PREP Course #13: The Importance of Diversity in Research and Clinical Trials

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CME Disclosure Statement

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- Course Director and Course Planner, Kevin Tracey, MD and Tina Chuck, MPH have nothing to disclose.
- Christine Metz, Phd is the speaker and has nothing to disclose.
Diversity in Research: Objectives

- Describe the Office of Diversity, Inclusion & Health Literacy
- Define Diversity, Inclusion, Health Literacy and Cultural Awareness/Competency
- Discuss the importance of diversity in medical research/clinical trials
- Describe how diversity in research could impact the results of clinical trials and patient outcomes
- Identify ways to increase diversity among research participants
Our ultimate goal is to deliver the highest quality care to all, regardless of race, ethnicity or cultural background, as well as language proficiency, literacy, age, gender, gender identity, sexual orientation, religion, disability or socioeconomic status.
Important Terms

**Diversity:**
Diversity encompasses acceptance and respect. It means understanding that each individual is unique, and recognizing our individual differences (age, race/ethnicity, etc).

**Inclusion:**  a basic human right
Miller and Katz (2002) defined inclusion as: “.. a sense of belonging: feeling respected, valued for who you are; feeling a level of supportive energy & commitment from others so that you can do your best.”

**Health Literacy:**
IOM: "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions."

**Cultural awareness:**
Understanding of one's own culture and the culture of others with openness and flexibility. Understanding that each person is UNIQUE

**Cultural competancy:**
The ability to operate within different value systems, respect and understand different cultures while not imposing one's own beliefs or attitudes onto others.
What is Ethnicity vs. Race?

- Self-identified -

**Ethnicity**: set of lifestyle/behavioral/cultural experiences (Hispanic/Latino vs. non-Hispanic/non-Latino)

-A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race.

**Race**: biological quality

-American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and White

Race = proxy for genetics

In racially stratified societies, genes, culture, and environment are strongly confounded

Cooper and Psaty, *Circulation* 2005
Some diseases predominantly affect certain groups more or less than others (or affect them differently):
Sickle cell anemia (African Americans)
Lupus, hypertension (women>men; African Americans)
Stroke, diabetes, kidney disease (Hispanic Americans)
Atrial fibrillation, Crohn’s (Caucasians)
Stomach cancer (Chinese, Japanese)
Cystic fibrosis (European heritage)
Multiple sclerosis (furthest from equator)
Melanoma (NZ, Australia)

Ethnicity/race - linked to GENETICS & ENVIRONMENT

DISEASE SUSCEPTIBILITY/DISEASE PROGRESSION/TREATMENT
Test new biologics and new devices
- Islet cell transplants (T1 diabetes) *INSULIN IS NOT A CURE*
- Teplizumab (mAb CD3) (prevent progression to T1 diabetes)

Test drug safety/device safety
- DES (1938-1971) to prevent miscarriages - found to cause cancers in daughters of exposed women

Identify effective drugs; compare drugs/trtmts

Identify new purposes for drugs/treatments
- Minoxidil — antihypertensive agent → hair growth
- Viagra — angina treatment → prolonged erections

*IMPORTANT: Assess effectiveness & safety of treatments in ALL IMPROVE HEALTH*
Out of 20 drugs tested, how many successfully complete Phases I – III?

1
Diversity

Pre-clinical studies-------------------Clinical Trials

Inclusiveness

Northwell Health℠
What is one of the main reasons why clinical trials fail?

...because they enroll too few subjects

Other reasons for the failure of clinical trials?

...because they don’t enroll diverse subjects
Translation of research evidence into clinical practice is effective only in populations that are adequately represented.

African Americans represent 12% of US population, but <5% of the clinical trial participation

Hispanics make up 16% of the US population, but 1% of the clinical trial participation

Consequences of clinical trials that are not inclusive?
Consequences of inadequate diversity in clinical trials

~50% of Asians and 75% of Pacific Islanders are unable to convert the antiplatelet drug clopidogrel (Plavix, approved 1997) into its active form; → At higher risk for adverse angioplasty outcomes (30% of all those living in HA)...


