

Socio-economic distribution of testicular cancer in Norway during four decades

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Abstract

The aim of this study is to study a possible social gradient for testicular cancer in Norway, and assess whether the gradient has changed since 1960. Testicular cancer has traditionally been considered a cancer of the affluent. The previous register-based studies are conflicting on whether there is a gradient, if the gradient is shifting and if there is a difference between seminomas and non-seminomas. We have used a linked file with data regarding social status from the censuses and data from the Cancer Registry of Norway regarding the occurrence of testicular cancer. We conducted a Cox-regression analysis of testicular cancer among all men ≥ 25 years when participating in the censuses of 1960, 1970 and 1980 and data extracted from the Personal register in 1990. For 1990, we did not have occupational data. The analysis was done for the following ten year intervals after each census. We found an increased risk associated with higher education during all periods in our study with an odds ratio over two when comparing the highest and lowest educated. Using occupational status we did only find an increased risk during the period 1981-1990, the period with both a large number of cases and occupational data. Even during that period, the effect of education was far more pronounced than occupation. The results were similar for seminomas and non-seminomas.

Introduction

Testicular cancer is primarily a cancer of the young, with a peak incidence around the age of 30 and a smaller second peak around 60 (1). Among the malignant tumours of the testis, most of them are germ cell tumours. These tumours are histologically divided into pure seminomas and non-seminomas (2), with seminomas accounting for around 60% of the germ cell tumours (3). The established risk factors are a family history of testicular cancer (4), contralateral cancer, cryptorchidism (5) and ethnicity, as blacks in the USA have a quarter of the white incidence rate (6). A registerbased study with a quantitative assessment of the proportions of cancer susceptibility accounted for by different factors showed 25% of the familiar variance could be explained by genetical factors, and 17% with shared childhood environmental factors (7).

It is most common in Western countries (1), with Norway among the most prevalent countries with an adjusted incidence rate of 11/100000 person years (3). There are great regional disparities in the incidence of testicular cancer, even among the Nordic countries, with Denmark and Norway having an incidence rate approximately twice that of Sweden and four times Finland (1). The large group of Finnish immigrants to Sweden retains their lower risk of testicular cancer compared to the Swedes after immigrating, without regards to the age of migration nor their duration of stay (8). Immigrants from non-Western countries to Denmark are also at lower risk (9).

The incidence of testicular cancer has risen in most Western countries since the end of WWII, this increase largely being a cohort effect (3). The birth cohorts born later are subject to a higher risk, except for men born during WWII in a number of European countries, including Norway. Those men are subject to a lower risk than those born previously or later (3). The register-based studies mainly show similar spatial and temporal trends for the histological subtypes seminomas and non-seminomas among the European nations (3). Some maternal and perinatal factors have also been investigated, and a register based study shows some associations with neonatal jaundice, retained placenta and maternal disease (10). Oestrogen exposure early in life has been implicated, but the indirect findings that could have supported the hypothesis are not conclusive (11;12).

There is evidence that semen quality and lower fertility even before diagnosis is associated with a higher risk of testicular cancer (13;14). Among the

Nordic countries the incidence of testicular cancer is associated with reduced semen quality in the male population (15). Therefore it has been hypothesised that testicular cancer belongs to an entity with chryptorchidism and low semen quality, and that the origin of this entity called testicular dysgenesis syndrome is very early in life, perhaps starting in utero (16). But it is argued that the association on individual basis could be due to other factors, and that this concept is not necessary (17).

The studies of socio-economic distribution of testicular cancer have yielded conflicting results. Testicular cancer was long considered to be a cancer of the affluent (18). Some register based studies using occupation as a marker of socio-economic status have found a positive gradient, showing an increased risk with higher status (19;20), whereas a newer study from Denmark using an untraditional classification of occupation did not show an increased risk associated with higher occupation or education (9).

Material and methods

We use data from the Norwegian censuses of 1960, 1970 and 1980 and data extracted from the Personal Register of 1990 in Statistics Norway for the purpose of determining the SES. The censuses are to cover the whole population, and participation is compulsory. Statistics Norway has collected data regarding occupation and education. The participants there were linked to a file from the Cancer Registry of Norway. Linkage between the files was done by Statistics Norway using the personal identification number given to all Norwegians which were later replaced with a participant number. For the occupation and employment to be better marker of the SES, we did only include the men with age ≥ 25 in the year of censuses in our analysis.

Dependent variables

Cancer diagnoses come from the Cancer Registry of Norway, from which we have the data for the first cancer episode. In this analysis we used date of diagnosis and the histological subtype. The notification of the Cancer Registry is mandated for all Norwegian practitioners and hospitals, and the registry covers entire Norway during the period we are studying. Regarding the histological

subtypes, we did only include the cases clearly coded as seminomas or non-seminomas in the analysis of the subtypes.

