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Death and hospital contact in a cohort from Thyborøn-Harboøre an environmentally contaminated site in Denmark

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We studied mortality and hospital contact in people from Thyborøn-Harboøre, an environmentally contaminated fishing community on the Danish West Coast. The population and a comparison group from other fishing communities on the Danish West Coast were identified from historical data in the Central Population Register. All persons were followed up for death and hospital contacts to March 2023. Event rates were compared with Poisson regression; adjusted rate ratios (aRR); and 95% confidence interval (CI). The old cohort included inhabitants in Thyborøn-Harboøre in 1968–1970 before pollution was controlled; 4914 persons/2485 deaths. All-cause mortality, aRR 1.06 (95% CI 1.01–1.11), and cancer mortality, aRR 1.17 (95% CI 1.05–1.30), were elevated; especially for kidney cancer aRR 1.82 (95% CI 1.07–3.12). Hospital contacts were elevated for psychiatric disorders; with an aRR of 4.07 (95% CI 1.41–11.72) for anxiety in men. As there is still considerable concern in the area about possible health consequences from stored chemicals, we included also a new cohort of newborn and immigrants to the area in 1990–2006; 2933 persons/302 deaths. All-cause mortality, aRR 1.26 (1.11–1.43) (men 1.15 and women 1.44), and cancer mortality, aRR 1.47 (95% CI 1.14–1.89) were elevated. Hospital contacts were elevated for ischemic heart disease/heart attack and indicated for autism/obsessive compulsive disorder in boys. In conclusion, mortality data confirmed incidence data of excess kidney cancer in the old cohort. The new cohort had a generally elevated mortality, possibly indicating selective immigration from other parts of Denmark. However, the new cohort is still relatively young, and the mortality pattern needs to be monitored.

Keywords Environmental contamination, Cohort study, Mortality, Hospital contact

Abbreviations

ADHD	Attention deficit hyperactivity disorder
aRR	Adjusted rate ratio—adjusted for sex (where relevant), running age, and calendar year
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CPR	Central population register
HH	Holmsland-Hanstholm
IBD	Inflammatory bowel diseases
ICD	International classification of diseases
NR	Not reported
OCD	Obsessive compulsive disorder
TH	Thyborøn-Harboøre

The possible long-term health consequences of exposure to chemical waste are an issue of concern both for the affected individuals and for the handling of chemical waste. However, the mixed exposures from chemical waste and the long-term latency of some diseases make it very difficult to identify possible causal associations between

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exposures and health risks¹. In the absence of ideal strategies to overcome these limitations, studies of worst case-scenarios from sites with appropriate health data have been suggested².

After World War II, chemical production expanded in Denmark with a focus on chemicals for use in agriculture. In 1953, one of the main producers moved to a small fishing community on the Danish West Coast called Thyborøn-Harboøre. Various chemicals were produced at the factory including phenoxy herbicides for weed control, and mercury compounds for protection of grain against fungus. However, parathion, an insecticide widely used on cereals, fruit, vines, vegetables, ornamentals and cotton³, soon became the main product.

Wastewater disposal to the North Sea, dumps of both liquid and solid waste in the sandy areas, and leakages from the factory ground polluted the area. As the pollution dates back to the 1950s, 1960s, and 1970s, quantitative data are unfortunately not available. However, a thorough investigation of the pollution in the late 1980s identified more than 100 xenobiotic compounds in the wastewater⁴. Furthermore, in Nissum Bredning, the water surrounding the factory ground, mercury accumulated in flounders, eels, and mussels; and in 1980–1982 concentrations of 2000–2500 ppb weight were found⁵. According to long-term Thyborøn inhabitants, fishing for private consumption was common in this water. The investigation was followed by initiation of regulation and better control, but the old contamination remained. The area also housed two smaller fishmeal-and oil processing companies, from where leakages of fish-oil and polluted wastewater were reported^{6,7}. Today the area is the chemically polluted area in Denmark of highest concern⁸.

In 2021, we found that people who lived in Thyborøn-Harboøre in 1968–1970 had a 20% higher cancer incidence than a comparison group of people who lived at the same time in other fishing communities at the Danish West Coast and without chemical factories⁹. The excess risk derived in particularly from cancers of the kidney and urinary bladder, where both men and women from Thyborøn-Harboøre had doubled risks. Furthermore, anecdotal cases of acutely blurred eye sights and gradual development of neurological disabilities have been reported from men working at the chemical factory in the pre-regulation period^{10,11}.

To get a comprehensive view of possible long-term health consequences for persons who have lived in Thyborøn-Harboøre, we used available register data to investigate causes of death and hospitalization. As present inhabitants in the area are concerned about possible health consequences of leakages from the stored chemicals in the area, we included also a cohort of newcomers to the area after 1990.

Materials and methods

Study-population

From the Danish Central Population Register (CPR) it is possible to identify all persons with a permanent address in Denmark at any time from 2 April 1968 until today. For each person, dates of immigrations, emigrations, internal movements in Denmark, and death are registered. Computerized population data were not available prior to 1968. We selected two subpopulations for the study. First, people who lived in Thyborøn-Harboøre in 1968–1970 representing the early living conditions in the area. Second, people who live in Thyborøn-Harboøre in 1990–2006 but not prior to 1990. The latter population was still young but included in the analysis as newcomers after pollution control started in the late 1980s. The cohort was further divided into people who moved into the area and people born there. Newcomers after 2006 were not included because new municipality codes did not allow identification of inhabitants from the small study areas. As in the cancer incidence study, reference cohorts from the two other fishing communities, Holmsland-Hanstholm, were identified⁹.

