

Risk of ischemic heart disease following occupational exposure to welding fumes: a systematic review with meta-analysis

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Abstract

Purpose Air pollution has been linked to an increased risk of ischemic heart disease (IHD), but less is known about occupational exposure to welding fumes and the risk of IHD. The objective of this paper was to review the epidemiological evidence on causal links between welding fume exposure and risk of IHD and to investigate whether the risk of IHD depends on specific welding characteristics.

Methods A systematic search in Medline 1979–2013 and EMBASE 1974–2013 identified 18 epidemiological studies with at least one risk estimate of IHD morbidity or mortality among workers exposed to welding fumes. Following an assessment of completeness of reporting, confounding, and bias, each risk estimate was characterized as more or less reliable. Pooled risk estimates were computed across studies by random effect meta-analyses.

Results The weighted relative risk (RR) for IHD following exposure to welding fumes was 1.09 [95 % confidence interval (CI) 1.00, 1.19]. We calculated a RR of 1.39 (95 % CI 0.96, 2.02) among studies using an internal reference group and 1.08 (95 % CI 0.99, 1.18) for studies using an external reference group. An increased risk was observed for acute myocardial infarction $RR = 1.69$ (95 % CI 1.18, 2.42) and other IHDs $RR = 1.06$ (95 % CI 0.98, 1.14). There was too limited evidence to evaluate the risk of IHD related to specific welding characteristics.

Conclusion Several studies indicate that welding is associated with a moderately increased risk of IHD; however,

bias and confounding cannot be ruled out with reasonable confidence.

Keywords Occupational exposure · Welding · Ischemic heart disease · Epidemiology · Welding fumes

Introduction

Worldwide ischemic heart disease (IHD) is the leading cause of death. There has long been broad scientific consensus that air pollution in major urban cities is associated with a modest increased risk of IHD among the elderly and ailing people (Fang et al. 2010). The epidemiological evidence on risk of IHD among welders, which may be exposed to levels of particles and gasses two orders of magnitude higher than urban citizens, has received limited attention in spite of the high occupational prevalence of metal welding that a global level approximates 5 % (World Health Organization and International Agency for Research on Cancer 1990).

The concentration of the welding fumes in ambient air at the workplace depends on the welding material, methods, welding intermittence (duration of welding, h/day), general and local exhaust ventilation, and space. Contamination of the environment can occur quickly in the absence of good ventilation and with welding in confined spaces. The Danish Welding Institute performed more than one thousand full-shift measurements of the particulates in the breathing air among welders in the 1980s and found average exposure to welding fume particulate in the range of 1–6 mg/m³, dependent on welding method (Hansen 1981). Similar exposures were found in a recent German study investigating particulate exposure to welding fumes among 241 welders in 33 worksites during 2007–2009. They found

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median mass concentrations of 2.48 mg/m³ for inhalable and 1.29 mg/m³ for respirable particles (Lehnert et al. 2012).

There exists only one earlier review on the risk of IHD in relation to welding exposure. Sjögren et al. (2006) reviewed in 2006 three Scandinavian studies addressing welding exposure and risk of IHD. However, one of the studies only addressed the risk of IHD stratified by ABO blood groups (Suadicani et al. 2002), and a second one used self-reported information on the outcome after welding exposure (Hilt et al. 1999). Because the majority of studies investigating risk of IHD welders use national mortality rates as reference, the review included only three studies in order to avoid healthy worker selection, as it may underestimate the true risk. To our knowledge, this is the first meta-analysis addressing the risk of IHD in relation to occupational exposure to welding fumes and gasses. The objective of this meta-analysis is to systematically evaluate the scientific evidence on causal links between occupational exposure to welding fumes and the risk of developing IHD, and whether the risk of IHD depends on specific welding characteristics.

Methods

This study is entirely based upon previously published data. We adhere to the international guidelines for reporting of systematic reviews and meta-analyses (Moher et al. 2009). The objective was formulated by the PICOS criteria (PICOS: Population = welders, Intervention = exposure to welding fumes, Comparison group = non-welders or general population, Outcome = ischemic heart disease, Study = cohort studies).

Literature search

We identified and retrieved original epidemiological papers providing estimates of IHD morbidity or mortality in relation to occupational metal welding. Two literature searches addressing morbidity and mortality were conducted. From Medline and EMBASE, we retrieved peer-reviewed English-language publications between January 1966 and April 2013 (EMBASE from 1974) by combining medical subject headings and generic terms for the exposure and outcomes (Fig. 1). For completeness, we also included unspecified cardiovascular disease because in particular older studies do not distinguish between IHD and other types of heart disease. Retrieved publications were limited to human studies. The literature search is presented in Table 1.

Our search in Medline and EMBASE yielded in total 409 hits, when duplicates were excluded. By sifting titles

and abstract, we excluded 283 reviews, case reports, and studies on other exposures and outcomes than those of interest (Fig. 1). The resulting 84 papers were retrieved in full. Sixty-eight of these failed to provide quantitative estimates of risk of cardiovascular morbidity or mortality in relation to occupational welding. In total, we thus identified 16 epidemiological studies for inclusion in this review. Since only three studies were explicitly designed to examine IHD risk in relation to welding, we scrutinized all tables and text to obtain risk estimates of morbidity/mortality that might be “hidden” in studies broadly describing morbidity or mortality in welding populations. Further, bibliographies of retrieved papers were reviewed to identify sources not obtained by the primary literature searches, which resulted in two additional papers. Our final database comprised in total 18 original articles (Tables 3 and 4).

