Guideline Driven Care Across the Lifespan: Where is the Evidence?
Where are the Gaps?

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• Takeda Oncology - consultant
Overview

• Prevalence of CV risk factors in cancer survivors

• Impact of CV risk factors on CVD in cancer survivors

• Guidelines for management of CV risk factors
Prevalence and Relevance of CV Risk Factors in Cancer Survivors

• Prevalence of CV risk factors is increased in cancer survivors
  – In CCSS, HTN, dyslipidemia, and DM increased vs. siblings
  – In adults cancer survivors, all CV RF increased vs. non-cancer controls
• In CCSS, hypertension, alone or in combination w/ other CV RF, increases risk of CVD and HF from thoracic RT or anthracyclines
• Adult cancer survivors w/ ≥ 2 CV RF are at increased risk of CAD, stroke or HF compared to cancer pts with < 2 RF and non-cancer controls.

Exercise and Mortality in Childhood Cancer Survivors

![Graph showing cumulative incidence of mortality over time with different exercise exposure levels.](image_url)

<table>
<thead>
<tr>
<th>Change in Exercise Exposure</th>
<th>RR (95% CI)</th>
<th>Favors High Maintenance or Increased Exercise Exposure</th>
<th>Favors Low Maintenance or Decreased Exercise Exposure</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low maintenance</td>
<td>1 [Reference]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased exposure</td>
<td>1.01 (0.81-1.27)</td>
<td></td>
<td></td>
<td>.91</td>
</tr>
<tr>
<td>Increased exposure</td>
<td>0.60 (0.44-0.82)</td>
<td></td>
<td></td>
<td>&lt;.01</td>
</tr>
<tr>
<td>High maintenance</td>
<td>0.56 (0.36-0.88)</td>
<td></td>
<td></td>
<td>.01</td>
</tr>
<tr>
<td>Recurrent or progressive primary cancer mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low maintenance</td>
<td>1 [Reference]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased exposure</td>
<td>1.00 (0.41-2.43)</td>
<td></td>
<td></td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Increased exposure</td>
<td>0.17 (0.02-1.35)</td>
<td></td>
<td></td>
<td>.09</td>
</tr>
<tr>
<td>High maintenance</td>
<td>0.39 (0.05-3.13)</td>
<td></td>
<td></td>
<td>.37</td>
</tr>
<tr>
<td>Health-related mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low maintenance</td>
<td>1 [Reference]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased exposure</td>
<td>1.08 (0.84-1.38)</td>
<td></td>
<td></td>
<td>.55</td>
</tr>
<tr>
<td>Increased exposure</td>
<td>0.67 (0.49-0.94)</td>
<td></td>
<td></td>
<td>.02</td>
</tr>
<tr>
<td>High maintenance</td>
<td>0.62 (0.39-1.00)</td>
<td></td>
<td></td>
<td>.05</td>
</tr>
</tbody>
</table>
• Awareness of CV Risk
• Assessment of Risk Factors and CV Risk

• Blood Pressure Control

• Cholesterol Management
• Cigarette Cessation

• Dietary Counseling
• Diabetes Management

• Exercise Promotion
CV 10-yr Risk Calculators Do Not Include Cancer Specific Parameters

AHA ASCVD Risk Calculator

Framingham General CVD Risk Score

- Age (years)
- Gender: Male, Female
- Race: African American, Other
- Total cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- Systolic blood pressure (mmHg)
- Diastolic blood pressure (mmHg)
- Treated for high blood pressure: No, Yes
- Diabetes: No, Yes
- Smoker: No, Yes

Results:
- Sex: Female, Male
- Risk Factors:
  - Age
  - Sys BP
  - Total Chol
  - HDL Chol
  - On hypertension medication
    - No (2.76157)
  - Cigarette smoker
    - No (0)
  - Diabetes present
    - No (0)
- Risk %
- Decimal Precision: 2