Follow-up

These populations were followed up in CPR for death and emigration until end of follow-up on 1 March 2023. Risk periods were calculated for each person starting from date of first registered address in Thyborøn-Harboøre until occurrence of the studied event, emigration, death or end of follow-up for the outcome. For the old cohort the first possible date was 2 April 1968, for the younger cohort it was 1 January 1990, and for both cohorts the last possible date was 1 March 2023, see Supplementary Table S1.

Cause of death was registered by linkage with the Cause of Death Register starting 1970 and ending 2021. The underlying cause of death was used in the analysis. The follow-up period included both deaths coded according to International Classification of Diseases (ICD)-8 and ICD-10. We used a conversion table developed by the Danish Health Authority¹², Supplementary Table S2. It should be noted that cause of death was missing for people with a permanent address in Denmark, but dying outside Denmark, and for people dying before 1 January 1970 or after 31 December 2021.

To identify hospitalizations, the cohorts were linked with the National Patient Register (LPR). Registration of somatic diagnoses in LPR started in 1977, registration of psychiatric diagnoses in LPR started in 1995, and both ended by 1 February 2023, person years were accumulated accordingly. Up until 1995, only in-patient contacts were included in the National Patient Register (LPR), but from that time onwards also out-patient hospital contacts were included in LPR. A person was considered a hospitalized case for a given disease on the first date of hospitalization for this disease. The main discharge diagnosis was used. Diseases were grouped according to the list used in the Grindsted-report¹³, Supplementary Table S3.

Statistics

Poisson regression with control for sex, running age and calendar time was used to compare cause-specific mortality/hospitalization rates between Thyborøn-Harboøre and Holmsland-Hanstholm. For the old cohort, we checked for interactions between area and sex, area and age, and area and calendar time for the old cohort for all-cause mortality by including two-factor interactions one at a time. We also adjusted the estimate of the difference between areas by including birth cohort in the model. Results were presented as adjusted rate ratios (aRR) with 95% confidence intervals (CI). Analysis was undertaken with SAS version 9.4 on the research server in Statistics Denmark.

Ethics

The study was a retrospective cohort study. Data were retrieved from the Danish Central Population Register, the Danish Cause of Death Register, and the Danish National Patient Register. These databases are not publicly available, but the databases can be used for research projects considered beneficial for the society. The use of data and the experimental protocol were approved by Region Zealand with the registration number REG-108-2018. Region Zealand is the public authority in charge of Nykøbing Falster Hospital, where the study was undertaken. According to Danish legislation, approval by the relevant public authority serves as ethical approval of studies based entirely on register-data. No contact was made to patients, their relatives, and/or treating physicians. Informed consent was thus waived by Region Zealand. The experimental protocol followed standard guidelines for cohort studies. To ensure data safety, numbers below 5 were not reported. The study was funded by the Central Region of Denmark, 1-30-72-172-18. The funder had no impact on the design, analysis, interpretation and reporting of the findings.

Results

Old cohort

In total, 4914 people were included in the old Thyborøn-Harboøre cohort, and 9537 in the old reference cohort from Holmsland-Hanstholm. The cohorts had been followed up for 40 years (Table 1). In the Thyborøn-Harboøre cohort, in total 2485 people died, compared with 4980 persons from Holmsland-Hanstholm, resulting in a borderline statistically significantly elevated aRR of 1.06 (95% CI 1.01–1.11) (Table 2). Only the interaction between area and calendar time was statistically significant indicating that the difference in mortality between the geographical areas decreased over time. Inclusion of birth cohort in the model did not change aRRs significantly.

Cancer mortality was statistically elevated in Thyborøn-Harboøre, aRR 1.17 (95% CI 1.05–1.30). Kidney cancer mortality was elevated, aRR 1.82 (95% CI 1.07–3.12), bladder cancer mortality to a lesser extent and not statistically significantly, aRR 1.25 (95% CI 0.74–2.12). Mortality was not statistically elevated for other cause of death.

The all-cause mortality in men from Thyborøn-Harboøre was aRR 1.07 (95% CI 1.01–1.14) as compared with men in Holmsland-Hanstholm (Table 2; Fig. 1). Neither cancer mortality, nor mortality from kidney or bladder cancer were statistically elevated in men; aRR 1.14 (95% CI 0.99–1.31); 1.28 (95% CI 0.62–2.62); and 1.09 (95% CI 0.59–1.98), respectively. Mortality from cardiovascular diseases, respiratory diseases and the residual group of other diseases was modestly, but not statistically significantly, elevated in men from Thyborøn-Harboøre, aRR 1.05 (95% CI 0.95–1.17); 1.04 (95% CI 0.82–1.31); and 1.06 (0.93–1.20), respectively. In women from Thyborøn-Harboøre the all-cause mortality was aRR 1.03 (95% CI 0.96–1.11). Both cancer mortality, and mortality from kidney and bladder cancer were elevated, thought the latter not statistically significantly; the aRRs being 1.21 (95% CI 1.03–1.43); 3.01 (95% CI 1.28–7.06); and 2.23 (0.71–6.97), respectively.

