A population-based case-control study on social factors and risk of testicular cancer

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A Population-based Case-Control Study on Social Factors and Risk of Testicular Cancer

Running head: Social Factors and Testicular Cancer

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Summary

Article focus:

- Background: It is controversial whether social position is associated with the risk of testicular cancer. Therefore the aims are a) the classification of social position based on job titles reported in an occupational history, and b) assessment of the association between risk of testicular cancer and job-title based social position.

Key messages:

- Job-title based social position is not associated with testicular cancer.
- Occupation as farmer or farm worker entails an elevated risk of testicular cancer, possibly due to related exposures.

Strengths and limitations:

- Occupational social factors were measured on the basis of a detailed lifetime history of occupations. This population based study allows examination of the full spectrum of social differences in the general population.
- The basis for the classification of social position is relatively valid because job histories usually are reported with good accuracy and the information was obtained by in-person interviews,
- A limitation is that the differential response of cases (76%) and controls (57%) may bias the effect estimates if possible selection effects differ between both groups. Also periods of unemployment and illness cannot be ranked by the scales utilised in this study.

Abstract:

Objectives: Incidence rates for testicular cancer have risen over the last few decades. Findings of an association between the risk of testicular cancer and social factors are controversial. The association of testicular cancer and different indicators of social factors were examined in this study.

Design: *Case-control study.*

Setting: *Population based multi-centre study in four German regions (*city states Bremen and Hamburg, the Saarland region and the city Essen*).*

Participants: The study included 797 control subjects and 269 subjects newly diagnosed with testicular cancer of which 170 cases were classified as seminoma and 99 as nonseminoma. The age of study subjects ranged from 15 to 69 years.

Methods: Social factors were based on the achieved educational level, post educational training, occupational sectors according to Erikson-Goldthorpe-Portocarrero (EGP) and the socioeconomic status (SES) on the basis of the International Socio-Economic Index of occupational status (ISEI). Odds ratios [ORs] and corresponding 95% confidence intervals [95%-CIs] were calculated for the whole study sample and for seminoma and nonseminoma separately.

Results: An increased testicular cancer risk was observed for subjects with an apprenticeship (OR=1.5 [95%-CI: 0.9-2.5]) or a university degree (OR=1.5 [95%-CI: 0.9-2.6]) relative to those whose education was limited to school. Analysis of occupational sectors revealed an excess risk for farmers and farm related occupations. No clear trend was observed for the analyses according the ISEI-scale.

Conclusions: Social factors based on occupational measures were not a risk factor for testicular cancer in this study. The elevated risk in farmers and farm related occupations warrants further research including analysis of occupational exposures.

Introduction

Subjects affected most by testicular cancer are men between 15 and 40 years of age. For men older than 40 years of age the risk of testicular cancer decreases continuously.[1, 2] The age distribution of testicular cancer is in sharp contrast to other neoplasms for which incidence rises with increasing age. Established risk factors for testicular cancer include a family history of testicular cancer and a history of an undescended testis.[3, 4] Exposure to endocrine disrupting chemicals in an occupational context or *in utero*, has been suggested as a factor in cancer development.[5] The incidence rates of testicular cancer have risen continuously in Western Europe and other industrialized countries, which may be due to changed environmental and life circumstances in these countries. In particular, in Germany the average numbers of testicular cancer per year in the 1980s and 1990s were 3196 and 3836. The corresponding age-standardised incidence rates were 7.7 and 8.9 per 100.000.[6] However, study results on the association of social factors and testicular cancer have been conflicting. Excess risks for higher levels of education or occupations related to higher social class, like administrators and managers and other professionals were observed in some studies.[7-10] Other studies did not observe an association between social status and testicular cancer [11-17] or even observed an inverse association.[18, 19] In one study the association of testicular cancer and socioeconomic status (SES) differed by histological type.[20] A register based study in Finland observed a decrease of testicular cancer incidence rates among subjects of higher social classes and an increase of incidence rates in the lower social classes between 1971 and 1995, leading to a levelling off of the social gradient.[21]

In this study, in addition to educational attainment at school and level of professional training as defined in a previous study[22] further social factors based on job histories were considered. In detail, socioeconomic status (SES) based on the International Socio-Economic Index (ISEI)[23] and social class based on the Erikson-Goldthorpe-Portocarrero (EGP)[24] classification was explored. Both the International Socio-Economic Index (ISEI) of occupation, which is a vertical grouping approach, and the Erikson-Goldthorpe-Portocarrero (EGP) classification of occupations which adopts a class schema, claim that employment relations are basic social characteristics of western society.

Study subjects and Methods

All participants were registered residents of the city states Bremen and Hamburg, the Saarland region and the city Essen. Study subjects randomly drawn from registration offices had to live in the study regions between July 1995 and December 1997. Incident cases, diagnosed between July 1995 and December 1997, were reported by an active registration system via hospitals and pathologists. In Hamburg cases were also identified via the state cancer registry.

Eligible cases had to have a diagnosis of tumour of the testis (ICD-10: C62.0-C62.9), epididymis (C63.0), spermatic cord (C63.1) or extragonadal germ cell tumours (C38.3; C48.0; C71.0-C71.9; ICD-O: M9060-9102).

A total of 353 eligible cases and 2014 potential controls were contacted for this study. Among cases, 54 persons were not reached, 29 persons refused participation. One case was excluded due to insufficient German language skills. Participation was denied by 552 control subjects, 512 moved or died and 182 persons were never reached.

Copies of pathology reports and histological material were obtained from hospitals. Pathology reports were reviewed centrally and compared with histological material when available by a reference pathologist to determine the histological type of tumour. Tumours were classified as seminomas (N=170, 63.2%) or nonseminomas (N=99, 36.8%) according to Parkin and co-workers.[25] The latter group also included extra-gonadal germ cell tumours. More detailed descriptions and demographic characteristics of the participants were published elsewhere.[22, 26-28]

Cases and controls had to be between 15 and 69 years of age. An n:m-matching for 5-year age strata and study region was chosen. To obtain sufficient power in this study, a matching ratio of 1:4 was realised for the age group 35-69, while for the age strata 15-34 a matching ratio of 1:2 was considered to be sufficient since most cases were expected in this age group. Inclusion criteria were fulfilled by 269 cases and 918 controls. Cases and controls were recruited in parallel. For this purpose controls were selected prospectively according to the expected case distribution. This left 121 controls for which no matching case interview was obtained.

Participants were interviewed face-to-face (N=984, 92.3%) or by telephone (N=82, 7.7%). Almost all interviews were performed with an index person (N=978, 91.7%). For deceased subjects or subjects too ill to answer the questions, a next-of-kin interview was solicited. The interview entailed questions about medical conditions since childhood, chemical and physical exposures and an occupational biography for every job held 6 months or longer.

For each employment period, the job title and industry and a brief summary of the job tasks were assessed. Each job was assigned a five-digit *International Standard Code of Occupations* (ISCO)[29] and a five-digit industry code (NACE).[30]

Assessment of Social Factors

Measures of social factors in this study were level of educational attainment at school, level of professional training, occupational sector based on EGP and SES based on ISEI.

Job title codes (ISCO) were linked to the *International Socio-Economic Index of Occupational Status* (ISEI).[23] The ISEI assigns values between 10 and 90 to job titles with respect to education and income. Judges, lawyers and physicians achieve the highest values, while unskilled labourers in agriculture and housekeepers the lowest values. In this scale a continuous hierarchical approach the distinctions of work related tasks and social patterns disappear in favour of a single parameter. The ISEI score provides a mechanism for ranking occupations related to both the level of education required and the income earned.[23] ISEI-Scores for the maximum ever achieved, the longest held and the last job were used to quantify the possible effect of socioeconomic status on testicular cancer risk. ISEI values were grouped into five categories employing the best possible equal distribution of controls.

