Title: International comparisons of the incidence and mortality of sinonasal cancer

Authors: Danny R Youlden^a, Susanna M Cramb^a, Susan Peters^b, Sandro V Porceddu^c, Henrik Møller^d, Lin Fritschi^b, Peter D Baade^a

^a Cancer Council Queensland, 553 Gregory Tce, Fortitude Valley QLD 4006, Australia.

^b Western Australian Institute for Medical Research, University of Western Australia, 35 Stirling Hwy, Crawley WA 6009, Australia.

^c Cancer Services, Princess Alexandra Hospital, 199 Ipswich Rd, Woolloongabba QLD 4102, Australia.

^d King's College London, Thames Cancer Registry, 42 Weston St, London SE1 3QD, United Kingdom.

Corresponding author: Mr Danny Youlden, Cancer Council Queensland, PO Box 201, Spring Hill, QLD 4004, Australia; Telephone: +61-7-36345351; Facsimile: +61-7-32598527.

Email addresses: DR Youlden - dannyyoulden@cancerqld.org.au;
SM Cramb - susannacramb@cancerqld.org.au;
S Peters - susan.peters@uwa.edu.au;
SV Porceddu - Sandro_Porceddu@health.qld.gov.au;
H Møller - henrik.moller@kcl.ac.uk;
L Fritschi - lin.fritschi@uwa.edu.au;
PD Baade – peterbaade@cancerqld.org.au.

Article category: Review

Word counts: Abstract – 240; Body of text – 3,685

Figure count: 3

Table count: 3

Reference count: 54

Abstract

Background: This paper reviews international patterns in sinonasal cancer incidence and mortality in light of changes in exposure to known risk factors. Sinonasal tumours are relatively rare, but they have the second highest occupational attributable fraction of all types of cancer, with a well-established link for workers exposed to wood dust.

Methods: Data for a variety of countries, mainly in Europe, North America and the Asia-Pacific region, were obtained from publicly accessible sources and supplemented with information requested from selected cancer registries. Rates were directly age-standardised to the World Health Organization Standard Population.

Results: The average annual incidence of sinonasal cancer was typically between 5-10 per million in males and between 2-5 per million in females between 2004-2008. Denmark reported the highest rates, with incidence continuing to increase, in contrast to trends in other countries which either remained relatively stable, or were decreasing slightly. There were significant recent decreases in sinonasal cancer mortality rates within two-thirds of the included countries.

Conclusions: Our observations are generally consistent with efforts to limit exposure to wood dust and other potentially causal substances in the workplace, as well as a reduction in the prevalence of smoking in many developed countries. Of concern is that occupational and behavioural risks related to sinonasal cancer are likely to increase among people in less developed countries into the future. However the incentive to intervene in these countries is limited by the lack of accurate and reliable cancer data.

Key words: sinonasal cancer; incidence; mortality; risk factors; international; epidemiology.

Introduction

Sinonasal cancer comprises cancer of the nasal cavity and paranasal sinuses, including the maxillary, ethmoid, frontal, and sphenoid sinuses and the middle ear. These cancers are uncommon; internationally they comprise about 0.2% of all cancers (excluding non-melanoma skin cancer) among males and 0.1% among females [1]. The majority of sinonasal cancers have an epithelial histology (up to 75%), with squamous cell carcinomas being the most common followed by adenocarcinomas [2].

Surgery continues to be the preferred treatment for sinonasal cancer [3]; resection of small tumours with clear margins offers excellent prognosis. However, many sinonasal cancers are detected in an advanced state due to late presentation, making complete surgical resection difficult. Post-operative radiotherapy is commonly employed in this situation but outcomes remain poor. Treatment is often limited due to the close proximity of disease to critical structures such as the eyes, brainstem and brain. More recently, investigators have been adding concurrent chemotherapy to post-operative radiotherapy but the benefits remain undefined [4, 5].

The primary risk factors for sinonasal cancer are occupational exposures, and in particular wood dust [6]. According to the International Agency for Research on Cancer (IARC), other established occupational risk factors include leather dust, nickel compounds, radium-226 and radium-228 as well as their decay compounds, and acids used in isopropyl alcohol production [7-9]. Associations between sinonasal cancer and occupational exposure to formaldehyde, textile dust, and hexavalent chromium compounds have also been suggested but the evidence for these are limited [7-9].

Sinonasal cancer is the second most important cancer site for occupational attribution, after mesothelioma [10]. In the United Kingdom, the occupational attributable fraction for sinonasal cancer was estimated to be 43% for men and 20% for women for cancers registered in 2004 [10].

While having less impact than occupational exposure, tobacco smoking has also been associated with an increased risk of sinonasal cancer [11-13], with the link being stronger for squamous cell carcinoma than for adenocarcinoma. There are few other known causes of sinonasal cancer.

The purpose of this study is to describe and compare current international patterns in sinonasal cancer incidence and mortality in light of documented changes in workplace exposures and smoking over time.

Materials and Methods

Sources of Data

Statistical information about sinonasal cancer (ICD-7/8/9: 160; ICD-10: C30-C31) was obtained from publicly available cancer registry and mortality databases. This was supplemented with data requested specifically from individual cancer registries. Further details are outlined below.

Selection of countries (incidence)

Unlike more common types of cancer, we were limited in the selection of countries for incidence because sinonasal cancer was not specifically included in the Globocan dataset [14]. Annual sinonasal cancer incidence data by age group and sex were, however, available from publicly accessible cancer registry datasets for nine countries, namely Denmark, Finland, Norway, and Sweden [15]; Hong Kong [16]; Ireland [17]; Italy [18]; the Netherlands [19]; and the United States of America (USA) [20]. We were also able to request similar information from the cancer registries of a further five countries/regions, including Australia, New Zealand, Canada, South Korea and South-East England. All of these registries are population-based and covered the entire country/region, with the exception of the USA (9% coverage for 1973-2010 and 28% coverage for 2004-2008) and Italy (10% coverage for 1992-2007 and an average coverage of 27% during 2004-2008).

Selection of countries (mortality)

Of those countries for which incidence data was available, we endeavoured to obtain mortality information from the same source to enable a direct comparison of recent incidence and mortality rates. This was not possible for four countries: Canada, Ireland, South Korea and the USA; instead, mortality data for these countries was obtained from the World Health Organization (WHO) mortality database [21]. Mortality data specifically for South-East England was not obtained.

