Assemblea AFEVA 2015

Il contributo degli studi sull'amianto dell'Istituto Ramazzini

Daniele Mandrioli

Direttore

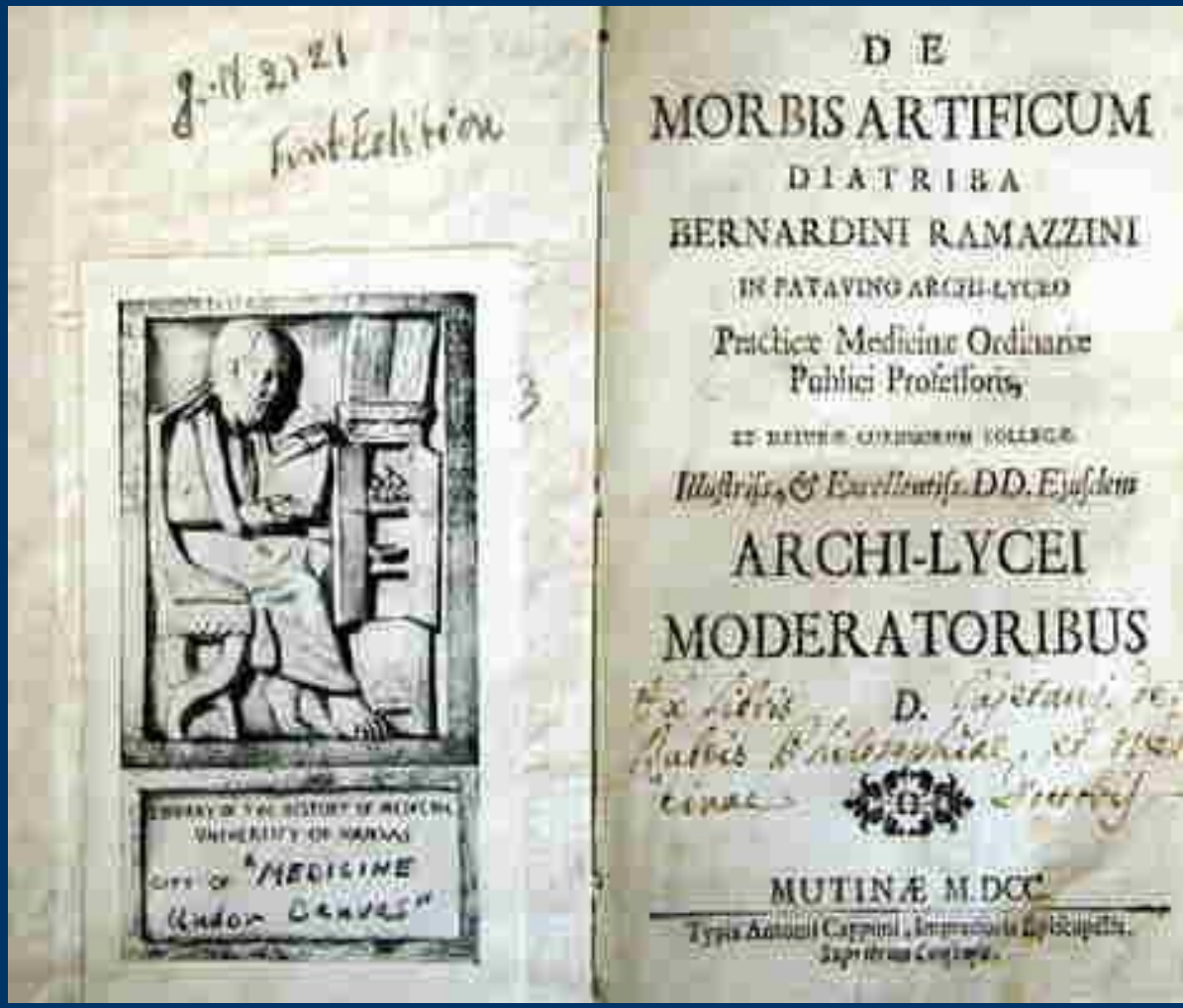
Centro di Ricerca sul Cancro Cesare Maltoni

