The Epidemiology of Therapy-Related MDS/AML in the Modern Treatment Era

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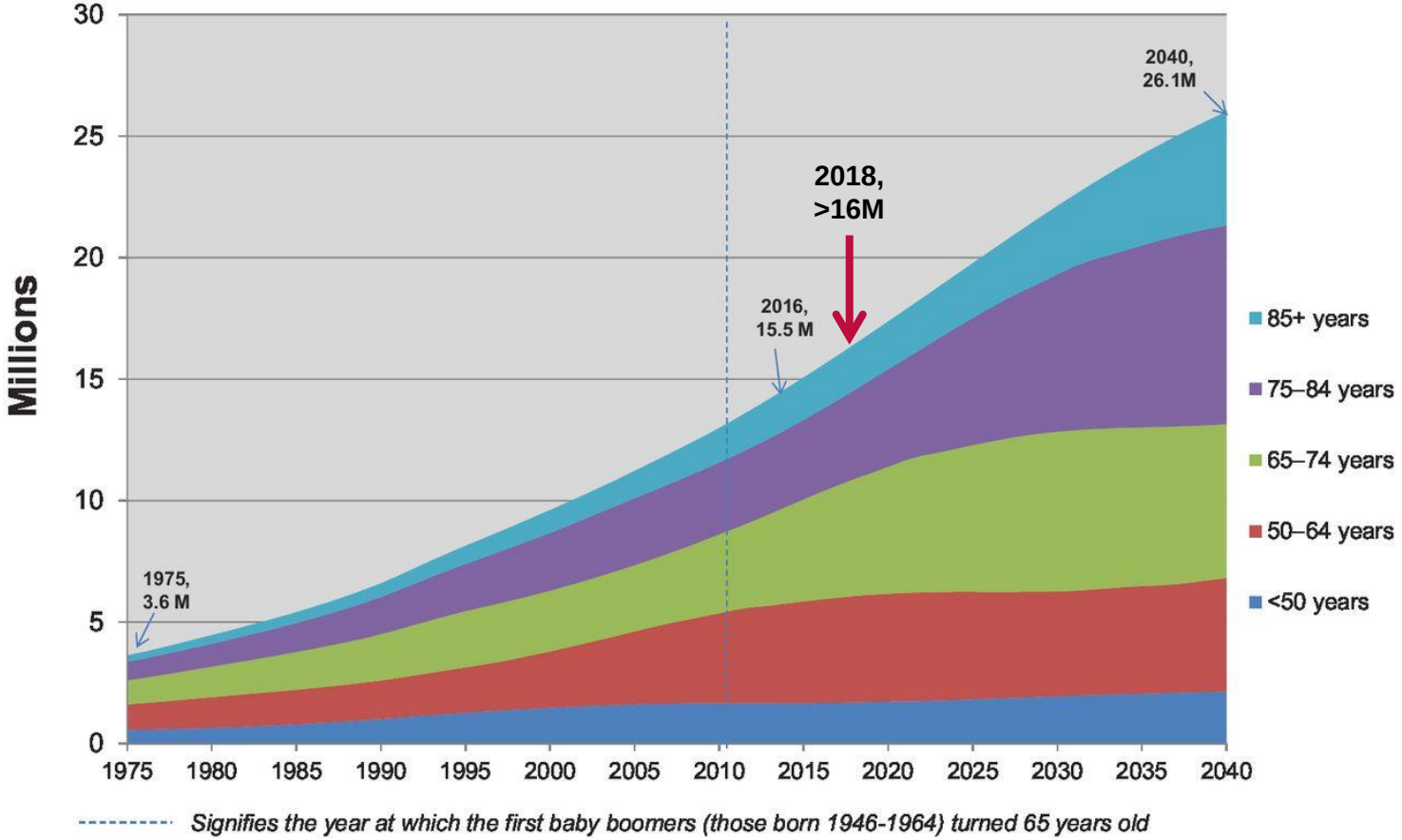
Growing population of cancer survivors



Bluethmann, Mariotto, Rowland. *Cancer Epidemiol Biomarkers Prev* 2016

Treatment-related leukemia

ASSOCIATION OF CANCER OF THE BREAST AND ACUTE MYELOCYTIC LEUKEMIA

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Four women are reported in whom carcinoma of the breast was diagnosed 1 to 11 months prior to the development of acute myelocytic leukemia. They were observed in a total population of 46 women with acute myelocytic leukemia seen between 1954 and 1964 in upper New York State. The coincidence was found about 30 times more frequently than would have been expected on the basis of individual occurrence rates applicable to the general population. The brief latency in these four patients who received no radiotherapy is in sharp contrast to the longer latency in a fifth patient who received radiotherapy and in 17 of 21 similar patients cited in the literature or observed in

