

Työpaikkojen rakenteisiin ja sisäilma-altisteisiin liittyvä syöpäriski

Occupational and environmental exposures and risk of cancers in Finland.

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Johdanto

Idea tähän tutkimushankkeeseen syntyi käytännön työterveyslääkäreiden havainnoista syöpäsairauksien ryvästymistä työpaikoilla. Sisäilmatutkimuksen yhteydessä on sivulöydöksenä tullut vastaan odotusarvoa suurempia syöpätapauksien keskittymiä, joko korjauksia seuranneiden vuosien aikana tai korjaamattoman rakennuksen selvittelyjen yhteydessä. On jopa havaintoja siitä, että vuosikymmenien aikana tietyssä luokahuoneessa useampi peräkkäinen työntekijä on sairastunut syöpään. Syöpärekisterin emeritusprofessori Eero Pukkala rohkaisi aloittamaan tutkimusta tästä aiheesta.

Syöpäsairaudet ovat väestössä yleisiä. Syövän ilmaantuvuus kasvaa iän myötä ja ikääntyvässä väestössä syöpä tuntuu yleistyvän, vaikka todellista ikävakioidun ilmaantuvuuden kasvua ei tapahtuisikaan. Syöpätapaukset herättävät huolta työyhteisöissä ja asiantuntevaa tutkimusta kaivataan lisää aiheettomien epäilysten hälventämiseksi ja toisaalta uusien työperäisten riskien varhaista toteamista varten.

Yksittäisen työpaikan tai työyhteisön syöpätapausten ryvästen etiologian epidemiologinen selvittely on hyvin vaikeaa, käytännössä mahdotonta. Sattuman osuus selittäjänä on suuri eikä tilastollisesti merkitseviä eroja saada esiin. Suomesta puuttuvat myös mekanismit ja asiantuntijoiden keskittymä, joka selvittelisi nimenomaan työperäisen syövän ryhmäkohtaista esiintyvyyttä paikallisesti tai työpaikkakohtaisesti.

Ammattitautidiagnostiikassa on mahdollista tarkastella yksittäisen työntekijän syövän työperäisyyttä ja todennäköisesti ja pääasiallisesti työstä aiheutunut syöpä voidaan myös korvata ammattitautina. Syövän työperäisyyden tarkastelussa pätevät samat säännöt kuin muissakin ammattitaudeissa: sairauden aiheuttajan ja syövän välinen yhteys on todettu epidemiologisin tutkimuksin ryhmätasolla ja yksilön kohdalla altistumisen ja sairauden välinen yhteys on vähintään todennäköinen. Esimerkkejä ammattitautina korvattavasta työperäisestä syövästä ovat asbestin ja eräiden kemikaalien aiheuttamat syövät (esim. bentseeni).

Kun on kyseessä uusi altiste tai aiemmin tuntematon yhteys, ei yksittäisen syöpätapauksen ja altistumisen välistä yhteyttä voida todentaa ilman edeltävää tutkimusnäyttöä. Jos edeltävää epidemiologista tutkimusta ei ole tehty, ei korvauskäytäntö tule muuttumaan ilman epidemiologista tutkimusta, vaikka tapaukset runsastuisivat tai havaittaisi paikallinen tapausten ryvästyminen.

Sisäilman ja työpaikkojen rakenteiden altisteista syöpävaarallisiksi tiedetään asbesti, radonkaasu, PAH-yhdisteet ja eläinkokeiden mukaan myös eräät hometoksiinit. Tupakoinnin osuus työperäisen syövän aiheuttajana on poistunut tai voimakkaasti vähentynyt tupakkalainsäädännön ansiosta. Koska tupakointi on väestössäkin vähentynyt, muiden syöpävaarallisten altisteiden osuuden tarkastelu on tullut helpommaksi. Työperäiseen syöpään kohdistuneita tutkimuksia on Suomessa tehty kuitenkin verrattain vähän. Näissä tutkimuksissa syöpävaaran lisääntymistä on kuitenkin todettu mm. naisilla liittyen homealtistumiseen.

Sisäilmaongelmien terveysvaikutustutkimusta on Suomessa tehty paljon, mutta tutkimus on kohdistunut pääasiassa astmaan ja muihin hengitystiesairauksiin ja työntekijöiden sijasta lapsiin. Em. syistä Turun yliopiston Trossi-yksikkö piti tärkeänä sisäilman työympäristöperäisten riskien kokonaisvaltaista tarkastelua yhteistyössä Syöpärekisterin kanssa. Aiheesta tulee yksikköömme jatkuvasti tiedusteluja. Eräät työpaikat ovat myös lasten oleskeluympäristöjä, minkä vuoksi heidänkin terveysriskinsä tarkastelu on perusteltua, koska heistä tulee tulevaisuuden työvoima

Työsuojelurahasto myönsi aiheen tutkimukseen apurahan, jonka avulla moniammatilliseen työryhmäämme saatiin rekrytoituksi väitellyt syöpäepidemiologi. Työsuojelurahasto piti myös

tämän senioritutkijan palkkaamista ratkaisevana hankkeen onnistumiseksi. Saimme rekrytoiduksi kokeneen tutkijan, joka on tehnyt tästä aiheesta epidemiologisen väitöskirjan. Laaja moniammatillinen syöpätutkimus edellyttäisi kuitenkin sekä pidempää aikajännettä että huomattavasti suurempaa resurssointia muista lähteistä kuin Työsuojelurahastolta.

Koska syöpäsairauksien ilmaantuvuudessa on viime vuosikymmeninä tapahtunut muutoksia tupakoinnin vähentymisestä huolimatta, syövän synnyn riskitekijöiden ja mahdollisten alueellisten erojen tutkiminen on entistäkin tärkeämpää. Tutkimuksen avulla saataneen selville myös ennaltaehkäisyyn mahdollisuuksia, mikä on tärkeää sekä yhteiskunnan resurssien, hoitomahdollisuuksien ja kustannusten näkökulmasta, myös – ja mikä tärkeintä – yksikön näkökulmasta inhimillisen kärsimyksen vähentämiseksi.

Tutkimus toteutettiin kokonaan rekisteritutkimuksena. Alkuperäistä tutkimussuunnitelmaa ei voitu aivan kaikilta osin noudattaa syöpärekisterin ja STUKin tietojen rajoitusten ja tietosuojamääräysten tulkinnan vuoksi. Tavoitteenamme oli tehdä kuntatason ja jopa työyhteistötason analyysejä ja monimuuttujamallituksia eri riskien ja tupakointihistorian synergistisen vaikutuksen tutkimiseksi.

Loppuraportti kirjoitettiin englanniksi ja tiivistelmä suomeksi tutkimukseemme kohdistuvan kansainvälisen mielenkiinnon vuoksi. Lisäksi tavoitteenamme on jatkaa tulosten raportointia kansainvälisissä tiedelehdissä englanninkielisen tutkijamme kanssa. Tutkimuskokonaisuudesta on julkaistu yksi kansainvälinen artikkeli tiedelehdessä ja lisäksi työn alla on useita artikkelikäsitkirjoituksia. Hanke on jo saanut jatkorahoitusta yksityisestä säätiöstä.

Tutkimusryhmämme kiittää kaikkia yhteistyökumppaneita datatiedostojen ja tilastojen jakamisesta sekä asiantuntija-avusta. Osoitamme kiitoksemme Työsuojelurahaston lisäksi erityisesti Syöpärekisterille, Säteilyturvakeskukselle ja Terveystieteiden ja hyvinvoinnin laitokselle.

Turussa, 17.10.2022

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Table of contents

1. Introduction
2. Materials and methods
 - 2.1. Radon exposure and risk of lung cancer
 - 2.2. Microbial exposures and risk of cancers
 - 2.3. Built environment and risk of cancers
- Results
3. Discussion
4. Conclusion
5. Future research needs and recommendations
6. References

List of tables and figures

Table 1. Radon exposure in selected municipalities and hospital districts in Finland.

Table 2. Incidence rate and total diagnosed lung cancer cases in Finland from 1955-2019, by hospital districts.

Table 3. Lung cancer incidence rate in radon-exposed municipalities with corresponding hospital districts in Finland from 1955-2019.

Table 4. Percentage of daily smokers in reference and exposed hospital districts in Finland.

Table 5. Exposure to mould in drinking water and risk of cancers in Finland, until 1970 and from 1971-2020.

Table 6. Exposure to actinomycetes in drinking water and risk of cancers in Finland, until 1970 and from 1971-2020.

Table 7. Exposure to both moulds and actinomycetes in drinking water and risk of cancers in Finland, until 1970 and from 1971-2020

Table 8. Breast cancer incidence in Finland, until 1970 and from 1971-2020.

Table 9. Larynx, epiglottis cancer incidence in Finland, until 1970 and from 1971-2020.

Table 10. Lung, and trachea cancer incidence in Finland, until 1970 and from 1971-2020.

Table 11. Lymphoid and haematopoietic tissue cancer incidence in Finland, until 1970 and from 1971-2020.

Table 12. Nasal cancer incidence in Finland, until 1970 and from 1971-2020.

Figure 1. Diagnosed lung cancer cases in selected radon-exposed municipalities in Finland from 1955-2019, by sex.

Figure 2. Lung cancer incidence rate in radon-exposed municipalities in Finland from 1955-2019.

Figure 3. Diagnosed lung cancer cases in Finland from 1955-2019, by hospital districts.

Figure 4. Type of housing in Finland before 1970.

Figure 4.1 Types of housing in Finland 1970 – 2019

Figure 5. Energy types and consumption in Finland, 2005 - 2019.

Publication plan

1. Groundwater radon exposure and risk of lung cancer: a population-based study in Finland. (*Published*)
Hadkhale, K., Atosuo, J., & Putus, T. (2022). Groundwater radon exposure and risk of lung cancer: A population-based study in Finland. *Frontiers in Oncology*.
<https://doi.org/10.3389/fonc.2022.935687>.
2. Moulds and actinomycetes exposure in drinking water and risk of cancers in Finland (submitted)
3. Occupational and environmental risk of indoor air exposure and risk of cancers.

1. Introduction

A high quality of indoor air is significant for the health and welfare of residents and employees. The Finnish working-age population spend about 90% of their time indoors and this figure is higher among children and elderly people (THL, 2022). Indoor air contamination is a mixture of pollutants consisting of microbes, chemicals and gases, man-made mineral fibres, street dust, organic dust (pollen, animal dander, dust mites), cleaning chemicals, biocides etc. Certain contaminants come directly from the soil (radon), the ground construction of the buildings (PAH, creosote, chloro-phenols) and timber and asbestos and other building materials. In Finland, the research on health effects caused by indoor air contaminants has been focused mainly on respiratory diseases and the symptoms caused by irritation. Likewise, exposure to microbes in drinking water is harmful to human health. Some moulds and bacteria can produce toxic carcinogens and exposure to such toxins are associated with the risk of cancer. At the population level, the impact on human health due to specific microbes is assessed primarily through epidemiological studies. However, there are difficulties and challenges when the microbial concentration is low but still harmful due to the toxigenic effect. Furthermore, pathogens are considered to have a greater health impact than chemicals (Craun, 1993 & Downs et al., 1999).

Naturally occurring radioactive elements are found in all groundwater and primarily in bedrock waters. Radon is the most significant among these elements and dissolves in groundwater. Exposure to these radioactive elements increases the risk of cancer and radon is primarily associated with the risk of lung cancer (Turtainen et al., 2010). Finland has a higher radon concentration compared to other European countries due to the geology, construction technology, climate and uranium concentration in Finnish soil (WHO, 2009). Groundwater is a source of indoor air radon as the radon transfers from water to air during various water-related activities such as laundry and taking a shower (Vinson et al., 2008, National Research Council 1999). Smoking increases the risk of cancer in asbestos exposure in a synergistic manner. Asbestos mainly causes lung cancer, mesothelioma, and cancer of the larynx in addition to lung fibrosis. Asbestos exposure may still occur during ship-building and the remediation of buildings, even though the use of asbestos was banned in the early 1990s (Martimo et al., 2010). Similar synergism was found between smoking and radon exposure and approximately 100-200 cases of lung cancer are estimated to be due to radon exposure (Auvinen et al 1996, Chen 2019). A case-control study from the collective data of nine European countries reported a similar hazard due to residential radon exposure accounting for up to 2% of all deaths from cancer in Europe (Darby et al. 2005). According to a recent

publication from Radiation and nuclear safety authority (STUK) Säteilyturvakeskus, in Finnish, 8% of daycare centres and 14% of school buildings have radon levels above the recommended value of 300Bq/m³ (Kojo and Kurttio 2020). In Finland, more than 200,000 people are municipal workers and approx. 100,000 are teachers in primary schools and kindergartens. The problem is present also in homes in certain regions in Finland (Darby et al. 2005).

In old buildings constructed before 1970, bitumen tar was used for moisture isolation between the ground construction and the walls. High PAH levels have been found in older school buildings after the installation of a mechanical ventilation system to replace the passive ventilation. The under-pressure in the indoor air may increase the emissions and exposure of PAH compounds. Approximately 40% of Finnish school buildings were built before the year 1970. At least 20-30% of Finnish housing stock has microbial problems due to construction (Reijula et al., 2012). This problem is well-known and has been well-documented in several studies by the Finnish Institute of Occupational Health (FIOH) and the National Institute of Health and Welfare (THL), the health effects have been the subject of intense research for more than three decades.

