High Cholesterol in Our Communities: Strategies for a Healthier Future

Co-Hosts: ABC Association of Black Cardiologists, Inc. AfPA Alliance for Patient Access National Minority Cardiovascular Alliance
Gary H. Gibbons, M.D.
Director
National Heart, Lung, and Blood Institute

National Hispanic Medical Association
Congressional Briefing
July 25, 2019
NHLBI Enduring Principles

- Value investigator-initiated fundamental discovery science.
- Maintain a balanced, cross-disciplinary portfolio (basic, translational, clinical, population science).
- Train a diverse new generation of leaders in science.
- Support implementation science that empowers patients and enables partners to improve the health of the nation.
- Innovate an evidence-based elimination of health inequities in the U.S. and around the world.
The burden of heart disease mortality persists among different ethnic groups.
Social Determinants of Heart Disease: Addressing Disparities in at-Risk Populations

Understanding the Interplay of Social and Biological Systems ...

Risk Factors
- High blood pressure
- Smoking
- High blood cholesterol
- Overweight/Obesity
- Physical inactivity
- Diabetes
- Family history
- Age

Geography
- Socioeconomic Status
  
Food Desert
- Unhealthy Diet

Biosocial Interface
- Microbiome
  
Immune System Activation

Heart Disease

... Describing and Understanding Prevalence and CVD Risk in Diverse Populations Through NHLBI-Supported Cohort Studies

- Longitudinal, multiethnic, community-based cohort study
- Original cohort: 6,814
- Ages: 45-84
- 1,437 Hispanic men and women enrolled

- Largest U.S. Hispanic/Latino health study
- Original cohort: 16,415
- Ages: 18-74
- 4,000 participants self-identified as Mexican/Mexican American; Puerto Rican; Cuban; Dominican; Central American; South American; Other

NIH
National Heart, Lung, and Blood Institute
The majority of US Hispanic/Latino adults had one or more risk factors for CVD, with significant variation by country of origin. In all groups, men had more risk factors for CVD than women.
Multifactorial, Multi-Level Influences of Cardiovascular Health Among Hispanics/Latinos

Demographics: Race, Subgroups, Gender, Geography

Socioeconomic Status: Income, Education, Employment

Health Systems: Access, Health Literacy, Language, Provider relationships

Psychosocial Factors: Acculturation, Culture

Different Adverse Risk Profiles by Hispanic Subgroup
Multifactorial, Multi-Level Influences of Cardiovascular Health Among Hispanics/Latinos

Demographics

- Racially diverse population
- Lower SES among Puerto Ricans assoc. with ↑BP

Socioeconomic Status (SES)

- SES comparable to NHB (income, poverty, education, occupation, wealth)
- Education strongest SES predictor of CVD (53% HS or greater vs. 90% in gen. pop)

Health System

- Large proportion lack insurance
  - 30% of uninsured vs. 11% NHW, 20% NHB
- Health literacy influences navigation & care
  - ↓health literacy predicts ↑mortality in HF

Psychosocial Factors

- Relationship b/w acculturation & CV risk
- Strong negative effects of ↑acculturation on CV risk factors but positive effects on prevention services
- Among Mexican women, highly acculturated ↑BMI and BP

Adapted from Rodriguez et al. Circ. 2014 Aug. 12; 130(7) HCHS Data Book Report 2013
A Dialogue with the NHLBI Circle of Partners: A Diverse Community Addressing the Health Equity Challenge

It takes all of us to address the health equity challenge.
High Cholesterol in Our Communities: Strategies for a Healthier Future

Co-Hosts: ABC, AfPA, National Minority Cardiovascular Alliance
Understanding Cholesterol in Hispanics/Latinos

Carlos Jose Rodriguez MD, MPH, FACC, FAHA
Vice Chair for Academic Affairs
Director of Clinical Cardiovascular Research
Montefiore Medical Center
Professor of Cardiovascular Medicine, Epidemiology and Population Health
Albert Einstein College of Medicine, Bronx, NY
Status of Cardiovascular Disease and Stroke in Hispanics/Latinos in the United States: A Science Advisory From the American Heart Association

