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Mortality risk associated to arsenic exposure after a major disaster. Results from the Manfredonia occupational cohort study 1976–2021

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ABSTRACT

Background: On September 1976, due to the explosion of an ammonia-washing column at the petrochemical plant in Manfredonia (Italy), 39 tonnes of arsenic were released into the atmosphere, contaminating the plants and the neighbourhoods close to it. The aim of this study is to present the results of a 45-year follow up of exposed workers with a focus on residential exposure.

Methods: We contacted Italian General Registries Offices and updated the vital status of persons involved in the clean-up activities following the disaster. The outcome of interest was the overall and cause-specific mortality. An accelerated failure time (AFT) approach was used when appropriate to model the risk of mortality.

Results: 1772 workers contributing 67,743 person years were considered in the analysis. For overall mortality, results of the age-adjusted AFT model show an accelerator factor of 0.89 (95%CI 0.80–0.99) among contract workers, which means a shortening of survival in comparison to the reference category (plastic area workers). When accounting for latency greater than 20 years, higher mortality rates for lung cancer were observed among workers residing in Manfredonia.

Discussion: An increased risk of mortality among workers who were more exposed to arsenic during the clean-up activities has been observed. In fact, a loss of 5 years of life among more exposed workers was calculated. Furthermore, the mortality rates of residents in Manfredonia were higher than those of workers residing elsewhere.

1. Introduction

From 1971 until 1994, a petrochemical plant operated in Manfredonia, producing plastic and fertilizer. The plant was about 2 km from Manfredonia, a coastal town with a population of around 50,000 in 1976. On the morning of the 26th September 1976, due to the explosion of an ammonia-washing column, 39 tonnes of arsenic were released into the atmosphere. Arsenic is well-known and widely documented as carcinogenic to humans. Furthermore, even low dose exposure to inorganic arsenic can increase mutagenesis in the long term (IARC, 2012). After the accident, part of the arsenic descended in the proximity of the plant and part of it dispersed in the direction of the city of Manfredonia, contaminating the neighbourhoods closer to the plant (Mangia et al., 2018). This industrial disaster followed the one that occurred in Seveso and had an international echo (De Marchi et al., 2017; Die Zeit, 1976).

In the first days after the accident, approximately 1800 workers from the plant as well as workers from contract companies and technicians who had arrived from other Italian sites of the same company started the clean-up activities and took soil samples to assess the degree of contamination. They worked without receiving any protective equipment from the company during the first days. The clean-up work officially ended on the 13th January 1977 (Ambrosi and Amicarelli, 1982). However, based on soils samples arsenic contamination in the plant was estimated until 1980 (Casciani and Attias, 1999).

In the days following the accident, a technical-health committee was set up, which established 100 µg/l as the threshold of urinary arsenic above which workers were not allowed in the plant and were required to repeat the analysis within a week. This threshold had rarely been exceeded during regular monitoring in the period before the accident (Soleo et al., 1982a). On the 12th October 1976, the technical committee

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published a report based on clinical examinations conducted among 700 workers, nearly half of whom (45%) showed arsenic in urine $>100 \mu\text{g/l}$ (Casciani and Attias, 1999). Thus, to ensure the continuation of clean-up activities that were still in progress, the threshold was raised to $300 \mu\text{g/l}$ (Ambrosi and Amicarelli, 1982).

Furthermore, 116 workers were admitted to the Manfredonia civil hospital with symptoms attributable to arsenic contamination, and 98 of them had arsenic levels $>3000 \mu\text{g/l}$ in their urine (Prencipe et al., 1979). In addition, at the Institute of Occupational Medicine at the University of Padua, subacute arsenic intoxication among 23 technicians who had been sent to Manfredonia from other company sites for measurement activities related to the accident was documented (Corsi et al., 1979).

Remarkably, in the period after the accident workers residing in Manfredonia showed total arsenic values in their urine on average higher than the values presented by workers residing in other municipalities. Some authors hypothesised the role of residential exposure to arsenic as a potential determinant (Soleo et al., 1982a, 1982b). Other authors suggested the potential role of a higher intake of organic arsenic, assimilable through fish and shellfish, which were assumed to be a richer part of the diet of persons living in coastal areas (Bertazzi et al., 1982; Foà et al., 1984).

