**Workers in Australian prebake aluminium smelters: update on risk of mortality and cancer incidence in the Healthwise cohort.**

Anthony Del Monaco1, Christina Dimitriadis1, Sophia Xie1, Geza Benke1, Malcolm R. Sim1, Karen Walker-Bone1

1. School of Public Health & Preventive Medicine, Monash University, Melbourne, Vic

**Word count: 3678**

**Name and address for correspondence:**

Professor Karen Walker-Bone

Monash Centre for Occupational and Environmental Health, Monash University

School of Public Health and Preventive Medicine, 553 St Kilda Road, Melbourne 3141

Victoria, Australia

Tel: +61 (0)399030525 Email: Karen.Walker-Bone@Monash.edu

**ABSTRACT**

**OBJECTIVES:** To investigate mortality and the rates of incident cancer amongst a cohort of aluminium industry workers.

**METHODS:** Amongst 4507 male employees who worked in either of two Australian prebake smelters for at least 3 months, data linkage was undertaken with the Australian National Death Index and Australian Cancer Database. Standardised Mortality Ratios (SMRs) and Standardised Incidence Rates (SIRs) were estimated for the whole cohort and for: production; maintenance and office workers. SMRs and SIRs were calculated by time since first employment.

**RESULTS:** Amongst production workers, there was an excess risk of mortality from mesothelioma (SMR 2.8, 95% CI 1.3-5.2), lung (SMR 1.4, 95% CI 1.0-1.8), prostate (SMR 1.9, 95% CI 1.3-2.7) and liver cancer (SMR 2.0, 95% CI 1.1-3.4) and the SIR was also increased for overall respiratory cancers, specifically lung cancers. An excess risk of death from stomach cancer (SMR 2.9, 95% CI 1.2-6.1) and Alzheimer’s disease (SMR 3.4, 95% CI 1.1-7.9) was seen amongst maintenance workers. The overall risk of death was similar to that of the Australian general population, as was mortality from cancers overall and non-malignant respiratory disease.

**CONCLUSIONS:** No excess risk of death from bladder cancer or non-malignant respiratory disease was found. Excess lung cancer mortality and incidence may be explained by smoking and excess mortality from mesothelioma may be explained by asbestos exposure. An excess risk of mortality from liver and prostate cancer have been shown in production workers and requires further investigation.

**KEYWORDS: Aluminium production; prebake smelters; cancer; mortality; mesothelioma; lung cancer; prostate cancer**

**What is already known on this topic?**

International Agency for Research on Cancer (IARC) has reported that aluminium production is carcinogenic. Excess risks of bladder cancer, lung cancer and cancers at other sites have been reported in Søderberg smelters. However, Søderberg smelters are also associated with greater exposure to emissions and it is not known whether prebake smelters have reduced the carcinogenic risks.

**What this study adds?**

Overall, there was no excess risk of death from cancer amongst aluminium production workers working in the prebake smelters although the SMR was increased (1.14). However, an excess risk was seen for deaths from mesothelioma, lung cancer, liver cancer and prostate cancer amongst production workers. An excess risk of death from stomach cancer was seen amongst maintenance workers, as was an excess risk of death from Alzheimer’s disease.

**How might this affect research, practice or policy in the foreseeable future?**

This paper provides additional evidence of reduction in rates of some types of cancer associated with prebake aluminium production (e.g. bladder) as compared with the increased risk previously reported in Søderberg smelters. However, there remains evidence of excess rates of some lung cancer and also mesothelioma and liver cancer.

**INTRODUCTION**
Aluminium is a ubiquitous metal with many common applications. Since 1984, The International Agency for Research on Cancer classified aluminium production as a definite (group 1) carcinogen 1,2. Workers in aluminium production are primarily exposed to polycyclic aromatic hydrocarbons (PAHs) although there are a range of other potential exposures, including: fluorides; sulfur dioxide, flourospar; carbon monoxide; carbon dioxide; trace metals (including chromium, nickel, vanadium); beryllium; asbestos; particulate matter; extreme heat; noise; and static magnetic fields2-4.

The processes of extraction of Aluminium have been refined over time in order to reduce exposure to PAHs4, sulfur dioxide and fluorides5 whilst there have also been improvements in control technology and better personal protection. As a result, it would be expected that the risk of occupational cancers (e.g. lung and bladder) which had strong dose-response relationships with coal tar pitch volatiles (CTPVs) such as those reported with Søderberg pots6, would be decreasing.

To explore this, the Australian Healthwise cohort of aluminium industry workers was established in 1995. The 2009 cancer and mortality findings showed no overall excess mortality or cancer but an increased incidence of kidney cancer and mesothelioma7. However, many of the relevant outcomes can have a long latency and therefore subsequent linkage was carried out to further investigate the risk of cancers of the lung, bladder and kidney, as well as deaths from malignant and non-malignant respiratory diseases.

**METHODS
Study population**

Healthwise is a longitudinal cohort of employees from two prebake aluminium smelters in Victoria, Australia, the characteristics of which have been described8. Both smelters used the Hall–Héroult process, the older smelter was in operation 1962-2014 and incorporated a rolling mill, power station and coal mine, whilst the newer smelter commenced operation in 1986 and remains active.

Employees were eligible for inclusion if they had worked a minimum of 90 days at a smelter after 1st January 1983 (date of commencement of complete Australian national cancer registration). The cohort included three groups: participants in a cross-sectional health survey 1995/1996 (n=1791, 35.1% of total cohort)9; workers who commenced employment after 1995/1996 and before December 2004 and participated in an inception cohort study of respiratory health (463, 9.1% of total cohort)10; and employees who commenced on or after 1 January 1983 and left before 1995/1996 (n=2847, 55.8% of total cohort). Participants in the two health studies were interviewed to collect demographic information, personal cigarette smoking history and a full employment history. For cohort members who left before 1995/1996, a full employment history (for each job: start date; site; operating centre; department and job title; end date), and data about cigarette smoking during employment were extracted from company records. For participants in the 1995/1996 health survey, company records were reviewed prior to the current linkage to obtain an updated employment history of all jobs held since interview. Data from the employment histories were used to classify workers into three groups (office, maintenance and production) estimating the number of years in each group. These groups were chosen as office workers tend to be unexposed, production workers are those most regularly exposed and maintenance workers tend to have more irregular and unpredictable exposure patterns, an approach used previously by us7,11 and others12. There was limited movement between the three categories over time: production and maintenance (n=347, 7.7%), production and office (n=637, 14.1%), maintenance and office (n=318, 7.1%) but, where movement occurred, all person-years and events were counted in each category. Participants without job history (n=12, 0.2%) were excluded from the analyses by work classification.

**Data linkage**

The National Death Index (NDI) and Australian Cancer Database (ACD), both held by the Australian Institute of Health and Welfare (AIHW), provide complete national coverage of deaths and cancers since 1983. For each cohort member, linkage was undertaken with the most recently available complete data, (cause of death until 30 November 2016 and registration of any cancer until 31 December 2014 (except cancer registrations for one state that were only complete until 2013)). As both smelters were located in Victoria and the vast majority of workers were also from that state, data linkage was also undertaken to the Victorian Cancer Registry, which provided complete cancer data until the end of 2016, enabling maximal cancer ascertainment for most participants13.

The AIHW used a probabilistic program to identify possible matches based on personal identifiers including surname, first name, birth date, death date (if known) and last contact date, and used multiple passes that grouped the data based on different matching criteria each time with each potential match scored by the probability of being a true match. Possible death matches were independently reviewed by two study team members and disagreements decided by a third team member. For ethical reasons, the ACD and VCR only provide “highly certain” cancer matches. Discrepancy checks were conducted comparing with previous linkages and also comparing cancer and death results to ensure maximum ascertainment and consistency. The underlying cause of death was coded to International Classification of Diseases, Ninth Revision (ICD-9)14 until 1996, or Tenth Revision (ICD-10) from 199715 onwards and cancer incidence records were coded to ICD-10. The broad and specific cause of death and cancer categories used in the analysis with the associated ICD-9 and ICD-10 codes are shown in supplementary tables S1 and S2.

 **Statistical Methods**

For classification into “ever work” category, workers commenced follow-up from the date of first employment in office, maintenance or productions jobs (offset by 90 days from date of first employment), or on 1 January 1983, whichever was the later. Time since first employment was calculated (>3 months to <20 years, 20–40 years and 40+ years) based on time since first employment in production or maintenance jobs. Workers continued to contribute person-years until the end of follow-up, based on when national death and cancer data were complete: 30 November 2016, and 31 December 2016, respectively, or until date of death, whichever was earliest. Only primary malignant cancers were included, however if a participant was diagnosed with more than one primary cancer at different anatomical sites, each cancer was counted.

