DOI: 10.1002/ajim.23154

AMERICAN JOURNAL OF INDUSTRIAL MEDICINE WILEY

LETTER TO THE EDITOR

Re Ferrante et al (2020). Mortality and mesothelioma incidence among chrysotile asbestos miners in Balangero, Italy: A cohort study

To the Editor,

We read with great interest the study by Ferrante et al[1] on mortality and mesothelioma incidence among chrysotile asbestos miners in Balangero, Italy, particularly as a paper on the same cohort was published only 2 years ago, by a different Italian research group, notably with slightly longer follow-up albeit published earlier.[2] While Ferrante et al[1] explain in their introduction that the methodological approach of the earlier study inspired them to reanalyse the data, considerable differences in analyzed mortality and exposure data between the two papers are not (thoroughly) discussed in their manuscript. We would like to ask Ferrante et al[1] to help explain and reconcile these differences for the reader and the research community.

1. Using similar inclusion criteria, unsurprisingly both studies demonstrate similar numbers of cohort members and person-years under risk (p-years); n = 974 and 35 362 p-years[1] compared with n = 1056 and 37 471 p-years.[2] Follow-up in both studies appears to start in 1946 and continues to 31 May 2013,[1] or 31 December, 2014,[2] resulting in a relatively low difference in p-years of about 6%. Both papers differ, however, considerably in the numbers of observed deaths, with an increase from 573 to 722 overall deaths (about 26%) and from 40 to 53 for lung cancer deaths (about 33%), between Ferrante et al[1] and Pira et al.[2] The obvious explanation is that standardized mortality ratios (SMR) in Ferrante et al[1] (Table 2) were presented only for the time period 1965 to 2013 (based on 21 175 p-years). Nevertheless, in the Poisson regression risk analyses (Table 4),[1] said to be based on the number of cases of the entire follow-up period, they list only a total of 41 lung cancer deaths, so that additional explanation for this difference is still needed.

2. From the original paper on this cohort study, it becomes clear that cumulative exposure was estimated from environmental measurements carried out from 1969 onward, and that for earlier periods exposure estimation was recreated based on working conditions.[3] Pira et al[2] also state that fiber counts were first carried out in 1969 and confirmed the simulations for the period between 1946 and 1969. Ferrante et al[1] claim that fiber concentrations had been performed during four surveys conducted between 1967 and 1970. Since 1975, systematic monitoring was carried out by the mining company itself. Ferrante et al[1] apparently used 1099 area and 484 personal measurements and the earlier mentioned simulation studies to estimate exposure for the cohort members. Although referring to another publication,[4] it remains unclear to the reader whether the methods and data used by Ferrante et al[1] were actually different from the earlier exposure assessment described by Piolatto et al[3] and by Pira et al[2] or, instead, whether different cutoff points were used in the epidemiological analyses.

3. Both papers investigate in more detail the mortality from lung cancer by presenting SMRs for the cohort vs the general population. Results are almost identical: SMR = 1.14 (95% confidence interval [CI], 0.81-1.55)[1] and 1.16 (CI, 0.87-1.52).[2] However, when they present analyses based on cumulative dust exposure (fiber/mL-y) marked differences are seen. Pira et al[2] present SMRs of 0.82 (CI, 0.44-1.40), 1.46 (CI, 0.89-2.26), and 1.25 (CI, 0.76-1.93) for exposure categories less than 100, 100 to less than 400, and 400+ compared with an external reference without exposure.[2] Ferrante et al[1] use the lowest exposure category of less than 27 fiber/mL-y as a reference category and present SMRs of 2.3 (CI, 0.8-6.8) and 2.6 (0.8-8.8) for the two higher tertiles of exposure, categorized as 27 to 345 and 346+.[1] This suggests a deficit of lung cancer deaths among cohort members with low exposure levels, indicated in Table SIII, with a SMR of 0.78 (CI, 0.25-1.82) for the low-dose group compared with the Piedmont reference population rates (of 1965-2013); but this does not fully explain the difference between the two papers.[1,2] The authors would help the reader tremendously by harmonizing exposure categories between the two studies, and by showing both cohort-internal and external comparisons, to help to understand the extent to which the differences arise from different data (cohort and exposure), different statistical approaches, and different follow-up time frames.