Istituto Ramazzini

12 Aprile 2025

Bernardino Ramazzini

Carpi, 1633 – Padua, 1714



De morbis artificum diatriba, (1700)

L'Istituto Nazionale "B. Ramazzini"

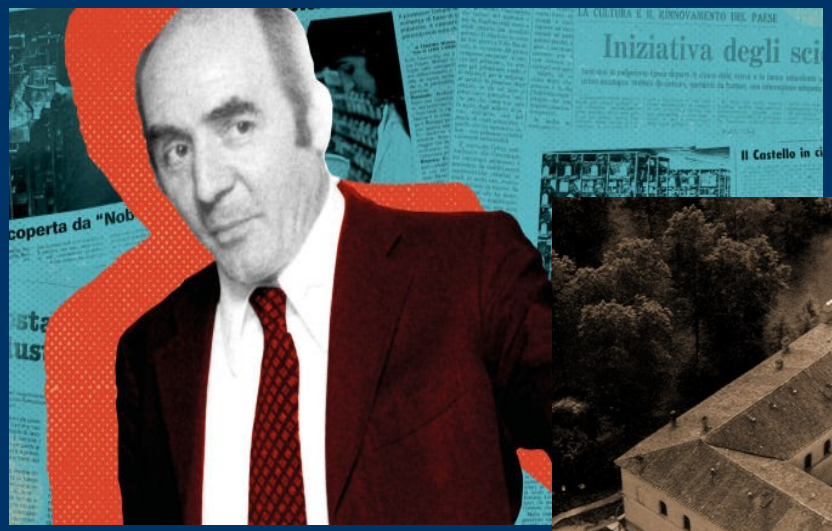
- L'Istituto Nazionale per lo studio e il controllo dei tumori e delle malattie ambientali "B. Ramazzini" è una cooperativa sociale ONLUS costituita nel 1987 che conta più di 35.000 soci

L'Istituto Nazionale "B. Ramazzini"

➢ Scopi dell'Istituto Ramazzini:

- l'attuazione di iniziative per la prevenzione di tumori attraverso una strategia basata sulla promozione della ricerca scientifica
- la formazione di personale specializzato
- la diffusione dell'informazione sui rischi cancerogeni ambientali e professionali
- la messa in atto di programmi clinici di diagnosi precoce dei tumori

CENTRO DI RICERCA SUL CANCRO CESARE MALTONI



CENTRO DI RICERCA SUL CANCRO CESARE MALTONI

- Con oltre 200 composti studiati per la loro cancerogenicità', è il secondo centro nel mondo per numero di sostanze studiate dopo il US National Toxicology Program
- Cancerogenicità:
  - Chiara evidenza (44%)
  - Evidenza borderline (16%)
  - No evidenza di cancro (40%)

James Huff, *Chemicals studied and evaluated in long-term carcinogenesis bioassays by both the Ramazzini Foundation and the National Toxicology Program: in tribute to Cesare Maltoni and David Rall*, in *Annals of the New York Academy of Sciences*, vol. 982, 1° dicembre 2002, pp. 208–230.

Il contributo degli studi sperimentali dell'IR su tutti i tipi di amianto

- **Saggi sperimentali su roditori: validità per l'identificazione dei rischi per l'uomo**
- **Condivisione di numerose basi genetiche, farmacologiche, tossicologiche, e risposte cancerogene**
- **Riproducibilità di risultati condotti indipendentemente in diversi laboratori**
- **Agenti dimostrati cancerogeni per l'uomo che risultano esserlo altrettanto in animali sperimentali quando adeguatamente studiati**
- **Strumento essenziale di prevenzione primaria poiché' permettono di testare la tossicità delle sostanze prima che queste possano provocare danni per la salute a uomini, donne e bambini**

Mandrioli D, Silbergeld EK. Evidence from Toxicology: The Most Essential Science for Prevention. *Environ Health Perspect*. 2016;124(1):6-11. doi:10.1289/ehp.1509880

Carcinogenesis bioassays: study duration and biological relevance. Food Chem Toxicol. 2001 Jul;39(7):739-44. Haseman J1, Melnick R, Tomatis L, Huff J.

