Women’s Heart Health Center
“YADUNA”

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**YADUNA: The First Lady Foundation**

Women Heart Health Center (WHHC): A project to promote women heart health

**Rational and Mandate**

*To become a model of excellence in women heart health and contribute to the improvement of CV health conditions of Lebanese women by providing screening, early diagnosis, raising awareness, spreading best practices and advance the understanding of the genetic, psychological, and health style factors leading to the large burden of disease.*
Coronary Heart Disease in Women:

- Address **Burden of Disease**
  - Understand relevance and prevalence of CV Risk factors; assess Public health Impact of Controlling R. factors
- Explore Prevalence of subclinical disease
- Review gender differences of Heart Disease
- Underscore the public health benefit of targeting women as partner in prevention and effectors of societal change.

**Women Heart Center: A pioneering National Initiative**
Global Burden Of CVD

- Globally, about 18 million people die annually from cardiovascular diseases:
  - An estimated 8 million due to **Coronary heart disease**
  - An estimated 6 million due to **Stroke**

- **Over 70%** of the global burden of heart attack and stroke is on poor countries.

- **Diabetes and hypertension** are major predisposing factors.

- Propelling the upsurge in cases of diabetes and hypertension is the growing prevalence of **overweight and obesity**.

Fuster V et al, Lancet 2005
The *greatest increase* in NCDs is anticipated in low- and middle-income countries:

By 2025, an anticipated increase:

- the prevalence of hypertension
  -- 24% in developed countries
  -- 80% in developing regions

- Diabetes > 200%

- Millions of people suffer unnecessarily, dying at an early age...
  Grave impact on economic security and stability

*Global Burden Of CVD*

Fuster V et al, Lancet 2005
Coronary Heart Disease: Increasing Burden in M. Eastern countries

- Genetic factors
- Cluster of risk factors
- Economic and political perils.
- Disparities of financial resources
- Limited and Underdeveloped surveillance, preventive and interventional opportunities

Large burden

10 years younger @ the first event

There is urgent need for Action:
Recognizing the global pandemic and burden of NCDs in a landmark decision, the United Nations held a high-level meeting on September 19, 2011 to determine priority actions and interventions in response to this crisis.

2ND in Hist of UN @ gen ASSEMBLY
Outcomes of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases (New York, September 2011)

- Acknowledge The enormous potential public health impact of various societal interventions to improve risk factor control

- The Declaration calls on Member States to give greater priority to
  - early detection, screening
  - diagnosis and treatment of NCDs &
  - improving the accessibility to essential medicines & technology for NCDs.

- Ensure that the provision of health care for NCDs is dealt with in the context of comprehensive overall health system
Burden of Coronary Heart Disease In Women
Burden of Coronary Heart Disease In Women

• A 49 year old woman, non diabetic, non smoker presented with progressive and severe dyspnea on exertion.
• She had consulted several physicians with similar but less severe symptoms, for one year.
• She denied chest pain at rest or @ effort.
• Symptoms dismissed as anxiety
• Examination was negative for bruits or murmurs. LV was normal.
• Coronary angiography:
Because of *atypical symptoms*, women seek medical care *later* than men and are more likely to be misdiagnosed.
Heart disease is the #1 killer of women:
"man's disease," ~ the same number of women and men die each year of heart disease & Stroke.

Lack of societal and professional awareness:
only 54% of women recognize that heart disease is their number 1 killer. (75% of women identified cancer as their leading cause of death)

Almost two-thirds (64%) of women who die suddenly of coronary heart disease have no previous symptoms.
Burden of Coronary Heart Disease In Women

Symptoms & risks Different in women!

Risk Factors Prevalent (~50%) worldwide:

- Diabetes and smoking are more consequential in women
- Acceleration of obesity and diabetes post menopause.
- Metabolic syndrome has a greater impact on women Vs men.
- Mental stress and depression affect women's hearts more than men's
- Low levels of estrogen after menopause pose a significant risk factor for developing cardiovascular disease
Women less likely to get immediate heart attack treatment

Women having heart attacks are less likely than men to get immediate treatment and more likely to die in the hospital, says a groundbreaking new study that tracked more than 1.1 million patients.