Carlos J. Rodriguez, Matthew Allison, Martha L. Daviglus, Carmen R. Isasi, Colleen Keller, Enrique C. Leira, Latha Palaniappan, Ileana L. Pina, Sarah M. Ramirez, Beatriz Rodriguez and Mario Sims

on behalf of the American Heart Association Council on Epidemiology and Prevention, Council on Clinical Cardiology, and Council on Cardiovascular and Stroke Nursing
• 17.4% of the US population is Hispanic
• >55 million Hispanics resided in the 50 states and DC
• US is projected to become more racially and ethnically diverse
• The public health impact of the Hispanic population is significant
US Hispanic population

The Distribution of the Nation’s Hispanic Population, 2011

Largest Hispanic Origin Group Shares in Select Metropolitan Areas, 2011

<table>
<thead>
<tr>
<th>Metropolitan Area</th>
<th>Mexican</th>
<th>Puerto Rican</th>
<th>Salvadoran</th>
<th>Cuban</th>
<th>Dominican</th>
<th>Guatemalan</th>
<th>Other</th>
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<tbody>
<tr>
<td>Los Angeles-Long Beach, CA</td>
<td>78</td>
<td>1</td>
<td>8</td>
<td>5</td>
<td>21</td>
<td>1</td>
<td>7</td>
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<tr>
<td>New York Northeastern NJ</td>
<td>12</td>
<td>28</td>
<td>5</td>
<td>21</td>
<td>2</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Miami-Hialeah, FL</td>
<td>6</td>
<td>18</td>
<td>54</td>
<td>4</td>
<td>1</td>
<td>30</td>
<td></td>
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<tr>
<td>Washington, DC/MD/VA</td>
<td>16</td>
<td>6</td>
<td>32</td>
<td>2</td>
<td>8</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Providence-Fall River-Pawtucket, MA/RI</td>
<td>8</td>
<td>28</td>
<td>6</td>
<td>26</td>
<td>15</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>
Genetic / Racial Diversity among Hispanics

- Being Hispanic is not a Race, it is an Ethnicity
- US concept of Race of only white or black is confusing to Hispanics
- Hispanics are an admixed population of varying racial admixture of
  - West African
  - European Caucasian
  - Native American ancestry
Hispanic Socioeconomic Status

Access to Health Care: Health Insurance

- Hispanics are twice more likely than non-Hispanic whites to lack health insurance.
- Despite employment at similar rates; Hispanics are disproportionately uninsured.
- Hispanics are three times LESS likely to have a regular health care provider.

Cumulative Lifetime Risk of Diabetes

**Male**
- Hispanic, 45.4 (40.5-51.0)
- Non-Hispanic Black, 40.2 (36.4-45.1)
- Other, 36.9 (29.6-46.0)
- Non-Hispanic White, 26.7 (24.4-29.5)

**Female**
- Hispanic, 52.5 (47.4-58.3)
- Non-Hispanic Black, 49.0 (44.6-53.7)
- Other, 43.3 (35.1-53.2)
- Non-Hispanic White, 31.2 (28.8-33.9)

Diabetes or Impaired Fasting Glucose: Latinos/Hispanics vs. Non-Hispanic Whites

<table>
<thead>
<tr>
<th>Racial / Ethnic Group</th>
<th>Overweight (BMI ≥ 25) Prevalence (%)</th>
<th>Obesity (BMI ≥ 30) Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black (non-Hispanic)</td>
<td>67.2</td>
<td>47.8</td>
</tr>
<tr>
<td>Mexican American</td>
<td>77.9</td>
<td>42.5</td>
</tr>
<tr>
<td>White (non-Hispanic)</td>
<td>67.2</td>
<td>32.6</td>
</tr>
</tbody>
</table>

Ogden, et al. JAMA.2014;311:806-14  
*Ages 20 and older*
LDL "Bad" Cholesterol + HDL "Good" Cholesterol + TRIGLYCERIDES/5 = TOTAL CHOLESTEROL
High Blood Cholesterol

- An estimated 28.5 million adults ≥20 years of age have serum TC levels ≥240 mg/dL (11.9% prevalence)
  - ≈5.8% of adults have undiagnosed hypercholesterolemia
- Women had higher prevalence of high TC (13.0%) than males (10.6%)
- Crude mean total cholesterol level in adults is <200 mg/dl
- From 1988 to 2014, mean serum TC for adults ≥20 years of age
  - Likely reflects greater uptake of cholesterol-lowering medications rather than changes in dietary patterns

