Comment on the paper "Boffetta et al. Validation of the diagnosis of mesothelioma and BAP1 protein expression in a cohort of asbestos textile workers from Northern Italy. Ann Oncol 2018; 29(2): 484-489"

D. Consonni[1*], C. Mensi[1]

[1]Epidemiology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

(*E-mail: dario.consonni@unimi.it)

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To the Editor,

in a recent paper on diagnostic evaluation of 127 deaths from pleural or peritoneal cancers (or malignant mesotheliomas, MM) among workers in an asbestos textile factory in Piedmont, Italy, sensitivity and specificity of the Regional Mesothelioma Registry of Piedmont (RMRP) were calculated [1]. We argue that those calculations are incorrect.

For 35 cases pathology samples were retrieved and MM diagnosis confirmed by morphological and immuno-histological (IHC) revision. A total of 76 cases were also listed in the RMRP (56 certain, 19 probable/possible and 1 non-MM). The RMRP, established in 1993, is part of a national mesothelioma registry (ReNaM, Registro Nazionale Mesoteliomi) organized as a network of regional registries which follow the same procedures for classifying the available diagnostic evidence [2-3].

The Authors crossed RMRP information with their revised diagnoses, and stated: "If we consider our diagnostic validation as gold standard, the sensitivity of the classification of the Registry (certain confirmed mesothelioma versus other) was 83% and the specificity 34% (results not shown in detail)" [1, p. 486]. The latter finding, if true, would be of major concern, implying 66% of false positives in the RMRP.

Based on figures in the paper [1, p.486], we reconstructed Table 1, which compares revised and RMRP diagnoses. Considering all MM, including probable and possible MM (main ReNaM statistics are based on all cases), sensitivity is (29+6)/35 = 100%. The two central columns are not informative, because no diagnostic validation was performed; considering all those cases as "non-MM", considering that RMRP classified 40 (= 27+13) as MM, is an evident mistake [1]. Strictly speaking, also the fourth column cannot be used in calculating specificity (the 5 non-MM cases did not undergo diagnostic revision). However, given that 3 were epithelial cancers, 1 was a non-neoplastic disease, and 1 had been classified as non-MM by the RMRP, it is plausible that IHC would have confirmed them as "true non-MM". In this case, specificity would be (1+4)/5 =100%. The 4 cases missing in the RMRP must be counted as non-MM, because they are not the target of MM registries (although some of them may be recorded because suspected diagnoses were scrutinized). Reasons for the high number of missing cases in the RMRP are: 1) death before 1993 (31 cases); 2) MM diagnosed in workers emigrated outside Piedmont (no information available); 3) diagnosis of non-MM (no information available except for the 4 cases noted above).

In conclusion, contrarily to what stated in the paper [1], a high quality of the RMRP emerges from the available data. Finally, we note that the Authors of the paper (on mesothelioma) have declared no conflict of interests [1]. This is odd, given that two of the Authors in a recent paper (on mesothelioma) reported "Consulting or Advisory Roles" for 4 large companies and one Author declared "Other relationships" with law offices [4]. These companies and law offices are currently involved in litigations regarding asbestos-related diseases.

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References

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Table 1. Comparison of revised and Regional Mesothelioma Registry of Piedmont (RMRP) diagnoses, 1963-2013

RMRP diagnoses	Revised diagnoses				Total
	IHC-MM	Registry-based MM	DCO-MM	Non-MM	
Certain MM	29	27		0	56
Probable/Possible MM	6	13		0	19
Non-MM	0	0	0	1	1
Missing	0	47		4	51
Total	35	33	54	5	127

DCO, death certificate only; IHC-MM, immunohistochemistry confirmed malignant mesothelioma cases; MM, malignant mesothelioma