Never Too Early, Never Too Late: Cardiovascular Health for Women Throughout the Lifespan

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Over the next year...

- 8.6 million deaths among women annually.
- Largest single cause of mortality; 1/3 of women’s deaths worldwide.
- In low- and middle-income countries, CVD death rates equivalent in women and men.
- Women in developing world more likely to die from CVD compared with women in industrialized nations.
- By 2020, coronary heart disease (CHD) will have increased by 120% among women from 1990’s levels.

Cardiovascular Disease Mortality Trends for Males and Females
United States: 1979-2003

Source: CDC/NCHS.

Source: NCHS and NHLBI. These data include coronary heart disease, heart failure, stroke and hypertension.

CHD Mortality in Younger Women
Women under 65 suffer the highest relative sex-specific CHD mortality.

Figure 1: Mean of death during hospitalization for coronary heart disease age and sex, according to age. The intervention rates are age and sex specific (NHANES I).


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Cardiovascular Health for Women Throughout the Lifespan

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Gender Differences in the Prevalence and Potency of CVD Risk Factors

Heart Disease is Preventable

- Not an inevitable part of life
- We have effective means to prevent heart disease
- We just don’t use these preventive strategies enough: particularly in women and minorities

Estimates for Ideal Cardiovascular Health based on AHA 2020 Goals
### Classification of CVD Risk in Women

**High risk**
- Established coronary heart disease
- Cerebrovascular disease
- Peripheral arterial disease
- Abdominal aortic aneurysm
- End-stage or chronic renal disease
- Diabetes mellitus
- 10-Year Framingham global risk >10%

**Optimal risk**
- Healthy lifestyle, with no risk factors, BP <120/80, Total cholesterol <200, BMI <25 kg/m², 150 min of activity per week, DASH diet

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### At risk
1 major risk factors for CVD, including:
- Cigarette smoking
- Poor diet
- Physical inactivity
- Obesity, especially central adiposity
- Family history of premature CVD (CVD at <55 years of age in male relative and <65 years of age in female relative)
- Hypertension
- Dyslipidemia
- Evidence of subclinical vascular disease (e.g., coronary calcification)
- Metabolic syndrome
- Poor exercise capacity on treadmill test and/or abnormal heart rate recovery after stopping exercise
- History of Gestational DM, Pregnancy induced HTN, preeclampsia
- Lupus, Rheumatoid Arthritis

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### Lifetime vs 10-Year CVD Risk Estimates

**Women**
- CVD risk levels
  - High short term (>10% 10-yr)
  - Low short term/high lifetime (<10% 10-yr/<39% lifetime)
  - Low short term/low lifetime (<10% 10-yr/<39% lifetime)
CVD Risk Factors in Women vs Men

<table>
<thead>
<tr>
<th>Factor</th>
<th>Prevalence vs Men</th>
<th>Relative Risk vs Men</th>
<th>Age Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>↓</td>
<td>↑↑↑</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>↑</td>
<td>↑↑</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>↑</td>
<td>↑↑</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>↑</td>
<td>↑↑</td>
<td></td>
</tr>
<tr>
<td>Physical Inactivity</td>
<td>↑↑</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>↑</td>
<td>↑↑</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>↑↑↑</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td>SLE/Rheumatoid Arthritis</td>
<td>↑↑↑</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>↑↑</td>
<td>↑</td>
<td></td>
</tr>
</tbody>
</table>

Gender Differences in the Effect of Smoking

- ↓ deaths due to smoking in men in all but 1 state (OK) but ↑ deaths in women in 18 states*
- Greater effect of Smoking in women vs men:
  - Meta-Analysis included 3,912,809 individuals and 67,075 coronary heart disease events from 86 prospective trials
  - Risk of smoking vs non smoking in those with heart disease was 25% greater in women vs men
  - Increased by 2% per year
  - Risk may be even higher because women often smoke less than men and women tend to start smoking later

*Alabama, Arizona, Arkansas, Georgia, Indiana, Kansas, Kentucky, Louisiana, Mississippi, Michigan, North Carolina, Ohio, Oklahoma, South Carolina, South Dakota, Tennessee, Texas, Washington, DC.