Gift JS1, Caldwell JC, Jinot J, Evans MV, Cote I, Vandenberg JJ. Scientific considerations for evaluating cancer bioassays conducted by the Ramazzini Institute. Environ Health Perspect. 2013 Nov-Dec;121(11-12):1253-63.

Il contributo degli studi sperimentali dell'IR su tutti i tipi di amianto

WORLD HEALTH ORGANIZATION

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

Non-occupational Exposure to Mineral Fibres

Edited by

J. Bignon, J. Peto and R. Saracci

IARC Scientific Publications No. 90

International Agency for Research on Cancer, Lyon, France

1989

RECENT RESULTS OF CARCINOGENICITY BIOASSAYS OF FIBRES AND OTHER PARTICULATE MATERIALS

C. Maltoni & F. Minardi

Institute of Oncology, Bologna, Italy

Summary. Different types of natural, commercial and modified asbestos fibres were tested in a highly standardized manner by peritoneal injection into rats and mice in order to assess their carcinogenicity.

Differences in mesotheliomatogenic effect were found between the various materials tested. Of particular interest is the finding that treatment of the fibres with phosphorus oxychloride and heating to 300°C markedly reduces the carcinogenicity of chrysotile fibres.

Introduction

A systematic and integrated study involving long-term experimental bioassays on particulate materials was started in January 1981 at the Bologna Institute of Oncology and is still in progress. The study covers a variety of fibrous and non-fibrous, natural and man-made materials, present in the occupational and/or general environment. Some of the materials studied are of major industrial importance.

The study is aimed at:

- identifying new potentially carcinogenic materials;
- assessing, in quantitative terms, the level of carcinogenic risk of a given material, and comparing the risks represented by different materials (assessment of the relative carcinogenic risk);
- helping to predict the target organs;
- defining the role in carcinogenesis of the physical and chemical characteristics of the test compounds.
- determining the role of different biological and experimental factors affecting the neoplastic response and, consequently, shedding some light on the pathogenesis of the possible oncogenic effects;
- helping to reconstruct the natural history of the tumours which may be induced by the test compounds.

Information on test materials and animals and the experimental procedures is given in Table 1. In view of the aims of the study, the experimental conditions are strictly standardized.

Table 4. Final results of tests on various types of natural asbestos and asbestos-cement (experiment BT 2101)[a]

Material	Peritoneal mesotheliomas		
	Tumour-bearing animals		Average latency time (weeks)
	No.	%	
Crocidolite (UICC)	39	97.5	59.5
Chrysotile (Canada, UICC)	32	80.0	92.2
Chrysotile (Rhodesia, UICC)	33	82.5	89.7
Chrysotile (California)	29	72.5	85.3
Amosite (UICC)	36	90.0	66.7
Anthophyllite (UICC)	35	82.5	73.3
Asbestos-cement	21	52.5	99.7
Water (controls)	0	-	-

[a]Sprague-Dawley rats (20 males and 20 females) were given a single intraperitoneal injection of the material (25 mg in 1 mg of water) and kept under observation for their full lifespan.

Table 3. Final results of tests on crocidolite, chrysotile (Canada) and sedimentary erionite[a]

Material	Peritoneal mesotheliomas			Pleural mesotheliomas		
	Tumour-bearing animals		Average latency time (weeks)	Tumour-bearing animals		Average latency time (weeks)
	No.	%		No.	%	
Crocidolite	39	97.5	59.5	18	45.0	104.8
Chrysotile (Canada)	32	80.0	92.2	26	65.0	111.1
Sedimentary erionite	20	50.0	106.1	35	87.5	64.2
Water (controls)	0	-	-	0	-	-

[a]Sprague-Dawley rats (20 males and 20 females) were given a single intraperitoneal and intrapleural injection of the material (25 mg in 1 ml of water) and kept under observation for their full lifespan.