According to international literature, aflatoxin is a well-documented carcinogenic mycotoxin found in humans and the exposure route is mainly via food and animal feed. Numerous other mycotoxins are known to cause malignant tumours in animals, among them T2-toxin, trichothecenes, sterigmatocystin, zearalenone and deoxynivalenol. The analysis of specific toxins in indoor air is very difficult to even when the toxin-producing fungi grow in the construction materials. The risk assessment of mycotoxins is therefore indirect, relying on documented tissue damage, and investigation of disease clusters in the exposed population. In farming, the toxin-producing fungi grow on hay, barley and corn and in a warmer climate, also in peanuts. The overall cancer risk among farmers is lower than in the general population, but on the other hand, e.g. in Norway, an increased risk of lip cancer was associated with the production of the crop, use of pesticides, construction work, equine farming and rainy summers (Nordby et al., 2004).

In previous research by the FIOH and THL, cancer risk was below average among farmers, but mould exposure significantly increased among women who were exposed to moulds (Laakkonen et al. 2008). Additionally, the drinking water in more than 20 towns and municipalities is contaminated with fungi and actinomycetes. This exposure has been going on for at least 15 years, and it is not possible to eradicate the microbiological contamination with conventional biocides used in water disinfection systems (Korhonen et al 2006, Hageskal

et al 2009). Currently, a study analysing the health risk associated with mould exposure in drinking water and showing the significant risk of certain chronic diseases is being conducted. In terms of radon exposure, STUK is responsible for monitoring related activities in Finland. According to STUK in Finland, over 300 lung cancer cases per year are diagnosed due to radon alone. The International Agency for Research on Cancer (IARC) has classified radon as a group 1 carcinogenic to humans [IARC, 2012]. Finland has a higher radon concentration compared to other European countries due to the geology, construction technology, climate and uranium concentration in Finnish soil [WHO, 2009]. The average radon concentration in Finnish homes is approximately 94 Bq/m³ [STUK, 2021]. Other factors increasing the risk for cancer are smoking, environmental tobacco smoke, certain chemicals and metals such as occupational exposure, diesel exhaust, shift work and ultraviolet radiation. Examples of occupations with increased cancer risk are fire fighters, construction workers and related occupations.

Aim of the study: This study aims to investigate the cancer risk associated with known or potential carcinogenic factors in built environments. Furthermore, the study observes occupational risk factors caused by exposure to natural radiation, radon exposure, microbes in drinking water, indoor air quality and construction materials in the Finnish housing stock, especially work places.

The specific objective of the study was to investigate the following:

- Groundwater radon exposure and risk of lung cancer.
- The risk of cancer from moulds and actinomycetes in drinking water.
- Indoor air exposure associated with environmental and occupational risk of cancers.

2. Materials and methods

This is a population-based study in Finland. The study utilises the data from the population register linked to the Finnish cancer registry to identify the number of cancer cases due to exposure to mould both in occupational and other environmental settings. Exposure to actinomycetes in drinking water in different municipalities in Finland was accessed through the national population register. The occupational history of the participants was obtained from the census records linked to the population register. Occupational groups were categorised e.g. those working on farms and others. Information on exposure to radon was obtained from STUK, Finland. The exposed municipalities were selected based on STUK's indoor radon measurements at groundwater treatment plants (Senja et al., 2021). In addition, information about the daycare centres and school buildings was obtained through the building

and dwelling register. This register provided information e.g. the age of the buildings as well as other real estate information associated with the buildings such as types of energy used etc. This information was utilised to identify information about the type of building used before the onset of the disease. We were also able to stratify the buildings based on the year of construction (before and after the 1970s) and types of energy consumption in Finnish homes. A unique personal identification number was used to link the data from different registries with the cancer registry to identify the number of cancer cases in the study. The personal identity code was deleted before the actual analysis. The controls were selected from those individuals who were alive and free of cancer at the time of the index date (date of diagnosis).

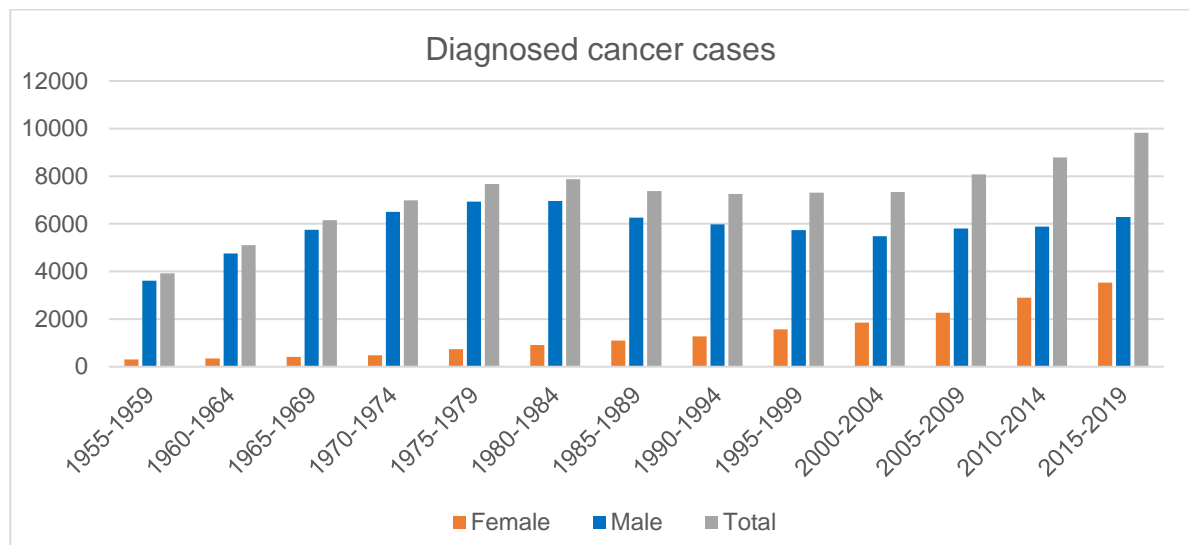
2.1 Radon exposure and risk of lung cancer

This sub-study was a population-based study in Finland. The exposed municipalities were selected based on STUK's indoor radon measurements at groundwater treatment plants [Senja et al., 2021]. According to the radiation act (859/2018), STUK is obliged to measure radon in the indoor air at water treatment plants if the indoor air at the workplace is in contact with groundwater or artificial groundwater. A total of 425 radon measurements at both groundwater and artificial groundwater facilities were made until 2020. Radon measurements were carried out in 211 workplaces by 51 employers. This measurement was conducted in 59 municipalities corresponding to the 14 hospital districts throughout Finland, respectively. Details about municipal exposure is available in the following report (Senja et al., 2021). Municipalities with radon exposure are categorised based on the following exposure estimates: maximum exposure value < 334 Bq/m³ (no exposure), 334 -1,499 Bq/m³ (low exposure) 1,500 -10,500 Bq/m³ (medium exposure) and > 10,500Bq/m³ (high exposure). However, for analysis, we categorised no exposure level, low and medium exposure level as low-risk hospital districts and high exposure level as high-risk hospital districts. Likewise, the lung cancer cases were calculated from the online tool of the Finnish cancer registry (Finnish cancer registry, 2022). In this study, we calculated the cancer cases from 14 selected hospital districts corresponding to their respective radon-exposed municipalities. A unique personal identification number supplied to every person in the Finnish population helped us to obtain information on health and various other matters. The Finnish cancer registry obtains cancer cases using the personal identification number from the population registry. The exact 95% confidence intervals (CIs) of the incidence rates were defined based on Poisson regression. We used two-sided tests for a statistical significance level of 0.05. We were unable to identify the incident of cancer cases in each of the exposed municipalities due to the fewer number of

cases. Hence, according to the data security and ethical guidelines, we estimated the lung cancer cases based on hospital districts of the respective municipalities. There are altogether 22 hospital districts within the 5 university hospital districts in Finland.

RESULTS

Figure 1. Diagnosed lung cancer cases in selected municipalities with radon exposed in Finland from 1955-2019, by sex.



Description: Lung cancer cases slightly increased until the mid-80s and started to decrease slowly until the late 90s. However, the cases started to increase again after 1990 in the radon-exposed municipalities in Finland.

The results are presented based on cancer incidence in each of the selected hospital districts from 1955 to 2019. Lung cancer cases were estimated according to the 5-year incidence rate and stratified by gender. Incidence rates are presented both in the overall rate of 100,000 as well as the age-standardised rate of Finland (2014) (table 2). Likewise, the high and low-risk municipalities were categorised based on the quantitative radon exposure estimates at the selected groundwater treatment plants (STUK report 2020) [Senja et al., 2021]. This study includes all the lung cancer cases from all the exposed municipalities. The selected university hospital districts include; the Uusimaa hospital district (without the Helsinki region), Kymenlaakso hospital district, Päijät-Häme hospital district, and the South Karelia hospital district in the Helsinki university hospital district (HYKS). Similarly, Satakunta hospital district in the Turku university hospital district (TYKS); Kanta-Häme and Pirkanmaa hospital districts in the Tampere university hospital district (TAYS); Southern Savo hospital district,

North Karelia hospital district; Northern Savo hospital district and central Finland hospital district in the Kuopio university hospital district (KYS) and Northern Ostrobothnia hospital district, Kainuu hospital district and Lapland hospital district in the Oulu university hospital district (OYS) (table 1).

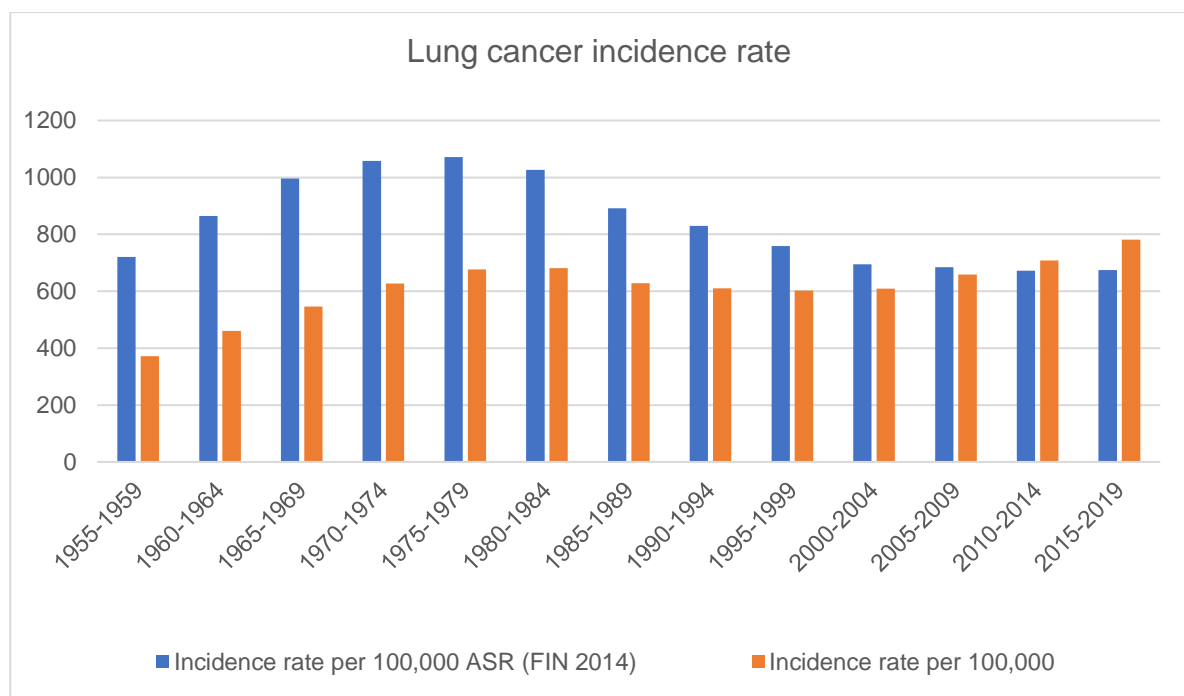
Table 1. Radon exposure in selected municipalities and hospital districts in Finland.

SN	Hospital districts	Municipalities	University hospital district.
1	Uusimaa hospital district (without Helsinki)	Hyvinkää, Mäntsälä, Nurmijärvi, Pornainen, Tuusula, Hanko, Sipoo	Helsinki university hospital district.
2	Kymenlaakso hospital district	Miehikkälä, Kouvola	Helsinki university hospital district.
3	Päijät-Häme hospital district	Pukkila, Hollola, Iitti, Lahti, Orimattila	Helsinki university hospital district.
4	South Karelia hospital district	Imatra, Parikkala, Lappeenranta	Helsinki university hospital district
5	North Karelia hospital district	Joensuu, Kitee, Kontiolahti, Nurmes, Outokumpu, Tohmajärvi, Valtimo	Kuopio university hospital district
6	Northern Savo hospital district	Kuopio, Leppävirta, Siilinjärvi, Tuusniemi	Kuopio university hospital district
7	Southern Savo hospital district	Mäntyharju	Kuopio university hospital district
8	Central Finland hospital district	Joutsa, Jyväskylä, Laukaa	Kuopio university hospital district
9	Northern Ostrobothnia hospital district	Haapajärvi, Kalajoki, Sievi	Oulu university hospital district
10	Lapland hospital district	Rovaniemi	Oulu university hospital district
11	Tampere region (Pirkanmaa) hospital district.	Kangasala, Nokia, Orivesi, Tampere, Ylöjärvi	Tampere University hospital district
12	Kanta-Häme hospital district	Riihimäki, Forssa, Hattula, Hausjärvi, Hämeenlinna, Janakkala	Tampere University hospital district
13	Kainuu hospital district	Kajaani	Oulu University hospital district
14	Satakunta hospital district	Honkajoki, Huittinen, Nakkila, Pori, Siikainen, Säskylä, Eura, Harjavalta, Kankaanpää, Karvia, Ulvila	Turku university hospital district

Description: Of the 22 hospital districts, 14 were selected for the study based on their exposure information. The table illustrates the hospital districts corresponding to the municipalities and university hospital districts in Finland.