	Thyborøn-Harboøre			Holmsland-Hanstholm		
	Total	Men	Women	Total	Men	Women
Old cohort 1968–1970						
Number of persons	4914	2595	2319	9537	5001	4536
Number of person years	199,046	101,695	97,350	376,676	191,106	185,571
Mean follow-up in years	40.5	39.2	42.0	39.5	38.2	40.9
Number of deaths	2485	1387	1098	4980	2755	2225
New cohort 1990–2006, Total						
Number of persons	2933	1594	1339	9537	5001	4536
Numbers of person years	67,374	36,348	31,026	230,879	118,415	112,463
Mean follow-up in years	23.0	22.8	23.2	24.2	23.7	24.8
Number of deaths	302	182	120	1197	755	442
New cohort 1990–2006, Moved-in						
Number of persons	1896	1039	857	7444	3951	3493
Number of person years	41,158	22,206	18,951	173,139	89,723	83,417
Mean follow-up in years	21.7	21.4	22.1	23.3	22.7	23.9
Number of deaths	295	177	118	1175	742	433
New cohort 1990–2006, Born in area						
Number of persons	1037	555	482	2093	1050	1043
Number of person years	26,216	14,142	12,075	57,739	28,693	29,047
Mean follow-up in years	25.3	25.5	25.1	27.6	27.3	27.8
Number of deaths	7	NR	NR	22	13	9

Table 1. Thyborøn-Harboøre and Holmsland-Hanstholm, Denmark. Old cohort 1968–1970, and new cohort 1990–2006 total and divided into people who moved-in and people born in the area. Number of people, person-years, mean follow-up in years, and number of deaths from 2 April 1968 and 1 January 1990, respectively, to 1 March 2023.

Cause of death	Total				Men				Women			
	Deaths		aRR	95% CI	Deaths		aRR	95% CI	Deaths		aRR	95% CI
	TH	HH			TH	HH			TH	HH		
All causes	2485	4980	1.06	1.01–1.11	1387	2755	1.07	1.01–1.14	1098	2225	1.03	0.96–1.11
Cancer	530	895	1.17	1.05–1.30	297	521	1.14	0.99–1.31	233	374	1.21	1.03–1.43
Kidney cancer	24	29	1.82	1.07–3.12	12	20	1.28	0.62–2.62	13	9	3.01	1.28–7.06
Bladder cancer	22	38	1.25	0.74–2.12	16	32	1.09	0.59–1.98	6	6	2.23	0.71–6.97
Cardiovascular disease	875	1921	1.03	0.95–1.11	503	1078	1.05	0.95–1.17	372	843	1.00	0.88–1.13
Respiratory diseases	193	414	0.98	0.82–1.16	107	225	1.04	0.82–1.31	86	189	0.92	0.71–1.18
Other diseases	678	1364	1.04	0.95–1.14	346	693	1.06	0.93–1.20	332	671	1.02	0.90–1.17
Kidney disease	22	52	1.01	0.61–1.67	13	28	1.05	0.54–2.04	9	24	0.99	0.45–2.14
Bladder disease	7	11	1.30	0.50–3.37	NR	5	NR	NR	NR	6	NR	NR
Liver disease	27	39	1.34	0.82–2.19	18	27	1.30	0.72–2.37	9	12	1.44	0.61–3.42
Dementia	62	109	1.07	0.78–1.46	13	36	0.69	0.37–1.31	49	73	1.24	0.86–1.78
External causes	121	250	0.98	0.79–1.22	83	165	0.99	0.76–1.29	38	85	0.95	0.65–1.40
Missing cause	88	136	1.24	0.95–1.62	51	73	1.37	0.96–1.96	37	63	1.08	0.72–1.63

Table 2. Thyborøn-Harboøre (TH) and Holmsland-Hanstholm (HH), Denmark. Comparison between areas for people living there 1968–1970. Mortality by cause of death. Disease categories with less than 5 cases in Thyborøn-Harboøre not shown. NR not reported.

In total, people living in Thyborøn-Holmsland in 1968–1970 had 4571 hospital-contact between 1977 and 1 February 2023 (Table 3) which was slightly elevated compared with the rates from Holmsland-Hanstholm; aRR 1.08 (95% CI 1.05–1.12). For hospital-contact attributed to any cancer, the aRR was 1.14 (95% CI 1.06–1.22), affecting both men and women; aRR 1.17 (95% CI 1.06–1.29) and 1.11 (95% CI 1.00–1.24), respectively. The aRR for anxiety in men was 4.07 (95% CI 1.41–11.72) based on 11 cases. For most other disease groups, the aRRs for Thyborøn-Harboøre compared with Holmsland-Hanstholm were almost identical, except a deficit risk for all neurological disorders in women, aRR 0.81 (95%CI 0.72–0.92). Inclusion of interactions in the model showed results similar to those for all-cause mortality.

