Ann Ist Super Sanità 2022 | Vol. 58, No. 4: 81-84
DOI: 10.4415/ANN_22_04_0

COMMENTARY

Health in contaminated sites: the contribution of epidemiological surveillance to the detection of causal links

Pietro Comba* **and Roberto Pasetto**

Dipartimento Ambiente e Salute, Istituto Superiore di Sanità, Rome, Italy
**Retired*

Abstract
The search for cause-effect relationships is a central aspect of epidemiological surveillance programs applied to populations living close to contaminated sites. Here are described needs for assessing causality in using different epidemiological study designs in association with the aim of promoting environmental public health, where uncertainties should be considered under a precautionary driven approach.

Key words
- contaminated sites
- epidemiological monitoring
- causality
- precautionary principle
- environment and public health

Several scientific papers and reviews published in the last few years have dealt with the health impact of residence in the neighborhood of industrial contaminated sites. The journal *Annali dell'Istituto Superiore di Sanità* has contributed to this exercise by publishing studies concerning contaminated areas both in Italy and abroad [1-11]. The purpose of the present Commentary is to examine one specific and to some extent controversial issue, that is the contribution of epidemiological surveillance to the detection of certain or suspected causal agents amenable to preventive action.

In Europe, earlier industrialization and poor environmental management practices have left a legacy of thousands of contaminated sites and the issue of contaminated sites has been included among the priorities of the Declaration of the Sixth Ministerial Conference on Environment and Health of the European Region of WHO [12].

Estimates of the overall health impact of contaminated sites in Europe are not yet available. Nevertheless, a series of documents provided by the COST Action Industrial Contaminated Sites and Health Network (a collaborative effort coordinated by the Istituto Superiore di Sanità – ISS, that involved experts and practitioners in the environmental and health fields of about 30 countries in the years 2014-2018 www.icshnet.eu), reported some tools for the assessment of health risk and impact associated to single contaminated sites including how to develop and feed communication strategies. A compilation of reviews on the main approaches to study health risks and impacts from industrially contaminated sites resulting from the ICSHNet activities are documented within a collection of articles published in a special issue dedicated to "environmental health challenges from industrial contamination" [13, 14].

When considering both the available evidence of an ascertained health impact of contaminated sites on the population living in their surroundings and the aims and procedures of *ad hoc* epidemiological surveillance programs, a red thread connecting the two issues is undoubtedly represented by the search for cause-effect relationships.

There is consensus in the international scientific literature about the requirements that epidemiological studies should meet to corroborate or confute a specific etiological hypothesis concerning the association between environmental exposures and health outcomes, and the criteria for such evaluation have been defined. A comprehensive discussion of such issues is included within the latest edition of the preamble of the IARC monographs on the evaluation of carcinogenic risk to humans [15].

The availability of a body of epidemiological evidence in assessing causal hypotheses has been thoroughly debated. The heart of the matter is that the possibility that bias, confounding or misclassification of exposure

Address for correspondence: Roberto Pasetto, Dipartimento Ambiente e Salute, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. E-mail: roberto.pasetto@iss.it.

and outcome that could explain the observed association should be ruled out with reasonable confidence. This generally implies that the epidemiological evidence be based on analytical studies adopting a cohort, case-control or other study designs with direct observation of the individual study subjects, rather than on geographic studies where the unit of observation is represented by spatially aggregated data [16]. Nevertheless, in the context of contaminated sites, optimal study designs for contributing to assessing causality are often infeasible due to scarce resources in economic, technical and temporal terms. In fact, analytical epidemiological studies are quite complex, generally designed to respond to single specific research questions, require years to be finished and are always expensive.

Epidemiological study models applied in contaminated sites are often based on descriptive approaches mostly useful for generating hypotheses, while analytic studies are mainly used for testing hypotheses, though each type of study can be used for both purposes [17].

Some study designs applicable in contaminated sites can potentially be used for epidemiological surveillance, that is, the capacity to assess the evolution of health risk and impact over time. Such models are principally based on cross-sectional area-based designs, while the best option among analytical designs is essentially based on a (residential) cohort approach that can be eventually modelled by combining different designs (e.g., with a nested biomonitoring study for a fine-grained evaluation of chemical exposure, if appropriate) [4, 14].