More than 93,000 cases of lung cancer cases were reported from the radon-exposed hospital districts from 1955 to 2019. The majority of the cases (approx. 80%) were males (Figure 3). The highest number of lung cancer cases were diagnosed in the Uusimaa hospital district (n = 16,606) and Pirkanmaa hospital district (n = 12,372) whereas the least were in the Southern Savo hospital district (n = 3,412) and Lapland hospital district (n = 3,751 (figure 3). During this period, the incidence rate of lung cancer increased until 1985 and then started to decrease until the late 1990s throughout the region. However, the incidence again started to increase after 2000 and has continued to increase (Figure 2).

Figure 2. Lung cancer incidence rate in radon-exposed municipalities in Finland from 1955-2019.



The number of new cancer cases per 100,000 people per year, if the age structure of the population was similar to that in Finland in 2014.

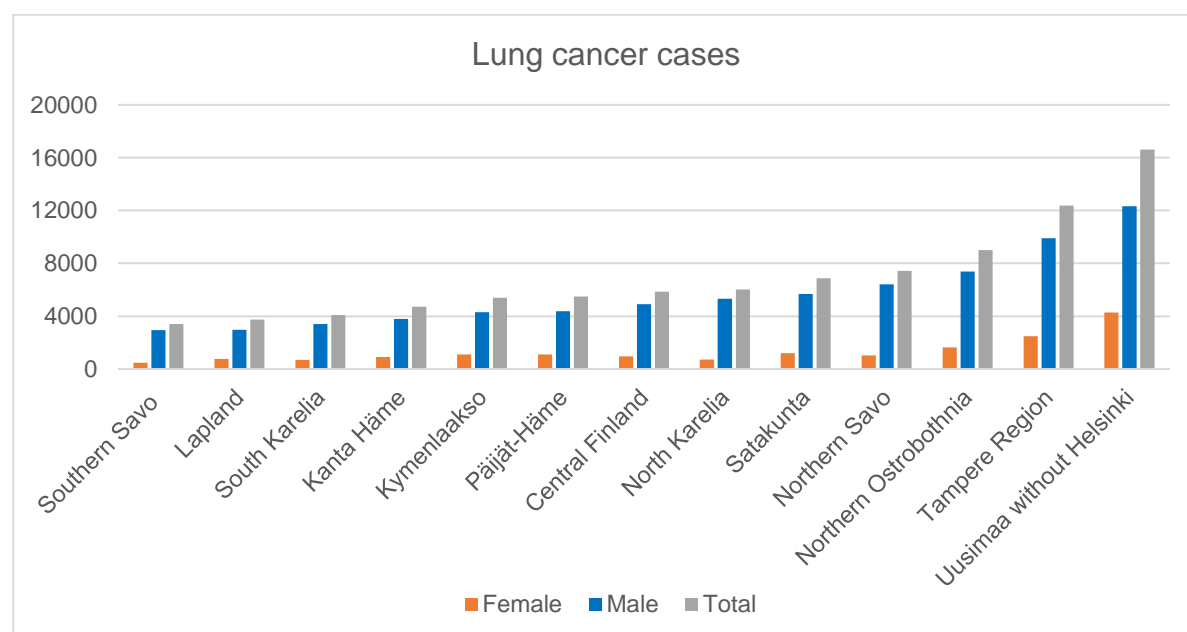
The number of new cancer cases per 100,000 people per year.

Description: The lung cancer incidence rate increased until the mid-80s and slowly started to decrease until the late 90s. However, the incidence started to increase again in the early 20s in the radon-exposed municipalities in Finland.

Stratification based on the hospital districts observed Lapland, North Karelia and Northern Ostrobothnia hospital districts as having the highest incidence rates whereas Southern Savo, central Finland, Päijät-Häme, Tampere region (Pirkanmaa), and South Karelia had the lowest. The age-standardized incidence rate was highest in Lapland (932.05), North Karelia (885.25) and Northern Ostrobothnia (853.42) and lowest in Southern Savo and Päijät- Häme hospital

districts according to the age structure of the Finnish population in 2014. Accordingly, the radon exposure estimate was observed to be the highest in the Lapland, North Karelia, and Northern Ostrobothnia hospital districts. The highest mean average risk ($> 10,000 \text{ Bq/m}^3$) was observed in Rovaniemi (Lapland hospital district), Joensuu, and Kontiolahti (North Karelia Hospital district), Ylöjärvi (Pirkanmaa hospital district), Sievi (Northern Ostrobothnia hospital district) and Tuusniemi (Northern Savo hospital district). Similarly, a lower risk or no risk was observed in the following municipalities: Huittinen, Nakkila, Pori, Siikainen, Säskylä, Eura, Harjavalta, Honkajoki, Kankaanpää (Satakunta hospital district) Pukkila (Päijät-Häme hospital district), Miehikkälä (Kymenlaakso hospital district), Orivesi, Nokia (Pirkanmaa hospital district), Riihimäki, Forssa (Kanta-Häme hospital district), Imatra, Parikkala (South Karelia hospital districts) (table 1). A statistically significant increased risk was observed in the high-risk hospital districts as compared to the low-risk hospital districts. The highest risk was observed (1.18, 1.14-1.23), (1.17, 1.13-1.22) and (1.13, 1.08-1.17) in Lapland, North Karelia and Northern Ostrobothnia hospital districts respectively as compared to the reference category (Table 3).

Figure 3. Diagnosed lung cancer cases in Finland from 1955-2019, by hospital district.



Description: The highest number of cases were identified in the Uusimaa hospital district followed by Tampere (Pirkanmaa) and Northern Ostrobothnia. Likewise, the lowest number of lung cancer cases was identified in the Southern Savo hospital district followed by Lapland and South Karelia hospital districts.

Table 2. Incidence rate and total diagnosed lung cancer cases in Finland from 1955-2019, by hospital districts.

	Hospital districts	*Incidence rate	** ASR (FIN)	Diagnosed cases
1	Central Finland hospital district	503.5	722.0	5,854
2	Kainuu hospital district	601.1	862.6	2,649
3	Kanta-Häme hospital district	584.5	732.3	4,716
4	Kymenlaakso hospital district	591.3	737.5	5,395
5	Lapland hospital district	603.0	932.1	3,751
6	North Karelia hospital district	655.9	885.3	6,033
7	Northern Ostrobothnia hospital district	516.6	853.4	9,014
8	Northern Savo hospital district	580.2	796.1	7,431
9	Päijät-Häme hospital district	543.4	709.0	5,483
10	Satakunta hospital district	590.2	758.9	6,880
11	South Karelia hospital district	589.0	732.2	4,094
12	Southern Savo hospital district	579.6	694.8	3,412
13	Tampere region hospital district	541.1	714.4	12,372
14	Uusimaa without Helsinki	480.0	811.7	16,606

*The number of new cancer cases per 100,000 people per year.

**The number of new cancer cases per 100,000 people per year, if the age structure of the population was similar to that in Finland in 2014.

Table 3. Lung cancer incidence rate in radon-exposed municipalities with corresponding hospital districts in Finland from 1955-2019.

Hospital districts	University Hospitals	IRR	95% CI
Reference (low)	Others	1.00	Reference
Lapland hospital district	Oulu University hospital district	1.18	1.14-1.23
North Karelia hospital district	Kuopio University hospital district	1.17	1.13-1.22
Northern Ostrobothnia	Oulu University hospital district	1.13	1.08-1.17

Low-risk hospital districts (reference): Central Finland hospital district, Kanta-Häme hospital district, Kymenlaakso hospital district, Northern Savo hospital district, Päijät-Häme hospital district, Satakunta hospital district, South Karelia hospital district, Southern Savo hospital district, Tampere region hospital district, Uusimaa without Helsinki hospital region.

High-risk hospital districts: Lapland hospital district, North Karelia hospital district and Northern Ostrobothnia hospital district.

2.2 Microbial exposure and risk of cancers.

This was a population-based ecological study in Finland. The exposure information is based on the municipalities that have drinking water that is exposed to 1) moulds only 2) actinomycetes only, and 3) those exposed to both moulds and actinomycetes. There is a total of 22 hospital districts under the 5 university hospital districts in Finland. In this study, we are using 17 hospital districts selected based on selected municipalities. Due to the ethical guidelines, the exposed municipalities are represented according to their respective hospital districts. Exposure classification was based on the following categories. Southern Savo and Eastern Savo hospital districts were categorized as having a low exposure to moulds in the drinking water. Similarly, Central Finland, Helsinki (municipality), Kainuu, Lapland, Päijät-Häme, South Karelia, and South Ostrobothnia were categorized as having a low exposure to actinomycetes and Kanta-Häme, Northern Savo, Päijät-Häme and Uusimaa (without Helsinki) hospital districts were categorized as having a medium exposure to actinomycetes. Kanta-Häme, Northern Savo, South Karelia, Pirkanmaa and Uusimaa without the Helsinki hospital districts were categorized as being exposed to both moulds and actinomycetes. Central Ostrobothnia hospital district, Northern Ostrobothnia hospital district, South-West Finland hospital district and Vaasa hospital districts were categorized as no exposure hospital districts (reference category) for all exposure types in the study. The incident of cancer cases were calculated from the Finnish cancer registry tool. (<https://cancerregistry.fi/statistics/cancer-statistics/>). In Finland, the Finnish cancer registry collects all the cancer cases throughout the country. The Finnish cancer registry obtains the cancer cases of all the residents with their identification numbers. A unique personal identity number is used to link information on health and various other matters. We were unable to identify the incidence of cancer cases in each of the exposed municipalities due to the small/limited number of cases. Hence, according to the data security and ethical guidelines, we estimated all the cancer cases based on the hospital districts of the respective municipalities.

RESULTS

Findings are presented with the cancer incidence rates for the selected non-exposed hospital districts used as a reference category. The exact 95% confidence interval (CIs) was defined based on a Poisson regression. For the purpose of categorization, exposure values were defined as follows: 0 - < 50 cfu/m³ as low exposure, > 50 cfu/m³ is medium exposure and, 0 cfu/m³ as no exposure or reference category. The following cancer outcomes were estimated

to compare the risk between exposed and reference categories: bladder and urinary tract, breast, kidney, larynx and epiglottis, liver, lung and trachea, lymphoid and haematopoietic tissue, and sinonasal cancer. The results were stratified based on the time period (until 1970 and from 1971- 2020) to observe the trends in cancer incidence and are presented as incidence rate per 100,000 and an age-standardized incidence rate according to the age structure of the Finnish population in 2014. The correlation coefficient was checked before the model fit and highly correlated variables were excluded from the model.

Until 1970, exposures to both moulds and actinomycetes were observed as slightly increasing the risk of bladder and urinary tract, breast, and kidney cancers in the Pirkanmaa hospital district as compared to the reference category. Similarly, until 1970, South Karelia observed an increased risk of lung, liver, lymphoid and haematopoietic, and larynx cancers whereas in Northern Savo this only applied to larynx cancers. Kanta-Häme hospital district observed an increased risk of kidney, lung, lymphoid and haematopoietic, and nasal cancer as compared to the reference category. For all the increased cancer incidences, the association was not statistically significant. After 1970 and until 2020, most smoking-related cancers were observed to have decreased as compared to the reference category. A statistically significant increased risk (rate per 100,000) of breast cancer was observed in the Kanta-Häme hospital district (1.14, 1.04-1.24) and Pirkanmaa hospital district (1.15, 1.05-1.25). A similar increased risk was also observed for the age-standardized incidence rate. However, the association was not statistically significant for the Kanta-Häme hospital district.

Table 4. Percentage of daily smokers in the exposed hospital districts and the non-exposed (reference category) in Finland.

Hospital districts	2013	2014	2015	2018
<i>Central Ostrobothnia hospital district</i>	17.7	20.2	15.6	15
<i>Northern Ostrobothnia hospital district</i>	18.7	17.5	15.8	14
<i>Southwest Finland Hospital District</i>	15.7	15.7	16.3	15.3
<i>Vaasa hospital district</i>	15.3	14.8	13.1	10.6
Central Finland hospital district	15.4	15.6	15.4	11.7
Helsinki and Uusimaa hospital district	16.1	15.8	14.9	12.6
Eastern Savo hospital district	20.9	*-	-	-
Kainuu hospital district	17.5	23	18.4	14.9
Kanta-Häme hospital district	18.9	17.7	19.4	13.8
Lapland hospital district	19.8	20.1	22.6	18.4

Northern Savo Hospital District	19.1	16.2	18.3	15.3
Pirkanmaa hospital district	16	17.1	15.8	13.7
Päijät-Häme hospital district	19.6	19.5	21.2	16.6
South Karelia hospital district	22.9	13.5	15.3	16.9
South Ostrobothnia hospital district	17.4	20.5	14.7	15.9
Southern Savo Hospital District	21.3	20.1	20.1	16.7

Description: The smoking trend has been similar in almost all hospital districts. The highest number of daily smokers was in 2013 and the least in 2019 signifying the decreasing trend of smoking in Finland throughout this period. Additionally, there is no significant difference in smoking incidence between the exposed and reference category.

Exposure to moulds only observed no significant risk of cancers until 1970, although a slight statistically insignificant risk of bladder and nasal cancers was observed in the Southern Savo hospital district. A similar observation was observed in cancers of the larynx, epiglottis, lung, lymphoid and haematopoietic tissue in the Eastern Savo hospital district. After 1970, a statistically significant increased risk of bladder (1.28, 1.09-1.49), breast (1.12, 1.02-1.22) kidney (1.22, 1.01-1.46), and lymphoid and haematopoietic cancers (1.16, 1.00-1.24) was observed in the Eastern Savo hospital district. A similar increased risk was also observed in Southern Savo for lymphoid and haematopoietic tissue cancer (1.13, 1.02-1.26) as compared to the reference category. For actinomycetes exposure, no such significant increased risk was observed in both low as well as medium exposed hospital districts as compared to the reference category. However, Helsinki municipality observed an increased risk of almost all types of cancers with cancers such as breast, kidney, liver, and lung showing a statistically significant risk in both periods. The latest strata period (1971-2020) shows decreased incidence of all smoking-related cancers as compared to the earlier period. Overall, we did not observe a significant difference in the risk of cancers in exposed hospital districts as compared to the hospital districts in the reference category (Tables 5, 6 and 7). Smoking figures show that the number of daily smokers has been decreasing in recent years with the highest percentage in the exposed municipalities as compared to the reference category. However, we do not have information on smoking in each of the hospital districts throughout the study period (Table 4).

