

# Occupational risk factors for testicular cancer: a registry-based case-control study in Rhineland Palatinate – Germany

## Berufliche Risikofaktoren für Hodenkrebs: eine Register-basierte Fall-Kontroll-Studie in Rheinland-Pfalz – Deutschland

### Abstract

**Objectives:** Testicular cancer affects mainly men below the age of 50. An association with occupation and social status has been suggested but risk factors are not well understood. A registry-based case-control study focusing on occupation was performed in Germany.

**Methods:** All 348 testicular cancer cases with available gainful occupational information registered between 2000 and 2005; as well as 564 suitable controls (from a pool of other cancers) were drawn from the Cancer Registry of Rhineland-Palatinate. Unconditional logistic regression was used to compute odds ratios (OR) and associated 95% confidence intervals (CI).

**Results:** Slightly elevated OR were observed for technicians and related professionals (OR 1.62, 95% CI 1.00–2.63) and for clerical support workers (OR 1.71, 95% CI 1.14–2.56). This increase was highest in the age group 20–50 for technicians (OR 2.02, 95% CI 1.23–3.33) and clerks (OR 2.00, 95% CI 1.30–3.09), respectively. An association with testicular cancer was observed for no other occupation.

**Conclusion:** An increased risk of testicular cancer was observed for technicians and related professionals and clerical support workers. This could be related to socioeconomic status or sedentary life style, two factors that were identified in previous studies. While the feasibility of a purely registry-based study was shown, missing occupational data and the choice of cancer controls represent challenges to the validity of this approach.

**Keywords:** cancer, clerical support workers, men's health, occupational health, sedentary life style, technicians

### Zusammenfassung

**Ziele:** Hodenkrebs betrifft vor allem junge Männer im Alter von unter 50 Jahren. Ein Zusammenhang zwischen erhöhtem Auftreten von Hodenkrebs und Beruf bzw. sozialem Status wurde untersucht (in Betracht gezogen), aber die Risikofaktoren sind bislang noch nicht umfassend erforscht. Eine Register-basierte Fall-Kontroll-Studie zur Untersuchung eines Zusammenhangs von beruflicher Erwerbstätigkeit und Hodenkrebs wurde in Deutschland durchgeführt.

**Methoden:** 348 Hodenkrebsfälle mit den verfügbaren Informationen zur Erwerbstätigkeit zwischen 2000 und 2005, sowie 564 geeignete Kontrollen (aus einem Pool anderer Krebsarten) wurden aus dem Krebsregister Rheinland-Pfalz gezogen. Mittels einer unbedingten logistischen Regression wurden Odds Ratios (OR) und deren 95%-Konfidenzintervall (CI) berechnet.

**Ergebnisse:** Eine leichte Erhöhung wurde für Techniker und verwandte Berufe (OR 1,62, 95% CI 1,00 bis 2,63) und für Bürokräfte (OR 1,71, 95% CI 1,14 bis 2,56) beobachtet. Dieser Anstieg war am höchsten in

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der Altersgruppe 20–50 für Techniker (OR 2,02, 95% CI 1,23 bis 3,33) sowie für Bürokräfte (OR 2,00, 95% CI 1,30 bis 3,09). Es wurde keine weitere Assoziation zwischen Hodenkrebs und anderen Berufen beobachtet.

**Fazit:** Ein erhöhtes Risiko für Hodenkrebs wurde für Techniker und verwandte Berufe sowie für Bürokräfte beobachtet. Dies könnte auf den sozioökonomischen Status bzw. die bewegungsarme Lebensweise zurückgeführt werden, was auch schon in früheren Studien gezeigt wurde. Während die Machbarkeit einer rein Register-basierten Studie gezeigt wurde, stellen die fehlenden beruflichen Daten sowie die Wahl der Krebskontrollen eine Herausforderung für die Richtigkeit dieses Ansatzes dar.

## Introduction

Testicular cancer is a rare disease; it occurs most commonly in young men in their third to fifth decade of life and accounts for about 1–3% of all cancers in men in Western countries and about 17% of cancers in men below 45 [1], [2]. Germany is one of the countries with the highest incidence rates of testicular cancer, with an estimated age-standardized incidence rate (Europe standard) of  $11.1/10^5$  in 2004 [3].