Exposure definition

The exposure of interest is welding exposure regardless of welded material (soft steel, mild steel, or stainless steel), welding processes (electrode welding or gas shielded welding), and welding intermittence.

Outcome definition

The outcome of interest is IHD in terms of AMI and other IHD (ICD-7; 400–468, ICD8; 410–414, ICD9; 410–414, ICD10; I20–I25), but due to a small number of scientific studies investigating the association between welding and IHD ($n = 12$), we included “circulatory disease” and “heart disease” if no explicit IHD diagnosis was provided.

Data extraction

Two of the authors (EM and PK) independently assessed exclusion and inclusion criteria for each paper and extracted information according to a scheme with variables defined a priori. Disagreements were resolved by consensus.

Completeness of reporting

The completeness of reporting of essential study characteristics was evaluated by two of the authors (EM and PK), and for each characteristic, we assessed whether sufficient detail was provided (yes/no). These study characteristics included eight items: population characteristics, study design, sampling procedure, inclusion and exclusion

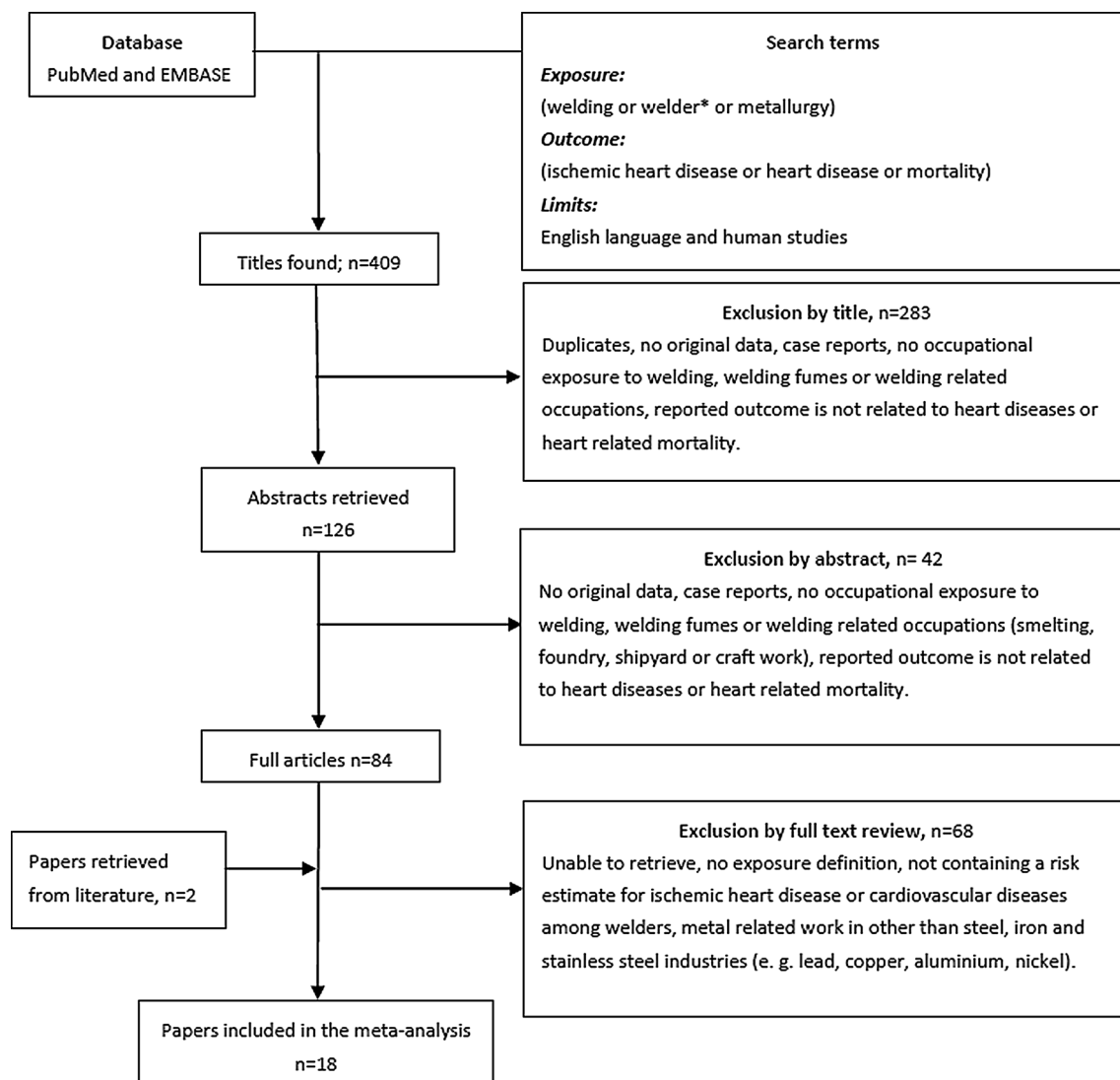


Fig. 1 Flowchart of the literature search. For more detailed search string, see Table 1

criteria, response rate, exposure ascertainment, and outcome ascertainment. Giving each study characteristic an equal weight (one point), we rated the completeness of reporting as adequate if the sum was six or more.

Confounding

If the risk estimates of interest were not adjusted for effects of age, gender, social class and smoking by analysis or design, the estimates were considered potentially biased unless it otherwise was apparent that the distribution of these risk factors was equal across the exposure groups. Information on other known risk factors for IHD such as hypertension, hypercholesterolemia, family history of IHD, obesity and physical inactivity were seldom available, but

social class was considered a useful proxy for these variables (Kaplan and Keil 1993; Marmot et al. 2008; Wilson et al. 1998).