Huxley RR et al. The Lancet 2011; 378: 1297 - 1305
Gender Differences in the Effect of Diabetes on Heart Disease

- Diabetes increases CAD risk 3-fold to 7-fold in women vs 2-fold to 5-fold in men
- Diabetes doubles the risk of second heart attack in women but not in men
- Finnish Study:
  - Burden of conventional risk factors in presence of Diabetes is greater in women vs men
  - Hazard Ratio of Major CHD events 2.9 (2.0-3.7) for diabetic man vs 9.5 (5.5-16.9) in diabetic woman, after controlling for other CVD risk factors
- Framingham Heart Study
  - Women with diabetes mellitus had relative risk of 5.4 for CAD vs women without diabetes
  - Men with diabetes had relative risk of 2.4
- Nurses’ Health Study
  - Relative risk of 6.3 for total cardiovascular (CV) mortality
  - Even if women had diabetes for <4 years, their risk of CAD was significantly elevated

Framingham Heart Study 30-Year Follow Up: CVD Events in Patients With Diabetes
(Ages 35-64)

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CVD</td>
<td>38</td>
<td>20</td>
</tr>
<tr>
<td>CHD</td>
<td>19</td>
<td>9</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>AMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>3*</td>
<td></td>
</tr>
</tbody>
</table>

Age-adjusted annual rate/1,000

Risk ratio

P<0.001 for all values except *P<0.05.


Diabetes: Temporal Gender Differences in All-Cause Mortality Rates

Men with Diabetes:
- death rates decreased by 18 deaths/1000 persons (similar decline in CVD mortality)

Women with Diabetes:
- death rates increased and more than double vs non-diabetic woman

**NHANES III: Age-Adjusted Prevalence of the Metabolic Syndrome***

- **Men**
  - White: 24.8%
  - African-American: 22.8%
  - Mexican-American: 25.7%

- **Women**
  - White: 16.4%
  - African-American: 28.3%
  - Mexican-American: 35.6%

*Criteria based on ATP III; diabetics were included in diagnosis.

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**Risk of Developing Diabetes, CHD, or Stroke by Metabolic Syndrome by Gender**

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes</strong></td>
<td>HR</td>
<td>HR</td>
</tr>
<tr>
<td></td>
<td>(95% CI)</td>
<td>(95% CI)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5.1</td>
<td>4.5</td>
</tr>
<tr>
<td>(4.2 – 6.3)</td>
<td>(3.7 – 5.6)</td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>2.3</td>
<td>1.5</td>
</tr>
<tr>
<td>(1.8 – 2.9)</td>
<td>(1.3 – 1.8)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>1.8</td>
<td>1.5</td>
</tr>
<tr>
<td>(1.2 – 2.8)</td>
<td>(1.0 – 2.2)</td>
<td></td>
</tr>
</tbody>
</table>

The presence of the Metabolic Syndrome was stronger predictor of DM, heart disease and stroke in women than in men.

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**Female-Specific Risk of Diabetes: Gestational Diabetes**

*Increased risk of CVD for GDM
• Attributable mostly due to development of Type 2 DM

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**ADA RECOMMENDATIONS**

- Women with a history of GDM should have lifelong screening for the DM or prediabetes at least every 3 years.
- Women with a history of GDM found to have prediabetes should receive lifestyle interventions or metformin to prevent DM.

**AHA GUIDELINES FOR WOMEN**

- GDM considered "At-Risk" Status
- Which women with GDM gets type 2 DM?
  - At 10 years, type 2 DM was 6X higher in "high-risk" GDM.
  - High-Risk Cluster = any 4 of cardiometabolic risk factors (BMI>30 kg m⁻², impaired glucose or insulin>7.8 mL L⁻¹, elevated triglycerides, low HDL or SBP>125 mm Hg) in pregnancy (5n 88.7% Sp 95.9%)

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Gender Differences in Lipids

Framingham Heart Study

![Graph showing gender differences in lipids](image)

Triglycerides are a significant risk factor for women, not men.

Coronary Heart Disease in Relation to HDL-C and Triglyceride Levels in Women

![Bar graph showing HDL cholesterol and triglycerides](image)

Castelli WP. Can J Cardiol. 1988;4:5A-10A.

Coronary Heart Disease in Relation to HDL-Cholesterol and Triglyceride Levels in Women

![Bar graph showing CHD mortality rates](image)

At all levels of LDL-C, CVD mortality rates in women with low HDL-C levels were 3 to 4 times greater compared with women with high HDL-C levels.


