

Childhood Cancer Survivor Study (U24 CA55727)

Report of the
Chronic Disease Working Group
Charles Sklar, M.D.

CCSS Investigator Meeting
Williamsburg, VA
June 9-10, 2010



Chronic Disease Working Group* 2010

Williamsburg
June 10, 2010

* Includes Neurology and Reproductive WGs

Chronic Disease Working Group

Core Members

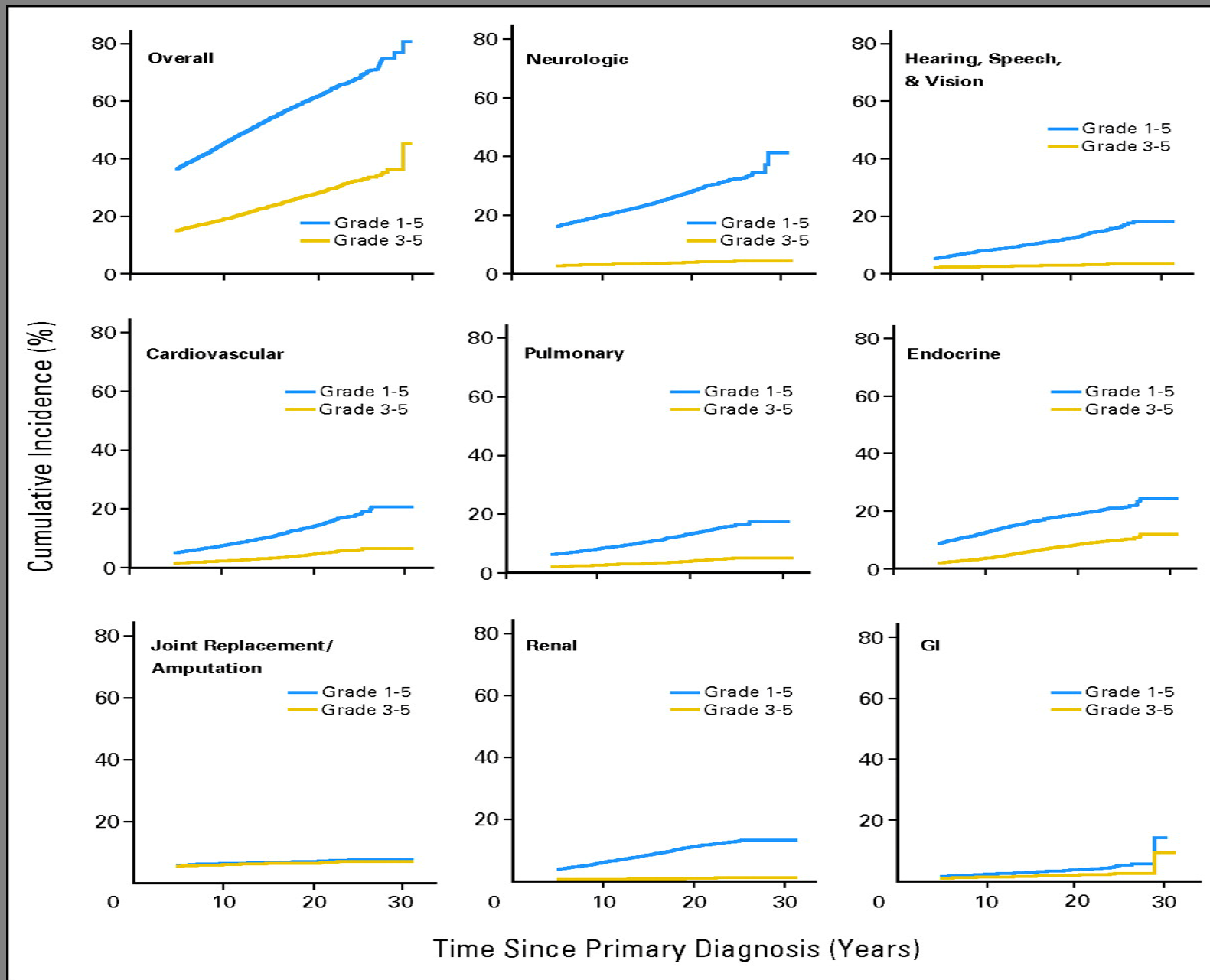
- Chuck Sklar (Co-Chair)
- Lisa Diller (Co-Chair)
 - Eric Chow
 - Dan Green
 - Kevin Oeffinger
 - Roger Packer