New cohort

Only 302 deaths were observed in the cohort living in Thyborøn-Harboøre in 1990–2006, but compared with Hanstholm-Holmsland it nevertheless represented an elevated mortality rate, aRR 1.26 (95% CI 1.11–1.43); less in men; aRR 1.15 (95% CI 0.98–1.36), than in women; aRR 1.44 (95% CI 1.18–1.76) (Table 4). Several causes of death contributed to the elevated mortality rate; cancer aRR 1.47 (95% CI 1.14–1.89); and to a less extent cardiovascular diseases aRR 1.31 (95% CI 0.98–1.74); respiratory diseases aRR 1.26 (95% CI 0.80–1.99); external causes aRR 1.25 (95% CI 0.84–1.88); and dementia aRR 2.21 (95% CI 1.12–4.39), which based on six cases was aRR 3.47 (95% CI 1.27–9.45) in men. Women had an increased risk of cancer death; aRR 1.81 (95% CI 1.26–2.62). Of the 39 cancer deaths in women, 18 were lung cancer deaths. No person in this cohort died from kidney cancer, but five people died from bladder cancer, aRR 2.87 (95% CI 0.97–8.45).

In the 1990–2006 cohort, people born in Thyborøn-Harboøre during the period contributed with only 39% of the person years and in the comparison area it was 25% (Table 1). Furthermore, these people were young and in Thyborøn-Harboøre only seven of 302 deaths occurred in people born there. Therefore, observations in the 1990–2006 cohort derived mainly from people moving there during 1990–2006. In Thyborøn-Harboøre, these immigrants had an excess mortality, aRR 1.28 (95% CI 1.13–1.46). In men, the aRR was 1.17 (95% CI 0.99–1.88), and the only statistically elevated cause of death was dementia, aRR 3.47 (95% CI 1.27–9.45) based on six cases. In women, the aRR was 1.48 (95% CI 1.21–1.81), and both death from cancer, aRR 1.82 (95% CI 1.26–2.63), and other diseases, aRR 1.50 (95% CI 1.01–2.22), were elevated.

In the 1990–2006 cohort, 2787 persons were registered with at least one hospital contact, which was similar to the rate in the comparison area, aRR 0.99 (95%CI 0.94–1.03) (Table 5). Contact regarding ischemic heart disease and heart attack were elevated; aRR 1.24 (95% CI 1.02–1.51) and 1.43 (95% CI 1.07–1.90), respectively. A remarkable difference between Thyborøn-Harboøre and the comparison area was the elevated rates for autism and obsessive compulsive disorder in boys though based on small numbers; aRR 1.85 (95% CI 0.64–5.35) and aRR 1.79 (95% CI 0.57–5.67), respectively.

Discussion

The study was initiated based on findings of a doubled incidence of kidney and bladder cancer in men and women living in Thyborøn-Harboøre at the time of heavy pollution in the area⁹. Kidney and bladder cancers are diseases with a good survival rate¹⁴. This means that while we had 39 and 107 incident cases of kidney and bladder cancers, respectively, we had only 25 and 22 deaths. Nevertheless, the mortality data supported the incidence data especially for women. For men, the mortality rates of the two cancers were elevated only modestly, which could possibly be explained by competing causes of death.