Carey et al. *Cancer* 1967

tMDS/AML risk varies by type of cancer therapy

- Leukemogenic treatments
  - Alkylating agents (melphalan > cyclophosphamide)
  - Platinum compounds (carboplatin > cisplatin)
  - Topoisomerase II inhibitors (etoposide > doxorubicin)
  - Antimetabolites (fludarabine)
  - Radiotherapy

➢ Risks in modern treatment era?

  ➢ New indications for standard agents

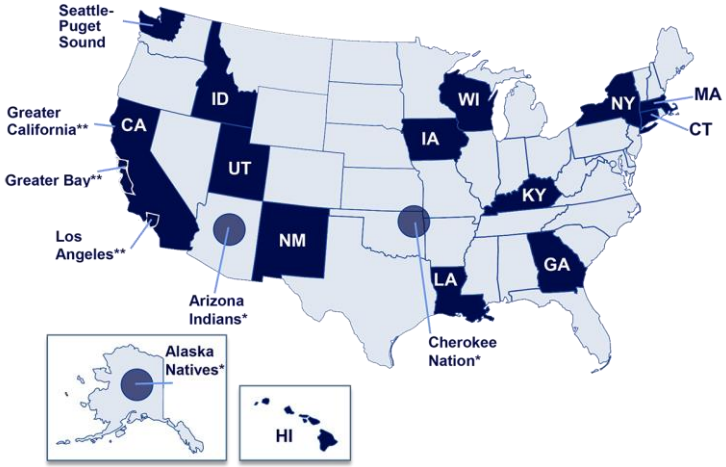
  ➢ Novel agents

Study designs for investigating tMN risk

Characteristic	Clinical trials, Case series, Case-control studies	Cancer registry data
Patients	Selected	Unselected
Sample size	Small	Large
Follow-up	?	Systematic, long-term
Treatment data	Detailed	Initial treatment yes/no only
tMDS/AML data	Detailed	Limited
Risk measure	Relative risk?	Relative & absolute risk

SEER: 2000-2014
tMDS/AML risks after chemotherapy for adult solid tumors

- 17 SEER registries, 2000-2014
- 700,612 adults treated with initial chemotherapy for 23 solid tumors
- 1619 cases of second primary MDS/AML
- Standardized incidence ratios (SIRs) compared risk with general population



Morton et al. *JAMA Oncol* 2019

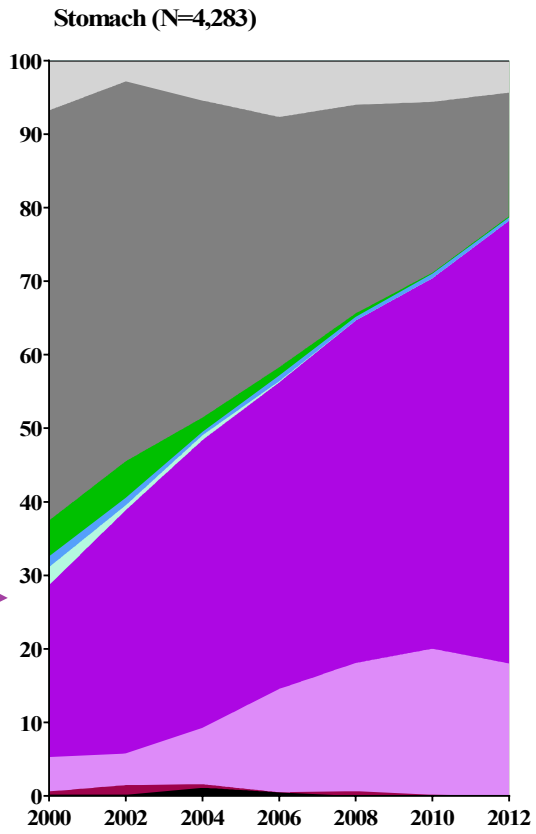
SEER: 2000-2014
tMDS/AML risks after chemotherapy for adult solid tumors