Have you or anyone in your family ever participated in clinical trials?

- Yes: 16%
- No: 77%
- Not sure: 7%

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.
Wide Majority of Americans Have Heard of Clinical Trials

Have you ever heard of a clinical trial?

- Yes: 80%
- No: 15%
- Not sure: 5%

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.
How much do you admire the following groups of people on a scale of 1 to 4?

- People who volunteer for clinical trials
- People who give blood
- People who donate an organ

### Organ donors
- 69: 4 (a great deal)
- 19: 3
- 3: 2
- 7: 1 (not at all)

### Blood donors
- 61: 4 (a great deal)
- 26: 3
- 43: 2
- 7: 1 (not at all)

### Clinical trial participants
- 37: 4 (a great deal)
- 38: 3
- 9: 2
- 4: 1 (not at all)
- 13: Not sure

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.
<10% of the US population participates in clinical trials – what is the number one reason for lack of participation?

Lack of Trust a Major Barrier to Participation in Clinical Trials

Fewer than 10% of Americans participate in clinical trials. Which of the following do you think is a reason that individuals don’t participate in clinical trials? (percentage saying lack of trust)

- African-American: 61%
- Non-Hispanic White: 54%
- Hispanic: 52%
- Asian: 51%

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.
Reasons for lack of trust?

U.S. Public Health Service Study of Untreated Syphilis at Tuskegee 1932-1972: The Most Infamous Clinical Study

Study of ‘untreated syphilis’: 600 African American men

- Promised free transportation to and from hospitals, free hot lunches, free medical care for diseases other than syphilis, and free burial after autopsies were performed.
- Subjects/victims never informed that they were research subjects, or that treatment for their syphilis could have been provided.
- Told they had “bad blood”, and required periodic medical examinations, including spinal taps.
- Subjects were not offered information regarding the available treatment, and were prevented from seeking it.
- Some subjects died of the disease, passed it on to wives, or passed congenital syphilis to children.
Aftermath of the Tuskegee Syphilis Study?

In 1974 Congress passed the National Research Act

Within the US Dept of Human and Health Services (DHHS), the Office of Human Research Protections was established to oversee clinical trials.

- INFORMED CONSENT
- Institutional Review Boards

-In 1997, President Bill Clinton formally apologized at a ceremony for surviving Tuskegee study participants.
Other barriers to participation in clinical research studies?

---Awareness----Enrollment----Retention--

- fears of exploitation in medical research; mistrust of medicine
- limited access to specialty care centers (referrals to clinical studies)
- financial constraints—lack of transportation, child/adult care
- competing demands of time
- lack of access to information about research (advertisement)
- unique cultural and linguistic differences
  (lack of research staff who share the same culture & language)
- fears of unintended outcomes
- health care discrimination
- negative experiences or lack of positive experiences
True or False?
Until 1988, clinical trials were almost exclusively conducted on men
True
Women were not typically included in clinical trials prior to the 1990s - even though women consume 80% of pharmaceuticals in the US

1992: women were first i.d. as under-represented!
(US Gov’t Accountability Office-GAO-1992)
WHY WERE WOMEN EXCLUDED FROM CLINICAL TRIALS (before 1988)?

- women were considered ‘little men’
- the only difference was in reproductive organs
- most researchers were men
- there were no guidelines to include women – there were guidelines to exclude women
WHY WERE WOMEN EXCLUDED FROM CLINICAL TRIALS (before 1988)?

-Cultural Bias: Protection of women and children

-Women (pregnant) = liability: Thalidomide trials

Thalidomide: a sedative agent developed in the 1950s – used for treating morning sickness

1957-1962 approved for use in the UK, Canada, Germany, and Japan
US: not approved but used in clinical trials (20,000 subjects)
~12,000 babies were born with phocomelia and other birth defects

1977 FDA guideline “…women of childbearing potential should be excluded from earliest dosing studies, Phase I and early Phase II.”
Implications of not including women?