In 1996, the Public Prosecutor's Office of Foggia initiated criminal proceedings against ten company managers and two physicians and asked for an occupational cohort study. The research team enrolled two sub-cohorts of workers. The first consisted of workers of permanent staff and the second consisted of contract workers who had reported an injury related to the accident or had urinary arsenic levels over the thresholds set by the authorities. Using this inclusion criterion, more than 300 of workers who took part in clean-up activities following the accident and were included in an epidemiological surveillance program, were excluded from the study. In 2016, there was an updated follow-up of the two sub-cohorts as originally enumerated (Gianicolo, 2021; Gianicolo et al., 2019; Gianicolo et al., 2019).

The role of residence in Manfredonia has not been investigated in depth in previous works, which is a crucial issue. In fact, in the days following the accident persons residing in Manfredonia but not working in the plant were admitted to the local hospital with acute arsenic intoxication and in some cases with arsenic in urine above $1000 \mu\text{g/l}$ (Prencipe et al., 1979). Thus, the aim of our study is to present results on the complete cohort of 1800 workers exposed to arsenic with a focus on residing in Manfredonia as a potential risk factor.

2. Materials and methods

2.1. Study population

Information about the area of work (fertilizer/plastic), type of contract, and demographic characteristics were available from the previous follow-ups. For cohort enumeration, two different data sources were used: personnel records for permanent staff (Comba and Pirastu, 2004) and a disease registry managed by the Worker's Health and Safety Board for the sub-cohort of contract workers. The list of the contract workers not previously enrolled (NPE) was retrieved from the archive, made available by the lower Marina Notarangelo of the court of Foggia.

2.1.1. Exposure

Since a measure of exposure to arsenic or concentrations of arsenic in urine were not available for the analysis, as done in previous studies, the area of work combined with the type of contract was used as a surrogate of exposure. Contract workers are assumed to be the most exposed, followed by fertilizer workers and plastic workers as the least exposed (Casciani and Attias, 1999; Gianicolo et al., 2019). This assumption is based on legal documents that reported concentrations of arsenic in soil in the range $0.22\text{--}4.50 \text{ mg/m}^2$ in the fertilizer area and between 0.01 and 0.12 mg/m^2 in the plastic area (Casciani and Attias, 1999). Contract workers were massively employed in clean-up activities, and during the

first days had no adequate protective equipment (Casciani and Attias, 1999).

We used a dichotomous variable to investigate the potential role of the residential exposure. Workers who were living in Manfredonia in 1976 constituted the first group. The second group included workers living in municipalities different from Manfredonia that were estimated, through a dispersion model, to be less or not at all contaminated by arsenic at the time of the accident (Mangia et al., 2018).

2.1.2. Follow-up

For the current study, the 26th September 1976 was chosen as starting point. We contacted the Italian General Registries Offices and updated the vital status of the persons in the cohort up to 30th March 2021.

The outcomes of interest were overall and cause-specific mortality. Causes of death were coded using the ninth Revision of the International Classification of Diseases (ICD IX). Based on previous literature on the causes of death associated with arsenic exposure, the following ICD-9 groups were analysed: a) Malignant neoplasm of respiratory and intrathoracic organs (160.0–165.9) with a focus on the subgroup "malignant neoplasms of lung" (162.0–162.9); b) Malignant neoplasm of genitourinary organs (179.0–189.9); c) Diseases of the circulatory system (390.0–459.9); d) Diseases of the respiratory system (460.0–519.9).

The fieldwork is documented in a flowchart reported in the supplementary material (Fig. S1). Briefly, in order to update the vital status of persons still alive at the second follow-up and the sub-cohort of contract workers not previously enrolled, 154 Italian General Registry Offices were contacted. Of these, 146 responded to our request (94%). After excluding those lost to follow up, analyses were restricted to 1722 male workers out of 1860 workers, as only 43 female workers were enrolled in the cohort and two of them were lost to follow up. The cause of death was provided for 91% of deceased workers (524 out of 576 deaths) (Table S1).

2.2. Statistical analysis

A complete case analyses was conducted. Persons-years were calculated from the date of the accident (26th September 1976) until date of death, date of loss to follow-up or 31st March 2021, whatever occurred first.

The nonparametric Kaplan-Maier estimator of survival probability was used to estimate the survival curve from the day of the accident for total and cause-specific mortality, according to the area of working (1. plastic, 2. fertilizer, 3. contract workers, 4. workers not previously enumerated (NPE)) and residence in Manfredonia (dummy). A log-rank test was used to test for differences in survival probability.