The key points to be considered in deciding on epidemiological study designs and their potential application to a given contaminated site are the following:

- the need to set goals before selecting the study design. This point, apparently obvious, is not always fulfilled since it is not rare to see chosen a study design before setting the goals because of previous knowledge and confidence with that design;
- the need to assess the feasibility of the study design in a given context;
- the validity of exposure assessment, considering that it is essential in weighing the value of results, in particular, if the study is chosen to verify a given hypothesis;
- the fact that "before initiating a new epidemiological study in a contaminated site, it is important to be certain that the expected goals are attainable and that the research itself will support – rather than interfere with – pursuit of needed public health actions" [18];
- the fact that "where data systems are in place, risk assessment combined with epidemiological surveillance may often be the most efficient, informative response to the exposure event in a contaminated site" [18].

As described above, the most common study design adopted in contaminated sites is represented by the analysis of current health information systems or data from pathology registries (e.g., cancer registries), often based on aggregated data (geographic or micro-geographic approaches).

In Italy, for example, an epidemiological surveillance project (Progetto SENTIERI) is being applied to monitor cause-specific mortality and hospitalization, cancer incidence and prevalence of malformations at birth in 46 among the main Italian sites of interest for remediation activities (almost all of them, with few exemptions mainly due to feasibility aspects) [19, 20].

In this frame, it should be stressed that in SENTIERI both environmental and health data are aggregated at the municipality level (around 310 out of a total of about 8,000 in Italy at large). Municipalities are characterized in terms of the presence/absence of the main sources of contaminants. For some contaminated sites, health outcomes are defined considering priority index contaminants identified through data and information collection on contamination, followed by an indepth analysis of intrinsic toxicological profiles of single contaminants and the likelihood of exposure for the population [20].

Some authors have criticized the geographic epidemiological study design adopted in SENTIERI, stating that "Establishing causal links between specific environmental exposures and complex, multifactorial diseases and conditions is a challenging endeavor and requires stronger evidence than the one provided by studies based on aggregated data" [21].

Soskolne, *et al.* [22] have criticized this last paper speaking of research financially supported by special interests as a common and worrisome practice.

Since, in this frame, we are dealing with epistemological, not deontological, issues, it seems appropriate to refer to the underlying selected study design in terms of the methodology of scientific research.

Some authors suggest adopting a consequential epidemiological approach that extends beyond etiologic studies to test and document solutions [23]. Galea [24] stated that the purpose of epidemiology has to do with health organization and disease reduction, where methods are tools convenient only insofar as they help us get there. Brownson, *et al.* [25] had previously raised the point that the natural observation unit is made not at the individual level but rather at multiple levels of an ecologic framework. This last point perfectly fits with the contribution of epidemiological surveillance based on aggregate data to causal inference: "Epidemiological surveillance should integrate general systems of observation at macro-area level with particular systems of observation at local level... Regulatory guidelines and adequate financial support would make possible the implementation of cohort or other analytical studies apt to pursue the epidemiological characterization of a given area" [26].

Epidemiological evidence generated by health information systems available at different levels of geographic aggregation may contribute to detecting causal links in the frame of an integrated multidisciplinary approach. The "epidemiological characterization" of a given contaminated area resulting from the application of different study models is apt to assess causal links at a local level and can be seen as analogous to "triangulation" in aetiological epidemiology, that is the practice of obtaining more reliable answers to research questions through integrating results from several different approaches, where each approach has different key sources of potential bias that are unrelated to each other [27].

For the evaluation of causal links, the gold standard remains the aforementioned IARC Monograph paradigm. In particular settings, geographic epidemiological methods and case series can constitute sufficient evidence of cancer risk in humans, as it was for fluoroedenite, the asbestiform fibre naturally occurring in soils at the slopes of the Etna Volcano in Sicily initially reported by ISS (see Bruno, *et al.* 2017 for a thorough reconstruction of the whole issue) and subsequently recognized by IARC as carcinogenic to humans with sufficient evidence [28].