Bias

Different types of bias are likely in observational studies addressing IHD—some causing overestimation of risk (inflationary bias) and other causing bias toward the null (deflationary bias).

The relative risk may be inflated by differential recall of exposure, if data on exposure are not defined by objective criteria and collected retrospectively by self-report after the disease was diagnosed. Specifically, in studies where the span between exposure and data collection is large, this is

Table 1 Systematic literature search 10.04.213**PubMed**

The following search string was used for the search in PubMed:

(((((“Metallurgy”[Mesh]) OR welding AND “Mortality”[Mesh])) OR (“Metallurgy”[Mesh]) OR welding AND “Cardiovascular Diseases”[Mesh])) AND (Humans[Mesh] AND English[lang]))

OR

(((((“Metallurgy”[Mesh]) AND “Mortality”[Mesh] AND (Humans[Mesh] AND English[lang])) OR (“Metallurgy”[Mesh] AND “Cardiovascular Diseases”[Mesh] AND (Humans[Mesh] AND English[lang])) AND (Humans[Mesh] AND English[lang]))

Limits: English language and Human studies

Total hits: 268

EMBASE

The following search string was used in EMBASE:

((metallurgy or weld*) and “heart disease*”)

OR

((metallurgy or weld*) and mortality)

Limits: English language and Human studies

Total hits: 182

When merged together and when duplicates were excluded, the final result of the searches was 409 hits

of concern. Furthermore, recruitment of participants may cause inflated risk estimates if exposed individuals with symptoms or disease are more likely to participate than referents without symptoms/disease. If these two types of bias were present according to the above criteria, the studies were classified as likely biased toward too high estimates.

Bias toward the null can be caused by non-differential misclassification of exposure, which is present if the participating individuals are classified in groups that poorly discriminate exposed from non-exposed or high-level exposed from low-level exposed. In studies using the general population as reference group, deflationary bias is likely due to healthy worker selection, because the general population includes sick and disabled people who are unable to work. If these two latter types of bias are present in the study, the study is classified as likely biased toward null.

Statistical analysis

The main outcome of interest was AMI and other types of IHD fulfilling ICD-7, 8, 9 and 10 criteria. Studies without CIs and broader heart-related diagnoses as outcome, such as cardiovascular diseases and diseases in the circulatory system, were not included in the meta-analyses in order to reduce heterogeneity in the outcome. For this reason, only nine studies were eligible for statistical analysis. To obtain an overall estimate of the risk of IHD in relation to welding, we computed the average risk across studies in random

effects models in which the contribution of each study was weighted by the inverse variance (Borenstein et al. 2009). This meta-analysis was performed using STATA software (metan, metabias and funnel commands) (Sterne 2009).

If a study provided more than one risk estimate, we prioritized the estimates in following order: (1) internal reference group rather than external (2) the most specific diagnosis of heart disease, e.g., AMI and (3) the estimate for any welding rather than a specific welding exposure.

First we computed a common risk estimate across all nine studies explicitly addressing IHD as outcome. Second, we stratified the analysis according to type of reference group (internal or external). The internal reference group was defined as workers working within the same industry in similar jobs, who were not directly exposed to welding fumes. If the reference group is the background population or just matched on age and sex without having similar employment, then it was defined as external. Third, we stratified the analysis on type of IHD, AMI and other IHD. Fourth, to check whether smoking affects the association between exposure to welding fumes and IHD, we stratified the analysis on studies that have controlled for smoking and those that have not. To check for publication bias, we produced funnel plots of the standard error (SE) by the logarithm of the relative risk.

Results**The study base**

We identified 18 follow-up studies that provided risk estimates for IHD (12 studies) or unspecified cardiovascular disease (six studies). The study characteristics are presented in Tables 1, 2 and 3. Two studies addressed IHD morbidity, and 16 were mortality studies. Among the 12 studies that provided risk estimates for IHD, four studies addressed the risk of AMI (Hilt et al. 1999; Hoshuyama et al. 2006; Ibfelt et al. 2010; Sjögren et al. 2002) and one study addressed other exposures (including welding) and IHD (Toren et al. 2007). Seven studies were published in the 2000s, four in the 1990s, six in the 1980s, and one in 1979. The studies have been conducted in about 10 different countries around the world, with the majority in Scandinavia. More than 66,998 persons at risk were included. The outcome of interest was identified mostly through death certificates, hospitalization registries and self-reports. Because the majority of the studies were based on registries, no information was included on lifestyle factors, such as smoking, which is a known determinant for IHD. Fourteen studies had a completeness of reporting score (CRS) ≥ 6 , and four of these were of higher quality (CRS ≥ 6 and no bias nor confounding) (Hilt et al. 1999; Moulin et al. 1993; Sjögren et al. 1987; Toren et al. 2007).