For the present analyses, ISCO codes were aggregated according to occupational sector and training required (EGP) assuming that internal homogeneity within a category is great and that a definable external social heterogeneity to members of other categories exists (24). The EGP is based on occupational group, required training, self support/independence, social mobility and leadership. Each reported job was classified into one of the following ten occupational categories: (I) higher service (includes mostly professionals, large enterprise employers and higher managers (>10 subordinates)); (II) lower service (includes mostly associate professionals, lower managers (1-10 subordinates), higher sales); (III) routine clericals/sales (includes routine clerical and sales workers); (IV) small employers (includes small entrepreneurs (1-10 subordinates); (V) self-employed (own account workers, no employees, artists); (VI) manual foremen (manual workers with supervisory status (>1 subordinate)); (VII) skilled manual (mostly craft workers, some skilled service, skilled machine operators, also gardeners); (VIII) semi-unskilled manual (mostly machine operators, elementary sales services and state work creation scheme); (IX) farm workers (employed farm workers, irrespective of skill level; also family farm workers); (X) farmers/farm managers (self-employed and supervisory farm workers, irrespective of skill level). Categories I and II, III, IV and V, VI and VII, IX and X were collapsed into for analysis.

Occupational histories excluded jobs starting within one year before the case diagnosis or before the first mailing to controls. For analysis of first job, last job, longest held job, job highest ranked and job lowest ranked the highest category formed the reference. Subjects which had never worked were excluded from analysis, except for the ever/never analysis of EGP. For this analyses, those subjects who did not work in the specific field under consideration were used as reference group in the ever/never analysis.

Educational level according to the German school system was classified into four levels (≤9 [no school degree, Sonderschulabschluss, Hauptschulabschluss], 10 [mittlere Reife], 12 [Fachabitur] and 13 [Abitur] years of school education). In addition, the highest professional post school level (none, apprenticeship, university or college degree, others) was analysed.

Statistical Analysis

Odds Ratios (OR) and 95%-confidence intervals [95%-CI] were calculated stratified for the five year age strata and study centres. All analyses were carried out for the whole study and by the two main histological subgroups. Odds ratios and corresponding confidence intervals were estimated by the maximum likelihood method using the procedure PHREG for conditional logistic regression analysis. The level of statistical significance was defined as $p<0.05$ (two-sided). All analyses were carried out using SAS 8.2. ORs were not reported if a given category included less than three cases.

Results

The proportion of medically confirmed cryptorchidism was higher in cases (4.8%) than in controls (1.0%). Among seminoma cases the proportion of medically confirmed cryptorchidism was 4.7% and 1.1% among the controls. In nonseminoma cases the prevalence of medical confirmed cryptorchidism was 5.1% while in the controls the prevalence was 1.0%. Overall, nonseminoma cases were on average 5 years younger than seminoma cases (nonseminoma: 31.1±8.4; seminoma: 36.9±8.8; controls: 38.0±11.7 [mean±sd]) (data not shown).

The distribution of number of occupations for cases and controls is shown in Table 1. Seven cases (six nonseminoma cases; one seminoma case) and 20 controls were still attending school or were students with no job history at the time of diagnosis (case) or first mailing (controls). Job histories of nonseminoma cases lasted 14.6±8.6 years, of seminoma cases 21.5±12.6 and of controls 21.0±12.9 years [mean±sd]. Except for the nonseminoma cases the number of occupational periods did not differ between cases and controls.

Table 1: Frequency of economically active periods for cases and controls for whole study and separated for analyses of age groups and histology.

Frequency	Cases N=269		Controls N=797	
Complete Study	N	%	N	%
0	7	2.6	20	2.5
1-2	108	40.2	324	40.7
3-4	98	36.4	281	35.3
5+	56	20.8	172	21.6
Seminoma	Cases N=170		Controls N=725	
0	1	0.6	13	1.8
1-2	43	25.3	192	26.5
3-4	74	43.5	299	41.2
5+	52	30.6	221	30.5

Nonseminoma	Cases N=99		Controls N=682	
0	6	6.1	20	2.9
1-2	37	37.4	193	28.3
3-4	40	40.4	274	40.2
5+	16	16.2	195	28.6

Stratification by educational level and professional degree is shown in Table 2. Risk estimates were not elevated for higher educational levels in the complete study group or in the histological subgroups. Subjects with professional degrees (i.e. apprenticeship, technical colleges, study at university and university for applied sciences) in the whole study group and in the analysis of seminoma cases as compared to subjects without professional training were at higher risk. For nonseminoma cases and their matched controls no increased risk was observed for professional training. No risk was observed for being employed before the age of 18 (OR=1.0; 95%-CI 0.7-1.4) (data not shown).

Table 2: Distribution of cases and controls by educational level and professional degrees and corresponding Odds Ratios with 95% confidence intervals

	Cases		Controls		
	N	%	N	%	
Complete Study	(269)		(797)		OR (95%-CI)
Years at school					
≤9	89	33.1	304	38.1	1.0†
10	61	22.7	192	24.1	0.8 (0.6-1.3)
12	25	9.3	78	9.8	0.9 (0.5-1.5)
13	94	34.9	222	27.9	1.0 (0.7-1.5)
Unknown	0	0.0	1	0.1	
Professional training					
None	24	8.9	95	11.9	1.0†
Apprenticeship	164	61.0	485	60.9	1.5 (0.9-2.5)
University degree	62	23.1	154	19.3	1.5 (0.9-2.6)
Other	19	7.1	63	7.9	0.9 (0.4-1.9)
Seminoma	(170)		(725)		
Years at school					
≤9	60	35,3	267	36,8	1.0†
10	39	22,9	180	24,8	0.8 (0.5-1.4)
12	17	10,0	75	10,3	0.9 (0.5-1.6)
13	54	31,8	202	27,9	1.0 (0.6-1.6)
Unknown	0	0,0	1	0,1	
Professional training					
None	12	7,1	88	12,1	1.0†
Apprenticeship	111	65,3	446	61,5	2.2 (1.1-4.3)
University degree	40	23,5	142	19,6	1.8 (0.9-3.7)
Other	7	4,1	49	6,8	1.6 (0.5-5.1)
Nonseminoma	(99)		(682)		
Years at school					
≤9	29	29,3	225	33,2	1.0†
10	22	22,2	172	25,4	0.8 (0.4-1.5)
12	8	8,1	73	10,8	0.8 (0.3-1.9)
13	40	40,4	206	30,4	1.1 (0.6-1.9)
Unknown	0	0,0	1	0,1	
Professional training					

None	12	12,1	80	11,7	1.0†
Apprenticeship	53	53,5	400	58,7	0.9 (0.5-1.9)
University degree	22	22,2	140	20,5	1.1 (0.5-2.5)
Other	12	12,1	62	9,1	0.5 (0.2-1.4)

†Reference.

No difference between cases and controls was observed (cases: mean score 42.8, median score 39; controls: mean score 42.4, median score 39) (data not shown). Risk estimates by ISEI-scores are presented in Table 3. Analyses of the maximum ISEI score reached during the lifetime showed no increased risks. A modest increased risk was observed for seminoma cases where the risk increase was restricted to the lowest category (OR=1.4; 95%-CI 0.8-2.4). For nonseminoma study sample no increased risk was observed as compared to the reference category. The analyses by ISEI of the job held longest and the last job held revealed no clear trends.