An accelerated failure time (AFT) approach was used for the analysis. This was preferred to the Cox regression model because it allows parameter estimates to be interpreted directly on the original time scale, thus facilitating the communication of the results to laypersons as well (Crowther et al., 2023; Wei, 1992). The independent variables used were age at time of the accident, area of work, type of contract, and place of residence at 1976. The most appropriate distribution for the AFT model, the Weibull distribution, was selected by means of a residual analysis (Fig. S2) and using both AIC and BIC as criterion. Parameters from an AFT model with Weibull distribution can be transformed to enable a direct comparison with Hazard Ratios from a Cox regression model (Kuss and Hoyer, 2021). Using the actual outcome of interest, observation time T, and modelling it multiplicatively, i.e., additively on a log scale:

$$\log(T) = \mu + \beta X + \sigma \varepsilon$$

With μ as the intercept, X the covariates, β the regression coefficients, σ a scale parameter, and ε the residual error with a specified distribution. It is a parametric model, which means that specific assumptions about the

Table 1
Persons under study, number of deaths, person-year, and crude mortality rate (per 1000) with 95% confidence interval, by characteristics of the cohort.

Type of worker	Person under study	Number of deaths	Person-years	Mortality rate per 1000 person-years	95% Confidence interval
All	1722	576	67743	8.50	7.82-9.23
Fertilizer area (ANIC)	649	175	26257	6.67	5.71-7.73
Plastic area (SCD)	232	50	9747	5.12	3.81-6.76
Contract workers	520	224	19667	11.40	9.95-12.98
Contract workers not previously included (NPE)	321	127	12072	10.52	8.77-12.52
Residence at 26.09.1976 in Manfredonia	911	303	36430	8.32	7.41-9.31
Residence at 26.09.1976 elsewhere	811	273	31313	8.72	7.71-9.82

distribution of the survival time T are associated with specific assumptions about the distribution of the residual error ϵ (Heinrich-Ramm et al., 2002). Given two survival times $S_1(t) = S_2(\gamma t)$ for the time t where $\gamma = \exp(\beta)$. We refer to the latter γ as the acceleration factor, which describes the contraction of the survival curves of a group when lower than one (with respect to the reference group), or the stretch if greater than one of the survival curves of a group (Kleinbaum and Klein, 2012). In other words, an acceleration factor lower than one corresponds to a higher risk with respect to the reference group. For specific causes of death, the assumption of proportional hazards in the AFT models were not met (Fig. S3) and a Poisson regression model was used. Additional analyses using the Poisson regression model were performed on the subgroup population with more than 20 years of follow-up. To account for the effect of immortal person-time bias, the immortal time of 20 years was excluded from the person-years count (Lash et al., 2021).

All statistical analysis were performed using the software R v.4.2.2 and package survival (R Core Team, 2023; Therneau, 2022).

3. Results

1722 workers contributed 67,743 person years (Table 1). The highest crude overall mortality rates were observed among contract workers, both for those included in previous follow up studies (11.40 deaths per 1000 person years; 95% confidence interval: 9.95–12.98) and for those not previously enrolled (10.52; 95% CI: 8.77–12.52).

	N. of deaths	AF (IC 95%)
Mansion		
- Plastic area	50	(ref)
- Fertilizer area	175	0.97 (0.87 - 1.08)
- Contract workers	224	0.89 (0.80 - 0.99)
- Contract Workers NPE	127	0.92 (0.82 - 1.04)
Residence at 1976		
- Elsewhere	273	(ref)
- Manfredonia	303	1.01 (0.95 - 1.07)

For overall mortality, results of the age-adjusted AFT model show an accelerator factor of 0.89 (95%CI 0.80–0.99) among contract workers, which means a contraction in the survival in comparison to that of the reference category (plastic area workers). In other words, the risk is higher among contract workers than plastic workers. In fact, the probability of the plastic area workers of surviving 45 years after the accident is equal to the survival probability of contract workers after 40 years. An accelerator factor of 0.92 (95% CI: 0.82–1.04) was observed among workers not previously enrolled. No contraction in the survival was observed for overall mortality among persons residing in Manfredonia (Fig. 1).

The complete results of Poisson models for cause-specific mortality are reported in the supplementary material (S3-S4). Mortality rates for neoplasms of lung and for neoplasm of respiratory and intrathoracic organ among workers residing in Manfredonia were higher than the rates observed among residents elsewhere (Relative Rate RR = 3.42; 95%CI: 1.89–6.64). Contract workers and non-previously recruited workers also showed an increase in the rate of lung cancer compared to plastic area workers (Table 2 and Table S2).