8 out of 10 drugs pulled from the market by the FDA (posed greater health risks to women)

Women: 1.5-2-fold greater chance of adverse drug rxns

EXAMPLES:
Drugs for insomnia (containing zolpiden)
e.g. Ambien, Edluar and Zolpimist (on the market for 20 yrs)

2013: FDA --> women should receive $\frac{1}{2}$ of the dose

Pregnant women require higher doses of Lamictal (for bipolar disorder)
1977-1993: few women included in clinical trials

NIH Revitalization Act of 1993

NIH Guideline that requires inclusion of women & minorities in clinical studies

-Women & minorities are to be included ALL human subject research

5 Races: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian/Pacific Islander, & White

2 ethnic groups: Hispanic/Latino and non-Hispanic/non-Latino

-They are to be included in ALL phases of clinical trials

-Costs cannot be a barrier

-Outreach must take place to include women AND minorities in trials
Pre-clinical Trials: Recent Reports

U.S. TO REQUIRE GENDER EQUALITY FOR MEDICAL LAB RATS EARLY-STAGE MEDICAL STUDIES TEND TO USE MORE MALE ANIMALS THAN FEMALE ONES. THAT'S BAD FOR THE HUMAN WOMEN WHO ULTIMATELY TAKE THESE DRUGS.

By Frances Diept   May 2014 Popular Science

Gender bias in cell and animal research may be one reason why women experience more side effects from drugs than men.

Policy: NIH to balance gender in cell & animal studies (October 2014)
Cardiovascular Disease-Related Clinical Trials
CVD: Cardiovascular Disease

True or False?

Since 1984, CVD deaths for males has exceeded those for females **FALSE - AHA**

Cardiovascular disease (CVD) is the most common cause of death in American women and accounts for a full one-third of all deaths (CDC)

Equal prevalence of CVD between the genders by the age of 40, and by the age of 60 more women than men are affected.

More women than men have died from CVD causes on a yearly basis since the mid 1980s
Overall trends in awareness that coronary heart disease is the leading cause of death in women

% aware of CHD as the leading cause of death in women

It depends on who you are?

National poll: 56% of ALL women
38% of Black women
34% of Hispanic women


Mosca et al, 2006
1993-2016 (23 yrs): How are we doing today?

~54% of participants in clinical trials for CVD are women (Women’s Health Study & Women’s Health Initiative)

However, in mixed gender CVD trials – women are under-represented (Kim and Menon 2009) – 38% and this has remained the same for 30 years!!!!
Inclusion, Analysis, and Reporting of Sex and Race/Ethnicity in Clinical Trials: Have We Made Progress?  

Gellier et al, 2011

86 RCT studies in published PubMed (in 2009)

75% of the studies did NOT report any outcomes by sex
21% did not report sample sizes by racial and ethnic groups
64% did not provide analyses based on racial or ethnic groups
Only 3 studies indicated that the generalizability of their studies may be limited by lack of diversity
No improvements over similar study performed in 2004!
Implications of inadequately representing women in cardiovascular clinical trials

Aspirin therapy for the 1° prevention of CVD has differential effects: In a meta-analysis of 6 trials including >95,000 individuals, aspirin was found to have a significant reduction in composite cardiovascular events in both men & women, 14% and 12%, respectively.

Type of cardiovascular event – gender specific:

Men: **32% reduction in myocardial infarction**
but no significant effect on stroke or mortality

Women: **17% reduction** in stroke
but no significant effect on MI or cardiovascular mortality

Type 2 Diabetes Clinical Trials
Disparity between U.S. diabetes trials participants and incidence

Incidence of Diabetes in the U.S.