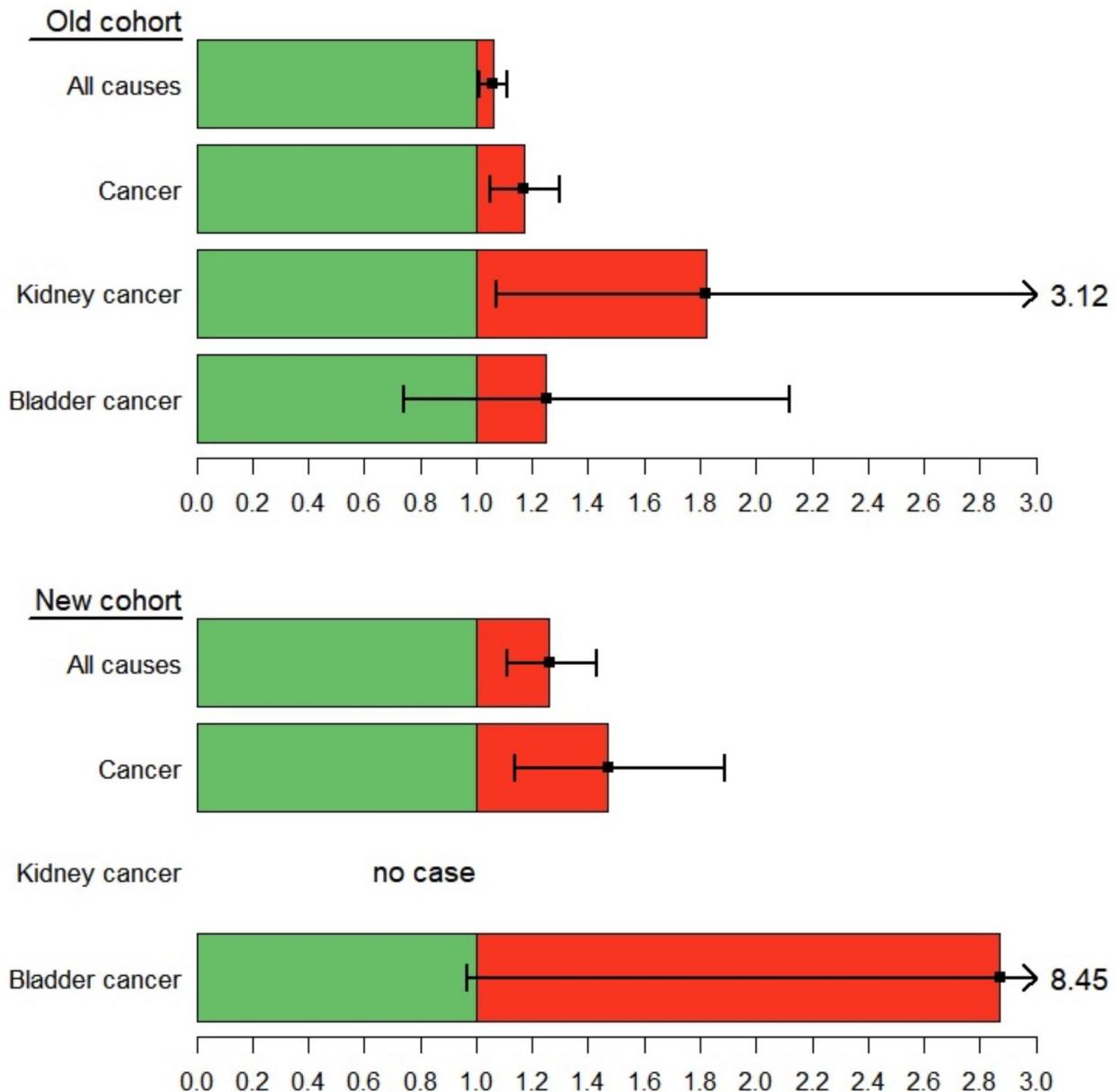


Fig. 1. Adjusted mortality rate ratio for persons living in Thyborøn-Harboøre compared with persons living in Holmsland-Hanstholm. Old cohort recruited 1968–1970; new cohort recruited 1990–2006. End of follow-up 1 March 2023.

During the follow-up period, for every 100 men dying in Holmsland-Hanstholm, 107 men died in Thyborøn-Harboøre; and for every 100 women dying in Holmsland-Hanstholm, 103 women died in Thyborøn-Harboøre. These modestly elevated risks in overall mortality originated from a broad spectrum of diseases, but only the risk of cancer mortality reached statistical significance. The amount of hospital contact in Thyborøn-Harboøre was overall in line with that of the comparison area. Elevated risk of hospital contact was seen for cancer and psychiatric disorders; the latter in particularly for affective disorders in both men and women, and where anxiety in men reached a 4-fold elevated risk.

To assess the possible impact of pollution in Thyborøn-Harboøre on present inhabitants, we included also a cohort of inhabitants who were either born there or had moved to the area after 1990. In the cancer incidence study, the only notable finding in this younger cohort was a more than double risk of lung cancer in women. Nevertheless, when we now had a longer follow-up period, we found a clearly elevated risk of 28% for all-cause mortality; particularly in women where it amounted to 44%, and to 48% in women who had moved to the area.

Since the environmental contamination from the Love Canal landfill was identified in 1978¹⁵, numerous studies of possible health consequences of residency in contaminated areas have been conducted¹⁶. It has

Disease initiation contact	Total					Men					Women				
	Contacts		aRR	95% CI		Contacts		aRR	95% CI		Contacts		aRR	95% CI	
	TH	HH		TH	HH	TH	HH		TH	HH	TH	HH		TH	HH
All contacts	4571	8695	1.08	1.05–1.12		2382	4458	1.14	1.08–1.20		2189	4237	1.03	0.98–1.09	
Cancer	1197	2065	1.14	1.06–1.22		643	1095	1.17	1.06–1.29		554	970	1.11	1.00–1.24	
Cardiovascular disease	2308	4411	1.01	0.96–1.07		1264	2367	1.05	0.98–1.13		1044	2044	0.97	0.90–1.05	
Ischemic heart dis.	781	1452	1.05	0.96–1.14		482	896	1.05	0.94–1.17		299	556	1.05	0.91–1.20	
Heart attach	413	861	0.94	0.84–1.06		281	552	1.00	0.86–1.15		132	309	0.84	0.69–1.03	
Stroke	568	1047	1.07	0.97–1.19		327	585	1.11	0.97–1.27		241	462	1.02	0.87–1.19	
Neurological disease	822	1672	0.91	0.84–0.99		457	853	1.01	0.90–1.13		365	819	0.81	0.72–0.92	
Dementia	107	190	1.09	0.86–1.38		49	89	1.07	0.75–1.52		58	101	1.11	0.80–1.53	
Parkinson disease	29	74	0.77	0.50–1.18		13	45	0.58	0.31–1.07		16	29	1.06	0.57–1.94	
Respiratory disease	1240	2348	1.02	0.95–1.09		691	1273	1.06	0.97–1.17		549	1075	0.97	0.88–1.08	
Asthma	114	229	0.93	0.75–0.117		60	94	1.20	0.87–1.66		54	135	0.75	0.55–1.03	
COPD	308	600	0.98	0.85–1.12		166	292	1.10	0.91–1.34		142	308	0.87	0.71–1.06	
Autoimmune disease	425	808	1.00	0.89–1.12		219	412	1.00	0.85–1.18		206	396	0.99	0.84–1.18	
IBD	83	137	1.14	0.87–1.50		37	70	0.99	0.66–1.47		46	67	1.30	0.89–1.90	
Rheumatoid arthritis	105	199	1.00	0.79–1.27		36	85	0.80	0.54–1.18		69	114	1.15	0.85–1.55	
Multiple sclerosis	13	33	0.73	0.39–1.39		NR	14	NR	NR		9	19	0.89	0.40–1.97	
Psychiatric disorders	286	516	1.04	0.90–1.20		149	261	1.07	0.87–1.31		137	255	1.01	0.82–1.25	
Affective disorders	42	93	0.85	0.59–1.22		17	35	0.90	0.50–1.60		25	58	0.81	0.51–1.30	
Anxiety	17	20	1.58	0.83–3.01		11	5	4.07	1.41–11.72		6	15	0.75	0.29–1.92	
Spontaneous abortion	NR	NR	NR	NR		NR	NR	NR	NR		232	423	1.04	0.89–1.22	

