G Ital Med Lav Erg 2022; 44:1, 51-58
ISSN 1592-7830

MEDICINA DEL LAVORO

*Federico Fassio[1], *Martino Bussa[1], Enrico Oddone[2], Ottavia Eleonora Ferraro[1], Mariangela Valentina Puci[1], Anna Morandi[1], Fabio Castaldo[3], Massimo Broi[3], Filippo Uberti[3], Simona Villani[1], Cristina Montomoli[1], Maria Cristina Monti[1]

Health status of petrochemical workers: a narrative review

[1] Unit of Biostatistics and Clinical Epidemiology, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Pavia, Italy
[2] Unit of Occupational Medicine "Salvatore Maugeri", Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Pavia, Italy
[3] Eni S.p.A.
* the authors equally contributed to the work

ABSTRACT. Professional exposure to benzene has been extensively investigated by occupational medicine, leading to strict regulation of exposure threshold values. However, the petrochemical industry utilizes many chemical substances, whose exposure, without effective control and mitigation actions, could influence the health status over time.
The aim of this narrative review is to describe health status of petrochemical workers related to occupational exposures, inquiring literature from 1980 to present. We used the PubMed and Web of Science search engines. As regards non-neoplastic diseases, despite heterogeneous prevalence estimates, we could say that standardized mortality rate (SMR) for hypertension, hypercholesterolemia and diabetes does not increase overall, compared to reference populations; a possible explanation may be the "healthy worker effect". Attention should be paid to color disperception and respiratory symptoms, due to toxic or irritating substances exposure. Studies concerning neoplastic pathology have mainly investigated mortality outcomes, finding no increase in cancer, except for melanoma or other skin cancers and leukemia. As regards the former, however, it is not excluded that other risk factors may contribute (e.g. UV rays in offshore workers), while for leukemia, only the most recent studies have analyzed various subtypes of hematopoietic tumors, highlighting a possible risk for the development of myelodysplastic syndrome. The risk of pleural mesothelioma was also increased, likely due to asbestos exposures, while the risk of death from prostate cancer remains controversial.

Key words: *refinery, health, workers, petrochemical, respiratory, visual, auditory, neoplastic, non-neoplastic.*

RIASSUNTO. STATO DI SALUTE DEI LAVORATORI DEL SETTORE PETROLCHIMICO: UNA REVISIONE NARRATIVA. L'esposizione professionale al benzene è stata ampiamente studiata nell'ambito della medicina occupazionale, portando a una rigida regolamentazione dei valori soglia di esposizione. Tuttavia, l'industria petrolchimica impiega molte sostanze chimiche, la cui esposizione, in assenza di misure di controllo efficaci, può influenzare lo stato di salute. Lo scopo di questa revisione narrativa è descrivere lo stato di salute dei lavoratori del settore petrolchimico relativamente alla loro esposizione professionale, revisionando la letteratura dal 1980 ad oggi. Abbiamo utilizzato i motori di ricerca PubMed e Web of Science. Per quanto riguarda le malattie non neoplastiche, nonostante eterogenee stime di prevalenza, si può affermare che il tasso di mortalità standardizzato per ipertensione, ipercolesterolemia e diabete non appare complessivamente aumentato rispetto alle popolazioni di riferimento; una possibile spiegazione potrebbe essere legata all'effetto "lavoratore sano". Occorre prestare particolare attenzione all'alterata percezione dei colori e ai sintomi respiratori dovuti

Introduction

Exposures to petroleum derived chemicals have steadily decreased over the years, since the half of last century, even due to regulations of occupational exposure levels to benzene and other air pollutants introduced over the decades (1-3). Data on benzene toxicity has guided to an increasingly active monitoring of exposure levels, environmental remediation and using personal protective equipment. This led to a decrease in pathologies strictly related to the inhalation of high doses of benzene and opening the research towards the impact that lower doses of this compound could have on health. Moreover, risk factors related to a sedentary lifestyle or shift work are always present in some job categories within petrochemical industry. All these issues reflect in difficult investigations, being mostly conducted on company health surveillance databases, often not containing exhausting medical information. Furthermore, information on the workers' disease state are often difficult to be linked to environmental sampling data, therefore leading to exposure levels estimated on self-reported work history. On the other hand, most epidemiological studies on workers in the oil processing industry have been conducted to address the problem of the carcinogenicity. The aim of this narrative review is to give a general overview on health status of petrochemical workers, exposed to several carcinogenic substances, to possibly provide an orientation on further studies for monitoring workers' health status within oil refining plants.

Methods

The narrative review was conducted searching the PubMed and Web of Science databases to identify studies addressing the health of petrochemical workers, published in peer-reviewed journals. Search strings were based on the topic of interest and included keywords such as: health, refinery, work or worker, petroleum or petrochemical, oil, cardiovascular, respiratory, mortality, surveillance; all the words have been combined in various ways (see Supplementary Material). The time period considered ranged from 1980 to 2021. Specific references cited by the articles, found through the listed research methods, were also con-

all'esposizione a sostanze tossiche o irritanti. Gli studi relativi alla patologia neoplastica hanno principalmente indagato gli esiti di mortalità, non trovando alcun aumento del rischio, ad eccezione del melanoma o di altri tumori della pelle e della leucemia. Per i primi, tuttavia, non è escluso che possano contribuire altri fattori di rischio (es. raggi UV nei lavoratori delle piattaforme petrolifere), mentre per le leucemie solo gli studi più recenti hanno approfondito le analisi relativamente ai diversi sottotipi di tumori ematopoietici, evidenziando un possibile rischio per lo sviluppo di mielodisplasia. Risulta aumentato anche il rischio di mesotelioma pleurico, verosimilmente legato all'esposizione all'amianto, mentre resta controverso il rischio di morte per cancro alla prostata.

Parole chiave: raffineria, salute, lavoratori, petrolchimico, respiratorio, visivo, uditivo, neoplastica, non-neoplastica.

sidered. We excluded articles covering the following topics: petrol pump workers, psychological status of workers and the Work Ability Index, other materials refineries (e.g. copper, nickel, aluminum) and health status of people living near petrochemical plants. Research ended on 31/12/2021.

Results

We found 933 results through the search strings. After a selection based on title and abstract content, we have identified 42 relevant primary studies or meta-analysis. Main findings are reported below.