After accounting for a latency greater than of 20 years, higher mortality rates are observed among residents in Manfredonia, in particular for mortality due to neoplasms of lung (RR = 4.95; CI95%: 2.43–11.50) and mortality due to neoplasms of respiratory and intrathoracic organs (RR = 3.15; CI95%: 1.73–6.20) (Fig. 2 and S4b).

4. Discussion and conclusion

This is the first study that considers the complete follow-up of the occupational cohort exposed to arsenic in the Manfredonia petrochemical plant 45 years after the disaster occurred in 1976.

As already observed in a previous study (Gianicolo et al., 2019), overall mortality and lung cancer mortality among contract workers, who were more exposed during the clean-up activities, are higher compared to those less exposed to arsenic.

After accounting for type of contract, area of working, and the

Table 2
Relative Rates (RR) with 95% confidence interval (IC95%) from the age adjusted Poisson regression according to categories of workers for malignant neoplasms of lung.

Type of worker	Number of deaths	RR	IC95%
All	63	-	-
Plastic area (SCD)	5	ref	
Fertilizer area (ANIC)	18	1.15	0.46-3.48
Contract workers	26	1.25	0.50-3.77
Contract workers not previously included (NPE)	14	1.47	0.55-4.65
Residence at 26.09.1976 in Manfredonia	13	ref	
Residence at 26.09.1976 elsewhere	50	3.42	1.89-6.64

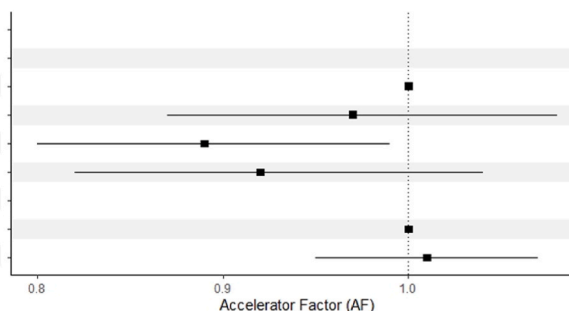


Fig. 1. Accelerator factor (AF) and 95% confidence intervals for overall mortality (total number of deaths = 576). Results from the age adjusted AFT model according to area of work and municipality of residence at 1976.

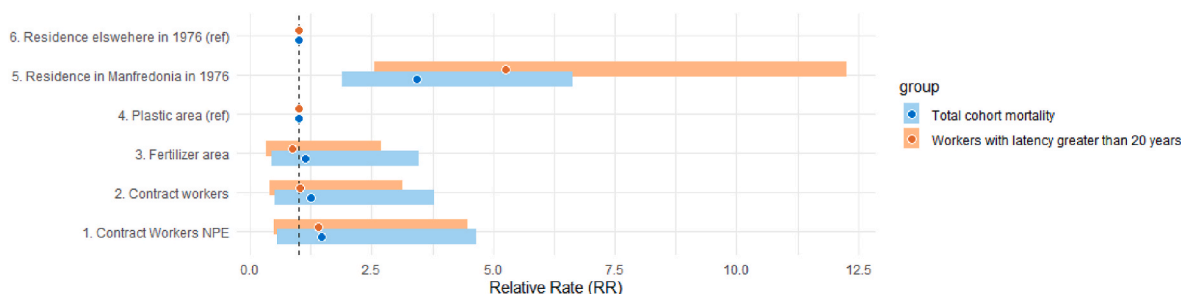


Fig. 2. Relative Rates (RR) for neoplasms respiratory and intrathoracic organs mortality with 95% confidence interval. Results from a Poisson regression model for the whole cohort and for a subgroup of workers accounting a latency greater than 20 years, according to area of work and municipality of residence at 1976.

confounding effect of age, workers residing in Manfredonia on the day of the accident showed a considerably higher lung cancer mortality rate than those residing elsewhere. The effect of residing in Manfredonia is higher when only workers surviving 20 years after the accident in 1976 are considered. This finding is consistent with Gianicolo et al. (2019), where increased rates for latency periods of 20 years were observed for lung cancer mortality. Overall, our results are in line with the monography published by IARC in 2012, which classifies arsenic and inorganic arsenic compounds as carcinogenic to humans (Group 1) and a cause of lung cancer (IARC, 2012).

