What are the psychosocial consequences of surviving childhood cancer?

Abstract: Each year 200 children and adolescents are diagnosed with cancer in Denmark. As a consequence of better treatment more than 75 per cent survive the first five years. It is a well-known fact, that cancer and even more so the active treatment will lead to late effects which may influence the survivors’ lives as far as somatic, psychological and social parameters (1-5) are concerned. However, the cancer does not just affect the child. The parents’ and siblings’ are also affected in their family situation, job wise and financially just as their health and use of medicine are affected on the long as well as on the short term.

There are now approximately 12,000 people who have suffered from childhood cancer. Therefore 24,000 parents and 15,000 – 20,000 siblings are directly affected by this type of cancer. We have already analysed part of the psychosocial late effects on childhood cancer survivors (6-8). However, we have hardly any knowledge about the significance of cancer on parents and siblings. We want to follow up on our previous survey, because the data are now 10 years old. The survivor group is larger and different now, because of changes in the active treatment, ensuring better survival and, hopefully, fewer late effects. We want to investigate the psychosocial late effects of survivors by matching them against a control group and matching the parents and siblings against the parents and siblings of the control group. Based on data from the Danish population based registries we want to map the socioeconomic, psychosocial and somatic late effects for childhood cancer survivors, their parents and siblings.

Children with cancer and their families are at present not followed up in a structured and systematic way for their health problems and psychosocial needs. Through this survey we are to contribute pointing out special groups at risk, to whom we should intensify the follow up and support. The knowledge we obtain is going to benefit other families, where children and adolescents are affected by serious chronic and potentially life-threatening disease.

Background: Studies of psychosocial consequences for childhood cancer survivors have indicated, that having cancer sets back the children’s educational achievements and affects their employment negatively (9;10). For some cancer and treatment types there is a documented decline in IQ and an increased prevalence of specific learning difficulties (9;11-13) leading to lower levels of education. Cancer survivors also have a higher rate of unemployment and low income (9;14;15). Some studies indicate, that cancer survivors stay unmarried, are divorced more frequently and have fewer children (9;14). Survivors with physical disability do not do well in some studies (16). Most of the studies are small and use siblings as controls.

Studies related to the parents are mostly conducted in the USA. Studies focusing on the economic situation of the families have examined the immediate effects and found that the families are affected (17-19). Most of the studies are old and obsolete, because treatment then was shorter and less intensive. They include few parents and have problems with selection
bias because of lack of follow up. We have conducted surveys on adult cancer survivors showing that they retire earlier (20), have a minor increased risk of unemployment (21), but their divorce frequency or frequency in change of cohabitation status (22).

siblings’ reaction to cancer is not well documented. So far the results from previous studies indicate that they react both emotionally and behaviourally at the time of diagnosis. They feel lonely and react with anxiety and adaptation. The results are of limited reliability, because the studies are limited and only have short follow-up (23-25). The fact that they are affected by this major life-event early in life, have increased the level of anxiety, awareness of disease and the feeling of guilt, and may lead to having fewer children, having children later in life, having more abortions and having an increased use of the health system.

Many of the studies mentioned carry with them methodological problems. Some have a large proportion of drop-out of both the cancer group and the control group. Most use hospital based control groups, not corresponding to the background population. The majority of the studies is small including less than 300 people examining only subgroups. Most of the studies are carried out in the USA, where the families and maybe insurance companies pay for a majority of the treatment. Thus the psychosocial lives of the families besides the cancer are also affected otherwise, and their results cannot be transferred to the Danish society without considering these conditions. We therefore only have insufficient data that cannot guide the planning of clinical praxis.

We already have carried through a registry survey of 5,396 childhood cancer survivors in Denmark. We examined how the survivors did psychosocially and found that survivors have a normal pattern in the following fields: Leaving home, education and establishing a family (6-8). Only children with a tumour in the CNS and especially children having cranial irradiation therapy did worse than standardized norms Having conducted these surveys we have a thorough experience with the sources of data, we want to use in this survey, and we have already defined the parameters, we want to measure.

**Strengths and limitations in the proposed survey:** Our survey uses administrative sources of data established independent of the hypothesis and without selection in reporting. In this way we steer clear of recall bias and selection bias. We also gather detailed clinical information from a national database including all children with cancer from 1985 up till now. Thus we take into account the clinical confounders, we *a priori* assume having an influence on both the determinant and the outcome.

Since the middle of the 1980’ies the surviving rate of children with cancer has increased due to more intense treatment and new chemotherapeuticals. The members of this group of survivors have now reached an age where we can measure the level of their psychosocial problems. It is possible, that we do not have enough power to show some of the outcomes. The survey should probably be repeated in 10 – 15 years, when the group of survivors is even larger and the members of the group older.

**We have the following hypothesis:**
- Childhood cancer survivors and their relatives as a group do well. They have normal patterns related to employment, establishing a family, leaving home and use of health services and medicine.
• A special group of children consisting of patients with CNS tumours, who had cranial irradiations therapy, were amputated or who received very intense or lengthy treatment is psychosocially not doing so well.
• This special group uses more antidepressants, anxiolytics, sedatives and antipsychotics compared to the background population.
• This special group have a higher degree of people living alone, have fewer children, have children later in life, and have more abortions.
• This special group is not so well educated is more often in part-time jobs, and live in poorer housing.
• The parents of this special group do socioeconomically worse than the background population with regard to income, affiliation to the labour market, housing and divorce and cohabitation status.
• The parents and siblings of this special group use more antidepressants, anxiolytics, sedatives and antipsychotics and are more frequently admitted to psychiatric wards than the background population.
• The siblings of this special group leave home later in life, have fewer children, have their children later in life and have more abortions.