All longer-term mortality trends were calculated based on data from the WHO mortality database [21]. Countries were selected according to the quality of mortality data (at least 95% coverage between 1990-2010), the number of years available (at least 10 years data) and the number of deaths due to sinonasal cancer (an average of at least 10 deaths per year for males and females combined). Consequently, mortality trends were analysed for Germany, Greece, Hungary, Poland, Romania, Spain and the United Kingdom in addition to the countries for which incidence trends were examined (except for Finland and Norway which did not have mortality information available on the WHO database) [21]. Although Japan and France both met the above selection criteria for mortality data, a change in coding during the mid to late-1990s corresponded with a dramatic drop in numbers, so they were excluded.

Statistical methods

All incidence and mortality rates were directly age-standardised to the WHO World Standard Population [22] and expressed per million population. Average annual estimates of incidence and mortality were calculated for the years 2004-2008 along with yearly rates for trend analysis for the selected countries.

Differences in the years of data available meant that the range of time for which trends were assessed ranged from four decades (1970-2011 eg. incidence data for some Nordic countries) to

1999-2009 (incidence data for South Korea). Trends were evaluated using the Joinpoint regression program v3.4.3 (© National Cancer Institute, Bethesda) under the specifications of at least eight observations between a joinpoint and the end of the data, and at least seven observations between two joinpoints. The modeling process started with the assumption of constant change over time (i.e. no joinpoint) and then checked whether adding joinpoints at various intervals significantly improved the fit of the model [23]. All possible combinations of trend lines were compared using Monte Carlo permutation tests [23], and the option with the fewest joinpoints that provided the best fit was objectively chosen. A maximum of three joinpoints was considered sufficient, despite the large number of years available for some countries, to avoid the trends being influenced by spurious fluctuations. The maximum number of joinpoints was decreased for countries with fewer years of data. Results were expressed in terms of the annual percentage change (APC) along with the associated 95% confidence interval (95% CI). The APC was considered to be statistically significant if $p < 0.05$.

The ratio of the mortality rate to the incidence rate (MR:IR) was also calculated to provide a proxy measure of the chances of survival. The closer that MR:IR is to 0 the more likely a person is to survive, while a ratio that is close to 1 indicates that most people die from the disease in question.

Results

Incidence

Of the countries for which incidence data on sinonasal cancer were available, most reported age-standardised rates of between 5 to 9 per million for males and between 2 to 5 per million for females (Table 1). The highest rates were in Denmark (12 per million for males and 7 per million for females). Sinonasal cancer was more common among males than females in each country, with the age-standardised incidence rate ratio for males:females varying from 1.3 in Norway to 2.5 in Italy and Finland (data not shown).

Variation was also observed in the age distribution between countries. Among males, more than half the cases were aged 65 years and over in all countries apart from Canada, Hong Kong, New Zealand, South Korea and the USA; for females, the exceptions were Ireland as well as Hong Kong, New Zealand and South Korea (Table 1). The proportion of women who were 65 years or older at the time of diagnosis tended to be higher than men, except for England and Ireland.

Incidence rate trends for sinonasal cancer by sex in selected countries are shown in Fig. 1, with the corresponding average annual percentage changes reported in Table 2. The largest contemporary decreases (2.7% per year for males and 1.9% per year for females) were in Hong Kong. Significant, ongoing decreases were also recorded for males and females in Finland and England, as well as for males in Australia, the Netherlands, New Zealand and Norway. In contrast, incidence was significantly increasing for both sexes in Denmark, particularly among females.

Data on sinonasal cancer histology was only readily available from the USA.[20] The majority (59%) of sinonasal cancers diagnosed in the USA between 2004 and 2008 were epithelial neoplasms, with squamous cell carcinomas and adenocarcinomas being the most common subtypes, accounting for 38% and 10% of all sinonasal cancers, respectively. Males (42%) had a higher proportion of squamous cell carcinomas than females (33%). However, incidence rates of sinonasal squamous cell carcinoma decreased significantly over time (Males: APC = -1.4%; 95% CI = -1.8%, -1.0%; females: APC = -0.9%; 95% CI = -1.6%, -0.3%) while adenocarcinoma rates remained stable for both sexes (Fig. 2).

The most common sites diagnosed with sinonasal cancer in the USA during 2004-2008 were the nasal cavity (46%) and maxillary sinus (29%).[20] This distribution has changed since the 1970s, when similar numbers were diagnosed for these sites (nasal cavity 39%, maxillary sinus 40%). Specifically,

incidence rates for tumours of the nasal cavity among males and females increased significantly between 1973-2010, while rates of maxillary sinus cancers have simultaneously decreased for both sexes (Fig. 2). More than half of sinonasal cancer patients in the USA were diagnosed at an advanced stage (57%), while a further 21% did not have stage information available.

Mortality

Similar to incidence, mortality rates were higher for males than females. For the countries included in Table 1, mortality rates between 2004-2008 varied from 1.3/100,000 in Sweden to 3.3/100,000 in Denmark for males and from 0.5/100,000 in the Netherlands to 1.5/100,000 in Denmark for females. The male:female age-standardised mortality rate ratio was usually between 1.5 and 2.5, but was as high as 3.7 in the Netherlands (data not shown).

The proportion of deaths that occurred after 65 years of age ranged from 42% in New Zealand to 70% in the Netherlands among males, and from 51% in Canada to 84% in Italy among females.

Significant, ongoing decreases in the mortality rate for sinonasal cancer dating back to the 1970s were found for both males and females in Australia, Canada, Greece, Hong Kong, Ireland, the Netherlands, Sweden, the United Kingdom and the USA, as well as for males in New Zealand and females in Hungary and Spain (Table 3 and Fig. 3). More recently, decreases were also observed for both sexes in South Korea and for females in Germany. Males in Romania, among whom the APC was +2.2% between 1999-2010, were the only group that experienced a significant increase in mortality rates due to sinonasal cancer over the past decade.

Marked differences were apparent in the mortality to incidence rate ratio, which varied from 0.21 in the Netherlands to 0.48 in South Korea for males, and from 0.12 in Norway and the Netherlands to 0.69 in New Zealand among females (Table 1). There was substantial disparity in the value of MR:IR

by sex in Norway, the Netherlands and South Korea, where the ratio was higher for males, and Finland, Ireland and New Zealand where the ratio was larger for females.