The person-years contributed by each participant was calculated using the STSET, STSPLIT, and STPTIME functions in the Stata statistical software package, version 15.1 (StataCorp. 2017. College Station, Texas), and were allocated into subgroups based on calendar year, sex and five-year age group. Australian population data were used to calculate the expected numbers of deaths and cancers for each outcome category based on 5-year age groups and sex-specific rates16,17. For cancer population incidence data for 2015-2016, the five-year mean of the 2009-2014 national population rates was applied, as national data was incomplete for these years. Population and cohort data include all primary incident cancers and multiple primary cancers in the same person. Standardised Mortality Ratios (SMRs) and Standardised Incidence Ratios (SIRs) with 95% confidence intervals (CIs) were calculated for overall death and cancer, and for major cancer and death categories respectively.

Ethics approval

The Monash University Human Research Ethics Committee approved the Healthwise Cancer and Mortality Study. An application to access national cancer and death data was approved by the AIHW Ethics Committee. Cancer Council Victoria Human Research Ethics Committee granted approval to access state cancer data for Victoria.

**RESULTS**

Rates of recruitment were 90% for the cross-sectional health survey9 and 77% for the inception cohort10. All company records were available for cohort participants who had left work. Since 20097, a small increase (n=140) in participants was achieved by: ongoing recruitment 2003-2004; subsequent employment at eligible sites for previously ineligible employees; and re-review of company records from 1983-1996, which identified a small number of additional employees.

The majority of the cohort was male (Table 1), mean age 59.8 years at time of linkage. The mean age at commencement of employment was 28 years, and 331 (6.5%) remained employed at the end of follow-up. There were 121,719 male person-years and 15,283 female person-years. Approximately 1/3 of the cohort had worked in the smelters for >20 years, and 80% had commenced employment before 1990, giving a mean follow-up of 27.7 years. Data linkage for cancer incidence and mortality was complete until 2016, adding an additional 14 years of follow-up compared with previously published findings7. Smoking information was available for around 90% men and 80% women in total although most of the missing smoking information related to the cohort of workers who left employment between 1983 and 1995/6 (20% missing). Given the small numbers of women, subsequent analyses were restricted to male workers.

Mortality rates for overall deaths and by category (Table 2) were comparable with those of the Australian population, as was the risk for most major categories of death, including non-malignant respiratory diseases. The overall risk of death from cancer was also similar to that of the Australian population. An increased risk of death from both mesothelioma /pleural cancer (SMR 2.42, 95% CI 1.25 - 4.23) and prostate cancer (SMR 1.53, 95% CI 1.07 - 2.10) were demonstrated amongst all smelter employees. In contrast, the risk of death from pancreatic cancer and brain/CNS cancer was lower than the Australian population. Once considered by type of work, the increased risk of mortality from mesothelioma/pleural (SMR 2.76, 95% CI 1.26 - 5.23), prostate (SMR 1.92, 95% CI 1.29 - 2.73) malignancies remained increased amongst production workers, as did the risk of death from lung and liver cancer. Maintenance workers showed excess risk of death from mesothelioma/pleural cancer, stomach cancer (SMR 2.94, 95% CI 1.18 - 6.05) and Alzheimer’s disease (SMR 3.38, 95% CI 1.10 - 7.88).

The cohort showed no increased risk of any incident cancers (Table 3) and pancreatic, melanoma and brain/CNS cancer cases were fewer than expected. An excess risk of incident respiratory and lung cancers (SIR 1.29, 95% CI 1.01 - 1.64) and mesothelioma (SIR 2.16, CI 0.99-4.11) was found amongst production workers.

Table 4 shows all-cause deaths amongst production or maintenance workers by time since first employment. The risk of death from all malignancies and all causes was lower than expected for workers who were first employed >3 months but <20 years before. There was an excess risk of suicide deaths for this time since first employment category (SMR 1.53, 95% CI 0.99-2.27). An excess risk of death from lung (SMR 1.45, 95% CI 1.07-1.92) and prostate cancer (SMR 1.79, 95% CI 1.11-2.74) was seen amongst workers who commenced work >20 years but <40 years ago. Amongst those first employed >40 years ago, no significantly increased risk of death for any cause was identified.

Exploring cancer incidence by time since first employment (Table 5), there was an excess risk of incident stomach cancer in production or maintenance workers employed >3 months but <20 years (SIR 2.56, 95% CI 1.03-5.27) and of lung cancer amongst those employed >20 years but <40 years ago (SIR 1.34, 95% CI 1.02-1.73). The risk of incident melanoma was reduced amongst those commencing employment >20 but <40 years ago.

**Table 1** Characteristics of participants of the Healthwise Cancer and Mortality cohort.

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristics** | **Male** | **Female** | **Total**  |
| Number of employees, N (%) | 4,507 (88.4) | 594 (11.6) | 5,101 (100) |
| Age commenced employment, median (IQR) | 27.36 (22.43-33.69) | 27.02 (22.21-33.65) | 27.35 (22.40-33.69) |
| Age at end of follow-up, median (IQR) | 59.07 (51.91-86.19) | 54.50 (48.63-61.57) | 58.53 (51.58-67.48) |
| Currently Employed End 2016, N (%) | 290 (6.43) | 41 (6.9) | 331 (6.49) |
| **Duration employment, N (%)** |
| < 5 years | 1,306 (28.98) | 268 (45.12) | 1,574 (30.86) |
| 5 - 9 years | 523 (11.60) | 123 (20.71) | 646 (12.66) |
| 10 - 19 years | 1,143 (25.36) | 137 (23.06) | 1,280 (25.09) |
| ≥ 20 years | 1,535 (34.06) | 66 (11.11) | 1,601 (31.39) |
| **Time Period started Employment, N (%)** |
| Before 1970 | 585 (12.98) | 9 (1.52) | 594 (11.64) |
| 1970 - 1979 | 826 (18.33) | 63 (10.61) | 889 (17.43) |
| 1980 - 1989 | 2,288 (50.77) | 278 (46.80) | 2,566 (50.30) |
| 1990 - 1999 | 616 (13.67) | 204 (34.34) | 820 (16.08) |
| 2000 - 2004 | 192 (4.26) | 40 (6.73) | 232 (4.55) |
| **Smoking status, N (%)** |
| Never Smoker | 1,249 (27.71) | 195 (32.83) | 1,444 (28.31) |
| Current Smoker  | 1,592 (35.32) | 138 (23.23) | 1,730 (33.91) |
| Former Smoker | 832 (18.46) | 98 (16.50) | 930 (18.23) |
| Non-Smoker\* | 516 (11.45) | 67 (11.28) | 583 (11.43) |
| Unknown  | 318 (7.06) | 96 (16.16) | 414 (8.12) |
| **Follow up until 31 December 2016** |
| Person-years of follow-up | 121,719 | 15,283 | 137,002 |
| Average follow-up in years (SD) | 27.87 (6.69) | 26.39 (6.17) | 27.70 (6.65) |
| **Mortality – Follow up until 30 November 2016** |
| No. deaths from death linkage (%) | 732 (16.24) | 22 (3.70) | 754 (14.78) |
| Median age (IQR) at death  | 68.57 (57.13-77.70) | 51.93 (48.62-63.01) | 68.23 (56.43-77.46) |
| **Cancer incidence – Follow up until 31 December 2016** |
| No. cancers from cancer linkage  | 735 | 62 | 797 |
| No. of participants with cancer (%) | 652 (14.47) | 57 (9.60) | 709 (13.90) |
| Median age (IQR) at first cancer | 62.58 (54.98-70.52) | 51.07 (45.82-63.40) | 61.97 (54.03-69.90) |

