



Chronic Disease Working Group 2008

Chuck Sklar

Lisa Diller

Niagara on the Lake

June 4, 2008

Chronic Disease Working Group 2008

1. Previous Work:

General Medical Health of Survivors

Overall burden of chronic medical disease in survivors

1. Hudson, Health Status. JAMA 2003
2. Oeffinger, Chronic medical conditions. NEJM 2006

Organ systems

A. Endocrine/growth

1. THYROID

Sklar, Thyroid disorders in HD. JCEM 2000

2. BONE

Kadan-Lottick, Osteonecrosis. JCO, in press

3. GROWTH/GH

Sklar, GH and risk of recurrence/smn. JCEM 2002

Gurney, Endocrine and cardiovascular disease in CNS. Cancer 2003

Gurney, Final height /bmi in CNS survivors. JCEM 2003

Brownstein, Impact of GH on final height. JCEM 2004

Chronic Disease Working Group 2008

1. Previous Work:

Organ systems

A. Endocrine/growth (cont)

3. GROWTH/GH (cont)

Ergun-Longmire, GH and smn. JCEM
2006

Chow, Final height ALL. J Pediatr 2007

4. WEIGHT

Oeffinger, Obesity ALL. JCO 2003

Ross, Genetic variation in leptinR and obesity
ALL. JCO 2004

Meacham, BMI across CCSS. Cancer
2005

Garmey, Longitudinal changes in obesity ALL.
JCO 2008, in press

5. PUBERTY/GONADAL FUNCTION

Chemaitilly, Acute ovarian failure. JCEM

2006

Sklar, Premature menopause. JNCI 2006

Chow, Timing menarche ALL. PBC 2008

Armstrong, Timing menarche CNS, submitted

Chronic Disease Working Group 2008

1. Previous Work:

Organ systems

B. Cardiovascular Health

1. CARDIAC

Gurney, Cardiovascular disease CNS survivors. Cancer 2003

Mulrooney, Late effects AML. Cancer 2008

Blanco, Genetic susceptibility to anthracycline cardiomyopathy. Cancer 2008, in press.

Mulrooney, Cardiac disease in CCSS, draft

2. VASCULAR

Bowers, Stroke in HD. JCO 2005.