* n = 850,000/year**

Type 2 diabetes disproportionately affects ethnic minorities

- Hispanic 36.0%
- White 24.0%
- Black 37.0%
- Other 2.0%
- Asian 1.0%

** NEED TO IMPROVE DIVERSITY

TO IMPROVE DIVERSITY
PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial  
Dormandy et al Lancet 2005  
n=5238 (global)  
**Males:** 67%  
**White:** 98%  

**Incidence of T2 diabetes:**  
White: 24%;  
African-American: 37%;  
Hispanic: 36%  

Action for Health in Diabetes (AHEAD) Trial (prevention of CVD):  
M Espeland et al Diabetes Care, 2007 (education and lifestyle changes)  
Ethnicity (n=5145)  
African-American (15.5%)  
American Indian / Alaskan Native (5.0%)  
Asian / Pacific Islander (1%)  
Hispanic / Latino (13%)  
**Non-Hispanic White** (63.3%)  
Other / multiple (1.9%)  

Predictors of New-Onset Diabetes in Patients Treated With Atorvastatin: Results From 3 Large Randomized Clinical Trials  
Waters et al 2011  
n=7593  
**Males:** Trial 1=82% (TNT); Trial 2=82% (IDEAL) and Trial 3=60% (SPARCL)  
**White:** 89% (TNT); 88% (LEAD)  
Black: 6% (TNT); 2% (Lead)  
Other: 5% (TNT); Asian 7%/Other 3% (LEAD)
“Much of what we know about treating cancer comes from **clinical trials that enroll just 3% of the patients diagnosed with cancer every year,**” says Hudis, who serves on CancerLinQ's board of governors. “With CancerLinQ, we're trying to learn from the remaining 97% who don't participate in these studies.”

Discussing the launch of CancerLinQ, a platform designed to deliver clinical benefits by analyzing aggregated electronic health records from thousands of oncology practices in late 2015, the American Society of Clinical Oncology (ASCO)
Prostate cancer statistics for new cases and deaths by race in the U.S. for the years 2006 – 2010

<table>
<thead>
<tr>
<th>RACE/ETHNICITY</th>
<th>INCIDENCE (New Cases)*</th>
<th>MORTALITY (Deaths)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All races</td>
<td>142.1</td>
<td>22.3</td>
</tr>
<tr>
<td>African American</td>
<td>219.8</td>
<td>49.8</td>
</tr>
<tr>
<td>Asian American or Pacific Islander</td>
<td>72.5</td>
<td>10.0</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>120.2</td>
<td>18.5</td>
</tr>
<tr>
<td>American Indian/Alaskan Native</td>
<td>97.9</td>
<td>21.2</td>
</tr>
<tr>
<td>White</td>
<td>133.2</td>
<td>20.7</td>
</tr>
</tbody>
</table>

* per 100,000

http://zerocancer.org/learn/statistics

from State Cancer Profiles
1998 Tamoxifen Trial

1998: 13,388 women studied over 5yrs (n=220 Black women, 1.6%)
‘Evidence’ → guidelines were written to counsel Black women against preventative tamoxifen therapy at ages 10 years younger than non-Black women (Black women: slightly lower breast cancer incidence but much higher mortality)

6 years later...

2004: Tamoxifen study in Black women – showed equally effective
McCASKILL-STEVENS et al *J Nat’l Cancer Inst* 2004
**Table 2.** Trial Enrollment for Minorities vs Whites According to Cancer Type, 2000-2002

<table>
<thead>
<tr>
<th>Racial/Ethnic Group</th>
<th>No. of Trial Participants</th>
<th>Enrollment Fraction, %</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cancers</td>
<td>37,635</td>
<td>1.7</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>32,633</td>
<td>1.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>1,094</td>
<td>1.3</td>
<td>0.72 (0.68-0.77)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Black</td>
<td>3,062</td>
<td>1.3</td>
<td>0.71 (0.68-0.74)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>745</td>
<td>1.7</td>
<td>0.95 (0.88-1.02)</td>
<td>.16</td>
</tr>
<tr>
<td>American Indian/ Alaskan Native</td>
<td>101</td>
<td>2.5</td>
<td>1.44 (1.18-1.76)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**ALL CANCERS TOTAL: 1.7% enrolled**
- Caucasian 1.8% enrolled
- Hispanic 1.3% enrolled P<0.001
- Black: 1.3% enrolled P<0.001
- Asian/Pacific Islander: 1.7% enrolled
Improvements Over Time (1996-2002)?