 **\*** Non-smoker from employment records (cannot rule out previously smoked)

 **Table 2** Deaths to the end of 2016 compared to the Australian population. **Male smelter employees – Ever worked in production, maintenance or office.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **All Smelter (N=4,507)** | **Ever Production (N=3,090)** | **Ever Maintenance (N=1,111)** | **Ever Office (N=1,473)** |
| **Cause of death categories+** | **O** | **E** | **SMR (95% CI)** | **O** | **E** | **SMR (95% CI)** | **O** | **E** | **SMR (95% CI)** | **O** | **E** | **SMR (95% CI)** |
| **All Malignancies**  | 273 | 269.40 | 1.01 (0.90 - 1.14) | 202 | 177.58 | 1.14 (0.99 - 1.31) | 56 | 69.07 | 0.81 (0.61 - 1.05) | 91 | 98.05 | 0.93 (0.75 - 1.14) |
| Oesophagus  | 11 | 10.17 | 1.08 (0.54 - 1.93) | 9 | 6.76 | 1.33 (0.61 - 2.53) | <3 | 2.52 | 0.79 (0.10 - 2.87) | <3 | 3.73 | 0.54 (0.06 - 1.94) |
| Stomach  | 16 | 9.32 | 1.72 (0.98 - 2.79) | 8 | 6.15 | 1.30 (0.56 - 2.56) | 7 | 2.38 | 2.94 (1.18 - 6.05) | 7 | 3.37 | 2.08 (0.84 - 4.28) |
| Colorectal  | 22 | 29.90 | 0.74 (0.46 - 1.11) | 14 | 19.73 | 0.71 (0.39 - 1.19) | 5 | 7.63 | 0.66 (0.21 - 1.53) | 8 | 10.90 | 0.73 (0.32 - 1.45) |
| Liver  | 15 | 9.72 | 1.54 (0.86 - 2.55) | 13 | 6.50 | 2.00 (1.06 - 3.42) | 4 | 2.38 | 1.68 (0.46 - 4.30) | 0 | 3.52 | - |
| Pancreas  | 6 | 13.65 | 0.44 (0.16 - 0.96) | 5 | 9.05 | 0.55 (0.18 - 1.29) | 0 | 3.42 | - | <3 | 5.01 | 0.40 (0.05 - 1.44) |
| Lung  | 73 | 61.84 | 1.18 (0.93 - 1.48) | 56 | 40.70 | 1.38 (1.04 - 1.79) | 17 | 15.86 | 1.07 (0.62 - 1.72) | 23 | 22.75 | 1.01 (0.64 - 1.52) |
| Mesothelioma, pleural  | 12 | 4.95 | 2.42 (1.25 - 4.23) | 9 | 3.27 | 2.76 (1.26 - 5.23) | 3 | 1.26 | 2.38 (0.49 - 6.96) | 5 | 1.84 | 2.72 (0.88 - 6.34) |
| Melanoma  | 11 | 11.24 | 0.98 (0.49 - 1.75) | 8 | 7.47 | 1.07 (0.46 - 2.11) | <3 | 2.78 | 0.36 (0.01 - 2.00) | 4 | 3.97 | 1.01 (0.27 - 2.58) |
| Prostate | 37 | 24.26 | 1.53 (1.07 - 2.10) | 30 | 15.66 | 1.92 (1.29 - 2.73) | 7 | 6.78 | 1.03 (0.41 - 2.13) | 13 | 8.98 | 1.45 (0.77 - 2.48) |
| Bladder  | 4 | 6.24 | 0.64 (0.17 - 1.64) | 4 | 4.07 | 0.98 (0.27 - 2.52) | <3 | 1.70 | 0.59 (0.01 - 3.28) | <3 | 2.29 | 0.44 (0.01 - 2.43) |
| Kidney  | 6 | 6.82 | 0.88 (0.32 - 1.91) | 5 | 4.53 | 1.10 (0.36 - 2.58) | <3 | 1.70 | 0.59 (0.01 - 3.27) | 3 | 2.48 | 1.21 (0.25 - 3.54) |
| Brain | 3 | 10.47 | 0.29 (0.06 - 0.84) | <3 | 7.02 | 0.28 (0.03 - 1.03) | <3 | 2.50 | 0.40 (0.01 - 2.23) | <3 | 3.66 | 0.27 (0.01 - 1.52) |
| **All Metabolic** | 24 | 26.75 | 0.90 (0.57 - 1.34) | 13 | 17.59 | 0.74 (0.39 - 1.26) | 6 | 7.03 | 0.85 (0.31 - 1.86) | 12 | 9.64 | 1.24 (0.64 - 2.17) |
| **All Mental And Behavioural** | 13 | 18.71 | 0.69 (0.37 - 1.19) | 10 | 12.19 | 0.82 (0.39 - 1.51) | 4 | 5.24 | 0.76 (0.21 - 1.95) | 4 | 6.28 | 0.64 (0.17 - 1.63) |
| **All Nervous System** | 15 | 23.37 | 0.64 (0.36 - 1.06) | 9 | 15.31 | 0.59 (0.27 - 1.12) | 8 | 6.28 | 1.27 (0.55 - 2.51) | 3 | 8.26 | 0.36 (0.07 - 1.06) |
| Alzheimer's Disease | 6 | 4.94 | 1.21 (0.45 - 2.64) | <3 | 3.17 | 0.63 (0.08 - 2.28) | 5 | 1.48 | 3.38 (1.10 - 7.88) | <3 | 1.80 | 1.11 (0.13 - 4.01) |
| Parkinson's Disease | 3 | 4.98 | 0.60 (0.12 - 1.76) | <3 | 3.20 | 0.31 (0.01 - 1.74) | <3 | 1.46 | 1.37 (0.17 - 4.97) | <3 | 1.82 | 0.55 (0.01 - 3.07) |
| **All Circulatory** | 207 | 228.33 | 0.91 (0.79 - 1.04) | 137 | 148.94 | 0.92 (0.77 - 1.09) | 53 | 61.52 | 0.86 (0.65 - 1.13) | 76 | 82.50 | 0.92 (0.73 - 1.15) |
| Ischaemic Heart Disease | 134 | 140.19 | 0.96 (0.80 - 1.13) | 90 | 91.59 | 0.98 (0.79 - 1.21) | 33 | 37.34 | 0.88 (0.61 - 1.24) | 47 | 50.74 | 0.93 (0.68 - 1.23) |
| Cerebrovascular | 36 | 38.25 | 0.94 (0.66 - 1.30) | 21 | 24.77 | 0.85 (0.52 - 1.30) | 12 | 10.63 | 1.13 (0.58 - 1.97) | 17 | 13.87 | 1.23 (0.71 - 1.96) |
| Other Heart Disease | 27 | 35.08 | 0.77 (0.51 - 1.12) | 19 | 22.96 | 0.83 (0.50 - 1.29) | 6 | 9.47 | 0.63 (0.23 - 1.38) | 8 | 12.50 | 0.64 (0.28 - 1.26) |
| **All Respiratory** | 57 | 54.19 | 1.05 (0.80 - 1.36) | 41 | 35.13 | 1.17 (0.84 - 1.58) | 16 | 15.00 | 1.07 (0.61 - 1.73) | 19 | 19.73 | 0.96 (0.58 - 1.50) |
| COPD | 29 | 30.49 | 0.95 (0.64 - 1.37) | 20 | 19.72 | 1.01 (0.62 - 1.57) | 9 | 8.45 | 1.06 (0.49 - 2.02) | 10 | 11.25 | 0.89 (0.43 - 1.63) |
| Asthma | 5 | 2.46 | 2.03 (0.66 - 4.75) | 4 | 1.60 | 2.50 (0.68 - 6.39) | <3 | 0.64 | 1.56 (0.04 - 8.71) | <3 | 0.83 | 1.21 (0.03 - 6.74) |
|  Asbestosis | <3 | 0.72 | 1.39 (0.04 - 7.73) | <3 | 0.47 | 2.15 (0.05 - 11.96) | 0 | 0.21 | - | <3 | 0.26 | 3.81 (0.10 - 21.22) |
| **All Digestive** | 32 | 30.31 | 1.06 (0.72 - 1.49) | 23 | 20.16 | 1.14 (0.72 - 1.71) | 8 | 7.63 | 1.05 (0.45 - 2.07) | 12 | 10.70 | 1.12 (0.58 - 1.96) |
| Liver Disease | 15 | 17.64 | 0.85 (0.48 - 1.40) | 11 | 11.90 | 0.92 (0.46 - 1.65) | 5 | 4.18 | 1.20 (0.39 - 2.79) | 5 | 6.14 | 0.81 (0.26 - 1.90) |
| **All Urinary** | 9 | 10.03 | 0.90 (0.41 - 1.70) | 4 | 6.48 | 0.62 (0.17 - 1.58) | <3 | 2.86 | 0.35 (0.01 - 1.95) | 6 | 3.64 | 1.65 (0.61 - 3.59) |
| **All Injury And Trauma** | 82 | 84.35 | 0.97 (0.77 - 1.21) | 58 | 55.83 | 1.04 (0.79 - 1.34) | 13 | 21.35 | 0.61 (0.32 - 1.04) | 19 | 24.78 | 0.77 (0.46 - 1.20) |
| Accidents | 38 | 46.78 | 0.81 (0.57 - 1.11) | 27 | 30.69 | 0.88 (0.58 - 1.28) | 5 | 12.10 | 0.41 (0.13 - 0.96) | 9 | 13.87 | 0.65 (0.30 - 1.23) |
| Suicide | 39 | 31.45 | 1.24 (0.88 - 1.70) | 27 | 21.06 | 1.28 (0.85 - 1.87) | 7 | 7.73 | 0.91 (0.36 - 1.87) | 10 | 9.11 | 1.10 (0.53 - 2.02) |
| **All Other Causes** | 16 | 29.09 | 0.55 (0.31 - 0.89) | 11 | 19.33 | 0.57 (0.28 - 1.02) | 6 | 7.39 | 0.81 (0.30 - 1.77) | <3 | 9.85 | 0.10 (0.00 - 0.57) |
| **All Death Causes Combined\*** | 732 | 774.53888 | 0.95 (0.88 - 1.02) | 512 | 508.54 | 1.01 (0.92 - 1.10) | 173 | 203.37 | 0.85 (0.73 - 0.99) | 243 | 273.43 | 0.89 (0.78 - 1.01) |

\* 4 deaths included in all deaths which have no cause of death coded. COPD = Chronic Obstructive Pulmonary Disease.+ Refer to Table S1 for ICD-9/ICD-10 definitions of death categories. Sum of number of deaths in the 3 work categories does not equal number of deaths in all smelters group, as ever work classification is not mutually exclusive.