NON-NEOPLASTIC PATHOLOGIES

Data coming from a large health surveillance project at 14 Shell refineries (4) reveal that, among 12,089 male employees, the five most common disease categories (72% of all absences lasting over 5 days) were: wounds/injuries (24.8%), respiratory diseases (16.7%), skeletal disorders (14.1%), digestive system diseases (9.1%) and hearth diseases (6.8%). As regards female workers (2,081), genitourinary diseases (9.9%) replaced hearth diseases (2.7%) in the top five categories. Workers in the production subgroup showed higher sickness rates than workers belonging to administrative and staff personnel. In general, the probability of an illness/absence was higher in subjects who had previously experienced long-term absences, in older workers, smokers and employees with health risk factors (high blood pressure, hypercholesterolemia and obesity). In 8 years of surveillance, 535,487 work days were lost due to illness events lasting over five days.

A ten-years retrospective study on 439 male workers of an Italian (5) refinery showed an increase in BMI values over the years (2000: 26.5 kg/m^2, 95%CI: 26.2-26.8 kg/m^2 – 2010: 27.4 kg/m^2, 95%CI: 27-27.7 kg/m^2), in particular for obesity (BMI≥30; 2000: 11% – 2010: 19%), while the number of subjects with hypercholesterolemia has slightly decreased over the years (2000: 30% – 2010: 23%), even though subjects with borderline levels (200-239 mg/dL) increased (2000: 31% – 2010: 39%). Unlike what observed in this study, the prevalence of hypertension in workers of a Brazilian refinery (6) increased between 2008 (27.2%) and 2017 (35.2%) (the prevalence of diabetes also underwent a growth trend, albeit not statistically significant: from 5.3% to 6.4%), while a decrease in prevalence of high cholesterol (14.7% to 11.6%) and cigarette smoking habits (8.4% to 3.8%) occurred. Specifically, shift workers showed a greater risk of hypertension (OR=1.33; 95%CI: 1.23-1.43) and high LDL cholesterol levels (OR=1.06; 95%CI: 0.99-1.14) than workers with fixed hours; the latter, on the other hand, showed a greater risk of prevalence as regards diabetes, cigarette smoking and arterial risk factors. In another analysis, shift petrochemical workers seem to have indeed an increased risk of metabolic syndrome (according to NCEP-ATPIII definition; OR=2.38; 95%CI: 1.13-4.98) compared to day workers, with higher levels of triglycerides and lower levels of HDL-C; however, no significant difference emerged in terms of BMI, blood pressure and total cholesterol (7). In an Iranian investigation, carried out on eight petrochemical plants, the multivariable regression model returned an increased risk of gastrointestinal disorder in shift workers (OR=1.52; 95%CI: 1.20-1.93) while no association emerged for cardiovascular health problems at the univariate analysis (8).

In another survey, benzene exposed workers showed an higher prevalence of hypertension compared to age/sex-matched unexposed group (30.5%; OR=2.44; 95%CI: 1.24-4.85); this observations was similar for the group exposed both to xylene and benzene (27.9%; OR=2.00; 95%CI: 1.11-3.61) (9). The prevalence of hypertension and its relation to noise exposure were investigated in a group of Brazilian refinery workers: 430/1729 subjects were found to be hypertensive (PAS≥140 mmHg of PAD≥90 mmHg), of which 12.7% were already under treatment. There seemed to be an association between hypertension and noise exposure: using the ≤75dB exposure as reference category, the risk of hypertension significantly increased in accordance with noise level ($OR_{75\text{-}85dB}$=1.56; 95%CI: 1.13-2.17 – $OR_{\geq 85dB}$=1.58; 95%CI: 1.10-2.26).

In an Italian cross-sectional study (10), conducted on 1,073 male workers, it was noted that the percentage of obese (BMI≥30) men over 53 years was higher than the national male estimates (27.5% *vs* 15.5%) and the condition of overweight or obesity affected more than half of the sample (62.4%). Just over a third of subjects (35.5%) had a condition of hypertension (which increased over 50% in the >53 years aged group) as well as high levels of triglycerides (29.7%), or cholesterol levels (24.3%); however, these data were in line with those of the general population.

A study conducted in Saudi Arabia (11) has for the first time investigated the potential association between prediabetes or type 2 diabetes with some occupational categories. It was found that the prevalence of prediabetes (HbA1c: 5.7-6.4%) in refinery workers (n=217) was 36.86%, while that of type 2 diabetes (HbA1c> 6.4%) was 16.12%; HbA1c levels were significantly higher in the exposed group compared to controls. It would seem that exposure to air pollutants can contribute to some degree of inflammation and also to oxidative stress, which is involved in one of the mechanisms of insulin resistance development. However, lower prevalence of diabetes (glu-

cose>126 mg/dL) were observed in other studies, ranging from 2% to 10% depending on the years (5,6,10).

Respiratory system

Petrochemical derivatives are a complex mixture of aromatic hydrocarbons with high volatility and can reach the deepest parts of the lungs, potentially resulting in an alteration of properties and concentration of the surfactant in the respiratory tree and contributing to the closure of small airways. What emerged in a refinery in Saudi Arabia (12) would seem to support this consideration with significantly reduced values of FEV_1 (Forced Expiratory Volume in the 1st second; Exposed: 3.08±0.16 L/s – Control: 3.99±0.14 L/s), Tiffeneau index (67.19±3.15 *vs* 76.66±2.01%), PEF (Peak Expiratory Flow; 4.80±0.37 *vs* 6.89±0.34 L/s), $FEF_{25\%}$ (Forced Expiratory Flow at 25% of FVC; 4.45±0.36 *vs* 6.39±0.33 L/s), $FEF_{50\%}$ (3.65±0.36 *vs* 6.39±0.33 L/s) in subjects considered exposed to benzene. Similar findings were observed in 80 refinery workers in Macedonia (13): a greater prevalence of respiratory (33.7% vs 22.5%) and nasal symptoms (36.2% vs 23.7%) emerged in subjects considered as exposed compared to subjects of the public administration. There was also a decrease in spirometry values: MEF_{50} (equivalent to FEF_{50}) (61.9% of predicted vs 67.4%) and in MEF_{75} (56.1% of predicted vs 62.9%), even stratifying by smoking habits. On the other hand, the prevalence of asthma (control *vs* exposed: 3.7% *vs* 5.0%), allergic rhinitis (control *vs* exposed: 10.0% *vs* 16.3%) and allergen sensitization (control *vs* exposed: 31.2% *vs* 35.0%) was found to be in line with data relating to Macedonian adult population.