Table 2 Characteristics of the 18 epidemiological studies

	<i>n</i> ^a
Population	
Welders only	16
Mixed job categories	2
Size of the cohort	
100–499	8
500–1,000	2
1,000–10,000	6
>10,000	3
Countries	Denmark, Sweden, Norway, Australia, Europe, USA, France, China, Italy
Outcomes assessed as stated in the papers ^b	
IHD	12
AMI	6
AP	4
Circulatory system	10
Follow-up time (years)	
0–10	2
10–20	3
>20	14
Morbidity/mortality studies	2/16
Intern/extern reference group	9/10

IHD Ischemic heart disease, *AMI* acute myocardial infarction, *AP* angina pectoris

^a The number provided is based on the amount of estimates, cohorts and outcomes included in the studies

^b We provided the outcome of interest as stated in the studies

Risk estimates

Eleven studies reported an increased risk for IHD and CD among workers exposed to welding fumes; however, of these, only six found a significant association (Ibfelt et al. 2010; Hoshuyama et al. 2006; McMillan and Pethybridge 1983; Moulin et al. 1993; Newhouse et al. 1985; Sjögren et al. 2002). The risk estimates among the significant findings spanned from a SMR and PMR of 106 for IHD (Sjögren et al. 2002) and AMI (McMillan and Pethybridge 1983) to a HRR of 2.79 for chronic IHD (Ibfelt et al. 2010). In contrast, Beaumont and Weiss (1980) found a significantly reduced risk for diseases of the circulatory system (SMR = 0.76, $p < 0.001$). Among the two studies concerning morbidity from IHD, Ibfelt et al. (2010) found a significantly increased risk for AMI and CIHD, but Hilt et al. (1999), whose study was one of the four higher quality studies, did not observe the same association. Among the three remaining higher quality studies, two did not find an association between welding exposure and IHD (Sjögren et al. 1987; Toren et al. 2007), while the study by Moulin et al. (1993) found a 66 % increased risk of CD (Tables 2, 3).

Welding material and process

Based on the few studies that assessed the risk of IHD among welders, we are unable to fully evaluate whether the risk of IHD is dependent on specific welding characteristics. However, three studies provide risk estimates for IHD according to the specific type of welding material (mild steel and stainless steel) (Hilt et al. 1999; Moulin et al. 1993), duration of employment and time since first employment (Moulin et al. 1993) and cumulative welding particulate exposure (Ibfelt et al. 2010).

Hilt et al. (1999) found that the risk of AMI did not differ between stainless steel and mild steel welding (total population size = 236). For angina pectoris, the risk among stainless steel welders was slightly increased, but still insignificant (OR 1.6 vs. 1.4 for mild steel). Moulin et al. (1993) found that ever stainless steel welders ($n = 9$) had an increased risk of 71 % (SMR, insignificant). For comparison, part time welders ($n = 5$) and mild steel welders only ($n = 14$) had a risk of 50 % (SMR, insignificant). The same authors found that the risk of IHD was positively associated with the duration of employment with a risk of 79 % ($p < 0.05$, $n = 24$) of IHD among those employed 20 years or more. Time since first employment was also associated with increased risk of IHD, those with a first employment 20 years or more ago had an elevated risk of 84 % ($p < 0.05$, $n = 23$) (Moulin et al. 1993). Only one study addressed dose–response relationship and found that the risk of AMI and chronic IHD increased with increasing exposure going from hazard rate ratio (HHR) = 1 at cumulative particulate exposure level 0–10 mg/m³ to HRR = 1.43 at exposure level of 50–100 mg/m³ ($n = 96$). For exposure level >100 mg/m³, the risk decreased to HRR = 1.03, which can be explained by selection bias: the healthiest stay and the sick leave (Ibfelt et al. 2010). The same pattern is observed for chronic IHD; however, the risk was significant (95 % CI 1.29, 6.04), going up to a HHR of 2.79 at exposure of 50–100 mg/m³ ($n = 83$) (Ibfelt et al. 2010).

Meta-analysis

We included nine studies with sufficiently homogeneous exposure and outcome information in a meta-analysis. Reasons for not being included in the meta-analysis were missing information on CIs (Beaumont and Weiss 1980; McMillan and Pethybridge 1983; Puntoni et al. 1979, 2001; Sjögren 1980; Stern et al. 1997), unspecified cardiovascular disease (Merlo et al. 1989; Simonato et al. 1991) and exposure only to stainless steel welding fumes (Sjögren et al. 1987). These nine studies included a total of 49,864 welders and persons with welding-related work. The majority of the studies included in the analyses were mortality studies,

Table 3 Risk of ischemic heart disease among welders and metal workers exposed to welding fumes (1983–2010)