**Table 3** Cancer incidence to the end of 2016 compared to the Australian population. **Male smelter employees – Ever worked in production, maintenance or office**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **All Smelter (N=4,507)** | **Ever Production (N=3,090)** | **Ever Maintenance (N=1,111)** | **Ever Office (N=1,473)** |
| **Cancer categories**+ | **O** | **E** | **SIR (95% CI)** | **O** | **E** | **SIR (95% CI)** | **O** | **E** | **SIR (95% CI)** | **O** | **E** | **SIR (95% CI)** |
| **Lip, Oral Cavity And Pharynx** | 36 | 36.62 | 0.98 (0.69 - 1.36) | 24 | 24.71 | 0.97 (0.62 - 1.45) | 9 | 8.70 | 1.03 (0.47 - 1.96) | 10 | 12.72 | 0.79 (0.38 - 1.45) |
| Lip  | 19 | 12.08 | 1.57 (0.95 - 2.46) | 13 | 8.12 | 1.60 (0.85 - 2.74) | 4 | 2.90 | 1.38 (0.38 - 3.53) | 5 | 4.05 | 1.23 (0.40 - 2.88) |
| Pharynx | 6 | 10.45 | 0.57 (0.21 - 1.25) | 5 | 7.08 | 0.71 (0.23 - 1.65) | <3 | 2.46 | 0.81 (0.10 - 2.94) | 0 | 3.67 | - |
| **Digestive Organs**  | 146 | 166.04 | 0.88 (0.74 - 1.03) | 106 | 110.63 | 0.96 (0.78 - 1.16) | 31 | 40.92 | 0.76 (0.51 - 1.08) | 40 | 60.30 | 0.66 (0.47 - 0.90) |
| Oesophagus  | 12 | 11.50 | 1.04 (0.54 - 1.82) | 10 | 7.67 | 1.30 (0.63 - 2.40) | 3 | 2.81 | 1.07 (0.22 - 3.12) | <3 | 4.21 | 0.48 (0.06 - 1.72) |
| Stomach  | 26 | 17.56 | 1.48 (0.97 - 2.17) | 18 | 11.65 | 1.55 (0.92 - 2.44) | 8 | 4.38 | 1.83 (0.79 - 3.60) | 7 | 6.37 | 1.10 (0.44 - 2.26) |
| Colorectal  | 83 | 101.83 | 0.82 (0.65 - 1.01) | 56 | 67.80 | 0.83 (0.62 - 1.07) | 17 | 25.13 | 0.68 (0.39 - 1.08) | 25 | 37.01 | 0.68 (0.44 - 1.00) |
| Colon  | 49 | 59.27 | 0.83 (0.61 - 1.09) | 33 | 39.39 | 0.84 (0.58 - 1.18) | 9 | 14.75 | 0.61 (0.28 - 1.16) | 16 | 21.63 | 0.74 (0.42 - 1.20) |
| Rectum  | 32 | 39.83 | 0.80 (0.55 - 1.13) | 22 | 26.58 | 0.83 (0.52 - 1.25) | 7 | 9.72 | 0.72 (0.29 - 1.48) | 9 | 14.48 | 0.62 (0.28 - 1.18) |
| Liver  | 12 | 12.35 | 0.97 (0.50 - 1.70) | 11 | 8.34 | 1.32 (0.66 - 2.36) | <3 | 2.97 | 0.67 (0.08 - 2.43) | <3 | 4.41 | 0.23 (0.01 - 1.26) |
| Gallbladder | 6 | 3.85 | 1.56 (0.57 - 3.40) | 5 | 2.55 | 1.96 (0.64 - 4.58) | <3 | 0.96 | 1.04 (0.03 - 5.80) | <3 | 1.41 | 1.42 (0.17 - 5.13) |
| Pancreas  | 4 | 15.82 | 0.25 (0.07 - 0.65) | 3 | 10.52 | 0.29 (0.06 - 0.83) | 0 | 3.92 |  - | <3 | 5.79 | 0.35 (0.04 - 1.25) |
| **Respiratory And Intrathoracic Organs**  | 101 | 91.42 | 1.10 (0.90 - 1.34) | 77 | 60.46 | 1.27 (1.01 - 1.59) | 22 | 23.00 | 0.96 (0.60 - 1.45) | 35 | 33.55 | 1.04 (0.73 - 1.45) |
| Larynx  | 8 | 8.39 | 0.95 (0.41 - 1.88) | 7 | 5.58 | 1.25 (0.50 - 2.59) | <3 | 2.05 | 0.49 (0.01 - 2.72) | <3 | 3.07 | 0.65 (0.08 - 2.35) |
| Lung  | 91 | 80.71 | 1.13 (0.91 - 1.38) | 69 | 53.32 | 1.29 (1.01 - 1.64) | 20 | 20.38 | 0.98 (0.60 - 1.52) | 33 | 29.68 | 1.11 (0.77 - 1.56) |
| **Melanoma**  | 62 | 90.28 | 0.69 (0.53 - 0.88) | 37 | 60.63 | 0.61 (0.43 - 0.84) | 16 | 21.56 | 0.74 (0.42 - 1.21) | 24 | 31.20 | 0.77 (0.49 - 1.14) |
| **Mesothelioma**  | 12 | 6.30 | 1.90 (0.98 - 3.33) | 9 | 4.16 | 2.16 (0.99 - 4.11) | 3 | 1.59 | 1.89 (0.39 - 5.52) | 5 | 2.34 | 2.14 (0.69 - 4.99) |
| **Male Reproductive Organs**  | 214 | 219.70 | 0.97 (0.85 - 1.11) | 138 | 146.61 | 0.94 (0.79 - 1.11) | 47 | 52.77 | 0.89 (0.65 - 1.18) | 86 | 81.55 | 1.05 (0.84 - 1.30) |
| Prostate  | 202 | 199.28 | 1.01 (0.88 - 1.16) | 131 | 133.11 | 0.98 (0.82 - 1.17) | 44 | 47.91 | 0.92 (0.67 - 1.23) | 82 | 74.39 | 1.10 (0.88 - 1.37) |
| Testis  | 11 | 9.55 | 1.15 (0.57 - 2.06) | 7 | 6.40 | 1.09 (0.44 - 2.22) | <3 | 2.38 | 0.84 (0.10 - 3.03) | 4 | 2.54 | 1.57 (0.43 - 4.03) |
| **Urinary Tract**  | 55 | 47.28 | 1.16 (0.88 - 1.51) | 39 | 31.47 | 1.24 (0.88 - 1.69) | 11 | 11.74 | 0.94 (0.47 - 1.68) | 23 | 17.06 | 1.35 (0.85 - 2.02) |
| Kidney  | 30 | 23.02 | 1.30 (0.88 - 1.86) | 23 | 15.52 | 1.48 (0.94 - 2.22) | 6 | 5.49 | 1.09 (0.40 - 2.38) | 14 | 8.17 | 1.71 (0.94 - 2.87) |
| Bladder  | 20 | 21.16 | 0.95 (0.58 - 1.46) | 13 | 13.90 | 0.94 (0.50 - 1.60) | 4 | 5.46 | 0.73 (0.20 - 1.88) | 8 | 7.75 | 1.03 (0.45 - 2.03) |
| **Brain And Other CNS**  | 5 | 13.07 | 0.38 (0.12 - 0.89) | 4 | 8.77 | 0.46 (0.12 - 1.17) | <3 | 3.13 | 0.32 (0.01 - 1.78) | <3 | 4.46 | 0.22 (0.01 - 1.25) |
|  Brain  | 5 | 12.55 | 0.40 (0.13 - 0.93) | 4 | 8.42 | 0.48 (0.13 - 1.22) | <3 | 3.01 | 0.33 (0.01 - 1.85) | <3 | 4.30 | 0.23 (0.01 - 1.30) |
| **Thyroid And Other Endocrine Glands**  | 6 | 7.27 | 0.83 (0.30 - 1.80) | <3 | 4.95 | 0.40 (0.05 - 1.46) | 4 | 1.72 | 2.32 (0.63 - 5.94) | <3 | 2.37 | 0.84 (0.10 - 3.05) |
|  Thyroid  | 5 | 6.72 | 0.74 (0.24 - 1.74) | <3 | 4.58 | 0.22 (0.01 - 1.22) | 4 | 1.59 | 2.51 (0.69 - 6.44) | <3 | 2.19 | 0.91 (0.11 - 3.30) |
| **Unknown Site**  | 17 | 18.40 | 0.92 (0.54 - 1.48) | 12 | 12.14 | 0.99 (0.51 - 1.73) | 5 | 4.72 | 1.06 (0.34 - 2.47) | <3 | 6.67 | 0.30 (0.04 - 1.08) |
| **Lymphoid, Haematopoietic + Related Tissue**  | 62 | 68.67 | 0.90 (0.69 - 1.16) | 35 | 45.88 | 0.76 (0.53 - 1.06) | 18 | 16.76 | 1.07 (0.64 - 1.70) | 22 | 24.17 | 0.91 (0.57 - 1.38) |
| Hodgkins | 6 | 3.60 | 1.66 (0.61 - 3.62) | 5 | 2.39 | 2.09 (0.68 - 4.87) | <3 | 0.89 | 2.24 (0.27 - 8.09) | 0 | 1.10 | - |
| Non-Hodgkin Lymphoma  | 29 | 32.20 | 0.90 (0.60 - 1.29) | 17 | 21.58 | 0.79 (0.46 - 1.26) | 8 | 7.76 | 1.03 (0.45 - 2.03) | 11 | 11.33 | 0.97 (0.48 - 1.74) |
| Multiple Myeloma  | 9 | 10.11 | 0.89 (0.41 - 1.69) | 5 | 6.75 | 0.74 (0.24 - 1.73) | <3 | 2.48 | 0.81 (0.10 - 2.91) | <3 | 3.69 | 0.54 (0.07 - 1.96) |
| Leukaemia  | 18 | 21.86 | 0.82 (0.49 - 1.30) | 8 | 14.56 | 0.55 (0.24 - 1.08) | 6 | 5.40 | 1.11 (0.41 - 2.42) | 9 | 7.74 | 1.16 (0.53 - 2.21) |
| **Other Cancers** | 19 | 28.48 | 0.67 (0.40 - 1.04) | 14 | 18.95 | 0.74 (0.40 - 1.24) | 6 | 7.10 | 0.84 (0.31 - 1.84) | 4 | 9.95 | 0.40 (0.11 - 1.03) |
| Connective Tissue | 4 | 5.10 | 0.78 (0.21 - 2.01) | 4 | 3.42 | 1.17 (0.32 - 2.99) | <3 | 1.24 | 0.81 (0.02 - 4.49) | <3 | 1.73 | 0.58 (0.01 - 3.22) |
| Myelodysplastic | 4 | 5.03 | 0.79 (0.22 - 2.03) | 3 | 3.31 | 0.91 (0.19 - 2.65) | <3 | 1.33 | 1.51 (0.18 - 5.44) | <3 | 1.85 | 0.54 (0.01 - 3.02) |
| **All Malignancies** | 735 | 793.53 | 0.93 (0.86 - 1.00) | 497 | 529.36 | 0.94 (0.86 - 1.03) | 173 | 193.71 | 0.89 (0.76 - 1.04) | 254 | 286.34 | 0.89 (0.78 - 1.00) |

