

**SCIENTIFIC SESSION IV**  
**Work of the Fellows (Poster Session)**

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## Diagnostic challenges of mixed dust pneumoconiosis

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*Background:* Exposures to multiple, mixed inorganic dusts occur in many worksites. Such exposures initiate inflammatory and fibrotic processes in the lung. By taking a detailed occupational history the diagnosis of leading pneumoconioses such as silicosis or asbestosis with typical radiologic pictures is mostly not difficult, e.g. when rounded or irregular opacities located in the upper and lower lung fields, respectively, dominate. However mixed dust exposures, e.g. quartz and carbon in hard coal mines, quartz, asbestos, various other components of cement and concrete dusts in the construction industry, may lead to considerable modification of the radiological and histopathological pictures. This is associated with diagnostic difficulties, especially with regard to the differential diagnosis of idiopathic pulmonary fibrosis subtypes.

*Methods:* The files of our outpatient department were searched for patients diagnosed as mixed dust pneumoconiosis.

*Results:* Five patients were identified whose detailed diagnostic workup during social court litigations (i.e. detailed clinical and occupational history, computed tomography, lung function testing, in one also case lung histology and dust analyses) demonstrated mixed dust pneumoconiosis. Dominating causative substances were quartz (3), quartz plus silicates (1), talkum (1), quartz plus aluminum compounds and silicon carbide (1), which were always combined with various other inorganic material. All cases were initially misdiagnosed as idiopathic pulmonary fibrosis because the assumed typical silicosis or asbestosis pattern was not visible in radiological examinations.

*Conclusions:* Diagnosis of interstitial lung disorders should always include a detailed occupational history that adequately considers that various inorganic dust exposures may cause mixed-dust pneumoconiosis with a broad spectrum of abnormal lung morphology.

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Dr. Baur is retired chair, Occupational Medicine at the University Hamburg and currently president of the European Society for Environmental and Occupational Medicine.

## Assessing the feasibility of preventing injury risks and improving work safety amongst factory workers in an urban slum: a participatory before-and-after intervention study: preliminary results

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**Background:** In Bangladesh an estimated 11.7 thousand workers suffer from fatal incidents and 24.5 thousand die from work-related diseases each year. Whilst addressing occupational injury and disease has been declared a national priority, there remains a critical lack of interventions to mitigate workplace risks. We aim to assess the feasibility of collaborating with factory owners/workers to design and implement occupational health interventions to improve work safety in two metal factories in Kamrangirchar, Dhaka.

**Methods:** We designed a participatory, mixed methods before-and-after study articulated over three phases. We present the preliminary analysis of data gathered during the first phase of the study. This documents the dynamic nature of incidents, near miss events, injury, hazards and ergonomics risks, and workers' perceptions and experiences of injury and risks, and aims to inform the design of appropriate intervention packages. Quantitative data were collected through hazard and ergonomics assessments, clinical data and surveillance. Qualitative data were collected using in-depth interviews. Data collected with different methods were integrated at multiple points, and findings from all data sets were triangulated at the end of the first phase.

**Results:** Overall 67 workers participated in the study. 166 incidents and 129 (77%) injuries occurred. Triangulation of findings consistently identified machine operators and children under 18 years old to be most at risk, poor ergonomics and a lack of personal protective equipment as the main risks. Workers recognised these risks but accepted them as an inevitable part of their work, largely due to practical barriers to mitigating them.

**Conclusions:** It was feasible to implement the study in collaboration with owners/workers. Incidents are frequent and identified risks are mitigable. Intervention packages will be finalized with owners/workers during phase two of the study. Findings will inform the development of a model that could be implemented more widely in Kamrangirchar or similar neglected contexts.

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Dr. Caleo is a Medical Doctor, and Public Health Specialist. She is the Public Health Advisor for Medecins Sans Frontieres (MSF) supporting research/interventions in Haiti, DRC, CAR, Guinea, Zambia, Niger, and Sierra Leone. In Bangladesh she worked extensively the MSF Occupational Health project to improve work safety and access to care. Grazia studied Epidemiology and Tropical Medicine at the London School of Hygiene and Tropical Medicine (LSHTM). She was an EPIET fellow and worked as consultant for WHO.

## The discovery of PFOA pollution in the Veneto region

Laura Facciolo<sup>1\*</sup>, Philippe Grandjean<sup>2,3</sup>

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*Background:* Serious PFAS pollution was discovered in the Veneto region that affected the Venetian aquifer system in the high plain at the foot of the Prealps. Even the Po River was found to be affected.