Discussion

Sinonasal cancer is a relatively rare cancer worldwide, with age-standardised incidence rates currently less than 10 per million in males and less than 5 per million in females for most of the countries in Europe, North America and the Asia-Pacific region that were included in this study. Incidence rates over time in these countries seem to be relatively stable, or decreasing slightly. The exception is Denmark, where incidence rates are higher than in other developed countries and continuing to trend upwards. Furthermore, compared to the histological distribution in the USA where squamous cell carcinomas outnumbered adenocarcinomas by almost 4 to 1, published data from Denmark for a hospital-based series of 242 sinonasal cancer patients diagnosed between 1995 and 2004 [24] showed considerable differences by histology, with proportionally more adenocarcinomas (29%) compared to squamous cell carcinomas (55%). It is unclear why the incidence of sinonasal cancer in Denmark should be so different. A study in 2007 based on data from the Danish National Board of Industrial Injuries found that 87% of 44 registered patients with sinonasal adenocarcinoma were deemed as being occupationally induced [25]. However, another 64 cases of sinonasal adenocarcinoma were not registered with the occupational compensation authority, and of these, only 32% of males and 0% of females had known wood-dust exposure.

Mortality rates for sinonasal cancer are typically less than half that of incidence and have also been decreasing over time in most of the countries for which sufficient and reliable data were available. Prognosis is heavily dependent on age and stage at diagnosis [26, 27]. For example, Turner and Reh [26] reported that the stage-specific 5-year relative survival for sinonasal cancers diagnosed in the USA between 1973-2001 varied from 81% for localised tumours to 49% for regional disease and 28% for metastatic cancers. Tumour location has also been reported as having a prognostic effect, with

tumours located in the sphenoid sinus being associated with a significantly lower probability of mortality within 5 years of diagnosis compared to either the frontal or maxillary sinus [27], while the evidence for histology appears mixed [27-29]. It is therefore feasible that differences in the distribution of age, stage, subsite and possibly histology of sinonasal cancers may contribute to the variation seen in the values of MR:IR between countries and also by sex within some countries.

Local recurrence continues to be the mainstay of treatment failure rather than distant disease [3]. Many sinonasal tumours grow to large sizes before they become symptomatic. Hence they can grow to adjoin or invade important structures before being detected. This often makes complete surgical excision difficult. Improved imaging techniques such as magnetic resonance imaging and positron emission tomography have aided in the delineation of both pre-operative and post-operative disease, improving the rate of resectability and accuracy of post-operative radiotherapy. Modern radiotherapy techniques, including intensity modulated radiotherapy, now make it possible to deliver high doses to areas of residual disease while limiting the dose to critical structures, such as the eye, optic nerves and optic chiasm. This reduces the risk of late complications such as blindness [4, 5, 30]. However, due to the infrequency of sinonasal cancer, randomized data comparing the benefits of post-operative radiotherapy, improved radiotherapy techniques and the addition of concurrent chemotherapy is lacking.

The main occupational risk factor that has been identified for sinonasal cancer is exposure to wood dust, which may occur in occupations including forestry and sawmill workers, furniture makers and carpenters, and workers in the pulp and paper industry. The association was first recognised in the 1960s when a cluster of nasal cancer among British woodworkers was observed [31]. Based on a range of studies since then, wood dust was classified as a Group 1 human carcinogen in 1995 by the IARC [6], with a particularly strong connection acknowledged between exposure to hardwood dust and sinonasal adenocarcinoma.

This decision was subsequently confirmed by other international and national institutions, followed by legislation to limit exposure levels. The Council of the European Union set the occupational exposure limit to 5 mg/m³ inhalable dust in 1999 [32], followed by a new limit of 1-1.5 mg/m³ in 2005 [33]. In the USA, thresholds were set at 5 mg/m³ for softwoods and 1 mg/m³ for most hardwoods in 1997 [34], and then further lowered in 2005 to 1 mg/m³ for all wood dust [35]. Similar occupational exposure standards have also been applied in Canada [36], New Zealand [37] and Australia [38].

Some of the factors that may influence disparities in the risk of developing sinonasal cancer between countries include the proportion of workers exposed to wood dust, differences in wood types, processing methods, when control measures were developed and the presence of other carcinogens in the workplace [39]. It has been estimated that 2.0% of the employed population of the European Union was occupationally exposed to wood dust between 2000-2003 [40]. Comparing the incidence rates of sinonasal cancer for males as presented in Table 1 with the percentage of workers exposed above the current limit of 1 mg/m³ inhalable wood dust, there is some suggestion of correlation. By highest to lowest incidence rates, the percentages exposed were: Denmark 1.7%; the Netherlands 1.3%; Italy 1.2%; Finland 1.2%; Sweden 0.8%; and Ireland 1.7% [40]. However, the use of specific wood species and working environments are likely to differ between the countries, and will consequently influence the observed relationship between exposure and incidence.

Occupational exposure to wood dust has generally decreased over time. In England, a decline of 10% per year was reported for furniture manufacturing between 1976-1983 [41], a Danish study found an annual decrease of about 8% in the same industry from 1997 to 2004 [42], a 6% decrease per year was described for the USA paper and pulp industry between 1979-1994 [43] and softwood dust exposure levels dropped 3% annually over the years 1981 to 1997 in Canadian lumber mills [44].

Combining data from various industries, decreasing trends were reported for occupational exposure to wood dust of 11% per annum (1979-1997) in the USA [45] and 8% per annum (1985-2005) in the United Kingdom [46].

Galea *et. al.* [46] linked the downward trend of wood dust exposure in the United Kingdom to factors such as technological changes in production processes, responses to new legislation, and enforcement agency inspections, together with global economic trends. In the Netherlands, the wood processing and construction industries have implemented several measures to prevent or diminish occupational exposure to wood dust since the late 1980s, coinciding with a decline in the incidence of sinonasal adenocarcinomas among males [47]. In many European countries, the use of chain saws has been replaced by forest harvesters and other equipment that reduces the level of occupational exposure to wood dust [40].

Other occupational exposures associated with either an established or suspected increased risk of sinonasal cancer affect considerably smaller numbers of workers worldwide compared to wood dust. The prevalence of occupational exposure to formaldehyde, hexavalent chromium, and nickel compounds was estimated to be 0.7%, 0.6%, and 0.4% of all workers in the European Union in 1990-1993, respectively [48]. Annual declines in occupational exposure levels to formaldehyde ranging from 4-5% in the USA (1979-2001) [49] to 7-9% in France (1986-2003) [50] have been reported for various industries. Symanski and colleagues [51] reported annual decreases in nickel exposure in the mining (-7%), smelting (-9%) and refining (-7%) sectors, but not in the milling (+4%) industry. This study was based on data from North American, European and Australian workplaces, with exposure levels documented to be falling more rapidly in North America than elsewhere [51].