+ Refer to Table S2 for ICD-10 definitions of cancer categories. Sum of number of deaths in the 3 work categories does not equal number of deaths in all smelters group, as ever work classification is not mutually exclusive.

**Table 4** Deaths to end of 2016 compared to Australian population by Time Since First Employment. **Male production and maintenance smelter employees**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **3 months to < 20 years** | **20- 40 years** | **> 40 years** |
| **Cause of death categories**+ | **O** | **E** | **SMR (95% CI)** | **O** | **E** | **SMR (95% CI)** | **O** | **E** | **SMR (95% CI)** |
| **All Malignancies**  | 21 | 35.59 | 0.59 (0.37-0.90) | 160 | 139.71 | 1.15 (0.97-1.34) | 56 | 51.56 | 1.09 (0.82-1.41) |
| Oesophagus  | 0 | 1.26 | - | 9 | 5.59 | 1.61 (0.74-3.06) | <3 | 1.68 | 0.60 (0.02-3.32) |
| Stomach  | 4 | 1.49 | 2.68 (0.73-6.87) | 7 | 4.93 | 1.42 (0.57-2.93) | 3 | 1.44 | 2.08 (0.43-6.09) |
| Colorectal  | 0 | 4.3 | - | 13 | 16.16 | 0.80 (0.43-1.38) | 5 | 4.73 | 1.06 (0.34-2.47) |
| Liver  | <3 | 1.1 | 0.91 (0.02-5.08) | 9 | 5.29 | 1.70 (0.78-3.23) | 5 | 1.76 | 2.85 (0.92-6.64) |
| Pancreas  | <3 | 1.61 | 0.62 (0.02-3.47) | 4 | 7.28 | 0.55 (0.15-1.41) | 0 | 2.56 | - |
| Lung  | 8 | 7.66 | 1.04 (0.45-2.06) | 49 | 33.82 | 1.45 (1.07-1.92) | 9 | 10.59 | 0.85 (0.39-1.61) |
| Mesothelioma, pleural  | <3 | 0.38 | 2.65 (0.07-14.77) | 6 | 2.55 | 2.35 (0.86-5.12) | 4 | 1.23 | 3.25 (0.89-8.32) |
| Melanoma  | <3 | 2.25 | 0.89 (0.11-3.21) | 7 | 5.33 | 1.31 (0.53-2.71) | 0 | 1.86 | - |
| Prostate | <3 | 1.08 | 0.93 (0.02-5.16) | 21 | 11.71 | 1.79 (1.11-2.74) | 11 | 7.81 | 1.41 (0.70-2.52) |
| Bladder  | 0 | 0.49 | - | <3 | 3.07 | 0.65 (0.08-2.35) | <3 | 1.73 | 1.16 (0.14-4.18) |
| Kidney  | 0 | 1 | - | 3 | 3.62 | 0.83 (0.17-2.42) | <3 | 1.1 | 1.81 (0.22-6.54) |
| Brain | <3 | 2.44 | 0.82 (0.10-2.96) | 0 | 5.27 | - | 0 | 1.06 | - |
| **All Metabolic** | 3 | 3.05 | 0.98 (0.20-2.87) | 8 | 12.98 | 0.62 (0.27-1.21) | 8 | 6.59 | 1.21 (0.52-2.39) |
| **All Mental And Behavioural** | 4 | 3.94 | 1.02 (0.28-2.60) | <3 | 5.37 | 0.37 (0.05-1.35) | 7 | 6.72 | 1.04 (0.42-2.15) |
| **All Nervous System** | <3 | 3.02 | 0.33 (0.01-1.85) | 7 | 9.71 | 0.72 (0.29-1.49) | 6 | 7.1 | 0.85 (0.31-1.84) |
| Alzheimer's Disease | 0 | 0.08 | - | <3 | 1.64 | 0.61 (0.02-3.39) | 5 | 2.51 | 1.99 (0.65-4.65) |
| Parkinson's Disease  | 0 | 0.08 | - | <3 | 1.88 | 0.53 (0.01-2.97) | <3 | 2.3 | 0.43 (0.01-2.42) |
| **All Circulatory** | 26 | 34.15 | 0.76 (0.50-1.12) | 101 | 111.87 | 0.90 (0.74-1.10) | 48 | 47.5 | 1.01 (0.75-1.34) |
| IHD | 20 | 23.15 | 0.86 (0.53-1.33) | 66 | 70.98 | 0.93 (0.72-1.18) | 27 | 24.53 | 1.10 (0.73-1.60) |
| Cerebrovascular | 3 | 4.4 | 0.68 (0.14-1.99) | 16 | 17.96 | 0.89 (0.51-1.45) | 11 | 10.16 | 1.08 (0.54-1.94) |
| Other Heart Disease | 3 | 4.99 | 0.60 (0.12-1.76) | 12 | 15.42 | 0.78 (0.40-1.36) | 8 | 9.36 | 0.86 (0.37-1.68) |
| **All Respiratory** | 3 | 4.89 | 0.61 (0.13-1.79) | 34 | 25.52 | 1.33 (0.92-1.86) | 13 | 15.62 | 0.83 (0.44-1.42) |
| COPD | <3 | 2.12 | 0.47 (0.01-2.63) | 17 | 15.43 | 1.10 (0.64-1.76) | 7 | 8.33 | 0.84 (0.34-1.73) |
| Asthma | <3 | 0.84 | 1.19 (0.03-6.61) | 3 | 1.02 | 2.94 (0.61-8.58) | 0 | 0.22 | - |
|  Asbestosis | 0 | 0.02 | - | <3 | 0.3 | 3.33 (0.08-18.55) | 0 | 0.29 | - |
| **All Digestive** | 3 | 5.98 | 0.50 (0.10-1.47) | 15 | 14.79 | 1.01 (0.57-1.67) | 9 | 4.78 | 1.88 (0.86-3.57) |
| Liver Disease | <3 | 4.46 | 0.45 (0.05-1.62) | 7 | 9 | 0.78 (0.31-1.60) | 4 | 1.33 | 3.00 (0.82-7.68) |
| **All Urinary** | 0 | 0.68 | - | <3 | 4.23 | 0.47 (0.06-1.71) | 3 | 3.63 | 0.83 (0.17-2.41) |
| **All Injury And Trauma** | 47 | 41.42 | 1.13 (0.83-1.51) | 20 | 25.53 | 0.78 (0.48-1.21) | 4 | 5.15 | 0.78 (0.21-1.99) |
| Accidents | 21 | 22.23 | 0.94 (0.58-1.44) | 8 | 13.8 | 0.58 (0.25-1.14) | 3 | 3.93 | 0.76 (0.16-2.23) |
| Suicide | 25 | 16.29 | 1.53 (0.99-2.27) | 9 | 9.76 | 0.92 (0.42-1.75) | 0 | 0.86 | - |
| **All Other Causes** | <3 | 7.29 | 0.27 (0.03-0.99) | 10 | 11.88 | 0.84 (0.40-1.55) | 3 | 5.46 | 0.55 (0.11-1.60) |
| **All Death Causes Combined\*** | 111 | 140 | 0.79 (0.65-0.95) | 362 | 361.6 | 1 .00 (0.90-1.11) | 157 | 154.11 | 1.02 (0.87-1.19) |

+ Refer to Table S1 for ICD-9/ICD-10 definitions of death categories.