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Publications 2009-2010

- ***Fertility of female survivors***, Green et al (**JCO**)
- ***Abnormal timing of menarche in BT survivors***, Armstrong et al (**Cancer**)
- ***Diabetes mellitus in survivors***, Meacham et al (**Arch Intern Med**)
- ***Outcomes in survivors of CNS tumors***, Armstrong et al, (**JNCI**)
- ***Outcomes in survivors of NB***, Laverdière et al (**JNCI**)
- ***Risk of thyroid dysfunction in ALL***, Chow et al (**PBC**)
- ***Ocular late effects***, Whelan et al (**PBC**)
- ***Chronic disease in CCSS***, Diller et al (**JCO**)
- ***Ovarian failure and reproductive outcomes in CCSS***, Green et al (**JCO**)
- ***Impact of RT and chemo on dental abnormalities***, Kaste et al (**Cancer**)
- ***Cardiac outcomes***, Mulrooney et al (**BMJ**)
- ***Late neurologic sequelae in survivors of ALL***, Goldsby et al (**JCO**)
- ***Fertility of male survivors***, Green et al (**JCO**)
- ***Cardiovascular risk factors***, Meacham et al (**Cancer Epi Biomarkers Prev**)
- ***Outcomes in survivors of osteosarcoma***, Nagarajan et al (**Cancer, in press**)
- ***Stillbirth and neonatal death in relation to RT***, Signorello et al (**Lancet, in press**)
- ***Long-term survivors of CNS malignancies***, Armstrong (**Eur J Neurol, in press**)

Cumulative incidence of chronic health conditions



Percentage of childhood cancer survivors with diabetes mellitus (DM) by age at interview for 3 treatment groups