The risk factors associated with testicular cancer are not very well known apart from the association with cryptorchidism (undescended testis) documented in multiple studies [4], [5], [6], [7], [8], [9], familial association [10] and exposure to high level of estrogen *in utero* [11].

Some occupational exposures were suggested to be associated with a higher risk for testicular cancer. These occupations include work in agriculture [12]. Rural residence during adulthood was associated with an increased risk of testicular cancer in Italy (Odds Ratio (OR) = 3.31; 95% confidence interval (CI) 1.36–8.01); use of pesticides in gardening was similarly associated with an elevated OR of 1.83 (95% CI 1.02–3.29) [13]. Further relevant occupations seem to include fire fighters and carpenters. In professional fire fighters in Florida the Standardized Incidence Ratio (SIR) was 1.60 (95% CI 1.20–2.09) [14], and similar results were obtained in New Zealand [15] and in Germany [16]. Studies concerning carpenters also showed an increased risk for testicular cancer; in New Jersey the SIR of testicular cancer for carpenters between 1979–2000 was 1.29 (95% CI 0.78–2.01). The incidence rate was increased after a 15-years lag from initial work date (SIR=2.40; 95% CI 1.29–4.32) [17], with similar results documented in Germany [18]. Results for selected other occupations have shown inconsistency associated with an increased risk of testicular cancer. A study on Vietnam war veterans showed a twofold elevated risk for testicular cancer with an OR of 2.5 (95% CI 1.1–5.7) [19]. No clear associations were seen for metal workers [20], but paper and pulp maintenance workers (and not process workers) in Sweden had higher risk of testicular cancer [21]. No clear risk was observed for professional and technical workers [22].

In order to shed more light on the occupational risk factors of testicular cancer and to assess the feasibility

of a registry-based case-control study, data from the cancer registry of the German federal state of Rhineland-Palatinate were used to conduct a case-control study for testicular cancer, where both the cases and controls were cancer patients registered in the years 2000–2005. Because of the small number of cases, only broad occupational categories, with limited specificity regarding occupational exposures were used.

## Material and methods

The study population includes cases and controls with registered malignancies in the Rhineland Palatinate cancer registry for the period 2000–2005. The registry has an overall completeness of over 90% for all cancers [3]. Cases of testicular cancer diagnosed between 2000 and 2005 in the cancer registry and having occupational information were compared to a set of cancer diagnoses which were chosen to represent the controls pool. These included primary cancer of the stomach, colon, pancreas, kidney, Hodgkin's lymphoma, thyroid, and lip, oral cavity and pharynx. These cancer types were selected because there was no strong indication of their association with occupational risk factors [23], [24], [25], [26], [27], [28], [29], [30]. Additionally, these cancers affect a wide age group including young patients which made it possible to broadly match them to testicular cancer patients basing on age groups [3], [23].

From the group of 15,868 potential controls, controls were matched by 5 years age groups ( $\leq 24$ , 25–29, 30–34, 35–39, 40–44, 45–49,  $\geq 50$ ), giving priority to controls with occupational information. The selection probabilities for the controls were 1 for the age groups  $\leq 24$ , 25–29, 30–34, 35–39, 0.26 for the age groups 40–44, 45–49 and 0.02 for the age group  $\geq 50$ . However, not all the cancer types included in the control pool eventually contributed controls to be matched to our cases, either due to absence of registered patients in specific age group (mostly people younger than 40 years) or because of missing occupational information. As a result of these restrictions, only a subset of cancers (colon, pancreas, kidney, thyroid cancers and Hodgkin's lymphoma) eventually formed our control population from the potential control pool.