Total enrollment increased by 50% (1996-2002)

The proportion of African Americans has declined!

Table 5. Composition of Trial Enrollees According to Race/Ethnicity, 1996-2002

<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. of enrollees</td>
<td>8154</td>
<td>8974</td>
<td>9742</td>
<td>10710</td>
<td>11792</td>
<td>13359</td>
<td>12484</td>
<td>Relative Risk Ratio (95% CI) P Value</td>
</tr>
<tr>
<td>Racial/ethnic group, % of total No. of enrollees</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>83.0</td>
<td>84.2</td>
<td>84.0</td>
<td>86.0</td>
<td>87.4</td>
<td>86.3</td>
<td>86.6</td>
<td>1.0 (Referent)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3.7</td>
<td>3.1</td>
<td>3.1</td>
<td>3.0</td>
<td>2.8</td>
<td>2.9</td>
<td>-3.0</td>
<td>0.88 (0.72-1.08) .23</td>
</tr>
<tr>
<td>Black</td>
<td>11.0</td>
<td>10.7</td>
<td>10.3</td>
<td>9.0</td>
<td>8.0</td>
<td>8.5</td>
<td>7.9</td>
<td>0.76 (0.65-0.89) &lt;.001</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>2.1</td>
<td>1.9</td>
<td>2.1</td>
<td>1.5</td>
<td>1.6</td>
<td>2.1</td>
<td>-2.2</td>
<td>0.99 (0.83-1.18) .91</td>
</tr>
<tr>
<td>American Indian/ Alaskan Native</td>
<td>0.3</td>
<td>0.2</td>
<td>0.5</td>
<td>0.5</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.80 (0.57-1.10) .17</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.
*Adjusted for age, sex, and cancer type using polytomous logistic regression.

Murthy, Krumholz and Gross

Participation in Cancer Clinical Trials: Race Sex-, & Age-Based Disparities
NCI sponsored trials from 2000-2002

How can we improve this?
"The Latino population is one of the fastest growing populations in the US [8], yet is underrepresented in clinical trials [9]. For example, only 3.1% participants of a population-based NCI study were Latino, while their proportion in the US population was 9.1% [9]. In a review of clinical trials covering 2001–2010, Latinos' enrollment constituted only 2.2% of accrued participants [10]. “

Motivators and barriers to Latinas' participation in clinical trials: The role of contextual factors by London et al
Contemporary Clinical Trials 11/2014
DOI:10.1016/j.cct.2014.11.013

How can we improve this?
Ethnic-specific trials vs. trials with diverse ethnic groups...
Circulation. 2005;112:3654-3666

Should ethnicity serve as the basis for clinical trial design?

Importance of Race/Ethnicity in Clinical Trials
Lessons From the African-American Heart Failure Trial (A-HeFT), the African-American Study of Kidney Disease and Hypertension (AASK), and the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)

Anne L. Taylor, MD; Jackson T. Wright, Jr, PhD, MD

ACE inhibitors and β-blockers work better in lowering BP in Caucasians
A-HeFT trial – first all Black cohort Isosorbide dinitrate/hydralazine **43% improved survival**, a **33% reduction in hospitaliz’n for heart failure & a significant improvement in qual of life**

African American hypertensives: 4-20-fold **↑** risk of progression to dialysis than Caucasians
AASK trial compared ACEI+Ca Channel blocker vs. ACEI+β-blocker

Represents major advances in the knowledge base for the trmt of heart and kidney diseases...WHY HAVE SEPARATE TRIALS???
## Cancer: Clinical Trials----AGE