Table 3.1 Induction of mesotheliomas by fluoro-edenite in Sprague-Dawley rats followed for up to 109 weeks

Material	Route of administration (dose)	No. of rats (sex)	No. of deceased rats at 109 wk	Incidence of mesotheliomas (%)	Significance[a]	Mean latency (wk)
Fibrous fluoro-edenite	Intraperitoneal injection (25 mg/rat)	40 (M)	40	92.5 (37/40)	[$P < 0.0001$]	61.6
Fibrous fluoro-edenite	Intraperitoneal injection (25 mg/rat)	40 (F)	40	72.5 (29/40)	[$P < 0.0001$]	66.4
Fibrous fluoro-edenite	Intrapleural injection (25 mg/rat)	40 (M)	37	10.8 (4/37)	NA	71.0
Fibrous fluoro-edenite	Intrapleural injection (25 mg/rat)	40 (F)	33	18.2 (6/33)	NA	72.8
Powdered prismatic fluoro-edenite	Intraperitoneal injection (25 mg/rat)	15 (M)	13	0 (0/13)	[NS]	NA
Powdered prismatic fluoro-edenite	Intraperitoneal injection (25 mg/rat)	15 (F)	13	0 (0/13)	[NS]	NA
Water (control)	Intraperitoneal injection (1 mL)	40 (M)	33	0 (0/33)	–	NA
Water (control)	Intraperitoneal injection (1 mL)	40 (F)	32	0 (0/32)	–	NA

[a] Calculated by the Working Group, Fisher exact test

F, female; M, male; NA, not applicable; NS, not significant; wk, week

From Soffritti et al. (2004)

Il contributo degli studi epidemiologici dell'IR su tutti i tipi di amianto

Icahn School of Medicine at Mount Sinai

Home Profiles Research units **Publications & Research Outputs** Press/Media

I mesoteliomi da amianto usato nelle ferrovie Italiane: Resoconto di 199 casi

Translated title of the contribution: Mesotheliomas due to asbestos used in the Italian railroads: Report of 199 cases

Cesare Maltoni, Luca Lambertini, Daniela Cevolani, Franco Minardi, Morando Soffritti

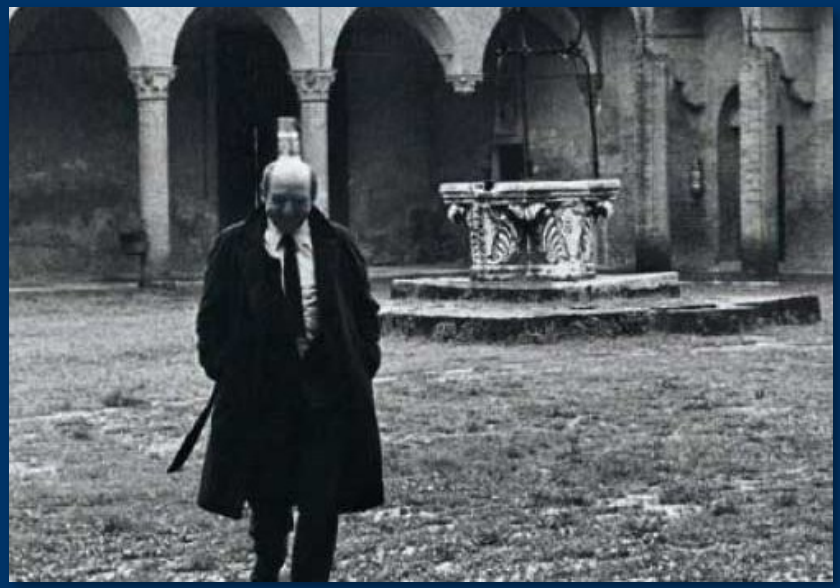
Research output: Contribution to journal › Article › peer-review