- SEER-Medicare claims, 2000-2014
- 165,820 older adults treated with initial chemotherapy
- Focus on use of known leukemogenic agents
- Increased use of platinum-based chemotherapy

Platinum

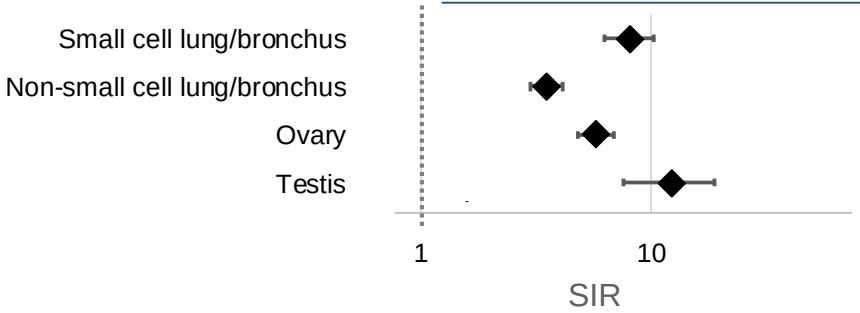
Platinum + topoisomerase II inhibitor

Topoisomerase II inhibitor



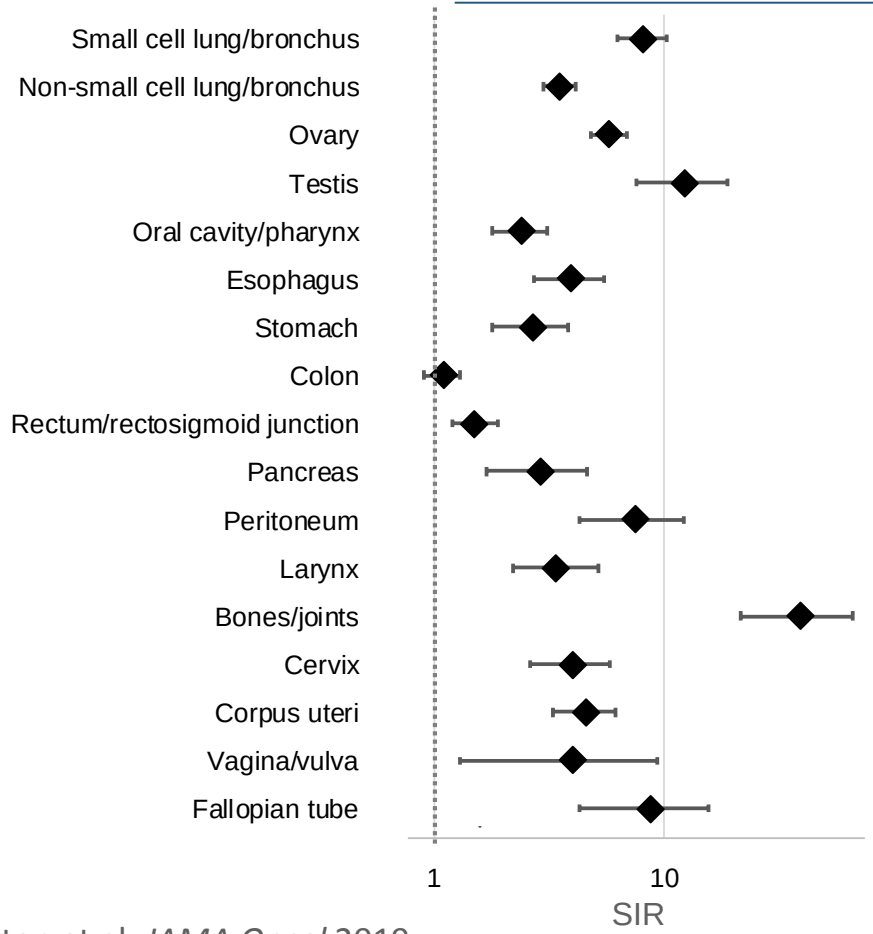
Morton et al. *JAMA Oncol* 2019

Platinum-based chemotherapy



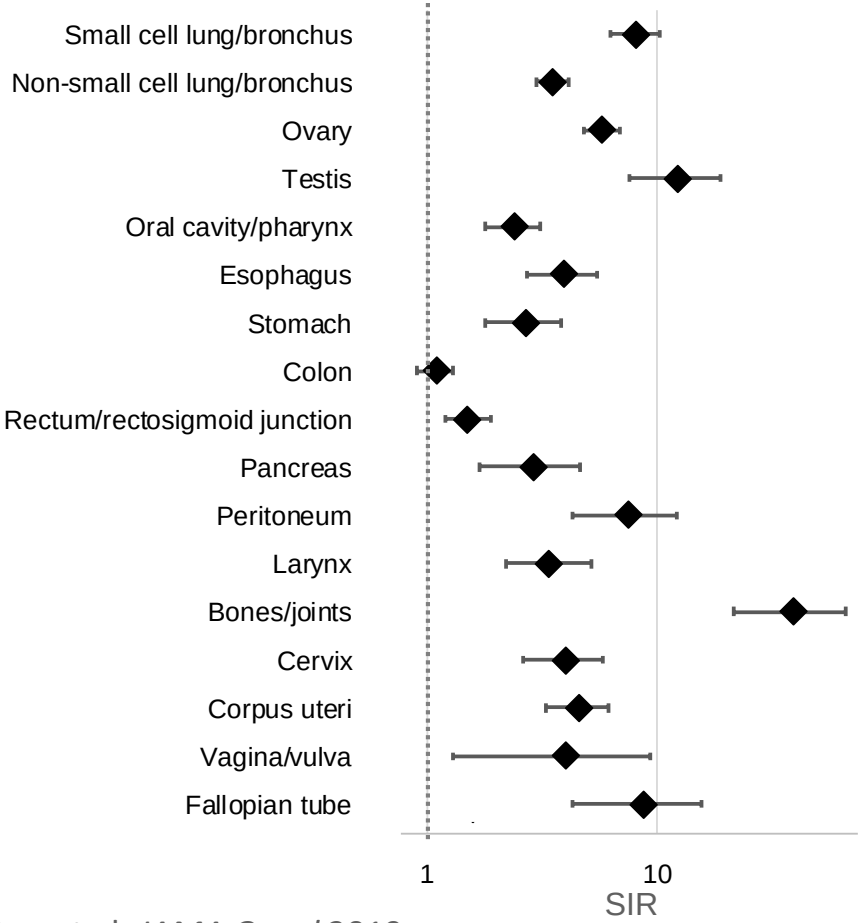
Morton et al. *JAMA Oncol* 2019

Platinum-based chemotherapy

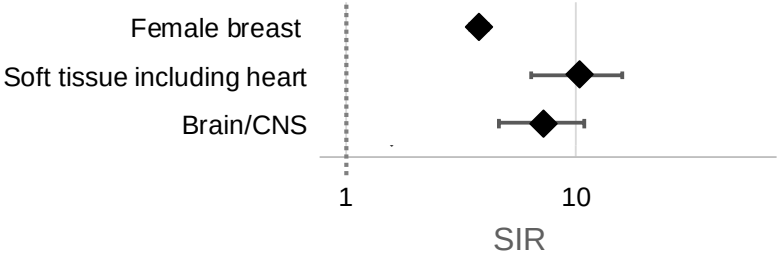


Morton et al. *JAMA Oncol* 2019

Platinum-based chemotherapy