The responses to a questionnaire from 5,983 workers within a petrochemical complex comprising 75 companies (refinery, production of organic chemicals compounds, synthetic rubber, fertilizers) highlighted an increased risk of having phlegm, wheezing or shortness of breath in smokers and subjects with a previous history of respiratory diseases or atopy, as well as in those who have declared to handle toxic materials (e.g. powders, metals, organic solvents and vapors; overall OR_{phlegm}=1.39; 95%CI: 1.11-1.73 – $OR_{wheezing}$=1.71; 95%CI: 1.31-2.44 – $OR_{shortness\ of\ breath}$ =1.80; 95%CI:1.37-2.38) and in those who did not wear or wear incorrectly protective devices (OR_{cpugh}=2.47; 95%CI: 1.21-5.06 – OR_{phlegm}=2.05; 95%CI: 1.29-3.27 – $OR_{wheezing}$=3.03; 95%CI: 1.65-2.43 – $OR_{shortness\ of\ breath}$ =2.05; 95%CI: 1.17-3.60). This study did not reveal an increase in the onset of respiratory symptoms in relation to the duration of work (set at ≥8.3 years on the basis of sample average), however the subdivision of the exposure values based on the job performed and aerial levels of compounds in the various structures is not clear (14).

Using two validated questionnaires, spirometry and FeNO measurement, in a cross-sectional study conducted in Algeria emerged a significant increased prevalence of respiratory and nasal symptoms in workers exposed to benzene, toluene, ethylbenzene and other compounds, employed in a hydrocarbons distribution company. Odd-ratios, adjusted for age, BMI and smoke, range approximatively form 2 to 10; even after additional adjustment for reported allergy, the main symptoms keep statistical significance (e.g. $OR_{cough,\ last\ 12\ months}$=3.25; 95%CI: 2.0-5.2 – $OR_{phlegm,\ at\ least\ 3\ months/yr}$=3.81; 95%CI: 1.9-7.6 – $OR_{breaths\ at\ rest,\ last\ 12\ months}$= 12.5; 95%CI: 3.7-41.4 – $OR_{asthma,\ last\ 12\ months}$=3.95; 95%CI: 1.3-12.2 – $OR_{nasal\ symptoms,\ throughout\ the\ year}$=3.96; 95%CI: 1.4-11.4). Authors observed, even after excluding subjects with rhinitis, a significant reduction of Tiffeneau index (81.9±8.6% *vs* 83.8±6.8%) and MEF_{25} (95.6±41.8% *vs* 105.8±49.7%) in exposed workers, as well as for others parameters, but without statistics relevance as regards the latter. Values of FeNO were significantly higher among exposed workers, both with and without adjustment for age, height and smoking category (15).

Visual and hearing system

The harmful substances present in the working environments of petroleum derivatives, inhaled in closed or poorly ventilated environments, especially if mixed with other impurities, can lead to disturbances not only of the respiratory system, but also of the nervous system (organic solvents can accumulate in organs rich in lipids): for example alteration of the visual and auditory system. In fact, organic solvents have been shown to be responsible for alterations in several components of the visual system, including the lens, retinal layers and the optic nerve. Occupational exposure to solvents such as styrene, toluene, n-hexane, carbon disulfide has been indicated as a possible causal event of acquired dyschromatopsia (16-18). In a Korean refinery (19) researchers saw an increase in the prevalence of dyschromatopsia, especially type III (concerning the perception of blue-yellow colors). Prevalence in left eye of workers without exposure was 22.7%, 24.0% in workers with low exposure, 26.5% in subjects with medium exposure and 30.2% in workers with high exposure; environmental pollutants were below the risk limit threshold, with the exception of benzene which was found to be on average 102% of the TLV. Using the CCI (Color Confusion Index) as parameter, it emerged that the level of exposure and duration in working years appeared to be statistically associated with the presence of type III dyschromatopsia in the left eye, even though this association was very weak (Spearman's correlation=0.131). The loss of color discrimination was also very weakly associated with chronological age (it should be noted that subjects with the highest exposure were also those with higher age). Similar disperception was weakly observed in 30 workers of an Indian refinery: blue-yellow vision defects were found in 16 of 30 workers *vs* 7 of 30 age-matched reference group. Furthermore, the Color Confusion Index (CCI) was higher in exposed than in unexposed (1.40±0.18 vs 1.28±0.21; p=0.037) (20). This latter association was not found in the study by Lee et al (except for not significant increase in the left eye) but only between CCI and age (p=0.002) (19).

Regarding the hearing system, it has been suggested that the association between chemical solvents and noise could have an additive effect even if levels are low or moderate (21,22). Morata et al (23) tried to evaluate a possible difference in the prevalence of hearing disorders

among workers of a refinery in South America, through audiometric and acoustic immittance tests: most of the toxic compounds (such as toluene, xylene, cyclohexane ethylbenzene) were found to be below exposure threshold levels in the various subgroups of workers, with the exception of benzene, which was found to be on average over-threshold for subjects involved in maintenance, refining of aromatic compounds and paraffins and workers in the internal laboratory for quality control. The result was a greater hearing loss at high frequencies in subjects considered to be more exposed to pollutants and noise (compared with reference categories not considered exposed due to environmental sampling with values below the detectable threshold for the pollutants analyzed; $p<0.005$). From the multiple regression model it was also observed that the risk of hearing loss was 3 times greater in maintenance subjects, again compared to the categories considered not exposed to noise or pollutants (95%CI: 1.3-6.9) and almost two and a half times higher in subjects operating in the refining of aromatics and paraffins (95%CI: 1.0-5.7). Subjects belonging to the subgroup of aromatic compound refinement and pipe-fitting, showed a significantly higher percentage of cases of decay of the acoustic reflex. Results, also considering the greater loss of reflex due to ipsilateral rather than contralateral stimulation, suggest that there may be retrocochlear involvement in the acoustic disturbances observed and that hearing loss may therefore not be attributable simply to cochlear damage following acute acoustic trauma or chronic.

A more recent Chinese study investigated the effect of combined exposure to noise and ethylbenzene in two refinery group workers compared to an unexposed group and to power station workers. Using the Neurobehavioral Core Test Battery, ia decrease in some of the function inspected, especially in people with 3 or more working age, was observed. There was also an increased risk of hearing loss ≥25 dB in the two petrochemical groups, but the estimate was not precise enough to get a conclusion (age-adjusted OR_1=107; 95%CI: 17.1-358 – OR_2=114; 95%CI: 34.2-343) (24).

