Is foundry work a risk for cardiovascular disease? A systematic review

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Aims

Foundry work has been associated with an increased risk of adverse cardiovascular events. The objective of this review was systematically and qualitatively to review the published literature to determine whether foundry work is significantly associated with cardiac disease.

Methods

MEDLINE and Cochrane databases were systematically searched to identify relevant English-language publications between 1966 and October 2002. Articles were rated as ‘good’, ‘fair’ or ‘poor’, using published quality review criteria. Additionally, variables suggesting causality were extracted. A qualitative summation of the literature was presented for two scenarios: all studies, or using only studies rated ‘fair’ and above.

Results

Fourteen studies were analysed. Four were found to be of ‘fair’ quality, the remainder ‘poor’. No ‘good’ quality studies were found. Nine studies show increased cardiac mortality among foundry worker groups and four studies also show a decreased risk. When only ‘fair’ quality studies are taken into consideration, two support increased risk of cardiac disease, one supports a protective effect of foundry work on cardiac disease and one revealed both increased and decreased risk for different cardiac outcomes.

Conclusions

The exploration of foundry workers’ risks of cardiac events reveals conflicting findings, which can only be partly attributed to confounders. Further prospective research to establish the independent contribution of foundry work to cardiac disease is needed.

Key words

Carbon monoxide; foundry; heart diseases; occupational disease; qualitative review; systematic review.

Introduction

Foundry workers may be exposed to various hazards such as heat, metal dusts, fumes, silica, polycyclic aromatic hydrocarbons (PAH), molten metal and machinery. Increased rates of lung disease, both malignant and non-malignant, have been associated with foundry work for some time [1]. Extremes of temperature have been associated with heart disease, usually in population settings [2]. Increased rates of heart disease have been found among occupations exposed to heat, namely potash miners and fire-fighters [2,3]. The mechanisms by which heat can lead to cardiac stress, usually in patients with underlying heart disease, are multiple [4].

Foundry workers may also be at increased risk of cardiac problems due to their exposure to carbon monoxide (CO). Exposure to CO is common in foundries, and generally occurs near furnaces (particularly in melting) or near idling vehicles [5,6]. There is still no clear consensus as to whether chronic moderate level exposure to CO is toxic to the heart. The biological plausibility for heart disease arising from occupational exposures in foundry workers relates to tissue hypoxia resulting from repeated CO exposure. CO binds with high affinity to
haemoglobin and shifts the oxyhaemoglobin dissociation curve to the left, displacing oxygen, lowering blood oxygen carrying capacity and reducing tissue delivery of oxygen [7], an effect which may be especially important to patients with underlying coronary disease. Carbon monoxide has also been shown to increase platelet adhesion, lower arrhythmia thresholds and, with chronic exposure, accelerate atherogenesis in model experiments [8–11]. More recent physiological experiments, which have taken into account nitric oxide (NO) effects on the cell, have also confirmed the potential oxidative stress caused by CO [12]. Other studies have not found an association between CO exposure and hypertension [13], atherogenesis development [14,15], or cardiovascular mortality [16]. In summary, there is biological plausibility that CO can affect at least people with underlying heart disease and may have a cardiotoxic effect on those with no pre-existing cardiac disease.

No published studies exist that specifically and prospectively examine the effect of CO and heat on development of cardiac disease among foundry workers. Several studies, however, look at the association between foundry work and cardiac disease. ‘Foundry work’ then becomes a surrogate marker for these exposures. In this review, the objective is systematically and qualitatively to review this published literature which addresses heart disease among foundry workers, in order to determine if there is sufficient fair to good quality evidence to establish that foundry work (i) is associated with a significant increase in cardiac disease and (ii) is an independent risk factor for cardiac disease.

Methods

A literature search using the MEDLINE database was carried out to identify relevant English-language publications between 1966 and October 2002, and included the MeSH headings ‘heart diseases’ and ‘occupational disease’ and the text words ‘foundry’, ‘heat’ and ‘carbon monoxide’. Retrieved publications were limited to English language and human studies. Bibliographies of retrieved publications were reviewed to identify sources not obtained in our search. Publications in abstract form were included to minimize publication bias. The Cochrane Library Clinical Trials Database was searched with the headings ‘occupational diseases’, ‘foundry’ and ‘carbon monoxide’. Articles not pertaining to foundry workers and articles without control groups were excluded.