*Approach:* The Mamme No PFAS organization was formed to inform residents on exposure sources, adverse health risks, and prevention efforts, and it is working with governmental agencies to remediate the problems and provide better protection against such pollution in the future. The organization is also working with scientists to obtain better documentation on health effects and to discover possible ways to lower PFAS levels in the body. The company responsible for the pollution will now be sued.

*Results:* The production company apparently knew of the environmental dissemination in 2006. However, in connection with a health study of teenagers, elevated blood concentrations of PFAS were found in 2017. The unexpected news of serious pollution with persistent chemicals was a shock to the affected population. The citizen group is providing links between exposed residents, scientists, and government, thereby empowering the people affected by the pollution and stimulation research and prevention. This development therefore illustrates the impact of environmental pollution seen from the side of the exposed people.

*Conclusions:* The early experience from the PFAS pollution in Veneto suggests that improved collaboration between scientists and exposed communities is crucial and also feasible. It also suggests that joint efforts are needed to obtain better prevention of chemical exposures in the future and worldwide.

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Laura Facciolo is Scientific Counselor of “Mamme No PFAS” (No PFASs MUMs), a group of citizens living in the so-called “Red Zone” of Veneto where, at the beginning of 2017, the 350.000 inhabitants suddenly discovered to have been highly exposed to PFASs due to serious contamination by wastewater from PFAS manufacture that reached the groundwater and also the Po river. Laura has a degree in Pharmaceutical Chemistry and lives in Montagnana (Padua).

## Effects of short and long-term alcohol-based fixation on Sprague-Dawley rat tissue morphology, protein and nucleic acid preservation

Federica Gnudi<sup>1\*</sup>, Simona Panzacchi<sup>1</sup>, Daniele Mandrioli<sup>1</sup>, Rita Montella<sup>1</sup>, Valentina Strollo<sup>1</sup>, Alex Merrick<sup>2</sup>, Fiorella Belpoggi<sup>1</sup>, Eva Tibaldi<sup>1</sup>

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*Background:* Safety concerns the toxic and carcinogenic effects of formalin exposure have drawn increasing attention to the search for alternative low risk fixatives in laboratories worldwide. Alcohol-based fixatives are considered some of the most promising alternatives.

*Methods:* We evaluated the performance of alcohol-fixed paraffin-embedded samples from Sprague-Dawley rats, analyzing tissue morphology, protein and nucleic acid preservation, after short and extremely long fixation times. Formalin-fixed paraffin-embedded samples were used as a comparator fixative.

*Results:* Short and long-term alcohol fixation as well gave generally comparable and satisfactory results regarding the structural status of tissues evaluated by scoring stained sections. Immunoreactivity of proteins, evaluated by immunohistochemistry, showed satisfactory results until 1 year. Alcohol fixation was superior compared to formalin, in terms of quantity of nucleic acid extracted from paraffin blocks, even after long time in alcohol.

*Conclusions:* Our results confirm that alcohol fixation is a suitable and safe alternative to formalin. There is a need for standardization of formalin-free methods and harmonization of diagnosis worldwide.

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Dr Gnudi is a postdoctoral researcher at the Cesare Maltoni Cancer Research Center, Ramazzini Institute, and she works in the pathology unit. Her work involve mainly the optimization of different procedures as IHC staining methods for protein pattern distribution analysis in order to provide technical, collaborative and consultative pathology support.

## Protecting decommissioning workers at hazardous remediation sites

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*Background:* “Decommissioning”, particularly the end of life decontamination and demolition of nuclear facilities and waste sites, has become a growth industry. The U.S. Department of Energy’s (DOE) nuclear weapons legacy at Hanford, Washington poses a huge remediation task with many challenges.

*Methods:* To help DOE anticipate and prevent worker risks, the multi-university/multi-disciplinary Consortium for Risk Evaluation with Stakeholder Participation (CRESP) team investigated the hazards facing decommissioning workers engaged in remediation of the Hanford tank farms, waste sites, and plutonium production facilities.

