Gender Health Disparities and Clinical Implications

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Health Disparities: Definition

“Health disparities are differences in the incidence, prevalence, mortality, burden of diseases and other adverse health conditions or outcomes that exist among specific population groups in the United States.”

National Institutes of Health, 1999
Basis of Health Disparities

• Gender
• Age
• Ethnicity
• Socioeconomic status
• Geography
• Sexual orientation
• Disability or special health care needs
Determinants of Health Disparities

- Natural, biological variation
- Inadequate access to essential health and other basic services
- Transient health advantage of one over another (first adopters of health promoting behavior)
- Health damaging behavior: no restriction on lifestyle choices
- Health damaging behavior: degree of lifestyle choices is severely restricted
- Exposure to unhealthy, stressful living and working conditions
- Natural selection (health related mobility) .... Sick people tend to move down the social scale.
Gender-Specific medicine is the *science* of how normal function and the experience of disease is influenced by the sex of the patient.
Gender and Sex: Definition

- **Gender**: introduced in the 1970s as an alternative to ‘sex’
- **Gender**: a social construct
- **Sex**: a biological term

*Krieger N., 2001;2003*
Sex, Gender & Health

- Explanations for many population and individual level health outcomes are not attributable to biology
- Income, income inequality, social connectedness, and social capital all show some association with health and illness

Sex and gender health association is a complex intertwined relationship
Access & Quality
Socioeconomic Disparity

• Below 100% of the Poverty Level (19-64 yo)
  ▪ Women: 17%
  ▪ Men: 13%

• Median earnings (>15 yo)
  ▪ Women: $22,224
  ▪ Men: $32,486

• Women earn 76.5 cents/$1.00 compared to men
Figure 7. Women Are More Likely Than Men to Have Access Problems in Past Year Because of Cost

Percent of adults ages 19–64 reporting the following problems in past year because of cost

- Did not fill a prescription
- Did not see specialist when needed
- Skipped medical test, treatment, or follow-up
- Had medical problem, did not see doctor or clinic
- Any of the four access problems

* Difference between men and women is significant at $p \leq 0.05$ or better.

Figure 6. Women Are More Likely Than Men to Have Cost-Related Access Barriers

Percent of adults ages 19–64 who have difficulty accessing health care:

- **Total**: Men 30, Women 43*
- **Insured continuously**: Men 23, Women 33*
- **Uninsured**
  - Men 49
  - Women 68*

* Difference between men and women is significant at p ≤ 0.05 or better.
^ Did not fill a prescription; did not see a specialist when needed; skipped recommended medical test, treatment, or follow-up; had a medical problem but did not visit doctor or clinic.
^^ Uninsured combines currently uninsured and currently insured but had a time uninsured in the past 12 months.

Figure 3. Women Are More Likely to Have Employer-Sponsored Insurance Through Their Spouses

Percent of adults ages 19-64 by insurance source

- Spouse’s Job
- Own Job

Men:
- Spouse’s Job: 52
- Own Job: 11

Women:
- Spouse’s Job: 64
- Own Job: 24

Figure 4. Women Under Age 65 Are More Likely Than Men to Take Prescription Medicines on a Regular Basis

Percent of adults who take prescription medicines on a regular basis

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>44</td>
<td>60</td>
</tr>
<tr>
<td>19-29</td>
<td>14</td>
<td>40</td>
</tr>
<tr>
<td>30-49</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>50-64</td>
<td>60</td>
<td>69</td>
</tr>
<tr>
<td>65+</td>
<td>85</td>
<td>89</td>
</tr>
</tbody>
</table>

* Difference between men and women is significant at $p \leq 0.05$ or better.

## Gender and Health Care Access

<table>
<thead>
<tr>
<th>Consumer Issue</th>
<th>Gender Majority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consumers of Health Care</td>
<td>Women</td>
</tr>
<tr>
<td>Part-time employment</td>
<td>Women</td>
</tr>
<tr>
<td>Preventative Services</td>
<td>Women</td>
</tr>
<tr>
<td>Lower Income</td>
<td>Women</td>
</tr>
<tr>
<td>Higher out-of-pocket expenses</td>
<td>Women</td>
</tr>
<tr>
<td>Coverage through spouse</td>
<td>Women</td>
</tr>
</tbody>
</table>
Connection to the System

• In general, women
  ▪ “are more likely to have a usual primary care provider than men” (Agency for Healthcare Research and Quality, 2004)
  ▪ “are more likely to enter treatment through primary care [as opposed to emergency services]” (Hauenstein et al., 2006)
  ▪ with a connection to the health care system are more likely to have their mental health needs met” (Sherbourne et al., 2001)
  ▪ may have fragmented care