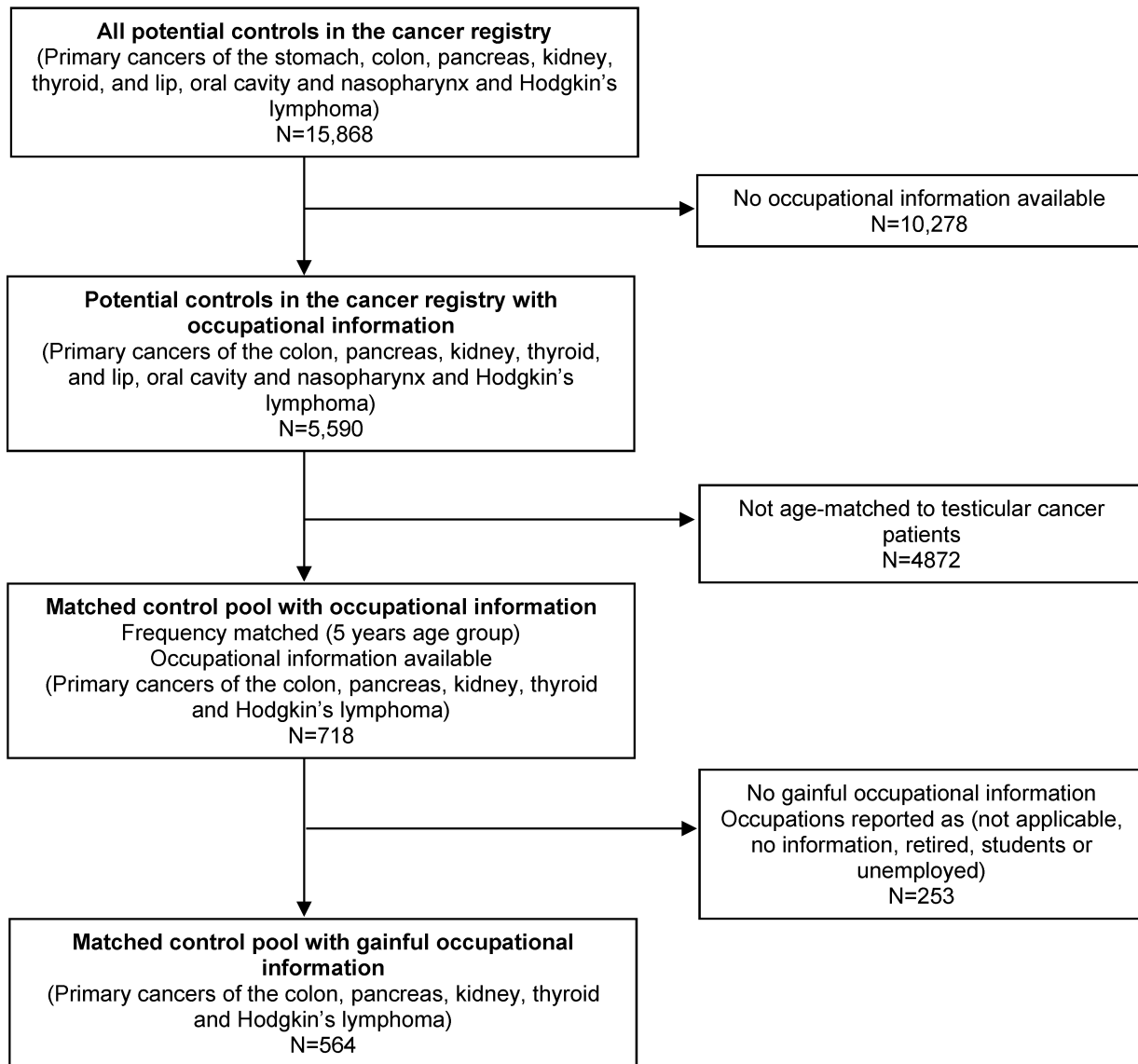


Figure 1: Stepwise selection of the controls population

Frequency matching was implemented because of the relatively young age of testicular cancer cases which rendered the selection of individually matched controls rather difficult. The occupations were originally coded according to the German Federal Employment Office coding system. They were re-coded according to the International Standard Classification of Occupations version 2008 [31], for better comparability with international results.

Due to the very large proportion of registrations with missing occupational information in the control population (about 70% of the potential controls in the cancer registry) a decision to include only cases and controls with job titles indicating gainful occupations in the analyses was made. The availability of job information for the potential controls in the age groups 25–49 was similar to that of testicular cancer patients as shown in Table 1. The stepwise process of controls selection is illustrated in more details in Figure 1.

Table 1: Availability of gainful occupational information for the testicular cancer cases and potential control population

Age group	Testicular cancer		All controls*	
	N	%	N	%
–24	18	19.15	17	25.76
25–29	38	37.62	21	41.18
30–34	79	43.17	39	44.83
35–39	93	44.50	82	44.81
40–44	73	46.79	135	41.16
45–49	23	47.92	301	41.35
50 +	24	32.88	4,995	34.63
Total	348	40.28	5,590	35.23

\* potential controls, before matching to testicular cancer cases

Because of the relatively small number of cases, the analysis included only the major occupational groups and the main subgroups rather than specific job titles to avoid diluting any possible effects.

