# Chapter 6
# Occupational Cancer Monitoring in Italy

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## 1.  The need for active occupational cancer monitoring

The monitoring of occupational cancer is indispensable for preventing cancer and protecting the health of the population as a whole. In fact, many human carcinogens have been first identified in occupational settings (e.g. asbestos, benzene, formaldehyde, etc.), with this information then used to limit (and hopefully avoid) the exposure of the general population.

In Italy, as a result of legislation on monitoring occupational cancers, three systems for monitoring the effects of occupational exposure to carcinogens have been implemented: the Italian national Mesothelioma Register (ReNaM), the Sinonasal Cancer Register (ReNaTuns) and the OCCAM monitoring system.

The registries relate to all incidences of cancer, recording cases of relevant occupational exposure: asbestos for mesothelioma and wood, leather, chromium for sinonasal cancers.

Since mesothelioma and sinonasal cancer are rare and caused by one or just a few substances, and as exposure to them is nearly always related to occupational settings, they are often referred to as "High etiologic fraction occupational neoplasms". In Italy, research into them is entrusted to Regional Operating Centres (COR) which record all cases and try to interview all patients or their representatives. This information is periodically sent to the Italian Workers' Compensation Authority (INAIL), where it is aggregated. This system is described elsewhere (Nesti *et al.* 2005).

Other cancers (e.g. lung, bladder, larynx, lympho-hematopoietic malignancies) that can also be attributable to occupational exposure are difficult to identify because:

—  they may be attributable to multiple causes other than occupational ones (e.g. smoking, air pollution, etc.);
—  they are common in the general population, meaning that interviewing all patients is not feasible.

Since the proportion of these neoplasms attributable to occupational causes is lower than mesothelioma and sinonasal cancer, they are often referred as "low occupational etiologic fraction neoplasms".

In Italy, the active search for these neoplasms is based on a monitoring system called OCCAM (Occupational CAncer Monitoring).

## 2. The OCCAM project

OCCAM is an information system used for studying occupational cancer risks and developing effective prevention strategies by studying cancer cases of occupational origin. The system is based on population-based case-control studies in which:

— incident cases ("cases") are identified by the available sources: cancer registries and/or hospital discharge records;
— control cases ("controls") are taken from health service population files;
— the economic activity of the workplaces where subjects (both cases and controls) worked is obtained via an automatic link to social security (National Institute for Social Security, INPS) records, and is considered as "exposure". The complete list of companies where subjects worked and their respective economic activity codes are linked to each case/control. Workers in a specific industrial sector are considered as "exposed" to that sector (e.g. "exposed" to the textile sector). For workers who have worked in several different sectors, the longest activity is considered as "exposure" in the analyses. People having worked only in the service and retail sectors, i.e. "unexposed", are used as the control (reference) category. The study thus covers individuals with a working career, whereby state records on working careers go back to 1974.

This system was developed at the Environmental Epidemiology and Cancer Registry Unit at the National Cancer Institute by the head of the Unit, Paolo Crosignani MD under an agreement with the National Institute for the Health and Safety (ISPESL) (now incorporated into Italian Workers' Compensation Authority (INAIL)) and with the collaboration of the Occupational Department of Pavia University (Crosignani *et al.* 2006).

Up to now carried out periodically by the OCCAM team, these studies are due to be performed in the future by the Regional Centres (CORs) under the supervision of INAIL which will be in charge of accessing the social security records.

The sources used to provide cases are cancer registries (CRs) and hospital discharge records (HDRs). CRs provide incident cases for all the cancers considered in the analyses. As for the HDRs, algorithms have been developed to identify incident cases, with only cancers known to be caused by occupational exposure being considered: larynx, lung, bladder, and lympho-hematopoietic neoplasms. As HDRs are used by the national health system in Italy as the basis for paying for care delivered, they are almost complete. Controls are taken randomly from the health service population files; sampling is carried out concurrently with case incidence.

Results, methodology and certain tools used to treat occupational carcinogens are available on the OCCAM website www.occam.it, of which much of the content is available in English.

# 3. Results

## 3.1 Cancer mapping by region, gender and type of cancer

Since 2002, more than 100,000 cancer cases have been examined. The main results are reported in the "Risultati" (Results) section of the OCCAM website. All these results have been sent to the regional health authorities to establish priorities in occupational cancer prevention. In some regions, measures targeting specific economic sectors have been carried out (e.g. in the Lombardy region for the metal-plating sector, where an increased risk of lung cancer had been found) (Panizza *et al.* 2012).

## 3.2 Case finding

A database containing the careers of all cases has been delivered to each Italian region involved in the OCCAM project, allowing local occupational health units (LHUs) to examine each case likely to be of occupational origin (e.g. all lung cancer cases among employees in the steelmaking or foundry sector). Knowing each production site and company, the LHUs are able to examine many cancer clusters that would otherwise have been ignored. Following in-depth investigations, about one-third of cases have now been recognised as caused by occupational exposure and reported for compensation.