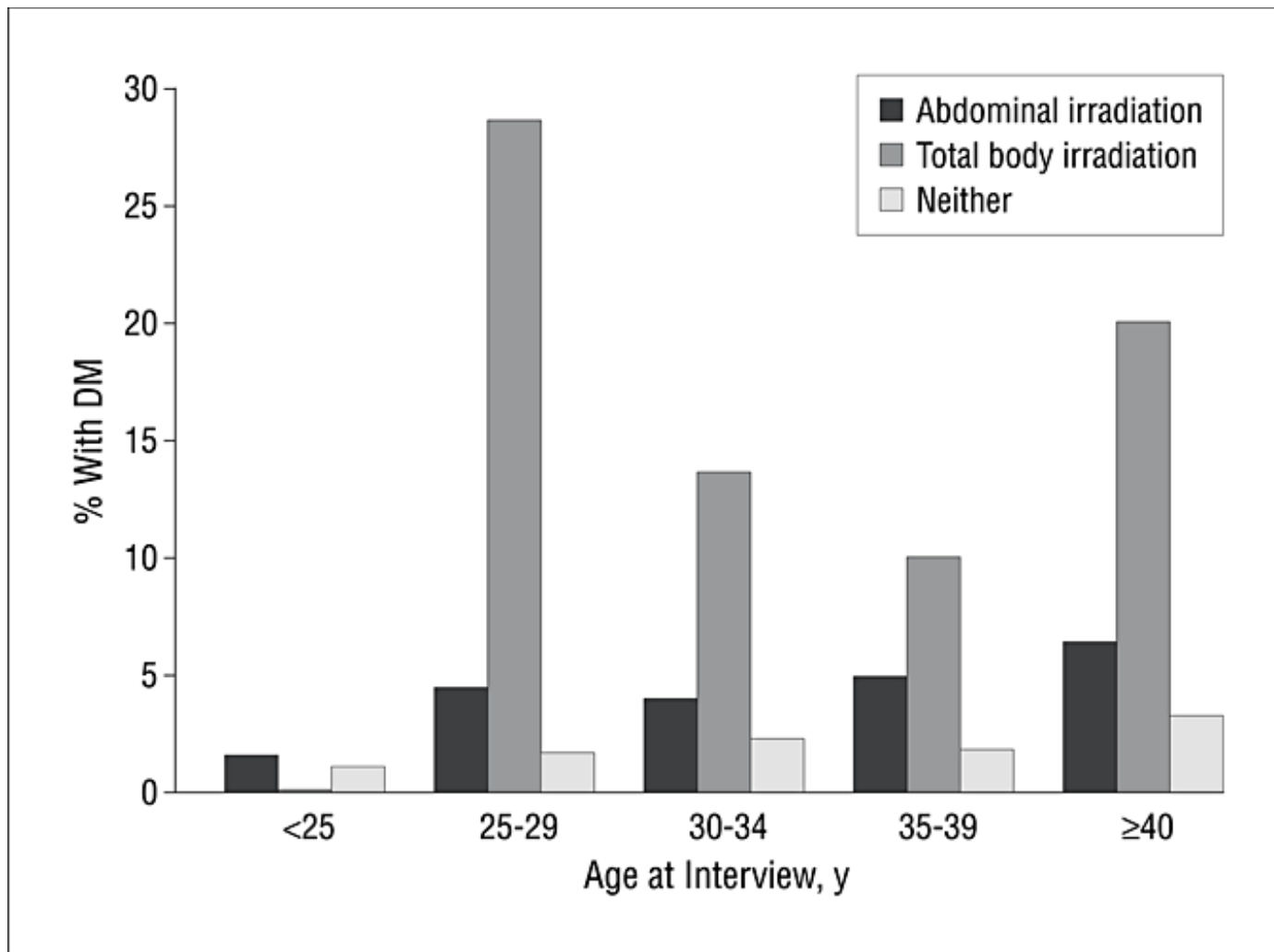
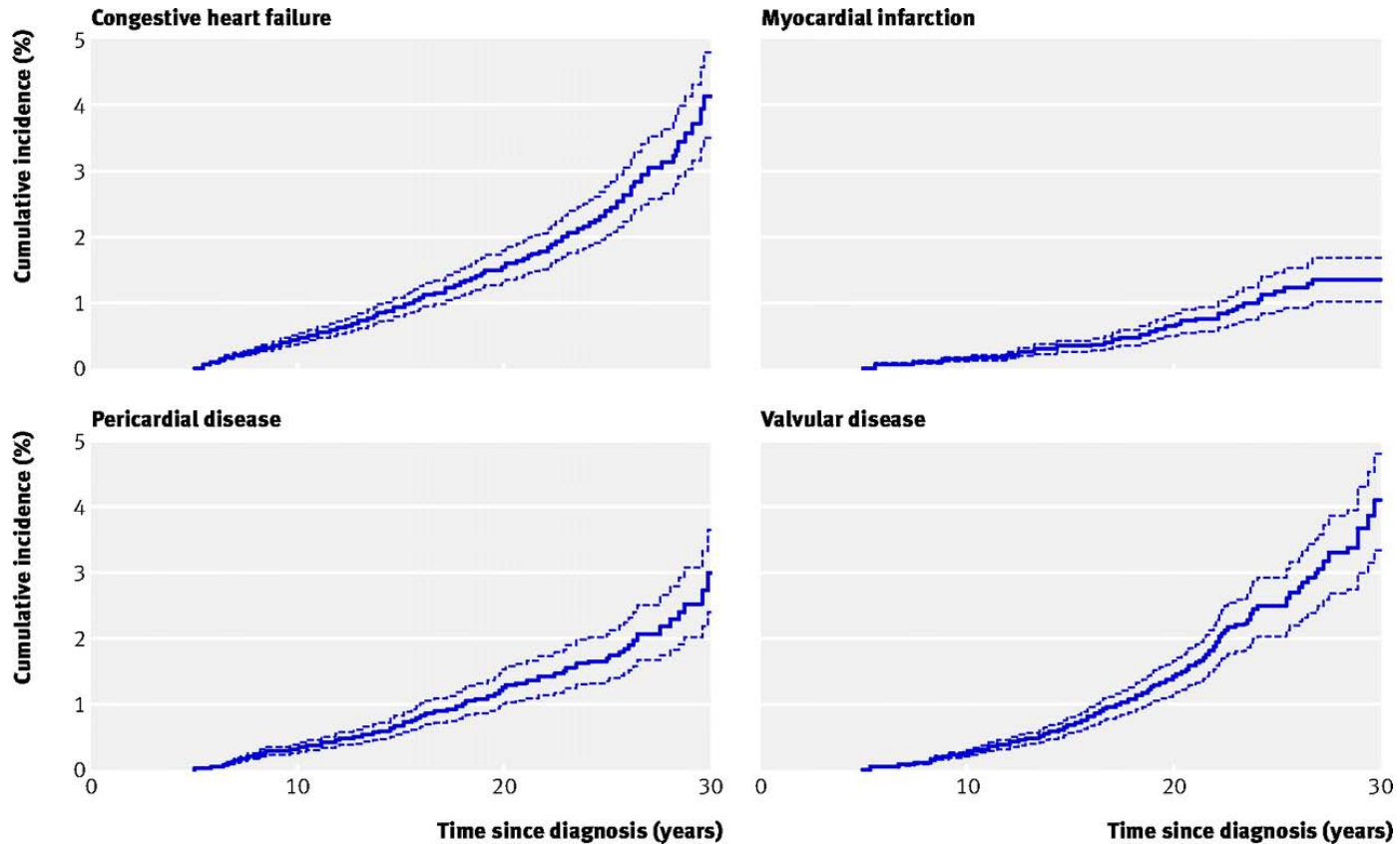