Independent variables

Occupation was classified according to the Erikson-Goldthorpe scheme in five groups based on employment (21). The Erikson-Goldthorpe scheme is most appropriate when studying urban populations. The farmers and the self-employed were excluded, as they were hard to fit in the Erikson-Goldthorpe hierarchical scheme. Those outside the working population at the time of censuses were also excluded. In 1990, Statistics Norway did not collect occupational data for the entire population, and therefore we did only do an analysis with education.

Education was defined as the highest obtained education in the Education Registry of Statistics Norway. The educational registry collects data regarding attained degrees from the Norwegian learning institutions and those with a degree from abroad who have registered their education. The immigrant's level of education was mostly registered by the Immigration Authorities, and this registration is the basis of the education if they did not register their previous degree later. The participants were divided into five groups based on the length of education necessary for achieving their highest degree: primary school (7-9 years), lower secondary school (10-11 years), upper secondary school (12 years), college (12-16 years) and university (over 16 years). For 1960, the groups with more than twelve years classified in one group. Those with unknown education that year were classified as primary school, because we considered those who did not have a known schooling at that time as having some education and basically having the same types of jobs as those with just primary.

Statistics

Age-adjusted hazard ratios were calculated using Cox regression assuming proportional hazards. The lowest level of education and the lowest social class were set as baseline. We used these measures of social status during the censuses in 1960, 1970 1980 and 1990 and calculated the hazard ratio for attaining testicular cancer in the following ten years. Those who died or emigrated were censored. We did this calculation for the total number of testicular tumours and for the tumours clearly classified as seminomas and non-seminomas. Some of the

tumours were not coded as seminomas and non-seminomas. Those were tumours other than germ cell tumours or tumours not classified in detail. Their numbers are small, under 6% of all tumours.

Results

The total number of cases for all men living in Norway from 25 years when participating in the censuses during the study period was 2927. The risk of acquiring testicular cancer was increased with higher education in all periods studied. For 1981-90 and 1991-2000, when the number of tumours was higher, the increase seemed to be stepwise. The hazard ratio was relatively unchanged during the decades we studied. On the contrary, SES classification using occupational categories resulted in no occupational gradient, except for the period 1981-90. The only occupational category in our study that was remarkable was those not included. This category had the lowest incidence in all periods studied. This covered about 15-25 % of the population. The results were relatively similar for seminomas and non-seminomas, with no obvious pattern distinguishing them from each other.

Discussion

When using the level of education as a SES indicator, we find a relatively constant positive social gradient in all periods. This difference seems convincing. Using occupation as a social gradient was not associated with an increase for those with higher status except for the period 1981-90, when the number of cases was substantially higher. For those excluded, there was a reduced risk compared to those in the lowest occupational category. If there was a higher odds with higher occupational status, the odds ratio would have been low. The association with occupation is in any case much weaker than with education. The results are the same for seminomas and non-seminomas.

Data considerations

Both occupational and educational data was at the beginning of each decade in the analyses. That gives us a fairly accurate indicator of the social status of the subjects at the time of diagnosis. Adult position will not catch socio-economic differences in the distribution of risk factors that are important earlier in life. The

size of material was relatively small for the first two decades. For the last two periods, the total number of cases was higher. The ratios for the last two periods are more suggestive of a stepwise pattern. One weakness when using occupational data are the number of participants who did not fit into our occupational classification. That includes students, farmers, self-employed, retired and those out of the labour force for other reasons. A large share of those outside the workforce tend to have a lower social status than the reference category, the unskilled workers. As testicular cancer is primarily a disease of the young, it could also be difficult to use occupational data to assess their social position. The educational registry was more reliable and covered practically speaking the whole population. As for those who are students, the educational registry will place them one rank lower than the education they will have the following decade.

Results

We have not found any similar register based studies where there was a discrepancy between education and occupation, so this finding is novel. The only occupational category showing a consistent deviation from the rest of the sample was those not included. As noted earlier, this category included those outside the labour force. In previous studies from Norway, a large share is the farmers, another share are those out of the labour force for other reasons. Those retired will also fall in this category. Some of those outside the labour force tend to have a more marginal position in the society. That might possibly account for at least a part of that difference. Pollan et al (19) uses the occupation of all men employed in 1970, and follows this cohort from 1971 to -89, having 1199 cases. The results were a positive socio-economic gradient, most obvious for seminomas. Another population based study from Finland follows the participants of the 1970 census in Finland from 1971-95. That study covers cases between the age of 45 and 64 years. That is a smaller sample of 174 cases. The result was a positive social gradient that is reduced during the study period. A newer population based study from Denmark with men over 30 years of age did not show this pattern, neither with occupation or level of education (9). This study has 1770 cases from the period 1994-2003. The occupational classification in that study was untraditional, based on the theory of the creative class by Richard Florida (22), perhaps not as

fitted for discriminating occupations based on social status. The educational classification consisted only of three groups.