Table 2: Main characteristics of the testicular cancer cases and controls included

Criteria	Cases (348)	Controls (564)
Mean age at diagnosis (years) $\pm$ SD	38 $\pm$ 12	45 $\pm$ 13
Cancer type	Testicular cancer (100%)	Colon Cancer (0.33%) Pancreatic Cancer (7.70%) Kidney Cancer (39.70%) Thyroid cancer (17.00%) Hodgkin's lymphoma (35.30%)
<b>Spread</b>		
Local	43.90%	30.90%
Regional	12.40%	26.70%
Distal	5.70%	10.90%
Unclear *	38.00%	31.50%
<b>Confirmation of the diagnosis</b>		
Clinical	0.09%	0.80%
Histology	95.50%	97.50%
Cytology	0.00%	0.30%
Others	0.00%	0.10%
Unclear *	4.40%	1.30%

\* Unclear indicates that no information was available in the cancer registry files

The analysis of the case-control study included calculating the odds ratio for the different jobs via unconditional logistic regression in relation to the different job titles. The reference group for the analysis was all the other occupations combined against the occupational title under study. To investigate the effect of this approach, a sensitivity analysis was done with another reference group including a set of occupational titles with no proven associations with testicular cancer risk reported in the literature (armed forces, services and sales workers, skilled agriculture, and elementary occupations). Age-group specific odds ratios for the occupational distribution of the patients in the highest risk age group (20–50) were also calculated. No additional adjustment for confounders could be done as no relevant additional information on cases and controls is available in the registry.

## Results

There were 864 primary testicular cancer cases and 718 age matched controls selected from the Rhineland-Palatinate cancer registry. For the analysis 348 cases and 564 cancer controls with gainful occupational information were available. The vast majority of the cases and controls were verified histologically (95.5% and 97.5% respectively) (Table 2).

The odds ratios for testicular cancer risk are shown in Table 3. There was a significant risk elevation for technicians and associate professionals, OR=1.62 (95% CI 1.00–2.63) and clerical support workers, OR=1.71 (95% CI 1.14–2.56) mostly for the subgroup general and keyboard clerics with an OR=1.83 (95% CI 1.21–2.77). In analyses stratified by age group the OR for the technicians and associate professionals and the clerical support workers was also elevated for the age-group 20–50 years, OR=2.02 (95% CI 1.23–3.33) and 2.00 (95% CI 1.30–3.09) respectively (Table 4).

When the OR was calculated against a selected group of occupations as reference (see methods), no significant increase was noted for any of the occupations, but the directions of associations were unchanged (Table 5).

## Discussion

This is the first registry-based case-control analysis to be conducted in the Rhineland Palatinate cancer registry, where both cases and controls were anonymously derived from the registry database. The registry has a good completeness of over 90% (and 95% for testicular cancer). The study showed a slight increase in the OR for testicular cancer in association with occupational codes related to “technicians and associate professionals” and to “clerical support workers”. However, due to the large number of missing occupational data these results need to be viewed with great caution.

The feasibility of the registry-based case-control approach was tested with a view to better utilize the data stored in the cancer registry. However, this approach was associated with some difficulties. The use of cancer cases as controls instead of the general population might raise concerns regarding the findings of this study. However, the cancer types included in our control group are generally not known to be strongly associated with occupational exposures. Thyroid cancer and Hodgkin's Lymphoma are considered to be associated with radiation exposure [23], [25], but this was not a limitation since testicular cancer does not seem to be associated with radiation [32]. Other difficulties encountered include the fact that the average age of male cancer patients is usually high while testicular cancer patients are mostly young or middle-aged men. This led to problems in finding appropriate age-matched controls for testicular cancer patients since there were very few cancers with relatively young age at occurrence. An additional limitation of this study was the high propor-

**Table 3: Age adjusted Odds ratio of testicular cancer risk in association with different occupational categories (ISCO-08). Gainful occupations only with all other occupations as reference group**