*Results:* DOE espouses a safety culture with responsibilities devolving on every level of subcontractors. This approach embodies sound principles when implemented consistently but incentivizes under-reporting. CRESP divided remediation hazards into 3 classes, each with its dedicated professionals: A: acute blast, burn, or radiation injury due to disasters (explosions, fires, collapses), the domain of Nuclear Safety; B: radiation and toxic chemical exposures from site-specific hazards, the domain of industrial hygiene (IH); C: industrial-type accidents, the domain of industrial safety. DOE has a well-established but incomplete protocol for Documented Safety Analyses (DSA) for each remediation project. Workers close to a Class A source have a high risk of injury or death, but DSAs estimate the initiating events as “highly unlikely” or less, hence estimate risks to workers as “low”. For Class B exposures, DOE and contractors emphasize radiation detection and personal protection, usually effectively. However, worker reports of illnesses from “vapors” at the tank farms are discounted because of inadequate IH. Class C accidents, including vehicles, struck-by, slips-trips-falls, are reported at a low rate. The DSA’s specifically exclude consideration of class C when estimating risks for a remediation project. The rationale is that these workers would be doing the same work elsewhere.

*Conclusion:* All three professional domains need to be involved in evaluating risks to workers for each remedy being evaluated at each contaminated facility whether, in the public or private sector.

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Dr. Gochfeld is professor emeritus at the Rutgers Robert Wood Johnson Medical School. He is an occupational physician and environmental toxicologist with interests in toxic waste remediation and heavy metal exposures. Dr. Burger is Distinguished Professor of Biology at Rutgers with an emphasis on ecological risk assessment and management. Both are founding participants of the Consortium for Risk Evaluation with Stakeholder Participation (CRESP), that provides technical expertise, risk communication, and research support to the U.S. Department of Energy (DOE).

## Asthmatic symptoms and airborne environmental pollution in the town of Terni, central Italy

Nicola Murgia<sup>1\*</sup>, Ilenia Folletti<sup>1</sup>, Giancarlo Pocetta<sup>1</sup>, Anna Miniucchi<sup>1</sup>, Lucio Casali<sup>1</sup>, Lamberto Briziarelli<sup>1</sup>

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**Background:** Airborne pollution is a risk factors for asthma symptoms. In the town of Terni, Central Italy, there are a large steel factory, other industries and a busy highway. Registry data suggest an increase in mortality and morbidity for respiratory diseases in Terni, but more detailed data are lacking. The aim of this study is to evaluate, by a re-analysis of the “Study on Allergy and Respiratory Health in Adults” (SARA) survey, the impact of environmental pollution on asthmatic symptoms.

**Methods:** 1660 subjects living in Terni municipality answered the SARA questionnaire, containing questions on socio-demographics characteristics and health- related outcomes. Having one or more asthmatic symptoms in the last 12 months was the main outcome of interest. Subjects reporting living close by an industrial area (< 500 m) and a busy road were considered at higher risk of airborne pollution. Chi- square test was used for categorical data and logistic regression models were used to assess the influence of environmental pollution on symptoms.

**Results:** More subjects at higher risk of environmental pollution reported asthmatic symptoms (32.1% vs 26.4%,  $p=0.016$ ). In the regression model, adjusted for sex, age, atopy, smoking and occupational status, there was an association between pollution and asthma symptoms that was of borderline statistical significance (OR 1.24, 95%CI 0.97-1.60). Including in the model the reported residence (urban vs rural) did not change the results.

**Conclusions:** Previous results from SARA were not conclusive on the relationship between respiratory symptoms environmental pollution; our results, considering subjects exposed to different sources of pollution at the same time, suggest an association between environmental exposures and asthmatic symptoms in these circumstances. Given the weakness of a postal questionnaire in assessing the exposure, further studies using more objective and robust indicators of exposure are needed.

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Nicola Murgia is Associate Professor of Occupational Medicine at the University of Perugia, Italy. His research focuses mainly on occupational and environmental respiratory diseases, in particular on the epidemiology of occupational and environmental lung diseases and on the development of non-invasive methods to study the effects of occupational risk factors on the respiratory system.

## Are sunscreens efficient to prevent the effect of UV radiation?

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*Background:* UV radiation is a frequent occupational exposure in many jobs outdoor. Our study tested the efficiency of nanoTiO<sub>2</sub> sunscreen to prevent the oxidative stress/inflammation caused by ultraviolet (UV) radiation using biomarkers in volunteers' blood.

*Methods:* Six identical subjects participated in three tests: A) nanoTiO<sub>2</sub> sunscreen; B) UV radiation; C) sunscreen + UV. The first samples were collected on day 1 before the test and the second samples after sunscreen application and/or UV exposure. On day 4, the third samples were collected, and the sunscreen was washed off. The fourth samples were collected one week later, on day 11. In all 3 studies, following biomarkers of oxidative stress and inflammation were measured using liquid chromatography-electrospray ionization-tandem mass spectrometry: malondialdehyde, 4-hydroxy-trans-hexenal, 4-hydroxy-trans-nonenal, aldehydes C6-C12, 8-isoProstaglandin F<sub>2α</sub>, o-tyrosine, 3-chlorotyrosine, 3-nitrotyrosine, 8-hydroxy-2-deoxyguanosine, 8-hydroxyguanosine, 5-hydroxymethyl uracil, and leukotrienes (LT).