**Table 5** Cancer incidence to end of 2016 compared to Australian population for Time Since First Employment **Male production or maintenance smelter employees**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **3 months to < 20 years** | **20- 40 years** | **> 40 years** |
| **Cancer categories** + | **O** | **E** | **SIR (95% CI)** | **O** | **E** | **SIR (95% CI)** | **O** | **E** | **SIR (95% CI)** |
| **Lip, Oral Cavity And Pharynx** | 10 | 8.67 | 1.15 (0.55-2.12) | 19 | 19.05 | 1.00 (0.60-1.56) | <3 | 2.97 | 0.34 (0.01-1.88) |
| Lip  | 7 | 3.73 | 1.88 (0.75-3.86) | 9 | 5.55 | 1.62 (0.74-3.08) | 0 | 0.88 | - |
| Pharynx | <3 | 2.16 | 0.46 (0.01-2.58) | 4 | 5.82 | 0.69 (0.19-1.76) | <3 | 0.76 | 1.32 (0.03-7.36) |
| **Digestive Organs**  | 21 | 22.40 | 0.94 (0.58-1.43) | 86 | 90.74 | 0.95 (0.76-1.17) | 22 | 25.99 | 0.85 (0.53-1.28) |
| Oesophagus  | <3 | 1.43 | 0.70 (0.02-3.88) | 9 | 6.39 | 1.41 (0.64-2.67) | <3 | 1.78 | 0.56 (0.01-3.12) |
| Stomach  | 7 | 2.74 | 2.56 (1.03-5.27) | 15 | 9.38 | 1.60 (0.89-2.64) | <3 | 2.61 | 0.77 (0.09-2.77) |
| Colorectal  | 10 | 13.93 | 0.72 (0.34-1.32) | 47 | 55.75 | 0.84 (0.62-1.12) | 14 | 15.68 | 0.89 (0.49-1.50) |
| Colon  | 4 | 7.79 | 0.51 (0.14-1.31) | 28 | 31.94 | 0.88 (0.58-1.27) | 9 | 10.02 | 0.90 (0.41-1.71) |
| Rectum  | 6 | 5.78 | 1.04 (0.38-2.26) | 17 | 22.33 | 0.76 (0.44-1.22) | 5 | 5.20 | 0.96 (0.31-2.25) |
| Liver  | <3 | 1.48 | 0.67 (0.02-3.76) | 7 | 7.02 | 1.00 (0.40-2.05) | 4 | 1.84 | 2.18 (0.59-5.58) |
| Gallbladder | 0 | 0.48 | - | 4 | 2.01 | 1.99 (0.54-5.10) | <3 | 0.73 | 1.37 (0.03-7.66) |
| Pancreas  | 0 | 1.86 | - | 3 | 8.49 | 0.35 (0.07-1.03) | 0 | 2.90 | - |
| **Respiratory And Intrathoracic Organs**  | 13 | 12.00 | 1.08 (0.58-1.85) | 64 | 49.90 | 1.28 (0.99-1.64) | 13 | 14.84 | 0.88 (0.47-1.50) |
|  Larynx  | <3 | 1.46 | 1.37 (0.17-4.94) | 5 | 4.65 | 1.08 (0.35-2.51) | 0 | 0.90 | - |
| Lung  | 11 | 9.98 | 1.10 (0.55-1.97) | 59 | 44.1 | 1.34 (1.02-1.73) | 11 | 13.68 | 0.80 (0.40-1.44) |
| **Melanoma**  | 19 | 21.81 | 0.87 (0.52-1.36) | 27 | 43.25 | 0.62 (0.41-0.91) | 4 | 10.51 | 0.38 (0.10-0.97) |
| **Mesothelioma**  | <3 | 0.62 | 1.61 (0.04-8.95) | 7 | 3.30 | 2.12 (0.85-4.38) | 3 | 1.37 | 2.20 (0.45-6.42) |
| **Male Reproductive Organs**  | 25 | 20.02 | 1.25 (0.81-1.84) | 114 | 126.98 | 0.90 (0.74-1.08) | 30 | 35.66 | 0.84 (0.57-1.20) |
| Prostate  | 17 | 13.63 | 1.25 (0.73-2.00) | 112 | 119.77 | 0.94 (0.77-1.13) | 30 | 32.30 | 0.93 (0.63-1.33) |
| Testis  | 8 | 5.98 | 1.34 (0.58-2.64) | <3 | 2.15 | 0.46 (0.01-2.59) | 0 | 0.06 | - |
| **Urinary Tract**  | 10 | 6.81 | 1.47 (0.70-2.70) | 30 | 25.24 | 1.19 (0.80-1.70) | 6 | 7.62 | 0.79 (0.29-1.71) |
| Kidney  | 6 | 3.81 | 1.58 (0.58-3.43) | 17 | 12.77 | 1.33 (0.78-2.13) | 3 | 2.68 | 1.12 (0.23-3.27) |
| Bladder  | 3 | 2.66 | 1.13 (0.23-3.29) | 10 | 10.89 | 0.92 (0.44-1.69) | 3 | 4.24 | 0.71 (0.15-2.07) |
| **Brain And Other CNS**  | 3 | 3.51 | 0.86 (0.18-2.50) | 0 | 6.25 | - | <3 | 1.20 | 0.83 (0.02-4.65) |
|  Brain  | 3 | 3.33 | 0.90 (0.19-2.64) | 0 | 6.03 | - | <3 | 1.16 | 0.86 (0.02-4.79) |
| **Thyroid and Other Endocrine Glands**  | <3 | 2.01 | 0.50 (0.01-2.77) | 4 | 3.57 | 1.12 (0.31-2.87) | <3 | 0.55 | 1.81 (0.05-10.07) |
|  Thyroid  | 0 | 1.83 | - | 4 | 3.33 | 1.20 (0.33-3.08) | <3 | 0.51 | 1.94 (0.05-10.83) |
| **Unknown Site**  | 3 | 2.84 | 1.06 (0.22-3.08) | 8 | 9.68 | 0.83 (0.36-1.63) | 5 | 2.97 | 1.68 (0.55-3.93) |
|  **Lymphoid, Haematopoietic + Related Tissue**  | 10 | 13.23 | 0.76 (0.36-1.39) | 26 | 34.56 | 0.75 (0.49-1.10) | 12 | 9.78 | 1.23 (0.63-2.14) |
|  Hodgkin’s | 4 | 1.57 | 2.54 (0.69-6.50) | <3 | 1.28 | 1.56 (0.19-5.64) | 0 | 0.19 | - |
| Non-Hodgkin Lymphoma  | 5 | 6.47 | 0.77 (0.25-1.80) | 14 | 16.16 | 0.87 (0.47-1.45) | 3 | 4.33 | 0.69 (0.14-2.03) |
| Multiple Myeloma  | <3 | 1.23 | 0.81 (0.02-4.54) | 4 | 5.47 | 0.73 (0.20-1.87) | <3 | 1.76 | 1.14 (0.14-4.10) |
|  Leukaemia  | 0 | 3.85 | - | 6 | 11.16 | 0.54 (0.20-1.17) | 7 | 3.34 | 2.09 (0.84-4.32) |
| **Other Cancers** | <3 | 5.39 | 0.37 (0.04-1.34) | 10 | 13.27 | 0.75 (0.36-1.39) | 6 | 5.29 | 1.13 (0.42-2.47) |
|  Connective Tissue | <3 | 1.33 | 0.75 (0.02-4.20) | <3 | 2.38 | 0.42 (0.01-2.34) | <3 | 0.59 | 3.41 (0.41-12.33) |
|  Myelodysplastic | 0 | 0.23 | - | 3 | 2.68 | 1.12 (0.23-3.27) | <3 | 1.97 | 0.51 (0.01-2.83) |
| **All Malignancies** | 118 | 119.32 | 0.99 (0.82-1.18) | 395 | 425.79 | 0.93 (0.84-1.02) | 104 | 118.75 | 0.88 (0.72-1.06) |

+ Refer to Table S1 for ICD-9/ICD-10 definitions of cancer categories.

**DISCUSSION**

This analysis of >121,700 person-years of follow-up amongst 4507 male employees in pre-bake aluminium smelters found no differences in the rates of overall mortality and, in particular, mortality from overall cancer and non-malignant respiratory disease, compared with the Australian population. Amongst the workers likely to have been most exposed (production and maintenance workers), there was a lower risk of overall death and overall cancer deaths in the 20 years after commencing work, consistent with results published previously7 and those from other studies18-19 amongst smelter workers and likely attributable to the healthy worker effect. An excess risk of lung (SMR 1.4, 95% CI 1.0-1.8), prostate (SMR 1.9, 95% CI 1.3-2.7) and liver cancer (SMR 2.0, 95% CI 1.1-3.4) was seen amongst production workers in whom an increased SIR for overall respiratory cancers (lung cancers) was also found. An excess risk of death from stomach cancer (SMR 2.9, 95% CI 1.2-6.1) and Alzheimer’s disease (SMR 3.4, 95% CI 1.1-7.9) was seen amongst maintenance workers. There was an excess risk of suicide in the first 20 years after commencing work.

