

## **Socio-demographic impact of platinum-induced ototoxicity in long-term survivors of childhood cancer.**

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### **Abstract**

**Objective:** Childhood cancer survivors (CCS) treated with platinum-based chemotherapy are at risk of treatment-induced ototoxicity. To date, there is limited knowledge on the effect of ototoxicity on socio-demographic factors, the burden to obtain insurances and psychological distress in CCS.

**Design:** Of the 653 CCS with completed questionnaires, 54 survivors had been treated with platinum. Ototoxicity (Münster score  $\geq 2b$ ) data were retrieved from pure-tone audiometry. All survivors completed a questionnaire consisting of the Distress Thermometer (DT), measuring the severity of distress and was recoded to a 0 (no distress)-10 (extreme distress) scale. The Hospital Anxiety and Depression Scale (HADS) was used to study the psychological distress (a score  $\geq 15$  is indicative for clinically significant distress).

**Results:** Median age at diagnosis was 6.2 years (range: 0.01-17.8) and median follow-up time from end of treatment to questionnaire was 15.6 years (range: 3.2-43.7). There were no differences in attempts to obtain insurances, highest education achievement and (un) employment between platinum-treated survivors and non-platinum treated survivors. Among the 54 platinum-treated CCS, median HADS score of hearing impaired survivors (n=22 (median score: 4.5, range: 0.0-29)) was not significantly different from survivors without ototoxicity (n=32 (median score 5.5, range: 0.0-11,  $p=0.337$ )). Similarly, DT scores were not significantly different between survivors with or without ototoxicity ( $p=0.441$ ). Compared to the 599 non-platinum treated survivors, median HADS and DT scores of platinum-treated survivors were not significantly different.

**Conclusion:** Based on this first, small study, we didn't find differences between CCS who suffer from platinum-related ototoxicity and survivors without hearing impairment, suggesting that CCS with ototoxicity do not necessarily encounter more socio-demographic challenges and psychological distress than CCS without ototoxicity.

**Keywords:** Childhood cancer, Survivor, Insurance, Hospital Anxiety and Depression Scale, Cisplatin, Ototoxicity.

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### **Introduction**

Over the past decades, survival rates for many pediatric tumors have increased substantially as a result of more effective treatment. This treatment has enabled long-term survival but also induced serious late side-effects in approximately 60% of all childhood cancer survivors (CCS) [1,2]. To date, numerous long-term physical effects of childhood cancer have been documented, of which one is ototoxicity, following platinum-based chemotherapy. Cisplatin and carboplatin are routinely used for the treatment of pediatric solid tumors.

As childhood cancer survivors are at risk of long-term complications of treatment, close medical surveillance which requires being accepted for health insurance, is an important issue. American studies have shown that CCS have significantly low rates of health insurance coverage and experience more difficulties to be accepted for in insurance than their siblings (Table 1) [3-8]. In the US, health insurance can be obtained individually, through employers, or through government programs such as Medicare or Medicaid. This system is different from the health care system in the Netherlands where it is mandatory to take on a basic level of health insurance.