Akylating agent and/or topoisomerase II-based chemotherapy



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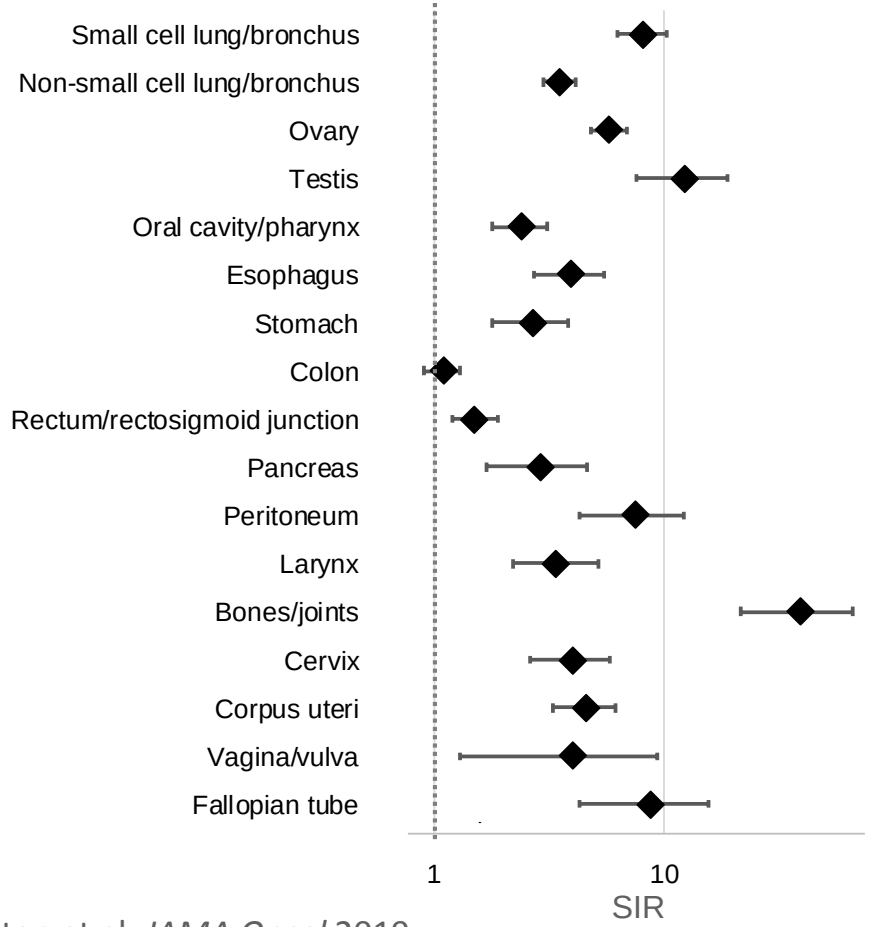
Platinum-based chemotherapy



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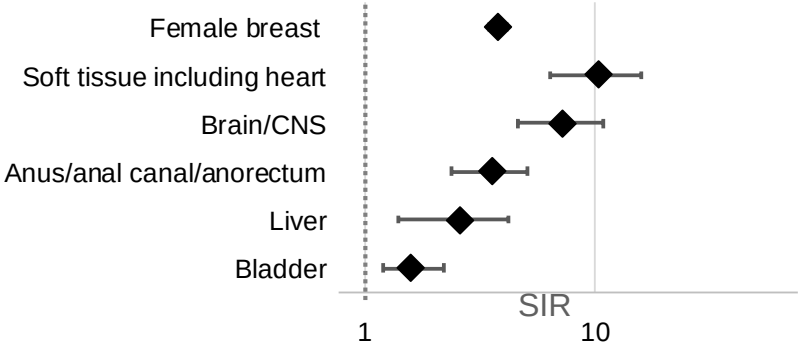
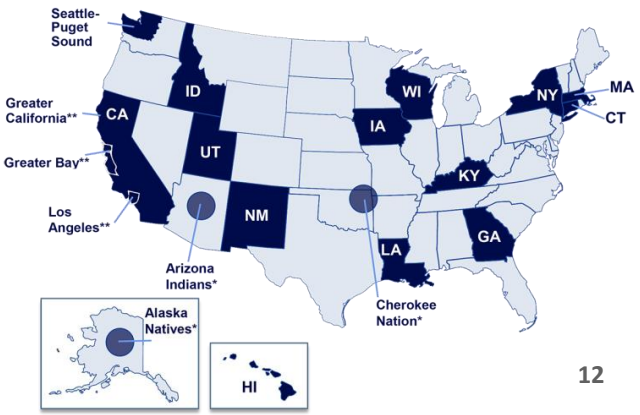