Murthy, Krumholz and Gross *JAMA* 2004

### Participation in Cancer Clinical Trials: Race-, Sex-, & Age-Based Disparities

NCI sponsored trials from 1996-2002

Participants in NCI Cooperative Group Breast, Colorectal, Lung, or Prostate Cancer therapeutic trials, 1996-2002 (n=75,215 subjects)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Trial Participants (%)</th>
<th>Proportion of Incident Cancer Pts</th>
<th>Proportion of US Population, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-64</td>
<td>51,145 (68)</td>
<td>37.5</td>
<td>78.5-over</td>
</tr>
<tr>
<td>65-74</td>
<td>17,851 (23)</td>
<td>31.4</td>
<td>11.3-over</td>
</tr>
<tr>
<td>75+</td>
<td>6219 (8.3)</td>
<td>31.2</td>
<td>10.2-under</td>
</tr>
</tbody>
</table>

Elderly patients, both minorities and whites, were strikingly underrepresented 2/3 of patients are elderly – but only 1/3 of elderly participate in clinical trials. **Older men more likely to enroll than older women….why?**
Elderly (ALL Ethnic Groups): Low Participation in Clinical Trials

<table>
<thead>
<tr>
<th>Age Group, y</th>
<th>No. of Trial Participants</th>
<th>Enrollment Fraction, %</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Racial/Ethnic Groups</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-64</td>
<td>25,199</td>
<td>3.0</td>
<td>Referent</td>
</tr>
<tr>
<td>65-74</td>
<td>9,140</td>
<td>1.3</td>
<td>0.43 (0.42-0.44)</td>
</tr>
<tr>
<td>≥75</td>
<td>3,296</td>
<td>0.5</td>
<td>0.15 (0.15-0.16)</td>
</tr>
<tr>
<td><strong>White</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-64</td>
<td>21,616</td>
<td>3.3</td>
<td>Referent</td>
</tr>
<tr>
<td>65-74</td>
<td>8,056</td>
<td>1.4</td>
<td>0.41 (0.40-0.42)</td>
</tr>
<tr>
<td>≥75</td>
<td>2,961</td>
<td>0.5</td>
<td>0.14 (0.14-0.15)</td>
</tr>
<tr>
<td><strong>Hispanic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-64</td>
<td>817</td>
<td>2.1</td>
<td>Referent</td>
</tr>
<tr>
<td>65-74</td>
<td>218</td>
<td>0.8</td>
<td>0.39 (0.34-0.45)</td>
</tr>
<tr>
<td>≥75</td>
<td>59</td>
<td>0.3</td>
<td>0.14 (0.11-0.18)</td>
</tr>
<tr>
<td><strong>Black</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>30-64</td>
<td>2,103</td>
<td>1.8</td>
<td>Referent</td>
</tr>
<tr>
<td>65-74</td>
<td>715</td>
<td>1.0</td>
<td>0.53 (0.48-0.57)</td>
</tr>
<tr>
<td>≥75</td>
<td>244</td>
<td>0.4</td>
<td>0.24 (0.21-0.27)</td>
</tr>
<tr>
<td><strong>Asian/Pacific Islander</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-64</td>
<td>586</td>
<td>2.7</td>
<td>Referent</td>
</tr>
<tr>
<td>65-74</td>
<td>130</td>
<td>1.0</td>
<td>0.37 (0.31-0.45)</td>
</tr>
<tr>
<td>≥75</td>
<td>29</td>
<td>0.3</td>
<td>0.10 (0.07-0.15)</td>
</tr>
<tr>
<td><strong>American Indian/Alaskan Native</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-64</td>
<td>77</td>
<td>3.4</td>
<td>Referent</td>
</tr>
<tr>
<td>65-74</td>
<td>21</td>
<td>2.2</td>
<td>0.63 (0.38-1.02)</td>
</tr>
<tr>
<td>≥75</td>
<td>3</td>
<td>0.4</td>
<td>0.10 (0.03-0.33)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.
*Racial and ethnic groups are mutually exclusive. P values for the pairwise comparison between each age group and the youngest age group (30-64 years) within each racial category were <.001, except for American Indian/Alaskan Native, 65 to 74 years of age, which was .08.*

How can we improve this?
Former President Jimmy Carter, 2015 (age 91)
Stage 4 melanoma in Aug 2015; radiation+Keytruda (PD-1/PD-L1)
-no tumors found in Nov 2015-

Keytruda: targets the activity of genes called PD-1 and PD-L1. The overall response rate of patients was 76 percent which means that most patients had reduction in cancer cells.
Older patients were included in Keytruda clinical trials (94 yrs). The label of the drug lists a trial with a median age of 61. That’s important: The age of the average melanoma patient is 62, according to the American Cancer Society, and the five-year survival rate when the cancer has spread is only about 15%.