Table 3: Distribution and frequency for achieved maximum ISEI scores and ISEI scores for the longest and last held job for whole study population and for histologic subgroups and corresponding Odds Ratios.

Complete Study	**Cases**		**Controls**		
Maximum	**N**	**%**	**N**	**%**	**OR (95%-CI)**
[16-37)	59	22.5	156	19.6	1.1 [0.7-1.8]
[37-44)	48	18.3	172	21.6	0.9 [0.5-1.4]
[44-55)	51	19.5	151	19.0	1.0 [0.6-1.6]
[55-66)	51	19.5	151	19.0	0.9 [0.6-1.5]
[66-88]	53	20.2	147	18.4	1†
Missing	7		20		
Last held job					
[16-37)	96	35.7	264	33.3	0.9 [0.6-1.4]
[37-44)	36	13.8	132	16.6	0.8 [0.5-1.3]
[44-55)	39	14.1	145	18.2	0.7 [0.4-1.1]
[55-66)	44	16.4	117	14.7	0.9 [0.6-1.5]
[66-88]	47	17.5	119	14.9	1†
Missing	7		20		
Longest held job					
[16-37)	104	38.7	277	34.9	0.9 [0.6-1.5]
[37-44)	41	15.2	150	18.8	0.8 [0.5-1.3]
[44-55)	33	12.3	144	18.1	0.6 [0.3-1.0]
[55-66)	43	16.0	106	13.3	1.0 [0.6-1.7]
[66-88]	41	15.2	100	12.6	1†
Missing	7	2.6	20	2.4	
SEMINOMA	Cases		Controls		
Maximum	N	%	N	%	
[16-37)	37	21.9	141	19.9	1.4 [0.8-2.4]
[37-44)	32	18.9	159	22.3	0.9 [0.5-1.6]
[44-55)	32	18.9	137	19.2	0.9 [0.5-1.6]
[55-66)	32	18.9	141	19.8	0.9 [0.5-1.6]
[66-88]	36	21.3	134	18.8	1†
Missing	1		13		
Last held job					
[16-37)	59	34.9	240	33.8	0.9 [0.6-1.6]
[37-44)	24	14.2	123	17.3	0.8 [0.5-1.5]
[44-55)	25	14.8	133	18.7	0.7 [0.4-1.3]
[55-66)	29	17.2	109	15.3	0.9 [0.5-1.6]
[66-88]	32	18.9	107	15.0	1†
Longest held job					
[16-37)	64	37.7	259	35.9	0.9 [0.5-1.5]

[37-44)	29	17.1	133	18.3	0.9 [0.5-1.5]
[44-55)	21	12.4	128	17.7	0.5 [0.3-1.0]
[55-66)	25	14.7	101	13.9	0.8 [0.4-1.5]
[66-88]	30	17.7	91	12.6	1†
Missing	1		12		

Table 3: continued

NONSEMINOMA	Cases		Controls		
Maximum	N	%	N	%	
[16-37)	22	23.7	128	19.5	0.9 [0.4-1.9]
[37-44)	16	17.2	148	22.3	0.7 [0.3-1.5]
[44-55)	19	20.4	129	19.5	0.9 [0.5-1.9]
[55-66)	19	20.4	133	20.1	1.0 [0.5-1.9]
[66-88]	17	18.3	124	18.7	1†
Missing	6				
Last held job					
[16-37)	37	39.8	223	33.8	0.9 [0.4-1.7]
[37-44)	12	14.0	110	16.6	0.7 [0.3-1.6]
[44-55)	14	14.0	126	19.0	0.7 [0.3-1.5]
[55-66)	15	16.1	103	15.5	0.9 [0.4-2.0]
[66-88]	15	16.1	100	15.1	1†
Longest held job					
[16-37)	40	40.4	230	33.9	1.1 [0.5-2.2]
[37-44)	12	12.1	130	19.1	0.7 [0.3-1.7]
[44-55)	12	12.1	128	18.8	0.6 [0.3-1.5]
[55-66)	18	18.2	91	13.3	1.4 [0.6-3.3]
[66-88]	11	11.1	83	12.2	1†
Missing	6	6.1	19	2.8	

†Reference.

ORs by occupational sectors (EGP) are shown in table 4. An increased risk for testicular cancer was observed for ever held an agriculture related job (OR=2.2 95%-CI 1.1-4.2). For seminoma cases the effect was of the same strength (OR=2.4 95%-CI 1.1-5.0), while for nonseminoma cases the OR estimate was smaller (OR=1.6 95%-CI 0.5-4.8). For all other classes no increased risk was observed. This pattern was replicated for almost all analysis presented in table 4. Compared with subjects in the highest EGP quintiles, increased risks were observed for category IX-X for first, last and occupation with highest category ever.

Table 4: Stratification and Odds Ratios with 95%-CI of occupational sectors according to Erikson, Goldthorpe and Protocarero for complete study group and histologic subgroups

	Complete Study					Seminoma					Nonseminoma[#]				
Category[1]	**Cases**		**Controls**			**Cases**		**Controls**			**Cases**		**Controls**		
	N	**%**	**N**	**%**	**OR [95%-CI]**	**N**	**%**	**N**	**%**	**OR [95%-CI]**	**N**	**%**	**N**	**%**	**OR [95%-CI]**
First held job															
I-II	25	9.5	69	8.9	1	15	8.9	63	8.8	1	10	10.8	60	9.1	1
III-V	40	15.3	140	18.0	0.9 [0.5-1.5]	24	14.2	126	17.7	0.9 [0.4-1.8]	16	17.2	126	19.1	0.8 [0.3-1.9]
VI-VII	134	51.1	404	52.0	1.1 [0.7-1.9]	90	53.3	372	52.2	1.3 [0.7-2.4]	44	47.3	335	50.8	0.9 [0.4-1.9]
VIII	56	21.4	148	19.0	1.1 [0.8-1.4]	34	20.1	138	19.4	1.1 [0.8-1.6]	22	23.7	128	19.4	1.0 [0.6-1.5]
IX-X	7	2.7	16	2.1	1.6 [0.5-4.6]	6	3.6	13	1.8	2.1 [0.6-6.7]	1	1.1	11	1.7	-
Last held job															
I-II	70	26.7	172	22.1	1	45	26.6	155	21.8	1	25	26.9	150	22.7	1
III-V	53	20.2	192	24.7	0.7 [0.4-1.0]	34	20.1	180	25.3	0.7 [0.4-1.2]	19	20.4	162	24.5	0.6 [0.3-1.1]
VI-VII	82	31.3	243	31.3	0.9 [0.6-1.3]	55	32.5	223	31.3	1.0 [0.6-1.6]	27	29.0	205	31.1	0.7 [0.4-1.3]
VIII	52	19.8	165	21.2	0.9 [0.7-1.1]	31	18.3	151	21.2	0.9 [0.7-1.2]	21	22.6	138	20.9	0.9 [0.6-1.2]
IX-X	5	1.9	5	0.6	3.0 [0.8-11.7]	4	2.4	3	0.4	4.3 [0.9-20.8]	1	1.1	5	0.8	-
Longest held job															
I-II	54	20.6	145	18.7	1	37	21.9	133	18.7	1	17	18.3	125	18.9	1
III-V	46	17.6	166	21.4	0.8 [0.5-1.2]	27	16.0	154	21.6	0.7 [0.4-1.2]	19	20.4	139	21.1	0.8 [0.4-1.6]
VI-VII	101	38.5	287	36.9	1.1 [0.7-1.6]	70	41.4	261	36.7	1.2 [0.8-2.0]	31	33.3	242	36.7	0.8 [0.4-1.5]
VIII	56	21.4	171	22.0	0.9 [0.8-1.2]	32	18.9	156	21.9	0.9 [0.7-1.2]	24	25.8	146	22.1	1.0 [0.7-1.4]
IX-X	5	1.9	8	1.0	1.3 [0.4-4.1]	3	1.8	8	1.1	1.0 [0.2-4.1]	2	2.2	8	1.2	-
Lowest category ever															
I-II	18	6.9	42	5.4	1	10	5.9	38	5.3	1	8	8.6	37	5.6	1
III-V	28	10.7	101	13.0	0.7 [0.3-1.4]	18	10.7	89	12.5	0.8 [0.3-2.0]	10	10.8	90	13.6	0.5 [0.2-1.5]
VI-VII	85	32.4	241	31.0	1.0 [0.5-1.8]	54	32.0	222	31.2	1.1 [0.5-2.5]	31	33.3	200	30.3	0.8 [0.3-1.8]
VIII	130	49.6	392	50.5	0.9 [0.7-1.3]	86	50.9	362	50.8	1.0 [0.7-1.5]	44	47.3	332	50.3	0.8 [0.5-1.3]
IX-X	1	0.4	1	0.1	-	1	0.6	1	0.1	-	0	0.0	1	0.2	-
Highest category ever															
I-II	86	32.8	231	29.7	1	58	34.3	211	29.6	1	28	30.1	201	30.5	1
III-V	58	22.1	194	25.0	0.8 [0.5-1.2]	35	20.7	183	25.7	0.7 [0.5-1.2]	23	24.7	167	25.3	0.8 [0.4-1.5]
VI-VII	105	40.1	307	39.5	1.1 [0.7-1.5]	71	42.0	276	38.8	1.2 [0.8-1.8]	34	36.6	257	38.9	0.9 [0.5-1.5]
VIII	10	3.8	40	5.1	0.8 [0.5-1.2]	2	1.2	38	5.3	0.5 [0.3-1.0]	8	8.6	31	4.7	1.0 [0.6-1.6]
IX-X	3	1.1	5	0.6	2.2 [0.5-10.4]	3	1.8	4	0.6	3.5 [0.7-17.7]	0	0.0	4	0.6	-