Table 5. Exposure to mould in drinking water and risk of cancers in Finland, until 1970 and from 1971-2020.

Hospital districts	Until 1970				1971-2020			
	¹ Rate per 100,000		² Age standardized (FIN 2014)		¹ Rate per 100,000		² Age standardized (FIN 2014)	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
Bladder and urinary tract cancer								
³ Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Eastern Savo (low)	0.96	0.52-1.76	1.08	0.72-1.61	1.28	1.09-1.49	1.05	0.91-1.22
Southern Savo (low)	1.10	0.62-1.96	1.09	0.73-1.63	1.06	0.90-1.25	0.89	0.76-1.05
Breast cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Eastern Savo (low)	0.77	0.55-1.06	0.73	0.57-0.95	1.12	1.02-1.22	0.93	0.85-1.01
Southern Savo (low)	0.78	0.58-1.10	0.72	0.56-0.94	1.10	1.00-1.20	0.93	0.85-1.02
Kidney cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Eastern Savo (low)	0.71	0.33-1.48	0.76	0.44-1.31	1.22	1.01-1.46	0.98	0.82-1.17
Southern Savo (low)	1.01	0.53-1.91	1.00	0.61-1.63	1.10	0.91-1.33	0.91	0.76-1.10
Larynx, epiglottis cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Eastern Savo (low)	1.09	0.55-2.16	1.34	0.82-2.21	0.98	0.61-1.55	0.84	0.55-1.29
Southern Savo (low)	0.91	0.44-1.90	0.88	0.49-1.57	1.08	0.70-1.68	0.90	0.59-1.37
Liver Cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Eastern Savo (low)	0.80	0.23-2.76	0.68	0.27-1.73	1.19	0.92-1.55	0.87	0.67-1.13
Southern Savo (low)	0.57	0.13-2.39	0.50	0.17-1.46	1.02	0.78-1.35	0.80	0.61-1.06

Lung, trachea cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Eastern Savo (low)	1.09	0.88-1.34	1.13	0.97-1.32	1.19	1.08-1.31	0.99	0.90-1.08
Southern Savo (low)	1.00	0.80-1.24	0.91	0.77-1.08	1.07	0.97-1.18	0.90	0.82-0.99
Cancer of the lymphoid and haematopoietic tissue								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Eastern Savo (low)	1.07	0.78-1.47	1.03	0.79-1.33	1.16	1.00-1.24	0.95	0.86-1.06
Southern Savo (low)	0.93	0.67-1.31	0.91	0.70-1.20	1.13	1.02-1.26	0.98	0.88-1.09
Nose, sinus cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Eastern Savo (low)	0.51	0.10-2.61	0.43	0.12-1.52	1.06	0.48-2.34	0.95	0.86-1.06
Southern Savo (low)	1.08	0.32-3.53	1.17	0.51-2.65	1.09	0.49-2.39	0.98	0.88-1.09

¹The number of new cancer cases per 100,000 people per year.

²The number of new cancer cases per 100,000 people per year, if the age structure of the population was similar to that in Finland in 2014.

³Reference hospital districts: No mould exposure (0 cfu/m³). These include 1) Central Ostrobothnia 2) Northern Ostrobothnia hospital district 3) South West Finland hospital district, and 4) Vaasa hospital district.

Low exposure to moulds (0 - 50 cfu/m³). These include 1) Eastern Savo hospital district, and 2) Southern Savo hospital district.

Description: Overall exposure to moulds in drinking water was observed as causing a slightly increased risk of certain types of cancers such as breast, lung, kidney etc. However, the age-standardized risk was observed as not being associated with a significantly increased risk. Hence, exposure to moulds in drinking water was not associated with an increased risk of cancers in exposed and non-exposed hospital districts. Non-exposed hospital districts are categorized as the reference category. Likewise, the overall incidence rate of all types of cancers were increased after the 1970s in both the exposed and non-exposed hospital districts.

Table 6. Exposure to actinomycetes in drinking water and risk of cancers in Finland, until 1970 and from 1971-2020.

Hospital districts	Until 1970				1971-2020			
	¹ Rate per 100,000		² Age standardized (FIN 2014)		¹ Rate per 100,000		² Age standardized (FIN 2014)	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
Bladder and urinary tract cancer								
³ Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Central Finland (low)	0.92	0.50-1.72	1.07	0.72-1.60	0.92	0.77-1.10	0.94	0.80-1.10
Helsinki (low)	1.32	0.78-2.27	1.14	0.77-1.69	0.96	0.81-1.40	1.02	0.88-1.19
Kainuu (low)	0.78	0.40-1.51	0.99	0.65-1.50	0.98	0.83-1.16	0.97	0.83-1.13
Lapland (low)	0.61	0.29-1.27	0.91	0.59-1.40	0.92	0.78-1.10	0.99	0.85-1.15
Päijät-Häme (low)	0.95	0.51-1.75	0.83	0.53-1.30	1.06	0.90-1.25	0.97	0.83-1.13
South Karelia (low)	1.01	0.56-1.83	0.91	0.59-1.40	1.10	0.93-1.29	0.96	0.82-1.11
South Ostrobothnia (low)	0.71	0.36-1.41	0.69	0.43-1.12	1.01	0.86-1.20	0.91	0.78-1.07
Kanta-Häme (Medium)	0.89	0.48-1.67	0.74	0.46-1.18	0.98	0.82-1.17	0.89	0.76-1.05
Northern Savo (Medium)	0.93	0.50-1.72	0.98	0.64-1.48	1.00	0.85-1.19	0.95	0.82-1.11
Päijät-Häme (Medium)	0.95	0.51-1.74	0.83	0.53-1.29	1.06	0.90-1.26	0.97	0.83-1.13
Uusimaa without Helsinki (Medium)	0.92	0.50-1.71	0.97	0.64-1.48	0.79	0.65-0.95	1.02	0.88-1.18
Breast cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Central Finland (low)	0.72	0.52-1.00	0.75	0.58-0.97	0.95	0.86-1.04	0.93	0.86-1.02
Helsinki (low)	1.71	1.35-2.18	1.57	1.29-1.90	1.33	1.22-1.45	1.39	1.29-1.50
Kainuu (low)	0.50	0.33-0.73	0.61	0.46-0.81	0.85	0.78-0.94	0.78	0.71-0.86

Lapland (low)	0.44	0.29-0.67	0.60	0.46-0.80	0.82	0.74-0.91	0.78	0.71-0.86
Päijät-Häme (low)	0.95	0.70-1.27	0.86	0.70-1.10	1.10	1.00-1.20	1.01	0.92-1.10
South Karelia (low)	0.81	0.59-1.11	0.78	0.60-1.00	1.08	0.98-1.20	0.95	0.87-1.04
South Ostrobothnia (low)	0.92	0.69-1.26	0.94	0.74-1.18	1.10	1.00-1.21	1.02	0.94-1.11
Kanta-Häme (Medium)	1.01	0.76-1.35	0.91	0.72-1.15	1.14	1.04-1.24	1.05	0.96-1.14
Northern Savo (Medium)	0.80	0.58-1.10	0.80	0.62-1.03	1.01	0.92-1.10	0.95	0.86-1.03
Päijät-Häme (Medium)	0.95	0.70-1.27	0.86	0.68-1.10	1.10	1.00-1.20	1.00	0.92-1.10
Uusimaa without Helsinki (Medium)	0.99	0.74-1.32	0.98	0.78-1.23	1.02	0.93-1.12	1.14	1.05-1.23
Kidney cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Central Finland (low)	0.82	0.41-0.65	0.80	0.46-1.37	0.85	0.69-1.05	0.81	0.67-1.00
Helsinki (low)	2.12	1.30-3.46	2.20	1.52-3.18	1.07	0.89-1.31	1.14	0.96-1.36
Kainuu (low)	0.35	0.12-0.97	0.39	0.18-0.82	1.04	0.85-1.26	0.94	0.78-1.13
Lapland (low)	0.65	0.30-1.40	0.86	0.51-1.45	0.95	0.77-1.16	0.97	0.81-1.16
Päijät-Häme (low)	1.16	0.64-2.13	1.00	0.61-1.64	1.16	0.96-1.40	1.07	0.90-1.28
South Karelia (low)	0.73	0.35-1.52	0.69	0.38-1.21	1.18	0.97-1.41	1.01	0.84-1.21
South Ostrobothnia (low)	0.61	0.28-1.35	0.50	0.26-0.97	0.97	0.80-1.19	0.86	0.71-1.04
Kanta-Häme (Medium)	1.14	0.62-2.10	1.04	0.63-1.69	1.16	0.96-1.40	1.05	0.88-1.26
Northern Savo (Medium)	0.80	0.39-1.62	0.77	0.44-1.32	1.17	0.91-1.33	1.01	0.85-1.21
Päijät-Häme (Medium)	1.17	0.64-2.13	1.09	0.61-1.64	1.16	0.97-1.40	1.07	0.90-1.27
Uusimaa without Helsinki (Medium)	1.06	0.63-2.13	1.05	0.72-1.83	0.92	0.76-1.14	1.14	0.96-1.35
Larynx, epiglottis cancer								

Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Central Finland (low)	1.08	0.54-2.14	1.15	0.68-1.95	0.95	0.59-1.51	0.95	0.62-1.43
Helsinki (low)	1.18	0.78-2.68	1.26	0.76-2.09	1.28	0.84-1.92	1.26	0.87-1.81
Kainuu (low)	0.79	0.36-1.72	1.01	0.58-1.76	1.14	0.74-1.76	1.06	0.72-1.57
Lapland (low)	1.07	0.54-2.12	1.47	0.91-2.38	1.10	0.71-1.71	1.15	0.78-1.68
Päijät-Häme (low)	0.87	0.41-1.84	0.79	0.43-1.47	1.14	0.74-1.76	1.00	0.67-1.50
South Karelia (low)	1.21	0.62-2.33	1.13	0.66-1.92	1.18	0.77-1.80	1.04	0.70-1.54
South Ostrobothnia (low)	1.01	0.50-2.05	0.96	0.55-1.70	1.11	0.71-1.71	0.99	0.67-1.49
Kanta-Häme (Medium)	0.81	0.38-1.77	0.73	0.38-1.37	1.00	0.63-1.58	0.87	0.57-1.33
Northern Savo (Medium)	1.00	0.49-2.03	0.97	0.55-1.71	1.17	0.76-1.79	1.08	0.73-1.60
Päijät-Häme (Medium)	0.87	0.41-1.84	0.79	0.42-1.47	1.14	0.74-1.76	1.00	0.67-1.50
Uusimaa without Helsinki (Medium)	1.04	0.52-2.08	1.11	0.65-1.91	0.89	0.55-1.43	1.07	0.72-1.59
Liver Cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Central Finland (low)	1.00	0.31-3.08	0.97	0.43-2.18	0.80	0.59-1.10	0.77	0.58-1.01
Helsinki (low)	2.80	1.27-6.15	2.59	1.46-4.58	1.37	1.07-1.76	1.45	1.17-1.81
Kainuu (low)	0.66	0.17-2.52	0.71	0.28-1.77	1.10	0.83-1.43	1.03	0.81-1.32
Lapland (low)	0.99	0.32-3.09	1.64	0.85-3.19	0.89	0.66-1.20	0.90	0.70-1.17
Päijät-Häme (low)	1.03	0.34-3.14	1.35	0.66-2.75	1.06	0.81-1.39	0.94	0.72-1.21
South Karelia (low)	1.11	0.38-3.28	0.90	0.39-2.10	1.03	0.78-1.36	0.89	0.69-1.16
South Ostrobothnia (low)	0.80	0.21-2.68	0.66	0.25-1.70	0.89	0.67-1.19	0.77	0.58-1.01
Kanta-Häme (Medium)	0.92	0.29-2.96	0.77	0.32-1.87	0.94	0.71-1.25	0.82	0.63-1.08

Northern Savo (Medium)	1.08	0.41-3.39	1.14	0.54-2.45	1.00	0.76-1.33	0.88	0.68-1.15
Päijät-Häme (Medium)	1.03	0.34-3.14	1.35	0.66-2.75	1.06	0.81-1.40	0.93	0.72-1.21
Uusimaa without Helsinki (Medium)	0.96	0.30-3.01	0.99	0.44-2.21	0.86	0.64-1.16	1.11	0.88-1.41
Lung, trachea cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Central Finland (low)	0.98	0.78-1.22	1.06	0.90-1.24	0.90	0.81-1.00	0.90	0.82-0.99
Helsinki (low)	1.32	1.09-1.61	1.16	0.99-1.34	1.11	1.00-1.22	1.12	1.03-1.22
Kainuu (low)	0.78	0.61-0.99	0.97	0.82-1.14	1.18	1.07-1.30	1.18	1.09-1.29
Lapland (low)	0.83	0.66-1.06	1.20	1.04-1.40	1.17	1.06-1.28	1.22	1.12-1.33
Päijät-Häme (low)	1.04	0.84-1.29	0.98	0.83-1.16	0.98	0.88-1.09	0.91	0.82-1.00
South Karelia (low)	1.12	0.91-1.38	1.04	0.88-1.21	1.06	0.96-1.17	0.93	0.84-1.02
South Ostrobothnia (low)	0.84	0.66-1.07	0.81	0.68-0.97	0.97	0.87-1.08	0.86	0.79-0.95
Cancer of the lymphoid and haematopoietic tissue								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Central Finland (low)	0.95	0.68-1.33	0.95	0.73-1.23	0.94	0.84-1.06	0.96	0.86-1.06
Helsinki (low)	1.47	1.10-1.94	1.49	1.19-1.87	1.04	0.92-1.15	1.08	0.98-1.19
Kainuu (low)	0.76	0.52-1.09	0.72	0.54-0.97	1.02	0.91-1.13	0.96	0.87-1.07
Lapland (low)	0.66	0.44-0.97	0.74	0.54-0.99	0.93	0.83-1.05	0.96	0.87-1.07
Päijät-Häme (low)	1.03	0.74-1.42	1.05	0.81-1.35	1.09	0.98-1.21	1.02	0.92-1.12