Mortality

As regards cardiovascular diseases mortality, a study carried out on a cohort of 1,583 workers of an Italian refinery (25) showed a lower risk of death (SMR=0.77; 95%CI: 0.64-0.93) compared to the general Lombard population (period 1949-1968). This result was in line with a previous study (26) conducted on workers of the same refinery, in which no increased risk emerged by comparing the sample with the Italian national population (SMR=0.88; $CI_{95\%}$: 0.68-1.12) and with the Lombard one (SMR=0.68; $CI_{95\%}$: 0.53-0.87). A further study (27) confirmed this mortality reduction (SMR=0.70; 95%CI: 0.63-0.78). Same mortality (SMR=0.90; 95%CI: 0.87-0.92) was found by a broader temporal analysis considering 28,555 employees who had worked at least 12 months from 1951 to 2003 in 8 refineries located in England, Scotland and Wales, using national population as reference. A significant reduction also emerged analyzing 2,203 workers employed between 1990 and 1998 in a chemical/refinery plant in Louisiana (OR=0.83; 95%CI: 0.72-0.94) (28) and also an older cohort of refinery and petrochemical Shell Oil Company workers (working period: 1948-1972; SMR 0.80) (29). A slight discrepancy from previous estimates was instead observed within a cohort of Canadian refinery workers, in which there seems to be an increase in the standardized mortality rate for arteries, arterioles and capillaries disease, compared to national population (SMR=1.31; 95%CI: 1.09-1.56). On the other hand, these workers showed a decreasing risk for acute myocardial infarction (SMR=0.84; 95%CI: 0.77-0.93). Aortic aneurysm mortality showed an insignificant increase for these refinery workers (SMR=1.21; 95%CI: 0.89-1.62), while it was for marketing and distribution sector ones, potentially exposed to petroleum products (SMR=1.56; 95%CI: 1.11-2.12) (30); in a previous study, mortality from diseases of the arteries was increase in the refinery subgroup (SMR=120; 95%CI: 107-135) (31).

Among three of the Italian (25,27) and English cohort (32) analyzed above, respiratory (SMR=0.54, 95%CI: 0.29-0.92; SMR=0.59, 95%CI: 0.44-0.78, SMR=0.76, 95%CI: 0.72-0.81 respectively) and gastrointestinal diseases mortality (SMR=0.54, 95%CI: 0.33-0.84; SMR=0.55, 95%CI: 0.42-0.71, SMR=0.80, 95%CI: 0.72-0.90 respectively) was decreased compared to the reference population.

Finally, within a cohort of 7,147 workers at a petrochemical plant in Southern Italy, the SMRs observed for cardiovascular (SMR=0.57; 95%CI: 0.50-0.65), respiratory (SMR=0.61; CI95%: 0.46-0.82) and gastrointestinal diseases (SMR=0.50; 95%CI: 0.38-0.65), calculated for 6,458 subjects with a follow-up of at least 10 years, were lower than the reference population (33).

NEOPLASTIC PATHOLOGIES

Data relating to malignancies mostly focus on mortality rates. Results of most of the studies in literature have been already summarized in some meta-analyzes. Published in 1989, a systematic review and meta-analysis of epidemiological studies on oil workers examined different types of solid and hematopoietic tumors (34): overall, there was no significant increase in mortality from any type of cancer in the oil industry. However, an increased risk of cancer mortality has been described in some small groups of petrochemical industry workers for the following cancers: prostate cancer in workers of methylethylketone (MEK) units in two US refineries, kidney cancer in petrol tanker drivers in a UK study, and melanoma in two out of eight UK refineries. Additionally, an increased risk of leukemia has been reported in three cohorts of workers within US refineries, especially those employed in the 1940s or earlier. No increased mortality was found for other types of cancers. These results were consistent with the evaluation of the International Agency for Research on Cancer (IARC, 1989): limited evidence for skin cancer and leukemia risk due to oil refineries, while inadequate evidence for other types of cancer (35). The authors stressed the lack of specificity of the analysis within the broad category of hematopoietic tumors in cohort studies: for instance, leukemias had not been analyzed for specific cell type. In addition, other hematopoi-

etic cancers, such as non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM), were not debated in most cohort studies. Nevertheless, subsequent systematic reviews and meta-analyzes of multiple myeloma and non-Hodgkin's lymphoma (36-38) did not reveal an increased risk of these hematopoietic tumors following occupational exposure to benzene or other petroleum products containing it. An update of this review (39), including a cohort of over 350,000 petrochemical workers, concluded that there was no increase in mortality from gastrointestinal cancers (stomach, colon, liver or pancreas), from pulmonary, bladder, kidney and brain tumor cancers. The summary standardized mortality ratios for each tumor type were below unity.

Association with Non-Hodgkin Lymphoma (NHL) and benzene was observed in a more recent meta-analysis, even after adjusting for the "healthy worker effect" (40). The summary relative risk for the 21 refinery studies analysed was 1.21 (Shore-adjusted 95%CI: 1.00-1.46) and 1.42 (Shore-adjusted 95%CI: 1.19-1.69) after adjusting for the healthy worker effect. Even after removing the largest sample size study or the one with the greater relative risk, the overall effect was confirmed. Considering only the 14 studies that assessed a higher exposure working category, the summary Relative Risk (RR) increased to 1.51 (Shore-adjusted 95%CI 1.07-2.14). This evidence is in contrast to what observed in a previous meta-analysis (41), which however not considered only refinery industries. It should be pointed up that some old studies report only risks for lymphosarcoma and reticulosarcoma, subcategories of NHL. Even Kane et al (42) highlighted the lack of association between gasoline exposure (not only refinery plants where considered) and NHL risk, with an overall risk, calculated with random effects analysis, of 1.02 (95%CI: 0.94-1.12. I^2=24.7%, p=0.077). The subtotal pooled risk for refinery and petrochemical plants resulted of 1.00 (95%CI: 0.91-1.09. I^2=0.0%, p=0.554).