Table 4: continued.

Ever held job															
I-II	86	32.0	231	29.0	1.1 [0.8-1.5]	58	34.1	211	29.1	1.1 [0.7-1.5]	28	28.3	201	29.5	1.2 [0.7-1.9]
III-V	92	34.2	308	38.6	0.7 [0.5-1.0]	58	34.1	286	39.4	0.6 [0.4-0.9]	34	34.3	268	39.3	0.9 [0.5-1.4]
VI-VII	166	61.7	494	62.0	1.2 [0.9-1.6]	110	64.7	453	62.5	1.2 [0.8-1.7]	56	56.6	413	60.6	1.1 [0.7-1.7]
VIII	130	48.3	392	49.2	1.0 [0.7-1.3]	86	50.6	362	49.9	1.0 [0.7-1.4]	44	44.4	333	48.8	1.0 [0.6-1.5]
IX-X	17	6.3	30	3.8	2.2 [1.1-4.2]	13	7.6	23	3.2	2.4 [1.1-5.0]	4	4.0	22	3.2	1.6 [0.5-4.8]

[1]Categories were assigned as follows: I=Higher service (includes mostly professionals, large enterprise employers and higher managers (>10 subordinates)); II=Lower service (Includes mostly associate professionals, Lower managers (1-10 subordinates), higher Sales); III=Routine clericales/sales (Includes routine clerical and sales workers); IV=Small employers (Includes small entrepreneurs (1-10 subordinates); V=Independent (Own account workers, no employees, artists); VI=Manual foremen (Manual workers with supervisory status (>1 subordinate)); VII=Skilled manual (Mostly craft workers, some skilled service, skilled machine operators, also gardeners); VIII=Semi-unskilled manual (Mostly machine operators, elementary sales services and state work creation scheme); XI=Farm workers‡ (Employed farm workers, irrespective of skill level; also family farm workers); X=Farmers/Farm managers (Self-employed and supervisory farm workers, irrespective of skill level). Frequencies and calculations for social status ever held. ‡: only Farm workers and forestry workers.

Discussion

Different methods of assigning social position may produce different results in terms of trends in health and inequality.[31, 32] Four indicators of social groupings were analysed in this study. School education was not observed to have an impact on testicular cancer risk. The elevated risk observed for professional training as compared to no training was restricted to the seminoma subgroup. Overall, there was no hint in this study that examined social factors are associated with testicular cancer. This result is in line with other newer studies.[11, 17]

Elevated risks in association with EGP other than agriculture were not observed in this study. An excess risk in agriculture and related occupations was also observed in several studies[9, 33-35] Increased risks in agriculture and related occupations are not explained by social factors but rather with exposures such as pesticides,[33, 35] fertilizers[36, 37] or contact with farm animals and zoonotic infections[33] which were not in the scope of this study.

No increased risks were observed for non-agricultural occupational sectors based on the EGP which is in line with other studies.[14, 21, 38] Also, no evidence was found that socioeconomic status (ISEI) is associated with testicular cancer. This indicates that factors other than occupation as a mediating variable between income and education may be responsible for testicular cancer risk.

Neither EGP categories nor continuous hierarchy by ISEI were a risk factor for testicular cancer in this study. If a social gradient for testicular cancer in Germany existed in the past and exposures were associated with this gradient, this gradient was attenuated by omnipresent exposures that do not differ by social circumstances. The rising trends of testicular cancer in industrialised countries may be an indirect indication for alignment of social dependent exposures.

This study has several limitations. First, the study suffered from low response (cases 76%, controls 57%). For the study region of Hamburg participation was lower among controls with lower education which might have resulted in an overestimation of the risk in the lower SES status groups. Hence, it is possible that a participation bias might have biased the effect estimates. Sensitivity analysis by leaving out Hamburg revealed similar findings, which could also be explained by specifics of the population structure of Hamburg.

Second, misclassification of social status is likely to have occurred. As the assessment of the social status is not based on a dichotomous variable, the direction of bias due to non-differential misclassification cannot be predicted.

Third, periods of unemployment and illness cannot be ranked by both scales utilised in this study. Non-consideration of such periods may lead to an underestimation of any social difference.[39]

The strength of this study is to measure occupational social factors on the basis of full detailed life history of occupations. This information was obtained by in-person interviews. Population based controls were used in this study, which permits full examination of social differences. Study subjects were not aware of this study hypothesis, and occupational biography is an unprejudiced variable, so reporting bias is not likely to occur. Different possible confounding variables were considered by adjusting for post-educational degree or medical confirmed undescended testis and job frequency. However, the results were stable in all analyses.

Conclusion

The absence of an effect was not specific to the ISEI score, as another occupational scaling method, the EGP, was not related to testicular cancer, except farming and farm related working. It is unclear how this negative finding for occupation can be explained, but it may point to different social indicators telling different things about groups differing in age or other characteristics. The findings support the hypothesis that social inequalities in testicular cancer are not be based upon differences in occupational sectors or derived SES. More information is needed on the specific social correlates (e.g. work characteristics, living areas), since education and occupation are not only indicators of access to material properties, but also correlates with psychosocial properties.

Contributorship statement: DIC, AS, K-HJ and WA contributed substantially to the conception of this manuscript and/or the interpretation of the data. These co-authors, as well as CS, IJ, CB-E and TB also contributed with the revision and final approval of the version to be published.