**Table 1.** Overview of literature on insurances in childhood cancer survivors (CCS)

Study	N Country	Cancer diagnosis	Having insurance (%)	Insurance type	Percentage of CCS reporting problems obtaining insurances	Costs of insurances	Control group	Compared to control group
Holmes et al. (1986) [29]	100 USA	Not specified	Life insurance (75%)/Health insurance (85%)	Life and health	Life insurance: 44% Health insurance: 24%	-	Siblings (n=100)	Life insurance (100%)/Health insurance (7%)
Vann et al. (1995) [7]	187 USA	Not specified	-	-	CCS: 24% Siblings: 2%	Health insurance excluding coverage for pre-existing health problems (OR: 5.5; 95% CI: 2.0-15.5)	Siblings (n=108)	-
Nagarajan et al. (2003) [4]	694 USA	Bone tumor	Any insurance (87%)	Health	30%	-	-	-
Pui et al. (2003) [8]	584 USA	ALL	Any insurance (80%)	Health	Not studied	Denial health insurance: 28%; prohibitive premiums: 19%; restrictions on health care: 7%	-	-
Oeffinger et al. (2004) [52]	9274 USA	Leukemia, solid tumor, CNS	Any insurance (84%)	Health	Not studied	-	-	-
Park et al. (2005) [3]	10671 USA	Leukemia, CNS, solid tumor	Private (83%)/Public (17%)	Health	CCS: 29% Siblings: 3%	Extra premium CCS: 2%; Extra premium siblings: 0.2%	Siblings (n=3553)	Private (91%, P<0.001)/Public (9%, P<0.001)
Castellino et al. (2005) [35]	8767 USA	Leukemia, solid tumor, CNS	Any insurance (83%)	Health	Not studied	-	-	-
Crom et al. (2007) [6]	1408 USA	Leukemia, solid tumor, CNS	Any insurance (88%)	Health	27%	65% is unable to afford higher premiums	General population	Private in CNS CCS (30%) vs. private in control (65%)
Mody et al. (2007) [36]	1136 USA	All	Private (78%)/Public (6%)	Health	Not studied	-	Siblings (n=1201)	Private (83%)/Public (3%) P=0.02
Klosky et al. (2008) [37]	801 USA	Leukemia, solid tumor, CNS	Private (90%)/Public (79%)	Health	Not studied	-	Non-attenders CCS (n=140)	Private (10%)/Public (21%) p<0.001
Mulrooney et al. (2008) [38]	272 USA	AML	Any insurance (85%)	Health	Not studied	-	Siblings (n=3899)	Any insurance (81%, P<0.001)
Zebrack et al. (2008) [34]	7147 USA	Leukemia, solid tumor, CNS	Any insurance (89%)	Health	Not studied	-	Siblings (n=388)	Any insurance (9%, p<0.02)
Boman et al. (2009) [39]	603 Sweden	CNS	Any insurance (33%)	Social**	Not studied	-	Randomly selected general population (n=996)	Any insurance (20%, p<0.0001)
Cassilas et al. (2010) [40]	8425 USA	Leukemia, solid tumor, CNS	Private (76%)/Public (7.6%)	Health	Not studied	-	-	-
Park et al. (2012) [5]	39 USA	Leukemia, solid tumor, CNS	Private (54%)/Public (10%)	Health	33%	Higher costs (50%)	-	-
Barakat et al. (2012) [42]	173 USA	Leukemia, solid tumor, CNS	Private (76%)/Public (24%)	Health	Not studied	-	-	-
Ottaviani et al. (2013) [42]	38 USA	Osteosarcoma	Any insurance (84%)	Health	Not studied	-	Osteosarcoma CCS: amputation (n=19) vs. limb salvage (n=19)	Not significant

Yagci-Küpel et al. (2013) [43]	201 Turkey	Solid tumor, CNS	Any insurance (91%)	Social*	Not studied	-	Normal population	Any insurance (87%, p<0.001)
Kirchhoff et al. (2013) [44]	32 USA	Leukemia, solid tumor, CNS	Employer-sponsored insurance (56%)	Health	Unable to afford insurance without an employer contribution	-	-	-
Park et al. (2015) [45]	698 USA	Leukemia, solid tumor, CNS	Employer-sponsored (79%)/ Public (12%)	Health	23%	-	Siblings (n=210)	Employer-sponsored (86%, p=0.04)/State (4.4%p=0.002)
Milam et al. (2015) [46]	193 USA	Leukemia, solid tumor, CNS	Private (36%)/ Public (32%)	Health	Not studied	-	-	-
Miller et al. (2016) [47]	193 USA	Not specified	Any insurance (80%)	Health	Not studied	-	-	-
Kuhlthau et al. (2016) [48]	443 USA	Not specified	Private (45%)/ Public (30%)	Health	Not studied	-	Healthy adults (n=1329)	Private (67%, p<0.0001)/ Government-sponsored (15% <0.0001)
Zheng et al. (2016) [49]	489 USA	Leukemia, solid tumor, CNS	Private (49%)/ Public (22%)	Health	Not studied	-	-	-
Berg et al. (2016) [50]	106 USA	Solid tumor, leukemia	Private (93%)/ Public (12%)	Health	11%	-	-	-
Dumas et al. (2017) [51]	1920 France	Solid tumor, CNS	Loan	Personal and home	Personal loan: 10.4% Home loan: 30.1%	-	-	-
Current study	54 The Netherlands	Solid tumor	-	Health, life, funeral, mortgage, risk, disability	24.1%	High premium: 38.5% Temporary increased: 0% Normal premium: 23% Not indicated: 38.5%	Leukemia survivors (n=599)	Problems controls: 19% High premium: 37.7% Temporary increased: 5.3% Normal premium: 27.2% Not indicated: 29.8%
*Social insurance covers all health expenditures, but also provides salary after retirement								
**Social insurance provides financial security, but it does not cover health care or unemployment. Social insurance is financed through a combination of employer and employee contributions, and through taxes								
CNS: Central Nervous System; CCS: Childhood Cancer Survivor; OR: Odds Ratio								

