**

- Qualifies biomarkers for specific applications in diagnosing disease, predicting therapeutic response, and improving clinical practice
- Employs rigorous, inclusive governance and project management with clearly defined goals and milestones
- Facilitate cross-sector partnerships across a broad range of disease and therapeutic areas
- Provides information to inform regulatory decision-making
- Enables pre-competitive sharing of data, resources, and expertise across stakeholders to collaboratively address unmet medical needs

# Biomarkers Consortium Governance Structure



# The MDSC Sarcopenia Project (2010-2013)

## Problem Statement

- Loss of muscle mass is common in aging and wasting conditions, and is associated with weakness, poor function and lower survival.
- This important clinical condition is currently poorly recognized.
- Multiple potential interventions exist to treat or prevent muscle mass loss.
- The field needs a clinical definition to proceed with specific regulation formulation.



# The MDSC Sarcopenia Project (2010-2013)

## Scope of the Problem

- Currently we are unable to identify patients that require treatment.

Clear and valid diagnostic criteria and outcome measures are needed to fulfill regulatory demands and support investments in testing interventions.



\* Your choice. Spend half an hour a day exercising or 24 hours a day dead.\*

- In the US the number of older adults ( $\geq 65$ years) is expected to double to 86.7 million near 2050 in the US.
- Expecting increased comorbidities and need for institutionalization.

# The Sarcopenia Project (2010-2013)

## The Ultimate Goal

Create an evidence-based definition by generating:

- Clear and valid diagnostic criteria and outcome measures acceptable to clinicians, FDA, and health insurers, including CMS
- Opportunities to develop and test potential interventions on low muscle mass and strength, to improve the health of older adults
- Clinical recognition and practice guidelines for screening, diagnosis and management