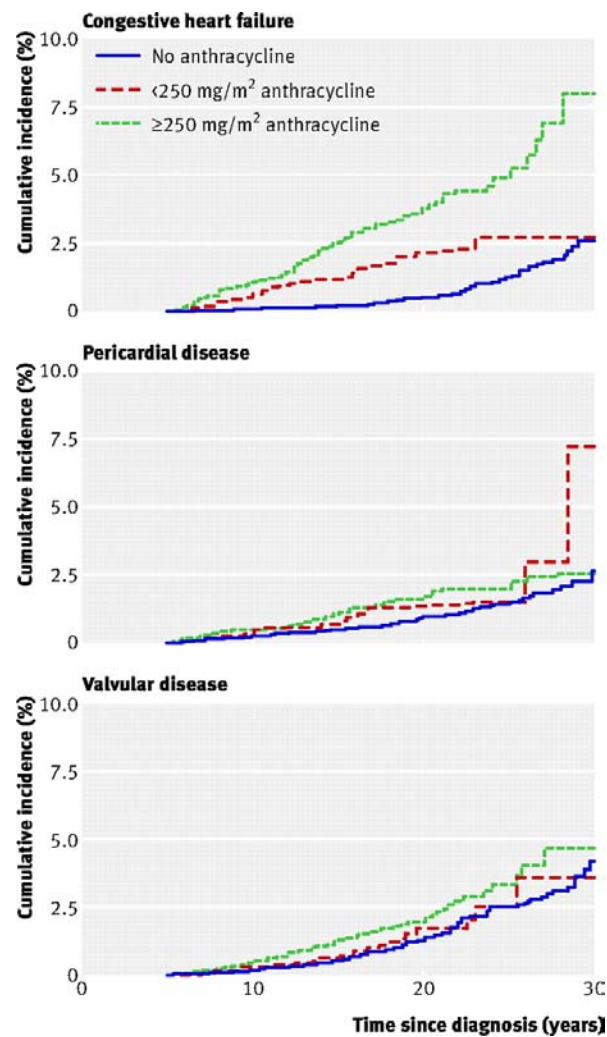