Women are less likely to get immediate treatment to stop the heart attack in its tracks: clot-busting drugs, balloon procedures to open the arteries or bypass surgery, the study says. Partly because of such delays, 15% of female heart attack patients die in the hospital, compared with 10% of men. Delaying care can be fatal.
Coronary Heart Disease in Women

• Because of *atypical symptoms*, women seek medical care *later* than men and are more likely to be misdiagnosed.

• Women presenting with MI and CAD are more likely to be older, have a history of DM, HTN, Hyperlipids, CHF, and unstable angina than male counterparts.

• Because of these comorbid conditions, there tends to be diagnostic confusion.

- Mortality from CABG-particularly among younger women-is double that among men, *due to procedural complications, suboptimal gender-based risk Stratification and possibly due to*

- Special predilection for microvessel disease, *(small vessel heart disease)* & Diastolic Heart Failure.
Peculiarities Of Heart Disease In Women Vs. Men

• Intrinsic Biologic Differences
  There is emerging evidence of gender differences in disease manifestations & predictive tests and tools for the early detection of CVD (eg. EKG Stress test)

• Disparities in delivery of Care
  There is need for better representation of women in clinical research.
  Use of guideline-indicated therapies differs based on sex

Rumsfeld et. al, EHJ 2004;25:101-103
Detecting *Sub*-Clinical Disease: *New Paradigm!!*

*Subclinical Changes of Function & Structure:*
*The More You Look The More You Find!*
In genetically susceptible individuals, factors that induce biochemical or physical injury can elicit pathophysiologic responses that include molecular, cellular, organ, structural or functional processes.
Coronary Artery Disease According to Age Quartiles

1,074 consecutive individuals who had undergone CTA evaluation with 64-slice multidetector computed tomography (MDCT) for general routine health evaluation in National University Bundang Hospital from Dec. 2005 - May 2006.

All, p < 0.001

Choi, E.-K. et al. J Am Coll Cardiol 2008;52:357-365
The majority of subjects had plaque and most bilateral.

Clear relation with age.

Fuster, V et al  AHA 2010
Optimizing Risk Evaluation in Primary Hypertension

Estimated and Observed Reductions in Deaths from Coronary Heart Disease in the United States between 1980 and 2000, Stratified According to Age and Sex.

Approximately half the decline in U.S. deaths from coronary heart disease from 1980 through 2000 may be attributable to reductions in major risk factors.

The Earlier, the Better

*NEJ Med 2007*
Managing The burden Of Coronary Heart Disease: From Global action to patient specific strategies.

Time To PERSONALIZE Prevention!

- New concepts
- **New tools**: Coronary calcium scoring improved risk classification in 25% of subjects in MESA
- New studies
- New Drugs
- New Guidelines
CV Markers & Surrogates Of CV of Risk

- Apo B apoprotein (LDL)/Apo A1 apoprotein (HDL)
  - ApoB/ApoA1 ratio (0.4-0.9)
- High sensitivity C-reactive protein (hs-CRP)
- Small dense LDL particles
- Obesity (BMI > 30)
- Hypertriglyceridemia
- Lipoprotein (a)
- LpPLA2
- Cell adhesion molecules (VCAM-1, ICAM-1, E-selectin)
- CAC
- UAE
- Sedentary life style

All Exaggerated In Diabetes

IOMedicine 2012
Lp-PLA$_2$ is Specific to Vascular Inflammation

N=90 Healthy Normals

Wolfert, AHA 2004
Lp-PLA$_2$ Predicts Major CV Events in CHD Patients: Mayo Heart Study