Age-adjusted Cardiovascular Disease Mortality in Women: Lipid Research Clinic Follow-Up

![Bar graph showing age-adjusted mortality](image)

HDL-C <50 mg/dL

HDL-C ≥50 mg/dL

< 131 mg/dL

131-160 mg/dL

> 160 mg/dL

LDL-Cholesterol
Gender Differences in Hypertension

NHANES 2005-2008

Female-Specific Risk of Hypertension: Pre-Eclampsia and Gestation HTN

The Northern Finland Birth Cohort 1966 included all expected births from 1 year (N=12,055 women).

- BP from prenatal care records
- Subsequent events from registries (~39.4 years)
- Gestational HTN: associated with increased risk of ischemic heart disease, MI, MI death, HF, ischemic stroke, kidney disease and DM.
- Isolated Systolic HTN was associated with increased risk of MI death, HF, and DM
- Isolated diastolic hypertension was associated with increased risk of ischemic heart disease

Source: NCHS and NHLBI. Hypertension is defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg, taking antihypertensive medication, or being told twice by a physician or other professional that one has hypertension.

Physical Activity in the USA-2010

<table>
<thead>
<tr>
<th>Gender</th>
<th>Meeting Guidelines</th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>25%</td>
</tr>
<tr>
<td>Female</td>
<td>16%</td>
</tr>
<tr>
<td>White Women</td>
<td>19%</td>
</tr>
<tr>
<td>Black Women</td>
<td>11%</td>
</tr>
<tr>
<td>Asian</td>
<td>18%</td>
</tr>
<tr>
<td>American-Indian</td>
<td>12%</td>
</tr>
<tr>
<td>Mexican-American</td>
<td>12%</td>
</tr>
</tbody>
</table>

Sources: National Health Interview Survey 2010

Risk of Death in Asymptomatic Women by Fitness

For each ↑1-MET, there was a 17% ↓ risk of death from all causes (P<0.001)* (*adjusted for traditional risk factors)

Risk of Death Among Women, By Expected Exercise Capacity for Age

Table 3. Hazard Ratios for Death From Any Cause and From Cardiac Causes among Women, According to the Deviation From the Expected Exercise Capacity for Age.

<table>
<thead>
<tr>
<th>Exercise Capacity</th>
<th>Death From Any Cause</th>
<th>Death From Cardiac Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Asymptomatic Women</td>
<td>Symptomatic Women</td>
</tr>
<tr>
<td></td>
<td>Asymptomatic Women</td>
<td>Symptomatic Women</td>
</tr>
<tr>
<td></td>
<td>Hazard ratio (95 percent confidence interval)</td>
<td></td>
</tr>
<tr>
<td>Exercise capacity</td>
<td>≥3 MET</td>
<td>≤3 MET</td>
</tr>
<tr>
<td>Observed v. pred. capacity (MET)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Hazard ratio</td>
<td>3.2 (1.01-10.7)</td>
<td>1.0 (0.40-2.48)</td>
</tr>
</tbody>
</table>

* The reference group is women whose exercise capacity was at least 85 percent of that predicted for age.
† This group served as the reference group.
Female-Associated Inflammatory Disorders

- Rheumatoid arthritis (RA ~1%) and Systemic Lupus Erythematosus (SLE ~1:2500): female predominance with 5-8 X greater risk of CAD
- Link between RA and SLE and CAD is inflammation - key role in all stages of atherosclerosis: endothelial dysfunction, plaque rupture, thrombosis.
- RA and SLE also have an influence on and accentuates some traditional CVD risk factors: dyslipidemia (low HDL), obesity, insulin resistance.
- Disease and Treatment impact CAD risk but exact mechanism is not completely clear
- Risk Estimation Formulas do not adequately predict risk in these patients

Inflammatory Disorders: CVD Effects

Conclusion

- Gender Differences exist in the impact of specific CVD risk factors: Tobacco, diabetes, metabolic syndrome, dyslipidemia, hypertension, fitness
- Female specific issues: Pregnancy induced HTN, pre-eclampsia, Gestational diabetes, PCOS
- Female preponderance diseases associated with markedly increased CVD risk: Rheumatoid Arthritis, SLE; need to develop risk assessment tool for this high risk population
- Other Issues for Women: Breast Cancer Therapy Effects, Chest Radiation
Which of the following is a true statement?

