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Increased Cardiac Risk After a Second Malignant Neoplasm Among Childhood Cancer Survivors, a FCCSS Study

Thibaud Charrier, Rodrigue S. Allodji, Aurélien Latouche, Florent de Vathaire, et al.



BACKGROUND

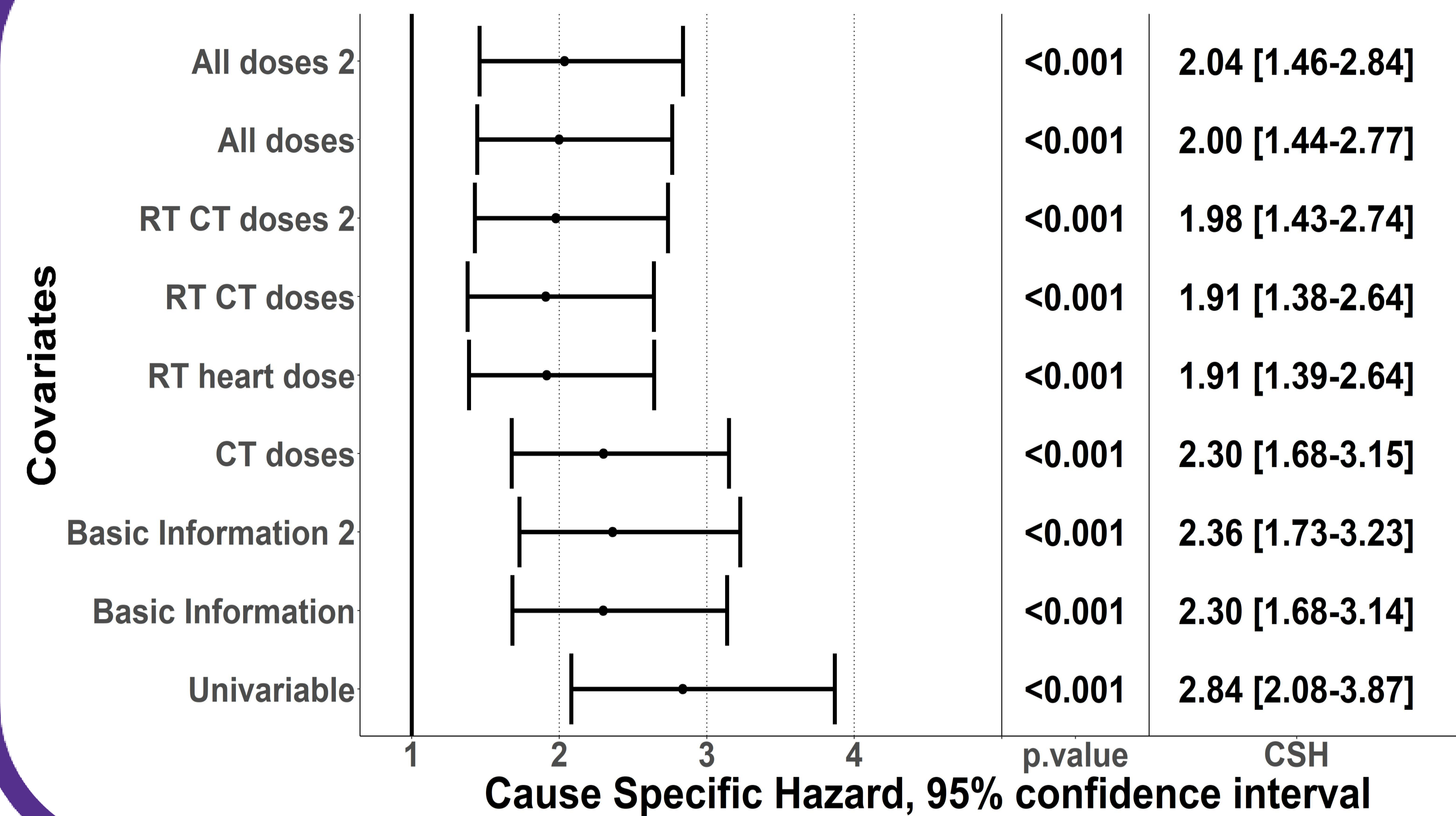
Advances in cancer treatment have significantly improved childhood cancer survival, with five-year survival exceeding 80% in most European and North American countries today. The adult population of childhood cancer survivors (CCS) exceeds 300,000 people in the USA alone, and is growing. Many late-effects have been observed at a higher rate than the general population.

Cardiac disease (CD) and second malignant neoplasms (SMN) are among the most serious and life-threatening late adverse effects experienced by CCS.

Previous work has identified important risk factors of CD, but the impact of other late-effects as SMN have been ignored.

We have studied the effect of a SMN on both the cumulative incidence and the instantaneous risk of CD accounting for the competing risk of death.