Mean Total Cholesterol Levels in US Adults

1988-1994: 208 mg/dL
1999-2002: 204 mg/dL
2007-2010: 198 mg/dL
Cardiovascular Health Disparities

- Lower CV health among minorities
  - 40% among whites,
  - 25% among Mexican Americans
  - 15% among African Americans
- Worsening CVH among whites has reduced persistent disparities in the heart health of minorities

Dyslipidemia and High Cholesterol among Hispanics/Latinos

- Among Hispanics with Hypercholesterolemia
  - 49% are not aware
  - 30% are receiving treatment
  - Of those receiving treatment, 64% are uncontrolled

- 2/3 (65%) of Hispanics had some form of Dyslipidemia
  - 41% had low HDL-C
  - 15% had high TGs
  - 35% have high non-HDL-C


Rodriguez C., J Am Heart Assoc. 2015 June; 4: e001867 doi: 10.1161/JAHA.115.001867
Hypercholesterolemia Prevalence by Hispanic Background (HCHS/SOL)

Daviglus, JAMA. 2012;308(17):1775-1784
Dyslipidemia by Race-Ethnicity: NOMAS

Rodriguez C., *Circulation* 2006; 113: e379
Rodriguez C., *Am J Cardiol* 2002; 89:178
<table>
<thead>
<tr>
<th></th>
<th>African Americans</th>
<th>Hispanics</th>
<th>Non-Hispanic Whites</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td># of patients (%)</td>
<td>462 (27)</td>
<td>546 (34)</td>
<td>612 (38)</td>
<td></td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>212.5</td>
<td>211.1</td>
<td>213.2</td>
<td>.782</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>143.8</td>
<td>139.4</td>
<td>140.7</td>
<td>.410</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>47.0</td>
<td>42.3</td>
<td>44.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>102.1</td>
<td>147.7</td>
<td>134.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LDL size (Å)</td>
<td>262.1</td>
<td>257.6</td>
<td>259.2</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

TC = total cholesterol; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; TG = triglycerides.

Evolution of Cholesterol Guidelines: ATP III to 2013 ACC/AHA to 2018 ACC/AHA

• Outcome being prevented:
  – Then: Coronary heart disease
  – Now: Atherosclerotic cardiovascular disease (MI, angina, stroke, TIA, PAD)
  PROBLEM: Less data on Hispanics

• 10 year Risk Calculator
  – Then: Modified FRS
  – Now: Pooled Cohort Equation- ASCVD risk estimator
  PROBLEM: Hispanics are not included in risk estimator

• Recommended Therapy:
  – Then: Any lipid drug; then later other lipid meds were added
  – Now: Statins alone; PCSK9
  PROBLEM: Poor screening, poor drug initiation among Hispanics

• Monitoring lipid levels
  – Then: no monitoring
  – Now: monitoring of LDLc after initiation of therapy
  PROBLEM: Less intensification of treatment and monitoring among Hispanics
Primary Prevention: Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle

Age 0-19 y
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of Familial Hypercholesterolemia → statin

Age 20-39 y
Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk
Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)

Age 40-75 y
LDL-C ≥190 mg/dL (≥4.9 mmol/L)
No risk assessment; High-intensity statin (Class I)

Diabetes mellitus and age 40-75 y
Moderate-intensity statin (Class IIa)

Diabetes mellitus and age 40-75 y
Risk assessment to consider high-intensity statin (Class IIa)

Age >75 y
Clinical assessment, Risk discussion

ASCVD Risk Enhancers:
- Family history of premature ASCVD
- Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g., preeclampsia, premature menopause)
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g., South Asian ancestry)

Lipid/Biomarkers:
- Persistently elevated triglycerides (≥275 mg/dL, ≥2.0 mmol/L)

In selected individuals if measured:
- hs-CRP ≥2.0 mg/L
- Lp(a) levels >50 mg/dL or >125 nmol/L
- apoB ≥130 mg/dL
- Ankle-brachial index (ABI) <0.9

Risk discussion:
- <5% “Low Risk”
- 5% - <7.5% “Borderline Risk”
- ≥7.5% - <20% “Intermediate Risk”
- ≥20% “High Risk”