Table 3. Thyborøn-Harboøre (TH) and Holmsland-Hanstholm (HH), Denmark. Comparison between areas for people living there 1968–1970. Hospital contact. Disease categories with less than 5 cases in Thyborøn-Harboøre not shown. *aRR* adjusted rate ratio—adjusted for sex (where relevant), running age, and calendar year, *CI* confidence interval, *COPD* chronic obstructive pulmonary disease, *HH* Holmsland-Hanstholm, *IBD* inflammatory bowel diseases, *NR* not reported, *TH* Thyborøn-Harboøre.

Cause of death	Total					Men					Women				
	Deaths		aRR	95% CI		Deaths		aRR	95% CI		Deaths		aRR	95% CI	
	TH	HH		TH	HH	TH	HH		TH	HH	TH	HH		TH	HH
All causes	302	1197	1.26	1.11–1.43		182	755	1.15	0.98–1.36		120	442	1.44	1.18–1.76	
Cancer	79	265	1.47	1.14–1.89		40	156	1.22	0.86–1.73		39	109	1.81	1.26–2.62	
Bladder cancer	5	10	2.87	0.97–8.45		NR	NR	NR	NR		NR	NR	NR	NR	NR
Cardiovascular disease	57	245	1.31	0.98–1.74		33	148	1.23	0.84–1.80		24	97	1.47	0.94–2.30	
Respiratory diseases	23	96	1.26	0.80–1.99		12	56	1.09	0.59–2.05		11	40	1.51	0.77–2.96	
Other diseases	82	359	1.12	0.88–1.42		49	239	0.97	0.72–1.33		33	120	1.39	0.95–2.05	
Liver disease	5	29	0.80	0.31–2.08		NR	22	NR	NR		NR	7	NR	NR	NR
Dementia	11	33	2.21	1.12–4.39		6	11	3.47	1.27–9.45		5	22	1.55	0.58–4.09	
External causes	31	101	1.25	0.84–1.88		24	77	1.19	0.75–1.88		7	24	1.40	0.60–3.27	
Missing cause	30	131	1.11	0.74–1.65		24	79	1.37	0.87–2.17		6	52	0.64	0.27–1.48	

Table 4. Thyborøn-Harboøre (TH) and Holmsland-Hanstholm (HH), Denmark. Comparison between areas for people living there 1990–2006. Mortality by cause of death. Disease categories with less than 5 cases in Thyborøn-Harboøre not shown. *aRR* adjusted rate ratio—adjusted for sex (where relevant), running age, and calendar year, *CI* confidence interval, *HH* Holmsland-Hanstholm, *NR* not reported, *TH* Thyborøn-Harboøre.

been a challenge in most of these studies to accurately identify the exposed population. A cohort study from the Love Canal area was based on follow-up of residents interviewed in 1978–1982, but not all residents had been interviewed, and a possible selection could not be excluded¹⁵. In a recent study, the life expectancy was compared between US census tracts with and without Superfund sites. Mortality data from 2010 to 2015 were used assuming that these data reflected the population residing in the census tract long enough for the site exposure to have an impact on the life expectancy¹⁷.