The publication of the WHO Report "Urban redevelopment of contaminated sites" [29] has recently contributed to the increase in collective awareness about the relevance of the health impact of contaminated sites in Europe and the need to develop appropriate strategies of monitoring and intervention. Among the key messages, it is important to translate scientific evidence into practical action and provide competent authorities with financial resources and operational tools to evaluate the success (in terms of health) of remediation interventions.

Epidemiological surveillance may thus contribute to priority setting for prevention and health promotion, assessment of the decreased occurrence of diseases regarded as being of etiological interest (based on *a priori* knowledge), with a specific focus on vulnerable subpopulations [19, 20].

Geographic epidemiological studies, conducted in the context of a permanent updating of environmental characterization of the contaminated sites, have the potential to indicate both preventive action of ascertained effectiveness and, in front of uncertainties, interventions justified in terms of the precautionary principle. Adopting a precautionary-driven approach is of great interest considering promoting public health in contaminated sites, especially in those areas where polluting industrial activities have operated for decades. In these places, whatever study design recently implemented would be unable to assess causal links without any uncertainties. Nevertheless, in such sites, the final aims of epidemiological studies from a public health perspective should be to promote actions to prevent future risks, that is, considering partial and uncertain evidence on observed past and present risks as signals (i.e., facts) when giving recommendations for interventions.

Another final aspect being highlighted is that epidemiological surveillance studies and systems, if appropriately designed, can be used not only for assessing the risks and impacts associated with contamination but also for considering issues arising from an environmental justice perspective [30].

Communities living where polluting human activities are located often show disadvantages associated with exposure to noxious environmental contaminants and socioeconomic deprivation [31]. For such communities, there is a need to assess inequalities and inequities associated with contaminated sites in terms of distributive and procedural injustice [32]. National assessments based on country surveillance systems like SENTIERI, can thus be designed to assess the presence of distributive injustices at a country level and by geographical macro-area. This means identifying communities close to contaminated sites where the potential exposure to harmful contaminants is combined with the presence of socioeconomic deprivation and with health profiles showing higher than expected observed risks [33]. The primary aim of such efforts is thus not to assess causal links between environmental exposure, socioeconomic deprivation and health profiles, but to identify the communities with an overburden of fragilities, while local surveillance systems can be developed to assess the contribution of different factors to health risks thus allowing specific actions to reduce them.

In different contexts, e.g., toxic torts litigations or criminal prosecution, the aim may be to pursue the identification of causal links, respectively "more likely than not" and "beyond any reasonable doubt". This may occur in some particular settings. For public health goals, though, the priority is to throw light on complex causal webs with the aim of reducing the likelihood of occurrence of environmentally-related adverse health effects with different degrees of credibility.

Conflict of interest statement

No potential conflict of interest.

Received on 1 September 2022.
Accepted on 6 September 2022.

REFERENCES

1. Comba P, Ricci P, Iavarone I, Pirastu R, Buzzoni C, Fusco M, Ferretti S, Fazzo L, Pasetto R, Zona A, Crocetti E; ISS-AIRTUM Working Group for the study of cancer incidence in contaminated sites. Cancer incidence in Italian contaminated sites. Ann Ist Super Sanità. 2014;50(2):186-91. doi: 10.4415/ANN_14_02_13
2. Bruno C, Tumino R, Fazzo L, Cascone G, Cernigliaro A, De Santis M, Giurdanella MC, Nicita C, Rollo PC, Scondotto S, Spata E, Zona A, Comba P. Incidence of pleural mesothelioma in a community exposed to fibres with fluoro-edenitic composition in Biancavilla (Sicily, Italy). Ann Ist Super Sanità. 2014;50(2):111-8. doi: 10.4415/ANN_14_02_02
3. Granieri A. Community exposure to asbestos in Casale Monferrato: from research on psychological impact to a community needs-centered healthcare organization. Ann Ist Super Sanità. 2015;51(4):336-41. doi: 10.4415/ANN_15_04_14
4. Pasetto R, Martin-Olmedo P, Martuzzi M, Iavarone I. Exploring available options in characterising the health impact of industrially contaminated sites. Ann Ist Super Sanità. 2016;52(4):476-82. doi: 10.4415/ANN_16_04_03
5. Ancona C, Bauleo L, Biscotti G, Bocca B, Caimi S, Cruciani F, Di Lorenzo S, Petrolati M, Pino A, Piras G, Pizzabiocca A, Rabbiosi S, Ruggieri F, Salatino C, Alimonti A, Forastiere F, ABC Study Group. A survey on lifestyle and level of biomarkers of environmental exposure in residents in Civitavecchia (Italy). Ann Ist Super Sanità. 2016;52(4):488-94. doi: 10.4415/ANN_16_04_05
6. Harari R, Harari F, Forastiere F. Environmental nickel exposure from oil refinery emissions: a case study in Ecuador. Ann Ist Super Sanità. 2016;52(4):495-9. doi:

10.4415/ANN_16_04_06
7. Soskolne CL. Ethical aspects of epidemiological research in contaminated sites. Ann Ist Super Sanità. 2016;52(4):483-7. doi: 10.4415/ANN_16_04_04
8. Bustaffa E, Minichilli F, Nuvolone D, Voller F, Cipriani F, Bianchi F. Mortality of populations residing in geothermal areas of Tuscany during the period 2003-2012. Ann Ist Super Sanità. 2017;53(2):108-17. doi: 10.4415/ANN_17_02_06
9. Murtas R, Andreano A, Greco MT, Tunesi S, Russo AG. Cancer incidence and congenital anomalies evaluation in the contaminated sites of Sesto San Giovanni – the SENTIERI Project. Ann Ist Super Sanità. 2019;55(4):345-50. doi: 10.4415/ANN_19_04_07
10. Gessoni F, Macciò S, Barbiellini Amidei C, Simonato L. Study on the health status of the population living in Marghera (Venice, Italy) through the use of a longitudinal surveillance system. Ann Ist Super Sanità. 2020;56(2):157-67. doi: 10.4415/ANN_20_02_05
11. De Rocchi D, Zona A, Tumino R, Egidi V, Pasetto R. Mortality temporal trends and cancer incidence profiles of residents in the petrochemical industrially contaminated town of Gela (Sicily, Italy). Ann Ist Super Sanità. 2021;57(2):174-82. doi: 10.4415/ANN_21_02_10
12. WHO Regional Office for Europe. Declaration of the Sixth Ministerial Conference on Environment and Health. WHO; 2017. Available from: www.euro.who.int/__data/assets/pdf_file/0007/341944/OstravaDeclaration_SIGNED.pdf.
13. Iavarone I, Pasetto R (Eds). Environmental health challenges from industrial contamination. Epidemiol Prev. 2018;42(5-6 Suppl. 1).
14. Colles A, Ardeleanu ER, Cendeias C, Ranzi A, Demeter Z, Hofer A, Kowalska M, Makris KC, Arrebola JP, Schoeters G, Hough R, Pérez-Carrascosa FM, Iavarone I, Martin-Olmedo P, Kalantzi OI, Ancona C, Ancona C, Pasetto R, Fletcher T, Hoek G, de Hoogh K. Human biomonitoring as a tool for exposure assessment in industrially contaminated sites (ICSs). Lessons learned within the ICS and Health European Network. Epidemiol Prev. 2019;43(4):249-59. doi: 10.19191/EP19.4.A03.070
15. International Agency for Research on Cancer, World Health Organizatoin. IARC Monographs on the identification of carcinogenic hazards to human. Preamble. Lyon, France: IARC, WHO; 2019. Available from: https://monographs.iarc.who.int/wp-content/uploads/2019/07/Preamble-2019.pdf.
16. Morgenstern H. Ecologic studies. In Rothman KJ, Greenland S, Lash TL (Eds). Modern epidemiology. 3th Ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008. pp 511-32.
17. De Sario M, Pasetto R, Vecchi S, Zeka A, Hoek G, Michelozzi P, Iavarone I, Fletcher T, Bauleo L, Ancona C. A scoping review of the epidemiological methods used to investigate the health effects of industrially contaminated sites. Epidemiol Prev. 2018;42(5-6S1):59-68. doi: 10.19191/EP18.5-6.S1.P059.088
18. Savitz DA. When is epidemiological research a helpful response to industrial contamination? Epidemiol Prev. 2018;42(5-6S1):89-92. doi: 10.19191/EP18.5-6.S1.P089.091
19. Zona A, Pasetto R, Fazzo L, Iavarone I, Bruno C, Pirastu R, Comba P (Eds). SENTIERI epidemiological study of residents in national priority contaminated sites. 5th Report. Epidemiol Prev. 2019;43(2-3 Suppl. 1).