Risk discussion: Emphasize lifestyle to reduce risk factors (Class I)
Risk discussion: If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class IIb)
Risk discussion: If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)
Risk discussion: Initiate statin to reduce LDL-C ≥50% (Class I)

If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥75th percentile, initiate statin therapy
Summary Recommendations

1. **Increase Health Care Access**: affect morbidity and mortality across different populations
2. **Diversifying the Health Care Workforce**: facilitated by expanding the numbers of non-physician providers
3. **Extend Cultural Competency Training Programs**
4. **Diversity in Randomized Clinical Trials**: most are industry-sponsored and do not include Hispanics
5. **Costs of Medications Are Prohibitive**: Insurance companies and Pharma can form a coalition to address this
6. **EMR data** can be de-identified and aggregated
7. **Increase NIH Research That Is More Inclusive Of Minorities**: translational, clinical, population science
CAPT Richardae Araojo, PharmD, MS
Associate Commissioner for Minority Health
Director, FDA Office of Minority Health and Health Equity
NHMA Congressional Briefing, July 2019
Disclaimer

• This presentation represents the personal opinions of the speaker and does not necessarily represent the views or policies of FDA

• No conflicts of interest to declare
Overview

• Overview of the U.S. Food and Drug Administration’s Office of Minority Health and Health Equity

• FDA Policy Strategies to Support Diverse Participation in Clinical Trials

• Communication & Outreach Strategies to Improve Diverse Participation in Clinical Trials and Cardiovascular Health
FDA Office of Minority Health and Health Equity (OMHHE)

**Mission**
To promote and protect the health of diverse populations through research and communication that addresses health disparities.

**Vision**
To create a world where health equity is a reality for all.
The Need for Diverse Participation

- Racial and ethnic minorities have been historically and remain under-represented in clinical trials
- Need representation to study the effects of medical products in the people who will ultimately use them
- Racial/ethnic minority populations may respond differently to medical products (ex: heart failure medications)
- To understand health disparities - diseases that occur more frequently or appear differently in diverse populations
Barriers to Diverse Participation

- Mistrust and distrust of the medical system due to historical abuses
- Lack of awareness on the patient’s part
- Inadequate recruitment and retention efforts
- Lack of minority physicians, researchers, and clinical investigators
- Misunderstanding of racial/ethnic minorities’ beliefs and values that contribute to their decision making process
- Lack of culturally/linguistically appropriate communication
- Perception that minorities do not want to participate
- Physicians/providers may not talk to their patients about clinical trials
- Enrollment criteria
- Return of Results
- Privacy concerns
- Lack of access
FDA Safety and Innovation Act (FDASIA) Section 907 Action Plan Priorities & Strategies

**Priority One**
Improve the completeness and quality of demographic subgroup data collection, reporting and analysis *(Quality)*

**Priority Two**
Identify barriers to subgroup enrollment in clinical trials and employ strategies to encourage greater participation *(Participation)*

**Priority Three**
Make demographic subgroup data more available and transparent *(Transparency)*

**FDA Guidance Documents**
Collection of Race and Ethnicity Data in Clinical Trials
Evaluation and Reporting of Age, Race, and Ethnicity Specific Data in Medical Device Clinical Studies

**Public Meetings**
Tools to support diverse clinical trial participation

**Drug Trials Snapshots**
(Center for Drug Evaluation and Research)
Drug Trials Snapshots: Summaries (2016-2018)

<table>
<thead>
<tr>
<th></th>
<th>WOMEN</th>
<th>BLACK or AFRICAN AMERICAN</th>
<th>ASIAN</th>
<th>WHITE</th>
<th>OTHER*</th>
<th>AGE 65 AND OLDER</th>
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<tr>
<td>2016</td>
<td>48%</td>
<td>7%</td>
<td>11%</td>
<td>76%</td>
<td>7%</td>
<td>21%</td>
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<tr>
<td>2017</td>
<td>55%</td>
<td>7%</td>
<td>11%</td>
<td>77%</td>
<td>14%</td>
<td>32%</td>
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<tbody>
<tr>
<td>2018</td>
<td>56%</td>
<td>11%</td>
<td>10%</td>
<td>69%</td>
<td>14%</td>
<td>15%</td>
</tr>
</tbody>
</table>

* The percentages of the categories “American Indian or Alaska Native (AI/AN),” “Native Hawaiian or Other Pacific Islander (NH/OP),” and “Unknown/Unreported” were small enough that we combined them into the “Other” category for the purposes of this review.