In general, health care insurances in the Netherlands are much more expensive for childhood cancer survivors than the normal population for being accepted [9]. Health insurance access for CCS has mainly been studied in the American population.

The significant impact of hearing impairment on speech and language acquisition, educational performance, and psychosocial functioning in young children has previously been documented [10-12]. Previous studies in non-CCS showed that severe hearing impaired subjects experience greater levels of anxiety and depression than the general population [13,14]. The St Jude Lifetime Cohort study has recently revealed that hearing loss in childhood cancer survivors is associated with an increased risk of non-independent living and unemployment [15]. This has not been confirmed in Dutch CCS as yet. Information on socio-demographics and the psychological impact of hearing impairment in Dutch CCS is lacking.

The objectives of the current study were to analyze the effect of ototoxicity on socio-demographic factors and the burden of survivors to obtain insurances, and to analyze emotional and psychological distress in adolescent and adult long-term survivors of childhood cancer with ototoxicity.

**Materials and Methods**

*Participants*

We included all adolescent and adult childhood cancer survivors (CCS) who visited the Erasmus Medical Center-Sophia Children’s Hospital for the first time between February 2001 and August 2009.

Adolescent and adult childhood cancer survivors who visited the outpatient clinic for the first time were asked to fill in the Dutch validated version of the Hospital Anxiety and Depression Scale (HADS) and the Distress Thermometer (DT) or received the questionnaires by mail. In total, 658 CCS completed either one of the two questionnaires. Both

the HADS and DT were completed by 645 CCS. The HADS alone was filled in by 646 survivors and the DT alone was completed by 653 survivors. Fifty-nine of the 658 CCS had been previously treated with cisplatin and/or carboplatin of which 54 had pure tone audiograms available. At the time of the questionnaires, CCS were at least 15 years of age, at least 5 years after cessation of treatment and in continuous complete remission. Follow-up time was defined as the period between cessation of treatment and the time of assessment at the outpatient late-effects clinic.

### ***Audiological Evaluations***

In a previous study we observed that hearing impairment after cessation of platinum treatment seemed to be irreversible [16]. Therefore, we defined ototoxicity as hearing loss Münster  $\geq$  grade 2b from stop treatment onwards, as hearing function does not seem to recover back to normal. Hearing function was evaluated by pure-tone audiometry measuring air conduction at frequencies of 0.25, 0.5, 1, 2, 4 and 8 kHz in decibel hearing level as previously described [17,18]. The worst ear was taken into account and when a patient had more than one audiogram after treatment, the audiogram after end of treatment and before the questionnaires and the closest time point to the questionnaire was used.

### ***Socio-demographics***

Socio-demographic factors such as age at diagnosis, gender, educational achievement, living situation, marital status, and employment were collected. Educational level was scored as primary school, secondary/vocational school, tertiary school and university/college. Living situation was scored as living with parents, independent living or living with partner. Marital status was scored as married or living as married, not married or divorced. Employment was scored as not employed, part time, fulltime or not indicated.