95% of patients with Lp-PLA$_2$ < 200 ng/ml were Event Free at 4Yr

A meta-analysis of 79,036 participants in 32 prospective studies found that Lp-PLA$_2$ levels are positively correlated with increased risk of developing CAD and Stroke

Brilakis ES et al. Mayo Heart Study. *Euro Heart J* 2005
Coronary Calcium reflects Macrophage recruitment & Inflamm in the vessel wall

Coronary calcium score @ age/gender/percentile distribution is predictive of future coronary events

Introduction of statin therapy retards calcification

Circulation 2007; V116: 2841
Prognostic Value of Coronary Artery Calcium Screening in Subjects With and Without Diabetes

Cumulative Survival

No Diabetes (n=9,474) vs. Diabetes (n=903)

Follow-up (Years)

0-10 (n=5,600)
11-100 (n=1,854)
101-400 (n=1,251)
401-1000 (n=508)
>1000 (n=261)

0-10 (n=351)
11-100 (n=189)
101-400 (n=182)
401-1000 (n=110)
>1000 (n=71)

A Road Map for Research/Prevention Concerning Women’s Cardiovascular Health.

Seeking solutions that could improve early detection, early diagnosis and treatment for women living with or @ risk of heart disease

Should take several factors into consideration beyond the Framingham risk score, including Medical and lifestyle history, Family history of CVD, Markers of preclinical disease, Surrogate markers

........................................the intensity of preventive therapy.
The First Lady Foundation launches a project to improve women heart health, by providing preventive services, raising awareness, & fostering research.
Women’s Heart Health Center @Yaduna

Unmet needs

- Spread awareness about women's heart disease
- Provide Comprehensive assessment of, & Intervention @ risk elements of cardiovascular disease by identifying relevant traditional and novel factors
- Address lifestyle, dietary issues and genomic factors peculiar to the Lebanese Women.
- Validate an adapted risk score applicable for Lebanese women
- Engage Women in efforts to improve their health / become partners as effective health advocates in the family and society: impacting childhood obesity and youth smoking, health promotion efforts during pregnancy and early childhood, & continuing prevention efforts throughout the life course
## Search for Markers, Surrogates

<table>
<thead>
<tr>
<th>Markers</th>
<th>CV predictive value</th>
<th>Availability</th>
<th>Cost</th>
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<tbody>
<tr>
<td><strong>Electrocardiography</strong></td>
<td>++</td>
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<tr>
<td><strong>Echocardiography</strong></td>
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<tr>
<td><strong>Carotid Intima-Media Thickness</strong></td>
<td>+++</td>
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<td><strong>Arterial stiffness (pulse wave velocity)</strong></td>
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<tr>
<td><strong>Ankle-Brachial index</strong></td>
<td>++</td>
<td>++</td>
<td>+</td>
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<tr>
<td><strong>Coronary calcium Score</strong></td>
<td>+</td>
<td>+</td>
<td>++++</td>
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<tr>
<td><strong>Endothelial dysfunction</strong></td>
<td>++</td>
<td>+</td>
<td>+++</td>
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<tr>
<td><strong>Cerebral lacunae/white matter lesions</strong></td>
<td>?</td>
<td>++</td>
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<tr>
<td><strong>Est. GFR</strong></td>
<td>+++</td>
<td>+++</td>
<td>+</td>
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<tr>
<td><strong>Microalbuminuria</strong></td>
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*Mancia et al. J Hypertension. 2007;25:1751-1762*
Distinctive features Of WHHC

- Dedicated National center which offers pioneering preventive, screening, diagnosis and therapeutic services to *underprivileged* women, in partnership with academic centers
- 2 Universities/academic health centers have assumed an important role in providing leadership & building research capacity.
- Precedes, and aligns with International call for action: IOM, WHO, Victoria Declaration
- Education, Screening, awareness, intervention, Technology, Essential Medications.
- Seek opportunities to create stronger collaboration with existing major national services, global initiatives & programs for increasing support of the center mission
1. What factors influence or explain disparities in cardiovascular disease epidemiology and disease outcomes between men and women?