Bowers, Stroke after CNS RT. JCO 2006

3. METABOLIC

Meacham, Incidence and risk factors DM, submitted

Meacham, Clustering CV risk factors, draft

C. Pulmonary

Mertens, Pulmonary disease in CCSS. Cancer 2002

D. Neurologic-neurosensory

Packer, Neurological outcomes in CNS. JCO 2003

Laverdiere, Late outcomes in NB. Submitted

Whelan, Visual dysfunction in CCSS, draft

Whelan, Auditory dysfunction in CCSS, draft

Chronic Disease Working Group 2008

1. Previous Work:

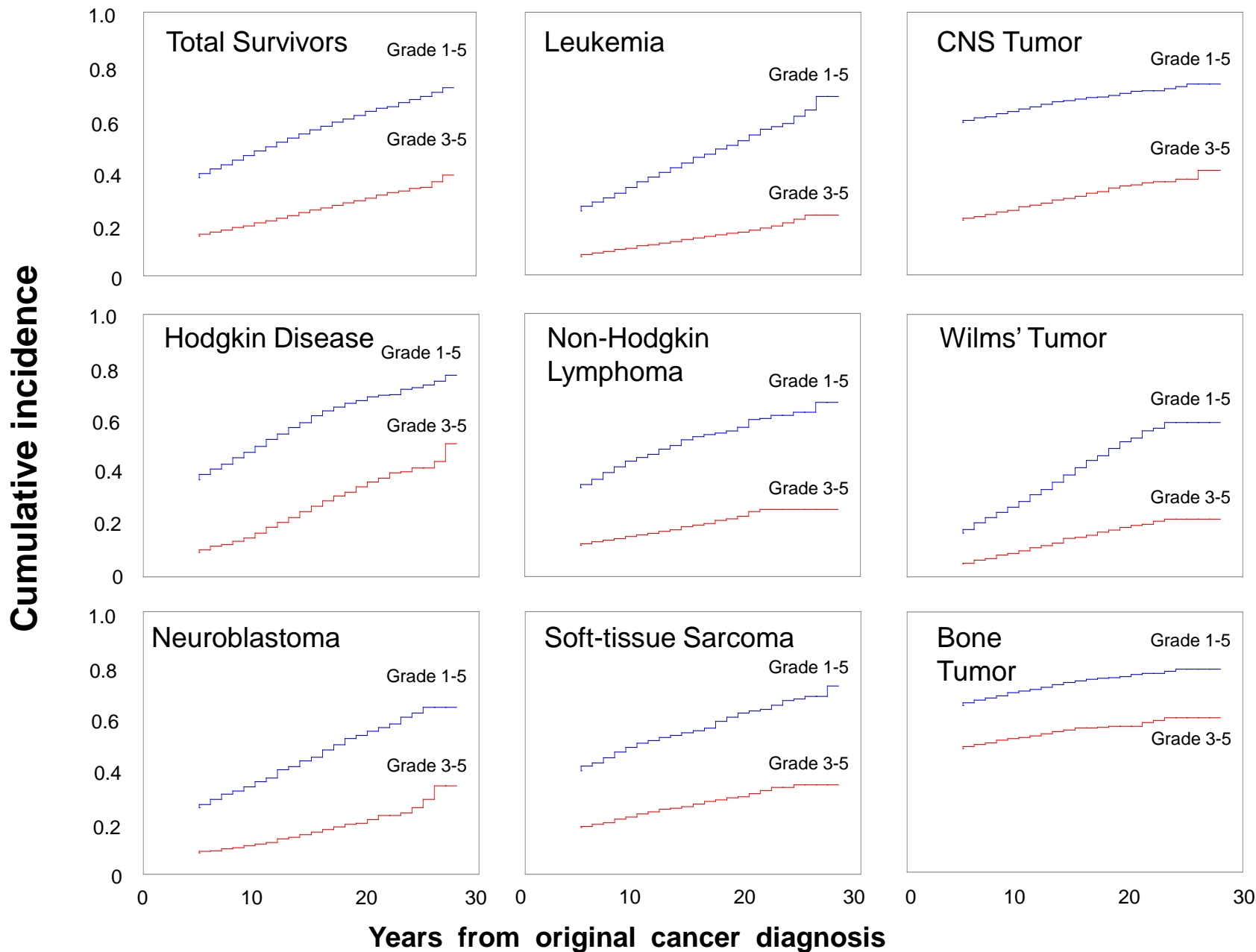
Highlighted Work

Chronic Medical Conditions

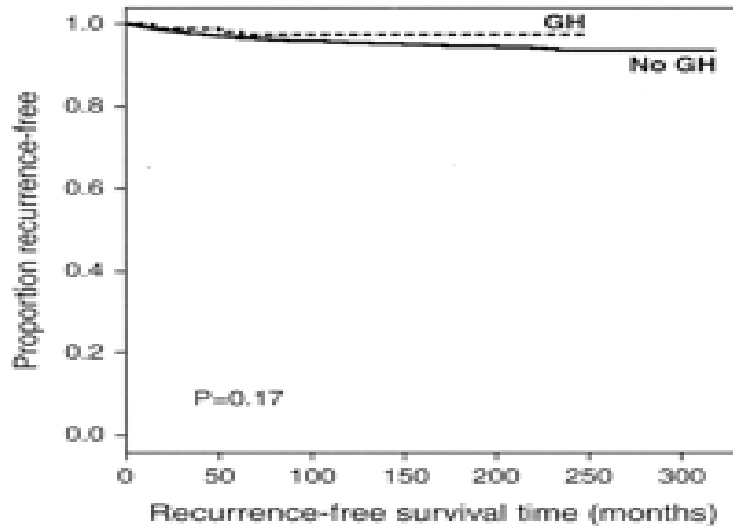
GH Therapy and Risk of Recurrence and
SMN