### ***Insurances***

CCS were asked to answer questions regarding health insurance status and difficulties obtaining insurances (Supplementary Figure 1). Insurance types included health insurance, mortgage, funeral insurance, life insurance and risk insurance. Those who reported being insured were asked about type of coverage, exclusions and extra premium charges related to their health history. Insurance was scored as no (no problems obtaining insurances), yes (problems obtaining insurances) and not applicable.

### ***Distress, Anxiety and Depression***

The HADS is a widely used self-report psychological instrument to screen for anxiety and depression. This psychological instrument is validated for different groups of the Dutch subjects and is stable across medical settings [19-21]. This tool includes 14 items, seven related to anxiety and seven related to depression, each scored

between 0 and 3 (total 21 points) [22]. As previously described, the scores were combined into a single scale, the total HADS score [22]. A higher HADS score is linearly associated with a higher level of emotional distress and a HADS score  $\geq$  15 is indicative of clinically significant emotional distress [22].

The DT was developed by the National Comprehensive Cancer Network (NCCN) as a screening tool [23]. It consists of a visual analogue scale ranging from 0-10 points, indicating the range of distress from 0 (no distress) to 10 (extreme distress) over the preceding week. The Dutch version of the distress thermometer has been validated [23].

### ***Statistical Analysis***

Mann-Whitney *U* test and  $\chi^2$  tests were used to compare characteristics of CCS with and without ototoxicity. The associations between hearing loss and socio-demographic and between psychological factors and hearing loss were analyzed with logistic regression and are expressed as odds ratios (ORs) with 95% confidence intervals (95% CI). Analyses were not performed when the number of patients per subgroup was below  $n=5$ . SPSS Statistics Version 21.0.0.1 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. *p*-values of  $<0.05$  were considered to be significant.

## **Results**

### ***Characteristics***

Of 658 CCS who were eligible for inclusion, 59 subjects were identified as being treated with platinum-based chemotherapy and 599 as being non-platinum treated. Pure-tone audiometry was available for 54 of the 59 platinum-treated CCS. Clinical data are depicted in Table 2. Of the included subjects, median age at diagnosis was 6.2 years (range: 0.01–17.8). Twenty-two of the survivors that were treated with platinum had bilateral hearing impairment (Münster  $\geq$  2b) and 32 did not have hearing impairment. Among the survivors with hearing loss 3/22 (14%) presented with grade 2b, 11/22 (50%) with grade 2c, 2/22 (9%) with grade 3a and 6/22 (27%) with grade 3b hearing impairment. Median follow-up time of audiometric assessment was 8.4 years (range: 0–23 years) and median age at audiometric assessment was 18.5 years (range: 4–40 years).

### ***Socio-demographics***

Socio-demographic characteristics did not differ between survivors with hearing impairment and those with normal hearing (Table 2 and Supplementary Table 1a). The median follow-up time since diagnosis and the questionnaire was 15.6 years (range: 3.2–43.7 years, Supplementary Figure 1 Q1-4) and median age at questionnaire was 23.5 years (range: 14.6–52.3 years). Among the CCS with ototoxicity, 3/22 (14%) completed primary education only and 8/32 (25%) survivors without ototoxicity completed primary education only. Eight of the 22 hearing impaired survivors

(36%) completed tertiary education or graduated from university or college. Of those without ototoxicity, 8/31 (26%) completed tertiary education or university/college. Among the CCS that were not treated with platinum compounds, 46/581 (8%) completed primary education only and 218/581 (38%) graduated from tertiary education or university/college. There was no statistically significant difference between those groups.

Among the CCS with ototoxicity, 5/22 (24%) was currently married or living as married and 5/31 (16%) of the survivors without ototoxicity were married or living as married. Among the CCS that were not treated with platinum compounds, 178/599 (30%) were married or living as married. Eight of the 22 CCS with ototoxicity (36%) were not employed at time of questionnaire of which two CCS indicated that they were still studying. Nine platinum-treated survivors

without ototoxicity (29%) were not employed at time of questionnaire of which one CCS indicated that she was completely rejected and one survivor indicated that she was not aiming for a job at the moment. Of the CCS who were not treated with platinum agents, 17% was not employed. Fulltime or part time employment was indicated in 41% of the hearing impairment survivors, in 58% of the survivors without ototoxicity and in 58% of the non-platinum treated survivors.