2. What are the best strategies to assess, modify, and prevent a woman’s risk of heart disease? 

   Framingham Risk Score fails to identify risk in a large number of women; Even up to age 80, more than three quarters of women are considered “low risk” by the Framingham Risk Score. Need an adapted & relevant score.

3. What are the most accurate and effective approaches to assess and recognize chest pain and other symptoms suggesting coronary heart disease in women? (Detecting obstructive (plaque) in the coronary arteries, &/Or microvascular vascular disease or dysfunction).

4. What role does a woman’s reproductive history and menopausal hormone therapy play in the development of heart disease?
Women Heart Health: The Big Questions

5. What are the risk factors for cardiovascular disorders associated with pregnancy and how are they best treated?

6. What is the best method for studying sex differences in vascular injury so that cardiovascular repair therapies may be improved?

7. What are the most effective treatments for diastolic heart failure (preserved syst. Function) in women?

8. Why are young women more likely than men to die after a heart attack or after surgical revascularization procedure?

9. How do psychosocial factors affect cardiovascular disease in women?

10. What biological variables are most influential in the development and clinical outcomes of heart disease and what can be done to reduce mortality rates in women?

The 2011 10Q report
My gratitude!

First Lady for vision, passion and generous r undertaking for a great national cause!

.. thanks all colleagues for their devotion of time and energy to this project.

....... a privilege and a pleasure to work with my fellow committee members, to learn from them in their respective capacities, and to engage with them in hearty discourse about the issues at hand.

“Knowing is not enough; we must apply. Willing is not enough; we must do.”

—Goethe
Thank You!
Flow diagram for CVD preventive care in women.

Evaluation of CVD Risk:
- Medical history/family history/pregnancy complication history
- Symptoms of CVD
- Depression screening in women with CVD
- Physical examination including blood pressure, body mass index, waist size
- Laboratory tests including fasting lipoproteins and glucose
- Framingham risk assessment if no CVD or diabetes

Non conventional Factors: CRP, CAC etc.

Implement Class I Lifestyle Recommendations (for all):
- Smoking cessation
- DASH-like diet
- Regular physical activity
- Weight management

Is Woman at High Risk of CVD (having ≥1 of the following)?
- Clinically established CHD
- Cerebrovascular disease
- Peripheral arterial disease
- Abdominal aortic aneurysm
- Diabetes mellitus
- Chronic kidney disease
- 10-year predicted CVD risk ≥10%

History of Paroxysmal Atrial Fibrillation?
- No
- Yes

Implement Class I Recommendations:
- Warfarin or
- Aspirin or
- Dabigatran

Recent cardiovascular event, procedure, or congestive heart failure symptoms?
- Yes
- No

Implement Class I Recommendations:
- Blood pressure control
- LDL-C-lowering therapy if ≥190 mg/dL

Refer to cardiac rehabilitation

Consider Class II Recommendations:
- Therapy for high LDL-C, non-HDL-C and triglycerides and/or HDL-C in select women
- Aspirin

Consider Class II Recommendations:
- LDL-C-lowering therapy (goal <70 mg/dL in very high-risk women)
- Non-HDL-C-lowering therapy (goal <130 mg/dL in very high-risk women with recent ACS or multiple poorly controlled cardiovascular risk factors)
- Glycemic control in diabetics
- Aspirin/antiplatelet agents
- Omega-3 fatty acids
Detecting *Sub*-Clinical Disease: New Paradigm!!

1. C-reactive protein, brain natriuretic peptides, and troponin remain the most clinically relevant serum biomarkers
2. *Conventional R. Factors*
3. Coronary calcium scoring improved risk classification in 25% of subjects in *MESA*.
4. *Role of imaging*

**Time To PERSONALIZE Prevention @ Existing Burden Of Disease!**

**Secondary Not Primary Prevention!**