South Karelia (low)	1.06	0.77-1.45	1.00	0.77-1.30	1.09	0.98-1.22	0.96	0.87-1.07
South Ostrobothnia (low)	0.95	0.68-1.33	0.87	0.66-1.14	1.14	1.03-1.27	1.04	0.95-1.16
Kanta-Häme (Medium)	1.10	0.80-1.51	0.97	0.74-1.26	1.11	1.00-1.24	1.02	0.91-1.12
Northern Savo (Medium)	0.90	0.65-1.28	0.90	0.69-1.19	1.04	0.93-1.16	0.99	0.89-1.10
Päijät-Häme (Medium)	1.02	0.74-1.42	1.05	0.81-1.35	1.09	0.98-1.21	1.02	0.91-1.12
Uusimaa without Helsinki (Medium)	1.02	0.74-1.41	1.02	0.78-1.32	0.92	0.83-1.04	1.11	1.00-1.22
Nose, sinus cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Central Finland (low)	0.76	0.19-2.99	0.72	0.26-1.96	0.97	0.42-2.20	0.89	0.42-1.90
Helsinki (low)	1.05	0.32-3.49	0.86	0.34-2.17	1.06	0.48-2.34	1.08	0.53-2.18
Kainuu (low)	0.95	0.27-3.31	1.28	0.58-0.84	0.95	0.41-2.17	1.06	0.52-2.14
Lapland (low)	0.47	0.10-2.54	0.58	0.19-1.75	0.85	0.36-2.02	0.96	0.46-2.00
Päijät-Häme (low)	0.95	0.27-3.31	0.76	0.28-2.03	0.72	0.29-1.83	0.67	0.28-1.58
South Karelia (low)	0.61	0.13-2.74	0.77	0.29-2.03	0.90	0.38-2.10	0.78	0.35-1.74
South Ostrobothnia (low)	0.62	0.14-2.77	0.66	0.24-1.88	1.09	0.50-2.39	0.99	0.48-2.10
Kanta-Häme (medium)	1.29	0.42-3.90	0.96	0.39-2.34	0.86	0.38-2.08	0.81	0.37-1.78
Northern Savo (medium)	0.80	0.21-3.06	0.64	0.22-1.83	1.06	0.48-2.34	1.10	0.54-2.21
Päijät-Häme (medium)	0.95	0.27-3.31	0.76	0.29-2.03	0.72	0.29-1.83	0.67	0.28-1.57
Uusimaa without Helsinki (medium)	0.72	0.18-2.92	0.67	0.24-1.90	0.84	0.35-2.01	1.00	0.48-2.07

¹The number of new cancer cases per 100,000 people per year.

²The number of new cancer cases per 100,000 people per year, if the age structure of the population in question was similar to that in Finland in 2014.

³Reference hospital districts: No actinomycetes exposure (0 cfu/m³). These are 1) Central Ostrobothnia 2) Northern Ostrobothnia hospital district 3) South West Finland Hospital district, and 4) Vaasa hospital district.

Low exposure to actinomycetes (0-50 cfu/m³). These include the Central Finland hospital district, Helsinki municipality, Kainuu hospital district, Lapland hospital district, Päijät-Häme hospital district, South Karelia hospital district, and South Ostrobothnia hospital district.

Medium exposure to actinomycetes (> 50 cfu/m³). These include Kanta-Häme hospital district, Northern Savo hospital district, Päijät-Häme hospital district, and Uusimaa (without Helsinki) hospital district.

Description: Overall, there is no significant difference in the risk of cancers in the exposed (low and medium) hospital districts as compared to the no-exposure (reference category) hospital districts. A slightly increased risk of cancers was observed in the Helsinki and Lapland hospital districts. However, the association was not statistically significant in all the cancer types. Furthermore, the Helsinki region receives water from lake Päijänne through a multistage cleaning process via a tunnel. Hence, there could be some other factors such as smoking and other lifestyle factors that lead to the risk of various types of cancers. Our sub-study observed the risk of radon exposure in some parts of Oulu university hospital District (OYS) which could be the reason behind the increased risk of cancers such as the lungs and larynx. However, we recommend further studies.

Table 7. Exposure to both moulds and actinomycetes in drinking water and risk of cancers in Finland, until 1970 and from 1971-2020.

Hospital districts	Until 1970				1971-2020			
	¹ Rate per 100,000		² Age standardized (FIN 2014)		¹ Rate per 100,000		² Age standardized (FIN 2014)	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
Bladder and urinary tract cancer								
³ Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Kanta-Häme (low)	0.89	0.48-1.67	0.74	0.46-1.18	0.98	0.83-1.20	0.89	0.76-1.05
Northern Savo (low)	0.93	0.50-1.73	0.98	0.64-1.48	1.00	0.85-1.19	0.95	0.82-1.11
South Karelia (low)	1.01	0.56-1.84	0.91	0.59-1.40	1.09	0.93-1.29	0.96	0.82-1.12
Pirkanmaa (low)	1.16	0.66-2.05	1.06	0.71-1.58	0.92	0.78-1.11	0.90	0.76-1.05
Uusimaa without Helsinki (low)	0.92	0.50-1.71	0.97	0.64-1.48	0.79	0.65-0.95	1.02	0.88-1.18
Breast cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Kanta-Häme (low)	1.01	0.76-1.35	0.91	0.72-1.15	1.14	1.04-1.24	1.05	0.96-1.14
Northern Savo (low)	0.80	0.58-1.10	0.80	0.63-1.03	1.01	0.92-1.11	0.95	0.86-1.03
South Karelia (low)	0.81	0.59-1.12	0.78	0.60-1.00	1.08	0.98-1.18	0.95	0.87-1.04
Pirkanmaa (low)	1.10	0.83-1.46	1.03	0.82-1.29	1.15	1.05-1.25	1.11	1.02-1.21
Uusimaa without Helsinki (low)	0.99	0.74-1.32	0.98	0.78-1.23	1.02	0.93-1.12	1.14	1.05-1.24
Kidney cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Kanta-Häme (low)	1.13	0.61-2.10	1.04	0.64-1.68	1.16	0.96-1.40	1.05	0.88-1.25
Northern Savo (low)	0.80	0.39-1.62	0.77	0.44-1.32	1.11	0.91-1.33	1.01	0.85-1.21
South Karelia (low)	0.73	0.35-1.52	0.69	0.38-1.21	1.17	0.97-1.41	1.01	0.85-1.21
Pirkanmaa (low)	1.07	0.60-2.00	1.04	0.65-1.69	1.08	0.89-1.31	1.04	0.87-1.24

Uusimaa without Helsinki (low)	1.16	0.63-2.13	1.15	0.72-1.83	0.93	0.76-1.14	1.14	0.96-1.35
Larynx, epiglottis cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Kanta-Häme (low)	0.81	0.38-1.77	0.73	0.38-1.38	1.00	0.63-1.58	0.87	0.57-1.33
Northern Savo (low)	1.00	0.49-2.03	0.97	0.55-1.70	1.17	0.76-1.79	1.08	0.73-1.60
South Karelia (low)	1.21	0.62-2.33	1.13	0.67-1.93	1.18	0.77-1.80	1.04	0.70-1.54
Pirkanmaa (low)	0.95	0.46-1.96	0.88	0.49-1.58	0.99	0.62-1.57	0.95	0.62-1.43
Uusimaa without Helsinki (low)	1.04	0.52-2.08	1.12	0.65-1.90	0.87	0.55-1.43	1.08	0.72-1.59
Liver Cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Kanta-Häme (low)	0.92	0.29-2.95	0.77	0.32-1.87	0.94	0.71-1.26	0.82	0.63-1.08
Northern Savo (low)	1.18	0.41-3.39	1.14	0.54-2.45	1.00	0.76-1.33	0.88	0.68-1.15
South Karelia (low)	1.11	0.38-3.28	0.90	0.39-2.08	1.03	0.78-1.35	0.89	0.69-1.16
Pirkanmaa (low)	1.05	0.35-3.18	1.05	0.48-2.30	0.85	0.63-1.14	0.81	0.61-1.06
Uusimaa without Helsinki (low)	0.96	0.30-3.01	0.99	0.44-2.21	0.86	0.64-1.16	1.11	0.88-1.41
Lung, trachea cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Kanta-Häme (low)	1.15	0.92-1.41	1.03	0.88-1.21	1.05	0.95-1.16	0.93	0.85-1.02
Northern Savo (low)	1.18	0.95-1.44	1.21	1.04-1.41	1.03	0.93-1.14	0.98	0.90-1.08
South Karelia (low)	1.11	0.91-1.38	1.04	0.88-1.22	1.06	0.96-1.18	0.93	0.84-1.01
Pirkanmaa (low)	1.04	0.84-1.29	0.96	0.81-1.14	0.97	0.88-1.08	0.92	0.84-1.01
Uusimaa without Helsinki (low)	1.05	0.85-1.31	1.07	0.91-1.25	0.83	0.75-0.93	1.06	0.97-1.15
Cancer of the lymphoid and haematopoietic tissue								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.

Kanta-Häme (low)	1.10	0.80-1.51	0.97	0.74-1.26	1.11	1.00-1.24	1.02	0.91-1.12
Northern Savo (low)	0.91	0.65-1.28	0.90	0.69-1.18	1.04	0.93-1.16	1.00	0.90-1.10
South Karelia (low)	1.06	0.77-1.45	1.00	0.77-1.30	1.09	0.98-1.21	0.97	0.87-1.07
Pirkanmaa (low)	1.06	0.77-1.46	0.99	0.76-1.29	1.02	0.91-1.13	1.00	0.90-1.11
Uusimaa without Helsinki (low)	1.02	0.73-1.41	1.02	0.79-1.32	0.92	0.83-1.04	1.11	1.00-1.22
Nose, sinus cancer								
Reference (no)	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Kanta-Häme (low)	1.29	0.42-3.90	0.96	0.39-2.33	0.88	0.38-2.08	0.81	0.37-1.78
Northern Savo (low)	0.80	0.21-3.10	0.64	0.22-1.83	1.06	0.48-2.34	1.10	0.54-2.21
South Karelia (low)	0.61	0.13-2.74	0.77	0.29-2.04	0.90	0.38-2.10	0.78	0.35-1.74
Pirkanmaa (low)	0.72	0.18-2.92	0.70	0.25-1.93	1.00	0.44-2.25	0.95	0.45-2.00
Uusimaa without Helsinki (low)	0.72	0.18-2.92	0.67	0.24-1.89	0.84	0.35-2.01	1.00	0.48-2.07

¹The number of new cancer cases per 100,000 people per year.

²The number of new cancer cases per 100,000 people per year, if the age structure of the population in question was similar to that in Finland in 2014.

³Reference category: No mould and actinomycetes exposure (0 cfu/m³). These include 1) Central Ostrobothnia hospital district 2) Northern Ostrobothnia hospital district 3) South West Finland hospital district, and 4) Vaasa hospital district.

Low exposure to moulds and actinomycetes (0 - 50 cfu/m³). These include the Kanta-Häme hospital district, Northern Savo hospital district, South Karelia hospital district, Pirkanmaa hospital district and Uusimaa (without Helsinki) hospital district.

Description: Overall exposure to moulds and actinomycetes in drinking water was not observed as an increased risk of cancers except for some cancers in the Helsinki region. However, this could also be due to other lifestyle-related habits. Hence, exposure to both moulds and actinomycetes in drinking was not associated with an increased risk of cancers in exposed and non-exposed hospital districts (reference category). Likewise, the incidence rate of some cancers was observed as an increased risk after the 1970s in both the exposed and non-exposed hospital districts. However, the association was not statistically significant.

2.3 The built environment and the risk of cancers.

This sub-study is an ecological study involving all hospital districts in Finland. There is a total of 22 hospital districts that come under the 5 university hospital districts in Finland. In this study, we utilized exposure information and cancer incidence from all the hospital districts. Exposure information was separately analysed as regards the building types and energy consumption (i.e. before 1970 and from 1970-2019). Accordingly, energy consumption was stratified based on the source. Information about energy consumption was only available up to 2005. The incidences of cancer cases were calculated from the same Finnish cancer registry tool. A unique personal identity number is used to link the cancer cases. We were unable to identify the incidences of cancer cases in each of the exposed municipalities due to the small number of cases. Hence, according to the data security and ethical guidelines, we estimated all the cancer cases based on the hospital districts of the respective municipalities. In this study, we selected the following cancer types based on the outcome of interest. These cancer types are breast, larynx and epiglottis, lungs and trachea, lymphoid and haematopoietic tissue, and nasal cancers. The incidence rate (IRR) was calculated for each cancer type.