Critical appraisal

Using this evidence, an overall assessment of causality was performed. For studies of cardiac disease among foundry workers, key data elements and quality criteria were summarized, when available, in tabular format. These included the strength of the association between exposure and outcome, the time sequence between exposure and outcome, and the dose–response relationship. In order to test the validity of any statistical association detected, the studies were additionally evaluated for sources of bias and confounding, using established evidence quality ratings [17]. Studies were rated as ‘good’, ‘fair’ or ‘poor’ quality, according to criteria for cohort studies established a priori. These are shown in Appendix 1.

The overall assessment of causality was performed for two groupings of studies: the first included only studies of ‘fair’ or ‘good’ quality; the second included all studies.

Results

Review of published literature concerning foundry workers

Study characteristics

No relevant publications were found in the Cochrane database. On abstract review of references retrieved from MEDLINE, 23 studies appeared eligible and full articles were retrieved. Subsequently, six of these were excluded as they presented data on the same groups reported by the authors in other publications [18–23]. In these cases, the study with the most cardiac information on the whole group was used. Two studies were excluded because of lack of controls [4,24] and one because it did not address cardiac outcomes [25]. As a result, 14 studies were abstracted for causality indicators and quality evaluation [1,5,26–37]. A summary of the studies is presented in Table 1 and their qualitative assessment is presented in detail in Appendix 2.

Association—increased cardiac risk

Three ‘fair’ [30,32,34] and six ‘poor’ [1,5,26,29,33,37] quality studies found an increased risk of cardiac disease among foundry workers for at least some of the outcomes studied. Table 2 reviews the key variables in each of these studies.

The most widely cited on this topic, Koskela et al. [30] have published several papers examining the risk of cardiac disease among foundry workers, representing different analyses of the same patient population. The key study, published in 1994, examined two groups in a mixed retrospective cohort (group 1, n = 2857)/cross-sectional (group 2, n = 931) design. The first ‘umbrella’ group represented a large retrospective cohort with known occupational histories and length of employment. Analysis of outcomes was via death registry and linkage to drug plan, looking at use of medications for heart disease. Group 2 was also a retrospective cohort, included in
three outcomes of hypertension, all cardiovascular disease and coronary artery disease (CAD) mortality in group 2 (rate of each is higher than ‘non-smoking, non-exposed’ and rate of both exposures highest).

Key problems in this study were use of a drug database as a surrogate outcome (may have obtained drugs elsewhere 0–20%) and use of initial smoking survey as record of smoking habits (1973 versus 1992 showed 70% overlap). No other major cardiac risk factors were controlled or corrected for (hypertension, cholesterol, family history of heart disease, diabetes, obesity). The external validity of the study may also be a problem because CO exposures have decreased in Finnish plants over time (94 versus 41 mg/m³ in smelting and casting areas) and are higher than current or past levels in North America.

The second ‘fair’ quality study is by Andjelkovich et al. [32], and studied 8774 male and 627 female foundry workers in a retrospective cohort design. The authors assessed the SMR using vital statistics verified by death certificates and other electronic databases, with a high follow-up rate. Definition of exposure took into account length of work in a foundry area. Smoking, although not assessed directly, was elegantly corrected for in the analysis in three ways.

‘Mortality patterns’ were the primary outcome. The subgroup of non-white males had an increased SMR of 126 (95% CI = 110–143) for the outcome of ‘ischaemic heart disease’. Interestingly, this study supports both increased and decreased cardiac risk among foundry workers (see next section). This study received a ‘fair’ rating because of its attention to detail in data collection and analysis, but cannot be considered ‘good’ quality because of the study design (retrospective), no mention of blinded outcome assessment and the inability to correct for key cardiac disease risk factors.

The third ‘fair’ quality study to find a positive association for CAD was published by Silverstein et al. in 1986 [34]. In a mixed case–control/retrospective design, 278 decedents who had worked in a US foundry were studied for the primary outcomes of mortalities from cardiovascular disease and non-malignant respiratory disease. Exposure was measured by years of employment and general air samples for dust, CO and ‘other contaminants’ (not specified).