*Results:* Sunscreen alone did not elevate plasma markers in study A, but UV exposure in study B increased all biomarkers in samples 2: malondialdehyde (p  
In study C the sunscreen prevented skin redness caused by UV radiation; however, it did not inhibit the elevation of all 15 oxidative stress/inflammatory markers: malondialdehyde (p

*Conclusions:* The markers of oxidative stress and inflammation were not significantly reduced by the prior use of the sunscreen. Its efficiency to prevent skin cancer may therefore be questioned.

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## Ethical issues in cancer prevention: A different challenge for behavioral and environmental risk factors

Annie Jeanne Sasco<sup>1\*</sup>

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*Background:* Ethics in the medical and health fields was the prime preoccupation of Hippocrates. By contrast, in recent centuries, it has largely been ignored. It became unavoidable, however, with the development of clinical trials for the testing of new therapeutic drugs becoming the “gold standard” for any human study. These clinical trials were generally in the domain of chronic diseases where the beneficial effects were quite small; no consideration whatsoever was devoted to iatrogenicity. The mythical randomized clinical trial was born and became a mandatory reference. Decades later, “meta-analysis” appeared on the scene when the need arose for assessing statistically significant differences in clinical outcomes.

*Methods:* The issue of ethics in prevention has been largely ignored and considered a non-issue. Nowadays, it is becoming “the right thing to do” to have charts of ethics in research, medical and university institutions. Some are truly excellent, but the majority correspond simply to vacuous words on a piece of paper or on a screen. Sometimes, when they are presented to the staff or students, the spoken words are invoked simply to minimize ethical concerns. Similarly, networks dealing with ethics do not themselves apply the very rules they prescribe for others.

*Results:* I shall explain how ethical principles need to be developed in prevention research and actions taken in reference to the field I know best, namely cancer prevention. Two classes of carcinogens will be contrasted because the implications for prevention are totally different. The first one belongs mostly to behavior or lifestyle; the second can be classified as environmental in the restricted (and only valid) sense of the word “environment”.

*Conclusions:* There are significant implications of how ethical principles are applied to prevention research.

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Dr Sasco founded in 1995 the first Research Unit of Epidemiology for Cancer Prevention at the IARC-WHO. Her objective was and still is the absolute need for epidemiological results to be translated into effective population health policies. Some of the students and fellows she trained all over the world are replicating this approach on a broad scale. Dr Sasco, now back at the Bordeaux University, is exceedingly active on issues of ethics and scientific integrity.

## The analysis of longitudinal data from life-span carcinogenicity bioassays on Sprague-Dawley rats

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*Background and aim of the work:* Long Term Carcinogenicity Bioassays (LTCB) are among the best instruments to strengthen the evidence on which regulatory agencies base their decision to classify harmful agents as human carcinogens; therefore, they are fundamental to protect public health. The statistical analysis is essential to validate the results from cancer and non-cancer outcomes in carcinogenicity bioassay. This work proposes and applies some methodologies for the analysis of non-cancer outcomes, such as body weights.

*Methods:* We used data from studies already concluded, evaluated and published: 4 bioassays aimed at testing the carcinogenic potential of Coca-Cola on Sprague-Dawley rats of different ages. The analysis of body weights of the second generation of rats was performed using mixed-effects models: linear and non-linear models were fitted, for non-linear models we have considered human non-linear growth functions.

*Results:* Linear models were fitted using the log-transformation of time and polynomial term of third order for time. Sex and treatment influence body weight, while age of dams during gestation doesn't. Growth models: Jenks-Bayley, Count and 1st order Berkey-Reed growth functions were evaluated; the latter best describes these data. Sex and treatment significantly influence all parameters. The direction, magnitude and significance of the effect of each variable is substantially similar in all models. The analysis of residuals highlights issues for all models: the extreme trends in the last part of life heavily affect the models' performance.

*Conclusions:* Mixed-effects models allowed to account for the structural effect of covariates that act the same way on all individuals, and to add random effects that introduce a correlation among subjects if clustering happens; nonlinear human growth models added information about the whole growth process, therefore these may be useful methods in studies focused on development and sexual maturation.