Job title	Against all other occupations			
	Cases	Control	OR*	95% CI
<b>Armed Forces Occupations</b>	5	9	0.75	0.24–2.28
<b>Managers</b>	2	8	0.39	0.08–1.93
Administrative and commercial	1	4	0.51	0.05–90.00
Chief executives, senior officials and legislators	1	4	0.79	0.09–32.00
<b>Professionals</b>	45	68	1.03	0.68–1.57
Science and engineering Professionals	18	17	1.82	0.88–3.77
Teaching professionals	7	16	0.58	0.22–49.00
Business and Administration Professionals	7	12	1.21	0.46–22.00
Information and communications	7	9	0.92	0.32–2.63
Health professionals	3	2	2.32	0.36–14.83
Legal, social and cultural professionals	3	12	0.29	0.08–1.06
<b>Technicians and associate professionals</b>	40	40	1.62	1.00–2.63
Science and engineering associate professionals	24	23	1.67	0.90–3.08
Legal, social, cultural and related associate professionals	10	11	1.35	0.55–3.32
Health associate professionals	6	6	2.41	0.73–8.02
<b>Clerical support workers</b>	61	59	1.71	1.14–2.56
General and keyboard clerks	60	58	1.83	1.21–2.77
Other clerical support workers	1	1	1.37	0.07–25.37
<b>Service and sales workers</b>	26	34	1.28	0.74–2.25
Sales workers	22	24	1.56	0.82–2.94
Protective services workers	1	3	0.74	0.07–7.46
Personal service workers	3	7	0.73	0.18–2.92
<b>Skilled agricultural, forestry and fishery workers</b>	16	21	1.46	0.71–3.01
Market-oriented skilled agricultural workers	14	20	1.54	0.72–3.30
Market oriented skilled forestry, fishing and hunting workers	2	1	2.81	0.23–34.36
<b>Craft and related trades workers</b>	119	195	1.04	0.77–1.40
Metal, machinery and related trades workers	56	59	1.44	0.95–2.19
Building and related trades' workers excluding electricians	38	77	0.88	0.57–1.36
Food processing, Wood working, Garment and other craft and related trades workers	15	31	0.65	0.33–1.27
Electrical and electronic trades workers	8	26	0.43	0.19–0.98
Handicraft and printing worker	2	2	2.00	0.26–15.40
<b>Plant and machine operators and assemblers</b>	32	63	0.76	0.48–1.21
Stationary plant and machine operators	9	17	0.79	0.32–1.95
Assemblers	5	10	0.76	0.24–2.39
<b>Elementary occupations</b>	2	3	1.14	0.17–7.54
Agricultural, forestry and fishery laborers	1	1	2.64	0.16–42.51
Refuse workers and other elementary workers	1	2	0.57	0.05–7.03

ISCO-08: International standard classification of occupations – version 2008  
CI: Confidence intervals  
\* The odds ratios for the different jobs were calculated via unconditional logistic regression. The reference group for the analysis was all the other occupations combined against the occupational title under study.

tion of missing occupational information for both the cases and controls. Less than 50% of all cases and a little more than 30% of the overall potential controls had occupational information available. To overcome this limitation the analysis was restricted to cases and controls

with gainful occupational information available in the registry. This may induce selection bias if availability of occupational information is linked to other differences relevant for the comparisons performed in this study, or if particular occupations had a higher probability to be

**Table 4: Odds ratios for different occupations in 20–50 years age category for testicular cancer patients gainful occupations only (main occupational categories)**

Job title	20–50			
	Cases	Control	OR	95% CI
Armed forces occupations	4	9	0.62	0.18–2.10
Managers	2	7	0.65	0.13–3.28
Professionals	39	62	0.86	0.55–1.34
Technicians and associate professionals	40	35	2.02	1.23–3.33
Clerical support workers	58	46	2.00	1.30–3.09
Service and sales workers	24	29	1.38	0.77–2.47
Skilled agricultural, forestry and fishery workers	15	13	1.76	0.80–3.85
Craft and related trade workers	108	169	0.88	0.62–1.19
Plant and machine operators, and assemblers	28	51	0.82	0.50–1.36
Elementary occupations	2	3	1.09	0.17–7.14

CI: Confidence intervals

**Table 5: Age adjusted Odds ratio of testicular cancer risk in association with different occupational categories gainful occupations only with selected occupations as the reference group**

Job title	Against selected occupations*			
	Case	Control	OR	95% CI
Managers	2	8	0.42	0.08–2.22
Professionals	45	68	0.74	0.42–1.30
Technicians and associate professionals	40	40	1.29	0.69–2.41
Clerical support workers	61	59	1.32	0.75–2.32
Craft and related trades workers	119	195	0.73	0.46–1.17
Plant and machine operators, and assemblers	32	63	0.65	0.36–1.17

CI: Confidence intervals  
\* Selected occupations serving as reference group: Armed forces, services and sales workers, skilled agriculture, and elementary occupations

noted in the registry. While this remains a possibility, we observed a wide range of occupational codes among both cases and controls. Additionally, the availability of occupational information in the high risk age groups was similar in testicular cancer patients and the selected controls.

