

## Peer Review File

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Review comments:

1) Why are childhood cancer survivors at risk of later effects? What changes have been made in childhood cancer treatment strategies in the past few decades to reduce the later impact?

-> We added in the in the manuscript (introduction)

Though survival rate is increasing, childhood cancer survivors (CCS) can develop many late complications due to delayed effects of treatment for childhood cancer.

Both physiologic and psychological consequences contribute to long-term mortality and morbidity. There have been efforts to reduce late complications such as development of proton therapy to reduce radiation hazard

2) How can cancer survivors conduct individually structured follow-up care to improve care for this rapidly growing patient population? 3) How to provide continuous care for childhood cancer survivors?

-> We added in the in the manuscript (introduction)

Well-established guidelines will be also helpful to survivors to conduct structured follow-up, which will provide continuous care and improve care for this rapidly growing patient population

3) What is the health-related quality of life?

-> We added in the in the manuscript (introduction)

Late complications can also impair health-related quality of life (HRQOL) which is defined by individual's or a group's perceived physical and mental health over time.

4) Does genetics play a role in the later impact risk? What strategies should be used to intervene and prevent later effects?

-> We added in the in the manuscript (introduction)

Genetic susceptibility are also thought to be related with late-complications But there are no definite model to predict occurrence of late complications, so early screening and timely intervention is essential to reduce adverse outcomes

5)What is the incidence of congenital malformations in the offspring of childhood cancer survivors?

->We added in the manuscript (page10)

As for effects on offsprings, children of cancer survivors do not have significantly increased risk for congenital anomalies due to their parent's exposure to mutagenic cancer treatments

6)Immune checkpoint inhibitors are novel anticancer agents, some of which are uniquely associated with hypophysitis. Can it improve the endocrine and metabolic consequences of childhood cancer survivors?

-> We added in the manuscript (page 5)

Despite the general consensus that checkpoint inhibitors are more easily tolerated than chemotherapy, their unique side effect profile is important to recognize given the possibility of life threatening adverse events.( Thorac Dis. 2018 Feb; 10(Suppl 3): S480–S489.)

7)How effective is growth hormone therapy for childhood cancer survivors? What kind of impact will it have?

->We added in the manuscript (page 10)

Growth hormone can increase final height of childhood cancer survivors. So it can be used in childhood cancer survivors who have GHD.

8)What are the chronic diseases of childhood cancer survivors as adults? What is the status of research?

survivors of all primary cancer diagnoses had an increased relative risk of development of chronic conditions when compared with siblings. There have been studies about chronic diseases, one of which is study from Childhood Cancer Survivor Cohort(J Clin Oncol. 2009 May 10; 27(14): 2339–2355)