### Insurances

At the time of completion of questionnaire, 129/653 CCS (19%) reported to ever have problems obtaining insurances due to childhood cancer history (Table 3, Supplementary Figure 1 Q5). Among the survivors with ototoxicity, 7/22 (32%) reported problems with obtaining insurances of which three survivors got accepted a higher premium and one got accepted

**Table 2.** Clinical characteristics of the childhood cancer survivors

	Platinum-Treated		Non-Platinum Treated
	Münster ≥ 2b N=22	Münster<2b N=32	N=599
<b>Gender, n (%)</b>			
Male	16 (72.7)	18 (56.3)	332 (55.4)
Female	6 (27.3)	14 (43.8)	267 (44.6)
<b>Age at diagnosis, years (range)</b>	6.8 (0.3-15.2)	10.6 (1.4-15.5)	6.0 (0.01-17.80)
Age at audiogram, years (range)	16 (4-40)	20 (5-32)	N/A
Age at socio-demographic QNR, years (range)	22 (18-33)	20 (18-30)	24 (15-52)
Age at DT and HADS, years (range)	21 (18-33)	20 (18-32)	24 (12-57)
<b>Childhood malignancy, n (%)</b>			
Sarcoma	5 (22.7)	13 (40.6)	60 (10)
Brain tumor	2 (9.1)	9 (28.1)	18 (3.0)
Hepatoblastoma	1 (4.5)	-	3 (0.5)
Neuroblastoma	5 (22.7)	2 (6.3)	40 (6.7)
Germ cell tumor	6 (27.3)	7 (21.9)	9 (1.5)
Other	3 (13.6)	1 (3.1)	35 (5.8)
Nephroma	-	-	81 (13.5)
Leukemia	-	-	219 (36.6)
Lymphoma	-	-	106 (17.7)
<b>Platinum, n (%)</b>			
Cisplatin alone	21 (95.5)	21 (65.6)	N/A
Carboplatin alone	-	11 (34.4)	N/A
Both	1 (4.5)	-	N/A
<b>Total cumulative dose, mg/m<sup>2</sup> (range)</b>			
Cisplatin alone	450 (300-800)	400 (100-720)	N/A
Carboplatin alone	N/A	2400 (1000-5850)	N/A
Cisplatin both	450	N/A	N/A
Carboplatin both	2600	N/A	N/A
<b>Cranial radiotherapy, n (%)</b>			
Yes	7 (31.8)	10 (31.3)	NAI
TCD (Gy)	54.4 (54.4-114)*	54 (40.5-66)	NAI
No	15 (68.2)	22 (68.7)	NAI

N/A: Not Applicable; NAI: No Additional Information; QNR: Questionnaire

\*Radiotherapy was given during primary treatment and relapse

eventually with a normal premium. Three survivors did not specify their premium.

Among the platinum-treated CCS without ototoxicity, 6/32 (19%) indicated to have problems with obtaining insurances. This was not significantly different from CCS with ototoxicity ( $p=0.497$ ). Two survivors got accepted at a higher premium, 2 got accepted eventually with normal premiums and 2 survivors did not specify their premium.

Nineteen percent of the 599 CCS (114/599) without platinum treatment, reported to ever have problems with obtaining insurances due to their childhood cancer history. This was not significantly different from platinum-treated CCS with ototoxicity ( $p=0.220$ ).

### ***Distress, Anxiety and Depression***

Low levels of anxiety and depression (HADS score  $<15$ ) were found in 21/22 survivors with ototoxicity, in 32/32 survivors without ototoxicity and in 555/599 non-platinum treated survivors. One survivor with ototoxicity and 33 non-platinum treated survivors stated high anxiety and depression levels (HADS score  $\geq 15$ ). Median HADS scores were not statistically significant between the three subgroups (Table 3).