The nested case–control study (15 cases/49 controls) found no association with circulatory disease among black males who died over age 60 (11 foundry/4 non-foundry cases, 1 foundry/4 non-foundry controls) with a crude OR of 11.0 (P = 0.06), but confidence intervals were wide due to small numbers (95% CI = 0.9–130). The study also noted a significant increase in non-malignant respiratory disease, suggesting either a contributing role of foundry work to this outcome, or increased rates of smoking as a confounder. The standardized proportional

<table>
<thead>
<tr>
<th>Table 1. Characteristics of 12 studies abstracted</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td>Pure foundry</td>
</tr>
<tr>
<td>Mixed foundry/non-foundry</td>
</tr>
<tr>
<td><strong>Patients studied</strong></td>
</tr>
<tr>
<td>100–999</td>
</tr>
<tr>
<td>1000–10 000</td>
</tr>
<tr>
<td>&gt;10 000</td>
</tr>
<tr>
<td><strong>Foundries in sample</strong></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2–5</td>
</tr>
<tr>
<td>10–20</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Countries</strong></td>
</tr>
<tr>
<td>Canada, Denmark, Finland, New Zealand, Norway, UK, USA</td>
</tr>
</tbody>
</table>

**Exposure levels documented (may have more than one)**
- Individual’s exposure measured: 0
- Direct plant measurement: 5
- Years of exposure calculated: 12
- None: 2

**Outcomes addressed**
- SMR/PMR with ICD codes: 10
- Odds ratios (OR) with ICD codes: 1
- Blood pressure: 2
- Medication for hypertension and cardiovascular deaths: 1

**Outcome ascertainment**
- Death certificate or other vital statistic documents: 12
- Direct patient assessment: 1
- Review of medical records: 1

**Quality assessment**
- Good: 0
- Fair: 4
- Poor: 10

group 1, but for whom baseline assessment health examination which recorded smoking habits was available. Definition of exposure took into account measurement of air and blood samples at site of work (blood samples were not clearly drawn from any of the study patients), length of work in a foundry area and regularity of exposure. Of potential confounders, smoking was corrected for in the second group studied, but not the first group, and PAH levels were measured but heat was not controlled for.

This is the only ‘fair’ quality study to address ‘morbidity and mortality from cardiovascular disease’ as a primary outcome measure. The authors found a rate ratio of 1.8 [95% confidence interval (CI) = 1.25–2.45] for the outcome of ‘all cardiovascular disease’ and 2.0 (95% CI = 1.28–2.92) for the outcome of ‘hypertension’ when they compared workers employed >5 years with regular CO exposure to workers employed <1 year with no CO exposure. Of note, no significant difference in cardiovascular mortality was observed between these groups, with a standardized mortality ratio (SMR) of 90 (no CI available). A Poisson regression also found a multiplicative effect of smoking and CO exposure on all
The mortality ratio (SPMR) was significantly elevated for the outcome of ‘all circulatory diseases’ alone, among black males, at 143 (95% CI = 110–186). This outcome was not increased among white males, SPMR = 92 (95% CI = 81–105). The SPMR for ‘arteriosclerotic heart disease’, although elevated, did not reach statistical significance.

Table 2. Studies finding a statistically significant increased risk of adverse cardiac outcomes among foundry workers