An excess risk of death from mesothelioma was found in production workers, along with increased incidence. The majority of mesothelioma cases were in former workers who stopped work before the 1995/1996 health survey and who have had the longest duration since exposure and would have also commenced employment at a time when there were greater levels of asbestos usage in Australian industry. Using an asbestos job exposure matrix, all 11 cases at the older smelter had some possible asbestos exposure and over half had >10 years of exposure at high levels (64%). It seems likely that most of this excess risk is attributable to asbestos exposure, some of which will have occurred in this industry.

In contrast with our previous findings7, longer follow-up has shown an increased mortality (18%) and incidence risk (13%) for lung cancer, with the highest risks amongst production workers and those who commenced employment >20 years but <40 years previously. Almost 80% of these lung cancer cases were in former or current smokers. In the cohort, production workers reported the highest current smoking rates (40.7%) (rates very similar to the national average rates for men at that time in Australia: 43% in 1983 and 30% in 1989)21. More definitive conclusions can only be drawn from future internal analyses, taking into account specific exposures, adjusting for smoking. Consideration of asbestos exposure in the lung cancer cases suggested that, although some will have had asbestos exposure, about half of cases occurred in the lowest exposure groups. An excess risk of lung cancer has been previously reported in aluminium smelters but mostly amongst those working in Søderberg smelters or mixed smelters3,21-24. In Søderberg smelters, the lung cancer risk has a dose-response relationship with exposure to benzo[a]pyrene (BaP) and benzene soluble material. Lower exposure to emissions in prebake smelters5,25 may be reducing the lung cancer risk but, given the possibility of greater peak particulate matter exposure and/ or more task-related exposure variability25, an excess lung cancer risk above the effect of smoking cannot yet be excluded.

Respiratory symptoms have long been attributed to aluminium smelting, including cough, wheeze, rhinitis and obstructive and restrictive lung diseases. So-called “potroom asthma” has been associated with dust and gas exposures in the potrooms4 but incidence rates have declined in parallel with better control over both types of exposure in the industry. One of the a priori aims of this research was to explore the risk of non-malignant respiratory deaths, and in particular, deaths caused by chronic obstructive pulmonary disease (COPD). Reassuringly, this follow-up linkage has shown no excess risk of death from non-malignant respiratory causes overall or related to asthma, COPD, or asbestosis.

An excess risk of death from liver cancer was found amongst production workers, but not a corresponding increase in liver cancer incidence. There is limited evidence of excess liver cancer risk from other studies3 but a significant excess of death from liver cancer was reported amongst carbon plant workers in China using an unspecified process involving high levels of exposure to CTPVs26. An association with mortality from liver cancer was shown in another study in prebake smelters27. More research is required.

An excess risk of death from prostate cancer was seen again in this cohort, with the risk highest amongst production workers who commenced employment >20 years previously. However, no excess of prostate cancer incidence was found. Investigations in other cohorts have shown an excess (but not significant) risk of prostate cancer mortality24,27,28 and incidence28 and no exposure-response relationship. Between-country comparison of incidence rates for prostate cancer is troublesome because of wide variation as to whether and when screening for prostate cancer is undertaken (in Australia, prostate specific antigen testing was introduced in the mid-1990s, resulting in substantial increases in prostate cancer diagnoses) and given its relatively long survival, mortality is also difficult to compare. At this time, therefore, it is unclear whether or not this is a chance finding.

For stomach cancer, a significant excess risk of death was seen amongst maintenance workers, but not production workers, and there were excesses of incident stomach cancers for maintenance workers. An elevated risk of stomach cancer has been reported in some other cohorts6,24,28,29 and, previously amongst office workers in this cohort7. However, studies which have looked for a dose-response relationship with BaP exposure have not found one. It is currently unclear therefore whether stomach cancer is truly a risk associated with this industry and indeed, if it is, what the cause might be.

The current study did not find an excess of bladder cancer mortality or incidence and continues to report lower than expected numbers of cases. This contrasts with older findings from Søderberg plants, in which an association with bladder cancer was consistently demonstrated with a dose-response relationship with BaP exposure3,4. As reported by others30, it seems that the risk of bladder cancer is being effectively mitigated in Aluminium smelters by the combination of engineering controls, improved work practices, technological advancement, and optimised use of personal protective equipment. Notably, our previous finding of an excess incidence of kidney cancer7 has not been replicated in this linkage. An excess risk has been shown in Canada8  and although not statistically significant, there were elevated risk ratios for kidney cancer incidence in this linkage. One further Healthwise linkage is envisaged and this risk will be further investigated after longer follow-up.

Elevated risks for death by suicide were found in this study amongst aluminium production workers employed > 3 months but < 20 years. No comparable studies of risk of suicide in this industry were identified. In Australia, rates of suicide have increased over the last decade, with the age-standardised rate for men increasing from 16.2 deaths per 100,000 population in 2011 to 18.2 in 202131. The biggest increase in these rates has occurred amongst younger working-aged men, particularly those with lower levels of educational attainment. Similar findings have been reported in the USA. Socio-economic factors are known to be importantly associated with suicide risk and it has been speculated that some of the excess risk in this socio-demographic group has been the long-term decline in manufacturing with the resultant decrease in good employment options for less educated adults who are therefore increasingly pushed towards precarious employment32. More research is required but we speculate that this is the most likely explanation for this finding in our cohort.

The finding of excess mortality from Alzheimer’s disease amongst maintenance workers is potentially of interest, although based on relatively small numbers. Excessive levels of aluminium in the central nervous system are neurotoxic and there are potential mechanisms by which aluminium could directly or indirectly impact the mechanism of Alzheimer’s disease33. Cognitive decline has been reported previously amongst workers in the aluminium industry34,35 with the decline associated with elevated blood aluminium levels36. Whilst there has not been any convincing evidence of an increased risk of deaths from Alzheimer’s disease amongst workers in the industry previously, cognitive impairment was found amongst Chinese workers in an aluminium factory with the highest plasma aluminium levels37. Given that the finding related to maintenance workers, but not production workers, this could be a chance finding but longer-term studies are required.

The findings from this study need to be considered alongside some limitations. Firstly, although every effort was made to recruit female workers, the numbers have proved too small to allow detailed investigation of their health risks. Secondly, although Healthwise is a large study, it is likely to have limited power to detect small increases in rare cancer and death outcomes. Thirdly, the cohort participants are currently aged 59.9 years (some are still working) and a longer duration of follow-up may yet yield more evidence of increased risks associated with exposures from this industry. Importantly, the majority of the cohort was first employed over 30 years before the latest linkage, so we might reasonably expect to see any long latency disease signals by now but latency periods for different types of cancer vary (dependent upon for example, mode of exposure, dose and duration, age at exposure, genetic factors, and other factors such as treatment with immunosuppression therapy). For this reason, another linkage is planned in 5 years’ time. Fourthly, although efforts were made to collect smoking data, there were differential levels of data available depending upon recruitment method: data from company records (about former employees) had more missing values. The Healthwise cohort started with a cross-sectional study in 1995/6, which recruited 90% of workers then employed by the company. Subsequently, data was obtained about everybody who had been employed by the Company between January 1983 and the commencement of the cross-sectional study but had left the company. Finally, new starters at the company (n=601) after December 1996 until December 2004 were offered participation and 77% consented. In consequence, a small number of potential cohort participants opted out of the research and a selection bias amongst this group cannot be ruled out, but the majority of workers came from company records in which no self-selection was possible. Another limitation is that exposure assessment was based on categorisation from the employment histories as: production; maintenance; or office workers and quantitative assessment was not available. Whilst these categories enable a “proxy” for high vs limited levels of exposure, the exposures will not be identical as, for example, production workers in prebake smelters (working in potrooms or the carbon plant) will have PAH exposure but those working in the rolling mill will not. It is our intention to undertake internal analyses to explore this further.

This study benefits from mandatory reporting of cancer in Australia across all states and territories so that the ACD is virtually complete, as is the NDI for deaths. Deaths occurring overseas are not recorded and, as this study does not actively track participants, it is not possible to account for participants who have died overseas or migrated permanently who will continue to contribute person-years without the possibility of having a death or cancer event recorded. The Time Since First Employment analysis means those workers with different exposure levels over different eras are grouped together and also allows examination for the potential exposure lag effects for cancer incidence over time, and there was little indication of increased cancer risk with workplace exposures.

In summary, there was an excess risk of death from mesothelioma, lung cancer, prostate cancer, liver and stomach cancer and increases in incidence of lung cancer and mesothelioma in production workers. However, there was no excess mortality from non-malignant respiratory disease or bladder cancer, perhaps explained by reduction in exposure to PAH. An excess risk of mortality from stomach cancer and Alzheimer’s disease was suggested in maintenance workers but further follow-up is required.