Significant increases in melanoma mortality have been reported in some small groups of UK refinery workers (SMR=1.78; 95%CI: 1.20-2.54) and Canadian upstream ones (SMR=6.00; 95%CI: 2.19-13.06) (43,44), but responsible agents have not been identified. However, none of the US cohort studies described a significant increase in skin cancer mortality (SMR=1.10; 95%CI: 0.95-1.27) (39). High mortality has been instead described for prostate cancer in short-term workers in a US refinery and in short-term workers employed in some crude oil operations. However, the absence of a growing trend in relation to length of service in these workers argues against the association between exposure to petroleum products and prostate cancer. Out of total oil workers, prostate cancer mortality was not increased (SMR=0.98; 95%CI: 0.94-1.03) (39). More recently, a systematic review and meta-analysis was performed with the aim of updating the IARC and Wong and Raabe reviews: particular attention was paid to mesothelioma, melanoma, and hematopoietic tumors (45). Studies using the most appropriate methods for case identification provided the best estimate of mesothelioma risk (meta-RR=3.22; 95%CI: 1.45-7.23), while a higher meta-RR was found in maintenance workers. A modest relative excess risk was found for acute lymphatic leukemia (ALL) (meta-RR: 1.51; 95%CI: 1.08-2.13) and melanoma (meta-RR: 1.23; 95%CI: 1.09-1.38). The relative risk for ALL was influenced by results of a large study, with some suspicion of diagnostic uncertainty, and the relative excess risk for melanoma was linked to two large studies on incidence. Furthermore, refinery workers may have a lower risk of lung cancer (meta-RR: 0.81; 95%CI: 0.76-0.86). The increased incidence of melanoma emerged in another meta-analyses (Standardized Incidence Rate or SIR=1.23: 95%CI: 1.11-1.36), but there is less evidence regarding mortality (SMR=1.02; 95%CI: 0.81-1.28), although the male subgroup analysis showed a greater association (SMR=1.19; 95%CI: 1.00-1.42). Regarding mortality, there appeared to be an association with the latitude of the Country in which studies were conducted (46).

In a mortality study conducted on a cohort of 5,112 male workers employed in Italian petrochemical plants, between 1949 and 2011 (average follow-up length of 49 years), the SMRs were calculated using regional rates, specific for age and gender (27). In the whole cohort there was an increased mortality for pleural mesothelioma (SMR 1.59; 95%CI: 0.71-3.53), brain tumor (SMR 1.47; 95%CI: 0.87-2.49) and lymphatic leukemia (SMR 1.81; 95%CI: 0.91-3.62), but without statistical relevance. All deaths from pleural cancer occurred after more than 10 years of latency and in workers with duration of exposure ≥20 years, while those from brain tumors occurred in workers with latency and duration of exposure <10 years. Cases of lymphatic leukemia, especially chronic type, involved workers with latency and duration of exposure ≥20 years. Four fatal cases of acute myeloid leukemia (AML) were observed in the group with latency ≥20 years (SMR 1.55, 95%CI: 0.58-4.12). A recent pooled analysis (47) of three case-control studies (48-50), updated with new cases of hematopoietic tumors (total of 370 cases and 1,587 controls), showed that occupational exposure was associated with an increased risk of myelodysplastic syndrome (MDS), but not acute myeloid leukemia (AML). In this analysis, a statistically significant dose-response relationship was found between MDS and benzene exposure, but similar results were not observed with AML; low benzene levels can cause MDS, but higher concentrations may be needed to develop AML. Some studies suggest that immune-mediated inflammation is an early stage in the development of benzene-induced MDS. Since MDS is prevalent in the elderly, the disease could remain at low grade for years and subsequently progress to the stage of full-blown disease with age-related decrease in immune defenses. In contrast, higher concentrations of benzene may be required for acute myeloid leukemia (AML). In this study, it was not confirmed that exposures occurring within 15 years of diagnosis are closely related to AML (or MDS and CML). The question of whether AML is an independent effect or a possible outcome of benzene-induced MDS also remains unanswered (47). Results of a subsequent analysis demonstrated the lack of association between benzene and chronic lymphocytic leukemia

(CLL) (51). Nevertheless, some studies identified elevated CLL mortality in petrochemical plant workers before 1950. As refineries represent a complex exposure environment, co-exposure in addition to benzene could contribute to the etiology. Finally, it must be said that previous studies probably reported an excess of cases of AML or aplastic anemia, rather than an excess of cases of MDS, since the diagnostic criteria for the last had yet not been defined (47).

In addition to cancer risk in residents living near petroleum facilities, the most recent meta-analysis has taken into consideration specific ones for workers within them. As in other studies, reduction in lung cancer risk was confirmed, although there was a strong heterogeneity between the included studies (SMR=0.82; 95%CI: 0.76-0.88) as well as the risk for mesothelioma (SMR 1.98; 95%CI: 1.46-2.67); this one is probably associated, in most cases, with exposure to asbestos, used in combustion petroleum pipes. Within the offshore workers sub-category, the risk of cutaneous melanoma (without statistical significance), leukemia (OR=1.47; 95%CI: 1.12-1.92), lung (OR=1.20; 95%CI: 1.03- 1.39) and mesothelioma (OR=2.47; 95%CI: 1.66-3.67) were increased, even though many of these associations appear to be due to other factors than those directly emerging from petroleum production (52).

Discussion and Conclusion

In the oil sector there are various risk factors which, in the absence of mitigation and control measures, can affect the health of workers. The presence of incorrect eating behavior, characterized by an excessive intake of high-calorific food, and work-related stress components, constitute important risk factors for the onset of cardiovascular diseases. From studies in literature, it was possible to note a slight increase in blood pressure, cholesterol and BMI values in petrochemical industry workers, but not evenly. The concept of promoting a balanced diet to reduce the onset of cardiovascular and metabolic diseases, as experimented in other industrial sectors (53), could therefore be extended to the oil industry, even to increase efficiency of labour. Greater attention to cardiovascular and coronary diseases should be given among shift workers (6,54,55). In almost all epidemiological studies concerning the occupational field, selection bias known as the "healthy worker effect" could underestimate the risk due to environmental pollutants. A possible strategy to minimize the effect of this bias could be to use as reference category a workers cohort, instead of general or local population (56). Along with others such as length and degree of exposure and limitation of the number of people included in the studies, this critical issue had already been highlighted in a literature review conducted more than 30 years ago on 120 articles (57).

The possible involvement of air pollutants with development of conditions of oxidative stress and inflammation make it necessary to continuously monitor the indices of predisposition to cardiovascular damage and the onset of diabetes; for the latter condition, more in-depth and targeted investigations should be conducted in this category of workers. The use of glycated hemoglobin would make it safer to determine a condition of diabetes or prediabetes, however it is a second level test in clinical practice, therefore annual blood glucose monitoring can still provide data that can be used to evaluate the general trend of the state glycaemic levels in workers and possibly correlating it with the role of environmental pollutants in refining plants.