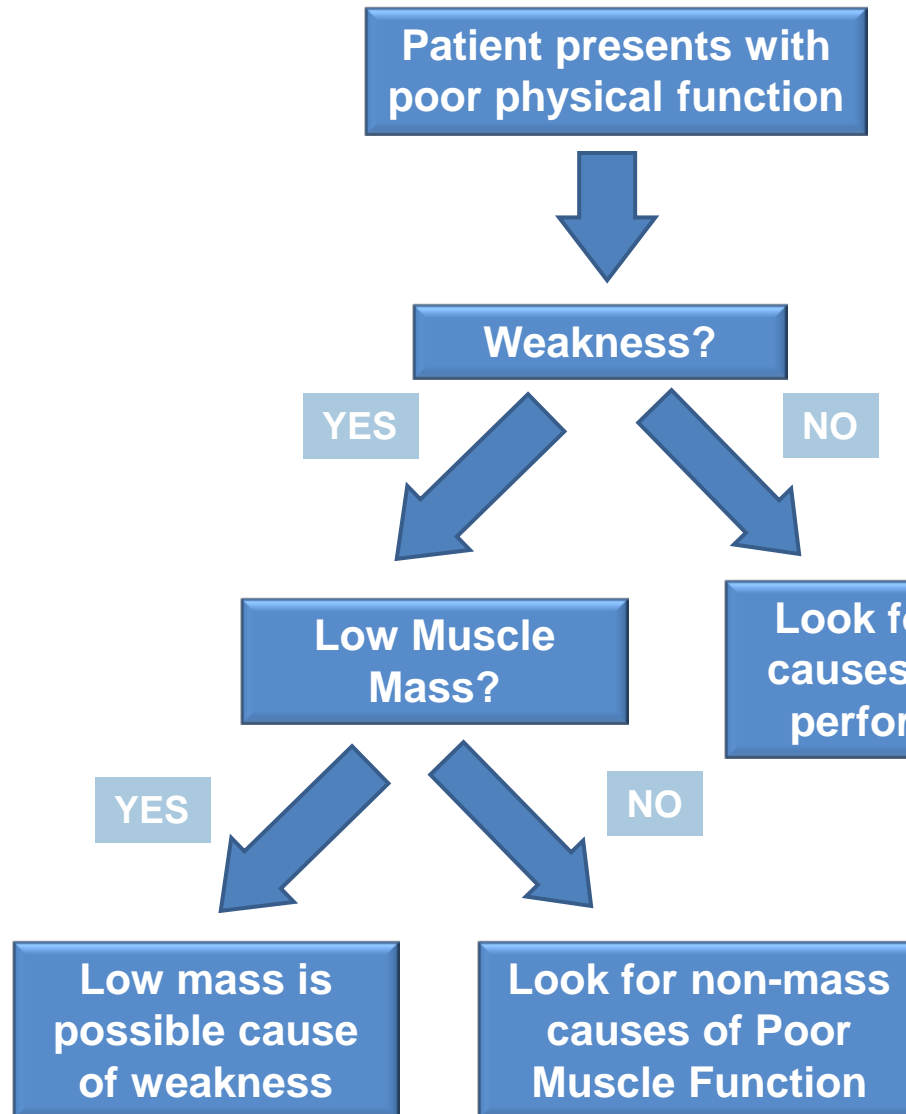
# Other Recent Sarcopenia Definitions

- European Working Group on Sarcopenia in Older People (EWGSOP)  
*Cruz-Jentoft et al, 2010*  
Low Muscle Mass (DXA ASM/ht<sup>2</sup>: ≤ 7.23 kg/m<sup>2</sup> men, ≤ 5.67 kg/m<sup>2</sup> women  
Low grip strength (< 30 kg men, < 20 kg women) OR **Gait Speed < 0.8 m/s**
- European Society of Parenteral and Enteral Nutrition Special Interest Groups (ESPEN)  
*Muscaritoli et al, 2010*  
Low Muscle Mass (<2 SD of 18-39 y, NHANES); **Gait Speed < 0.8 m/s**
- Society of Sarcopenia, Cachexia, and Wasting Disorders  
*Morley et al, 2011*  
Lean appendicular muscle mass < 2SD below healthy individuals age 18-30 y, same ethnicity; **Gait speed < 1 m/s OR walking distance < 400m in 6 minutes**
- International Working Group on Sarcopenia (IWG)  
*Fielding et al, 2011*  
Low appendicular mass relative to height (DXA ASM/ht<sup>2</sup>):<7.23kg/m<sup>2</sup>men &<5.67kg/m<sup>2</sup> women. **Gait Speed < 1m/s**

## Questions Remaining

When is low lean mass empirically grounded to its relationship to strength and function?

# Current Clinical Paradigm



**What is the best measure of poor physical function?**

**What is the best measure of weakness?**

**What is the best measure of muscle mass?**

# The Sarcopenia Project (2010-2013)

## MDSC Sarcopenia Project Goals

- Use cross-sectional and prospective data from several aging studies to evaluate criteria for sarcopenia diagnosis, based on shared operational definitions of performance, strength, body composition (pooled analyses completed)
- Present findings to a broad professional audience for feedback and recommendations (Consensus Meeting, co-sponsored by FDA, FNIH and NIA took place on May 8-11, 2012 in Baltimore, MD)
- Publish findings and define a consensus/multi-stakeholder definition of clinically important sarcopenia (manuscripts ready for submission)

# Data Pooled from Longitudinal Clinical Studies

Study	Baseline sample size	Age range	gender	ethnicity	# follow ups	Max follow up
<b>Cawthon</b> MrOS	5995, almost all with DXA. First entrants 2000	64-100	All male	4.1% AA 2.1% Hispanic	Up to 6; most have at least 3	8.8 years
<b>Dam</b> Rancho Bernardo	2000 depending on study purpose and wave. Sample sizes for key measures varies. First study 1988	50-99	about 2/3 F	Mostly white; About 200-450 Hispanic and AA recruited 1995-2000	Up to 6	22 years
<b>Sceppa</b> Boston Puerto Rican Health Study	1449 First study entry 2004	45-75	70% F	All Puerto Rican	1	6 years
<b>Kenney</b> 6 clinical trials	About 700 in 6 clinical trials	60+	80% F	Small % AA and Hispanic	Up to 4	Up to 2 years
<b>Alley</b> InChianti	842 age 70+, 1154 total Study began 1998	20-90+	60% F	All white	3	9 years
<b>McLean</b> Framingham Original	861 with DXA	70+	2/3 F	White	Up to 7	18 years
<b>McLean</b> Framingham Offspring	2700 who are 50+with DXA	50+	50% F	white	Up to 4	14 years
<b>Harris/Newman</b> Health ABC	3075	70-79	51% women	42% AA	Up to 6	12 years
<b>Harris</b> AGES	5762	65+		White	1	About 8 years