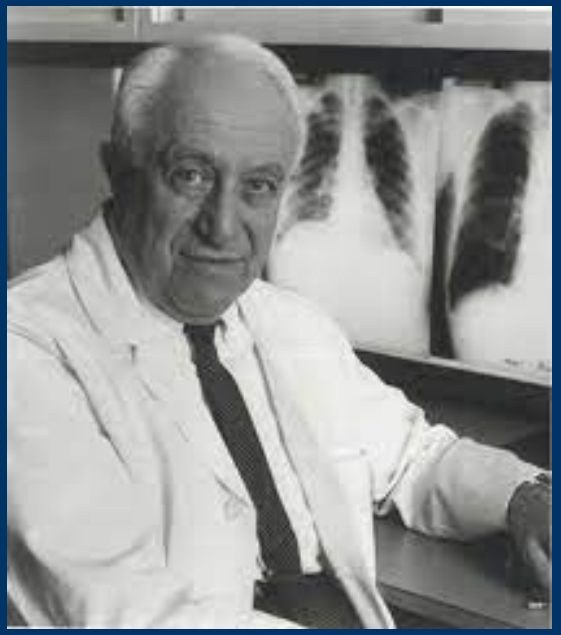
Overview Fingerprint

Abstract

The data on the cases of mesothelioma and other asbestos-related pathologies, collected by the European Foundation of Oncology and Environmental Sciences "B. Ramazzini" among people exposed in various circumstances to the asbestos used in railroads, are herein presented. Up to now, the series includes 199 cases of mesothelioma (179 pleural, 1 pericardial, 9 peritoneal, 1 pleuro-peritoneal and 9 with unspecified origin) and 151 cases of asbestosis and other mesothelialnon mesothelioma pathologies. The onset of some cases of mesothelioma due to the pollution of general environment and to family contact is emphasized. More research is needed in order to better quantify the risk due to asbestos exposure as well as to adopt preventive measures and provide compensation for tumours arisen after work exposure.

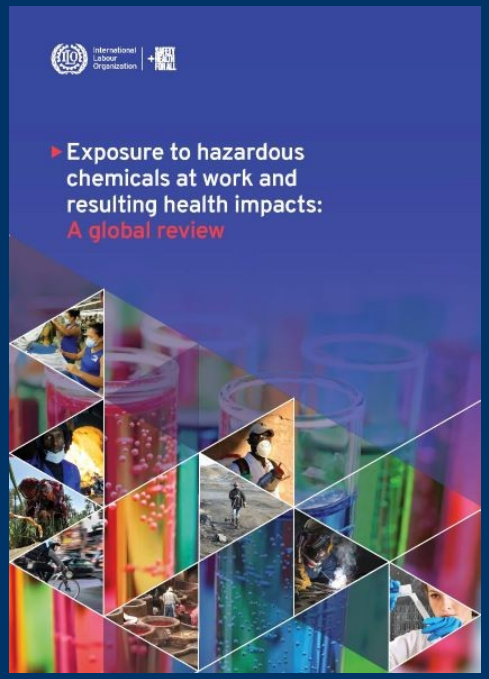
Collegium Ramazzini





ESPOSIZIONI A SOSTANZE CHIMICHE: PRIORITA' GLOBALI

Secondo l'Organizzazione Internazionale del Lavoro (ILO), ogni anno più di 1 miliardo di lavoratori è esposto a sostanze pericolose, inclusi inquinanti, polveri, vapori e fumi nei loro ambienti di lavoro.



Le principali esposizioni chimiche identificate come prioritarie includono:

1. **Amianto**
2. **Silice**
3. **Metalli pesanti**
4. **Solventi**
5. **Coloranti**
6. **Nanomateriali artificiali (MNM)**
7. **Sostanze perfluorurate (PFAS)**
8. **Interferenti endocrini (EDC)**
9. **Pesticidi**
10. **Inquinamento dell'aria**

PRIORITA' GLOBALI (ILO): AMIANTO

MAIN SECTORS OF EXPOSURE	PRIMARY HEALTH IMPACTS	GLOBAL BURDEN OF OCCUPATIONAL EXPOSURES	WORK-RELATED HEALTH IMPACT
Mining Construction Agriculture; plantations; other rural sectors Automotive industry Protective textiles	Cancer (mesothelioma, cancer of the lung, larynx, ovary) Asbestosis and pleural disease	>125,000,000 (WHO 2018)*	>233,000 deaths annually (GBD 2019)