As regard neoplastic pathologies, it has been observed an overall reduction in relative or mortality risks, likely explained by the "healthy worker effect". Some exceptions were found in specific studies, maybe linked to particular cohort of subjects or to higher level of environmental pollutants. Considering the variety of volatile compounds present in petrochemical plants, it is often difficult to demonstrate the association of each ones to a specific type of tumor, hence the desire to give a general overview of cancer risk in this industrial sector. Help comes from in vitro or animal studies, which linked the exposure to a single chemical compound with a specific neoplasm, even though the additive effect of other pollutants present in the workplace cannot be excluded. The increased risk for certain type of cancers, for example mesothelioma or lung, could not be closely related to exposure to substances derived from benzene but to materials such as asbestos, for a long time present in industrial sector, therefore also in petrochemical plants (58-60). Furthermore, in older studies, some categories of haematopoietic tumors did not have the same current classification, creating a certain difficulty in comparing the trend of these diseases. For example, MDS diagnostic criteria were recently defined, and it seems to be a relationship between benzene exposure and this syndrome (61), even at low doses, so new studies on petrochemical workers should be implemented. Overall, the association between benzene exposure and leukemia is confirmed by various studies in the literature (62) while there is heterogeneity in risks for the different type of leukemia (AML, CML, CCL), maybe linked to different dose exposure (for CCL and AML could be necessary high dose). Otherwise, the association with lymphomas (in particular NHL) is not so clear. Except for some small studies, no association between working in refineries and prostate cancer was found, even though in literature we could find some evidence of association of this neoplasm with BTX exposure (63); the correct use of PPE and environment monitoring, to keep toxic compound below threshold levels, could partially explain these findings.

Major problems, emerging from cross-sectional and retrospective studies analyzed, are mostly linked to data collection through company health surveillance databases, often not conceived for in-depth epidemiological research and without standardized classification systems. Therefore, information obtained could be hardly comparable and sometimes lack in details. Another matter is the low sample size, which could fail in finding precise Standardized Mortality Ratio or Standardized Incidence Ratio (i.e. with wide confidence interval), especially for rare pathologies.

In almost all of the studies analyzed, a univocal opinion emerged on the need to implement workers health monitoring programs through different strategies, such as specific direct examinations or simply medical counseling, also in order to reduce absenteeism due to health problems.

References

1) 1910.1028 - Benzene. | Occupational Safety and Health Administration. https://www.osha.gov/laws-regs/regulations/standardnumber/1910/1910.1028 [Accessed January 5, 2022]
2) Directive (EU) 2017/ of the European Parliament and of the Council of 12 December 2017 amending Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work.9.
3) Feitshans IL. Law and regulation of benzene. Environ Health Perspect (1989) 82:299-307. doi: 10.1289/ehp.8982299
4) Tsai SP, Dowd CM, Cowles SR, et al. Prospective morbidity surveillance of Shell refinery and petrochemical employees. Occupational and Environmental Medicine (1991) 48:155-163. doi: 10.1136/oem.48.3.155
5) Mannocci A, Pignalosa S. Cardiovascular Diseases Risk Factors in oil and gas workers: a ten years observational retrospective cohort. Annali di Igiene: Medicina Preventiva e di Comunità (2016) 122-132. doi: 10.7416/ai.2016.2091
6) Carvalho FC, Godinho MR, Ferreira AP. Cardiovascular risk factors among oil refinery workers: ecological study. Revista Brasileira de Medicina do Trabalho (2020) 18:11-19. doi: 10.5327/Z1679443520200476
7) Esquirol Y, Bongard V, Mabile L, et al. Shift Work and Metabolic Syndrome: Respective Impacts of Job Strain, Physical Activity, and Dietary Rhythms. Chronobiology International (2009) 26:544-559. doi: 10.1080/07420520902821176
8) Choobineh A, Soltanzadeh A, Tabatabaee H, et al. Health Effects Associated With Shift Work in 12-Hour Shift Schedule Among Iranian Petrochemical Employees. International Journal of Occupational Safety and Ergonomics (2012) 18:419-427. doi: 10.1080/10803548.2012.11076937
9) Kotseva K, Popov T. Study of the cardiovascular effects of occupational exposure to organic solvents. Int Arch Occup Environ Health (1998) 71 Suppl:S87-91.
10) Mannocci A, Pignalosa S, Saulle R, et al. Prevalence of major cardiovascular risk factors among oil and gas and energy company workers.6.
11) Meo SA, Al-khlaiwi T, Abukhalaf AA, et al. The Nexus between Workplace Exposure for Wood, Welding, Motor Mechanic, and Oil Refinery Workers and the Prevalence of Prediabetes and Type 2 Diabetes Mellitus. IJERPH (2020) 17:3992. doi: 10.3390/ijerph17113992
12) Meo SA, Alrashed AH, Almana AA, et al. Lung function and fractional exhaled nitric oxide among petroleum refinery workers. J Occup Med Toxicol (2015) 10:37. doi: 10.1186/s12995-015-0080-7
13) Minov J, Karadzinska-Bislimovska J, Vasilevska K, et al. Respiratory and nasal symptoms, immunological changes and lung function among petroleum refinery workers. (1901) 101:14.
14) Park J, Lee C, Ryu S. Factors Related to the Prevalence of Respiratory Symptoms in Workers in a Petrochemical Complex. Jrnl of Occup Health (2006) 48:216-222. doi: 10.1539/joh.48.216
15) Sekkal S, Haddam N, Scheers H, et al. Occupational Exposure to Petroleum Products and Respiratory Health: A Cross-Sectional Study From Algeria. Journal of Occupational & Environmental Medicine (2012) 54:1382-1388. doi: 10.1097/JOM.0b013e31825fa6c9
16) Muttray A, Wolff U, Jung D, et al. Blue-yellow deficiency in workers exposed to low concentrations of organic solvents. Int Arch Occup Environ Health (1997) 70:407-412. doi: 10.1007/s004200050237
17) Gobba F, Cavalleri A. Color Vision Impairment in Workers Exposed to Neurotoxic Chemicals. NeuroToxicology (2003) 24:693-702. doi: 10.1016/S0161-813X(03)00037-8
18) Paramei GV, Meyer-Baron M, Seeber A. Impairments of Colour Vision Induced by Organic Solvents: A Meta-Analysis Study. NeuroToxicology (2004) 25:803-816. doi: 10.1016/j.neuro.2004.01.006
19) Lee E-H, Eum KD, Cho S-I, et al. Acquired dyschromatopsia among petrochemical industry workers exposed to benzene. NeuroToxicology (2007) 28:356-363. doi: 10.1016/j.neuro.2006.05.005
20) Indhushree R, Monica R, Coral K, et al. Visual functions of workers exposed to organic solvents in petrochemical industries. Indian J Occup Environ Med (2016) 20:133. doi: 10.4103/0019-5278.203138
21) Hormozi M, Ansari-Moghaddam A, Mirzaei R, et al. The risk of hearing loss associated with occupational exposure to organic solvents mixture with and without concurrent noise exposure: A systematic review and meta-analysis. Int J Occup Med Environ Health (2017) doi: 10.13075/ijomeh.1896.01024
22) Sliwinska-Kowalska M, Zamyslowska-Szmytke E, Szymczak W, et al. Hearing loss among workers exposed to moderate concentrations of solvents. Scand J Work Environ Health (2001) 27:335-342. doi: 10.5271/sjweh.622
23) Morata TC, Engel T, Durão A, et al. Hearing Loss from Combined Exposures among Petroleum Refinery Workers. Scandinavian Audiology (1997) 26:141-149. doi: 10.3109/01050399709074987
24) Zhang M, Wang Y, Wang Q, et al. Ethylbenzene-Induced Hearing Loss, Neurobehavioral Function, and Neurotransmitter Alterations in Petrochemical Workers. Journal of Occupational & Environmental Medicine (2013) 55:1001-1006. doi: 10.1097/JOM.0b013e31829f3142
25) Consonni D, Pesatori AC, Tironi A, et al. Mortality study in an Italian oil refinery: Extension of the follow-up. Am J Ind Med (1999) 35:287-294. doi: 10.1002/(SICI)1097-0274(199903)35:3<287::AID-AJIM9>3.0.CO;2-F
26) Bertazzi PA, Pesatori AC, Zocchetti C, et al. Mortality study of cancer risk among oil refinery workers. Int Arch Occup Environ Heath (1989) 61:261-270. doi: 10.1007/BF00381424
27) Bonzini M, Grillo P, Consonni D, et al. Cancer risk in oil refinery workers: a pooled mortality study in Italy. La Medicina del Lavoro (2019) 110:3-10. doi: 10.23749/mdl.v110i1.7842
28) Tsai SP, Dowd CM, Cowles SR, et al. Prospective morbidity surveillance of Shell refinery and petrochemical employees. Occupational and Environmental Medicine (1991) 48:155-163. doi: 10.1136/oem.48.3.155
29) Marsh GM, Enterline PE, McCraw D. Mortality patterns among petroleum refinery and chemical plant workers. Am J Ind Med (1991) 19:29-42. doi: 10.1002/ajim.4700190105
30) Lewis RJ. Updated mortality among diverse operating segments of a petroleum company. Occupational and Environmental Medicine (2000) 57:595-604. doi: 10.1136/oem.57.9.595
31) Rushton L. A 39-year follow-up of the U.K. oil refinery and distribution center studies: results for kidney cancer and leukemia. Environmental Health Perspectives (1993) 101:77-84. doi: 10.1289/ehp.93101s677
32) Sorahan T. Mortality of UK oil refinery and petroleum distribution workers, 1951-2003. Occupational Medicine (2007) 57:177-185. doi: 10.1093/occmed/kql168
33) Pasetto R, Biggeri A, Comba P, et al. Mortality in the cohort of workers of the petrochemical plant in Gela (Sicily) 1960-2002. (2007) 7.
34) Wong O, Raabe GK. Critical review of cancer epidemiology in petroleum industry employees, with a quantitative meta-analysis by cancer site. Am J Ind Med (1989) 15:283-310. doi: 10.1002/ajim.4700150305
35) Occupational Exposures in Petroleum Refining (IARC Summary & Evaluation, Volume 45, 1989). https://inchem.org/documents/iarc/vol45/45-01.html [Accessed February 4, 2022]
36) Wong O, Raabe GK. Cell-Type-Specific Leukemia Analyses in a Combined Cohort of More Than 208,000 Petroleum Workers in the United States and the United Kingdom, 1937-1989. Regulatory Toxicology and Pharmacology (1995) 21:307-321. doi: 10.1006/rtph.1995.1044
37) Wong O, Raabe GK. Multiple Myeloma and Benzene Exposure in a Multinational Cohort of More Than 250,000 Petroleum Workers. Regulatory Toxicology and Pharmacology (1997) 26:188-199. doi: 10.1006/rtph.1997.1162
38) Wong O, Raabe GK. Non-Hodgkin's Lymphoma and Exposure to Benzene in a Multinational Cohort of More Than 308,000 Petroleum Workers, 1937 to 1996: Journal of Occupational and Environmental Medicine (2000) 42:554-568. doi: 10.1097/00043764-200005000-00016