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Conflict of interest: None declared.

Data sharing statement: No additional unplublished data from this study.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *case-control studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	**1**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	4-5
Methods			
Study design	4	Present key elements of study design early in the paper	**5**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,5,6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	5,6
		(*b*) For matched studies, give matching criteria and the number of controls per case	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6,7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5,6,7*
Bias	9	Describe any efforts to address potential sources of bias	14,15
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5,6,15
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, explain how matching of cases and controls was addressed	6
		(*e*) Describe any sensitivity analyses	14

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	10
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	Table 1 – Table 4
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8
		(*b*) Report category boundaries when continuous variables were categorized	7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Table 1 – Table 4
Discussion			
Key results	18	Summarise key results with reference to study objectives	14,15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14,15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

A Population-based Case-Control Study on Social Factors and Risk of Testicular Germ Cell Tumours

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A Population-based Case-Control Study on Social Factors and Risk of Testicular Germ Cell Tumours

Running head: Social Factors and Testicular Cancer

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Keywords: Case control study; education; male germ cell cancer; occupational risk factors; social position; socioeconomic status

Word count: 2.642

Abstract: 254

Summary: 191

Summary

Article focus:

- Background: It is controversial whether social position is associated with the risk of testicular cancer. The aims of this analysis are a) to classify social position based on job titles reported in an occupational history, and b) to assess the association between testicular cancer and job-title based social position.

Key messages:

- Job-title based social position is not associated with testicular cancer.
- Occupation as farmer or farm worker entails an elevated risk of testicular cancer, possibly due to related exposures.

Strengths and limitations:

- Occupational social factors were measured on the basis of a detailed lifetime history of occupations. This population-based study allows examination of the full spectrum of social differences in the general population.
- The basis for the classification of social position is relatively valid because job histories usually are reported with good accuracy and the information was obtained by in-person interviews,
- A limitation is that the differential response of cases (76%) and controls (57%) may bias the effect estimates if possible selection effects differ between both groups. Also periods of unemployment and illness cannot be ranked by the scales utilised in this study.

Abstract:

Objectives: Incidence rates for testicular cancer have risen over the last few decades. Findings of an association between the risk of testicular cancer and social factors are controversial. The association of testicular cancer and different indicators of social factors were examined in this study.

Design: *Case-control study.*

Setting: *Population-based multi-centre study in four German regions (*city states Bremen and Hamburg, the Saarland region and the city of Essen*).*

Participants: The study included 797 control subjects and 266 subjects newly diagnosed with testicular cancer of which 167 cases were classified as seminoma and 99 as non-seminoma. The age of study subjects ranged from 15 to 69 years.

Methods: Social position was classified by educational attainment level, post educational training, occupational sectors according to Erikson-Goldthorpe-Portocarrero (EGP) and the socioeconomic status (SES) on the basis of the International Socio-Economic Index of occupational status (ISEI). Odds ratios [ORs] and corresponding 95% confidence intervals [95%-CIs] were calculated for the whole study sample and for seminoma and non-seminoma separately.

Results: Testicular cancer risk was modestly increased ámong subjects with an apprenticeship (OR=1.7 [95%-CI: 1.0-2.8]) or a university degree (OR=1.6 [95%-CI: 0.9-2.8]) relative to those whose education was limited to school. Analysis of occupational sectors revealed an excess risk for farmers and farm related occupations. No clear trend was observed for the analyses according the ISEI-scale.

Conclusions: Social factors based on occupational measures were not a risk factor for testicular cancer in this study. The elevated risk in farmers and farm related occupations warrants further research including analysis of occupational exposures.

Introduction

Subjects affected most by testicular cancer are men between 15 and 40 years of age. For men older than 40 years of age the risk of testicular cancer decreases continuously.[1, 2] The age distribution of testicular cancer is in sharp contrast to other neoplasms for which incidence rises with increasing age. Established risk factors for testicular cancer include a family history of testicular cancer and a history of an undescended testis.[3, 4] Exposure to endocrine disrupting chemicals in an occupational context or *in utero*, has been suggested as a factor in cancer development.[5] The incidence rates of testicular cancer have risen continuously in Western Europe and other industrialized countries, which may be due to changed environmental and life circumstances in these countries. In particular, in Germany the average numbers of testicular cancer per year in the 1980s and 1990s were 3196 and 3836. The corresponding age-standardised incidence rates were 7.7 and 8.9 per 100.000.[6] However, study results on the association of social factors and testicular cancer have been conflicting. Excess risks for higher levels of education or occupations related to higher social class, like administrators and managers and other professionals were observed in some studies.[7-10] Other studies did not observe an association between social status and testicular cancer [11-17] or even observed an inverse association.[18, 19] In one study the association of testicular cancer and socioeconomic status (SES) differed by histological type.[20] A register based study in Finland observed a decrease of testicular cancer incidence rates among subjects of higher social classes and an increase of incidence rates in the lower social classes between 1971 and 1995, leading to a levelling off of the social gradient.[21]

In this study, in addition to educational attainment at school and level of professional training as defined in a previous study[22] further social factors based on job histories were considered. In detail, socioeconomic status (SES) based on the International Socio-Economic Index (ISEI)[23] and social class based on the Erikson-Goldthorpe-Portocarrero (EGP)[24] classification was explored. Both the International Socio-Economic Index (ISEI) of occupation, which is a vertical grouping approach, and the Erikson-Goldthorpe-Portocarrero (EGP) classification of occupations which adopts a class schema, claim that employment relations are basic social characteristics of western society.

Study subjects and Methods

All participants were registered residents of the city states Bremen and Hamburg, the Saarland region and the city of Essen. Study subjects randomly drawn from registration offices had to live in the study regions between July 1995 and December 1997. Incident cases, diagnosed between July 1995 and December 1997, were reported by an active registration system via hospitals and pathologists. In Hamburg cases were also identified via the state cancer registry. Eligible cases had to have a new diagnosis of tumour of the testis (ICD-10: C62.0-C62.9; ICD-O: M9060-M9102).

A total of 353 eligible cases and 2014 potential controls were contacted for this study. Among cases, 54 persons were not reached, 29 persons refused participation. One case was excluded due to insufficient German language skills. Participation was denied by 552 control subjects, 32 were excluded due to insufficient language skills, 512 had moved away, had died or were never reached.

Copies of pathology reports and histological material were obtained from hospitals. Pathology reports were reviewed centrally and compared with histological material when available by a reference pathologist to determine the histological type of tumour. Tumours were classified as seminomas (N=167, 62.8%), including seminoma not other specified (ICD-O, M9061: n = 160), anaplastic seminoma (M9062: n = 4), or non-seminomas (N=99, 37.2%), including embryonal carcinoma (M9070: n = 26), yolk sac tumor (M9071: n = 1), malignant teratoma not other specified (M9080: n = 2), teratocarcinoma (M9081: n = 15), malignant teratoma, intermediate (M9083: n = 5), mixed germ cell tumor (M9085: n = 49), and choriocarcinoma (M9100: n = 1) according to Parkin and co-workers.[25] More detailed descriptions and demographic characteristics of the participants were published elsewhere.[22, 26-28] Cases and controls had to be between 15 and 69 years of age. A n:m-group-matching for 5-year age strata and study region was chosen. To obtain sufficient power in this study, a matching ratio of 1:4 was realised for the age group 35-69, while for the age strata 15-34 a matching ratio of 1:2 was considered to be sufficient since most cases were expected in this age group. Due to overlap of the age distribution of seminoma and non-seminoma cases, the majority of controls matched to both seminoma and non-seminoma cases. Thus, for the analyses by histologic subgroup, 725 controls were matched by age and region to the seminoma cases while 682 controls were matched by age and region to the non-seminoma cases. Inclusion criteria were fulfilled by 266 cases and 918 controls. Cases and controls were recruited in parallel. For this purpose controls were selected prospectively according to the expected case distribution. This left 121 controls for which no matching case interview was obtained.