How can we improve the enrollment of elderly subjects in clinical trials?
Patient Income Level and Cancer Clinical Trial Participation

Unger et al, *Journal of Clinical Oncology* 2013, n=5,499 subjects

40% discussed clinical trials with their physicians

in 45% of cases, physicians offered clinical trial participation to pts

51% of these patients participated in clinical trials

Overall participation rate = 9% of which Males: 38%

White: 94%; African American: 2.5%; Asian/Pac Isl: 1.1%; Native Am: 0.4%

Lower income patients are less likely to participate in clinical trials
(patients with incomes <$20,000 showed a 44% lower odds of participation)

Older patients were less likely to participate in clinical trials

<table>
<thead>
<tr>
<th>Household income distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bottom 10%</strong></td>
</tr>
<tr>
<td>$0 to $10,500</td>
</tr>
</tbody>
</table>

Source: US Census Bureau, 2006; income statistics for the year 2005

How can we improve participation of low income patients?
SUMMARY: Who Is Underrepresented in U.S. Clinical Trials?

- **Women:** 8 of the 10 drugs eliminated from the market in the 1990’s because of unexpected side--effects that affected women more than men (*Science.* 2005;308:1517)
- **Elderly:** Nearly 2/3 of cancer pts are >65 yrs old, but <1/3 of all trial enrollees.
- **Children:** Study of 31 1 U.S. pediatric hospitals found that 79% of kids were given at least one medication not been approved for children (*Arch Pediatr Adolesc Med.* 2007;161:282).
- **Adolescents:** Only 10% of 15---19 year old cancer patients enter into trials, while 60% under age 15 take part (*Curr Opin Pediatr.* 2002;14:1-4.)
- **Low income:** Regardless of race or ethnicity, low socio-economic status has a negative impact on clinical research participation.
- **Those who live in rural areas:** Among patients enrolled in NCI sponsored trials, investigators found that suburban areas had the highest participation.
- **Others:** Additional populations who are underrepresented in clinical trials include those with special health needs (disabled, chronic illness, co-morbidities) and the uninsured (*J Clin Epidemiol.* 1999;52:1143-56)
Recommendations for Improving the Success of Clinical Trials

Recruit minority and female healthcare workers & research staff
Educate to raise awareness of clinical trials and their importance
Involve communities
Foster collaborations with communities of ethnic groups
Assess diversity throughout study period
Re-examine trial design and ethics
Build trust through communication
Build trust through communication
Build trust through communication
Seven out of 10 Say Practitioners Don’t Talk About Medical Research

Has your doctor or other health care professional ever talked to you about medical research?

- Yes: 22%
- No: 70%
- Not sure: 8%

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.
Most Would Participate if Asked by Someone They Trust

Do you agree or disagree with the following: I would take part in a clinical trial if I was asked by someone I trust.

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.
Were there any differences in side effects among sex, race and age?
Subgroup analyses were conducted for sex, race and age.
**Sex:** The risk of bleeding is higher among women taking ZONTIVITY than men.
**Race:** There were too few non-Caucasian patients to make a reliable assessment of bleeding risk by race.
**Age:** ZONTIVITY increases the risk of bleeding in all age groups. Because older patients have a higher risk of bleeding in general, there is more bleeding in older patients taking ZONTIVITY.
QUESTIONS???
Our goal is to be a national health care leader, committed to excellence, compassion and improving the health of the community.