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality rating</th>
<th>Population</th>
<th>Outcome</th>
<th>Strength of association</th>
<th>Timing of exposure to outcome</th>
<th>Dose–response relationship</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andjelkovich et al., 1990 [32]</td>
<td>Fair</td>
<td>931</td>
<td>Rate ratio for 1. CV mortality 2. All CV disease 3. Hypertension</td>
<td>3.4 (1.13–12.11)</td>
<td>Not specified</td>
<td>Significant association of mortality with ‘years since hire’ (P = 0.001)</td>
<td>Indirect adjustment for smoking three ways attempt to correct for this confounder Cardiac disease not a primary outcome. Controlled for job rotation</td>
</tr>
<tr>
<td>Silverstein et al., 1986 [34]</td>
<td>Fair</td>
<td>278</td>
<td>SPMR ‘all circulatory diseases’, ‘black’ men</td>
<td>143 (110–186a)</td>
<td>Not specified</td>
<td>Not specified</td>
<td>Trend toward association between mortality and exposure found for circulatory disease among black males in case–control part of study</td>
</tr>
<tr>
<td>Burns et al., 2002 [37]</td>
<td>Poor</td>
<td>53 782</td>
<td>SMR ‘all heart disease’, foundry cohort Males Females</td>
<td>109 (104–115) 97 (73–110)</td>
<td>Not specified</td>
<td>Not specified</td>
<td>Cardiac disease one of many outcomes</td>
</tr>
<tr>
<td>Park, 2001 [5]</td>
<td>Poor</td>
<td>1113</td>
<td>OR heart disease Skilled trade: foundry Moulding</td>
<td>1.89 (1.19–2.99)</td>
<td>Not specified</td>
<td>Some association seen in non-foundry workers exposed to CO</td>
<td>Multiple sub-group analyses, therefore a few significant results not unexpected</td>
</tr>
<tr>
<td>Firth et al., 1999 [26]</td>
<td>Poor</td>
<td>3522</td>
<td>SMR ‘circulatory diseases’ for total workforce</td>
<td>1.16 (1.07–1.27a)</td>
<td>Not specified</td>
<td>No trends of increased risk with increased exposure</td>
<td>Main hypothesis was to explore relationship of foundry work to lung cancer, not cardiac disease</td>
</tr>
<tr>
<td>Hobbesland et al., 1997 [29]</td>
<td>Poor</td>
<td>14 730</td>
<td>SMR ‘Sudden death’ ‘Hypertension’</td>
<td>1.55 (1.33–1.80a)</td>
<td>No clear trend for length of employment</td>
<td>Significant associations for type of work (certain furnace workers, but not others)</td>
<td>Multiple sub-group analyses, therefore a few significant results not expected</td>
</tr>
<tr>
<td>Sorahan et al., 1994 [1]</td>
<td>Poor</td>
<td>10 438</td>
<td>SMR ‘circulatory diseases’</td>
<td>111 (106–116a)</td>
<td>Addressed, but not for cardiac outcomes</td>
<td>Addressed, but not for cardiac outcomes</td>
<td>Cardiac disease not a primary outcome</td>
</tr>
<tr>
<td>Wojtczak-Jaroszowa, 1987 [33]</td>
<td>Poor</td>
<td>427</td>
<td>Blood pressure among foundry workers (F) compared to glass blowers with (G) and without CO exposure (C) (percentage, by age category)</td>
<td>Age 24–49: F = 26%, G = 24%, P = NS F = 26%, C = 6%, P = 0.005 Age 35–49: F = 15%, G = 52%, P = 0.001 F = 15%, C = 17%, P = NS Age 50–64: no difference</td>
<td>Addressed, but not for cardiac outcomes</td>
<td>Appears to be a cross-sectional study—not applicable</td>
<td></td>
</tr>
</tbody>
</table>

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*aValue in parentheses is 95% CI.

*bNS, not significant.
among black males, at 133 (95% CI = 89–199). Deaths from ‘arteriosclerotic heart disease’ were not significantly increased among white men, although deaths from emphysema were, again suggesting that smoking may be an important confounder among foundry workers.

Silverstein’s study assembled comparable groups, used reliable outcome measures (death registries and death certificates), an adequate observation period and excellent follow-up. Some confounders (prior employment in in coal mine or zinc foundries) and contamination (rotation of jobs) were addressed in data collection. Additionally, the analysis attempted to correct for smoking in the retrospective cohort (76% rate among whites and 52% among blacks) and for smoking and prior occupation in the case–control study. Weaknesses limiting validity of this study are: no apparent blinding to outcome assessment; lack of power from multiple subgroup analyses; and, most importantly, as in the other studies, no corrections are made for potentially significant confounders such as hypertension or other key cardiac risk factors.

The other six ‘poor’ quality studies finding a positive association between foundry workers and cardiac disease were rated to be of insufficient methodological quality to allow assessment for causation [1,5,26,29,33,37]. Details of these studies are outlined in Table 2.

**Association—decreased cardiac risk**

Two ‘fair’ and two ‘poor’ quality studies found a statistically significant decrease in cardiac risk in foundry workers [31,32,35,36]. These are detailed in Table 3.

Rotimi et al. [31] represents the largest ‘fair’ quality study addressing mortality among foundry workers. They examined 21 013 workers in two engine manufacturing plants employed for an average of 10 (women) or 15 (men) years in a retrospective cohort design. Exposures were not well described. The primary outcome measure was the SMR. All point estimates of ‘circulatory disease’ were decreased, but only ‘black men’, at an SMR of 72 (95% CI = 61–86), and ‘all men’, at an SMR of 91 (95% CI = 85–97), reached statistical significance, with 133 and 803 observed deaths, respectively. Indirect correction for smoking suggested a lower rate of smoking in the cohort.

Strengths of this study lie in its careful recording of comparable groups with reliable outcome measures (even including employment records) and adequate observation period. Follow-up was borderline at 87%, with 13% presumed alive because they were not recorded in any registers. This bias would act to decrease apparent SMR and potentially exaggerate the negative findings. To correct for this, the authors re-analysed the data with and without the ‘unknown status’ cohort, without a significant change in findings. Again, this study did not receive a ‘good’ quality rating because of its retrospective design, lack of blinding to outcome assessment and large risk of confounding for other cardiac risk factors.