• In general, men
  ▪ use less medical services
  ▪ have less frequent preventative ambulatory visits
  ▪ tend to wait until there is an emergent need
Measurable Outcomes

HEDIS: The nation’s most widely used tool of health care quality measurement, developed and maintained by NCQA

Gender Difference
  ▪ Cholesterol

No Gender Difference
  ▪ Blood Pressure
  ▪ HgA1C

National Committee for Quality Assurance (NCQA), 2005
Research
Clinical Research in Women

WE HAVE STUDIES OF FRUIT FLIES, MICE, HAMSTERS, FROGS, MONKEYS AND MEN WITH THIS CONDITION - BUT MEDICAL RESEARCH USING WOMEN AS SUBJECTS JUST NEVER OCCURRED TO ANYBODY.
Formation of “Women’s Health”

• 1980-1990’s
  ▪ Public Health Services Task Force on Women’s Health
  ▪ Creation of the Office of Research on Women’s Health
  ▪ FDA reversed its 1977 edict excluding women from clinical trials
  ▪ National Institutes of Health Revitalisation Act 1993
    • 1998 65% of NIH studies included women
Scientists had made the assumption without confirmatory testing and that what is learned from studying men could be extrapolated to women without modification.

At the time researchers did not report gender analysis, perform gender sub-analysis, or power studies to assess the impact of gender.

2/3 of all research on diseases that affected both sexes had been performed exclusively in men.
Cardiovascular Disease
AHA Guidelines

Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women

Expert Panel/Writing Group*
Lori Mosca, MD, PhD (Chair); Lawrence J. Appel, MD; Emelia J. Benjamin, MD; Kathy Berra, MSN, ANP; Nisha Chandra-Strobos, MD; Rosalind P. Fabunmi, PhD; Deborah Grady, MD, MPH; Constance K. Haan, MD; Sharonne N. Hayes, MD; Debra R. Judelson, MD; Nora L. Keenan, PhD; Patrick McBride, MD, MPH; Suzanne Oparil, MD; Pamela Ouyang, MD; Mehmet C. Oz, MD; Michael E. Mendelsohn, MD; Richard C. Pasternak, MD; Vivian W. Pinn, MD; Rose Marie Robertson, MD; Karin Schenck-Gustafsson, MD, PhD; Cathy A. Sila, MD; Sidney C. Smith, Jr, MD; George Sopko, MD, MPH; Anne L. Taylor, MD; Brian W. Walsh, MD; Nanette K. Wenger, MD; Christine L. Williams, MD, MPH
Hypertension

31 studies (103,268 men and 87,349 women)

Major Drug Classes Included
- ACE Inhibitors
- Angiotensin-receptor Blockers
- B-Blockers
- Calcium Channel Blockers
- Diuretics

Major Outcomes
- Non-fatal stroke or death from cerebrovascular disease
- Non-fatal myocardial infarction or deaths from CHD
- Heart failure causing death or requiring hospitalization
- Total major cardiovascular events
- Total cardiovascular deaths
- Total mortality

Achieved blood pressure reductions were comparable for both men and women.

Lipids
Do Satins Work Equally Well for Men and Women?

Time Magazine March 31, 2010
Representation of ♀ in Clinical Trials of Cholesterol Lowering Medicines

<table>
<thead>
<tr>
<th>Trials</th>
<th>Number of Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1° Prevention Trials with Statins</td>
<td>20,566</td>
</tr>
<tr>
<td>Male</td>
<td>2,939</td>
</tr>
<tr>
<td>Female</td>
<td>17,627</td>
</tr>
<tr>
<td>2° Prevention Trials with Statins</td>
<td>32,956</td>
</tr>
<tr>
<td>Male</td>
<td>11,001</td>
</tr>
<tr>
<td>Female</td>
<td>21,955</td>
</tr>
<tr>
<td>Fibrate Trials</td>
<td>13,945</td>
</tr>
<tr>
<td>Male</td>
<td>373</td>
</tr>
<tr>
<td>Female</td>
<td>13,572</td>
</tr>
</tbody>
</table>
Representation of ♀ in Clinical Trials of Cholesterol Lowering Medicines

JUPITOR, MEGA, AFCAPS/TeXCAPS: Primary Prevention
ASCOT-LLA, ALLHAT-LLA: < 15% with CVD
HPS, PROSPER: No Gender Subset Analysis
Justification of the Use of Statins (JUPITER)

- Study Design
  - Randomized placebo controlled trial
  - 20mg rosuvastatin
  - 11,000
  - Men > 50 yo Women > 60 yo
  - CRP < 2.0 ng/l LDL < 130 mg/dl
- The rates of the primary end point were 0.77 and 1.36 per 100 person-years of follow-up in the rosuvastatin and placebo groups
- The rosuvastatin group did have a higher incidence of physician-reported diabetes.
- NNT 120 for 1.9 years to prevent 1 event