4. Even more dramatic differences occur in the comparison of mesothelioma data between the two papers. These are presented as combined pleural and peritoneal malignancies in Ferrante et al[1] (n = 6 + 2 deaths [1965-2013]; n = 6 mesothelial incident cancer cases [1990-2012]),[1] and as pleural malignancies only by Pira et al[2] (n = 7 deaths; ie, one additional death of pleural cancer and omitting two deaths from cancer of the peritoneum).[2] Although Ferrante et al[1] explain they followed an a priori defined protocol, it would have been helpful to show alternative analytic approaches for comparison. Noteworthy are unexplained differences between these two analyses; for example, Pira et al[2] have grouped three pleural cancer deaths into an exposure category of less than 10 years duration, while there is only one case in the less than 11 years exposure-duration category in

Ferrante et al[1] (Table 3). Which of the analytical decisions cause the differences is again not self-explanatory to the reader of both papers but should be explained for full transparency.

We appreciate the authors' support in leaving no questions unanswered in the comparison of two papers based on the virtually same cohort material, for the sake of clarity and transparency among scientists, so that debate can focus on the science of exposure and illness rather than be pulled into unedifying corners that serve only to prolong nonscientific disputes.[5]

ETHICS STATEMENT

The authors performed the work as staff members at the above-mentioned institutions. No ethical approval was required.

DISCLAIMER

Where authors are identified as personnel of the International Agency for Research on Cancer/World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer/World Health Organization.

Joachim Schüz PhD[1]
Hans Kromhout PhD[2]

[1]*International Agency for Research on Cancer (IARC/WHO), Section of Environment and Radiation, Lyon, France*
[2]*Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands*

Correspondence
Joachim Schüz, PhD, International Agency for Research on Cancer (IARC/WHO), Section of Environment and Radiation, 150 cours Albert Thomas, F-69372 Lyon, France.
Email: schuzj@iarc.fr

Joachim Schüz and Hans Kromhout contributed equally to the writing of this letter to the editor.

ORCID

Joachim Schüz http://orcid.org/0000-0001-9687-2134
Hans Kromhout https://orcid.org/0000-0002-4233-1890

REFERENCES

1. Ferrante D, Mirabelli D, Silvestri S, et al. Mortality and mesothelioma incidence among chrysotile asbestos miners in Balangero, Italy: a cohort study. *Am J Ind Med*. 2020;63(2):135-145.
2. Pira E, Romano C, Donato F, Pelucchi C, Vecchia C, Boffetta P. Mortality from cancer and other causes among Italian chrysotile asbestos miners. *Occup Environ Med*. 2017;74(8):558-563.
3. Piolatto G, Negri E, La Vecchia C, Pira E, Decarli A, Peto J. An update of cancer mortality among chrysotile asbestos miners in Balangero, northern Italy. *Br J Ind Med*. 1990;47(12):810-814.
4. Silvestri S, Magnani C, Calisti R, Bruno C. The Experience of the Balangero Chrysotile Mine in Italy: Health Effects Among Workers Mining and Milling Asbestos and the Health Experience of Persons Living Nearby. In: Nolan RP, Langer AM, Ross M, Vicks FJ, Martin RF, eds. *The Health Effects of Chrysotile Asbestos. Contribution of Science to Risk-management Decisions*. Toronto, Canada: The Canadian Mineralogist special publication, Mineralogical Association of Canada; 2001:177-186.
5. Michaels D. *Doubt is Their Product*. Oxford, UK: Oxford University Press; 2008.