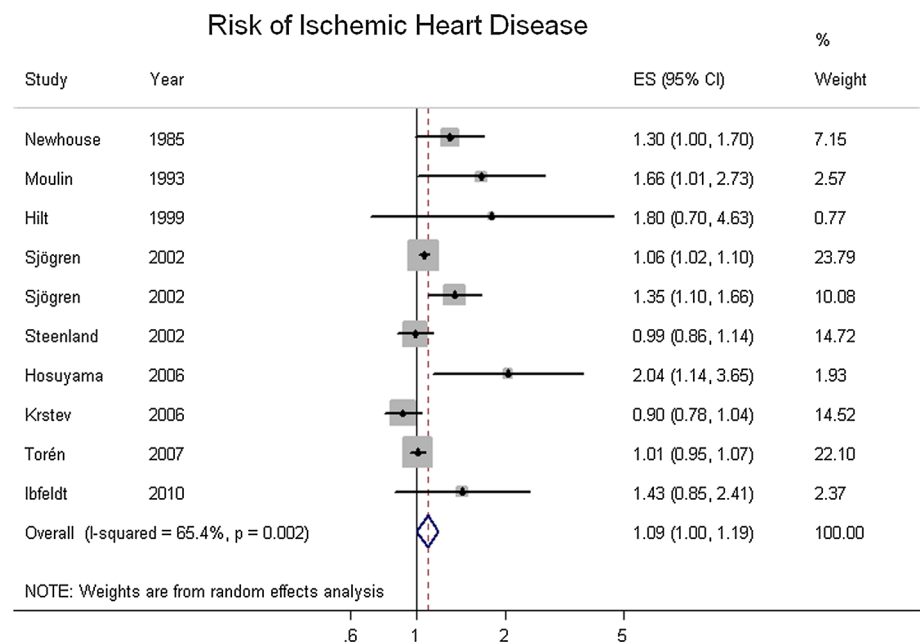
Study	Population	Follow-up (years) and population at risk (<i>n</i>)	Exposure contrast	Outcome	Risk estimate (95 % CI)	Potential			Comments
						Bias	Confounding	Score for complete reporting	
Ibfelt et al. (2010)	Welders	(1986–2006) 5,866	External: Exposure divided into categories (0–10, 10–50, 50–100 and >100 mg/m ³ × years) vs general population internal: the highest exposure group versus the lowest exposure group	ICD-8 and ICD-10 AMI (410, I21) AP (413, I20) CIHD (412, I25)	External, SIR, AMI = 1.12 (1.01, 1.24) AP = 1.11, (1.01, 1.22) CIHD = 1.17 (1.05, 1.31) Internal, HRR, AMI = 1.43 (0.85, 2.41) AP = 1.41 (0.84, 2.36) CIHD = 2.79 (1.29, 6.04)	Yes in the external analyses, leading the estimates toward one. No in the internal analyses.	Yes	8	In the internal analyses, the estimates presented here are from the 50–100 mg/m ³ × years group, because the estimate from the highest group, > 100 mg/m ³ × years could be biased by HWE, since all the estimates were lower than in the 50–100 group. An analysis where the welders who welded before 1960 were excluded showed higher estimates, which possibly reflects the HWE
Sjögren et al. (2002)	Welders	(1970–1995) 31,722 (1990–1995) 28,068	Welders versus gainfully employed men	Mortality by IHD (ICD-7 and ICD-8; 410–414)	SMR, cohort 1970–1995 1.06 (1.02, 1.11) Cohort 1990–1995 1.35 (1.10, 1.64)	No	Yes	5	
Toren et al. (2007)	Construction workers	(1971–2001) mortality cases 831	Metal fumes versus non-exposed	Mortality by IHD (ICD-9 and ICD-10; 410–412 and I21–I25)	RR, 1.01 (0.95, 1.08)	No	No	7	

Table 3 continued

Study	Population	Follow-up (years) and population at risk (<i>n</i>)	Exposure contrast	Outcome	Risk estimate (95 % CI)	Potential		Confounding	Score for complete reporting	Comments
						Bias	Confounding			
Hilt et al. (1999)	Welders	(1960–1993) 236	Any or stainless steel welding versus non-welders from the general population	AMI AP (self-reported, checked health information with general practitioner)	OR, any welding: AMI = 1.8 (0.7, 4.4) AP = 1.4 (0.5, 4.2) OR, Stainless steel welding: AMI = 1.8 (0.7, 4.7) AP = 1.6 (0.5, 5.0)	No for AMI. Yes for AP (misclassification)	No		8	Both the dependent and independent variable was self-reported. The sensitivity for AP was 22 % in the study group and 29 % in the control group
McMillan et al. (1983)	Welders	(1955–1976) 131	Welders versus boilermakers, shipwrights, electrical fitters, painters and joiners	Mortality by AMI (ICD-9; unspecified)	PMR, 106 ($\chi^2 = 0.02$)	No	Yes		5	Very short method section. Not much information. There were two control groups and the PMR was calculated from the three groups
Sjögren et al. (1987)	Stainless steel welders	(1950–1984) 234 and 208	High exposed versus low exposed stainless steel welders	Mortality by IHD (ICD-8; 410–414)	RR, 0.86 (0.39, 1.87)	No	No		8	Provides data only on stainless steel welding
Krstev et al. (2007)	Shipyard workers (shipfitters, welders and cutters)	(1950–2001) 184	Shipfitters, welders and cutters versus general population	Mortality by arteriosclerotic heart disease (ICD-9; 410–414, 429.2)	SMR, 0.90 (0.78, 1.03)	Yes, leading the estimate toward one	Yes		7	The exposed group consisted of several job categories; therefore, the result does not clarify the risk for heart disease among welders only
Stern et al. (1997)	Welders	(1984–1991) mortality cases 752	Welders versus general population	Mortality by IHD (ICD-9; 410–414)	PMR, 0.91 (NS)	Yes, leading the estimate toward one	Yes		7	Females and non-white men were included. The CIs were not presented in the tables with the estimates

Table 3 continued

Study	Population	Follow-up (years) and population at risk (<i>n</i>)	Exposure contrast	Outcome	Risk estimate (95 % CI)	Potential		Score for complete reporting	Comments
						Bias	Confounding		
Steenland (2002)	Mild steel welders	(1950–1998) 4,459	Welders versus general population	Mortality by IHD (ICD-9; 410–414)	SMR, 0.99 (0.86, 1.14)	Yes, leading the estimate toward one	Yes	5	This study is an update on an earlier study about lung cancer. The method section is very short and the author refers to the earlier study which we were not able to retrieve in full
Newhouse et al. (1985)	Welders	(1940–1982) 1,027	Welders versus general population	Mortality by IHD (ICD-8; 410–414)	SMR, 130 (104, 156)	Yes, leading the estimate toward one	Yes	7	
Moulin et al. (1993)	Welders	(1975–1989) 2,721	Welders versus other manual workers at the same factories	Mortality by IHD (ICD-8; 410–414)	RR, 1.66 (1.01, 2.68)	No	No	8	
Hoshuyama et al. (2006)	Welders	(1980–1993) 2,818	Welders versus non-exposed blue-collar workers	Mortality by AMI and IHD (ICD-9; 410 and 411–412)	SRR, AMI = 204 (114, 363) IHD = 95 (86, 103)	No	Yes	7	

Fig. 2 Forest plot of the relative risk of ischemic heart disease based on ten populations

with only two addressing morbidity from IHD and AMI (Hilt et al. 1999; Ibfeldt et al. 2010).