For causes of death among the middle aged in Norway, a previous study using both educational and occupation status in Norway has shown different patterns for different diseases, with sometimes remarkable differences e.g. pancreatic cancer and lung cancer (23). This study shows the importance of using both education and occupation as a social marker when doing a register based study with long follow-up because the differences can be substantial. One explanation could be that education is a more relevant indicator of SES-status in Norway and the other Nordic countries. Another explanation could be that people with different education do different type of work in each category. The trends are similar for seminomas and non-seminomas. That suggests that the relevant risk-factors that are causing this SES gradient have the same impact on the risk of seminomas and non-seminomas.

Occupational exposures affecting the risk of obtaining testicular cancer are previously mostly considered for certain type of industrial workers and has been centred on chemical exposures (19). Those findings can not explain a positive socio-economic gradient. The impact of other traditional factors involved in other cancer types as smoking, diet, physical activity and smoking have been inconsistent (24), and the distribution of them among the different classes can not explain a positive socio-economic gradient. Testicular cancer is mostly a cancer of the young, and the environmental factors early in life may affect the risk of subsequent cancer. Therefore future studies with an estimation of perinatal and childhood socio-economic factors would be of interest. A socio-economic pattern or a lack of thereof will give rise to new hypothesis regarding the causes.

Table 1 Men in Norway aged 25 years and above at start of each study period, testicular cancers 1961-2000 in Norway and two histological subgroups across socio-economic status.

	All cases of cancer ^a				Seminomas ^a		Non-seminomas ^a	
	Population	% pop	n	OR	n	OR	n	OR
1960 census								
<i>Education</i>								
Primary	790735	75.5	234	1	162	1	57	1
Lower secondary	188625	18.0	106	2.19 (1.74-2.754)	73	2.19 (1.66-2.89)	28	2.28 (1.45-3.59)
Upper secondary	35568	3.4	23	3.00 (1.95-4.613)	15	2.87 (1.69-4.88)	8	3.91 (1.86-8.21)
Higher education	32612	3.1	17	2.00 (1.22-3.267)	13	2.21 (1.26-3.89)	4	1.86 (0.67-5.12)
<i>Occupation</i>								
Unskilled workers	240569	22.9	80	1	57	1	22	1
Skilled workers	340314	32.5	129	1.03 (0.78-1.36)	87	0.97 (0.70-1.36)	32	0.96 (0.56-1.65)
Low level employees	90202	8.6	41	1.40 (0.96-2.04)	27	1.30 (0.82-2.05)	11	1.36 (0.66-2.80)
Mid level employees	132407	12.6	49	1.08 (0.76-1.54)	35	1.08 (0.71-1.64)	13	1.05 (0.53-2.09)
High level employees	92112	8.8	38	1.17 (0.79-1.71)	30	1.29 (0.82-2.00)	7	0.79 (0.34-1.86)
Not included ^b	151936	14.5	43	0.54 (0.37-0.79)	27	0.47 (0.30-0.76)	12	0.63 (0.31-1.29)
Total number ^c	1047540	100	380		263		97	
1970 census								
<i>Education</i>								
Primary	730488	65.2	252	1	165	1	69	1
Lower secondary	144448	12.9	73	1.70 (1.31-2.21)	45	1.62 (1.16-2.25)	24	1.98 (1.24-3.15)
Upper secondary	125666	11.2	48	1.34 (0.98-1.83)	30	1.30 (0.88-1.92)	17	1.66 (0.98-2.83)
College	55493	5.0	36	2.44 (1.72-3.46)	24	2.59 (1.65-3.90)	10	2.34 (1.20-4.54)
University	58962	5.3	37	2.19 (1.55-3.09)	20	1.83 (1.15-2.91)	16	3.31 (1.92-5.70)
Other/unknown	5414	0.5	5	2.79 (1.15-6.76)	4	3.44 (1.27-9.26)	1	2.04 (0.28-14.7)
<i>Employment</i>								
Unskilled workers	344207	30.7	140	1	87	1	49	1
Skilled workers	286650	25.6	117	1.07 (0.84-1.38)	79	1.18 (0.87-1.60)	32	0.83 (0.53-1.29)
Low level employees	88306	7.9	40	1.29 (0.91-1.83)	24	1.26 (0.80-1.98)	14	1.25 (0.69-2.26)
Mid level employees	98134	8.8	57	1.75 (1.29-2.39)	42	2.12 (1.47-3.07)	13	1.09 (0.59-2.01)
High level employees	82404	7.4	38	1.19 (0.83-1.71)	22	1.12 (0.70-1.78)	15	1.33 (0.75-2.37)
Not included ^b	220770	19.7	59	0.50 (0.37-0.68)	34	0.46 (0.31-0.69)	14	0.37 (0.20-0.67)
Total number ^c	1120471	100	451		288		137	