Participants were interviewed face-to-face (N=984, 92.3%) or by telephone (N=82, 7.7%). Almost all interviews were performed with an index person (N=978, 91.7%). For deceased subjects or subjects too ill to answer the questions, a next-of-kin interview was solicited. The interview entailed questions about familial characteristics, family history of cancer and other diseases, medical conditions since childhood, chemical and physical exposures and an occupational biography for every job held 6 months or longer.

For each employment period, the job title and industry and a brief summary of the job tasks were assessed. Each job was assigned a five-digit *International Standard Code of Occupations* (ISCO)[29] and a five-digit industry code (NACE).[30]

Assessment of social factors

Measures of social factors in this study were level of educational attainment at school, level of professional training, occupational sector based on EGP and social status based on ISEI.

Job title codes (ISCO) were linked to the *International Socio-Economic Index of Occupational Status* (ISEI).[23] The ISEI assigns values between 10 and 90 to job titles with respect to education and income. Judges, lawyers and physicians achieve the highest values, while unskilled labourers in agriculture and housekeepers the lowest values. In this scale a continuous hierarchical approach the distinctions of work related tasks and social patterns disappear in favour of a single parameter. The ISEI score ranks occupations by both, level of education and income.[23] ISEI-Scores were defined for the maximum score ever achieved and the longest held and the last job, respectively.. ISEI scores were grouped into five categories employing the best possible equal distribution of controls.

For the present analyses, ISCO codes were classified by occupational sector according to Erikson-Goldthorpe-Portocarrero (EGP). The EGP typology is based on occupational group, required training, self support/independence, social mobility and leadership. Within a category it assumes social homogeneity in terms of the market situation (sources and levels of income, degree of economic security and chances of economic advancement) and in terms of the work situation (autonomy in performing work-tasks and roles) (24). Each reported job was classified into one of the following ten occupational categories: (I) higher service (includes mostly professionals, large enterprise employers and higher managers (>10 subordinates)); (II) lower service (includes mostly associate professionals, lower managers (1-10 subordinates), higher sales); (III) routine clericals/sales (includes non-manual administration and sales workers); (IV) small employers (includes small entrepreneurs (1-10 subordinates); (V) self-employed (own account workers, no employees, artists); (VI) manual foremen (manual workers with supervisory status (>1 subordinate)); (VII) skilled manual (mostly craft workers, some skilled service, skilled machine operators, also gardeners); (VIII) semi-unskilled manual (mostly machine operators, elementary sales services and state work creation scheme); (IX) farm workers (employed farm workers, irrespective of skill level; also family farm workers); (X) farmers/farm managers (self-employed and supervisory farm workers, irrespective of skill level). Categories were collapsed into five groups (I and II; III to V; VI and VII; VII; IX and X) for analysis.

Occupational histories excluded jobs starting within one year before diagnosis in cases or before the first mailing to controls. The highest category served as the reference for the analysis of first job, last job, longest held job, job ranked highest and job ranked lowest,. Subjects who had never worked were excluded, except for the ever/never analysis of EGP. All subjects who did not belong to the group under consideration were used as the reference group in the ever/never analysis.

Educational level was classified by years of schooling into four levels according to the German school system (≤9 years [no school degree, Sonderschulabschluss, Hauptschulabschluss], 10 years [mittlere Reife], 12 years [Fachabitur] and 13 years [Abitur]). In addition, the highest professional level attained after school (none, apprenticeship, university or college degree, others) was analysed.

Statistical analysis

Odds Ratios (OR) and 95%-confidence intervals [95%-CI] were calculated stratified for the five year age strata and study centres. All analyses were carried out for the whole study group and stratified by histological subgroups. Controls were excluded from the subgroup analyses if no matching case was available in an age-group×study region stratum. Odds ratios and corresponding confidence intervals were estimated by conditional logistic regression using the procedure PHREG. The level of statistical significance was defined as $p<0.05$ (two-sided). The study was designed as an exploratory study as the risk factors of testicular cancer are largely unknown. The study was powered to detect an OR of 1.8 for any risk factor with a prevalence of 20%, and an OR 0f 2.0 for any risk factor with a prevalence of 10%. The study was not powered to confirm any risk for seminoma and non-seminoma cases separately. All analyses were carried out using SAS 8.2. ORs were not reported if a given category included less than three cases.

Results

The proportion of medically confirmed cryptorchidism was higher in cases (9.9%) than in controls (3.6%). Overall, non-seminoma cases were on average 5 years younger than seminoma cases and controls (non-seminoma: 30.0 [21-41]; seminoma: 35 [28-49]; controls: 35 [26-58] (median [10^{th} percentile – 90^{th} percentile])).

The distribution of number of occupations for cases and controls is shown in Table 1. Seven cases (six non-seminoma cases; one seminoma case) and 20 controls were still attending school or were students with no job history at the time of diagnosis (case) or first mailing (controls). Job histories of non-seminoma cases lasted 13 [4-25] years, of seminoma cases 19 [8-32] and of controls 18 [6-41] years (median [10^{th} percentile – 90^{th} precentile]). Except for the non-seminoma cases the number of occupational periods did not differ substantially between cases and controls.

Table 1: Frequency of economically active periods for cases and controls for whole study sample and for seminoma and non-seminoma.

Study group/ number of job periods	Number of cases	Percent	Number of conrols	Percent
Complete study sample	266	100.0	797	100.0
0	7	2.6	20	2.5
1-2	79	29.7	213	26.7
3-4	112	42.1	321	40.3
5+	68	25.6	243	30.5
Seminoma	167	100.0	725	100.0
0	1	0.6	13	1.8
1-2	42	25.2	192	26.5
3-4	72	43.1	299	41.2
5+	52	31.1	221	30.5
Non-seminoma	99	100.0	682	100.0
0	6	6.1	20	2.9
1-2	37	37.4	193	28.3
3-4	40	40.4	274	40.2
5+	16	16.2	195	28.6

The distribution of cases and controls by educational level and professional degree is shown in Table 2. Subjects with professional degrees (i.e. apprenticeship, technical colleges, study at university and university for applied sciences) were at higher risk as compared to subjects without professional training in the whole study group and in the the seminoma subgroup but not in the non-seminoma subgroup. No risk was observed for being employed before the age of 18 (OR=1.0; 95%-CI 0.7-1.3) (data not shown).