RESULTS

The results are presented in the following tables (Tables 8-12, Figures 4 & 5). The findings of the study show that all the selected cancers increased after the 1970s. Primarily, lung cancer has increased sharply compared to the other types. The most high-risk hospital districts are Helsinki (municipality), North Karelia, Lapland and Northern Ostrobothnia. In addition, the number of apartment buildings has also sharply increased since the 1970s and terraced housing has increased proportionately during this period, mostly during the 80s. Information on energy consumption was not available for the entire duration but only from 2005 onwards. This figure shows that electricity is the most common form of energy used in Finnish homes. The next common type was oil or gas. District heating has become the most common form of energy in recent years. Despite improved housing and other conditions, we observed an increased risk of cancer incidence; it was thought that indoor air conditioning and ventilation etc. could have played a role in indoor air quality and consequently resulted in the increased incidence of cancers in the respective hospital districts. Additionally, buildings constructed before the 70s used various construction materials such as asbestos, PAH and tar. This could have an indirect effect on indoor air pollution e.g. in day care buildings and schools as well as a direct effect on the risk of cancers among the construction workers. Long-term exposures can cause a higher risk among teachers and school children as well.

Table 8. Breast cancer incidence in Finland, until 1970 and from 1971-2020.

Hospital districts	Until 1970				1971-2020			
	¹ Rate per 100,000		² Age standardized (FIN 2014)		¹ Rate per 100,000		² Age standardized (FIN 2014)	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
Central Ostrobothnia	1.13	0.74-1.72	1.23	0.90-1.68	0.99	0.88-1.12	1.02	0.91-1.14
Eastern Savo	1.06	0.70-1.63	0.97	0.69-1.36	1.18	1.05-1.32	1.00	0.89-1.11
Helsinki (municipality)	2.38	1.65-3.44	2.08	1.57-2.77	1.40	1.26-1.58	1.48	1.33-1.64
Kanta-Häme	1.40	0.94-2.10	1.21	0.88-1.66	1.19	1.07-1.35	1.12	1.00-1.24
Kainuu	0.70	0.42-1.11	0.81	0.57-1.15	0.90	0.80-1.02	0.83	0.74-0.94
Kymenlaakso	1.39	0.93-2.10	1.27	0.93-1.74	1.25	1.11-1.40	1.11	1.00-1.23
Lapland	0.61	0.37-1.01	0.80	0.56-1.13	0.86	0.76-0.98	0.83	0.74-0.94
Länsi-Pohja	0.79	0.50-1.26	0.87	0.61-1.22	0.98	0.86-1.10	0.94	0.84-1.06
North-Karelia	0.99	0.62-1.50	1.00	0.72-1.38	0.99	0.87-1.11	0.91	0.81-1.02
Northern Ostrobothnia	0.88	0.56-1.37	0.95	0.68-1.33	0.83	0.73-0.95	0.94	0.84-1.05
Northern Savo	1.11	0.72-1.70	1.06	0.77-1.47	1.07	0.95-1.20	1.00	0.90-1.12
Päijät-Häme	1.31	0.87-1.97	1.14	0.83-1.58	1.16	1.03-1.30	1.07	0.96-1.20
Satakunta	1.33	0.89-2.00	1.28	0.94-1.75	1.17	1.03-1.31	1.07	0.96-1.20
South Karelia	1.13	0.74-1.72	1.03	0.74-1.42	1.14	1.00-1.28	1.01	0.91-1.14
South Ostrobothnia	1.29	0.85-1.94	1.24	0.91-1.70	1.16	1.04-1.31	1.09	0.98-1.21
South-West Finland	1.71	1.17-2.53	1.47	1.10-1.99	1.25	1.11-1.40	1.19	1.07-1.33
Southern Savo	1.11	0.72-1.69	0.96	0.69-1.24	1.15	1.02-1.30	1.00	0.88-1.11
Tampere (Pirkanmaa) region	1.52	1.03-2.27	1.37	1.00-1.86	1.21	1.08-1.36	1.18	1.06-1.32
Uusimaa without Helsinki	1.37	0.91-2.05	1.30	0.94-1.77	1.08	0.96-1.21	1.21	1.09-1.35
Vaasa	1.81	1.24-2.67	1.65	1.23-2.22	1.14	1.01-1.28	1.11	1.00-1.25
Åland	1.80	1.23-2.64	1.39	1.03-1.89	1.09	0.97-1.23	1.02	0.91-1.14

Table 9. Larynx, epiglottis cancer incidence in Finland, until 1970 and from 1971-2020.

Hospital districts	Until 1970				1971-2020			
	¹ Rate per 100,000		² Age standardized (FIN 2014)		¹ Rate per 100,000		² Age standardized (FIN 2014)	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
Central Ostrobothnia	0.97	0.41-2.32	1.06	0.55-2.02	0.84	0.45-1.55	0.89	0.52-1.52
Eastern Savo	1.01	0.42-2.39	1.17	0.61-2.19	1.03	0.57-1.84	0.89	0.52-1.52
Helsinki (municipality)	1.34	0.60-3.01	1.10	0.57-2.08	1.33	0.77-2.31	1.32	0.81-2.16
Kanta-Häme	0.76	0.30-1.92	0.63	0.29-1.33	1.05	0.58-1.87	0.92	0.54-1.56
Kainuu	0.73	0.29-1.87	0.90	0.44-1.73	1.19	0.68-2.10	1.12	0.67-1.86
Kymenlaakso	0.87	0.36-2.12	0.81	0.40-1.61	1.26	0.72-2.20	1.07	0.64-1.78
Lapland	0.99	0.42-2.35	1.28	0.69-2.38	1.15	0.65-2.04	1.21	0.74-1.99
Länsi-Pohja	0.92	0.38-2.21	0.96	0.50-1.87	1.12	0.63-2.00	1.10	0.66-1.83
North-Karelia	1.21	0.53-2.75	1.11	0.59-2.11	1.26	0.72-2.19	1.16	0.71-1.93
Northern Ostrobothnia	0.95	0.40-2.27	0.95	0.49-1.85	1.03	0.60-1.86	1.20	0.73-1.99
Northern Savo	0.93	0.39-2.24	0.84	0.42-1.67	1.22	0.70-2.14	1.14	0.69-1.89
Päijät-Häme	0.81	0.32-2.01	0.69	0.33-1.42	1.19	0.70-2.11	1.06	0.63-1.77
Satakunta	0.97	0.41-2.31	0.86	0.43-1.70	1.36	0.78-2.35	1.24	0.76-2.04
South Karelia	1.12	0.48-2.60	0.98	0.51-1.90	1.23	0.70-2.16	1.10	0.66-1.83
South Ostrobothnia	0.94	0.39-2.27	0.84	0.42-1.67	1.15	0.66-2.05	1.05	0.62-1.76
South-West Finland	0.92	0.38-2.23	0.78	0.39-1.58	1.18	0.67-2.09	1.10	0.65-1.80
Southern Savo	0.84	0.34-2.09	0.76	0.37-1.54	1.13	0.64-2.01	0.95	0.56-1.60
Tampere (Pirkanmaa) region	0.88	0.36-2.15	0.76	0.38-1.55	1.04	0.58-1.87	1.00	0.60-1.68
Uusimaa without Helsinki	0.96	0.40-2.30	0.97	0.50-1.88	0.92	0.51-1.69	1.13	0.68-1.88
Vaasa	0.87	0.36-2.12	0.68	0.33-1.42	1.13	0.64-2.02	1.05	0.62-1.75
Åland	1.29	0.57-2.91	1.14	0.61-2.17	1.52	0.89-2.61	1.38	0.85-2.24

Table 10. Lung, and trachea cancer incidence in Finland, until 1970 and from 1971-2020.

Hospital districts	Until 1970				1971-2020			
	¹ Rate per 100,000		² Age standardized (FIN 2014)		¹ Rate per 100,000		² Age standardized (FIN 2014)	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
Central Ostrobothnia	0.90	0.65-1.17	0.92	0.75-1.13	1.00	0.87-1.14	1.02	0.91-1.16
Eastern Savo	1.11	0.84-1.46	<i>1.07</i>	<i>0.87-1.30</i>	1.31	1.15-1.49	1.10	0.97-1.23
Helsinki (municipality)	1.35	1.04-1.75	<i>1.10</i>	<i>0.89-1.33</i>	1.23	1.08-1.40	1.24	1.11-1.40
Kanta-Häme	1.17	0.90-1.53	0.97	0.79-1.19	1.16	1.02-1.32	1.03	0.91-1.16
Kainuu	0.80	0.59-1.07	0.92	0.75-1.13	1.31	1.15-1.49	1.31	1.17-1.46
Kymenlaakso	1.10	0.83-1.44	0.97	0.79-1.18	1.20	1.05-1.37	1.04	0.92-1.17
Lapland	0.90	0.64-1.15	1.13	0.94-1.38	1.29	1.13-1.47	1.36	1.21-1.51
Länsi-Pohja	0.93	0.70-1.24	1.05	0.86-1.28	1.27	1.11-1.49	1.27	1.13-1.42
North-Karelia	1.37	1.05-1.79	1.33	1.10-1.61	1.29	1.13-1.47	1.19	1.07-1.34
Northern Ostrobothnia	0.84	0.62-1.13	0.97	0.79-1.19	1.07	0.94-1.23	1.26	1.12-1.41
Northern Savo	1.20	0.92-1.57	1.14	0.94-1.39	1.14	1.00-1.30	1.09	0.97-1.23
Päijät-Häme	1.06	0.80-1.40	0.92	0.75-1.13	1.08	0.95-1.24	1.00	0.89-1.13
Satakunta	1.11	0.85-1.46	0.99	0.81-1.21	1.18	1.04-1.35	1.07	0.95-1.21
South Karelia	1.14	0.87-1.50	0.98	0.80-1.19	1.17	1.03-1.34	1.03	0.91-1.15
South Ostrobothnia	0.86	0.64-1.15	0.77	0.61-0.95	1.07	0.94-1.22	0.96	0.85-1.08
South-West Finland	1.17	0.89-1.53	0.93	0.76-1.14	1.17	1.02-1.34	1.06	0.94-1.19
Southern Savo	1.02	0.77-1.35	0.86	0.69-1.06	1.18	1.04-1.35	1.00	0.89-1.12
Tampere (Pirkanmaa) region	1.07	0.81-1.41	0.91	0.74-1.11	1.08	0.94-1.23	1.02	0.91-1.15
Uusimaa without Helsinki	1.08	0.82-1.42	1.00	0.82-1.23	0.92	0.80-1.06	1.17	1.04-1.31
Vaasa	1.20	0.91-1.57	0.95	0.78-1.17	1.18	1.04-1.35	1.08	0.96-1.21
Åland	1.11	0.84-1.46	0.80	0.65-0.99	1.12	1.00-1.28	0.98	0.87-1.11

Table 11. Lymphoid and haematopoietic tissue cancer incidence in Finland, until 1970 and from 1971-2020.

Hospital districts	Until 1970				1971-2020			
	¹ Rate per 100,000		² Age standardized (FIN 2014)		¹ Rate per 100,000		² Age standardized (FIN 2014)	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
Central Ostrobothnia	0.86	0.55-1.33	1.00	0.71-1.40	1.03	0.89-1.19	1.03	0.90-1.17
Eastern Savo	1.13	0.74-1.70	1.08	0.76-1.50	1.17	1.02-1.35	1.00	0.87-1.13
Helsinki (municipality)	1.54	1.05-2.26	1.58	1.16-2.14	1.09	0.95-1.26	1.13	1.00-1.28
Kanta-Häme	1.15	0.77-1.74	1.02	0.72-1.43	1.18	1.02-1.35	1.06	0.93-1.20
Kainuu	0.80	0.51-1.26	0.76	0.52-1.09	1.07	0.93-1.23	1.00	0.88-1.14
Kymenlaakso	1.11	0.73-1.67	1.04	0.74-1.45	1.24	1.08-1.42	1.08	0.95-1.22
Lapland	0.70	0.43-1.11	0.78	0.54-1.11	0.99	0.85-1.14	1.00	0.88-1.14
Länsi-Pohja	0.76	0.48-1.20	0.80	0.56-1.14	1.04	0.91-1.20	1.05	0.91-1.19
North-Karelia	1.00	0.63-1.48	0.99	0.71-1.39	1.12	0.98-1.30	1.03	0.90-1.17
Northern Ostrobothnia	0.90	0.58-1.39	0.95	0.68-1.34	0.90	0.77-1.05	1.01	0.88-1.15
Northern Savo	0.95	0.62-1.47	0.95	0.68-1.34	1.10	0.96-1.27	1.03	0.91-1.17
Päijät-Häme	1.08	0.71-1.64	1.10	0.79-1.53	1.15	1.00-1.33	1.06	0.93-1.20
Satakunta	1.01	0.66-1.55	0.98	0.69-1.38	1.14	0.99-1.31	1.02	0.90-1.16
South Karelia	1.11	0.73-1.68	1.05	0.75-1.47	1.16	1.00-1.33	1.00	0.88-1.14
South Ostrobothnia	1.00	0.65-1.53	0.91	0.65-1.29	1.21	1.05-1.39	1.09	0.96-1.24
South-West Finland	1.29	0.87-1.92	1.18	0.85-1.63	1.22	1.06-1.40	1.13	1.00-1.29
Southern Savo	1.00	0.64-1.51	0.96	0.68-1.36	1.20	1.04-1.38	1.02	0.90-1.16
Tampere (Pirkanmaa) region	1.11	0.74-1.68	1.04	0.75-1.46	1.10	0.93-1.24	1.04	0.91-1.19
Uusimaa without Helsinki	1.07	0.71-1.62	1.08	0.78-1.50	0.98	0.85-1.13	1.15	1.01-1.31
Vaasa	1.15	0.77-1.74	1.08	0.78-1.51	1.07	0.93-1.23	1.00	0.88-1.13
Åland	1.31	0.89-1.96	1.07	0.77-1.49	1.26	1.10-1.44	1.15	1.02-1.31

Table 12. Nasal cancer incidence in Finland, until 1970 and from 1971-2020.