As mentioned previously, Andjelkovich et al. [32] noted both increased and decreased mortality measures among foundry workers. This retrospective ‘fair’ quality study, described in the previous section, noted that SMRs for ‘circulatory disease’ and ‘ischaemic heart disease’ were significantly reduced among white men, with values of 87 (95% CI = 78–96) and 87 (95% CI = 77–98), respectively. Statistical association in this large study is most likely valid, given the large number of observed deaths and narrow confidence intervals for the outcomes of interest.

The other two studies finding a negative association between foundry workers and cardiac disease were rated to be of insufficient methodological quality to allow assessment for causation [35,36] (Table 3).

**No association between foundry work and cardiac risk**

All the ‘fair’ quality studies found no significant association between foundry work for some of the cardiovascular endpoints used (Table 4). Koskela [30] noticed no change in overall cardiovascular mortality. Andjelkovich et al. [32] found no associations for the outcomes of cerebrovascular disease among white males and no association for circulatory disease or cerebrovascular disease among ‘non-white’ males. Silverstein et al. [34] reported no significant associations for any of the cardiac outcomes for ‘whites’ and no association for ‘all vascular deaths’ for ‘blacks’. Rotimi et al. [31], the last of the ‘fair’ quality studies, did not note a change in the main endpoint ‘circulatory disease’ SMR among the largest group, ‘white’ men, where they observed 803 deaths, with an SMR of 95 (95% CI = 88–101).

Two ‘poor’ quality studies found no association for any of their measured outcomes [27,28] and one ‘poor’ quality study found no association for most of its outcomes [29].

**Discussion**

One of the main putative cardiotoxic agents in foundry work is CO. Biological plausibility for the role of CO in the worsening or development of cardiac disease clearly exists.

Secondly, the validity of the statistical association should be determined: is association due to bias and what are potential sources of bias? Could the association be due to confounding, and what would the sources of confounding be? Other factors that support exposure as being the actual cause of the disease are the strength of association, a compatible time sequence, and evidence of a dose–response relationship. Finally, consistency with other studies would support such an association not being spurious.
Is there a valid statistical association?

The resultant epidemiological exploration of foundry workers’ risks of cardiac events is unfortunately not conclusive. The foundry literature in which cardiac outcomes are addressed as primary or secondary reveals conflicting results. When considered as a whole, nine studies show some increased cardiac mortality among foundry worker groups. Four studies also show a decreased risk. Finally, virtually all studies show no association for at least some of their cardiac outcomes.

When only the best quality studies are taken into consideration, assuming these are more likely to account for confounders, thus yielding ‘truer’ results, the results are again conflicting: three show increased risk for some cardiac outcomes and two show decreased risk for at least some of the cardiac outcomes.

Potential sources of bias

Healthy worker effect

Much of the negative association for outcomes is credited to the healthy worker effect (HWE), which states that, among certain employment groups, healthier people are hired to begin with and only those with continuing good health stay in that employment, creating a bias that masks all but marked increases in mortality. The foundry worker studies reviewed meet certain generic risk criteria for suffering from HWE bias. HWE has been suggested to be likely in cohort studies looking at chronic diseases, such as cardiac disease [3]. In this respect, all but Silverstein’s case–control study are ‘at risk’ of suffering from HWE. Occupations that require stringent hiring of healthy workers also increase the likely bias from HWE. Since foundry work involves physical labour, this may play a role. Using the general population as a comparison group increases the chance of HWE bias: only the studies of Koskela [30] and Silverstein et al. [34] compared one foundry group to another. Length of employment of <1 year and follow-up of <10 years are also said to increase the chances of the HWE. Of the fair quality studies, all had adequate observation periods (>10 years), but one included employees exposed for <1 year (criterion >6 months) [32]. In summary, there are certain features of the foundry work literature that indicate increased HWE. It is still not clear how correction can be made for the HWE. Taking into consideration that the study least likely to be suffering from HWE [30] and another which corrected for HWE statistically [5] show a positive association with cardiac disease and the study most likely to be showing an effect from HWE [32] shows a decreased association of foundry work with cardiac disease, interpretation of the literature shifts slightly towards a valid statistical association of foundry work with cardiac disease.