Table 2: Distribution of cases and controls by educational level and professional degrees and corresponding odds ratios with 95% confidence intervals

	Cases		Controls		
	N	%	N	%	OR (95%-CI)
Complete study sample	269	100.0	797	100.0	
Years at school					
≤9	89	33.1	304	38.1	1.0†
10	61	22.7	192	24.1	0.9 (0.6-1.3)
12	25	9.3	78	9.8	0.9 (0.5-1.5)
13	9	34.9	222	27.9	1.1 (0.8-1.6)
Unknown	0	0.0	1	0.1	-
Professional training					
None	22	8.3	95	11.9	1.0†
Apprenticeship	163	61.3	485	60.9	1.7 (1.0-2.8)
University degree	62	23.3	154	19.3	1.6 (0.9-2.8)
Other	19	7.1	63	7.9	1.0 (0.4-2.3)
Seminoma	170	100.0	725	100.0	
Years at school					
≤9	57	35.3	267	36.8	1.0†
10	39	22.9	180	24.8	0.9 (0.6-1.4)
12	17	10.0	75	10.3	0.9 (0.5-1.7)

13	54	31.8	202	27.9	1.0 (0.7-1.7)
Unknown	0	0.0	1	0.1	-
Professional training					
None	10	7.1	88	12.1	1.0†
Apprenticeship	110	65.3	446	61.5	2.5 (1.3-5.1)
University degree	40	23.5	142	19.6	2.1 (1.0-4.6)
Other	7	4.1	49	6.8	2.3 (0.7-7.2)
Non-seminoma	99	100.0	682	100.0	
Years at school					
≤9	29	29.3	225	33.2	1.0†
10	22	22.2	172	25.4	0.8 (0.4-1.5)
12	8	8.1	73	10.8	0.8 (0.3-1.9)
13	40	40.4	206	30.4	1.1 (0.6-1.9)
Unknown	0	0.0	1	0.1	-
Professional training					
None	12	12.1	80	11.7	1.0†
Apprenticeship	53	53.5	400	58.7	0.9 (0.5-1.9)
University degree	22	22.2	140	20.5	1.1 (0.5-2.5)
Other	12	12.1	62	9.1	0.5 (0.2-1.4)

†Reference.

No difference in average ISEI-score was observed between cases and controls (cases: mean score 42.5, median score 39; controls: mean score 42.4, median score 39). Risk estimates by ISEI-scores are presented in Table 3. Analyses of the maximum ISEI score reached during lifetime showed no increased risks, neither for the complete study sample, nor for the seminoma and non-seminoma study samples. Similarly, the analyses by ISEI of the job held longest and the last job held revealed no associations with testicular cancer.

Table 3: Distribution of achieved maximum ISEI score and of ISEI scores for the longest and last held job for whole study population and for histologic subgroups with corresponding odds ratios.

ISEI score	**Cases**		**Controls**		
	N	**%**	**N**	**%**	**OR (95%-CI)**
Complete study sample					
Maximum ISEI score					
[16-37)	5	22.0	156	19.6	1.1 [0.7-1.7]
[37-44)	47	18.1	172	21.6	0.8 [0.5-1.3]
[44-55)	51	19.7	151	19.0	1.0 [0.6-1.5]
[55-66)	51	19.7	151	19.0	0.9 [0.6-1.5]
[66-88]	53	20.5	147	18.4	1†
Missing	7		20		
Last held job					
[16-37)	95	36.7	266	34.2	0.9 [0.6-1.4]
[37-44)	35	13.5	131	16.8	0.8 [0.5-1.3]
[44-55)	38	14.7	145	18.6	0.7 [0.4-1.1]
[55-66)	44	17.0	117	15.0	0.9 [0.5-1.5]
[66-88]	47	18.1	119	15.3	1†
Missing	7		20		
Longest held job					

[16-37)	102	39.4	277	34.9	0.9 [0.6-1.4]
[37-44)	40	15.4	150	18.8	0.8 [0.4-1.3]
[44-55)	33	12.7	144	18.1	0.6 [0.3-1.0]
[55-66)	43	16.6	106	13.3	1.0 [0.6-1.6]
[66-88]	41	15.8	100	12.6	1[†]
Missing	7		20	2.4	
SEMINOMA					
Maximum ISEI score					
[16-37)	34	20.5	141	19.9	1.2 [0.7-2.2]
[37-44)	32	19.3	159	22.3	0.9 [0.5-1.5]
[44-55)	32	19.3	137	19.2	0.9 [0.5-1.6]
[55-66)	32	19.3	141	19.8	0.9 [0.5-1.6]
[66-88]	36	21.7	134	18.8	1[†]
Missing	1		13		
Last held job					
[16-37)	56	33.7	241	33.8	0.9 [0.5-1.5]
[37-44)	24	14.5	123	17.3	0.8 [0.5-1.5]
[44-55)	25	15.1	133	18.7	0.7 [0.4-1.3]
[55-66)	29	17.5	109	15.3	0.9 [0.5-1.6]
[66-88]	32	19.3	107	15.0	1[†]
Longest held job					
[16-37)	61	36.7	259	35.9	0.8 [0.5-1.4]
[37-44)	29	17.5	133	18.3	0.8 [0.5-1.5]
[44-55)	21	12.7	128	17.7	0.5 [0.3-1.0]
[55-66)	25	15.1	101	13.9	0.8 [0.4-1.5]
[66-88]	30	18.1	91	12.6	1[†]
Missing	1		13		
NON-SEMINOMA					
Maximum ISEI score					
[16-37)	22	23.7	128	19.5	0.9 [0.4-1.9]
[37-44)	16	17.2	148	22.3	0.7 [0.3-1.5]
[44-55)	19	20.4	129	19.5	0.9 [0.5-1.9]
[55-66)	19	20.4	133	20.1	1.0 [0.5-1.9]
[66-88]	17	18.3	124	18.7	1[†]
Missing	6				
Last held job					
[16-37)	37	39.8	223	33.8	0.9 [0.4-1.7]
[37-44)	12	14.0	110	16.6	0.7 [0.3-1.6]
[44-55)	14	14.0	126	19.0	0.7 [0.3-1.5]
[55-66)	15	16.1	103	15.5	0.9 [0.4-2.0]
[66-88]	15	16.1	100	15.1	1[†]
Longest held job					
[16-37)	40	40.4	230	33.9	1.1 [0.5-2.2]
[37-44)	12	12.1	130	19.1	0.7 [0.3-1.7]
[44-55)	12	12.1	128	18.8	0.6 [0.3-1.5]
[55-66)	18	18.2	91	13.3	1.4 [0.6-3.3]
[66-88]	11	11.1	83	12.2	1[†]
Missing	6	6.1	19	2.8	

[†]Reference.

ORs by EGP categories are shown in Table 4. An increased risk for testicular cancer was observed for ever holding an agriculture related job (OR=1.9 95%-CI 1.0-3.8). For seminoma cases the effect was of the same strength (OR=2.1 95%-CI 1.0-4.5), while for non-seminoma cases the OR estimate was smaller and statistically non-significant (OR=1.6 95%-CI 0.5-4.8). For all other classes no increased risk was observed. This pattern is seen for almost all analyses presented in Table 4. Compared with subjects in the highest EGP category, increased risks were observed for category IX-X for the first, the last and the occupation with the highest EGP category ever.