We found an increased risk of testicular cancer in two groups, technicians and associate professionals; and clerical support workers. An increase in testicular cancer risk in these groups was also reported in some previous studies [22], [33]. However, in a large prospective study that included 7,519 incident cases of testicular cancer from Denmark, Finland, Iceland, Norway and Sweden (NOCCA study), the Standardized Incidence Ratios (SIR) for these occupations were only slightly elevated. The SIR for technician workers and clerical workers were 1.06 (95% CI 0.99–1.15) and 1.14 (95% CI 1.02–1.27) respectively. In the NOCCA study, physicians were found to have the highest risk for testicular cancer, with an SIR of 1.48 (95% CI 1.15–1.88) [34]. In our study the risk for health professionals and health associate professionals was non-significantly elevated, OR 2.32 (95% CI 0.36–14.83) and 2.41 (95% CI 0.73–8.02) respectively. Combining both groups into one “health related jobs” group resulted in an OR of 1.82 (95% CI 0.73–4.54). Obviously, the Nordic study included a much larger number of cases in comparison to our study, did not rely on cancer controls

and was much less afflicted by missing data issues, which once again underlines the need for caution when interpreting our data. It is, however, interesting to note that both studies indicate risk elevations associated with medical occupations.

The two groups (technicians and associate professionals and clerical support workers) with elevated OR noted in our analysis share a similar job environment, including long hours of office work. The increase of testicular cancer risk in both technicians and clerical support workers could be expected to be related to their socioeconomic status which, although not available in the cancer registry data, may be higher than in comparison groups. Several studies have indicated that testicular cancer is associated with higher socioeconomic status [35], [36], [37], but more detailed mechanisms are not understood. A possible explanation of our findings is the sedentary life style characteristic of these two groups. In a review discussing the lifestyle factors associated with testicular dysfunction, sedentary work habits were suggested to increase testicular temperature [38]. An increase in testicular temperature has long been associated with the increase in testicular cancer incidence; however, in a study conducted in the United States, exposure to elevated temperatures ( $\geq 80^{\circ}\text{F}$  or  $26.7^{\circ}\text{C}$ ) was not significantly associated with testicular cancer risk (OR 1.20; 95% CI 0.80–1.80) [39]. Other studies investigating the effect

of raised temperature on testicular cancer incidence have also failed to detect an association [8], [40], [41], [42]. The specific work environment may also lead to reduced physical activity. The UK testicular cancer study group reported a protective effect of exercise against testicular cancer, whereas a positive association with sedentary life style was reported [8]. A Canadian study also showed protective effects of moderate to high levels of recreational and – somewhat less clearly – for occupational activities [5]. An inverse association between physical activity during childhood and the risk of testicular cancer was also reported [43]. Contrary to the above findings, many studies reported no effect [44], [45] or even positive associations [46] between testicular cancer and physical activity.

In conclusion, we found a slightly increased risk of testicular cancer for both technicians and associate professionals and for clerical support workers. Whether this increase is related to specific occupational exposure in those people including the lifestyle factors associated with these occupations such as increased scrotal temperature or lack of physical activity due to prolonged periods of sitting, or exposure to electromagnetic fields from electrical equipments such as laptops [32], [47] is still an open question. These exposures (heat, physical activity and exposure to electromagnetic fields) were previously discussed as possible causes for testicular cancer among other possibilities in pulp and paper workers in Sweden, a relationship was not confirmed though [21]. Further studies are needed to investigate these associations in more detail. The feasibility of a registry-based case-control study in the cancer registry could be demonstrated, while limitations were highlighted. For the future, such studies are likely to become more informative if the amount of missing data can be reduced, as physicians provide more complete data to the registry wherever possible.

## Notes

## Competing interests

The authors declare that they have no competing interests.

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## Authorship

All authors participated in planning the study and writing the manuscript.

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