a) More men than women have hypertension in those over the age of 65
b) Pre-eclampsia increases the risk of future hypertension, stroke and diabetes
c) Women have an increased prevalence of diabetes but a diabetic woman has better CVD outcomes when compared to a diabetic man.
d) Pre-eclampsia increases the risk of future hypertension and stroke, but not diabetes
e) The Framingham Risk Score will accurately assess a woman’s risk of a myocardial infarction in the next 10 years if she had Rheumatoid Arthritis

Cardiovascular Health Improvement/Risk Reduction in Women: What works?
**Atherosclerosis Prevention**

- **Lifestyle interventions** —
  - Cornerstone of prevention
  - First step in risk factor management
- **Of particular importance** —
  - Smoking cessation
  - Ideal body weight
  - Promoting regular physical activity
  - Promoting heart healthy dietary patterns
  - Stress reduction

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**Prominent Risk Factors:**

**Premenopausal**

- **Abnormal ovarian function** *(Barton 2013)*
  - Loss of protective benefits of estrogen
  - Inadequate ovarian reserve: associated with unhealthy cardiometabolic risk profile *(Bail 2013)*
- **Polycystic ovary syndrome**
- **Metabolic syndrome** *(Simkova et al 2013)*
- **History of lactation < 3 mos** *(McClure 2012)*

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**Perimenopausal**

- **Decrease in exercise > decrease in calorie intake** (weight gain, waist circumference)
- **Decreased social interaction d/t:**
  - Mood disorders
  - Sleep disturbance
  - Vasomotor symptoms
  - Changes in work patterns *(ESHRE Capri Workshop Group 2011)*
- **Alterations in lipid profiles**
Prominent Risk Factors: Postmenopausal
• Dyslipidemia
• Hypertension
• Metabolic Syndrome
• Lack of exercise
• Psychosocial function
  – Social support
  – Dysphorias

Elements of Successful Interventions
Program components
Delivery strategies
Community participation

Successful Program Components
Promotion of Behavior Change:
Cognitive-Behavioral Strategies
  Goal setting
  Self-monitoring
  Frequent and prolonged contact
  Feedback and reinforcement
  Self-efficacy enhancement
  Modeling
  Motivational Interviewing
  Problem solving and Relapse Prevention
Delivery Strategies

• Group-based interventions work well in women
  – Offer social support
  – Similar challenges in modifying lifestyle
  – Successful in white and minority populations

• Individual-Focused Interventions/Personalized goal setting

• Computer Technology
  – Internet-based
  – Technology

Improving Cardiovascular Health in the Community

• Principles of Community-based participatory research
  – Work with community members to understand social and cultural context of population
  – Identify appropriate settings for the intervention
  – Include local community members in the design and implementation of the intervention
  – Use culturally sensitive approaches
  – Use churches and local residents as health promoters

Cardiac Risk Reduction Intervention for At Risk Young Black Women

American Heart Association: Clinical Research Grant # 12CRP11910021
Involving the Community
Cultural Sensitivity

• Theory of Planned Behavior – theoretical framework
• Motivation to lose weight, become more physically active differs by cultural group based on differing views of body size and shape (Kumanyika, 1993)
• Recent AHA Scientific Statement highlights need for more evidence for intervention trials aimed at physical activity and dietary changes in all populations (Artinian et al., 2010)
• Higher incidence of DM2, HTN, Heart disease, stroke, Hypercholesteremia in Black women (CDC, 2007; World Health Organization, 2006)

Involving the Community
Cultural Sensitivity

• Evidence supports churches are conducive environments for behavioral treatment programs for Black women (Kennedy 2005, Ramirez 2007, Sbrocco 2012)
  — Church provides an inviting social environment
  — Familiarity and the program is church sanctioned
  — Social support plays a vital role in behavior change (Dallow & Anderson, 2003)
Community Advisory Board – from inception of the idea, support with grant, aiding and guiding every aspect of the study...PRICELESS!