**FUNDING STATEMENT**The Healthwise study was funded by Alcoa of Australia Ltd (PO Box 252, ApplecrossWA 6953) (Award Number: Not applicable). The sponsor had no direct involvement in study design, the collection, analysis, and interpretation of data, the writing of the report or in the decision to submit the paper for publication.

ACKNOWLEDGEMENTS

The Healthwise study was overseen by an independent scientific advisory board chaired by Professor Neil Pearce and consisting of union representatives, Alcoa of Australia Ltd representatives being Dr James Wesdock, Dr Michael Donoghue, and academic experts, being Professor Mark Cullen and Professor Harvey Checkoway. We would like to thank the board members for their comments on the analysis and manuscript.

CONTRIBUTORSHIP

MS was awarded funding for the study and conceived the design. AdM, CD and GB undertook the data collection and analyses and provisional report writing. KWB drafted the manuscript. All co-authors reviewed the draft manuscript prior to submission.

COMPETING INTERESTS

All authors confirm that they have no competing interests to declare.

DATA SHARING/AVAILABILITY

Linkage data were obtained from the Australian Institute for Health and Welfare and permission would need to be obtained from them for additional data usage.

ETHICS APPROVAL

This study was approved by the Monash Research Ethics Committee (ref: 9941).

**REFERENCES**

1. IARC. Monograph 34: polynuclear aromatic compounds, Part 3, industrial exposures

in aluminium production, coal gasification, coke production, and iron and steel

founding. Geneva: World Health Organisation, 1984

1. A review of human carcinogens. Part F: Chemical agents and related occupations / IARC Working Group on the Evaluation of Carcinogenic Risks to Humans (2009: Lyon, France). Available from: <https://monographs.iarc.who.int/wp-content/uploads/2018/06/mono100F-22.pdf>. (Date last accessed November 2022)
2. Gibbs GW, Labreche F. Cancer risks in aluminium reduction plant workers. JOEM 2014;56: S40-59.
3. Wesdock JC, Arnold IMF. Occupational and environmental health in the Aluminium industry. JOEM 2014;56: S5-11.
4. Benke G, Abramson M, Sim M. Exposures in the alumina and primary aluminium

industry: an historical review. Ann Occup Hyg 1998;42:173–89

1. Spinelli J, Demers P, Le N, et al. Cancer risk in aluminium reduction plant workers

(Canada). Cancer Causes Control 2006;17:939–48

1. Sim MR, Del Monaco A, Hoving JL, Macfarlane E, McKenzie D, Benke G, et al. Mortality and cancer incidence in workers in two Australian prebake aluminium smelters. Occup Environ Med. 2009;66(7):464-70.
2. Fritschi L, Beach J, Sim M, Abramson M, Benke G, Musk AW, et al. Respiratory symptoms and lung function in two prebake aluminum smelters. Am J Ind Med. 1999;May;35(5):491-8.
3. Fritschi L, Sim MR, Forbes A, Abramson MJ, Benke G, Musk AW, et al. Respiratory symptoms and lung-function changes with exposure to five substances in aluminium smelters. Int Arch Occup Environ Health. 2003 Mar;76(2):103-10.
4. Abramson MJ, Benke GP, Cui J, de Klerk NH, Del Monaco A, Dennekamp M, et al. Is potroom asthma due more to sulphur dioxide than fluoride? An inception cohort study in the Australian aluminium industry. Occup Environ Med. 2010;Oct;67(10):679-85.
5. Benke G, Sim M, Fritschi L, Aldred G. A task exposure database for use in the alumina and primary aluminium industry. Applied Occupational Environmental Hygiene 2001;16(2):149-53.
6. Moulin JJ, Clavel T, Buclez B, et al. A mortality study among workers in a French

aluminium reduction plant. Int Arch Occup Environ Health 2000;73:323–30.

1. Hoving JL, Del Monaco A, MacFarlane E, Fritschi L, Benke G, McKenzie D, et al. Methodological issues in linking study participants to Australian cancer registries using different methods: lessons from a cohort study. Aust N Z J Public Health. 2005;29(4):378-82.
2. International Classification of Diseases. Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death. Ninth Revision Conference 1975 (ICD-9). Geneva: World Health Organization; 1977.
3. The International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). Geneva: World Health Organisation; 1992.
4. Causes of Death, Australia, 2017: Australian Bureau of Statistics; 2018 [Available from: [http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/3303.0Explanatory%20Notes12017?OpenDocument](http://www.abs.gov.au/AUSSTATS/abs%40.nsf/Lookup/3303.0Explanatory%20Notes12017?OpenDocument).
5. Cancer Incidence and Mortality (ACIM) books, 2014: Australian Institute of Health and Welfare (AIHW). (Available from: https://www.aihw.gov.au/reports/cancer/ cancer-data-in-australia/acim-books).
6. Friesen MC, Demers PA, Spinelli JJ, Eisen EA, Lorenzi MF, Le ND. Chronic and acute effects of coal tar pitch exposure and cardiopulmonary mortality among aluminum smelter workers. Am J Epidemiol. 2010;172(7):790-799.
7. Maltseva A, Serra C, Kogevinas M. Cancer risk among workers of a secondary aluminium smelter. Occup Med (Lond). 2016 Jul;66(5):412-4.
8. Greenhalgh, EM, Scollo, MM, Winstanley, MH. Tobacco in Australia: Facts and issues. Melbourne: Cancer Council Victoria; 2022. Available from [www.TobaccoInAustralia.org.aus](http://www.TobaccoInAustralia.org.aus) (Date last accessed 22/11/22).
9. Rønneberg A, Langmark F. Epidemiologic evidence of cancer in aluminium reduction

plant workers. Am J Ind Med 1992;22:573–90.

1. Andersen A, Dahlberg BE, Magnus K, et al. Risk of cancer in the Norwegian

aluminium industry. Int J Cancer 1982;29:295–8.

1. Spinelli JJ, Band PR, Svirchev LM, et al. Mortality and cancer incidence in aluminium reduction plant workers. J Occup Environ Med 1991;33:1150–5
2. Gibbs G, Armstrong B, Sevigny M. Mortality and cancer experience of Quebec

aluminium reduction plant workers. Part 2: Mortality of three cohorts hired on or

before January 1st, 1950. J Occup Environ Med 2007;49:1105–23.

1. Debia M, Weichenthal S, Tardif R, Dufresne A. Ultrafine particles (UFP) exposures in an aluminium smelter: Soderberg vs prebake potrooms. Environment & Pollution 2012; 1(1). 10.5539/ep.v1n1p2.
2. Liu N, Wang Z, Dong D, et al. Cancer mortality among carbon workers in China: a retrospective cohort study. J Occup Health 1997;39:325-30.
3. Milham S. Mortality in aluminium reduction workers. J Occup Med 1979;21:475-80.
4. Gibbs GW, Sevigny M. Mortality and cancer experience of Quebec aluminium reduction plant workers. Part 3: monitoring the mortality of workers first employed after January 1, 1950. J Occup Environ Med 2007;49:1269-87.
5. Konstanstinov VG, Simakhina PG, Gotlib EV, Kuz’minykh AI. Problem of the carcinogenic hazard in aluminium electrolysis halls. Porfessional ‘nyi Rak. 1974;87-91.
6. Taiwo OA, Slade MD, Cantley LF, Tessier-Sherman B, Galusha D, Kirsche SR, Donoghue AM, Cullen MR. Bladder cancer screening in aluminium smelter workers. J Occup Environ Med. 2015 Apr;57(4):421-7.
7. Australian Institute for Health and Welfare 2022. Suicide and self-harm monitoring. Available from: Deaths by suicide over time - Australian Institute of Health and Welfare (aihw.gov.au) (Date last accessed 22/11/22).
8. Eisen EA, Chen KT, Elser H, Picciotto S, Riddell CA, Combs MA, Dufault SM, Goldman-Mellor S, Cohen J. Suicide, overdose and worker exit in a cohort of Michigan autoworkers. J Epidemiol Community Health. 2020;74:907-912.
9. Krewski D, Yokel RA, Niebour E, Borchelt D, Cohen J, et al. Human health risk assessment for aluminium, aluminium oxide and aluminium hydroxide. J Toxicol Environ Health B Crt Rev 2007; 10(Suppl 1): 1-269.
10. Hosovski E, Mastelica Z, Sunderic D, et al. Mental abilities of workers exposed to aluminium. Med Lav 1990;81:119-23.
11. White DM, Longstreth WT, Rosenstock L et al. Neurologic syndrome in 25 workers from an aluminium smelting plant. Arch Intern Med 1992;152:1443-8.
12. Riihimaki V, Aitio A. Occupational exposures to aluminium and its biomonitoring in perspective. Crit Rev Toxicol 2012;42:827-53.
13. Meng H, Wang S, Guo J, Zhao Y, Zhang S, Zhao Y, et al. Cognitive impairment of workers in a large-scale aluminium factory in China: a cross-sectional study. BMJ Open 2019;9:e027154.