Genetic Variation and Risk of Obesity

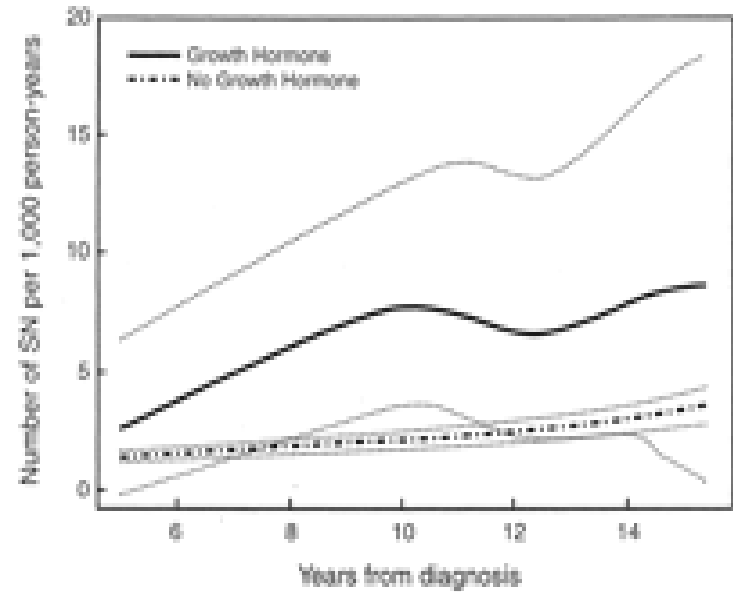
Figure 1. Cumulative incidence of chronic health conditions in 10,397 adult survivors of pediatric cancer



Risk of Recurrence



Risk of SMN



Risk of SMN, Updated

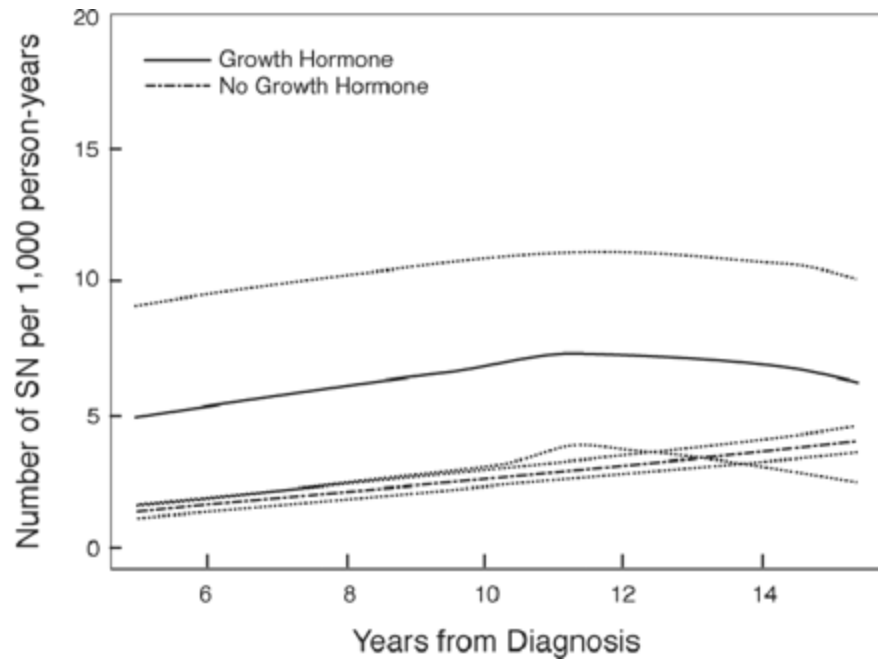


Table 3. Sex-Specific ORs and 95% CIs for Being Overweight or Obese (BMI \geq 25 kg/m²) by CRT and Age at Diagnosis in 600 Adult White, Non-Hispanic Survivors of Childhood ALL