Relocation of industrial activities from the Western world to developing countries might also play a role in the observed patterns. For example, in the Netherlands there has been a decrease in the

number of men employed in the furniture, leather or building industries, with leather processing being moved to low-income countries during the 1980s and 1990s [47].

Cigarette smoking and environmental tobacco smoke are established risk factors for sinonasal cancer [12, 13], principally for squamous cell carcinoma. Smoking rates have been decreasing in many developed countries since the 1970s [52]. We would therefore expect a concomitant reduction in sinonasal cancer over time, such as has been occurring with lung cancer in males. That this was not uniformly seen in the data that we presented, even in countries where the reduction in smoking has been marked, suggests that other factors may have a greater influence on the observed trends. For instance, Denmark, while having much higher incidence rates of sinonasal cancer, has very similar smoking rates to other Northern European countries [53]. It could also be that by considering trends for all sinonasal cancers combined we have reduced our ability to detect the ecological association that smoking has with squamous cell carcinoma. Indeed, when we analysed incidence trends by histology using data from the USA, we found that rates of adenocarcinoma had remained stable while the incidence of squamous cell carcinoma had significantly decreased, which is consistent with smoking patterns.

There is increasing interest in the suggestion of an association between the human papillomavirus (HPV) and sinonasal cancer, with a recent meta-analysis finding around a 30% prevalence of HPV in cases of sinonasal squamous cell carcinoma [54]. While current evidence is equivocal, if a causal link is demonstrated then it is possible that the extensive dissemination of the HPV vaccine may also influence future trends for some forms of sinonasal cancer incidence.

Due to the small number of sinonasal cancers diagnosed, the estimates of incidence and mortality rates and trends often had relatively wide confidence intervals. This limited our ability to assess whether rates were truly remaining stable or changing over time. Furthermore, annual age and sex-

specific incidence data that were required to calculate standardised rates could only be accessed for a limited number of countries. While it would be ideal to have data for the same range of years to compare trends between countries, this was not possible, and we acknowledge that differences in the time periods considered may introduce biases. Factors such as data quality and coding practices vary from country to country and can therefore also influence the reported comparisons. We were only able to obtain information from two Asian countries and no African or South American countries. Thus, we do not know whether the incidence and mortality data for sinonasal cancer reported here are consistent across these other regions.

In conclusion, after being officially recognised as human carcinogens, measures have been put in place to limit exposure to both wood dust and tobacco in many developed countries. These actions appear to be having some impact on the incidence and mortality of sinonasal cancer at the population level, with significantly decreasing rates evident over recent years in several of the countries included in this study. Of concern, however, is that unless similar regulations are implemented in less developed countries, sinonasal cancer is likely to become an increasing problem in those parts of the world. This further highlights the need for access to reliable and up to date cancer statistics for people who live in less developed countries, which would enable monitoring of recent trends and thus enhance advocacy for cancer control activities.

Acknowledgements

The authors gratefully acknowledge the provision of data extracts from: the Cancer and Screening Unit of the Australian Institute of Health and Welfare; the Ministry of Health, New Zealand; the National Cancer Control Institute, South Korea; the Thames Cancer Registry, England; and Statistics Canada.

Conflict of interest

Nil.

Funding

Lin Fritschi was supported by fellowships from the Australian National Health and Medical Research Council (#513706) and the Cancer Council of Western Australia. Peter Baade was supported by an Australian National Health and Medical Research Council Career Development Fellowship (#1005334).

Ethical approval

Ethical approval was not required or sought for this study.

References

- [1] Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M et al. Cancer Incidence in Five Continents, Vol. IX. IARC Scientific Publications No. 160. Lyon: IARC. 2007.
- [2] Franchi A, Miligi L, Palomba A, Giovannetti L, Santucci M. Sinonasal carcinomas: recent advances in molecular and phenotypic characterization and their clinical implications. *Crit Rev Oncol Hematol* 2011;79(3):265-277.
- [3] Robbins KT, Ferlito A, Silver CE, Takes RP, Strojan P, Snyderman CH et al. Contemporary management of sinonasal cancer. *Head Neck* 2011;33(9):1352-1365.
- [4] Porceddu S, Martin J, Shanker G, Weih L, Russell C, Rischin D et al. Paranasal sinus tumors: Peter MacCallum Cancer Institute experience. *Head Neck* 2004;26(4):322-330.
- [5] Hoppe BS, Stegman LD, Zelefsky MJ, Rosenzweig KE, Wolden SL, Patel SG et al. Treatment of nasal cavity and paranasal sinus cancer with modern radiotherapy techniques in the postoperative setting--the MSKCC experience. *Int J Radiat Oncol Biol Phys* 2007;67(3):691-702.
- [6] World Health Organization. Wood Dust. *IARC Monogr Eval Carcinog Risks Hum* 1995;62:35-37.
- [7] Straif K, Benbrahim-Tallaa L, Baan R, Grosse Y, Secretan B, El Ghissassi F et al. A review of human carcinogens--part C: metals, arsenic, dusts, and fibres. *Lancet Oncol* 2009;10(5):453-454.
- [8] El Ghissassi F, Baan R, Straif K, Grosse Y, Secretan B, Bouvard V et al. A review of human carcinogens--part D: radiation. *Lancet Oncol* 2009;10(8):751-752.
- [9] Baan R, Grosse Y, Straif K, Secretan B, El Ghissassi F, Bouvard V et al. A review of human carcinogens--Part F: chemical agents and related occupations. *Lancet Oncol* 2009;10(12):1143-1144.
- [10] Rushton L, Hutchings SJ, Fortunato L, Young C, Evans GS, Brown T et al. Occupational cancer burden in Great Britain. *Br J Cancer* 2012;107(Suppl 1):S3-7.
- [11] Benninger MS. The impact of cigarette smoking and environmental tobacco smoke on nasal and sinus disease: a review of the literature. *Am J Rhinol* 1999;13(6):435-438.
- [12] 't Mannetje A, Kogevinas M, Luce D, Demers PA, Begin D, Bolm-Audorff U et al. Sinonasal cancer, occupation, and tobacco smoking in European women and men. *Am J Ind Med* 1999;36(1):101-107.
- [13] International Agency for Research on Cancer, World Health Organization. Tobacco Smoke and Involuntary Smoking. *IARC Monogr Eval Carcinog Risks Hum* 2002;83.
- [14] Ferlay J, Shin H, Bray F, Forman D, Mathers C, Parkin DM. GLOBOCAN 2008: Cancer incidence, mortality and prevalence worldwide. IARC CancerBase No. 10 (version 1.2). Lyon: IARC Press. 2010.
- [15] Engholm G, Ferlay J, Christensen N, Johannesen TB, Klint Å, Kjørtum JE et al. NORDCAN: Cancer Incidence, Mortality, Prevalence and Survival in the Nordic Countries, Version 5.3 (25.04.2013). Association of the Nordic Cancer Registries, Danish Cancer Society. Available at <http://www.ancre.nu>; accessed June 2013.
- [16] Hong Kong Cancer Registry. Cancer Statistics Query System (CanSQS) by ICD-10. Available at http://www3.ha.org.hk/cancereg/e_a1b.asp; accessed June 2013.
- [17] National Cancer Registry Ireland. The National Cancer Registry Ireland: Data download, 1994-2010. Available at <http://www.ncr.ie/ncr>; accessed June 2013.
- [18] Italian Association of Cancer Registries (AIRTUM). ITACAN: Cancer in Italy, Version 1. Available at <http://www.registri-tumori.it>; accessed June 2013.
- [19] Netherlands Cancer Registry. Dutch Cancer Figures. Groningen: Comprehensive Cancer Centre the Netherlands (IKNL) 2013. Available at <http://www.iknl.nl/cijfers/index.php?taal=en>; accessed June 2013.