Fig 2 Cumulative incidence and 95% CI of cardiac disorders among childhood cancer survivors

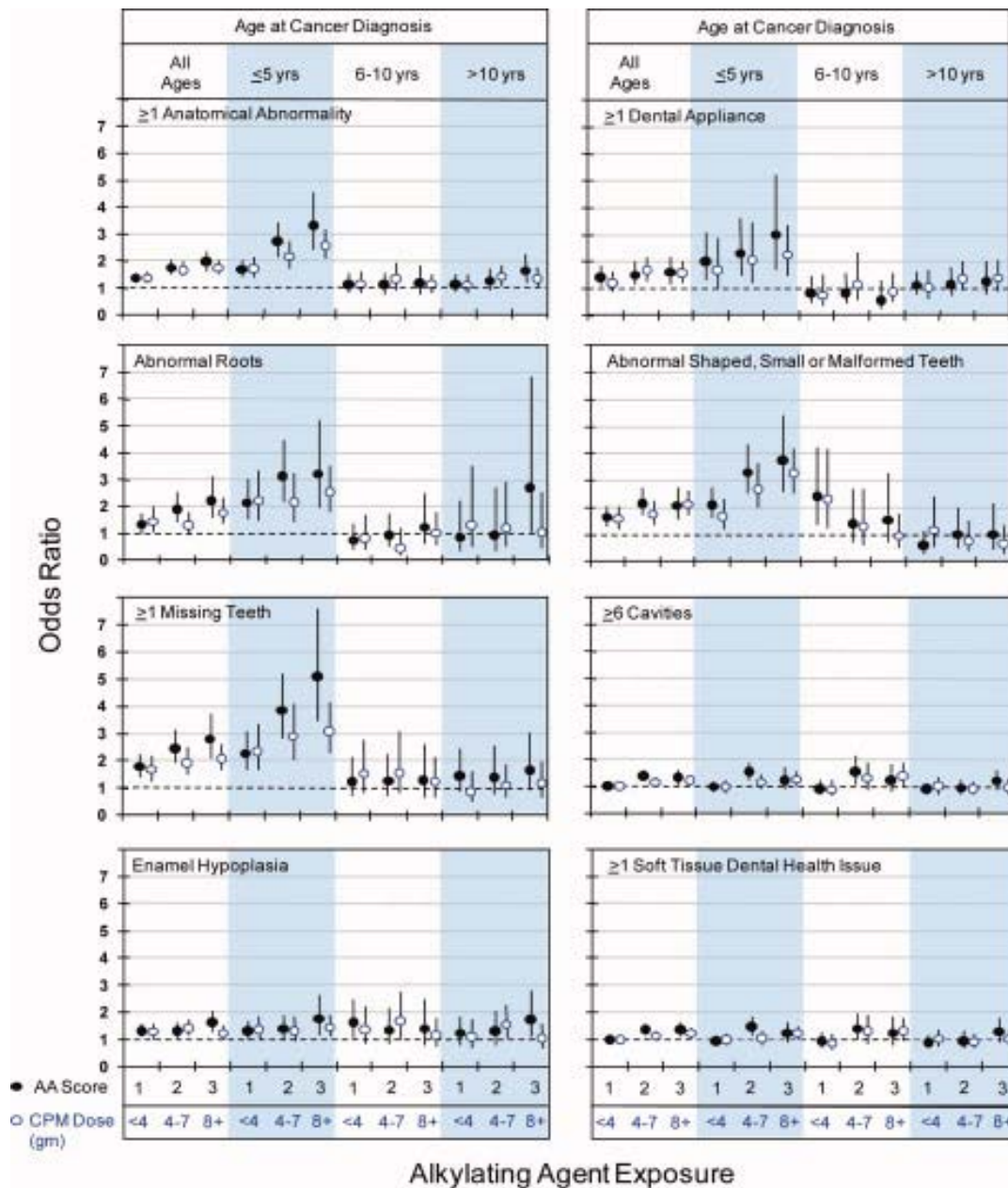


Mulrooney, D. A et al. *BMJ* 2009;339:b4606

