Cardiovascular Disease Risk in Cancer Survivors

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Assistant Professor
Emory University, Nell Hodgson Woodruff School of Nursing
Speaker Disclosers

Principal Investigator receiving funding for CVD disease research in Cancer Survivors

• Internal funding Kennedy Survivorship Pilot Grant Award, Emory University: *Novel Testing for Subclinical Cardiovascular Disease in Lymphoma Survivors*

• Funding from Radiation Therapy Oncology Group sponsored by National Cancer Institute: *The Relationship between Radiation Dose Volume and Adverse Cardiovascular Disease Outcomes in Cancer Survivors who Received Therapeutic Thoracic Radiation*
### Pollen Count

**Total Pollen Count for 4/11/2014:**

- **4054**

#### Trees:
- Oak, Birch, Sweetgum, Mulberry
- Oak, Birch, Sweetgum, Mulberry, Pine, Sycamore

- Extremely High: L=0.14, M=15.89, H=90.1499, E=1500+

#### Grass:
- Grass

- Low: L=0.4, M=5.19, H=29.199, E=200+

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**Last Week**

**This Week**

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**Non-Drowsy Claritin**

- Original Prescription Strength
- loratadine tablets 10 mg/antihistamine
- 30 Tablets

- Relief of:
  - Sneezing
  - Runny nose
  - Itchy, watery eyes
  - Itchy, dry eyes
  - Itchy or rashy skin

*When taken as directed. See Drug Facts Panel.*

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**Windshield Washer Fluid**

- Windshield Washer Fluid and De-Icer
- 1 gallon
- Concentrated
- Full strength

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*CLEAN*
Objectives

• Discuss the growing population of cancer survivors
• Present an epidemiological model explaining the elevated CVD risk in cancer survivors.
• Differentiate which cancer survivors are at risk for CVD.
• Identify screening recommendations.
• Discuss effective prevention strategies.
Facts and Figures

Morbidity and Mortality Weekly Report (MMWR)QuickStats: Age-Adjusted Death Rates for Heart Disease and Cancer --- United States, 1999—2009* Weekly June 3, 2011 / 60(21);713
All-site Cancer Survival Today

Percent Surviving
5 years

65.8%

What does this mean for Preventive Cardiology Nurses?
A 65 year old woman presents for her annual Survivorship Visit following treatment 5 years ago for Stage IIB breast cancer (T2, N1, M0). At that time, she received bilateral mastectomies with axilla lymph node removal and radiation to the left axilla. What will most likely be the cause of her mortality?

1. Breast cancer recurrence
2. Cancer metastasis to brain or bone
3. Cardiovascular disease
4. Cancer metastasis to lung
How the numbers stack up

- Risk of CVD death in cancer survivors is higher than the actual risk of tumor recurrence
- 7-fold higher mortality than general population
  - 15-fold increased risk of developing heart failure
  - 10-fold increased risk ischemia
- Higher incidence of hypertension, dyslipidemia, acute coronary syndromes, CVA.
Epidemiology of CVD in Cancer Survivors

Native Risk Factors
- Genetics
- Environmental

Treatment Risk Factors
- Chemotherapy
- Radiotherapy
- Surgery

Health Behaviors
- Tobacco, obesity, sedentary lifestyle, metabolic syndrome, insulin resistance

Pathophysiology
- Cardiomyopathy
- Fibrosis

Cardiovascular Disease
Epidemiology of CVD in Cancer Survivors

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- Genetics
- Environmental

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- Radiotherapy
- Surgery

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Tobacco, obesity, sedentary lifestyle, metabolic syndrome, insulin resistance

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Cardiovascular Disease
Epidemiology of CVD in Breast Cancer Survivors

Native Risk Factors


Treatment Risk Factors

Cardiovascular Disease

Health Behaviors

Pathophysiology
Epidemiology of CVD in Breast Cancer Survivors

Native Risk Factors

• Boerman (2014)
• Haque (2014)
• Obi (2014).


Cardiovascular Disease

Treatment Risk Factors

• Obi (2014).


Health Behaviors

Pathophysiology
A 65 year old woman presents for her annual Survivorship Visit following treatment 5 years ago for Stage IIB breast cancer (T2, N1, M0). At that time, she received bilateral mastectomies with axilla lymph node removal and radiation to the left axilla.