- [20] Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov). *Research Data (1973-2010)*. National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2013, based on the November 2012 submission. Available at www.seer.cancer.gov; accessed June 2013.
- [21] World Health Organization Statistical Information System. WHO mortality database detailed data files. May 2013 update [online database], Geneva: WHO 2013. Available at <http://www.who.int/whosis/mort/download/en/index.html>; accessed June 2013.
- [22] Ahmad O, Boschi-Pinto C, Lopez A, Murray C, Lozano R, Inoue M. Age standardization of rates: a new WHO standard. GPE Discussion Paper Series No. 31. Geneva: World Health Organization. 2001.
- [23] Kim H, Fay M, Feuer E, Midthune D. Permutation tests for joinpoint regression with applications to cancer rates. *Statistics in Medicine* 2000;19(3):335-351.
- [24] Thorup C, Sebbesen L, Dano H, Leetmaa M, Andersen M, Buchwald C et al. Carcinoma of the nasal cavity and paranasal sinuses in Denmark 1995-2004. *Acta Oncol* 2010;49(3):389-394.
- [25] Hansen J, Rasmussen TR, Ommand O, Olsen JH. Registration of selected cases of occupational cancer (1994-2002) with the Danish National Board of Industrial Injuries. *Ugeskr Laeger* 2007;169(18):1674-1678.
- [26] Turner JH, Reh DD. Incidence and survival in patients with sinonasal cancer: A historical analysis of population-based data. *Head Neck* 2012;34(6):877-885.
- [27] Wu AW, Suh JD, Metson R, Wang MB. Prognostic factors in sinonasal sarcomas: analysis of the surveillance, epidemiology and end result database. *Laryngoscope* 2012;122(10):2137-2142.
- [28] Airolidi M, Garzaro M, Valente G, Mamo C, Bena A, Giordano C et al. Clinical and biological prognostic factors in 179 cases with sinonasal carcinoma treated in the Italian Piedmont region. *Oncology* 2009;76(4):262-269.
- [29] Koivunen P, Makitie AA, Back L, Pukkila M, Laranne J, Kinnunen I et al. A national series of 244 sinonasal cancers in Finland in 1990-2004. *Eur Arch Otorhinolaryngol* 2012;269(2):615-621.
- [30] Dirix P, Nuyts S, Geussens Y, Jorissen M, Vander Poorten V, Fossion E et al. Malignancies of the nasal cavity and paranasal sinuses: long-term outcome with conventional or three-dimensional conformal radiotherapy. *Int J Radiat Oncol Biol Phys* 2007;69(4):1042-1050.
- [31] Acheson ED, Cowdell RH, Hadfield E, Macbeth RG. Nasal cancer in woodworkers in the furniture industry. *Br Med J* 1968;2(5605):587-596.
- [32] The Council of the European Union. Council Directive 1999/38/EC. *Official Journal of the European Communities* 1999;138:66-69.
- [33] Scientific Committee on Occupational Exposure Limits. Recommendation from the Scientific Committee on Occupational Exposure Limits: risk assessment for wood dust. SCOEL/SUM/102 2003. Available at ec.europa.eu/social/BlobServlet?docId=3876&langId=en; accessed 13 Mar 2013..
- [34] United States Department of Labor. Occupational Safety and Health Guideline for Wood Dust, All Soft & Hardwoods Except Western Red Cedar. Available at <http://www.osha.gov/SLTC/healthguidelines/wooddustallsoftandhardwoodsexceptwesternredcedar/recognition.html>; accessed 27 Feb 2013.
- [35] American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices – Wood Dusts (7th edition). Cincinnati: ACGIH. 2005.
- [36] CAREX Canada. Surveillance of environmental and occupational exposures for cancer prevention: wood dust. Available at http://www.carexcanada.ca/en/wood_dust/; accessed 27 Feb 2013.