Potential sources of confounding

Understanding the role of confounders is of key importance in interpretation of the foundry data. For relatively rare lung diseases, which occur almost uniquely from exposures, use of the epidemiological model of SMR as applied to a general workforce is a valid design.
Cardiovascular deaths, of which 75% are related to coronary disease, are the leading cause of mortality in the United States, accounting for about one-third of all deaths in subjects >35 years of age [38]. As a result, this model can only be associative, not conclusive: too many risk factors are well documented to play a role in the development of heart disease and stroke. The studies reviewed in this paper have shown that foundry populations may have rates of smoking which are different from the general population, suggesting the importance of correcting for this confounder [27,34,36]. Additionally, we know nothing of their rates of diabetes, hypercholesterolaemia or hypertension. All of these are significant independent risk predictors and must be considered [39].

Can the valid association be judged as cause and effect?

Most of the positive results presented for either cardiac or ‘cardiovascular disease’ give rate ratios in the range of 1.8–3.4 and SMRs and SPMRs from 107 to 155. This association is significant in several studies, but seldom consistent even within studies for different endpoints. Although there is no absolute cut-off of what constitutes a ‘strong’ association, the association for cardiovascular disease seen in the foundry literature could be considered moderate.

To address whether the time sequence was compatible, we would have to have a sense of time to development of disease from start of employment for the cases. These data are not presented: only average length of employment. In one of the studies, evidence of a dose–response relationship is examined: those employed >5 years and exposed to CO, especially smokers, carried a statistically significant increased cardiac disease risk [30].

Conclusions and future directions

With extensive review and qualitative analysis of published empirical studies looking at the effect of foundry work on cardiac disease, some suggestion of foundry work being a risk factor has emerged. The study least

Table 4. Studies in which one or more cardiac outcomes are not significantly associated with foundry work

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality rating</th>
<th>Population Outcome</th>
<th>Strength of association</th>
<th>Timing of exposure to outcome</th>
<th>Dose–response relationship</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koskela, 1994 [30]</td>
<td>Fair</td>
<td>2857</td>
<td>Rate ratio for 1. CV mortality 2. All CV disease 3. Hypertension</td>
<td>Not significant 1.8 (1.25–2.45) 2.0 (1.28–2.92)</td>
<td>Not specified</td>
<td>Not for mortality data</td>
</tr>
<tr>
<td>Andjelkovich et al., 1990 [32]</td>
<td>Fair</td>
<td>8774</td>
<td>SMR ‘Non-white’ men ‘Circulatory disease’</td>
<td>104 (94–115$^a$)</td>
<td>Not specified</td>
<td>Not addressed since outcome not elevated</td>
</tr>
<tr>
<td>Silverstein et al., 1986 [34]</td>
<td>Fair</td>
<td>278</td>
<td>SMR white males All circulatory diseases ASHD All vascular SMR circulatory disease</td>
<td>92 (81–105$^a$) 96 (81–113$^a$) 68 (36–127$^a$)</td>
<td>Not specified</td>
<td>No association between mortality and exposure found among white males Not specified</td>
</tr>
<tr>
<td>Rotimi et al., 1993 [31]</td>
<td>Fair</td>
<td>21 103</td>
<td>Women White men Blood pressure and headaches</td>
<td>86 (41–158$^a$) 95 (88–101$^a$) Exp BP 121/80, 7% on meds; control BP 123/81, 2% on meds, P = 0.20 95 (85–106$^a$)</td>
<td>Not specified</td>
<td>No dose response between exposure and prevalence of headache, not assessed for BP 60% of foundry workers smoked</td>
</tr>
<tr>
<td>Jarvinen, 1998 [27]</td>
<td>Poor</td>
<td>123</td>
<td>SMR ‘circulatory disease’</td>
<td>Not specified</td>
<td>Not specified</td>
<td></td>
</tr>
</tbody>
</table>

ASHD, atherosclerotic heart disease.

$^a$Value in parentheses is 95% CI.
likely to suffer from bias [30] suggests an increased risk, but is still seriously flawed in that it does not account for other cardiac risk confounders. Additionally, exposures are much reduced currently compared with 30 years ago in the Finnish foundries in question. The populations are also sufficiently different in their cardiac risks [40] to cast serious doubt on the applicability of these results to the North American foundry workers. From this literature, we can conclude that there is a moderate association of foundry work with cardiac disease, but cannot conclude causality at all.