### Justification of the Use of Statins (JUPITER)

<table>
<thead>
<tr>
<th>Outcome Event</th>
<th>Men p-value</th>
<th>Women p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Event</td>
<td>&lt;0.0001</td>
<td>0.02</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>&lt;0.0001</td>
<td>0.18</td>
</tr>
<tr>
<td>Any MI</td>
<td>0.0006</td>
<td>0.11</td>
</tr>
<tr>
<td>Any Stroke</td>
<td>0.0005</td>
<td>0.40</td>
</tr>
<tr>
<td>Arterial revascularization and hospitalization</td>
<td>0.002</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MI, Stroke, Death from CVD</td>
<td>&lt;0.0001</td>
<td>0.16</td>
</tr>
<tr>
<td>Any Death</td>
<td>0.08</td>
<td>0.12</td>
</tr>
<tr>
<td>New Onset DM</td>
<td>0.29</td>
<td>0.008</td>
</tr>
</tbody>
</table>
Carotid Atorvastatin Study in Hyperlipidemic Postmenopausal Women (CASHMERE)

• 12 month trial
• Postmenopausal Women
• Moderate Dyslipidemia
• Randomized Placebo Controlled
• 80mg Atorvastatin vs. Placebo (n=192 vs 206)
• Results: No change in intimal medial thickness (IMT)
Primary Prevention with Statins in Women

The risk benefit ratio of statins for primary prevention of CVD in women has not been definitively established.

The differing results in men compared to women may be due to the diminished effect of elevated LDL in women compared to men or the lack of evaluation of more unique risk factors
The Aspirin Connection
Women’s Health Study Aspirin
New England Journal
March 2005

• 40,000 Women
• Aspirin 100 mg every other day vs placebo
• Followed for 10 years
• Results
  ▪ Non-fatal Stroke
  ▪ Non-fatal Heart Attack
  ▪ Hemorrhagic Stroke
  ▪ Cardiovascular disease death

Ridker P, et al. NEJM 2005
Figure 3. Aspirin in the Primary Prevention of Myocardial Infarction and Stroke among Men and Women.

The results of a sex-specific random-effects meta-analysis of data from six trials are shown: the British Doctors’ Trial (BDT), the Physicians’ Health Study (PHS), the Thrombosis Prevention Trial (TPT), the Hypertension Optimal Treatment (HOT) study, the Primary Prevention Project (PPP), and the current Women’s Health Study (WHS). The relative risk (RR) and 95 percent confidence interval (in parentheses) are shown for each trial (indicated by the box and horizontal line through each box, respectively), and the relative risk is shown for the combined results (indicated by the diamond and the dashed line in each graph). For the relative risk of myocardial infarction among women, the dashed line is coincident with the solid line at 1.00. The size of the box is proportional to the amount of information in the corresponding trial.
Relative risks and 95% confidence intervals of myocardial infarction stratified by percentage of male participants

<table>
<thead>
<tr>
<th>Male (%)</th>
<th>Non-fatal MI</th>
<th>p*</th>
<th>Fatal MI</th>
<th>p*</th>
<th>Both fatal and non-fatal MI</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–66</td>
<td>0.87 (0.71–1.06)</td>
<td>0.26</td>
<td>0.87 (0.65–1.17)</td>
<td>0.86</td>
<td>0.86 (0.79–0.95)</td>
<td>0.52</td>
</tr>
<tr>
<td>70–89</td>
<td>0.72 (0.61–0.86)</td>
<td>0.23</td>
<td>0.91 (0.75–1.11)</td>
<td>0.24</td>
<td>0.82 (0.71–0.95)</td>
<td>0.13</td>
</tr>
<tr>
<td>100</td>
<td>0.62 (0.54–0.71)</td>
<td>0.48</td>
<td>0.55 (0.20–1.53)</td>
<td>0.01</td>
<td>0.63 (0.46–0.85)</td>
<td>0.02</td>
</tr>
<tr>
<td>Total</td>
<td>0.72 (0.64–0.81)</td>
<td>0.03</td>
<td>0.88 (0.75–1.03)</td>
<td>0.19</td>
<td>0.79 (0.72–0.87)</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

MI, myocardial infarction.

*Test for heterogeneity, p value is from $\chi^2$ test. Random effects model was used in all combinations.