**These particular subgroups were calculated as part of a Geriatrics Report and are not a regular feature of the Drug Trial Snapshots.
Clinically Relevant Enrollment

• FDA expectations are that sponsors enroll participants who **reflect the demographics for clinically relevant populations** with regard to age, gender, race, and ethnicity

• A plan to address inclusion of clinically relevant **subpopulations** should be submitted for discussion to the Agency at the earliest phase of development and, for drugs and biologics, no later than the end of the phase 2 meeting
Ongoing FDA Efforts

• FDA Reauthorization Act of 2017

• 21st Century Cures Act
  – Patient Engagement Efforts
Diversity in Clinical Trials Campaign

BE A #CLINICALTRIALSCHAMPION

Videos
Newsletters & E-alerts
Webpage
Stakeholder Collaboration
Podcasts
Social Media
Communications Toolkit
Graphics
Latinos Can Make a Difference in Clinical Trials
Diverse Participation in Clinical Trials Videos and Podcast

Highlights the importance of racial and ethnic minority participation in clinical trials.

Each video features a different theme and key message.
Diversity in Clinical Trials Resources

**Factsheet: Clinical Trials**

Clinical trials are research studies that determine whether medical products like medicines, vaccines, or devices are safe and effective. These studies may show which medical approaches work best for certain illnesses or groups of people.

Office of Minority Health

4 Things You Should Know About the Importance of Diversity in Clinical Trials

1. **Clinical trials are conducted to identify new medical treatments.**
   - Different populations may respond differently to treatments.
   - Participation in clinical trials helps ensure that a treatment is safe and effective for all people.

2. **Clinical trials provide important information for patients.**
   - Patients can get access to new treatments.
   - Patients can have their voices heard.

3. **Clinical trials help improve the standard of care for all people.**
   - New treatments are often developed based on clinical trial results.
   - Clinical trials can lead to better care for patients.

4. **Clinical trials are conducted in a variety of settings.**
   - Clinical trials can be conducted in hospitals, clinics, and other locations.
   - Clinical trials can be conducted with people of all ages and backgrounds.

**Minorities in Clinical Trials**

**HOJA INFORMATIVA**

Las minorías en los estudios clínicos

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Las minorías en los estudios clínicos son estudios de investigación que determinan si los productos médicos como medicamentos, vacunas o dispositivos son seguros y efectivos. Estos estudios pueden demostrar que estos productos funcionan mejor para ciertas enfermedades o grupos de personas.

**La importancia de la participación de las minorías en los estudios clínicos**

Participar en estudios clínicos es necesario para garantizar que los productos médicos sean seguros y efectivos. Las minorías en los estudios clínicos pueden beneficiarse de participar en estos estudios y contribuir a la investigación en salud.

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Cardiovascular Health

- Research & Collaboration
  - Intramural
  - Extramural/Centers of Excellence in Regulatory Science and Innovation (CERsIs)
Outreach & Communication

- Culturally and linguistically competent education and resources
- Partnerships and Collaborations
Stakeholder Engagement & Collaboration

• The Alliance of Multicultural Physicians

• National Minority Cardiovascular Alliance

• Puerto Rico Clinical Research Summit (May 2018 & 2019)
  – Co-organized by FDA OMHHE, Puerto Rico Consortium for Clinical Investigation, Yale University, Universidad de Puerto Rico, Universidad Central del Caribe, Ponce Health Sciences University, and Puerto Rico Science, Technology & Research Trust

• Yale and FDA OMHHE Memorandum of Understanding
  – To advance the Yale Cultural Ambassadors Program and engagement of community partners to increase diverse participation in clinical research
Connect with OMHHE

Follow us on twitter @FDAHealthEquity

healthequity@fda.hhs.gov

www.fda.gov/healthequity

Join webinars and stakeholder calls
High Cholesterol in Our Communities: Strategies for a Healthier Future

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