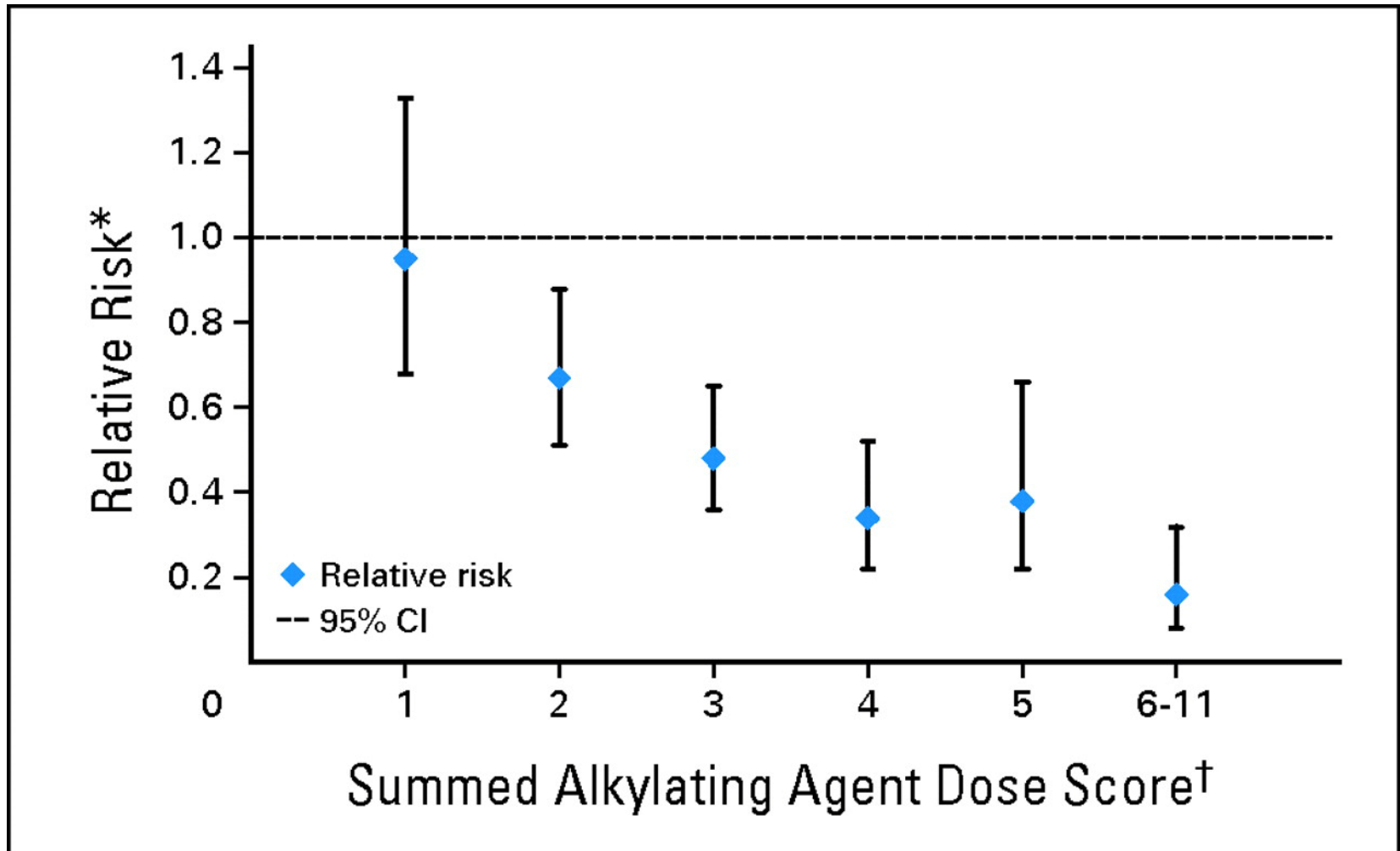
Fig 3 Cumulative incidence of cardiac disorders among childhood cancer survivors by anthracycline dose