Disease initiating contact	Total				Men				Women			
	Contacts		aRR	95% CI	Contacts		aRR	95% CI	Contacts		aRR	95% CI
	TH	HH			TH	HH			TH	HH		
All contacts	2787	9892	0.99	0.94–1.03	1498	5111	0.95	0.89–1.01	1289	4781	1.03	0.97–1.10
Cancer	195	801	1.14	0.97–1.33	96	416	1.05	0.84–1.32	99	385	1.23	0.99–1.54
Cardiovascular disease	512	2190	1.05	0.95–1.15	274	1215	0.96	0.84–1.10	238	975	1.17	1.01–1.35
Ischemic heart dis.	130	500	1.24	1.02–1.51	79	329	1.12	0.87–1.43	51	171	1.50	1.09–2.05
Heart attach	60	203	1.43	1.07–1.90	41	137	1.40	0.99–1.99	19	66	1.47	0.88–2.46
Stroke	97	378	1.23	0.99–1.54	59	232	1.16	0.87–1.55	38	146	1.35	0.95–1.94
Neurological disease	413	1607	1.01	0.91–1.13	225	856	1.01	0.87–1.17	188	751	1.02	0.87–1.20
Dementia	25	107	1.17	0.76–1.82	14	61	1.12	0.62–2.01	11	46	1.23	0.63–2.38
Parkinson disease	5	22	1.22	0.46–3.23	NR	16	NR	NR	NR	6	NR	NR
Respiratory disease	689	2220	1.06	0.98–1.16	374	1192	1.02	0.91–1.15	315	1028	1.12	0.98–1.27
Asthma	104	351	0.93	0.74–1.16	59	172	0.99	0.73–1.33	45	179	0.86	0.62–1.19
COPD	69	295	1.10	0.84–1.42	39	165	1.08	0.76–1.53	30	130	1.12	0.75–1.66
Autoimmune disease	137	611	0.91	0.76–1.10	73	326	0.88	0.68–1.14	64	285	0.95	0.73–1.25
IBD	29	145	0.76	0.51–1.14	14	67	0.74	0.42–1.32	15	78	0.78	0.45–1.36
Rheumatoid arthritis	39	140	1.16	0.81–1.66	13	56	0.92	0.50–1.69	26	84	1.33	0.85–2.06
Multiple sclerosis	5	42	0.47	0.19–1.19	NR	16	NR	NR	NR	26	NR	NR
Psychiatric disorders	396	1346	1.02	0.91–1.15	217	724	1.01	0.87–1.18	179	622	1.04	0.88–1.23
Affective disorders	63	228	0.97	0.73–1.28	23	82	0.94	0.59–1.50	40	146	0.98	0.69–1.40
Anxiety	25	97	0.87	0.56–1.35	9	38	0.77	0.37–1.61	16	59	0.93	0.53–1.62
ADHD in children	25	102	0.66	0.42–1.02	16	61	0.67	0.39–1.17	9	41	0.63	0.31–1.30
Autism in children	7	12	1.45	0.57–3.69	5	8	1.85	0.64–5.35	NR	NR	NR	NR
OCD in children	8	13	1.72	0.71–4.16	NR	7	1.79	0.57–5.67	NR	6	NR	NR
Spontaneous abortion	NR	NR	NR	NR	NR	NR	NR	NR	118	452	1.05	0.86–1.29

Table 5. Thyborøn-Harboøre (TH) and Holmsland-Hanstholm (HH), Denmark. Comparison between areas for people living there 1990–2006. Hospital contact. Disease categories with less than 5 cases in Thyborøn-Harboøre not shown. *ADHD* attention deficit hyperactivity disorder, *aRR* adjusted rate ratio—adjusted for sex (where relevant), running age, and calendar year, *CI* confidence interval, *COPD* chronic obstructive pulmonary disease, *HH* Holmsland-Hanstholm, *IBD* inflammatory bowel diseases, *NR* not reported, *OCD* obsessive compulsive disorder, *TH* Thyborøn-Harboøre.

The availability of long-standing population registers in the Nordic countries provides a possibility to overcome these limitations and to accurately identify individuals exposed to environmental hazards. For instance, in both Sweden¹⁸ and Finland¹⁹ all inhabitants living in areas affected by radiation fallout from the Chernobyl accident were identified from the population registers and individually followed up for later cancer occurrence. In Denmark, children born in 1940–1970 and attending schools near an asbestos-cement factory were identified from the city archive and followed up for occurrence of mesothelioma and other asbestos-related cancers²⁰.

In a setting similar to the one reported on here, an investigation of mortality and health events covered Grindsted, a provincial town in Jutland, where a chemical factory started in 1924^{13,21}. Event occurrence over time in Grindsted was compared with that in comparable towns across Jutland. The analysis was adjusted for covariates as e.g. education. In total, 39,000 people who had lived in Grindsted at some point in time were included in the analysis. The overall mortality rate was in line with that of the comparison towns, e.g. in 2011–2021 incidence rate ratio (IRR) 0.97 (95% CI 0.91–1.03). Cancer incidence was similar in the two areas, IRR 1.03 (95% CI 0.96–1.11) with some increased prostate cancer incidence among Grindsted-inhabitants in earlier years. Kidney cancer was not increased, and bladder cancer data not reported. Incidence of cardiovascular diseases was increased; IRR 1.08 (95% CI 1.03–1.14), but this excess did not derive from acute myocardial infarction, ischemic heart disease, or stroke. Occurrence of psychiatric disorders was slightly increased IRR 1.05 (95% CI 0.99–1.11). Although addressing similar problems, the methodologies were somewhat different, e.g. in definition of risk populations, and it was therefore not possible directly to compare the results of the Grindsted-report with those from the present study.

The elevated mortality in persons who moved to Thyborøn-Harboøre during the years 1990 to 2006, resembled the pattern seen in Danish citizens moving to other marginal geographic areas in Denmark during this period. In the rural-provincial area of Lolland-Falster, which includes the two southern Danish islands, people who moved in during 1998–2007 had a mortality rate ratio of 1.57 (95% CI 1.52–1.63) compared with Danes in general²². Health-related geographical relocation has thus contributed to mortality inequalities in Denmark. In the Thyborøn-Harboøre study, one may wonder why the risk estimates for cancer mortality was higher for the new than for the old cohort, especially because the opposite pattern was seen in the previous study of the cancer incidence⁸. However, it should be taken into account that in the cancer incidence study only

cancers diagnosed after a given person had moved to Thyborøn-Harboøre were considered. In the mortality study, all cancer deaths after a given person had moved to Thyborøn-Harboøre were considered. So given the relatively long survival time for some cancer, e.g. bladder cancer, “sick” immigration could have contributed to the differences in the results.