Table 1 continued

	All cases of cancer ^a				Seminomas ^a		Non-seminomas ^a			
	Population	% pop	n=	OR	n	OR	n	OR		
1980 census										
<i>Education</i>										
Primary	503293	40.3	234	1	126	1	85	1		
Lower secondary	262778	21.0	171	1.67 (1.37-2.03)	108	1.96 (1.52-2.54)	57	1.45 (1.04-2.03)		
Upper secondary	257210	21.0	197	2.02 (1.67-2.43)	122	2.33 (1.82-2.96)	64	1.70 (1.23-2.35)		
College	100849	8.1	93	2.58 (2.03-3.29)	59	3.07 (2.25-4.19)	29	2.04 (1.34-3.12)		
University	100518	8.0	95	2.63 (2.07-3.34)	65	3.38 (2.50-4.56)	27	1.89 (1.23-2.92)		
Other/unknown	25416	2.0	13	1.36 (0.78-2.37)	9	1.76 (0.90-3.46)	4	1.08 (0.39-2.93)		
Missing ^d	141	<0.0	1		1		0			
<i>Occupation</i>										
Unskilled workers	255331	20.4	157	1	88	1	62	1		
Skilled workers	264142	21.1	187	1.19 (0.96-1.47)	119	1.35 (1.02-1.78)	64	1.02 (0.72-1.44)		
Low level employees	102390	8.2	85	1.47 (1.13-1.92)	54	1.68 (1.20-2.36)	25	1.07 (0.67-1.70)		
Mid level employees	178282	14.2	149	1.49 (1.19-1.87)	92	1.65 (1.23-2.22)	48	1.18 (0.81-1.72)		
High level employees	136202	10.9	118	1.42 (1.12-1.81)	78	1.67 (1.23-2.27)	37	1.12 (0.74-1.68)		
Not included ^b	313858	25.1	108	0.40 (0.31-0.51)	59	0.40 (0.28-0.55)	30	0.31 (0.20-0.48)		
Total number ^c	1250064	100	804		490		266			
1990 extraction										
<i>Education</i>										
Primary	395012	29.3	221	1	147	1	57	1		
Lower secondary	282171	20.9	280	2.05 (1.72-2.45)	170	1.89 (1.51-2.35)	95	2.581 (1.86-3.56)		
Upper secondary	364550	27.0	445	2.79 (2.37-3.28)	292	2.80 (2.29-3.41)	138	3.123 (2.29-4.26)		
College	123977	9.2	143	2.53 (2.05-3.12)	95	2.55 (1.97-3.31)	43	2.765 (1.86-4.11)		
University	145375	10.8	180	2.73 (2.24-3.33)	114	2.63 (2.06-3.36)	56	3.074 (2.12-4.45)		
Other/ unknown	38889	2.9	24	1.37 (0.90-0.09)	19	1.66 (1.03-2.67)	4	0.830 (0.30-2.29)		
Missing ^d	1630	0,1	0		0		0			
Total number ^c	1349974	100	1293		837		393			

Explanation table 1

^a: Number of cases the following decade.

^b: Those with no occupation at the time of census or extraction.

^c: Number of men \geq 25 years during the censuses or the data collection of 1990.

^d No values assigned.