Different ecological studies have been published on the population living in the area at high risk of environmental crisis of Manfredonia. The World Health Organisation performed an analysis for the period 1980–1994 using the Apulia Region as the reference, and showed an increased cumulative mortality risk among persons aged 0–74 years in the area (Martuzzi et al., 2002). An ecological study on the mortality of residents in Manfredonia from 1970 to 2013 compared directly age-adjusted mortality rates x 10,000 (ADR) and standardised mortality ratios (SMR), assuming the Apulia Region and the Province of Foggia as the reference populations (Gianicolo et al., 2016). General mortality rates decreased during the study period. ADR decreased from 92 to 52 among men, and from 70 to 39 among women. However, while in 1970 the overall mortality in Manfredonia was lower than in the Province and in the Region, from 1970 Manfredonia residents progressively lost their advantage over the regional average (men: from –20% to –10%; women: from –20% to +1.5%). According to the authors, this can be potentially related to both changes in the demographic composition due to migration flows and the actual deterioration in the health of the population following the accident at the plant (Gianicolo et al., 2016).

Some limitations should be considered while interpreting the results of this study. We do not have any information about the individual exposure, such as urinary arsenic levels. Knowing the levels of urinary arsenic would have resulted in more accurate exposure estimates than assuming the level of exposure based on the working area, the type of contract, and the estimates of soil contamination in different areas of the plants. Thus, misclassification of the exposure cannot be ruled out. In addition, in the model we consider the place of residence in September 1976. Thus, misclassification of the residence due to migration cannot be ruled out. However, persons who resided in Manfredonia at the time of the accident experienced the most acute phases of exposure in the hours immediately following the dispersion of arsenic in the residential area.

Another important limitation of this work is the lack of information about smoking habits. As reported in our previous publication (Gianicolo et al., 2019), using a bias quantification approach and an indirect adjustment following the method proposed by Axelson and Steenland allowed us to conclude that the confounding by smoking was likely to be minimal (Axelson and Steenland, 1988).

Despite the limitations, this is the first study that considers the complete cohort of individuals exposed to arsenic and a follow-up with a length of 45 years. In fact, this is the first study that reports results on

those workers who, even though involved in the decontamination activities, were not enumerated in the original cohort. For these workers no injuries or urinary arsenic above the thresholds set by the authorities were reported in the registry maintained by the Worker's Health and Safety Board, and this was used as exclusion criterion in previous studies. However, our analysis showed that this category of workers had shorter survival compared to the reference category of workers. It follows that raising thresholds prioritized clean-up activities over the health of workers.

A further strength of the study is the robustness of the information on the outcome, which was obtained from public offices.

The present study provides two key findings. Firstly, the increased relative mortality rates among workers who were more exposed to arsenic during the clean-up activities, already found in previous work, is confirmed by an acceleration factor, corresponding to the loss of 5 years of life for contract workers compared to plastics area workers. Secondly, the mortality rate of residents in Manfredonia began diverging from that of residents elsewhere 20 years after 1976, resulting in a mortality rate for lung cancer that was three times higher for residents than for other workers and nearly five times higher considering a latency greater than 20 years.

CRediT authorship contribution statement

R. Di Staso: Writing – original draft, Software, Formal analysis, Data curation. **D. Wollschläger:** Writing – review & editing, Validation. **M. Blettner:** Writing – review & editing. **E. Gianicolo:** Supervision, Project administration, Methodology, Conceptualization.

Declaration of competing interest

All of the authors declare that they do not have any competing interests.

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This manuscript is dedicated to the memory of Rosanna Giordano.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijheh.2024.114428>.