It was a strength of the study that we had the comprehensive cohort of people living in Thyborøn-Harboøre during 1968–1970. In Denmark, the CPR allows for individual follow-up of all people who even had a permanent address in Denmark. Limitations were that causes of death were available only from 1970 onwards, hospital contact for somatic diseases only from 1977 onwards, and for psychiatric diseases from 1995. To map possible health problems for those living in Thyborøn-Harboøre after pollution came under control in the 1980s, we included a cohort of persons living in the area only in 1990–2006 and primarily consisting of people who had moved there. It was a strength that we could include a comparison cohort of people living at other fishing communities on the Danish West Coast during the same calendar years. In this way we controlled for possible differences in general living conditions, for occupational differences, and for possible dietary differences. By using individual data in the analysis, we controlled also for sex and age, and calendar time of follow-up. In our previous cancer incidence study, it was possible also to use comparison between study outcomes as an indirect control for confounding, e.g. we found excess risks for bladder and kidney cancer but not for lung cancer, indicating that tobacco smoking was not the causal agent behind the excess risks of bladder and kidney cancers. We could thus exclude a number of possible explanatory factors for the observed disease pattern, but it is not possible in an observational epidemiological study to conclusively identify causal associations. We found interaction between geographical area and calendar time, but this will not have affected our results, as calendar time was adjusted for in the calculation of risk estimates. Only the interaction between area and calendar time was statistically significant indicating that the difference in mortality between the geographical areas decreased over time. While mortality data were comprehensive, there may be some inaccuracies in registration of causes of death²³. Use of hospital contacts may further be negatively affected by travel distances to hospitals²⁴, and positively affected by limited access to private specialists, e.g. private, office-based psychiatrists. Finally, we did not have data on socioeconomic conditions, e.g. on people receiving public income support in pre-pensionable age, which might indicate presence of health-problems.

The mortality analysis confirmed the finding from the cancer incidence study of an elevated risk of kidney and bladder cancer in people living in Thyborøn-Harboøre in 1968–1970. Further investigation of possible causes is warranted. Otherwise, the Thyborøn-Harboøre inhabitants from 1968 to 1970 had a slightly elevated mortality rate and a hospital contact pattern similar to that of people living in other Danish West Coast fishing communities. One signal that deserves future monitoring was occurrence of psychiatric disorders, in particularly in men and boys.

Finally, in the 1990s and early 2000s, the data could indicate a possibly selective immigration to Thyborøn-Harboøre of people with health problems. Among women this was illustrated by an overall 48% elevated mortality rate compared with women moving to Holmsland-Hanstholm in the same period. Geography-related redistribution of health is known from Lolland-Falster, another marginal area of Denmark²⁵. A careful follow-up of health in the present population is needed to assess whether selection at migration or exposures in the area are responsible for the elevated mortality rate in people who had moved to Thyborøn-Harboøre in 1990 to 2006.

This study was initiated to assess possible health consequences of the historical environmental pollution in Thyborøn-Harboøre. A doubled risk of kidney and bladder cancer has been found previously, and this finding was confirmed in the present study. Compared with men from other Danish West Coast communities, the overall mortality rate for men in Thyborøn-Harboøre was slightly elevated with small contributions from a broad range of causes of death. The pattern in use of hospital contact was well in accordance with that of the comparison area. Based on small numbers, the study indicated a need for future monitoring of occurrence of psychiatric disorders. The study could further indicate selective immigration to Thyborøn-Harboøre in the 1990s and early 2000s of people with health problems.

Data availability

The data that support the findings of this study are not openly available due to reasons of sensitivity. Pseudonymized data are stored in Statistics Denmark and can be accessed according to EU-data protection rules. Contact to: forskerservice@dst.dk and elsebeth@sund.ku.dk.

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Author contributions

E.L. and S.L. designed the study. S.L. undertook the analysis. E.L. wrote the main manuscript text. All authors reviewed the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval, consent to participate and experimental protocol

The study was a retrospective cohort study. Data were retrieved from the Danish Central Population Register, the Danish Cause of Death Register, and the Danish National Patient Register. These databases are not publicly available, but the databases can be used for research projects considered beneficial for the society. The use of data and the experimental protocol were approved by Region Zealand with the registration number REG-108-2018. Region Zealand is the public authority in charge of Nykøbing Falster Hospital, where the study was undertaken. According to Danish legislation, approval by the relevant public authority serves as ethical approval of studies based entirely on register-data. No contact was made to patients, their relatives, and/or treating physicians. Informed consent was thus waived by Region Zealand. The experimental protocol followed standard guidelines for cohort studies. To ensure data safety, numbers below 5 were not reported. The study was funded by the Central Region of Denmark, 1-30-72-172-18. The funder had no impact on the design, analysis, interpretation and reporting of the findings.

Additional information

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