In our random effect meta-analysis, we found an overall borderline significant increased risk of IHD of 9 % (95 % CI 1.00, 1.19) (Fig. 2). The analysis was based on 10 risk estimates from nine studies. The study by Sjögren from 2002 provided two estimates, because it included two cohorts (Sjögren et al. 2002). In the stratified analysis by smoking, we observed an increased but insignificant risk of 14 % (95 % CI 0.86, 1.53) among studies with adjustment for smoking (Fig. 3).

We also stratified our analyses according to the use of an internal or external comparison group. Three studies have used an internal reference group, five have used an external reference group, and one study used both an internal and external reference groups. Typically, the external comparison groups were based on the general population rate of IHD. The risk estimate for the internal reference analysis was based on four studies, and for the external reference analysis was based on six studies, again where Sjögren from 2002 provides two risk estimates. Because the study by Ibfeldt et al. (2010) provides an estimate for both the internal and external analysis, it is included in both analyses. In the analysis of the studies using internal reference groups, we found an RR of 1.39 (95 % CI 0.96, 2.02). The RR was 1.08 (95 % CI 0.99, 1.18) for the external reference analysis (Fig. 4).

In the analyses of the specific outcome, we estimated an increased significant risk of 69 % (95 % CI 1.18, 2.42) of AMI (based on three studies), but found no association with other IHD (RR = 6 %; 95 % CI 0.98, 1.14, based on nine studies) (Fig. 5).

In the analysis of possible publication bias, we found that there was no small study effect ($p = 0.09$) (Fig. 6).

Discussion

Through the systematic literature search, we identified 18 epidemiological cohort studies that addressed the risk for heart disease among welders. Only two studies examined the risk of incident IHD (Hilt et al. 1999; Ibfeldt et al. 2010), and therefore, we chose to include mortality studies even though mortality is a less sensitive measure of IHD, because of the large and increasing survival rate for acute as well as chronic IHD morbidity (Unal et al. 2009). However, only nine studies were eligible for formal meta-analysis.

The epidemiological evidence of welders' risk for IHD seems contradictory. Eleven of the 18 studies reported an increased risk spanning a SMR of 104 for cardiovascular diseases (Merlo et al. 1989) and HRR of 2.79 for chronic IHD (Ibfeldt et al. 2010). Six of these studies reported a significantly increased risk (Hoshuyama et al. 2006; Ibfeldt et al. 2010; McMillan and Pethybridge 1983; Moulin et al. 1993; Newhouse et al. 1985; Sjögren et al. 2002), while one other study reported a significantly reduced risk (Beaumont and Weiss 1980).

The overall meta-analysis indicated a small borderline significant risk of IHD among the welders. Stratifying the analysis on studies who have controlled for smoking and those who have not, we found an insignificant but still increased risk of IHD. The findings indicate that smoking does not play a significant role as a confounder among these study populations (Table 4).

Fig. 3 Forest plot of the relative risk of IHD stratified by adjustment for smoking