# Statistical Approach: Classification and Regression Tree Analyses to Derive Grip Strength + Lean Mass Cutpoints

## Strengths

- Our findings are generalizable because of the:
  - Large, diverse and well-characterized set of populations
  - Pooled sample had both genders, diversity of race/ethnicity, multiple geographic regions, and a range of health and functional states
- We have an explicit conceptual framework and did extensive sensitivity and cross-validation analyses
- A range of sensitivity + supplementary analyses was possible because:
  - Alternate measures of physical function, strength and body composition were used to evaluate whether findings would differ substantially using different cut points and measures
- Our primary indicator, gait speed  $< 0.8\text{m/s}$  is associated with reduced survival and increased disability

# Sarcopenia Project Accomplishments

Pooled data from multiple aging studies was used to develop preliminary evidence-based cutpoints for grip strength and lean body mass that are potentially clinically relevant.

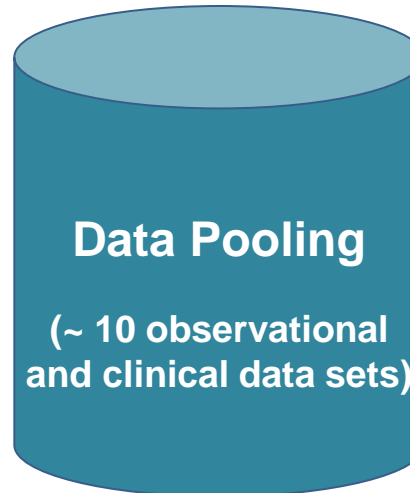
1. The FNIH Sarcopenia Project: Rationale, Study Description and Recommendations  
(*Studenski S, et al.*)

2. Cut-points in grip strength for the clinical definition of slowness with weakness  
(*Alley D, et al.*)

3. Cut points for low appendicular lean mass identifying older adults with weakness  
(*Cawthon P, et al.*)

4. Criteria for clinically important weakness and reduced muscle mass and their longitudinal association with incident mobility disability and mortality  
(*McLean R, et al.*)

5. Consensus Definition Comparisons  
(*Dam T, et al.*)



**Joint Team Recommendations**

**Project Team**

**Consensus Conference**  
May 2012 – Baltimore, Maryland



# The Sarcopenia Project Findings

## Conclusions

- Through the Sarcopenia Project, evidence-based candidate criteria were established as follows:

**For men:** grip strength (GS<sub>MAX</sub>) < 26 kg and an index of < 0.789 for appendicular lean mass adjusted for body mass (ALM<sub>BMI</sub>)

**For women:** GS<sub>MAX</sub> < 16 kg and ALM<sub>BMI</sub> < 0.512

- Based on this consensus, further biomarker analyses become possible in future clinical trials
- A series of five manuscripts submitted to the Journal of Gerontology Medical Sciences (JGMS) in 2013 and under review before publication

# Sarcopenia Results Dissemination Strategy

- Publications of results as a series of papers in JGMS, Spring 2014
- Public announcements, webinar, conference to disseminate the findings of the research after the paper publications to be organized by NIA, NIH
- FNIH press-release currently planned
- Findings presented at the ASBMR Annual Meeting in October 2013 and as an Innovator Presentation at the Partnering for Cures Meeting, organized by Faster Cures in New York, NY in November 2013

## Questions to be Addressed in Follow Up Studies

- Confirmation of the established criteria in populations with more severe mobility limitation
- Taking comorbidities into consideration
- Accounting for differences in measurement on Hologic and Lunar DEXA machines

# Creating an Overarching Sarcopenia Initiative

## Sarcopenia Future Project Goals

- Validate and confirm the predictive validity of the candidate criteria established by the first Sarcopenia Project through analysis of populations with higher levels of mobility limitation and with muscle wasting disorders
- Establish the reproducibility of repeated measures of body composition and demonstrate how changes in muscle mass affect function

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# Thank You

**For more information and questions,  
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