| Effect | Effect of Gln223Arg Polymorphism (Arg/Arg v Gln) | | | | | Arg/Gln and Gln/Gln | | | | |
|--|--|-----|------------|------|-----------------|---------------------|------------|-----|--|--|
| | Female (n = 294) | | | | | Male (n = 306) | | | | |
| | No. of Patients | OR | 95% CI | P | No. of Patients | OR | 95% CI | P | | |
| Overall main effect of polymorphism* | 50 v 244 | 2.5 | 1.3 to 4.8 | .004 | 71 v 235 | 1.3 | 0.7 to 2.2 | .39 | | |
| Stratum-specific effects of the polymorphism | | | | | | | | | | |
| Treatment only | | | | | | | | | | |
| < 20 Gy CRT or chemotherapy only | 28 v 117 | 1.4 | 0.6 to 3.3 | .44 | 35 v 119 | 0.9 | 0.4 to 2.0 | .88 | | |
| \geq 20 Gy CRT | 22 v 127 | 6.1 | 2.1 to 22 | .002 | 36 v 116 | 1.8 | 0.8 to 4.0 | .16 | | |
| P for interaction | | | .04 | | | | .44 | | | |
| Treatment/age at diagnosis | | | | | | | | | | |
| < 20 Gy CRT/age at DX 0-4 years | 7 v 33 | 3.1 | 0.6 to 16 | .19 | 13 v 34 | 1.0 | 0.3 to 3.7 | .98 | | |
| < 20 Gy CRT/age at DX 5-21 years | 21 v 84 | 1.1 | 0.4 to 2.9 | .92 | 22 v 85 | 1.0 | 0.4 to 2.5 | .91 | | |
| \geq 20 Gy CRT/age at DX 0-4 years | 12 v 48 | 4.2 | 1.0 to 29 | .085 | 16 v 52 | 1.5 | 0.5 to 4.9 | .52 | | |
| \geq 20 Gy CRT/age at DX 5-21 years | 10 v 79 | 7.1 | 1.6 to 50 | .018 | 20 v 64 | 2.0 | 0.7 to 6.3 | .20 | | |
| P for interaction | | | .16 | | | | .62 | | | |

Table 3. Sex-Specific ORs and 95% CIs for Being Overweight or Obese (BMI ≥ 25 kg/m²) by CRT and Age at Diagnosis in 600 Adult White, Non-Hispanic Survivors of Childhood ALL

| Effect | Effect of Gln223Arg Polymorphism (Arg/Arg v Gln) | | | | | Arg/Gln and Gln/Gln | | | | |
|--|--|-----|------------|------|-----------------|---------------------|------------|-----|--|--|
| | Female (n = 294) | | | | | Male (n = 306) | | | | |
| | No. of Patients | OR | 95% CI | P | No. of Patients | OR | 95% CI | P | | |
| Overall main effect of polymorphism* | 50 v 244 | 2.5 | 1.3 to 4.8 | .004 | 71 v 235 | 1.3 | 0.7 to 2.2 | .39 | | |
| Stratum-specific effects of the polymorphism | | | | | | | | | | |
| Treatment only | | | | | | | | | | |
| < 20 Gy CRT or chemotherapy only | 28 v 117 | 1.4 | 0.6 to 3.3 | .44 | 35 v 119 | 0.9 | 0.4 to 2.0 | .88 | | |
| ≥ 20 Gy CRT | 22 v 127 | 6.1 | 2.1 to 22 | .002 | 36 v 116 | 1.8 | 0.8 to 4.0 | .16 | | |
| P for interaction | | | .04 | | | | .44 | | | |
| Treatment/age at diagnosis | | | | | | | | | | |
| < 20 Gy CRT/age at DX 0-4 years | 7 v 33 | 3.1 | 0.6 to 16 | .19 | 13 v 34 | 1.0 | 0.3 to 3.7 | .98 | | |
| < 20 Gy CRT/age at DX 5-21 years | 21 v 84 | 1.1 | 0.4 to 2.9 | .92 | 22 v 85 | 1.0 | 0.4 to 2.5 | .91 | | |
| ≥ 20 Gy CRT/age at DX 0-4 years | 12 v 48 | 4.2 | 1.0 to 29 | .085 | 16 v 52 | 1.5 | 0.5 to 4.9 | .52 | | |
| ≥ 20 Gy CRT/age at DX 5-21 years | 10 v 79 | 7.1 | 1.6 to 50 | .018 | 20 v 64 | 2.0 | 0.7 to 6.3 | .20 | | |
| P for interaction | | | .16 | | | | .62 | | | |