**Based on estimates from 2018. A new WHO/ILO joint estimate is under development*

COLLEGIUM RAMAZZINI: CRITERI DI HELSINKI

Journal List > J Occup Health > v.58(2); 2016 Mar 20 > PMC5356971

Journal of Occupational Health
Open Access

J Occup Health. 2016 Mar 20; 58(2): 224–227.
Published online 2016 Mar 31. doi: 10.1539/joh.16-2004-LT

PMCID: PMC5356971
PMID: 27040481

Comments on the 2014 helsinki consensus report on asbestos

Collegium Ramazzini[1]

COLLEGIUM RAMAZZINI: CAUSALITA' MESOTELIOMA

INDUSTRIAL HEALTH
National Institute of Occupational Safety and Health
This Journal | For Authors | Submissions

Ind Health. 2016 Jan; 54(1): 92–93.
Published online 2016 Jan 29. doi: 10.2486/indhealth.cr02
PMCID: PMC4791299
PMID: 26822314

Comments on the causation of malignant mesothelioma: rebutting the false concept that recent exposures to asbestos do not contribute to causation of mesothelioma

In summary, the Collegium Ramazzini concludes that risk of malignant mesothelioma is related to cumulative exposure to asbestos in which all exposures—early as well as late—contribute to the totality of risk. The Collegium Ramazzini rejects as false, mendacious, and scientifically unfounded the claim put forth by the Italian asbestos industry and its expert witnesses that in cases of prolonged exposures to asbestos only the earliest periods of exposure contribute to mesothelioma induction, while all subsequent exposures have no causal role. The Collegium Ramazzini is deeply concerned that acceptance of this false claim will contribute to the unjust denial of workers' compensation and civil damages to affected workers, that it will hinder efforts to diagnose and prevent malignant mesothelioma, and that ultimately it will undermine the health of the public in Italy and in countries around the world.

TOOLKIT PER LA VALUTAZIONE DEGLI STUDI EPIDEMIOLOGICI

Environ Health. 2021; 20: 90.
Published online 2021 Aug 19. doi: 10.1186/s12940-021-00771-6
PMCID: PMC8375462
PMID: 34412643

Toolkit for detecting misused epidemiological methods

Colin L. Soskolne,[✉1] Shira Kramer,[2] Juan Pablo Ramos-Bonilla,[3] Daniele Mandrioli,[4] Jennifer Sass,[5,6] Michael Gochfeld,[7] Carl F. Cranor,[8] Shailesh Advani,[9,10] and Lisa A. Bero[11]

Associated Data

▸ **Data Availability Statement**

Abstract

Go to: ▸

Background

Critical knowledge of what we know about health and disease, risk factors, causation, prevention, and treatment, derives from epidemiology. Unfortunately, its methods and language can be misused and improperly applied. A repertoire of methods, techniques, arguments, and tactics are used by some people to manipulate science, usually in the service of powerful interests, and particularly those with a financial stake related to toxic agents. Such interests work to foment uncertainty, cast doubt, and mislead decision makers by seeding confusion about cause-and-effect relating to population health. We have compiled a toolkit of the methods used by those whose interests are not aligned with the public health sciences. Professional epidemiologists, as well as those who rely on their work, will thereby be more readily equipped to detect bias and flaws resulting from financial conflict-of-interest, improper study design, data collection, analysis, or interpretation, bringing greater clarity—not only to the advancement of knowledge, but, more immediately, to policy debates.

CONFLITTI DI INTERESSE: FONTE DI BIAS DEGLI STUDI

Ci sono prove sufficienti che i conflitti di interesse finanziarii siano in grado di influenzare i risultati degli studi (ovvero siano fonte di "bias"), sia negli studi umani che non umani, in molti campi tra cui l'epidemiologia e la tossicologia

I conflitti di interesse finanziari introducono "bias" a tutti i livelli del processo di ricerca e pubblicazione (legami finanziari dell'autore, sponsorizzazione del lavoro e finanziamento delle riviste)

D'altra parte, non ci sono prove che i cosiddetti "COI non finanziari" costituiscano una fonte sistematica di bias.