**True or False: She is at increased risk for CVD because she has been treated for breast cancer?**

1. True
2. False
ARS Question # 3

A 65 year old woman presents for her annual Survivorship Visit following treatment 5 years ago for Stage IIB breast cancer (T2, N1, M0). At that time, she received bilateral mastectomies with axilla lymph node removal and radiation to the left axilla.

Her increased risk for developing CVD is most influenced by:

1. History of 30 pack year smoker, HTN, hypercholesterolemia, BMI 35,
2. Receipt of left axilla radiation
3. Failure to receive Tamoxifen during her cancer treatment
A 45 year old woman presents for her annual Survivorship Visit following treatment 5 years ago for Stage IIB breast cancer (T2, N1, M0). At that time, she received bilateral mastectomies with axilla lymph node removal, chemotherapy with CAF (**cyclophosphamide**, **doxorubicin** (**Adriamycin**), and **5-FU**), and radiation to the left axilla.

True or False: She is at increased risk for CVD because she has been treated for breast cancer?

A. True  
B. False
A 45 year old woman presents for her annual Survivorship Visit following treatment 5 years ago for Stage IIB breast cancer (T2, N1, M0). At that time, she received bilateral mastectomies with axilla lymph node removal, chemotherapy with CAF (cyclophosphamide, doxorubicin (Adriamycin), and 5-FU), and radiation to the left axilla.

**True or False: She is at increased risk for CVD because she has been treated for breast cancer?**

1. True
2. False
Known Cardiotoxic Chemotherapies

Coronary Ischemia:
  - Fluorouracil (5-FU)
  - Interleukin-2
  - Sorafenib

Arrhythmias:
  - Thalidomide
  - Vandetanib

LV dysfunction:
  - Anthracyclines
  - Tratuzumab
  - Sunitinib
CVD Risk from Radiation

• Routine mapping often prevents radiation induced disease now.
• When occurs, commonly involves pericardium, aortic valve, vascular diseases, baroreflex failure
• Radiation-induced CVD: oxidative stress, fibrosis, and inflammation
• Risk factors for radiation-associated CVD: dose > 30-35 Gy, dose per fraction> 2 Gy, large volume of irradiated heart, younger age at exposure, longer time since exposure, use of cytotoxic chemotherapy, and presence of other CVD risk factors.
Epidemiology of CVD in Cancer Survivors

Native Risk Factors
- Genetics
- Environmental

Treatment Risk Factors
- Chemotherapy
- Radiotherapy
- Surgery

Health Behaviors
- Tobacco, obesity, sedentary lifestyle, metabolic syndrome, insulin resistance

Cardiovascular Disease

Pathophysiology
- Cardiomyopathy
- Fibrosis
Cardiovascular risk factors among long-term survivors of breast, prostate, colorectal, and gynecologic cancers: a gap in survivorship care?

Kathryn E. Weaver • Randi E. Foraker • Catherine M. Alfano • Julia H. Rowland • Neeraj K. Arora • Keith M. Bellizzi • Ann S. Hamilton • Ingrid Galdey-Girvan • Gretchen Keel • Noreen M. Aziz

Received: 31 October 2012 / Accepted: 23 January 2013 / Published online: 16 February 2013
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Abstract
Purpose: Individuals diagnosed with high survival cancers will often die of cardiovascular disease (CVD) rather than a recurrence of their cancer, yet CVD risk factors may be overlooked during survivorship care. We assess the prevalence of CVD risk factors among long-term cancer survivors and compare results to survey data from the general population in the same geographic region. We also characterize how often at-risk survivors discuss CVD-related health behaviors with their health care providers.

Methods: Survivors (n=1,582) of breast, prostate, colorectal, and gynecologic cancers, 4–14 years after diagnosis, were recruited from two California cancer registries for a cross-sectional mail survey. We assessed CVD risk factors, including smoking, body mass index, physical inactivity, hypercholesterolemia, hypertension, and diabetes, as well as report of discussions with health care providers about diet, exercise, smoking, and lifestyle change assistance.