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Dr. Sgargi is a member of the Biostatistics Unit at the Cesare Maltoni Cancer Research Centre of the Ramazzini Institute. She obtained a PhD in Statics at the University of Bologna. She works at the analysis of results of bioassays, and at systematic reviews of the literature (collaborating to the WHO/ILO Joint Methodology for the Global Burden of Diseases). She is part of a project with the Sant'Orsola Hospital (Bologna) on Toxicant-associated fatty liver diseases.

## Dietary intake of acrylamide and risk of breast, endometrial and ovarian cancers: systematic review and dose-response meta-analysis

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*Background:* Acrylamide is probable human carcinogen that occurs naturally in starchy foods during cooking processes at high temperatures. Aside from occupational exposures and smoking, main source of human exposure is diet, particularly consumption of potatoes, grain products, and coffee. High acrylamide intake has been associated with altered sex-steroid hormone concentrations and increased risk of hormone-dependent gynecologic neoplasms.

*Objective:* We performed a systematic review of the papers investigating the association between acrylamide intake and risk of breast, endometrial and ovarian cancer. We also examined a possible dose-response relation by carrying out a dose-response meta-analysis of these studies.

*Methods:* We searched in PubMed up to September 10, 2019 the non-experimental human studies investigating risk of breast, endometrial, or ovarian cancer in relation to dietary intake of acrylamide. We also carried out a dose-response meta-analysis using a restricted cubic spline model.

*Results:* We retrieved 18 studies: 11 cohort, 5 case-cohort, and 2 case-control studies. Since some studies assessed more than one cancer type, we found a total of ten studies on risk of breast cancer, seven on endometrial cancer, and seven on ovarian cancer. In the dose-response meta-analysis, acrylamide intake was associated with slightly increased risks of endometrial and ovarian cancers, with a stronger and almost linear increased risk among never smokers. Conversely, for breast cancer we found no evidence to support an increased risk following acrylamide exposure, except for a positive association among premenopausal women exposed to at least 20 µg/day of acrylamide.

*Conclusions:* Based on the relatively small number of studies published to date, acrylamide intake was associated with increased risk of endometrial and ovarian cancer in a dose-response fashion, with a slightly stronger association observed among never smokers. Acrylamide intake was associated with an increased risk of breast cancer only among premenopausal women and at intakes greater than 20 µg/day.

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Dr. Filippini, MD, is a Researcher and a PhD student in Public Health at the University of Modena and Reggio Emilia. He works in the studies of health effects of environmental risk factors, particularly dietary risk factors and outdoor pollutants, with specific reference to the risk of chronic diseases such as neurodegenerative diseases and cancer.

## Exposure to inorganic selenium in drinking water and incidence of amyotrophic lateral sclerosis: A long-term followup of a natural experiment

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**Background:** Some studies have reported an association between overexposure to selenium and risk of amyotrophic lateral sclerosis (ALS), a rare degenerative disease of motor neurons. From 1986 through 2015, we followed a cohort in Northern Italy that had been inadvertently consuming tap water with unusually high concentrations of inorganic hexavalent selenium from 1974 to 1985.

**Methods:** We had previously documented an excess incidence of ALS in this cohort during 1986-1994. Here, we report extended follow-up of the cohort for an additional 21 years, encompassing 50,100 person-years of the exposed cohort and 2,233,963 person-years of the unexposed municipal cohort. We assessed ALS risk using a Poisson regression analysis, adjusting for age, sex and calendar year.

**Results:** We identified 7 and 112 incident ALS cases in the exposed and unexposed cohorts, respectively, yielding crude incidence rates of 14 and 5 cases per 100,000 person-years. The Poisson regression analysis produced an overall incidence rate ratio (IRR) for ALS of 2.8 (95% confidence interval (CI) 1.3, 6), with a substantially stronger IRR in 1986-1994 (8.2, 95% CI 2.7, 24.7) than in 1995-2015 (1.5, 95% CI 0.5, 4.7), and among women (5.1, 95% CI 1.8, 14.3) than men (1.7, 95% CI 0.5, 5.4).

**Conclusions:** Overall, these results indicate an association between high exposure to inorganic selenium, a recognized neurotoxicant, and ALS incidence, with declining rates after cessation of exposure and stronger effects among women.

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Dr. Vinceti is full professor of Public Health at the Department of Biomedical, Metabolic and Neural Sciences at University of Modena and Reggio Emilia where he works in the study of health effects of environmental and dietary risk factors, specifically regarding risk of chronic diseases as neurodegenerative diseases and cancer.