**Material and methods:** We compare a series of parameters (outcomes) for childhood cancer survivors, parents and siblings with the parameters for a matched control group and the parents and siblings of the control group. The control group is matched on sex and date of birth. The group is identified in the Danish population.

For this register based survey we use the Danish Cancer Register which covers virtually all incident cases of cancer that have occurred in Denmark since 1943. The disease must be diagnosed before the cases reach the age of 20 years. From the Danish Cancer Register we collected the following information: Diagnosis (IARC-classification), date of diagnosis, tumour histology according to ICD-O, tumour location and vital status.

The Central Population Register (CPR): Since 1968, all residents of Denmark have been registered in the Central Population Register and assigned a unique personal identification number. Individual information is kept under this identification number in all Danish national registers, ensuring accurate linkage of information between registers. We obtain the control group as a random sample of the population who was alive in 1980 or born later. We then frequency match the control group on sex and date of birth with the case group reaching a total of 100,000 persons in the control group. For both childhood cancer survivors (cases) and controls we identify all parents and siblings through the CPR.
The Integrated Database for Labour Market Research: Since 1980 Statistics Denmark has administered this register. Information on education, labour market and family structures for both cases and controls and their parents and siblings is obtained by data linkage to the CPR. The core variables in the database are derived once a year by linkage with the Danish administrative registries.

Hospital-Discharge Register and Danish Psychiatric Central Register: We gather information on dates of admittance and discharge on both somatic and psychiatric departments from these registers.

Register of Medicinal Product Statistics: This register contains information on all prescription medicine coupled to the CPR. We can identify all medicine prescribed to cases, controls, their parents and siblings. We are to focus on antidepressants, anxiolytics, sedatives and antipsychotics.

Analyses and statistics: The linking of registers will be made at Statistics Denmark and will be delivered as a set of data from which it is impossible to link to individuals. The analyses are to be conducted using the statistical programme SAS on the research computer at Statistics Denmark. The analyses consist of comparisons of cases and controls and the parents and siblings of both groups.

1. For cases, controls, their parents and siblings: The frequencies of admittance to somatic and psychiatric departments and their use of antidepressants, anxiolytics, sedatives and antipsychotics.
2. For parents of both cases and controls: Their income, sick-leave, absence from work, affiliation to labour market, education, housing and private means.
3. For parents of both cases and controls: Their divorce and change in cohabitation status and number of children after the date of cancer diagnosis.
4. For cases, controls and their siblings: Date of first child and consecutive children, the number of children and abortions.
5. For siblings of cases and controls: Family structure, divorce, change in cohabitation status and education.

These variables are to be analysed considering type of cancer, education, type of job, age, sex, number of siblings, vital status for the childhood cancer patients and level of historical rate of employment as independent variables. We are also going to make an analysis for interaction by comparing a model of analysis which allows for interaction with another model without interaction.

Calculation of power: As for divorces we know, that 33 per cent of marriages of the background population from 1950 to 2006 have been dissolved (26). For the difference to be clinically significant we demand the difference between parents of cases and controls to be 7 per cent point. With a level of significance of 5 per cent and a number of controls 5 times that of cases and a power of 80 per cent it means, that we need 2,241 couples of the parents of the control group and 449 couples of the parents of the cases. This is substantially less than is represented in the two groups.

Regarding use of antidepressants we know that 16 per cent of women and 9 per cent of men have had \( \geq 2 \) prescriptions (27). In order for the difference to be clinically significant we demand that the difference between the controls and their parents and siblings and the cases
and their parents and siblings be 5 per cent point. With a level of significance of 5 per cent and a number of controls 5 times that of cases and a power of 80 per cent it means, that we need 2,447 women from the control group and 490 women of the case group and 1459 men from the control group and 292 men from the case group.

We are going to compare data regarding personal means, income and housing from before the diagnosis with after diagnosis. Thus a power calculation is not relevant. With regard to the number of children of cases and siblings, the event is so frequent, that we need no power calculation.

**Time frame:**
The survey is to begin June 1, 2009.

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**Analyses**

- Use of medicine and number of admittances for cases, controls and their relatives
- Composition of publications number 1 and 2.
- Psychosocial and socioeconomic consequences for parents and siblings
- Composition of publication number 3 and writing the PhD. thesis

1st publication: Admittance and use of medicine among childhood cancer survivors and their relatives. A population based study in Denmark
2nd publication: Psychiatric disease and suicide among people who have had childhood cancer and their relatives. A population based study in Denmark
3rd publication: Psychosocial and socioeconomic consequences for parents and siblings to childhood cancer survivors. A population based study in Denmark

**Perspectives:** Children with cancer and their families today do not receive systematic and structured psychological and social support. Despite major knowledge about physical problems, only a few studies on psychosocial consequences for survivors and their relatives are methodologically strong. This means that we have only limited knowledge on this important field. Through this survey we want to be able to find patients and families at risk of psychosocial comedown at an early stage. By the aid of our survey the clinicians are going to be able to target the intervention to those most in need.

Because of a comprehensive welfare system in Denmark our survey is going to isolate the psychosocial consequences derived from the cancer from those stemming from the society’s way of handling the families. It is our aim that it will to be possible to use the results internationally to optimize the follow-up of children with cancer and their families.
The data we generate from this project is going to have impact both on intervention and support to the families most in need. But it is also going to help families with children suffering from other serious and potentially life threatening diseases.

**Ethics:** The survey has been approved by the Danish Data Protection Agency and is going to be carried through according to Danish legislation. No information about individuals in the dataset used in the final report can be used to identify individuals. The results are exclusively to be processed as statistical analyses and as such it is impossible to identify individuals.

Reference List