EFFECT OF SMN ON CAUSE SPECIFIC HAZARD OF CD



METHODS

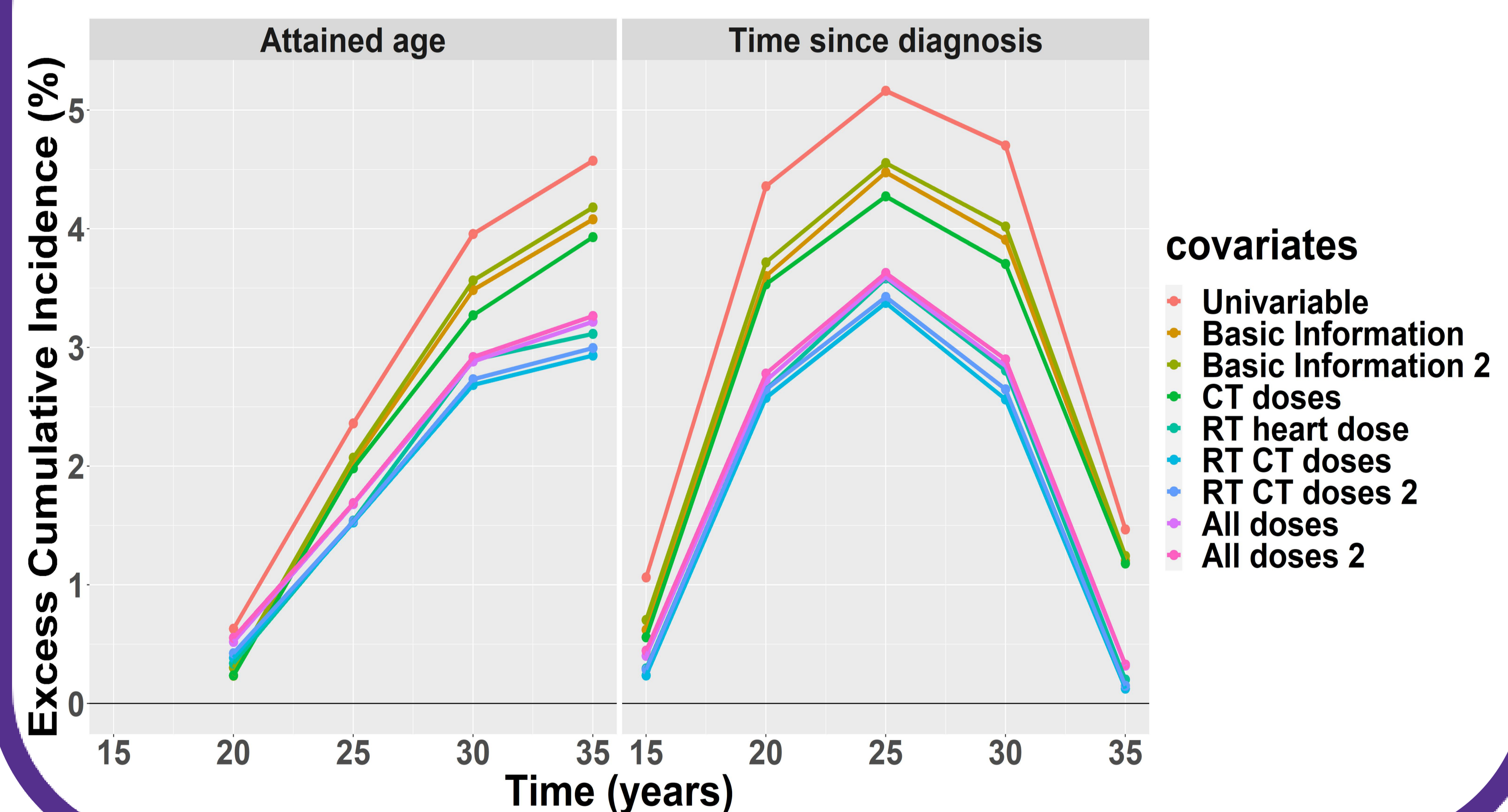
Population: Analysis included 7670 CCS diagnosed between 1945 and 2000, treated with combinations of surgery, radiotherapy (RT) and chemotherapy (CT).

Cumulative Incidence: To account for the time dependance of the occurrence of SMN, we employed the landmark approach considering an additive regression model for the cumulative incidence of CVD.

Instantaneous Risk: Next, the effect of SMN on the instantaneous risk of CVD was estimated using a proportional cause specific hazard model considering SMN as a time-dependent exposure.

Shared technique: In both models, we included death as a competing event, and adjusted for childhood cancer treatment information (age at diagnosis, radiotherapy doses, anthracyclines, ...).

ADDITIVE EFFECT OF SMN ON CUMULATIVE INCIDENCE OF CD



RESULTS

- ◆ Overall, after a median follow-up of 29 years, 470 CVDs including 63 experimenting a SMN were identified.
- ◆ An increased cumulative incidence of CVD was estimated for patients experimenting a SMN before they reached 35 years old.
- ◆ This increase was of 4.8% [95%CI: 1.0-8.6%] at 30 years old, with a cumulative incidence of 6%.
- ◆ No increase in the cumulative incidence of CVD was observed for later landmark times.
- ◆ SMN has been estimated to multiply the cause-specific-hazard by a 2.2 fold [95% CI: 1.6-3.0].

CONCLUSION

- × SMN occurrence does increase instantaneous risk of CD at all age.
- × SMN occurrence before 35 years old does increase the cumulative incidence of CD.
- × Our results provide new insight into the CVD risk after a SMN that may impact long-term follow-up of CCS.