Reference List

- (1) World Health Organization, International Agricultural Research Centre. Cancer incidence in five continents. 2002.
- (2) Ulbright TM. Germ cell tumors of the gonads: a selective review emphasizing problems in differential diagnosis, newly appreciated, and controversial issues. *Mod Pathol* 2005 Feb;18 Suppl 2:S61-S79.
- (3) Bray F, Richiardi L, Ekbom A, Pukkala E, Cuninkova M, Moller H. Trends in testicular cancer incidence and mortality in 22 European countries: continuing increases in incidence and declines in mortality. *Int J Cancer* 2006 Jun 15;118(12):3099-111.
- (4) Westergaard T, Olsen JH, Frisch M, Kroman N, Nielsen JW, Melbye M. Cancer risk in fathers and brothers of testicular cancer patients in Denmark. A population-based study. *Int J Cancer* 1996 May 29;66(5):627-31.
- (5) Akre O, Pettersson A, Richiardi L. Risk of contralateral testicular cancer among men with unilaterally undescended testis: a meta analysis. *Int J Cancer* 2009 Feb 1;124(3):687-9.
- (6) Brown LM, Pottern LM, Hoover RN, Devesa SS, Aselton P, Flannery JT. Testicular cancer in the United States: trends in incidence and mortality. *Int J Epidemiol* 1986 Jun;15(2):164-70.
- (7) Czene K, Lichtenstein P, Hemminki K. Environmental and heritable causes of cancer among 9.6 million individuals in the Swedish Family-Cancer Database. *Int J Cancer* 2002 May 10;99(2):260-6.
- (8) Ekbom A, Richiardi L, Akre O, Montgomery SM, Sparen P. Age at immigration and duration of stay in relation to risk for testicular cancer among Finnish immigrants in Sweden. *J Natl Cancer Inst* 2003 Aug 20;95(16):1238-40.
- (9) Marsa K, Johnsen NF, Bidstrup PE, Johannesen-Henry CT, Friis S. Social inequality and incidence of and survival from male genital cancer in a population-based study in Denmark, 1994-2003. *Eur J Cancer* 2008 Sep;44(14):2018-29.
- (10) Wanderas EH, Grotmol T, Fossa SD, Tretli S. Maternal health and pre- and perinatal characteristics in the etiology of testicular cancer: a prospective population- and register-based study on Norwegian males born between 1967 and 1995. *Cancer Causes Control* 1998 Oct;9(5):475-86.
- (11) Dieckmann KP, Endsinn G, Pichlmeier U. How valid is the prenatal estrogen excess hypothesis of testicular germ cell cancer? A case control study on hormone-related factors. *Eur Urol* 2001 Dec;40(6):677-83.
- (12) Zhang Y, Graubard BI, Klebanoff MA, Ronckers C, Stanczyk FZ, Longnecker MP, McGlynn KA. Maternal hormone levels among populations at high and low risk of testicular germ cell cancer. *Br J Cancer* 2005 May 9;92(9):1787-93.

- (13) Jacobsen R, Bostofte E, Engholm G, Hansen J, Olsen JH, Skakkebaek NE, Moller H. Risk of testicular cancer in men with abnormal semen characteristics: cohort study. *BMJ* 2000 Sep 30;321(7264):789-92.
- (14) Jacobsen R, Bostofte E, Engholm G, Hansen J, Skakkebaek NE, Moller H. Fertility and offspring sex ratio of men who develop testicular cancer: a record linkage study. *Hum Reprod* 2000 Sep;15(9):1958-61.
- (15) Jorgensen N, Asklund C, Carlsen E, Skakkebaek NE. Coordinated European investigations of semen quality: results from studies of Scandinavian young men is a matter of concern. *Int J Androl* 2006 Feb;29(1):54-61.
- (16) Skakkebaek NE. Testicular dysgenesis syndrome. *Horm Res* 2003;60 Suppl 3:49.
- (17) Akre O, Richiardi L. Does a testicular dysgenesis syndrome exist? *Hum Reprod* 2009 Sep;24(9):2053-60.
- (18) Rimpela AH, Pukkala EI. Cancers of affluence: positive social class gradient and rising incidence trend in some cancer forms. *Soc Sci Med* 1987;24(7):601-6.
- (19) Pollan M, Gustavsson P, Cano MI. Incidence of testicular cancer and occupation among Swedish men gainfully employed in 1970. *Ann Epidemiol* 2001 Nov;11(8):554-62.
- (20) Pukkala E, Weiderpass E. Socio-economic differences in incidence rates of cancers of the male genital organs in Finland, 1971-95. *Int J Cancer* 2002 Dec 20;102(6):643-8.
- (21) Eriksson R, Goldthorpe JH. *The constant flux*. Oxford: Oxford University Press, 1999.
- (22) Florida RL. *The rise of the creative class and how it's transforming work, leisure, community and everyday life*. New York, NY: Basic Books, 2002.
- (23) Naess O, Claussen B, Thelle DS, Smith GD. Four indicators of socioeconomic position: relative ranking across causes of death. *Scand J Public Health* 2005;33(3):215-21.
- (24) Garner MJ, Turner MC, Ghadirian P, Krewski D. Epidemiology of testicular cancer: an overview. *Int J Cancer* 2005 Sep 1;116(3):331-9.