- [37] Department of Labour. Workplace Exposure Standards: Consideration Paper on Lowering the Workplace Exposure Standard for Softwood Dust. Wellington: DOL 2010.
- [38] Australian Safety and Compensation Council. Benchmarking of exposures to wood dust and formaldehyde in selected industries in Australia. Canberra: Australian Government. 2008.
- [39] Blot WJ, Chow WH, McLaughlin JK. Wood dust and nasal cancer risk. A review of the evidence from North America. *J Occup Environ Med* 1997;39(2):148-156.
- [40] Kauppinen T, Vincent R, Liukkonen T, Grzebyk M, Kauppinen A, Welling I et al. Occupational exposure to inhalable wood dust in the member states of the European Union. *Ann Occup Hyg* 2006;50(6):549-561.
- [41] Jones PA, Smith LC. Personal exposures to wood dust of woodworkers in the furniture industry in the High Wycombe area: a statistical comparison of 1983 and 1976/77 survey results. *Ann Occup Hyg* 1986;30(2):171-184.
- [42] Schlunssen V, Jacobsen G, Erlandsen M, Mikkelsen AB, Schaumburg I, Sigsgaard T. Determinants of wood dust exposure in the Danish furniture industry--results from two cross-sectional studies 6 years apart. *Ann Occup Hyg* 2008;52(4):227-238.
- [43] Coble JB, Lees PS, Matanoski G. Time trends in exposure measurements from OSHA compliance inspections of the pulp and paper industry. *Appl Occup Environ Hyg* 2001;16(2):263-270.
- [44] Hall AH, Teschke K, Davies H, Demers P, Marion S. Exposure levels and determinants of softwood dust exposures in BC lumber mills, 1981-1997. *AIHA J (Fairfax, Va)* 2002;63(6):709-714.
- [45] Teschke K, Marion SA, Vaughan TL, Morgan MS, Camp J. Exposures to wood dust in U.S. industries and occupations, 1979 to 1997. *Am J Ind Med* 1999;35(6):581-589.
- [46] Galea KS, Van Tongeren M, Sleguwenhoek AJ, While D, Graham M, Bolton A et al. Trends in wood dust inhalation exposure in the UK, 1985-2005. *Ann Occup Hyg* 2009;53(7):657-667.
- [47] Kuijpers JH, Louwman MW, Peters R, Janssens GO, Burdorf AL, Coebergh JW. Trends in sinonasal cancer in The Netherlands: more squamous cell cancer, less adenocarcinoma. A population-based study 1973-2009. *Eur J Cancer* 2012;48(15):2369-2374.
- [48] Kauppinen T, Toikkanen J, Pedersen D, Young R, Ahrens W, Boffetta P et al. Occupational exposure to carcinogens in the European Union. *Occup Environ Med* 2000;57(1):10-18.
- [49] Lavoue J, Vincent R, Gerin M. Formaldehyde exposure in U.S. industries from OSHA air sampling data. *J Occup Environ Hyg* 2008;5(9):575-587.
- [50] Lavoue J, Vincent R, Gerin M. Statistical modelling of formaldehyde occupational exposure levels in French industries, 1986-2003. *Ann Occup Hyg* 2006;50(3):305-321.
- [51] Symanski E, Chang CC, Chan W. Long-term trends in exposures to nickel aerosols. *AIHAJ* 2000;61(3):324-333.
- [52] Thun M, da Costa e Silva V. Introduction and overview of global tobacco surveillance. In Shafey O, Dolwick S, Guindon G (eds): Tobacco control country profiles 2003, 2nd Edition. Atlanta: American Cancer Society, 2003. p. 7-12.
- [53] World Health Organization. WHO report on the global tobacco epidemic, 2011: Warning about the dangers of tobacco. Geneva: WHO; 2011.
- [54] Syrjanen K, Syrjanen S. Detection of human papillomavirus in sinonasal carcinoma: systematic review and meta-analysis. *Hum Pathol* 2013;44(6):983-991.

Table 1: Sinonasal cancer incidence and mortality rates (per million population) in selected countries by sex, 2004-2008.

Males

Country ^a	Cases/year	% aged 65+ yrs	ASR ^b	[95% CI]	Deaths/year ^c	% aged 65+ yrs	ASR ^{b,c}	[95% CI]	MR:IR
Denmark	47.8	50.6%	11.9	[10.4, 13.6]	14.2	64.8%	3.3	[2.6, 4.2]	0.28
Netherlands	101.8	54.8%	8.8	[8.0, 9.6]	22.0	70.0%	1.9	[1.5, 2.3]	0.21
USA (SEER) ^d	420.4	44.5%	8.7	[8.4, 9.1]	n.a.	n.a.	n.a.	n.a.	n.a.
USA (Total) ^d	n.a.	n.a.	n.a.	n.a.	270.8	53.1%	1.4	[1.3, 1.5]	n.a.
Hong Kong	35.4	38.4%	8.1	[6.9, 9.4]	10.0	60.0%	2.2	[1.6, 3.0]	0.27
Australia ^e	102.0	50.7%	7.6	[6.9, 8.4]	23.0	56.5%	1.7	[1.3, 2.0]	0.22
South Korea	183.4	37.9%	7.3	[6.8, 7.8]	83.2	49.8%	3.5	[3.2, 3.9]	0.48
Norway	23.4	52.1%	7.2	[5.9, 8.7]	6.0	43.3%	1.8	[1.2, 2.6]	0.25
Canada ^f	142.2	48.5%	6.9	[6.4, 7.4]	36.2	55.7%	1.6	[1.4, 1.8]	0.23
Italy ^g	84.4	56.6%	6.6	[6.0, 7.3]	25.8	69.0%	1.9	[1.5, 2.2]	0.28
Finland	24.0	55.0%	6.3	[5.2, 7.6]	11.4	57.9%	3.0	[2.2, 3.9]	0.47
Sweden	43.4	53.0%	6.1	[5.3, 7.0]	10.0	66.0%	1.3	[1.0, 1.8]	0.22
Ireland	14.2	59.2%	5.8	[4.5, 7.4]	5.0	64.0%	2.0	[1.3, 3.0]	0.34
New Zealand	13.0	38.5%	5.3	[4.0, 6.7]	6.2	41.9%	2.5	[1.7, 3.6]	0.47
England (South-East)	37.4	54.5%	5.0	[4.3, 5.8]	n.a.	n.a.	n.a.	n.a.	n.a.

Females

Country ^a	Cases/year	% aged 65+ yrs	ASR ^b	[95% CI]	Deaths/year ^c	% aged 65+ yrs	ASR ^{b,c}	[95% CI]	MR:IR
Denmark	31.4	63.1%	6.7	[5.6, 7.9]	8.2	63.4%	1.5	[1.1, 2.2]	0.23
Norway	22.0	64.5%	5.3	[4.3, 6.6]	3.2	81.3%	0.6	[0.3, 1.1]	0.12
USA (SEER) ^d	304.0	54.7%	5.2	[4.9, 5.4]	n.a.	n.a.	n.a.	n.a.	n.a.
USA (Total) ^d	n.a.	n.a.	n.a.	n.a.	201.0	69.1%	0.8	[0.7, 0.8]	n.a.
Hong Kong	22.6	41.6%	4.4	[3.6, 5.4]	6.0	63.3%	1.1	[0.7, 1.6]	0.24
Netherlands	56.4	56.0%	4.2	[3.7, 4.8]	8.0	67.5%	0.5	[0.4, 0.7]	0.12