- Expanded patient population at risk
- Balance treatment risks/benefits

Morton et al. *JAMA Oncol* 2019

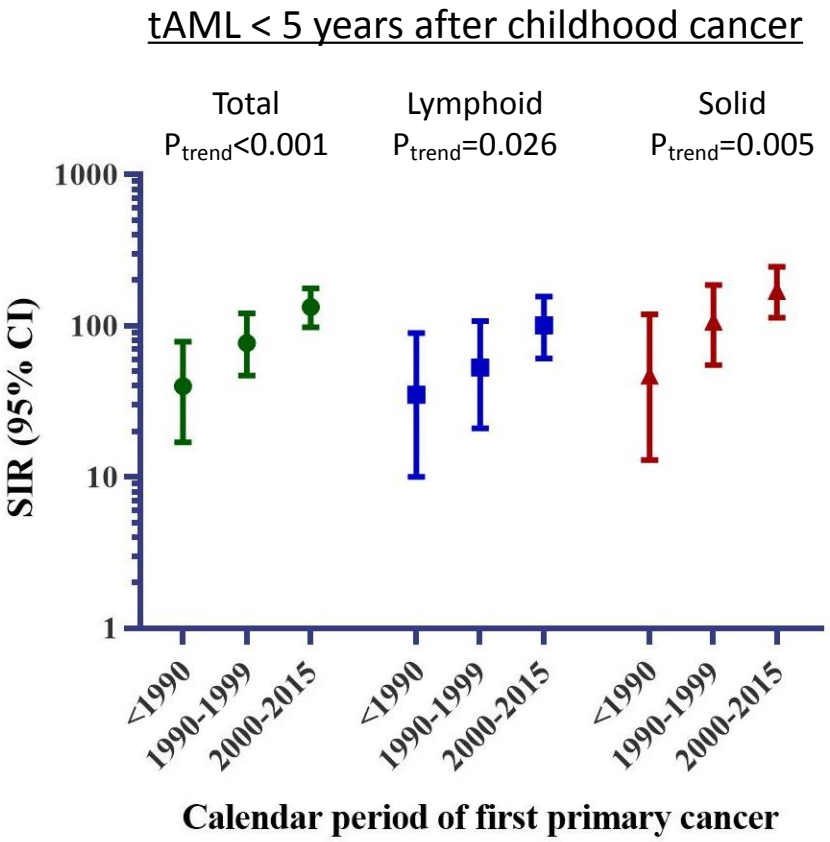
Role of chemotherapy for childhood cancer in tMDS/AML

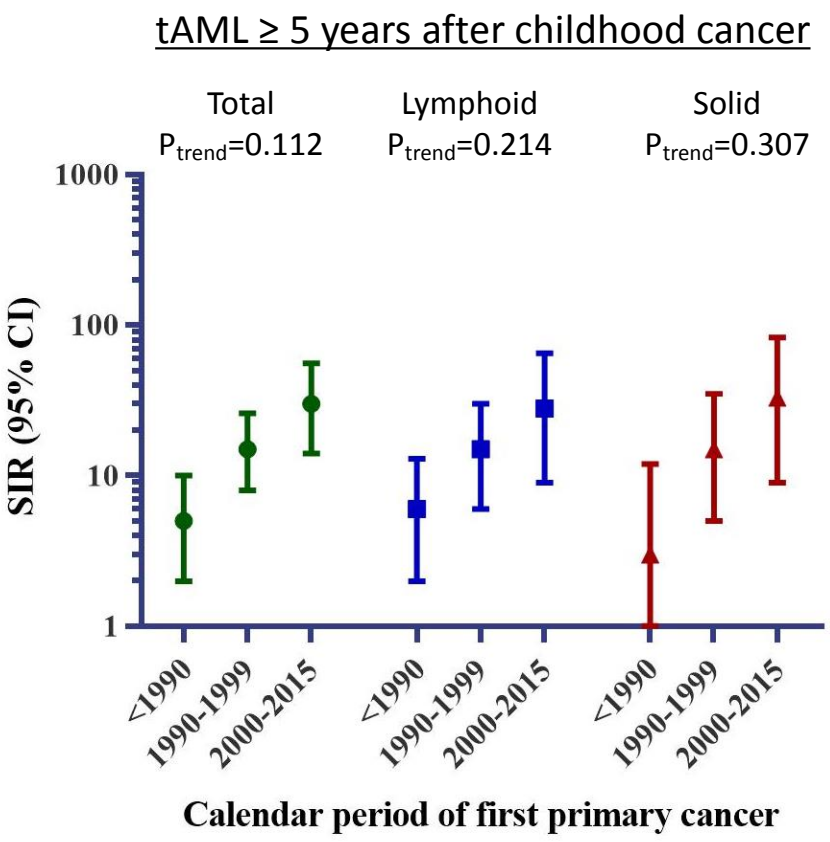
- Established risk for tMDS/AML after childhood cancer based on small case-control studies
- Advances in childhood cancer treatment, risks for current patients?
- Initial chemotherapy for childhood cancer
- 9 SEER registries, 1975-2015 (N=25,933)
- 17 SEER registries, 2000-2015 (N=36,975)



