Response to reviews No 05199120 and 05123031:

Considering the suggestions from the reviewers, we have edited the manuscript in order to address the required changes. We have rephrased the title in order to better reflect the content and offer an insight on the current status.

Furthermore, we have rephrased the aspects related to the rare occurrence of pancreatic cancer, in order not to be misleading and to clearly mention that pancreatic cancer is a rare entity in pediatric population, not among adults. We have also added data regarding the suggestion of concluding whether the multiple pancreatic associated tumors mentioned above in childhood are associated with pancreatic cancer in adulthood. For this purpose, we have added data available from the National Cancer Database and also from other recently published studies with information about the evolution and survival among these patients.

Moreover, as suggested by the reviewer, we have also summarized current evidence on how several factors (such as BMI)-page 16 of the manuscript- and conditions existing from childhood, such as diabetes, chronic pancreatitis or McCune-Albright syndrome diagnosed at pediatric age – on pages 17,19 and 21 of the manuscript- may be associated with the development of pancreatic cancer in adulthood. This information has been added in the sections dedicated for each pathology and we also outlined the findings in the conclusion sections.

Review No 05123031

Pancreatic cancer is not a rare disease worldwide, in China or in the United States. Pancreatic cancer is about the sixth or seventh most common cancer among all cancers. Of course, the incidence of pancreatic cancer in children is very low and its occurrence is very rare. Therefore, whether the risk factors of pancreatic cancer have been hidden in childhood is indeed worth further study to reduce the mortality rate of pancreatic cancer in adulthood. The authors analyzed the incidence of pancreatic cancer in childhood, which has important implications for the identification of pancreatic cancer risk groups and the early screening of pancreatic cancer. However, it is well known that cases of pancreatic cancer in childhood are rare and the incidence is low. Therefore, how to predict the development of pancreatic cancer in adulthood through childhood is very critical. Pancreatic malignant tumors in children include pancreatoblastoma, solid pseudo-papillary tumors, insulinoma, gastrinoma, vasoactive intestinal peptide secreting tumors (vipoma), acinar cell carcinoma, ductal adenocarcinoma, mucinous cystic neoplasms, lymphoma, germ cell tumors, primitive neuroectodermal tumors, and mesenchymal tumors. The authors should conclude whether the multiple pancreatic associated tumors mentioned above in childhood are associated with pancreatic cancer in adulthood. Risk factors for pancreatic cancer include Obesity, Diabetes mellitus, glucose metabolism and insulin resistance, Chronic pancreatitis, Cystic fibrosis, McCune-Albright syndrome, Multiple endocrine neoplasia type 1 (MEN 1), von Hippel Lindau disease (vHL), and Li Fraumeni Syndrome (LFS). The analysis of these factors does provide better prevention strategies for the development of pancreatic cancer in adulthood. To provide better guidance to people at risk for pancreatic cancer. However, the authors do not address in depth in this manuscript how childhood risk factors influence the development of pancreatic cancer in adulthood. If the authors can correlate the incidence of adult pancreatic cancer with the risk factors in childhood, it will provide

good guidance for the prevention of adult pancreatic cancer. Overall, this paper provides a relatively new perspective on the link between pancreatic cancer from childhood to adulthood. The author should give careful consideration to the issues mentioned above before publishing this article.

Response to Review No 05199120

This review reports the main pancreatic cancers diagnosed during childhood, the most important childhood diseases predisposing to the development of pancreatic malignancies and the gene mutations associates with pancreatic malignant tumors. Generally speaking, it is good. However, I do not think that the title reflects the main subject.