Canada ^f	99.2	53.8%	4.2	[3.8, 4.6]	23.2	51.4%	0.9	[0.7, 1.1]	0.22
South Korea	114.8	49.1%	3.8	[3.5, 4.1]	43.0	61.4%	1.4	[1.2, 1.6]	0.37
Sweden	29.2	60.3%	3.5	[2.9, 4.2]	5.8	58.6%	0.6	[0.4, 1.0]	0.18
Australia ^e	51.8	52.7%	3.4	[2.9, 3.9]	9.3	73.0%	0.6	[0.4, 0.9]	0.18
Ireland	8.4	38.1%	3.3	[2.4, 4.6]	4.4	59.1%	1.5	[0.9, 2.4]	0.46
England (South-East)	28.6	52.4%	3.2	[2.7, 3.9]	n.a.	n.a.	n.a.	n.a.	n.a.
Italy ^g	44.8	65.6%	2.6	[2.2, 3.1]	15.0	84.0%	0.7	[0.5, 0.9]	0.25
Finland	13.4	68.7%	2.5	[1.9, 3.4]	9.2	80.4%	1.6	[1.2, 2.3]	0.64
New Zealand	7.2	44.4%	2.5	[1.7, 3.5]	5.0	56.0%	1.7	[1.1, 2.6]	0.69

Data sources: Australian Institute of Health and Welfare (personal communication), Hong Kong Cancer Registry [16], Italian Association of Cancer Registries (AIRTUM) [18], Ministry of Health New Zealand (personal communication), National Cancer Control Institute South Korea (personal communication), National Cancer Registry Ireland [17], Netherlands Cancer Registry [19], Association of the Nordic Cancer Registries (NORDCAN) [15], Statistics Canada (personal communication), Surveillance, Epidemiology, and End Results (SEER) Program [20], and the Thames Cancer Registry (personal communication).

Abbreviations: MR:IR = ratio of mortality rate to incidence rate; 95% CI = 95% confidence interval; n.a. = not available.

Notes:

- a. Countries are sorted in descending order of incidence rate.
- b. Age-standardised rate using the WHO world standard population [22], expressed per 1,000,000 population.
- c. Mortality data had the same data source as incidence data where possible. Exceptions were Ireland, Canada, South Korea and USA which had their mortality data from the WHO mortality database.
- d. Incidence and mortality counts for the USA are not comparable due to using different geographic regions. USA (SEER) covers 28% of the population.
- e. Australian data are for the years 2004-2007.
- f. Canadian incidence data includes some non-invasive cases (98.2% of cases were invasive).
- g. Italian Registries cover approximately 27% of the population.

Table 2: Trends (expressed as annual percentage change (APC)) in sinonasal cancer incidence rates by sex for selected countries.^{a,b,c}

	Males				Females			
	Time period 1	APC1 [95% CI]	Time period 2	APC2 [95% CI]	Time period 1	APC1 [95% CI]	Time period 2	APC2 [95% CI]
Australia	1982-2007	-0.6* [-1.1, -0.0]			1982-2007	-0.2 [-1.2, +0.7]		
Canada	1992-2009	-0.9 [-2.2, +0.4]			1992-2009	-0.3 [-1.7, +1.1]		
Denmark	1970-2011	+0.7* [+0.3, +1.1]			1970-2011	+1.6* [+0.8, +2.3]		
Finland	1970-2011	-0.8* [-1.3, -0.3]			1970-2011	-1.0* [-1.7, -0.3]		
Hong Kong	1983-2010	-2.7* [-3.8, -1.5]			1983-2010	-1.9* [-3.0, -0.8]		
Ireland	1994-2009	-1.9 [-5.4, +1.8]			1994-2002	+6.0 [-2.5, +15.4]	2002-2009	-8.0 [-16.5, +1.4]
Italy	1992-2007	+0.5 [-1.7, +2.7]			1992-2007	+1.5 [-2.2, +5.3]		
Netherlands	1989-2011	-1.2* [-1.9, -0.5]			1989-2011	+1.0 [-0.3, +2.4]		
New Zealand	1970-2009	-1.6* [-2.5, -0.7]			1970-2009	-0.3 [-1.4, +0.8]		
Norway	1970-2010	-0.9* [-1.3, -0.4]			1970-2010	+0.3 [-0.5, +1.1]		
South-East England	1970-2009	-0.8* [-1.3, -0.4]			1970-2009	-0.6* [-1.1, -0.2]		
South Korea	1999-2009	-1.1 [-2.4, +0.1]			1999-2009	-0.1 [-2.1, +1.9]		
Sweden	1970-1978	-5.8* [-10.5, -1.0]	1978-2010	-0.2 [-0.9, +0.5]	1970-1977	-7.5* [-13.5, -1.1]	1977-2010	+0.4 [-0.3, +1.1]
USA	1973-2010	+0.0 [-0.3, +0.3]			1973-2010	+0.2 [-0.2, +0.6]		

Data sources: Australian Institute of Health and Welfare (personal communication), Hong Kong Cancer Registry [16], Italian Association of Cancer Registries (AIRTUM) [18], Ministry of Health New Zealand (personal communication), National Cancer Control Institute South Korea (personal communication), National Cancer Registry Ireland [17], Netherlands Cancer Registry [19], Association of the Nordic Cancer Registries (NORDCAN) [15], Statistics Canada (personal communication), the Surveillance, Epidemiology, and End Results (SEER) Program [20], and the Thames Cancer Registry (personal communication).

Abbreviations and symbols: 95% CI = 95% confidence interval; * = The APC is statistically significant from zero ($p < 0.05$).

a Countries were selected based on the availability of incidence data by age group and year of diagnosis.

b Rates were age-standardised to the WHO World Standard population [22].

c Trends modelled using Joinpoint Regression Programme (version 3.4.3), National Cancer Institute.

Table 3: Trends (expressed as annual percentage change (APC)) in sinonasal cancer mortality rates by sex for selected countries.^{a,b,c}