Results: With the exception of current smoking, CVD risk factors were more common among survivors than the general adult population. Of survivors, 02.0 % were overweight, or obese; 55.0 % reported hypertension, 20.7 % reported diabetes, 18.1 % were inactive, and 5.1 % were current smokers. Compared to white, non-Hispanic survivors,
Epidemiology of CVD in Cancer Survivors

Native Risk Factors
- Genetics
- Environmental

Treatment Risk Factors
- Chemotherapy
- Radiotherapy
- Surgery

Health Behaviors
- Tobacco, obesity, sedentary lifestyle, metabolic syndrome, insulin resistance

Cardiovascular Disease

Pathophysiology
- Cardiomyopathy
- Fibrosis
What about other cancers?
Adult and Pediatric Cancers

Top 10 Cancer Sites: 2009, Male and Female, United States—All Races

- Lung and Bronchus: 43.5
- Female Breast: 22.2
- Prostate: 22.0
- Colon and Rectum: 15.7
- Pancreas: 10.8
- Ovary: 7.8
- Leukemias: 7.0
- Non-Hodgkin Lymphoma: 6.3
- Liver and Intrahepatic Bile Duct: 5.8
- Brain and Other Nervous System: 4.4

Childhood Cancer Incidence and Mortality Rates (per 100,000)

Screening recommendations
Screening recommendations

• No evidenced-based guidelines for adults!

• There is one consensus based clinical practice guidelines:
  *Boveli, Plataniotis and Riola (2010). European Society of Medical Oncology Clinical Practice Guidelines*

• IOM 2005 Report “From Cancer Patient to Cancer Survivor: Lost in Transition”
  • Importance of risk-based care with individualized recommendations

• Children’s Oncology Group Guidelines: www.survivorshipguidelines.org
<table>
<thead>
<tr>
<th>Screening (condition)</th>
<th>US Preventive Services Task Force</th>
<th>COG</th>
<th>UK Children’s Cancer Study Group</th>
<th>AAP / AHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure (hypertension)</td>
<td>Annually for adults</td>
<td>Annually if treatment risk factors present</td>
<td>Regularly for all survivors</td>
<td>Measured at every healthcare episode if &gt;3yo</td>
</tr>
<tr>
<td>Fasting lipids (dyslipidemia)</td>
<td>Males 20-34yo / females 20-44yo with CHD risk</td>
<td>2y after completing therapy and q2y if risk factors present</td>
<td>Consider if received chest radiation or BMT</td>
<td>All cancer survivors</td>
</tr>
<tr>
<td>EKG / ECHO (cardiomyopathy)</td>
<td>N/A</td>
<td>EKG 2y after therapy / ECHO q1-5 yrs depending on exposures</td>
<td>ECHO q3-5 y depending on exposures</td>
<td>N/A</td>
</tr>
<tr>
<td>Fasting glucose (glucose intolerance / diabetes)</td>
<td>Only asymptomatic adults with blood Pressures &gt;135/80mmHg</td>
<td>q2y in cancer survivors exposed to specific treatments</td>
<td>Survivors who received BMT</td>
<td>Baseline for all cancer survivors</td>
</tr>
<tr>
<td>Age at Treatment*</td>
<td>Radiation with Potential Impact to the Heart$</td>
<td>Anthracycline Dose †</td>
<td>Recommended Frequency</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>-----------------------------------------------</td>
<td>----------------------</td>
<td>----------------------</td>
<td></td>
</tr>
<tr>
<td>&lt;1 year old</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>&lt;200 mg/m²</td>
<td>Every 2 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥200 mg/m²</td>
<td>Every year</td>
<td></td>
</tr>
<tr>
<td>1-4 years old</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;100 mg/m²</td>
<td>Every 5 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>≥100 to &lt;300 mg/m²</td>
<td>Every 2 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
<td></td>
</tr>
<tr>
<td>≥5 years old</td>
<td>Yes</td>
<td>&lt;300 mg/m²</td>
<td>Every 2 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>&lt;200 mg/m²</td>
<td>Every 5 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥200 to &lt;300 mg/m²</td>
<td>Every 2 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥300 mg/m²</td>
<td>Every year</td>
<td></td>
</tr>
<tr>
<td>Any age with decrease in serial function</td>
<td></td>
<td></td>
<td>Every year</td>
<td></td>
</tr>
</tbody>
</table>
Current Clinical Practice of Monitoring