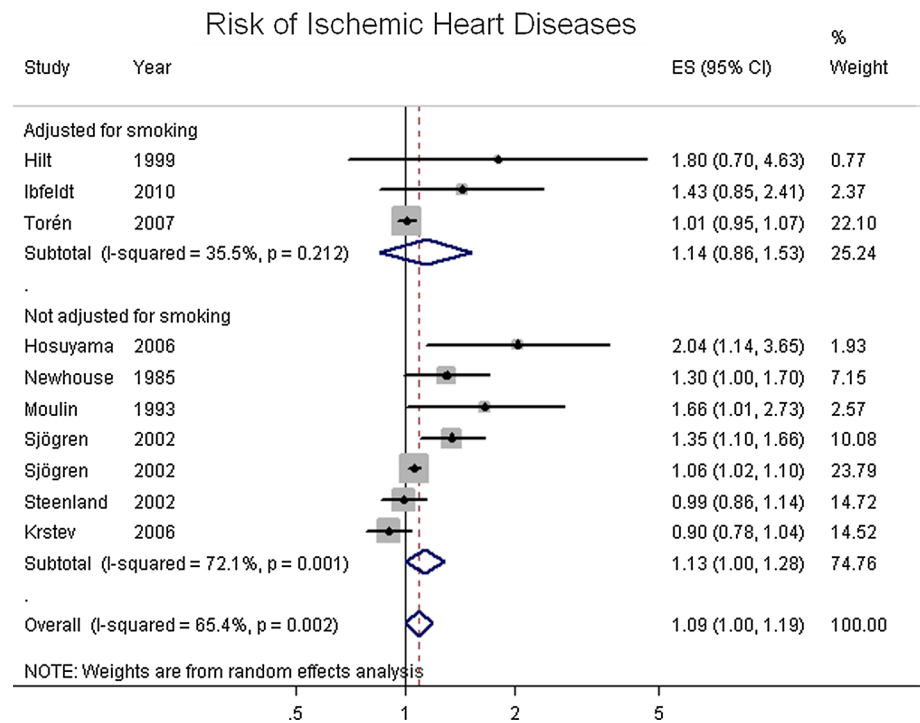
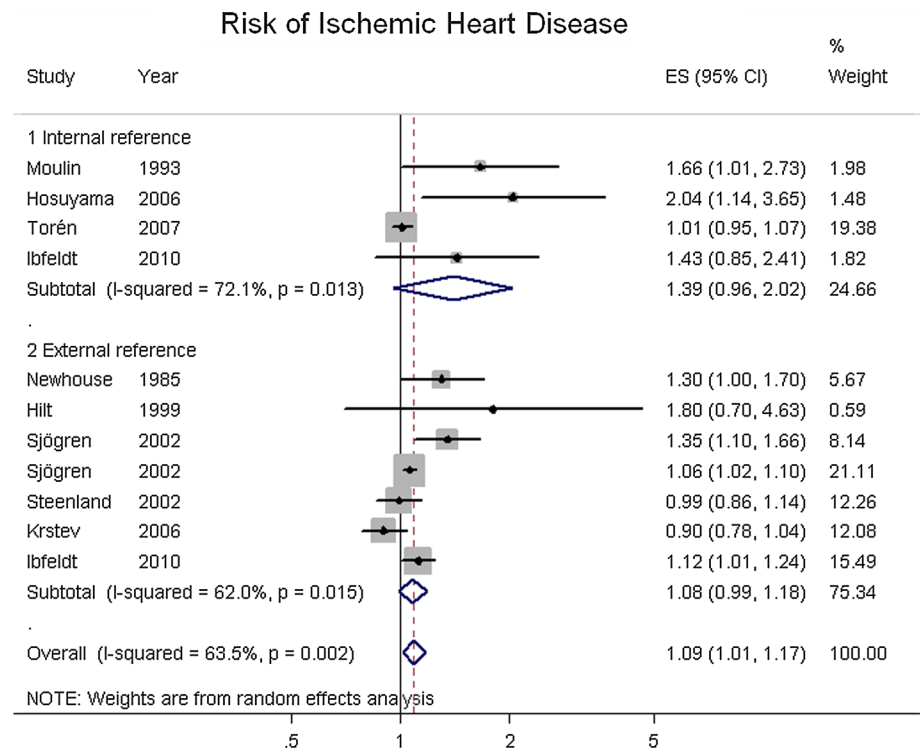
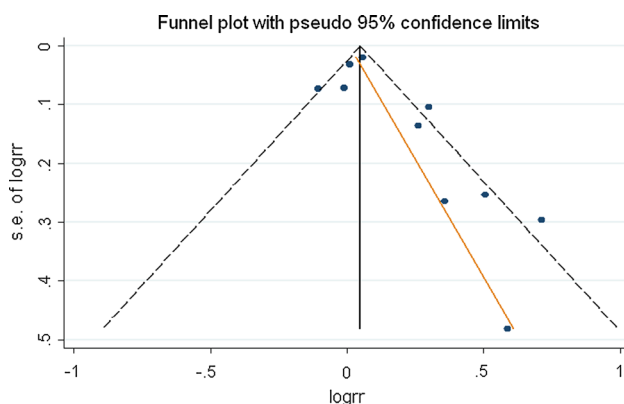
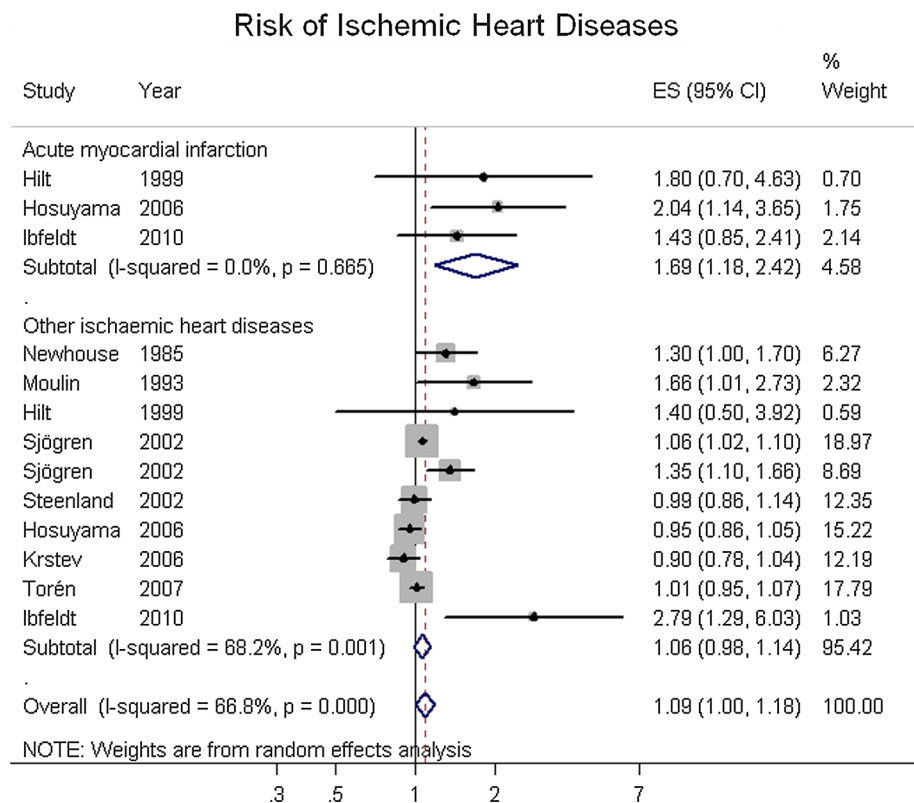


Fig. 4 Forest plot of the relative risk of ischemic heart disease stratified by reference group



When we stratified the analysis by reference group, risk estimates based on internal analyses were higher than risk estimates based upon external reference groups, most often the general population. Assuming that welding is indeed related to increased risk of IHD, an obvious explanation for these divergent results is bias toward null in mortality

studies with background population as reference because of the well-known selection of healthy workers into the population of employed (McMichael 1976). When death rates of welders are compared with national death rates, underestimation of the true risk is expected as the total population includes sick and disabled people that are unable to work.