	Deaths/ year ^d	Period 1	APC 1 [95% CI]	Period 2	APC 2 [95% CI]	Period 3	APC 3 [95% CI]	Period 4	APC 4 [95% CI]
<i>Males</i>									
Australia	22.3	1970-2011	-3.0* [-3.6, -2.4]						
Canada	33.6	1970-2005	-2.8* [-3.2, -2.4]						
Denmark	12.1	1970-2006	-0.1 [-1.1, +1.0]						
Germany	111.1	1979-1994	+2.5* [+1.2, +3.8]	1994-2002	-7.0* [-10.6, -3.3]	2002-2011	+2.1 [-0.5, 4.8]		
Greece	8.4	1970-2010	-2.6* [-3.5, -1.6]						
Hong Kong	9.9	1970-2011	-5.3* [-6.0, -4.6]						
Hungary	23.9	1970-2011	+0.2 [-0.5, +0.8]						
Ireland	4.9	1970-2009	-2.5* [-3.7, -1.2]						
Italy	91.9	1970-1978	-10.5* [-13.9, -7.0]	1978-1992	+4.1* [+2.3, +6.0]	1992-1998	-5.2 [-11.5, +1.6]	1998-2010	+0.3 [-1.4, +2.1]
Netherlands	20.1	1970-2011	-2.6* [-3.2, -2.0]						
New Zealand	5.8	1970-2009	-2.0* [-2.9, -1.2]						
Poland	68.7	1999-2011	-1.5 [-3.7, +0.8]						
Romania	84.7	1999-2010	+2.2* [+0.5, +3.9]						
South Korea	60.9	1995-2002	+14.9* [+8.3, +21.8]	2002-2011	-5.5* [-8.1, -2.8]				
Spain	63.8	1971-2010	-0.4 [-0.9, +0.1]						
Sweden	10.4	1970-1977	+8.3 [-3.2, +21.2]	1977-2010	-2.2* [-3.2, -1.3]				
UK	72.4	1970-2010	-3.4* [-3.7, -3.1]						
USA	266.7	1979-2007	-2.2* [-2.5, -1.9]						
<i>Females</i>									
Australia	11.7	1970-2011	-3.3* [-3.8, -2.7]						
Canada	21.5	1970-2005	-2.3* [-2.9, -1.6]						
Denmark	7.9	1970-1993	+4.0* [+1.2, +7.0]	1993-2006	-5.0 [-9.8, +0.0]				
Germany	60.9	1979-1986	+4.6 [-0.4, +10.0]	1986-2011	-2.7* [-3.5, -2.0]				
Greece	4.7	1970-2010	-3.7* [-4.7, -2.7]						
Hong Kong	5.2	1970-2011	-5.2* [-6.1, -4.3]						

Hungary	13.2	1970-2011	-1.1* [-1.8, -0.4]		
Ireland	5.0	1970-2009	-1.5* [-2.6, -0.4]		
Italy	56.2	1970-1977	-9.4* [-14.9, -3.5]	1977-2010	-0.5 [-1.2, +0.2]
Netherlands	10.5	1970-2011	-1.5* [-2.4, -0.7]		
New Zealand	4.8	1970-2009	-0.9 [-1.9, +0.1]		
Poland	43.5	1999-2011	-1.0 [-2.7, +0.7]		
Romania	46.1	1999-2010	-0.9 [-3.7, +2.0]		
South Korea	34.0	1995-2003	+11.7* [+4.2, +19.7]	2003-2011	-5.6* [-10.2, -0.8]
Spain	28.1	1971-2010	-1.8* [-2.5, -1.2]		
Sweden	7.1	1970-2010	-2.4* [-3.5, -1.3]		
UK	52.9	1970-2010	-3.6* [-3.9, -3.2]		
USA	192.5	1979-2007	-2.0* [-2.4, -1.5]		

Data source: Data obtained from WHO Mortality Database [21].

Abbreviations/Symbol: 95% CI = 95% confidence interval; * The APC is statistically significant from zero ($p < 0.05$).

a Countries were selected based on data quality (at least 95% estimated coverage over the examined time period), the number of years available (at least 10 years data) and the number of deaths due to sinonasal cancer (an average of at least 10 deaths per year for males and females combined). No coverage data were available for Hong Kong. Most countries have estimated coverage available between 1990-2010.

b Rates were age-standardised to the WHO World Standard population [22].

c Trends modelled using Joinpoint Regression Programme (version 3.4.3), National Cancer Institute.

d. Deaths/year is the average number of deaths over the most recent 10-year period.

Figure 1: Trends in sinonasal cancer incidence rates by sex for selected countries, 1970–2011

Data sources: Australian Institute of Health and Welfare (personal communication), Hong Kong Cancer Registry [16], Italian Association of Cancer Registries (AIRTUM) [18], Ministry of Health New Zealand (personal communication), National Cancer Control Institute South Korea (personal communication), National Cancer Registry Ireland [17], Netherlands Cancer Registry [19], Association of the Nordic Cancer Registries (NORDCAN) [15], Statistics Canada (personal communication), Surveillance, Epidemiology, and End Results (SEER) Program [20], and the Thames Cancer Registry (personal communication).

Notes: Countries were selected based on the availability of incidence data by age group and year of diagnosis. y-Axis represents 'Incidence rate per 1,000,000 population per year' and is portrayed on a log base 10 scale, while x-axis represents 'Year'.

Rates were age-standardised to the WHO World Standard population [22] and trends were modelled using the Joinpoint Regression Programme (version 3.4.3), National Cancer Institute.

Figure 2: Trends in sinonasal cancer incidence by morphology, site and sex, United States of America, 1973-2010

Data source: Surveillance, Epidemiology, and End Results (SEER) Program [20].

Notes: Adenocarcinoma defined as morphology types 814-838. Squamous cell carcinoma defined as morphology types 805-808. Nasal cavity defined as ICD C300. Maxillary sinus defined as ICD C310. y-Axis represents 'Incidence rate per 1,000,000 population per year' and is portrayed on a log base 10 scale, while x-axis represents 'Year'. Rates were age-standardised to the WHO World Standard population [22] and trends were modelled using the Joinpoint Regression Programme (version 3.4.3), National Cancer Institute.

Annual percent trends, 1973-2010 (95% CI):

Adenocarcinoma: Males +0.1% (-0.8%,+1.1%), Females -0.2% (-1.0%,+0.5%).

Squamous cell carcinoma: Males -1.4% (-1.8%,-1.0%), Females -0.9% (-1.6%,-0.3%).

Nasal cavity: Males +0.6% (+0.1%,+1.1%), Females +0.9% (+0.4%,+1.3%).

Maxillary sinus: -1.2% (-1.7%,-0.7%), Females -0.9% (-1.4%,-0.3%).

Figure 3: Trends in sinonasal cancer mortality rates by sex for selected countries, 1970–2011

Data source: World Health Organization [21].

Notes: Countries were selected on the basis of having data of sufficient quality (at least 95% of the country covered) and quantity (at least 90 deaths over the most recent 10 years). y-Axis represents 'Mortality rate per 1,000,000 population per year' and is portrayed on a log base 10 scale, while x-axis represents 'Year'. Rates were age-standardised to the WHO World Standard population [22] and trends were modelled using the Joinpoint Regression Programme (version 3.4.3), National Cancer Institute.