The median follow-up time between cessation of treatment and completion of the DT was 15.6 years (range: 3.2-41.6 years). As shown in Table 3 and Supplementary Table 1b, we did not observe statistically significant differences in median DT score between non-platinum treated survivors (median: 1 (range: 0-10)) and platinum-treated CCS with ototoxicity (median: 0 (range: 0-8),  $p=0.711$ ), nor between platinum-treated survivors with and without ototoxicity (median: 0 (range: 0-6),  $p=0.441$ ).

### **Discussion**

The current study seems to indicate the following in CCS with and without platinum-induced hearing impairment: 1) educational level, employment, living situation and marital status was similar across all childhood cancer survivors; 2) survivors in this study had similar rates of problems with obtaining insurance; and 3) survivors with and without platinum-induced hearing loss experience equal levels of psychological distress.

In the general population in the Netherlands aged between 18 and 57 years old, 14% completed primary education, 51% is educated at secondary level and 76% is highly educated (i.e., tertiary education of university/college) [27]. Our study showed that childhood cancer survivors within this age range have similar or even higher education levels as the normal population and hearing impairment did not seem to lead to lower education levels. The overall rate of unemployment in our cohort was 18% and is similar to other studies in childhood cancer survivors [6,28].

The results of this small study could suggest that hearing impaired childhood cancer survivors in the Netherlands do

not experience more difficulties in obtaining (a different) insurance or more coverage than non-ototoxic survivors that were platinum-treated, or non-platinum treated survivors. We showed that 32% of the platinum-treated survivors with ototoxicity, 19% of platinum-treated survivors without ototoxicity and 19% of non-platinum treated CCS had problems obtaining insurances although the exact reason is not known. This is in line with previous reports showing that about 29% to 44% of American childhood cancer survivors experience difficulty obtaining insurances because of health reasons [3-7,29]. In the Netherlands patients will be automatically insured for health care through the parents if they are  $<18$  years of age, but children can also stay insured for health care through the parents if they are above 18 years of age. The result of this study can therefore be an underestimation of the problems experienced by survivors trying to obtaining a different health care insurance or more coverage of their health insurance.

Previous studies showed inconsistent results with regard to the occurrence of depression and anxiety following hearing loss in CCS. Some studies showed that survivors reveal significantly more mental health issues and insurance problems than healthy siblings [28,30,31]. A study by Prasad et al. observed that childhood cancer survivors experience higher self-reported rates of depression and anxiety compared with siblings by using the Brief Symptom Inventory-18 (BSI-18), a standardized self-report for symptoms of depression and anxiety [32]. On the other hand, a study in pediatric brain tumor survivors reported that survivors do not experience more distress (5%) than siblings (11%) on the BSI-18 test [33]. As in the general population where 3% to 10% have symptoms of depression or distress and in line with previous studies in childhood cancer survivors where 4 clinical depression or distress rates between 4-11% were reported, we found that up to 6% of the childhood cancer survivors experience emotional distress [34].

Our study observed no differences in HADS score between survivors with (4.5) and without hearing loss (5.5), although numbers were limited.

### **Conclusion and Future Perspectives**

Although we included more than 600 survivors of childhood cancer survivors, the subgroup of platinum-treated survivors was small and did not allow us to perform multivariate analysis. Other limitations of the study are the limited detail with regard to self-reported data and lack of detailed insurance data. Childhood cancer survivors were not asked when they tried to obtain insurance coverage.

Based on our sample size of platinum-treated survivors of  $n=54$ , a standard deviation of 3.2 and a significance level of 0.05, the beta (type II error) would be 0.63 (37%). This indicates that the current study lacked power to completely

Table 3. Socio-demographic outcomes, psychological distress (HADS) and emotional distress (DT)

