**Supplemental Digital Content 2.** Risk of bias assessment criteria for observational studies

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| **Study group** | **Selection bias** | | | |
|  | Is the study group representative? | | | |
|  | yes/no/unclear | | | |
|  | Yes if:  •the study group consists of more than 75% of the original cohort of patients curative treated for childhood cancer with external beam three dimensional planned radiotherapy and survived at least 90 days after radiotherapy  or  •it was a random sample with respect to the cancer treatment | No if:  •the study group consists of less than 75% of the original cohort of patients curative treated for childhood cancer with external beam three dimensional planned radiotherapy and survived at least 90 days after radiotherapy  or  •if it was not a random sample with respect to cancer treatment | Unclear if:  no or incomplete numbers are mentioned about the study group to enable full assessment according to these criteria | |
|  |  |  |  | |
| **Follow-up** | **Attrition bias** | | | |
|  | Is the follow-up adequate? | | | |
|  | yes/no/unclear | | | |
|  | Yes if:  the outcome was assessed for more than 75% of the study group | No if:  the outcome was assessed for less than 75% of the study group (irrespective of reason for missing outcome assessment; can include death) | Unclear if:  no numbers are mentioned | |
|  |  |  |  | |
| **Outcome** | **Detection bias** | | | |
|  | Are the outcome assessors blinded for important determinants related to the outcome? | | | |
|  | yes/no/unclear | | | |
|  | Yes if:  the outcome assessors were blinded for important determinantsa related to the outcome | No if:  it is mentioned that the outcome assessors were not-blinded for important determinantsa related to the outcome | Unclear if:  it is not mentioned of the assessors are blinded for the important determinantsa | |
|  | a: Determinants are defined as: type of radiotherapy, radiotherapy field and radiotherapy dose | | | |
|  |  |  |  | |
| **Risk estimation** | **Confounding** | | | |
|  | Are the analyses adjusted for important confounding factors? | | | |
|  | yes/no/unclear/not applicable | | | |
|  | Yes if:  important prognostic factors (i.e. age, gender, co-treatment, follow-up) were taken adequately into account | No if:  important prognostic factors (i.e. age, gender, co-treatment, follow-up) were not taken adequately into account | Unclear if:  it is not mentioned if the analyses are adjusted for important confounding factors. | Not applicable (NA) if:  no risk estimation has been performed on the adverse outcomes |