Hospital districts	Until 1970				1971-2020			
	¹ Rate per 100,000		² Age standardized (FIN 2014)		¹ Rate per 100,000		² Age standardized (FIN 2014)	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
Central Ostrobothnia	1.49	0.29-7.60	2.06	0.67-6.34	0.91	0.31-2.66	1.01	0.38-2.68
Eastern Savo	0.70	0.94-4.91	0.60	0.13-2.71	1.10	0.39-3.04	1.12	0.43-2.89
Helsinki (municipality)	1.40	0.27-7.21	1.19	0.33-4.15	1.10	0.39-3.04	1.21	0.48-3.07
Kanta-Häme	1.69	0.35-8.26	1.33	0.39-4.51	0.91	0.31-2.66	0.90	0.33-2.47
Kainuu	1.25	0.23-6.76	1.79	0.56-5.65	0.98	0.34-2.79	1.18	0.46-3.01
Kymenlaakso	0.80	0.12-5.28	0.70	0.17-2.96	1.05	0.37-2.94	1.00	0.37-2.63
Lapland	0.62	0.82-4.73	0.81	0.21-3.22	0.88	0.29-2.58	1.08	0.41-2.80
Länsi-Pohja	0.69	0.98-4.95	0.97	0.25-3.61	1.55	0.60-4.00	1.62	0.68-3.90
North-Karelia	1.28	0.23-6.85	1.44	0.43-4.78	1.31	0.49-3.50	1.28	0.51-3.20
Northern Ostrobothnia	1.13	0.20-6.34	1.19	0.33-4.15	0.92	0.31-2.67	1.20	0.46-3.01
Northern Savo	1.05	0.18-6.10	0.88	0.23-3.34	1.10	0.39-3.04	1.23	0.49-3.11
Päijät-Häme	1.25	0.23-6.76	1.06	0.29-3.83	0.75	0.24-2.31	0.75	0.26-2.14
Satakunta	1.41	0.27-7.30	1.48	0.45-4.88	1.22	0.45-3.30	1.20	0.47-3.04
South Karelia	0.80	0.12-5.28	1.06	0.29-3.84	0.92	0.32-2.68	0.87	0.31-2.39
South Ostrobothnia	0.81	0.12-5.33	0.92	0.24-3.50	1.12	0.41-3.10	1.11	0.43-2.86
South-West Finland	1.20	0.21-6.57	1.03	0.28-3.75	1.15	0.42-3.15	1.16	0.46-2.98
Southern Savo	1.42	0.28-7.32	1.62	0.50-5.22	1.12	0.41-3.11	1.04	0.39-2.73
Tampere (Pirkanmaa) region	0.95	0.16-5.76	0.97	0.26-3.62	1.03	0.36-2.90	1.07	0.41-2.79
Uusimaa without Helsinki	0.95	0.16-5.76	0.93	0.25-3.52	0.87	0.29-2.56	1.12	0.43-2.90
Vaasa	1.45	0.28-7.42	1.27	0.37-4.37	1.15	0.42-3.15	1.13	0.44-2.91
Åland	0.78	0.12-5.20	0.85	0.21-3.31	1.05	0.37-2.94	0.90	0.33-2.45

Figure 4. Type of housing in Finland before 1970.

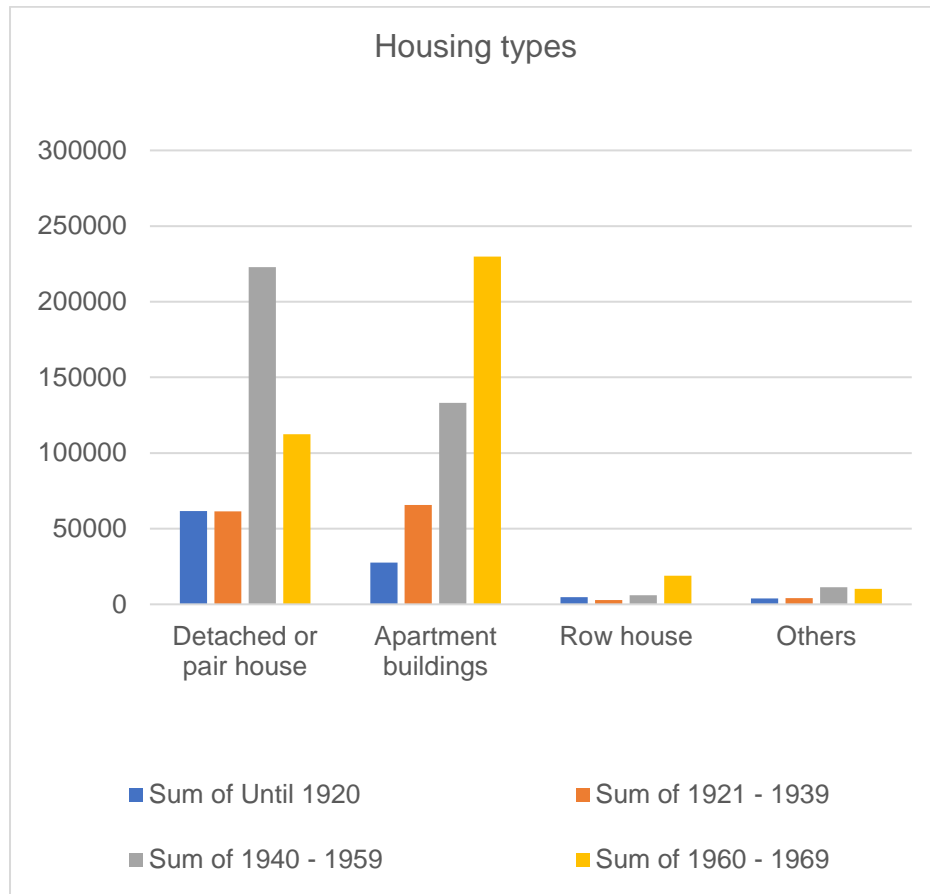
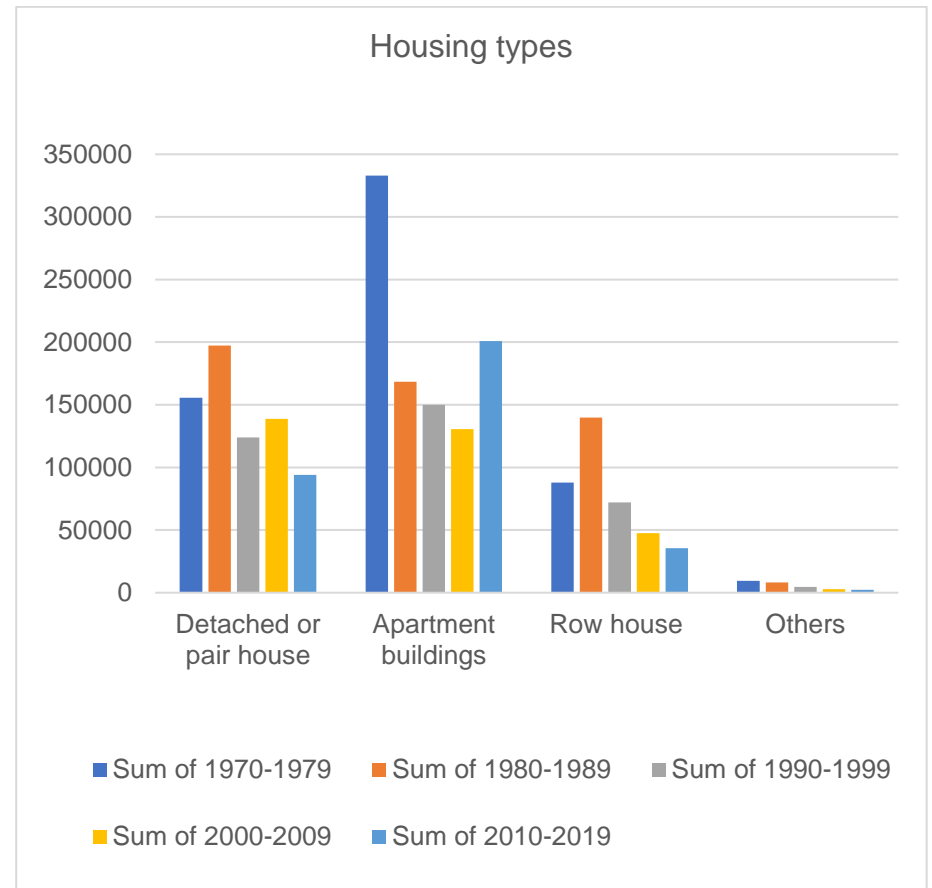
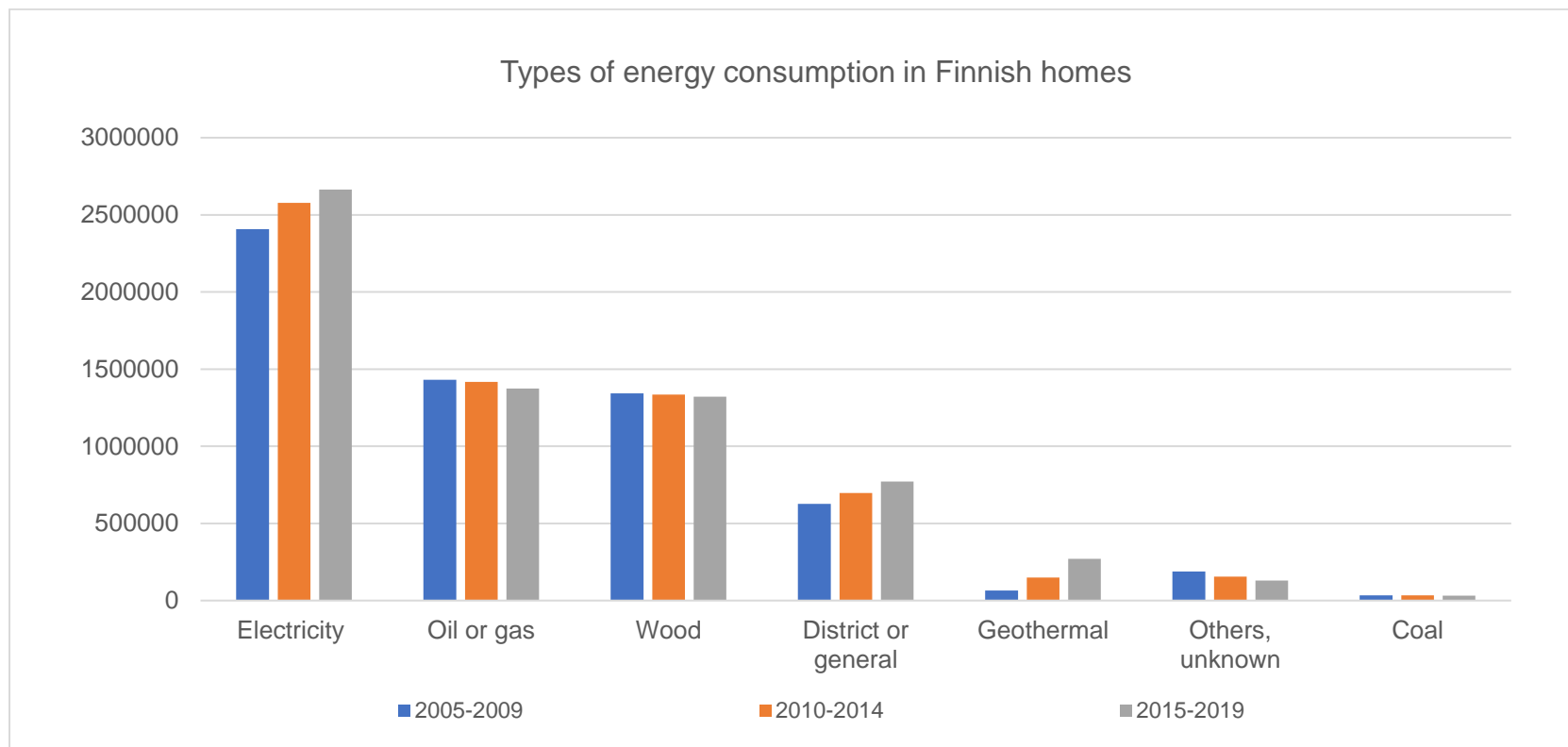


Figure 4.1. Types of housing in Finland from 1970 - 2019.



Description: Housing types dramatically changed after the 1970s. Previously, houses were mainly detached and there were fewer apartment buildings; however, after the 70s, the housing changed to mainly apartment buildings and terraced houses.

Figure 5. Energy types and consumption in Finland, 2005 - 2019.



Description: Electricity is the most common form of energy from 2005 onwards. However, consumption has widely increased in the later decades. Oil and gas are now the second most common form while coal is the least common in Finnish homes.

3. Discussion

Based on the radon concentration at the groundwater treatment plants and incidences of lung cancer, our study observed that almost all municipalities and their corresponding hospital districts with the highest radon exposure level correlated with a higher incidence rate of lung cancer as compared to municipalities with lower or no exposure levels. Hence, we can conclude that groundwater radon exposure is associated with the increased risk of lung cancer in these regions. Similarly, we also observed environmental and occupational exposure associated with the increased risk of cancers such as lung and breast cancers. Other cancers such as lymphoid and haematopoietic tissue cancer and nasal cancers were also increased but the risk was statistically insignificant. Consequently, some indication of exposure associated risk for these types of cancer is also indicated. In this study, we were not able to obtain information on construction materials used in Finnish housing such as asbestos, PAH compounds and bitumen tar that would help to provide an in-depth understanding of the exposure associated risk. Cancer risks were observed to be very high after the 1970s. Similarly, exposure to moulds and actinomycetes in the drinking water was not observed as an increased risk of cancer as compared to no-risk hospital districts (reference category). In this sub-study, we were not able to identify the cancer risk of exposure to microbes in the Finnish drinking water at the population level. Concerning human health and drinking water, even a small risk constitutes a great effect. Hence, individual-level data would possibly provide the most clear association. Future studies are recommended.