39) Wong O, Raabe GK. A Critical Review of Cancer Epidemiology in the Petroleum Industry, with a Meta-analysis of a Combined Database of More Than 350,000 Workers. Regulatory Toxicology and Pharmacology (2000) 32:78-98. doi: 10.1006/rtph.2000.1410
40) Steinmaus C, Smith AH, Jones RM, et al. Meta-analysis of benzene exposure and non-Hodgkin lymphoma: biases could mask an important association. Occupational and Environmental Medicine (2008) 65:371-378. doi: 10.1136/oem.2007.036913
41) Lamm SH, Engel A, Byrd DM. Non-Hodgkin lymphoma and benzene exposure: A systematic literature review. Chemico-Biological Interactions (2005) 153-154:231-237. doi: 10.1016/j.cbi.2005.03.027
42) Kane EV, Newton R. Occupational exposure to gasoline and the risk of non-Hodgkin lymphoma: A review and meta-analysis of the literature. Cancer Epidemiology (2010) 34:516-522. doi: 10.1016/j.canep.2010.05.012
43) Rushton L. Further follow up of mortality in a United Kingdom oil refinery cohort. Occupational and Environmental Medicine (1993) 50:549-560. doi: 10.1136/oem.50.6.549
44) Schnatter AR, Thériault G, Katz AM, et al. A retrospective mortality study within operating segments of a petroleum company. American Journal of Industrial Medicine (1992) 22:209-229. doi: 10.1002/ajim.4700220207
45) Schnatter AR, Chen M, DeVilbiss EA, et al. Systematic Review and Meta-Analysis of Selected Cancers in Petroleum Refinery Workers. Journal of Occupational & Environmental Medicine (2018) 60:e329-e342. doi: 10.1097/JOM.0000000000001336
46) Vujic I, Gandini S, Stanganelli I, et al. A meta-analysis of melanoma risk in industrial workers. Melanoma Research (2020) 30:286-296. doi: 10.1097/CMR.0000000000000531
47) Schnatter AR, Glass DC, Tang G, et al. Myelodysplastic Syndrome and Benzene Exposure Among Petroleum Workers: An International Pooled Analysis. JNCI Journal of the National Cancer Institute (2012) 104:1724-1737. doi: 10.1093/jnci/djs411
48) Schnatter AR, Armstrong TW, Nicolich MJ, et al. Lymphohaematopoietic malignancies and quantitative estimates of exposure to benzene in Canadian petroleum distribution workers. Occupational and Environmental Medicine (1996) 53:773-781. doi: 10.1136/oem.53.11.773
49) Rushton L, Romaniuk H. A case-control study to investigate the risk of leukaemia associated with exposure to benzene in petroleum marketing and distribution workers in the United Kingdom. Occupational and Environmental Medicine (1997) 54:152-166. doi: 10.1136/oem.54.3.152
50) Glass DC, Gray CN, Jolley DJ, et al. Leukemia Risk Associated With Low-Level Benzene Exposure: Epidemiology (2003) 14:569-577. doi: 10.1097/01.ede.0000082001.05563.e0
51) Rushton L, Schnatter AR, Tang G, et al. Acute myeloid and chronic lymphoid leukaemias and exposure to low-level benzene among petroleum workers. Br J Cancer (2014) 110:783-787. doi: 10.1038/bjc.2013.780
52) Onyije FM, Hosseini B, Togawa K, et al. Cancer Incidence and Mortality among Petroleum Industry Workers and Residents Living in Oil Producing Communities: A Systematic Review and Meta-Analysis. IJERPH (2021) 18:4343. doi: 10.3390/ijerph18084343
53) Leighton F, Polic G, Strobel P, et al. Health impact of Mediterranean diets in food at work. Public Health Nutr (2009) 12:1635-1643. doi: 10.1017/S1368980009990486
54) Engin A. "Circadian Rhythms in Diet-Induced Obesity.," In: Engin AB, Engin A, editors. Obesity and Lipotoxicity. Advances in Experimental Medicine and Biology. Cham: Springer International Publishing (2017). p. 19-52 doi: 10.1007/978-3-319-48382-5_2
55) Kecklund G, Axelsson J. Health consequences of shift work and insufficient sleep. BMJ (2016)i5210. doi: 10.1136/bmj.i5210
56) Karvonen MJ, Mikheev MI eds. Epidemiology of occupational health. Copenhagen: Albany, NY: World Health Organization, Regional Office for Europe; WHO Publications Center USA [distributor] (1986). 392 p.
57) Harrington JM. Health experience of workers in the petroleum manufacturing and distribution industry: A review of the literature. Am J Ind Med (1987) 12:475-497. doi: 10.1002/ajim.4700120503
58) Gun RT, Pratt N, Ryan P, et al. Update of mortality and cancer incidence in the Australian petroleum industry cohort. Occupational and Environmental Medicine (2006) 63:476-481. doi: 10.1136/oem.2005.023796
59) Montanaro F, Ceppi M, Puntoni R, et al. Asbestos Exposure and Cancer Mortality among Petroleum Refinery Workers: A Poisson Regression Analysis of Updated Data. Archives of Environmental Health: An International Journal (2004) 59:188-193. doi: 10.3200/AEOH.59.4.188-193
60) Tsai SP, Waddell LC, Gilstrap EL, et al. Mortality among maintenance employees potentially exposed to asbestos in a refinery and petrochemical plant. Am J Ind Med (1996) 29:89-98. doi: 10.1002/(SICI)1097-0274(199601)29:1<89::AID-AJIM11>3.0.CO;2-W
61) Copley GB, Schnatter AR, Armstrong TW, et al. Hospital-Based Case-Control Study of MDS Subtypes and Benzene Exposure in Shanghai. Journal of Occupational & Environmental Medicine (2017) 59:349-355. doi: 10.1097/JOM.0000000000000952
62) Khalade A, Jaakkola MS, Pukkala E, et al. Exposure to benzene at work and the risk of leukemia: a systematic review and meta-analysis. Environmental Health (2010) 9:31. doi: 10.1186/1476-069X-9-31
63) Blanc-Lapierre A, Sauvé J-F, Parent M-E. Occupational exposure to benzene, toluene, xylene and styrene and risk of prostate cancer in a population-based study. Occup Environ Med (2018) 75:562-572. doi: 10.1136/oemed-2018-105058