Yerman et al. *BMC Medicine* 2007

total of 23 trials (n = 113,494 participants)
Gender and Aspirin

• Men
  ▪ Decrease Risk of MI
  ▪ No/Slight Decrease Risk of Stroke
  ▪ Recommendations
    • Men with known CAD
    • Men with a $\geq 10\%$ 10 yr risk
    • Men $> 45$ yo when benefit $>\text{risk}$

• Women
  ▪ ? decrease of MI
  ▪ Decrease in Risk of Stroke
  ▪ Recommendations
    • Women with known CAD
    • Women with a $\geq 10\%$ 10 yr risk
    • Women $> 55$ yo if benefit $>\text{risk}$
Cardiovascular Disease

- Women arrive at the hospital later than men.
- Younger women were less likely to be treated with aspirin.
- Women were more likely to be given a diagnosis other than coronary artery disease.
- Less women discharged on beta-blockers.
- Women have a slightly higher 30 day mortality.
- Women had longer door-to-needle time (12.5 min).
Model of Microvascular Angina in Women

Hormonal Alterations coupled with:

Pro-atherogenic factors
- Hyperlipidemia
- HTN
- Smoking
- Metabolic dysfunction
- Inflammation

Sex-specific precursors
- PCOS
- Hypoestrogenemia
- Menopause

Subendocardial or epicardial ischemia

Nonobstructive atheroma

Microvascular dysfunction

Accelerating factors
- Early menopause
- Risk factor clustering

Vascular dysfunction symptoms
- Atypical symptoms, including prolonged symptoms at rest, shortness of breath, unusual fatigue, and more frequent pattern

Shaw, L. et al, JACC Nov 2009
Mental Health
Antidepressants

• Prescribing rate for antidepressants increased by 48% between 1995-2002
• 118 million prescriptions (CDC, 2005)
• Most commonly prescribed medication (CDC, 2005)
## Gender and Depression

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Women as compared to Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset</td>
<td>Earlier</td>
</tr>
<tr>
<td>Lifetime Prevalence Rate</td>
<td>Higher (20% vs. 10%)</td>
</tr>
<tr>
<td>Duration of episodes</td>
<td>Longer</td>
</tr>
<tr>
<td>Relapse Rate</td>
<td>Higher</td>
</tr>
<tr>
<td>Effect of Seasonal Changes</td>
<td>Greater</td>
</tr>
<tr>
<td>Response to SSRI</td>
<td>Women</td>
</tr>
<tr>
<td>Co-morbid anxiety</td>
<td>Greater</td>
</tr>
<tr>
<td>Co-morbid Alcohol and Substance Abuse</td>
<td>Less</td>
</tr>
<tr>
<td>Association of Gonadal Hormones</td>
<td>Greater</td>
</tr>
<tr>
<td>Suicide Attempts</td>
<td>Greater</td>
</tr>
<tr>
<td>Suicide Completion</td>
<td>Less</td>
</tr>
</tbody>
</table>

Kornstein S, Primary Psychiatry. 2003;10(12):58-61
Nicotine Addiction
Effect of Nicotine on Women

- **Nicotine**
  - Women: calming effects on stress-induced mood changes
  - Men: enhance aggressive moods

- **Nicotine + alcohol**
  - Women: appears to enhance the effects of alcohol.
  - Men: appears to dilute some of the sedating and intoxicating effects of alcohol.

- **Women may be more responsive than men to non-nicotine stimuli**
Smoking Cessation

• Quitting Smoking
  ▪ Women less successful than men
  ▪ Women relapse more often and for different reasons than men

• Women > Men
  ▪ Join smoking cessation groups
  ▪ Experience severe withdrawal symptoms
  ▪ Worry about weight gain

• Men > Women
  ▪ Benefit from nicotine replacement therapy

• Women = men
  ▪ Effectiveness of bupropion
Gender and Diabetes

- Women vs. Men with OSA
  - New-onset DM: OR 11.8
- Severe Diabetic Retinopathy
  - M > F
- Risk of sudden death in patients with adult-onset DM
  - 300% (F) vs 50% (M)
- Skin Disorders in DM
  - Lipodystrophy F>M
  - Acanthosis Nigricans F>M
- Baseline albuminuria
  - M>F

Celen YT et al, J Clin Sleep Med. 2010 Jun 15;6(3):244-50
Gender-Specific Medicine

- Encompasses all Aspects of Medicine
- Proven Gender Differences
- Future Applications in Clinical Practice
- Improved Clinical Care
- Expand Research and Education Programs
- Benefits Both Men and Women
The study of sex- and gender-based differences in healthcare continues to be limited by:

- a historical deficit in data on women
- an emerging understanding of unique issues about women’s gender specific medicine
- the absence of standardized reporting mechanisms to collect and analyze data
Challenges

• To determine where and when sex- and gender-based differences in health emerge
• To determine the clinical significance of observed differences
Gender Disparities Exist

The Journal of Men’s Health & Gender
September 2004

Thank you for Your Attention