Table 3. Sex-Specific ORs and 95% CIs for Being Overweight or Obese (BMI ≥ 25 kg/m²) by CRT and Age at Diagnosis in 600 Adult White, Non-Hispanic Survivors of Childhood ALL

| Effect | Effect of Gln223Arg Polymorphism (Arg/Arg v Gln) | | | | | Arg/Gln and Gln/Gln | | | | |
|--|--|-----|------------|------|-----------------|---------------------|------------|-----|--|--|
| | Female (n = 294) | | | | | Male (n = 306) | | | | |
| | No. of Patients | OR | 95% CI | P | No. of Patients | OR | 95% CI | P | | |
| Overall main effect of polymorphism* | 50 v 244 | 2.5 | 1.3 to 4.8 | .004 | 71 v 235 | 1.3 | 0.7 to 2.2 | .39 | | |
| Stratum-specific effects of the polymorphism | | | | | | | | | | |
| Treatment only | | | | | | | | | | |
| < 20 Gy CRT or chemotherapy only | 28 v 117 | 1.4 | 0.6 to 3.3 | .44 | 35 v 119 | 0.9 | 0.4 to 2.0 | .88 | | |
| ≥ 20 Gy CRT | 22 v 127 | 6.1 | 2.1 to 22 | .002 | 36 v 116 | 1.8 | 0.8 to 4.0 | .16 | | |
| <i>P</i> for interaction | .04 | | | | | .44 | | | | |
| Treatment/age at diagnosis | | | | | | | | | | |
| < 20 Gy CRT/age at DX 0-4 years | 7 v 33 | 3.1 | 0.6 to 16 | .19 | 13 v 34 | 1.0 | 0.3 to 3.7 | .98 | | |
| < 20 Gy CRT/age at DX 5-21 years | 21 v 84 | 1.1 | 0.4 to 2.9 | .92 | 22 v 85 | 1.0 | 0.4 to 2.5 | .91 | | |
| ≥ 20 Gy CRT/age at DX 0-4 years | 12 v 48 | 4.2 | 1.0 to 29 | .085 | 16 v 52 | 1.5 | 0.5 to 4.9 | .52 | | |
| ≥ 20 Gy CRT/age at DX 5-21 years | 10 v 79 | 7.1 | 1.6 to 50 | .018 | 20 v 64 | 2.0 | 0.7 to 6.3 | .20 | | |
| <i>P</i> for interaction | .16 | | | | | .62 | | | | |

Chronic Disease Working Group 2008

2. Topics Under Discussion

A. GI complications

B. GU complications

C. Genetic risk factors for ovarian failure

Chronic Disease Working Group 2008

3. Gaps in Knowledge

A. Renal outcomes

B. GI outcomes

C. Bone density in adult survivors

D. Fracture risk

E. Interaction between normal aging process and major organ dysfunction, especially cardiovascular disease

F. Interaction between cardiovascular risk factors (eg, insulin resistance, dyslipidemia), direct organ damage from prior therapy (eg, anthracycline, RT), and lifestyle choices (eg, smoking, alcohol)

Chronic Disease Working Group 2008

4. Opportunities within CCSS

A. CP (Existing Data)

1. GI outcomes
2. Renal outcomes
3. Solid organ transplants
4. Infectious complications

B. CP (Future Data)

1. Interaction of CV risk factors, lifestyle choices, treatment exposures and CV mortality
2. Impact of aging on burden of chronic medical conditions
3. Incidence and risk factors for bone fracture
4. Renal/tubular dysfunction in expanded cohort

Chronic Disease Working Group 2008

4. Opportunities within CCSS (cont.)

C. Ancillary studies

1. Direct measurement studies

- a. Assessment of markers for CVD (eg, fasting insulin/glucose, CRP, lipids) in subset of survivors
- b. Assessment of BMD in subset of survivors
- c. Blood indices of chronic organ system dysfunction (eg, BUN, creat)

2. Intervention studies to reduce risk (eg, exercise, diet) in survivors at high risk for CVD

Chronic Disease Working Group 2008

5. RFA

A. Studies designed to improve our understanding of the interaction between metabolic risk factors for CVD, cardiotoxic therapeutic exposures, and lifestyle choices on CVD disease and CV mortality

B. Studies designed to assess incidence of and risk factors for reduced BMD in adult survivors of childhood cancer