Supplementary material

Search strings used in PubMed:

- health[Title/Abstract] AND refinery[Title/Abstract] AND workers[Title/Abstract] (1980-2021)
- health[Title/Abstract] AND petrochemical[Title/Abstract] AND workers[Title/Abstract] (1980-2021)
- cardiovascular[Title/Abstract] AND refinery[Title/Abstract] AND workers[Title/Abstract] (1980-2021)
- cardiovascular[Title/Abstract] AND petrochemical[Title/Abstract] AND workers[Title/Abstract] (1980-2021)
- respiratory[Title/Abstract] AND refinery[Title/Abstract] AND workers[Title/Abstract] (1980-2021)
- respiratory[Title/Abstract] AND petrochemical[Title/Abstract] AND workers[Title/Abstract] (1980-2021)
- surveillance[Title/Abstract] AND petrochemical[Title/Abstract] AND workers[Title/Abstract] (1980-2021)
- surveillance[Title/Abstract] AND refinery[Title/Abstract] AND workers[Title/Abstract] (1980-2021)
- refinery[Title] AND smok*[Title] (1980-2021)
- mortality oil petrochemical(1980-2021)
- mortality AND oil AND worker AND petroleum(1980-2021)
- mortality[Title/Abstract] AND oil refinery[Title/Abstract] (1980-2021)

Search strings used in Web of Science:

- Refinery (abstract) and health (abstract) and worker*(abstract)
- Refinery (abstract) and cardiovascular (abstract) and worker*(abstract)
- Petro* (abstract) and cardiovascular (abstract) and worker*(abstract)
- Refinery (abstract) and respiratory (abstract) and worker*(abstract)
- Petro* (abstract) and respiratory (abstract) and worker*(abstract)
- Petro* (abstract) and vision (abstract) and worker*(abstract)
- Refinery (abstract) and vision (abstract) and worker*(abstract)
- Petro* (abstract) and hear* (abstract) and worker*(abstract)
- Oil refinery (abstract) and mortality (abstract)
- Petroleum (abstract) and mortality (abstract) and meta-analysis (All fields)

Correspondence: *Maria Cristina Monti, Dipartimento di Sanità Pubblica, Medicina Sperimentale e Forense, Via Forlanini 2, 27100 Pavia (PV), Italy, Tel. 0382-987182, cristina.monti@unipv.it*