Advani et al. *Leukemia* (In press)

tAML after childhood cancer, 1975-2015





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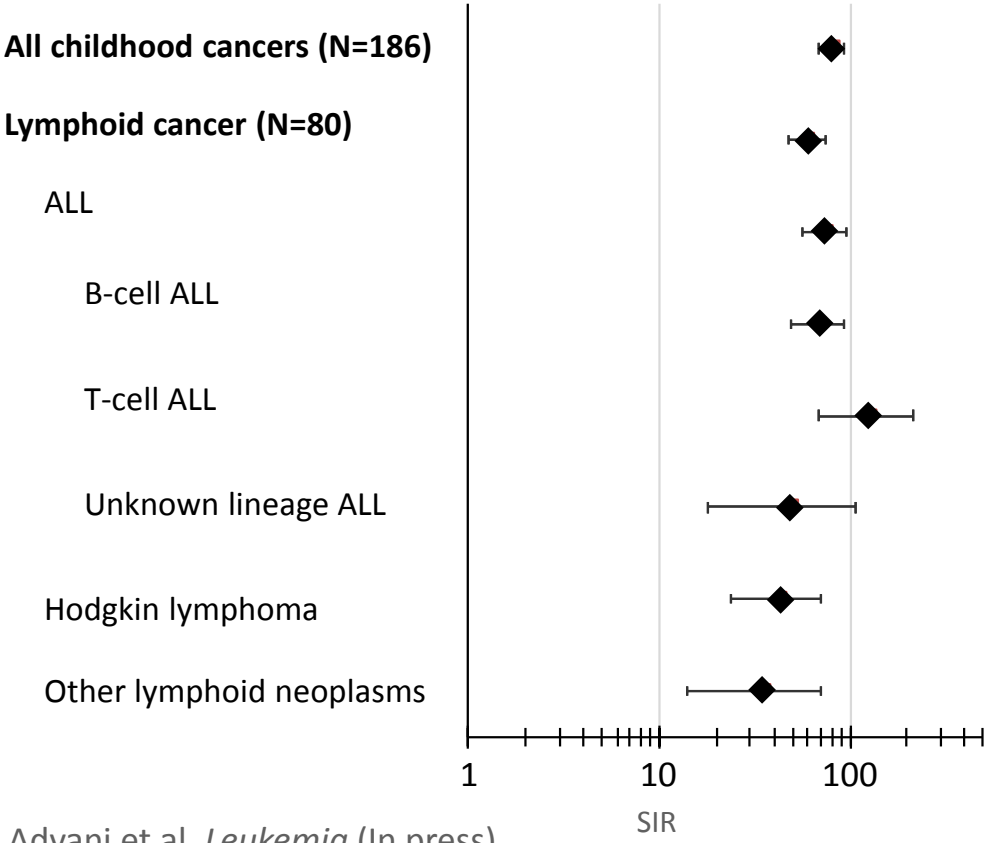
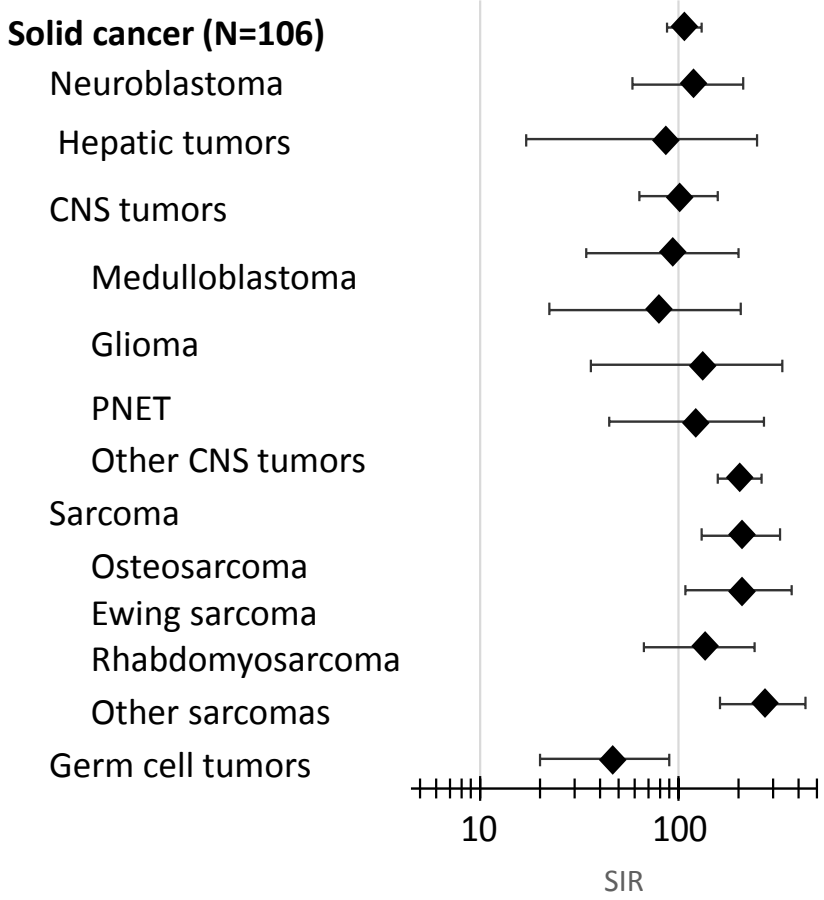
tMDS/AML after childhood cancer, 2000-2015