References

- Ambrosi, L., Amicarelli, V., 1982. L'incidente di Manfredonia: la cronistoria degli avvenimenti. *Med. Lavoro* 73 (Suppl. 3), 271–275.
- Axelson, O., Steenland, K., 1988. Indirect methods of assessing the effects of tobacco use in occupational studies. *Am. J. Ind. Med.* 13, 105–118.
- Bertazzi, P.A., Metelka, L., Riboldi, L., Guercilena, S., Foa, V., Dompe, M., 1982. Valutazione dell'arsenico urinario totale quale indicatore di esposizione professionale. *Med. Lavoro* 73 (Suppl. 3), 353–364.
- Casciani, M., Attias, L., 1999. Expert Testimony in Lawsuit Number 8437/96. *Court of Law, Foggia*, p. 206.
- Comba, P., Pirastu, R., 2004. Indagine Epidemiologica di Mortalità dei Lavoratori Presenti nello Stabilimento Enichem di Manfredonia il 26.9.1976 e nel Periodo Successivo. *Procura della Repubblica di Foggia*.
- Corsi, G., Rossi, A., Maestrelli, P., Bartolucci, G.B., Picotti, G., 1979. Rilievi su un episodio di intossicazione subacuta da composti arsenicali inorganici. *Med. Lavoro* 70, 282–291.
- Crowther, M.J., Royston, P., Clements, M., 2023. A flexible parametric accelerated failure time model and the extension to time-dependent acceleration factors. *Biostatistics* 24, 811–831.
- De Marchi, B., Biggeri, A., Cervino, M., Mangia, C., Malavasi, G., Gianicolo, E., Vigotti, M.A., 2017. A participatory project in environmental epidemiology: lessons from the Manfredonia case study. *WHO Public Health Pap.* 3, 321–327.
- Die Zeit, 1976. Arsen auf Mandelbäumen, *Die Zeit*.
- Foà, V., Colombi, A., Maroni, M., Buratti, M., Calzaferri, G., 1984. The speciation of the chemical forms of arsenic in the biological monitoring of exposure to inorganic arsenic. *Sci. Total Environ.* 34, 241–259.
- Gianicolo, E., Mangia, C., Cervino, M., Bruni, A., De Marchi, B., Biggeri, A., Porcu, R., Vigotti, M.A., 2016. Studio ecologico sulla mortalità dei residenti a Manfredonia dal 1970 al 2013. *Epidemiol. Prev.* 40, 281–289.
- Gianicolo, E., Mangia, C., Cervino, M., Bruni, A., Portaluri, M., Comba, P., Pirastu, R., Biggeri, A., Vigotti, M., Blettner, M., 2019. Long-term effect of arsenic exposure: results from an occupational cohort study. *Am. J. Ind. Med.* 62, 145–155.
- Heinrich-Ramm, R., Mindt-Prufert, S., Szadkowski, D., 2002. Arsenic species excretion after controlled seafood consumption. *J. Chromatogr., B: Anal. Technol. Biomed. Life Sci.* 778, 263–273.
- IARC, 2012. A review of human carcinogens. Part C: arsenic, metals, fibres, and dusts. Available from: <http://monographs.iarc.fr/ENG/Monographs/vol100C/index.php> (Lyon, France).
- Kleinbaum, D.G., Klein, M., 2012. *Survival Analysis A Self-Learning Text*. Third Edition. Springer, New York, NY.
- Kuss, O., Hoyer, A., 2021. A proportional risk model for time-to-event analysis in randomized controlled trials. *Stat. Methods Med. Res.* 30, 411–424.
- Lash, L., VanderWeele, T.J., Haneuse, S., Rothman, K.J., 2021. *Modern Epidemiology*, fourth ed. Wolters Kluwer.
- Mangia, C., Cervino, M., Gianicolo, E., 2018. Arsenic contamination assessment 40 years after an industrial disaster: measurements and deposition modeling. *Air Quality, Atmosphere & Health* 11, 1081–1089.
- Martuzzi, M., Mitis, F., Biggeri, A., Terracini, B., Bertollini, R., 2002. Ambiente e stato di salute nella popolazione delle aree ad alto rischio di crisi ambientale in Italia. *Epidemiol. Prev.* 26 (Suppl. 1), 1–53.
- Prencipe, D., Pellegrino, L., Gatta, R., Tomaiuolo, P., Tomaiuolo, M., Esposito, N., 1979. Intossicazione, acuta da arsenico: 150 casi. *Gazzetta Sanitaria Dauno-Lucana* 29, 43–56.
- R Core Team, 2023. R: A Language and Environment for Statistical Computing [Internet]. R Foundation for Statistical Computing, Vienna, Austria.
- Soleo, L., Assennato, G., Misciagna, G., Basso, A., Colella, A., Matera, L., Cassano, F., Martino, M.G., 1982a. L'incidente di Manfredonia: l'intervento del primo momento. *Med. Lavoro* 73 (Suppl. 3), 309–323.
- Soleo, L., Assennato, G., Misciagna, G., Colella, A., Basso, A., Matera, L., Scrutinio, D., Solimini, R., Gagliardi, T., 1982b. L'incidente di Manfredonia: l'indagine sanitaria a distanza. *Med. Lavoro* 73 (Suppl. 3), 324–335.
- Therneau, T., 2022. A package for survival analysis in R. R package version 3, 5–7.
- Wei, L.J., 1992. The accelerated failure time model: a useful alternative to the Cox regression model in survival analysis. *Stat. Med.* 11, 1871–1879.