Le revisioni sistematiche e la metodologie evidence-based più avanzate in epidemiologia e tossicologia tengono conto dei conflitti di interesse finanziari quando si valuta il rischio di bias e la qualità dell'evidenza dello studio

Mandrioli D, Kearns CE, Bero LA. Relationship between Research Outcomes and Risk of Bias, Study Sponsorship, and Author Financial Conflicts of Interest in Reviews of the Effects of Artificially Sweetened Beverages on Weight Outcomes: A Systematic Review of Reviews. PLoS One. 2016 Sep 8;11(9):e0162198. doi: 10.1371/journal.pone.0162198.

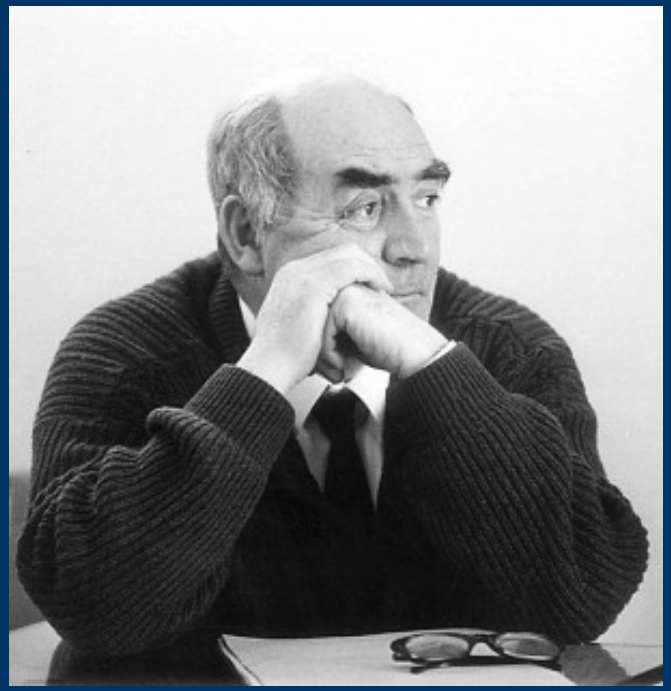
Bero LA, Grundy Q. Why Having a (Nonfinancial) Interest Is Not a Conflict of Interest. PLoS Biol. 2016 Dec 21;14(12):e2001221. doi: 10.1371/journal.pbio.2001221.

Woodruff TJ, Sutton P. The Navigation Guide systematic review methodology: a rigorous and transparent method for translating environmental health science into better health outcomes. Environ Health Perspect. 2014 Oct;122(10):1007-14. doi: 10.1289/ehp.1307175. Epub 2014 Jun 25.

Pega F, Norris SL, Backes C, Bero LA, Descatha A, Gagliardi D, Godderis L, Loney T, Modenese A, Morgan RL, Pachito D, Paulo MBS, Scheepers PTJ, Schlünssen V, Sgargi D, Silbergeld EK, Sørensen K, Sutton P, Tenkate T, Torreão Corrêa da Silva D, Ujita Y, van Deventer E, Woodruff TJ, Mandrioli D. RoB-SPEO: A tool for assessing risk of bias in studies estimating the prevalence of exposure to occupational risk factors from the WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury. Environ Int. 2020 Feb;135:105039. doi: 10.1016/j.envint.2019.105039. Epub 2019 Dec 18.

GRAZIE

Istituto "B. Ramazzini"



"Gli alti costi [umani ed economici] probabilmente rappresentano la ragione per cui, nel settore della cancerogenesi ambientale e sperimentale, le parole si sostituiscono a fatti, le opinioni ai dati, e i congressi e i resoconti delle commissioni sommergono i buoni dati di laboratorio"
[Cesare Maltoni]

C. Maltoni, G. Lefemine e A. Ciliberti, *Carcinogenicity bioassays of vinyl chloride monomer: a model of risk assessment on an experimental basis*, in *Environmental Health Perspectives*, vol. 41, 1° ottobre 1981, pp. 3–29.