Fig. 5 Forest plot of the relative risk of acute myocardial infarction and other ischemic heart diseases**Fig. 6** Funnel plot of SE and relative risk as a function of log (relative risk) in nine studies with 10 risk estimates

All except one study that indicate a negative association of welding and IHD have used national mortality rates as reference, and therefore, a truly elevated risk may be underestimated and even reversed.

By dividing the outcome into AMI and other IHD, we found the risk of AMI significantly increased by some 70 %, but no increased risk for other IHD. Again, if welding is related to IHD, this result may reflect that two of the three studies that explicitly address AMI are incidence studies of morbidity, which are more sensitive than

mortality studies where the outcome represents a mix of etiologic and prognostic factors, or that AMI is less prone to misclassification than other IHD that may include a more heterogeneous group of diseases.

In addition to inappropriate reference groups, use of mortality rates rather than disease incidence rates and outcome misclassification—which all would tend to leave a truly elevated risk undetected—the available data have several other limitations, which preclude strong conclusions as the causal relations between welding exposure and risk of IHD. First, considering heterogeneity with respect to exposures and outcomes across studies, the number of studies are few and do not allow for detailed analysis of exposure–response, timing between exposure and outcome or susceptible subgroups. Second, potential confounding factors are not adequately dealt with in the majority of studies. For instance, only five studies adjusted for tobacco smoking (Hilt et al. 1999; Ibfeldt et al. 2010; Moulin et al. 1993; Sjögren et al. 1987; Toren et al. 2007)—a strong determinant if IHD in all age groups. A Norwegian study found that a slightly higher number of welders were more prone to smoke and smoked more than occupationally active men from the general population (Hilt et al. 1999). Also, a Swedish study found that 29 % were smokers in the general population compared with 42 % among the welders (Sjögren et al. 2002). By lack of control for smoking in the analyses or by study design, the risk of IHD may be

Table 4 Risk of unspecified heart disease among welders and metal workers exposed to welding fumes (1979–2001)

Study	Population	Follow-up (years) and population at risk, n	Exposure contrast	Outcome	Risk estimate (95 % CI)	Potential			Score for complete reporting	Comments
						Bias	Confounding			
Simonato et al. (1991)	Welders	(14.8 person-years/person) 11,092	Welders versus general population	Mortality due to circulatory system (ICD-8; 390–458)	SMR, 94 (86, 103)	Yes, leading the estimates toward one	Yes		7	
Puntoni et al. (2001)	Electric arc welders and gas welders	(1960–1996) 267 and 228	Electric arc or gas welders versus general population	Mortality by Cardiovascular disease (ICD-9; 390–459)	SMR, electric arc = 91 (n.a) Gas = 122 (n.a)	Yes, leading the estimates toward one	Yes		7	No CIs were presented for the analysis of job titles. The results were insignificant
Sjögren (1980)	Stainless steel welders	(1950–1978) 234	Stainless steel welders versus general population	Mortality by cardiovascular disease (Unspecified source)	Ratio (observed/expected), 1.2 (n.a)	Yes, leading the estimate toward one	Yes		7	Only a ratio is calculated and no CI
Puntoni et al. (1979)	Autogenous welders and electrical arc welders	(1960–1975) 136 and 78	Autogenous or electric arc welders versus hospital staff	Mortality by cardiovascular disease (unspecified source)	RR, Autogenous: 1.19 (NS) Electrical: 0.91 (NS)	No	Yes		5	
Beaumont et al. (1980)	Welders	(1950–1977) 3,247	Welders versus general population	Mortality by diseases of the circulatory system (ICD-7; 400–468)	SMR, 0.76 ($p < 0.001$)	Yes, leading the estimate toward one	Yes		7	The authors state that the welders were relatively young, and this could explain the decreased risk
Merlo et al. (1989)	Oxyacetylene and electric arc welders	(1960–1982) 274 and 253	Oxyacetylene or electric arc welders versus general population	Mortality by cardiovascular diseases (ICD-8; 390–458.9)	SMR, All welders: 104 (78, 135) Oxyacetylene: 124 (89, 168) Electric arc: 72 (40, 119)	Yes, leading the estimates toward one	Yes		7	

overestimated and results among the studies that did adjust for smoking are conflicting. Third, the small magnitude of risk elevation observed in the meta-analysis raises in itself concern for biased results. Fourth, few studies were specifically designed to examine the association between welding and IHD (Hilt et al. 1999; Ibfelt et al. 2010; Sjögren et al. 2002). Although this may be seen as a strength because publication bias may be less likely, the lack of stringent designs addressing the welding-IHD association results in crude exposure assessment and analyses with higher risk of falsely negative results.

Conclusion

There is a strong heterogeneity in estimates of risk for IHD according to occupational metal welding across a limited number of observational studies. Although some large higher quality studies indicate a slightly increased risk, these findings are not corroborated by other studies. Overall, available data are too limited to draw reliable conclusions as to possible risk of IHD in relation to metal welding and whether the risk is dependent on the specific welding characteristics.

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Conflict of interest The authors declare that they have no conflict of interest.

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