Future research

In light of increasing claims of cardiovascular disease among foundry workers past and present, it is critical to establish whether foundry work independently increases the risk of cardiac disease. Prospective studies of foundry workers are desperately needed, carefully detailing exposures and confounders. These could detect an effect from foundry work as early as 5 years, if surrogate clinical markers such as angina, increased cholesterol or hypertension were examined.

Acknowledgements

The author gratefully acknowledges the support provided by the Ontario Workplace Safety and Insurance Board (WSIB). The opinions expressed in this paper are strictly those of the author and no endorsement by the WSIB of these opinions is suggested or implied.

References

26. Firth HM, Elwood JM, Cox B, Herbison GP. Historical
Appendix 1. Criteria for assigning levels of quality to cohort studies

**Good**

Studies are graded ‘good’ only if all of the following are met:

- Consideration of inception cohorts
- Follow-up at least 80%
- Interventions are spelled out clearly
- All important outcomes are considered, outcome assessment is blinded
- Reliable and valid measurement instruments are used and applied equally to the groups
- Appropriate consideration of potential confounders with either restriction or measurement for adjustment in the analysis

**Fair**

Studies are graded fair if any of the following problems occur, without the fatal flaws listed in the ‘poor’ category:

- Generally comparable groups, or some minor problems with follow-up
- Some but not all important outcomes are considered
- Measurement instruments acceptable, although not ideal and generally applied equally
- Some but not all important confounders are accounted for
- Lack of blinding to outcome assessment

**Poor**

Studies are graded poor if any of the following fatal flaws exist:

- Groups assembled are not comparable, either initially or throughout study
- Unreliable or invalid measurements are used, or are not applied equally
- Key confounders are not addressed or adjusted for
- Inadequate power of study to detect equivalency
## Appendix 2. Summary of quality assessment for cohort studies of adverse cardiac outcomes in foundry workers