- **Quality**: To become the leader in providing quality health care which can be defined and measured.
- **Research**: To improve the human condition by advancing disease-oriented, basic scientific and clinical research.
- **Education**: To provide an exceptional learning environment.
- **Operational Performance**: To act as a system and be recognized as the provider of choice which is operationally efficient and financially successful.
- **Service Excellence**: To provide an environment in which patients, their families, and physicians are highly satisfied with the services provided through the Health System.
- **Workforce Development**: To become the employer of choice through the development and support of a competent, motivated and productive workforce.
- **Promoting Community Health & Advocacy**: To become an indispensable community asset by responding to identified health needs through education, advocacy, partnerships and programs which result in improved access to care and health outcomes.
- **Physician Partnerships**: To become the preferred hospital partner for physicians practicing in the service area.
Why is Diversity a critical component of successful biomedical research and clinical trials?
Clinical and Biomedical Research Still Lacks Diversity

Despite Congressional directives for 30 years to diversify clinical research, the number of studies that include minorities and the diversity of scientists being funded have not improved. **Published Online:** January 01, 2016

Priyam Vora

Researchers compiled 30 years of raw data regarding the percentage of clinical studies that include racial and ethnic minorities. The data included funding for research by non-white scientists and 2 decades of analyses from the National Institutes of Health (NIH).

The researchers found that out of more than 10,000 cancer studies, only 2% studies have included enough minorities to make the conclusions relevant. Additionally, less than 5% of NIH-funded respiratory research programs included ethnic minorities. A separate study showed that scientists from minority communities—who can also help in reaching out to the study participants—are consistently less likely to receive NIH funding. These findings have persisted despite the 1993 NIH Revitalization Act, which mandated all federally funded clinical research programs to prioritize the inclusion of women and minorities.

The Need to Study Diverse Groups

Most scientists rely on research deduced from a largely homogeneous population, usually white and male. The study asserts that this lack of variety in research programs could have negative consequences on our ability to care for the nearly 40% of the current US population whose heritage includes non-European races. It is critical to address this gap because according to forecasts, the proportion of minority residents will exceed 50% by 2044.

The study finds that race/ethnicity and ancestral background can strongly influence disease patterns, clinical presentations and remedial response. While every study doesn’t need to consider genetic variation, at least clinical and biomedical research should include these variations to derive meaningful results. For example, up to 75% of Pacific Islanders are unable to convert the antiplatelet drug clopidogrel into its active form putting them at a higher risk for adverse outcomes after angioplasty.

Minorities Are Under-Studied

The enrollment of minorities in cancer clinical trials remains lacking despite striking racial/ disparities in cancer incidence and mortality. The same is true for minority representation in research for cardiovascular diseases and diabetes.

While some NIH reviewers have argued that including diverse groups might increase the financial costs, not including them has greater financial consequences. For instance, bridging the disparity gap would have cut down medical costs by more than $1.2 trillion during 2003-2006. It is a question of short-term expenses versus long-term economic benefits.

Understanding the Hurdles to Diversify Research

Inadequate access to specialty care centers and fear of being exploited in medical research are some of the most-cited barriers to research diversity. The study cites other barriers such as lack of access to information, not fully understanding the scope of the research, cultural and linguistic differences, insufficient time, inadequate funds, fears of unintended outcomes, stigmatization, and healthcare discrimination. It is imperative that funders, academic institutions, investigators and potential research participants all get together in this effort to bridge the gap in research diversity.

- See more at: http://www.ajmc.com/newsroom/clinical-and-biomedical-research-still-lacks-diversity#sthash.BPYwdxmE.dpuf
PROBLEM:
The NIH guidelines only apply to federally funded clinical trials

What percentage of clinical trials were federally funded?

20%: Federally funded

80%: Sponsored by pharmaceutical companies (ref: US General Acct’ing Office) and these are regulated by the FDA

FDA: Modernization Act of 1997
and
Guidance for Industry Collection of Race and Ethnicity Data in Clinical Trials

U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Center for Biologics Evaluation and Research (CBER) Center for Devices and Radiologic Health (CDRH) Office of the Commissioner (OC)
September 2005 Clinical Medical

- Guidelines -