Mulrooney, D. A et al. BMJ 2009;339:b4606



Summed alkylating agent dose score and the relative risk for siring a pregnancy



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Approved Concept Proposals

- ***Outcomes in survivors of Ewing's***, Ginsburg et al (Provisionally accepted JNCI)
- ***Outcomes in survivors of HD***, Castellino et al (Submitted)
- ***Auditory outcomes***, Whelan et al (Draft)
- ***Outcomes in survivors of Wilms'***, Termuhlen et al (Draft)
- ***Fertility in female survivors after CRT < 30 Gy***, Green et al (Draft)
- ***GI outcomes***, Goldsby et al (Manuscript in prep)
- ***Anti-depressant use and risk of obesity***, Green (Manuscript in prep)
- ***Female psychosexual functioning***, Ford et al (Analysis completed)
- ***Outcomes in HSCT survivors***, Baker et al (Analysis ongoing)
- ***Male sexual health***, Meacham et al (Analysis ongoing)
- ***GU outcomes***, Shnorhavorian et al (Analysis ongoing)
- ***Outcomes for infant survivors***, Vrooman (Analysis ongoing)
- ***Cataracts after RT***, Chodick et al (Analysis ongoing)
- ***Radiosensitivity of human oocyte***, Wallace (Analysis ongoing?)
- ***Chronic medical conditions in BMTSS vs CCSS***, Armenian et al (Data set in process)
- ***CV risk factor clustering and risk of cardiac m/m***, Armstrong et al (Awaiting data)
- ***First and recurrent stroke***, Fullerton et al (Awaiting data)
- ***Risk score algorithm to predict CVD***, Chow (Awaiting data)
- ***M/M underweight survivors***, Meacham (Awaiting data)

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Approved AOI's

- **Risk of osteoporosis and fractures, Kadan-Lottick***
- **Solid organ transplantation, Termuhlen ***
- **Infectious complications, Perkins***
- **M/M in HD survivors with contemporary tx, Castellino***
- **Outcome of pregnancies exposed to chemo/RT, Mulvihill***
- **Diseases of thyroid after RT, Viega**
- **Longitudinal assessment of chronic health conditions, Armstrong**
- **Health and functional status in survivors of medulloblastoma, King**
- **Health status of older survivors, Kinney**
- **Scoring AA exposure, Green**
- **Long-term outcomes in Ewing's survivors, Marina**

* Approved > 6months ago

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Ancillary studies

- **Completed**

- **Safety/efficacy of GH**, Sklar (Genentech Fdn)

- *Risk of recurrence and SN*, Sklar et al, JCEM 2002
- *Factors that affect final height*, Brownstein et al, JCEM 2004
- *Risk of SN update*, Ergun-Longmire et al, JCEM 2006

- **Premature menopause**, Sklar (R01 NCI)

- *Acute ovarian failure*, Chemaitilly et al, JCEM 2006
- *Premature menopause*, Sklar et al, JNCI 2006
- *Psychosexual functioning*, Ford et al, analysis completed

- **Metabolic Syndrome in survivors of ALL**, Gurney (R21)

- *MS and GHD in ALL*, Gurney et al, Cancer 2006
- *Body composition and muscle strength/mobility*, Ness et al, PBC 2007
- *Health knowledge about heart/stroke*, Gurney et al, Ann Epidemiol 2007
- *Endothelial function*, Dengel et al, J Pediatr Hem/Onc 2008
- *Poor adherence to dietary guidelines*, Robien et al, J Pediatr Hem/Onc 2008
- *Bone density in survivors of ALL*, Thomas et al, Cancer 2008

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Ancillary studies

- **Active**
 - **Testicular and sexual dysfunction in male survivors,** Meacham (LAF)
 - Data collection complete, analysis underway
- **Proposed**
 - **Genetic susceptibility to obesity,** Kamdar, submitted Leukemia & Lymphoma Society
 - **Late neurologic sequelae in survivors of CNS tumors,** Ullrich, in prep

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Future Research Priorities

- **Develop models to predict premature menopause**
 - Using both exposure data, patient info, and biomarkers
- **Impact of changes in therapy on neuro outcomes in survivors CNS tumor**
- **Impact of newer agents (eg, ifosfamide, cisplatin) on a variety of medical and reproductive outcomes**
- **Impact of aging on organ system function in survivors**
- **Improved understanding of genetic component of chronic organ system dysfunction following cancer therapy**
- **Direct measurement studies**
 - Assessment of metabolic markers for CVD (eg, fasting insulin/glucose, CRP, lipids) in subset of survivors
 - Assessment of BMD in subset of survivors
 - Blood indices of chronic organ system dysfunction (eg, BUN, creat)
- **Intervention studies to reduce risk (eg, exercise, diet) in survivors at high risk for CVD**