<table>
<thead>
<tr>
<th>Author</th>
<th>Quality rating</th>
<th>Comparable groups</th>
<th>Reliable outcome measurement instruments</th>
<th>Adequate observation period</th>
<th>Blinded outcome assessment</th>
<th>Key confounding factors addressed</th>
<th>Analysis corrects for confounders</th>
<th>Sufficient power</th>
<th>Adequate follow-up (&gt;80%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Firth et al., 1999 [26]</td>
<td>Poor</td>
<td>Yes—compared to age- and time-matched population of New Zealand</td>
<td>Yes—vital statistics established by multiple sources; deaths linked to death registry</td>
<td>Yes—1945-1991</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes—86.2%</td>
</tr>
<tr>
<td>Jarvinen, 1998 [27]</td>
<td>Poor</td>
<td>No—similar age otherwise no data about workplace, exposures</td>
<td>Yes—BP measured first and last day of work week</td>
<td>No</td>
<td>Some—blurring of vision, medications, systemic disease, smoking; 59% core makers and 31% referents smoked ($P = 0.003$)</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Not applicable—cross-sectional</td>
</tr>
<tr>
<td>Hansen, 1997 [28]</td>
<td>Poor</td>
<td>Yes—age-matched, ‘skill’ matched, e.g. farm labourers, better than population matching</td>
<td>Yes—death certificate</td>
<td>Yes—22 years</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>$87%$ 22 years study group, $97%$ controls</td>
</tr>
<tr>
<td>Hobbesland et al., 1997 [29]</td>
<td>Poor</td>
<td>Yes—Norwegian male population</td>
<td>Yes—death certificate computer linkage to statistics Norway</td>
<td>No</td>
<td>Yes—288 886 person-years</td>
<td>No—corrected for time of employment, nil else</td>
<td>No</td>
<td>Yes</td>
<td>Yes—96%</td>
</tr>
<tr>
<td>Sorahan et al., 1994 [1]</td>
<td>Poor</td>
<td>No—population control, but excluded 625 of 10 438 workers with ‘Indian, Pakistani, or Arab surnames, with suspiciously low SMR, due to inadequate tracing’</td>
<td>Yes—subjects censored at age 85 or on ‘exit from study; SMR</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes—1946–1990, mean 29.2 years, 94.8% had vital statistics information</td>
</tr>
<tr>
<td>Koskela, 1994 [30]</td>
<td>Fair</td>
<td>Yes—large retrospective cohort</td>
<td>Yes—population data register; medication records by health insurance database</td>
<td>Yes—931 cross-sectional, 653 members of above cohort</td>
<td>No</td>
<td>Some—smoking not corrected for in group 1, but corrected by data from 1993 questionnaire in group 2 (53% smokers, 31% ex-smokers, 16% non-smokers)</td>
<td>Yes—Poisson regression accounting for age, calendar year, factory, employment state, period of follow-up, duration of employment in foundry area, duration in fettling shop, duration in foundry/fettling shop, duration in industry, but not smoking or other cardiac risk factors</td>
<td>Yes</td>
<td>Not applicable given cross-sectional retrospective cohort design</td>
</tr>
<tr>
<td>Author</td>
<td>Quality</td>
<td>Comparable groups</td>
<td>Reliable outcome measurement instruments</td>
<td>Adequate observation period</td>
<td>Blinded outcome assessment</td>
<td>Key confounding factors addressed</td>
<td>Analysis corrects for confounders</td>
<td>Sufficient power</td>
<td>Adequate follow-up (&gt;80%)</td>
</tr>
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<td>------------------------</td>
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<tr>
<td>Rotimi et al., 1993 [31]</td>
<td>Fair</td>
<td>Yes—general US population</td>
<td>Yes—ICD9, death certificate, several computerized sources/complete employment records</td>
<td>Yes—13 years</td>
<td>No</td>
<td>No</td>
<td>Yes—race/gender/age specific mortality/calendar time; indirect correction for smoking suggests lower rate of smoking related deaths (emphysema COPD) in cohort; analysed with and without ‘unknown status’ cohort</td>
<td>No</td>
<td>Yes—87% (13% presumed living, bias is to decrease SMR)</td>
</tr>
</tbody>
</table>
| Andjelkovich et al., 1990 [32] | Fair    | Yes—SMR age, sex, race, year and cause specific, as well as geographical adjustment | Yes—vital statistics from several sources                       | Yes—1950–1984              | No                       | No                               | Yes—indirect adjustment for smoking three ways: (1) Do SMRs with high smoking-specific mortality move together? (2) Dose–response (i.e. length of employment) should not have an effect if smoking-related. (3) Calculated SMRs based on automotive workers’ smoking habits and smoking-attributable risk
| Burns et al., 2002 [37]   | Poor    | Yes—age, sex and geographical adjustment                                             | Yes—vital statistics from several sources                       | Yes—1940–1961 (foundry cohort) | No                       | No                               | No                               | Yes for men, no for women                |
| Park, 2001 [5]            | Poor    | No controls—cause of death unlikely to be exposure-related                          | Yes—ICD9, nosologist-coded death certificate, single computerized source | Yes—19 years                | No                       | No                               | Yes—vital statistics for 85%                  |
| Wojtczak-Jaroszowa, 1987 [33] | Poor    | No—control group glass factory workers (G) and glass workers (G), the latter exposed to heat, not CO, CS or lead | Yes—medical documentation and personal interviews                | No                         | No                       | Yes—matched for age, country of birth, physical workload, number of years worked, smoking status, ETOH, but only surrogate outcomes assessed (not cardiac death) | No               | Not applicable as cross-sectional design |
### Appendix 2. Continued

<table>
<thead>
<tr>
<th>Author</th>
<th>Quality rating</th>
<th>Comparable groups</th>
<th>Reliable outcome measurement instruments</th>
<th>Adequate observation period</th>
<th>Blinded outcome assessment</th>
<th>Key confounding factors addressed</th>
<th>Analysis corrects for confounders</th>
<th>Sufficient power</th>
<th>Adequate follow-up (&gt;80%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silverstein et al., 1986 [34]</td>
<td>Fair</td>
<td>Yes—US death registry corrected for sex, race and year of death</td>
<td>Yes death certificates, certified nosologists</td>
<td>Yes—&gt;10 years</td>
<td>No</td>
<td>Some—prior employment in coal mine or zinc foundry</td>
<td>Some—smoking history recorded (76% white, 52% black); case–control analysis corrected for age at death, smoking, prior occupation</td>
<td>No—a lot of subgroup analysis</td>
<td>Yes—98% of death certificates found</td>
</tr>
<tr>
<td>Decoufle and Wood, 1979 [35]</td>
<td>Poor</td>
<td>Yes—US male population</td>
<td>Yes—death certificates nosologist ICD5–7, also revision of ICD codes may be an issue</td>
<td>Yes—30 years</td>
<td>No*</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Egan et al., 1979 [36]</td>
<td>Poor</td>
<td>Yes—US male population</td>
<td>Yes—death certificates</td>
<td>No—4 years (1971–1975)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes—86%</td>
</tr>
</tbody>
</table>