Significance

• Women ages 25-45 increases in morbidity and mortality—Significantly higher in Black women
• Higher prevalence of risk factors than white women elevates the risk for:
  — Early onset of CVD
  — Premature death due to heart disease or stroke
• Gender–based interventions limited
  — Participation in studies by young black women (YBW) underrepresented or non-existent
• Little evidence of targeted behavior change interventions in this population
Design and Methods

- Community-based RCT comparing the effectiveness of a self-management risk reduction program combined with wireless coaching to usual care.
- Sample: N= 90 young black women ages 25-45 yrs. (45 Intervention & 45 Usual Care) having 2 or more CVD risk factors
- Community-Based Advisory Board from 2 churches in LA area. Participants randomized by church.

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Baseline</th>
<th>3 months</th>
<th>6 months</th>
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</thead>
<tbody>
<tr>
<td>Clinical Measures</td>
<td>Waist, BMI, BP, CRP- Inflammation, Lipids</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Food Frequency Questionnaire (Computer)</td>
<td>Diet Patterns/ Nutrition</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Newest Vital Sign</td>
<td>Anxiety</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Demographics- Health History</td>
<td>Safety &amp; Medical</td>
<td>X</td>
<td></td>
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<tr>
<td>Brief Symptom Inventory</td>
<td>Sleep</td>
<td>X</td>
<td></td>
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<td>Patient Health Questionnaire</td>
<td>Depressive Symptoms</td>
<td>X</td>
<td>X</td>
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<td>Medical Outcomes Study -SAS</td>
<td>Adherence</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Stanford Brief Activity Survey</td>
<td>Perceived</td>
<td>X</td>
<td>X</td>
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<tr>
<td>MOS-SF-12</td>
<td>Quality of Life</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Protection Motivation Theory</td>
<td>Health threat of heart disease, self efficacy</td>
<td>X</td>
<td>X</td>
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<tr>
<td>INTERHEART STRESS</td>
<td>Stress</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Perceived Social Support Scale</td>
<td>Social Support</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Rosenberg Self-esteem</td>
<td>Self-esteem</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

Intervention

- Heart Health Package
  - Whole health approach
  - One-on-one
  - Small groups at the church
- Promotion of self-management
- Skill-based
- Individualized goals
  - Feedback
  - Unique barriers addressed
- Culturally sensitive
Heart Health Education

- Self-management
- Heart healthy eating
  - Reading food labels, portion control (first regardless of other choices)
  - The facts about fats revealed
  - How to eat enough fruits and vegetables
  - Whole grains, high fiber
  - Meats, poultry, fish – how much, how often
  - Low fat dairy
- Physical activity for heart health
- Medication adherence
- Stress management
- Smoking cessation and avoiding second-hand smoke
- Healthy salt intake for life

Intervention: Wanda-CVD

- Self-management risk reduction program
  - Wireless Coaching
    - Automated transmission of messages
    - Examine activity level using wearable smartphone
    - Daily/Weekly questionnaires
    - Blood pressure measurement
    - Wireless transmission to database with data analytics
    - Easy to use Graphical User Interface (GUI) for clinicians
  - Tablet and Web-based portal
- Goal of 6 month study
  - Study usefulness of education and technology in reducing CVD risk
  - 90 women (45 intervention, 45 control)
  - Examine effectiveness of risk factor reduction
  - Blood pressure, weight, BMI, lipid profile, hsCRP
  - Examine activity level and food consumption
  - Test acceptability and feasibility (i.e. adherence)

Wanda-CVD System Design
Wanda-CVD App: User Settings

Wanda-CVD App: Daily Questionnaire

<table>
<thead>
<tr>
<th>Monday</th>
<th>Tuesday</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>1</td>
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<tr>
<td>2</td>
<td>2</td>
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<td>4</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Wanda-CVD App: Blood Pressure Monitor

WANDA App: Blood Pressure Monitor
WANDA App: Activity Monitoring

- Activity Monitoring
  - Continuous
  - Seamless
  - Wireless
  - Activity Intensity
  - METs

Wanda-CVD: Wireless Coaching

Motivational Message:

“People who take care of themselves are better equipped to take care of others”

What we hope to achieve...

- To test a self-management intervention to determine whether it is efficacious in at risk young Black women in preventing or halting the progression of heart disease.
- By giving them the tools and social support and delivering information in a manner that is familiar and salient to them over a 6 month period we are hoping for sustainability and a better quality of life for Black women as they age.
Questions and Answers
• Use the “CHAT” box on the Right of your screen to submit a question for the Q&A Session