Calculate
### Blood Pressure Guidelines

<table>
<thead>
<tr>
<th>BP Category</th>
<th>Systolic BP</th>
<th>Diastolic BP</th>
<th>Treatment or Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120 mm Hg</td>
<td>&lt;80 mm Hg</td>
<td>Evaluate yearly; encourage healthy lifestyle changes to maintain normal BP</td>
</tr>
<tr>
<td>Elevated</td>
<td>120-129 mm Hg</td>
<td>&lt;80 mm Hg</td>
<td>Recommend healthy lifestyle changes and reassess in 3-6 months</td>
</tr>
<tr>
<td>Hypertension:</td>
<td></td>
<td></td>
<td>Assess the 10-year risk for heart disease and stroke using the atherosclerotic cardiovascular disease (ASCVD) risk calculator</td>
</tr>
<tr>
<td>stage 1</td>
<td>130-139 mm Hg</td>
<td>80-89 mm Hg</td>
<td>- If risk is less than 10%, start with healthy lifestyle recommendations and reassess in 3-6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- If risk is greater than 10% or the patient has known clinical cardiovascular disease (CVD), diabetes mellitus, or chronic kidney disease, recommend</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>lifestyle changes and BP-lowering medication (1 medication); reassess in 1 month for effectiveness of medication therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- If goal is met after 1 month, reassess in 3-6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- If goal is not met after 1 month, consider different medication or titration</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Continue monthly follow-up until control is achieved</td>
</tr>
<tr>
<td>Hypertension:</td>
<td>≥140 mm Hg</td>
<td>≥90 mm Hg</td>
<td>Recommend healthy lifestyle changes and BP-lowering medication (2 medications of different classes); reassess in 1 month for effectiveness</td>
</tr>
<tr>
<td>stage 2</td>
<td></td>
<td></td>
<td>- If goal is met after 1 month, reassess in 3-6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- If goal is not met after 1 month, consider different medications or titration</td>
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<td>- Continue monthly follow-up until control is achieved</td>
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Whelton et al. JACC 2018;71(19):e127-248
Recommendations for Lipid Screening

• COG guidelines recommend q2 yr screening in CCS with cranial, TBI or abdominal RT
• Adult Guidelines recommend screening and managing modifiable CV risk factors in patients receiving cardiotoxic therapies
Lipid Management Guidelines

ASCVD Risk Enhancers:
- Family h/o premature ASCVD
- Chronic kidney disease
- Metabolic syndrome
- Premature menopause
- Inflammatory Diseases
- Ancestry (e.g., S. Asian)

Biomarkers
- Persistently ↑LDL ≥160 mg/dl
- Persistently ↑Triglycerides ≥175 mg/dl
- hsCRP ≥ 2.0 mg/L
- Lp(a) > 50 mg/dl
- apoB ≥ 130 mg/dl
- Ankle brachial index < 0.9

https://doi.org/10.1016/j.jacc.2018.11.003
CV Medications and CV Outcomes in Cancer

Head & Neck Cancer Pts w/ Neck RT
- Incidental Statin Use During RT

CV Med Adherence and CAD Hosp.
- Pts w/ Pre-existing CAD & Incident CA


Screening for Diabetes in Children

- COG: q2 yr HbA1c screening in CCS who received TBI or abdominal RT
- COG: annual BMI assessment in CCS who received cranial RT (esp. leukemia and brain cancer)

### Table 2.5—Risk-based screening for type 2 diabetes or prediabetes in asymptomatic children and adolescents in a clinical setting*

<table>
<thead>
<tr>
<th>Criteria</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Overweight (BMI &gt;85th percentile for age and sex, weight for height &gt;85th percentile, or weight &gt;120% of ideal for height)</td>
<td>A</td>
</tr>
</tbody>
</table>

Plus one or more additional risk factors based on the strength of their association with diabetes as indicated by evidence grades:

- Maternal history of diabetes or GDM during the child’s gestation | A |
- Family history of type 2 diabetes in first- or second-degree relative | A |
- Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander) | A |
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight) | B |

*Diabetes Care 2018;41(supplement 1)*
Screening for Diabetes in Adults

Table 2.3—Criteria for testing for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in overweight or obese (BMI ≥ 25 kg/m² or ≥ 23 kg/m² in Asian Americans) adults who have one or more of the following risk factors:
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - History of CVD
   - Hypertension (≥ 140/90 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - Women with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)

2. Patients with prediabetes (A1C ≥ 5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at age 45 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

- ↑ risk w/ steroids, PI3Kinase inhibitors, mTOR inhibitors

Diabetes Care 2018;41(supplement 1); Hwangbo et al. JAMA Oncol 2018;4(8):1105-99.
# Diagnostic Criteria for Type II Diabetes