- Echocardiogram for baseline and serial assessment of LVEF
- BP and weight with survivorship clinic
- May or may not get lipid panel with routine labs
- No consistency of when these should be measured or how frequent.
Purpose

1) to describe the subclinical incidence and calculated risk for the two most prevalent CVDs (HF and CAD), and

2) to examine perceived risk, knowledge and behaviors related to cardiovascular health in the lymphoma cancer survivorship population.
Methods

A cross-sectional, correlation study, with a purposive sample of 50 asymptomatic patients who are 2 to 10 years post diagnosis and treatment for lymphoma.

A secondary aim of this study will be to explore patients’ perspectives on the content and delivery approaches of a patient-specific cardiac risk reduction plan developed from the clinical findings collected in this research, integrating survivorship and preventive cardiology services.
# Instruments & Measures

<table>
<thead>
<tr>
<th>Antecedents and Screening</th>
<th>Concepts</th>
<th>Instruments/ Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Demographic/ clinical factors</td>
<td>Demographic/ clinical factors</td>
</tr>
<tr>
<td></td>
<td>Cognitive Screening</td>
<td>Blessed Orientation-Memory-Concentration (BOMC)</td>
</tr>
<tr>
<td></td>
<td>Previous cardiac events or symptoms</td>
<td>Shortened WHO Rose Angina Questionnaire</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Routine Noninvasive Measures</th>
<th>Concepts</th>
<th>Instruments/ Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Routine Lab testing: CBC, Chemistry &amp; Lipid panels</td>
<td>Routine Lab testing: CBC, Chemistry &amp; Lipid panels</td>
</tr>
<tr>
<td></td>
<td>Calculated CVD risk</td>
<td>Framingham Risk Assessment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Novel/ Investigational Measures</th>
<th>Concepts</th>
<th>Instruments/ Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Biomarkers of inflammation &amp; myocardial injury</td>
<td>Biomarkers: HS-CRP, cTnI, BNP</td>
</tr>
<tr>
<td></td>
<td>Atherosclerosis</td>
<td>Coronary Artery Calcification Computed Tomography (CAC-CT)</td>
</tr>
<tr>
<td></td>
<td>Myocardial Dysfunction</td>
<td>Echocardiogram</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Reported Measures</th>
<th>Concepts</th>
<th>Instruments/ Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Heart Disease Knowledge</td>
<td>Heart Disease Knowledge Questionnaire</td>
</tr>
<tr>
<td></td>
<td>CVD risk-reducing behaviors</td>
<td>Health-Promoting Lifestyle Profile II (HPLPII)</td>
</tr>
<tr>
<td></td>
<td>Physical and psychological symptoms</td>
<td>Memorial Symptom Assessment Scale- Heart Failure (MSAS-HF)</td>
</tr>
<tr>
<td></td>
<td>HRQL</td>
<td>SF-36 &amp; EQ-5D</td>
</tr>
</tbody>
</table>
## Early Evaluation (N=20)

<table>
<thead>
<tr>
<th>Sociodemographic &amp; Risk Variables</th>
<th>Value</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Gender</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>Working Full-time</td>
<td>70%</td>
<td></td>
</tr>
<tr>
<td>Low annual income</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Average Age</td>
<td>47.5 years</td>
<td>(29-73)</td>
</tr>
<tr>
<td>Heart disease in 1 Degree Relative</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>1 current/ 4 former</td>
<td></td>
</tr>
<tr>
<td>Exercise minutes per week</td>
<td>91.11 (SD 76)</td>
<td>(0-210)</td>
</tr>
<tr>
<td>• 150min/ week or greater</td>
<td>35%</td>
<td></td>
</tr>
<tr>
<td>History</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• HTN</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>• Hyperlipidemia</td>
<td>25%</td>
<td></td>
</tr>
</tbody>
</table>
### Identification of the Metabolic Syndrome - Any 3 of the Following:

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal obesity*</td>
<td>Waist circumference**</td>
</tr>
<tr>
<td>Men</td>
<td>&gt;102 cm (&gt;40 in)</td>
</tr>
<tr>
<td>Women</td>
<td>&gt;88 cm (&gt;35 in)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>150 mg/dL</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>&lt;40 mg/dl</td>
</tr>
<tr>
<td>Men</td>
<td>&lt;50 mg/dl</td>
</tr>
<tr>
<td>Women</td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>130/85 mmHg</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>110 mg/dL</td>
</tr>
</tbody>
</table>

Early Evaluation (N=20)

<table>
<thead>
<tr>
<th>Concerning CV Findings</th>
<th>Value</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist to hip ratio</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• &gt; .85 in women</td>
<td>50%</td>
<td>(.75-1)</td>
</tr>
<tr>
<td>• &gt; .90 in men</td>
<td>80%</td>
<td>(.75-1)</td>
</tr>
<tr>
<td>Triglycerides &gt; 150</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• &lt;40 in men</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>• &lt;50 in women</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>Blood pressure &gt; 130/85</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>Fasting Glucose &gt; 110 mg/dl</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Total patients with metabolic syndrome</td>
<td>25%</td>
<td></td>
</tr>
</tbody>
</table>
Early Evaluation (N=20)

<table>
<thead>
<tr>
<th>Concerning CV Findings</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Cardiac CT</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Heart Dysfunction</td>
<td></td>
</tr>
<tr>
<td>• Systolic Dysfunction</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>• Diastolic Dysfunction</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Diagnosed with hyperlipidemia</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>Framingham Risk</td>
<td></td>
</tr>
<tr>
<td>• Moderate (11-19% risk of having event in next 10 years)</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>• High (&gt;30% risk of having even in next 10 years)</td>
<td>1 (5%)</td>
</tr>
</tbody>
</table>
Challenges in cardio-oncology care

- Improve the evidence base
- Develop, approve, disseminate, and adhere to guidelines
- Cost effectiveness?
- Limit additional risk
- Risk Prediction
Prevention Strategies
Prevention strategies

• Incorporate preventive cardiology within Survivorship Clinics

• Support Survivorship Clinics!

• Routine monitoring of CVD risk factors and patient centered counseling to address

• Start with AHA’s Simple 7
Education

AHA’s Simple Seven
1. Get Active
2. Control Cholesterol
3. Eat Better
4. Stop Smoking
5. Manage Blood Pressure
6. Lose Weight
7. Reduce Blood Sugar

Source: American Heart Association
Effects of Physical Activity Guidelines on Cancer and CVD Mortality: The Cooper Center Longitudinal Study

N=53,000

CE Barlow, WL Haskell, SG Lakoski: Meeting the Physical Activity Guidelines and Risk of Cardiovascular Disease and Cancer Mortality: Cooper Center Longitudinal Study. AHA Scientific Sessions (2013), Dallas, TX
Influence of Conventional Cardiovascular Risk Factors and Lifestyle Characteristics on Cardiovascular Disease After Hematopoietic Cell Transplantation


ABSTRACT

Purpose
To determine the influence of modifiable lifestyle factors on the risk of cardiovascular disease after hematopoietic cell transplantation (HCT).

Patients and Methods
HCT survivors of ≥1 year treated from 1970 to 2010 (n = 3,893) were surveyed from 2010 to 2011 on current cardiovascular health and related lifestyle factors (smoking, diet, recreational physical activity). Responses (n = 2,326) were compared with those from a matched general population sample (National Health and Nutrition Examination Survey [NHANES]; n = 1,192).

Results
Compared with NHANES participants, HCT survivors (median age, 55.9 years; median 10.8 years since HCT; 71.3% allergenoid) had higher rates of cardiomyopathy (4.0% vs 2.6%), stroke (4.8% vs 3.3%), dyslipidemia (33.9% vs 22.3%), and diabetes (14.3% vs 11.7%, P < .05 for all comparisons). Prevalence of hypertension was similar (27.9% vs 30.0%), and survivors were less likely to have ischemic heart disease (6.1% vs 9.9%, P < .01). Among HCT survivors, both smoking and obesity were associated with ischemic heart disease risk, whereas smoking was not associated with increased cardiovascular disease risk.

The journal is printed by Blackwell Publishing, Inc., 350 Main St., MA 01901-3197, USA.