	Platinum-Treated			Non-Platinum Treated	
	Münster ≥ 2b N=22	Münster<2b N=32	P-value <sup>a</sup>	N=599	P-value <sup>b</sup>
<b>Socio-Demographics</b>					
<b>Educational level</b>					
Primary	3 (13.6)	8 (25.8)	N/A	46 (7.9)	N/A
Secondary/Vocational	11 (50)	15 (48.4)	0.733	317 (54.6)	0.874
Tertiary	5 (22.7)	5 (16.1)	1.000	122 (21)	0.715
University/College	3 (13.6)	3 (9.7)		96 (16.5)	
Missing	0	1		18	
<b>Employment</b>					
Not employed	8 (36.4)	9 (29)		100 (17.2)	
Part time	6 (27.3)	9 (29)	0.688	183 (31.4)	0.096
Fulltime	3 (13.6)	9 (29)	N/A	152 (26.1)	N/A
Yes, not specified	5 (22.7)	4 (12.9)	N/A	147 (25.3)	N/A
Missing	0	1		17	
<b>Living situation</b>					
Living with parents	12 (54.5)	21 (72.4)	0.316	275 (47.7)	
Independent living	4 (18.2)	3 (10.4)		125 (21.7)	N/A
Living with partner	6 (27.3)	5 (17.2)	0.914	176 (30.6)	0.916
Missing	0	3		23	
<b>Marital status</b>					
Married or living as married	5 (23.8)	5 (16.1)		178 (30.4)	
Not married	16 (76.2)	26 (83.9)	0.493	397 (67.6)	0.488
Divorced	0	0	N/A	11 (1.9)	N/A
Missing	1	1		13	
<b>Insurances</b>					
<b>Problems obtaining insurances</b>					
<b>No, n (%)</b>	11 (50)	15 (46.9)		329 (54.9)	
<b>Not applicable, n (%)</b>	4 (18.2)	11 (34.4)	0.320	156 (26)	0.654
<b>Yes, n (%)</b>	7 (31.8)	6 (18.8)	0.497	114 (19)	0.220
Funeral insurance	3 (30)	2 (33.3)		23 (16.2)	
Life insurance	2 (20)	0		46 (32.4)	
Health insurance	2 (20)	2 (33.3)		32 (22.5)	
Mortgage	1 (10)	0		33 (23.3)	
Risk insurance	1 (10)	0		0	
Disability insurance	0	0		4 (2.8)	
Not specified	1 (10)	2 (33.3)		4 (2.8)	
<b>Premium, n (%)</b>					
Increased	3 (43)	2 (33)		43 (38)	
Temporary increased	0	0		6 (5)	
Normal	1 (14)	2 (33)		31 (27)	
Not indicated	3 (43)	2 (34)		34 (30)	
<b>Emotional and Psychological Distress</b>					
<b>HADS</b>					
<15, n (%)	21 (95.5)	32 (100)		555 (92.7)	
≥ 15, n (%)	1 (4.5)	0 (0)		34 (5.7)	
Missing, n (%)	0 (0)	0 (0)		10 (1.7)	

HADS score, median (range)	4.5 (0-29)	5.5 (0-11)	0.337	6 (0-35)	0.862
Anxiety score, median (range)	3 (0-14)	3 (0-7)	0.411	4 (0-18)	0.486
Depression score, median (range)	1 (0-15)	2 (0-6)	0.363	1 (0-19)	0.685
<b>DT score, median (range)</b>	<b>0 (0-8)</b>	<b>0 (0-6)</b>	<b>0.441</b>	<b>1 (0-10)</b>	<b>0.711</b>

HADS: Hospital Anxiety and Depression Scale; DT: Distress Thermometer

<sup>a</sup>Münster ≥ 2b vs. Münster < 2b, <sup>b</sup>Münster ≥ 2b vs. no audiogram

rule out false negative conclusions, i.e. that hearing impaired survivors do not encounter more psychological distress than normal hearing survivors with audiogram.

In summary, based on this first study, with a small sample size, we didn't find differences between hearing impaired survivors of childhood cancer who were treated in the Netherlands and survivors without hearing loss, suggesting that CCS with ototoxicity do not encounter more problems obtaining insurance coverage or with psychological distress when compared to non-ototoxic platinum-treated survivors and non-platinum treated survivors. Future prospective studies should comprise larger cohorts, including a healthy reference group and should elucidate more on insurances.

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### Ethical Standards

This study has been submitted by the medical ethical committee and was approved as a non-WMO study (MEC-2015-269) because only data was retrieved from databases and medical records

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