**Table 2.2—Criteria for the diagnosis of diabetes**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG $\geq 126$ mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.</td>
<td>* Metformin, SGLT-2 inhibitors and GLP-1 agonists have CV benefit</td>
</tr>
<tr>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>2-h PG $\geq 200$ mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.</td>
<td>* Metformin, SGLT-2 inhibitors and GLP-1 agonists have CV benefit</td>
</tr>
<tr>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>A1C $\geq 6.5%$ (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.</td>
<td>* Metformin, SGLT-2 inhibitors and GLP-1 agonists have CV benefit</td>
</tr>
<tr>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose $\geq 200$ mg/dL (11.1 mmol/L).</td>
<td>* Metformin, SGLT-2 inhibitors and GLP-1 agonists have CV benefit</td>
</tr>
</tbody>
</table>

Diabetes Care 2018;41(supplement 1)
## Non-Pharmacologic Interventions for Heart Health

<table>
<thead>
<tr>
<th>Nonpharmacological Intervention</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight loss</strong></td>
<td>Weight/body fat</td>
</tr>
<tr>
<td><strong>Healthy diet</strong></td>
<td>DASH dietary pattern</td>
</tr>
<tr>
<td><strong>Reduced intake of dietary sodium</strong></td>
<td>Dietary sodium</td>
</tr>
<tr>
<td><strong>Enhanced intake of dietary potassium</strong></td>
<td>Dietary potassium</td>
</tr>
</tbody>
</table>
| **Physical activity** | Aerobic | 90–150 min/wk  
65%–75% heart rate reserve |
| Dynamic resistance | 90–150 min/wk  
50%–80% 1 rep maximum  
6 exercises, 3 sets/exercise, 10 repetitions/set |
| Isometric resistance | 4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk  
8–10 wk |
| **Moderation in alcohol intake** | Alcohol consumption | In individuals who drink alcohol, reduce alcohol† to:  
Men: ≤2 drinks daily  
Women: ≤1 drink daily |

Whelton et al. JACC 2018;71(19):e127-248
Summary

• Cancer survivors have an increased prevalence of CV risk factors
• CV risk factors are associated with increased incidence of CVD in cancer survivors
• Risk assessment scores do not include cancer treatment and may underestimate CV risk
• Aggressive surveillance for and treatment of CV risk factors may lead to decreased CV events in cancer survivors
• Lifestyle modifications, especially exercise, can significantly impact cardiac and cancer mortality in cancer survivors
Question

- 32 yo man w/ HL @ age 22. Treated w/ ABVD x 3 cycles + IFRT to R neck/supraclavicular nodes. Now presents w/ recurrent large B cell lymphoma. Plan to give R-CHOP x 6 cycles.
- No other PMH, meds, or relevant FH
- Physical Exam:
  - HR 93 BP 135/74, BMI 39.83
  - Exam unremarkable.
- Labs:
  - Glucose 133, HbA1c 6.2
  - Chol 201, Trig 590, HDL 25, LDL 117
- Echo: EF 57%, no abnormalities
- 10 yr CVD risk: 4.5%
Question

Which of the following would you recommend?

A. Healthy lifestyle recs and reassess in 3 months
B. Healthy lifestyle recs + metformin for metabolic syndrome
C. Healthy lifestyle recs + BP medication
D. Healthy lifestyle recs + statin for hypertriglyceridemia
E. B, C and D
A 21 y.o. male with a h/o childhood ALL, diagnosed at age 6 months presents for his first visit to the adult survivorship clinic. He was treated with chemotherapy per protocol 95-001 (induction with asparaginase, doxorubicin, vincristine, Ara-C, prednisone, and MTX, followed by intensive treatment with Ara-C, MTX, asparaginase, 6-MP) as well as 18 Gy RT for CNS prophylaxis. His cumulative anthracycline exposure was 350 mg/m2.
Question

Based on his prior treatment exposures, what is the recommended surveillance schedule?

A. Echocardiogram to look for left ventricular dysfunction every year.
B. Echocardiogram to look for left ventricular dysfunction every 2 years.
C. Echocardiogram to look for left ventricular dysfunction every 5 years.
D. Echocardiogram to look for left ventricular dysfunction every year until age 30 years and if normal, no further surveillance is recommended.