20. Zona A, Fazzo L, Pasetto R, Benedetti M, Bruno C, De Santis M, Iavarone I (Eds). SENTIERI epidemiological study of residents in national priority contaminated sites. Sixth report. Epidemiol Prev. 2022. In press.
21. Ciocan C, Franco N, Pira E, Mansour I, Godono A, Boffetta P. Methodological issues in descriptive environmental epidemiology. The example of study Sentieri. Med Lav. 2021;112(1):15-33. doi: 10.23749/mdl.v112i1.10099
22. Soskolne CL, Kramer S, Ramos-Bonilla JP, Mandrioli D, Sass J, Gochfeld M, Cranor CF, Advani S, Bero LA. Toolkit for detecting misused epidemiological methods. Environ Health. 2021;20(1):90. doi: 10.1186/s12940-021-00771-6
23. Frumkin H. Work that matters: toward consequential environmental epidemiology. Epidemiology. 2015;26(2):137-40. doi: 10.1097/EDE.0000000000000240
24. Galea S. An argument for a consequentialist epidemiology. Am J Epidemiol. 2013;178(8):1185-91. doi: 10.1093/aje/kwt172
25. Brownson RC, Hartge P, Samet JM, Ness RB. From epidemiology to policy: toward more effective practice. Ann Epidemiol. 2010;20(6):409-11. doi: 10.1016/j.annepidem.2010.03.003
26. Pasetto R, Pirastu R. Studio di coorte nel contesto dei siti inquinati. In: Bianchi F, Comba P (eds). Indagini epidemiologiche nei siti inquinati: basi scientifiche, procedure metodologiche e gestionali, prospettive di equità. Roma: Istituto Superiore di Sanità; 2006. (Rapporti ISTISAN 06/19).
27. Lawlor DA, Tilling K, Davey Smith G. Triangulation in aetiological epidemiology. Int J Epidemiol. 2016;45(6):1866-86. doi: https://doi.org/10.1093/ije/dyw314
28. IARC Monographs. Some nanomaterials and some fibres. IARC monographs on the evaluation of carcinogenic risks to humans; volume 111; 2017. Available from: https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Some-Nanomaterials-And-Some-Fibres-2017.
29. WHO Regional Office for Europe. Urban redevelopment of contaminated sites: a review of scientific evidence and practical knowledge on environmental and health issues. Copenhagen: WHO; 2021. Available from: https://apps.who.int/iris/handle/10665/340944.
30. Pasetto R, Iavarone I. Environmental Justice in industrially contaminated sites. From the development of a national surveillance system to the birth of an international network. In Mah A, Davis T (eds): Toxic truths: environmental justice and citizen science in a post-truth age. Manchester University Press; 2020. pp. 199-219. Available from: www.manchesteropenhive.com/view/9781526137005/9781526137005.00023.xml.
31. Di Fonzo D, Fabri A, Pasetto R. Distributive justice in environmental health hazards from industrial contamination. A systematic review of national and near-national assessments of social inequalities. Soc Sci Med. 2022;297:114834. doi: 10.1016/j.socscimed.2022.114834
32. Pasetto R, Marsili D, Rosignoli F, Bisceglia L, Caranci N, Fabri A, Innocenti-Malini G, Melis G, Minardi V, Zengarini N, Zona A, Mannarini T. Promozione della giustizia ambientale nei siti industriali contaminati. Epidemiol Prev. 2020;44(5-6). doi: 10.19191/EP20.5-6.A00
33. Pasetto R, Di Fonzo D, Porcu R, De Santis M, Zona A. Environmental health inequalities among municipalities affected by contaminated sites in Italy. Environmental Justice 2021. Ahead of print. doi: 10.11089/env.2021.0068