Table 4: Distribution of study subjects and corresponding odds ratios with 95%-CI by occupational sectors according to Erikson, Goldthorpe and Protocarero for complete study group and histologic subgroups

	Complete study sample					Seminoma					Non-seminoma#				
Category[1]	**Cases**		**Controls**			**Cases**		**Controls**			**Cases**		**Controls**		
	N	**%**	**N**	**%**	**OR [95%-CI]**	**N**	**%**	**N**	**%**	**OR [95%-CI]**	**N**	**%**	**N**	**%**	**OR [95%-CI]**
First held job															
I-II	25	9.5	69	8.9	1	15	8.9	63	8.8	1	10	10.8	60	9.1	1
III-V	40	15.3	140	18.0	0.9 [0.5-1.5]	24	14.2	126	17.7	0.9 [0.4-1.8]	16	17.2	126	19.1	0.8 [0.3-1.9]
VI-VII	132	49.6	404	52.0	1.1 [0.8-1.5]	88	52.7	372	52.2	1.2 [0.8-1.7]	44	47.3	335	50.8	0.9 [0.4-1.9]
VIII	55	21.4	148	19.0	1.1 [0.8-1.4]	33	20.1	138	19.4	1.1 [0.8-1.6]	22	23.7	128	19.4	1.0 [0.6-1.5]
IX-X	7	2.7	16	2.1	1.6 [0.5-4.6]	6	3.6	13	1.8	2.1 [0.6-6.7]	1	1.1	11	1.7	-
Last held job															
I-II	70	26.7	172	22.1	1	45	26.6	155	21.8	1	25	26.9	150	22.7	1
III-V	533	20.2	192	24.7	0.7 [0.4-1.0]	34	20.1	180	25.3	0.7 [0.4-1.2]	19	20.4	162	24.5	0.6 [0.3-1.1]
VI-VII	81	30.5	243	31.3	0.9 [0.6-1.3]	54	32.3	223	31.3	1.0 [0.6-1.6]	27	29.0	205	31.1	0.7 [0.4-1.3]
VIII	50	19.8	165	21.2	0.9 [0.7-1.1]	29	18.3	151	21.2	0.9 [0.7-1.2]	21	22.6	138	20.9	0.9 [0.6-1.2]
IX-X	5	1.9	5	0.6	3.0 [0.8-11.7]	4	2.4	3	0.4	4.3 [0.9-20.8]	1	1.1	5	0.8	-
Longest held job															
I-II	54	20.6	145	18.7	1	37	21.9	133	18.7	1	17	18.3	125	18.9	1
III-V	46	17.6	166	21.4	0.8 [0.5-1.2]	27	16.0	154	21.6	0.7 [0.4-1.2]	19	20.4	139	21.1	0.8 [0.4-1.6]
VI-VII	100	38.6	287	36.9	1.1 [0.8-1.6]	69	41.3	261	36.7	1.2 [0.8-2.0]	31	33.3	242	36.7	0.8 [0.4-1.5]
VIII	54	23.9	171	22.0	0.9 [0.6-1.3]	30	18.0	156	21.9	0.0 [0.5-1.2]	24	25.8	146	22.1	1.0 [0.7-1.4]
IX-X	5	1.9	8	1.0	1.3 [0.4-4.1]	3	1.8	8	1.1	1.0 [0.2-4.1]	2	2.2	8	1.2	-
Ever held job															
I-II	86	32.0	231	29.0	1.1 [0.8-1.5]	58	34.1	211	29.1	1.1 [0.7-1.5]	28	28.3	201	29.5	1.2 [0.7-1.9]
III-V	92	34.2	308	38.6	0.7 [0.5-1.0]	58	34.1	286	39.4	0.6 [0.4-0.9]	34	34.3	268	39.3	0.9 [0.5-1.4]
VI-VII	164	61.7	494	62.0	1.2 [0.9-1.6]	108	64.7	453	62.5	1.2 [0.8-1.7]	56	56.6	413	60.6	1.1 [0.7-1.7]
VIII	128	48.1	392	49.2	1.0 [0.7-1.3]	84	50.3	362	49.9	1.0 [0.7-1.4]	44	44.4	333	48.8	1.0 [0.6-1.5]
IX-X	16	6.0	30	3.8	1.9 [1.0-3.8]	12	7.2	23	3.2	2.1 [1.0-4.5]	4	4.0	22	3.2	1.6 [0.5-4.8]

[1]Categories were assigned as follows: I=Higher service (includes mostly professionals, large enterprise employers and higher managers (>10 subordinates)); II=Lower service (includes mostly associate professionals, lower managers (1-10 subordinates), higher sales); III=Routine clerical/sales (includes routine clerical and sales workers); IV=Small employers (includes small entrepreneurs (1-10 subordinates); V=Independent (own account workers, no employees, artists); VI=Manual foremen (manual workers with supervisory status (>1 subordinate)); VII=Skilled manual (mostly craft workers, some skilled service, skilled machine operators, also gardeners); VIII=Semi-unskilled manual (mostly machine operators, elementary sales services and state work creation scheme); X=Farmers/farm managers (self-employed and supervisory farm workers, irrespective of skill level); XI=Farm and forestry workers (employed farm workers, irrespective of skill level; also family farm workers).

Discussion

Different methods of assigning social position may produce different results in terms of trends in health and inequality.[31, 32] Four indicators of social position were analysed in this study. School education was not associated with testicular cancer risk. The elevated risk observed for professional training versus no training was restricted to the seminoma subgroup. Overall, our data provide no evidence that the examined social dimensions are associated with testicular cancer. This result is in line with other studies.[11, 17]

Elevated risks for EGP categories other than agriculture were not observed in this study. An excess risk in agriculture and related occupations have been observed in several previous studies.[9, 33-35] It has been suggested that the observed risks in agriculture and related occupations could be associated with specific exposures such as pesticides,[33, 35] fertilizers[36, 37] or contact with farm animals and zoonotic infections[33] which were not in the scope of this analysis. The absence of increased risks for non-agricultural occupational sectors based on the EGP corroborates previous studies.[14, 21, 38]

Social status based on ISEI was no risk factor for testicular cancer in this study. If a social gradient for testicular cancer in Germany existed in the past and exposures were associated with this gradient, this gradient may have been attenuated by an increase in exposures that do not differ by social position or for which the social gradient declined over time. The rising trends of testicular cancer in industrialised countries might be an indirect indication for such an increase of exposures that are (or have become) independent of social position.

This study has some limitations. First, the study suffered from only modest response among controls (cases 76%, controls 57%). In particular in the study region of Hamburg participation was lower among controls with lower education which might have resulted in an overestimation of the risk in the lower social status groups. Hence, it is possible that a participation bias might have biased the effect estimates. However, a sensitivity analysis excluding Hamburg revealed similar findings.

Second, some non-differential misclassification of social status is likely to have occurred. As the assessment of social status is not based on a dichotomous variable, the direction of bias due to non-differential misclassification cannot be predicted. However, our classification is based on occupational titles which are known to be reported with good validity. Moreover, the fact that different indicators of social position give similar results increases confidence in our findings.

Third, periods of unemployment and illness cannot be ranked by both scales utilised in this study. Non-consideration of such periods may lead to an underestimation of any social difference.[39]

The strength of this study is to measure occupational social factors on the basis of a complete history of occupations. This information was obtained by in-person interviews. The population-based design of this study alows permits full examination of social differences. Study subjects were not aware of this study hypothesis, and occupational biography is an unprejudiced variable, so reporting bias is unlikely to occur. Different possible confounding variables were considered by adjusting for post-educational degree or medical confirmed undescended testis and job frequency but the results remained stable in all analyses.

Conclusion

The absence of an effect was not specific to the ISEI score, as another occupational scaling method, the EGP typology, showed no associations with testicular cancer, except for farming and farm related jobs. Different social indicators may mean different things with regard to correlates of social position. Our data indicate that a simple social gradient of testicular cancer risk – if it had existed in the past – may no longer exist. Rather, our findings support the hypothesis that social inequalities in testicular cancer are not related occupation-based social position. More information is needed on the specific social correlates (e.g. work characteristics, living areas). It should be noted that education and occupation are not only indicators of access to material properties, but are also related to psychosocial properties.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *case-control studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4, 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	4, 5
		(*b*) For matched studies, give matching criteria and the number of controls per case	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	14
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6*
Bias	9	Describe any efforts to address potential sources of bias	13
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how matching of cases and controls was addressed	5
		(*e*) Describe any sensitivity analyses	13

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	9,10
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	Table 1 – Table 4
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	14
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Table 1 – Table 4
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.