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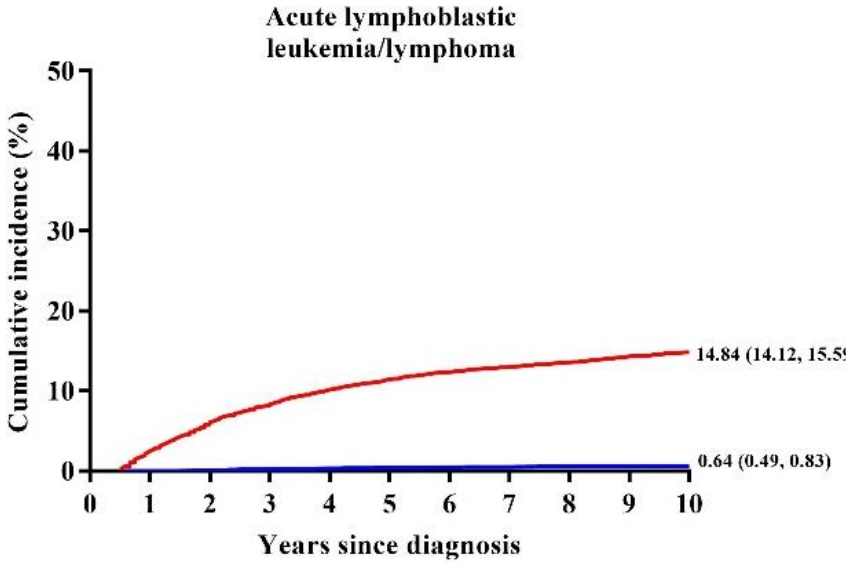

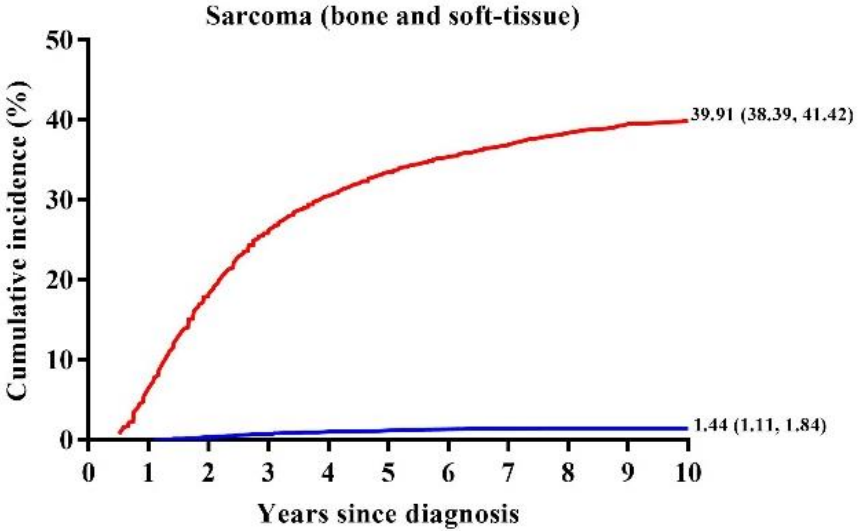

tMDS/AMLrisk

Competing risk

Advani et al. *Leukemia* (In press)

Conclusions

- Increased risk of tMDS/AML after radiotherapy and chemotherapy in the modern treatment era
- tMDS/AML is rare
- Consider gains in survival vs. adverse effects
  - Particularly for survivors of first primary cancers with a favorable prognosis
- Continued efforts to develop effective agents and cancer treatment approaches with fewer late sequelae are critical
- Need to better understand mechanisms of leukemogenesis

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