Studies on indoor radon exposures and lung cancer are well represented in prior research, including the pathway combination for radon (Darby et al., 2005, Krewski et al., 2006, Messier et al., 2017], however, there are very few studies on the association between groundwater radon and the risk of cancer. Our findings were consistent with other epidemiological studies on groundwater radon concentration and lung cancer risk. This study in North Carolina, USA observed a significant positive association between groundwater radon concentration and lung cancer incidence rates [Messier et al., 2020]. According to the study, groundwater radon exposure was associated with an odds ratio (OR) of 1.13 (95% CI 1.04 -1.23) suggesting an overall 3% increase in the incidence rate of lung cancer for every 100Bq/l increase. The study was adjusted for various confounding factors such as age, gender, smoking, race, indoor air radon etc. Another study from Maine also observed a significant positive correlation with lung cancer (Hess et al., 1983). Individual case-control studies from European, North American and African studies are also consistent with our findings (Darby et al., 2005, Krewski et al., 2005, Darby et al., 2006, Krewski et al., 2006, Orosun et al., 2021). Our findings are also parallel to other Finnish sub-studies. Few epidemiological studies have observed chemical exposure to be associated with the

risk of cancers in Finland (Koivusalo et al., 1994 & Koivusalo et al., 1997). However, microbial exposure and cancer risk are very limited. A study by Miettinen and colleagues observed that about 2% of the drinking water from the distribution network in Finland contained microbes in the drinking water. However, the study did not report the associated risk of cancers to this exposure in the study (Miettinen et al., 2007). This small proportion of moulds and actinomycetes in the drinking water could be the reason for the taste and odour experienced in some distribution networks (Korhonen et al., 2006). According to the report from the Finnish Institute of drinking water, microbial growth in Finnish drinking water is phosphorous limited instead of carbon limited. Hence, analysis of phosphorous compounds would give a better indication of the growth potential of microbes (Mäkinen, 2008). In the report, a small proportion (0.03-0.09%) of the sample contained at least one of the microbes in the drinking water. Microbial contamination was more common in well water than in the distribution channel. In general, moulds appear to decrease in the distribution channel due to dilution while the actinomycetes increased as a result of microbial growth (Miettinen et al., 2007). In an occupational setting, a Finnish cohort of 1.8 million economically active participants estimated the risk of cancer exposed to moulds and bacteria (Laakkonen et al., 2008). The study observed a significant increased risk of cervical and lip cancer among women in the highest exposure category but not among males. A Finnish job-exposure matrix quantitatively estimated the exposure to moulds and bacteria among the economically active Finnish workers in the study. Hence, these studies were not able to show a clear association between microbial exposure and cancer risk. Findings from this study are consistent with our study. Hence, we assume that exposure to drinking water circulated via distribution channels is not associated with cancer risks. Further research is needed to demonstrate whether moulds and actinomycetes in the drinking water could have detrimental health outcomes other than cancer.

Likewise, indoor air exposure was associated with some cancer types such as lungs. Epidemiological studies observed similar cancer risks at the population level. A United States study reported a high risk of lung cancer, particularly adenocarcinoma, among the never smokers suggesting there were other risk factors including indoor air pollution and occupational exposures (Rivera et al., 2016). Another Chinese study observed degrading indoor air quality relating to housing quality such as poor ventilation was associated with an increased risk of lung cancer among non-smoking women (Mu et al., 2013). Similarly, the use of asbestos in older buildings and the risk of cancer was observed. A review published in Iceland reported the risk of mesothelioma and lung cancer due to asbestos in the buildings (Gudmundsson and Tomasson, 2019). According to the study, even though modern housing bans the use of asbestos, the risk was

still observed due to the latency period. The latent time from exposure to disease can be up to 40 years. Hence the study of such harmful agents should be continued especially among older buildings and populations exposed for a long time such as construction workers, daycare and school teachers etc.

The limitation of the study is the study design where the incidence rate was assigned at the population level and the estimated cancer risk at the municipal level had to be based on the hospital district. This was because there were very few cases in some smaller municipalities in Finland and therefore according to the data regulation and ethical principle, the dataset was provided based on the hospital districts. Hence, we decided to choose 22 hospital districts for our study. Likewise, we were unable to obtain the groundwater radon figures from all regions of Finland and that limited our choice of exposure information and classification in this study. Due to this, we cannot ignore the likelihood of exposure misclassification which could dilute the association and bias of the observed effect towards null. For example, in the sub-analysis of microbial exposure (actinomycetes) in drinking water, Päijät-Häme was included in both the low and medium exposed categories. In some cases, the exposed population were a small proportion of the total population which limited the choice of exposure category in the study. This could result in an under or over-estimation of the true exposure. This can not only underestimate the true occurrence of both moulds and actinomycetes exposure estimation but also the categorization (exposed vs. unexposed) in the study. However, we were able to consider a large number of exposed populations as regards indoor air exposure both at environmental and occupational levels and could therefore estimate the risk of various cancers in all the hospital districts in Finland. This could address the exposure misclassification in the study. However, we cannot ignore the residual confounding in the study. We did not have direct information on smoking throughout the study period therefore we were unable to adjust for a possible confounding effect. Hence, we had to restrict the study to a limited period based on the data. However, this limited information was able to determine the smoking trend in recent years. The average smoking prevalence in the reference category was not different from the exposed categories meaning that there was no statistical difference in smoking patterns in the exposed and non-exposed hospital districts. We observed a decreasing trend in the number of smokers in 2013, 2014, 2015, and 2018 in all hospital districts in Finland (THL, 2022). Though we were not able to estimate the exposure at the individual level as well as municipal level, we were able to observe the current situation at the population level where the exposure levels of microbes, primarily moulds, actinomycetes and groundwater radon were all measured above the reference level. Another limitation of the study was the lack of information on the occupation and smoking status of the individual patients.

The strength of the study is the large sample size. This study utilized data with a full coverage of cancer cases in all the selected hospital districts in Finland. We were able to observe the time trends in cancer incidences despite the declining prevalence of smoking. The use of the personal identity code enabled a linking of the various registers that ensured a complete ascertainment of all relevant events (Pukkala et al., 2011). The completeness and accuracy of the cancer registers in Finland are of top quality in international rankings (Pukkala et al., 2018). Despite the smoking information being limited, strong and precise data from the National Institute of Health and Welfare (THL) helped to understand the smoking trend in recent years. At the population level, there was a public health concern about microbial exposure in drinking water associated with cancer risk. Even though the risk is low, the effect on the population level is high. In this study, we were able to address this issue and safely conclude that the risk is not significantly higher at the population level. However, future research is needed to estimate the risk at the individual level. Additionally, we were not able to separately estimate the exposure in specific occupational categories but we can assume that the risk of cancer is not remarkably higher based on our findings. Future studies with individual-level quantitative exposure adjusted to smoking among directly exposed occupational groups such as water distribution workers, residents in older and newer housing (and both) and other similar categories would provide the strongest evidence.

4. Conclusion

Based on the findings of these studies, we were able to observe the association between groundwater radon exposure and an increased risk of lung cancer. Future studies with high-quality individual-level quantitative exposures are required to explore the association between lung cancer and possibly other cancer risks. Similarly, indoor air exposure was associated with an increased risk of certain types of cancers such as lung and breast cancer. The risk was primarily associated with occupational and environmental exposure. Despite the decreasing trends in smoking habits, we observed an increased incidence of certain types of cancers. However, we were not able to identify the cancer risk associated with exposure to moulds and actinomycetes in drinking water in Finland.

5. Future research needs and recommendations

Future studies with individual-level quantitative exposure adjusted to smoking among highly exposed occupational categories would provide the strongest evidence. Further research into radon exposure needs to be conducted with other cancer outcomes such as breast cancer. Incidences of some cancers are declining while others are increasing; this needs future research to learn more about the most recent trends in cancer incidence. Similarly, exposure to the

construction materials such as asbestos, PAH, tar etc. in Finnish housing could be further explored among construction workers or other highly exposed groups such as daycare and school teachers. Since the latent period of hazardous substances can take up to 40 years, future research among these highly exposed occupational groups is recommended.

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Tulosten tiivistelmä, tutkimuksen rajoitukset ja suositukset

Syöpärekisterin viimeaikaisten tilastojen mukaan syövän ilmaantuvuudessa on havaittavissa lisääntymistä mm. pään ja kaulan alueen syövässä sekä tupakoimattomien keuhkosyövässä. Aikaisemman tutkimuksen mukaan homealtistumisen aiheuttama syöpäsairastuvuuden riski kohdistui selvemmin naisiin kuin miehiin, joilla ei lisäriskiä havaittu. Homeelle altistuneilla naisilla syövän lisäriski kohdistui mm. huulisyöpään (Laakkonen ym. 2008).

Tutkimuksemme mukaan pohjaveden radonin pitoisuuden ja alueen syöpien välillä havaittiin yhteys keskussairaala-alueen tasolla. Mittauksia tehtiin vesilaitoksilla. Kuntatason tai työpaikkatason tarkastelua ei päästy tekemään tietosuojamääräysten tulkinnan vuoksi. Radonin on aiemmin arvioitu aiheuttavan 100-200 ylimääräistä syöpätapausta vuosittain. Radonalueilla syöpäriski kohdistuu työntekijöiden lisäksi myös lapsiin ja nuoriin asunnoissa, päiväkodeissa ja kouluissa. Tämä altistuminen vaikuttaa heidän terveyteensä työiässä. Radonalueilla altistumista tapahtuu työpaikoilla, julkisissa rakennuksissa alimmassa kerroksessa ja asuinrakennusten pohjakerroksissa. Epidemiologisen tutkimuksen avulla ei työperäistä ja muun ympäristön altistumista voi erottaa toisistaan.

Juomaveden homeiden ja sädesienten vaikutus syöpäsairastavuuteen oli vähäinen eikä saavuttanut tilastollista merkitsevyyttä minkään syövän osalta. Juomaveden kautta tapahtuva altistuminen kohdistuu ko. alueella koko väestöön, myös työpaikoilla työikäiseen väestöön.

Hallussamme olleita työpaikkakohtaisia altistumismittaustietoja (radon, PAH-yhdisteet, homeet, sädesienet) ei voitu hankkeessa käyttää toivotulla tavalla tietosuojamääräysten vuoksi. Ositekohtaiset sairausluvut olisivat olleet niin pieniä, että yksittäisen potilaan henkilöllisyys olisi voinut paljastua, joten syöpärekisteri ei toimittanut tietoja kunnan tarkkuudella. Sama koski kunta- ja työpaikkakohtaisia tunnuslukuja STUK:in radonmittausten ja muiden altistemittausten osalta. Pienimmäksi tarkasteltavaksi alueeksi jäi näin ollen sairaanhoitopiiri tässä raportissa. Tutkimusta tulisi kuitenkin jatkaa, koska alueellisia eroja havaittiin.

Merkittävä rajoite oli myös havaintokohtaisen tupakointitiedon puuttuminen syöpärekisterin tiedoista. Tupakointitietona voitiin käyttää vain THL:n tarjoamaa yleistä väestön alueellista tupakointitietoa. Tämän vuoksi suunniteltua monimuuttujamallitusta ei voitu toteuttaa synergismianalyysin tekemiseksi. Tupakointi on kiistatta merkittävin sekoittava tekijä syöpätutkimuksessa, kun yritetään arvioida työ- (tai ympäristö)peräisiä riskejä. Tupakansavu saattaa lisäksi lisätä muiden syöpävaarallisten tekijöiden, kuten radonkaasun, PAH-yhdisteiden ja sienten toksiinien syöpävaarallisuutta (synergismi). Ravintotekijöitä ei huomioitu tässä tutkimuksessa.

Suosituks

Tutkimuksemme perusteella syntyi useita merkittäviä kehitys- ja jatkotutkimustarpeita. Yhteistyötä tulisi lisätä tutkimuslaitosten, yliopistojen ja syöpärekisterin välillä. Syöpätutkimus tarvitsisi runsaamman rahoituksen ja pitkäaikaisen, ohjelmatyyppisen tutkimusotteen. Olemme esittäneet kansallisen syöpätutkimuskeskuksen perustamista epidemiologisen tutkimuksen vahvistamiseksi. Kansalliset terveystietorekisterit ovat vajaakäytöllä.

Työryhmämme suosittelee nykyisen ja aikaisemman tupakointitiedon sekä ammatin lisäämistä syöpärekisterin havaintokohtaisiin tietoihin. Altistumistiedon ja sairauskohtaisen tiedon tietoturvallinen yhdistäminen tulisi olla mahdollista jonkin ulkopuolisen tahon esim. FIMM:n anonymisointipalvelun avulla. Muuten heikkoja signaaleja ei havaita työ- tai ympäristöaltisteiden syöpävaarallisuudesta elleivät vasteet ole tavattoman suuria. Harvinaisten syöpien tutkimus on mahdollista vain hyvin suurista aineistoista ja tulisi järjestää kansallinen tai pohjoismainen

datapankki, josta tietojen louhinta olisi mahdollista ilman yksilötason tietosuojan vaarantumista. Kansallisen yhteistyön lisäksi myös kansainvälistä tutkimusyhteistyötä tulisi lisätä. Syöpäsairauksien merkitys työelämässä ja työlääketeieteessä tulee kasvamaan väestön ikääntyessä, työurien pidentyessä ja syövän hoitotulosten parantuessa. Syövästä toipuvien työterveyshuoltoa tulisi räätälöidä ja kehittää.

Kiitokset

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