## 3.3 Analytical Studies

The OCCAM data set has also been used to perform analytical studies on occupational cancer risks, providing cases, controls and the setting where to carry out the study.

Increased breast cancer risks have been observed in the textiles, rubber, paper and electrical manufacturing sectors in Lombardy (Italy) (Oddone *et al.* 2013), as well as in the Province of Milan (Italy) (Oddone *et al.* 2014a), giving rise to a growing suspicion of a possible link to a single large electrical manufacturing plant located there. To this aim, all cases of breast cancer registered in 2002 - 2009 in women who had worked at least one year in the factory and resided in Lombardy were selected. Controls were randomly sampled from all women in the same plant and residing in Lombardy on 31 December 2005. The odds ratios (ORs) for breast cancer were significantly higher in women exposed to chlorinated solvents (OR 1.65, 95% confidence interval (CI) 1.04-2.62), with a twofold increase (OR 2.10, 95% CI 1.21-3.66) among women exposed for at least 10 years. No other significantly increased ORs by exposure or job title were observed. All these analyses were carried out – pursuant to the OCCAM methodology – using company records and without interviewing the employees (Oddone *et al.* 2014b), thereby saving time and money.

An increased breast cancer risk has also been observed among women employed in the health sector. Only cases and controls having worked as nurses were considered for being interviewed on their exposure to shift work. Restricting cases and controls to the health sector allowed the OCCAM team to carry out a case-control study on shift work solely among employees working shifts. This study is currently under way. Preliminary analyses show an increased breast cancer risk among nurses exposed to shift work (Massari *et al.* 2015).

Moreover, studies based on the OCCAM methodology observed an increased risk of breast cancer among women steel foundry workers in Umbria (Italy) (Oddone *et al.* 2014), lung cancer in electroplating industry in Lombardy (Italy) (Panizza *et al.* 2012) and bladder cancer in leather and printing industries also in Lombardy (Amendola *et al.* 2007).

## 3.4   Estimating cancer risks by factory

Where the observation period given by a CR or an HDR is long enough (at least 10 years) and a factory has a sufficient number of employees (100 or more), the workforce cancer risk can be estimated without performing a cohort study. Instead an OCCAM case-control study can be performed, where:

— exposed cases are those (of a particular type of cancer and gender, e.g. male lung cancer cases) who worked in that factory (recall that OCCAM provides a history of companies where the subject has worked);
— exposed controls are healthy subjects from the population sample who also worked in the factory concerned;
— unexposed cases and controls are those who worked in the retail sector, i.e. the reference category used in the OCCAM case-control design.

This case-control design is equivalent to a case-control study embedded in the cohort of those who worked in that company. Even though the cohort is not enumerated, the completeness of the case series and the sampling of the source population make this analysis equivalent to a formal cohort study. In this way we evaluated the lung cancer risk in the rubber sector (Aiani *et al.* 2011). Moreover, the use of other (unexposed) workers as reference mitigates the underestimation of the true risk caused by the "healthy worker effect".

## 3.5   Mapping factories at risk

Cancer estimation by factory can also be carried out systematically for all factories in a specific geographical area and present in the OCCAM database. A list of factories with increased cancer risk has been produced for the Greater Milan area using HDRs from 2000 to 2010. An increased male lung cancer risk has been found in a number of factories belonging to the automotive and building sectors. A list of the factories still in operation has been compiled. All this information will be processed by the Local Occupational

Units to check whether carcinogens are still present in the work environment and also as a reference for compensating lung cancer cases with a potential occupational origin.

## 4.   Other support systems

Within the OCCAM context, two tools have been developed to deal with the problem of recognising low-incidence occupational cancer cases: the literature matrix and the general practitioner (GP) system.

The OCCAM Matrix systematically collects all positive results (i.e. a statistically significant increased risk of specific cancers among employees of a specific economic sector) and sorts them in a "Matrix" by type of cancer and economic sector. This matrix is intended as a tool for supporting connections between the type of cancer, gender and area found during cancer mapping.

The Italian GP system (named MMG from the Italian "Medici di Medicina Generale") is designed to allow GPs to recognise which of their patients suffer from a neoplasm of potential occupational origin. Based on information on the type of cancer and a patient's occupation, the MMG tool might recommend the GP to refer the patient to the Local Occupational Health Unit for a more in-depth case investigation. This system is table-driven, allowing a regular update taking account of the latest findings in the literature or from international bodies (e.g. the IARC Monograph no 100). It is available for field test at the web address: www.occam.it/mmg

## 5.   Outlook

There can be no doubt that, without a systemic and organized effort, most, if not all, occupational cancer cases will be ignored. In Italy all these activities are supported by the Occupational Safety Act (legislative decree 81/2008, art. 244). Following the retirement of the head of project, Paolo Crosignani, it is to be expected that the Milan National Cancer Institute will discontinue the work, with it being taken over by the Italian Workers' Compensation Authority (INAIL).

As a research tool, OCCAM provides unique opportunities to perform in-depth studies on occupational cancer risks, providing cases, controls and settings enabling such studies to be performed at very low cost.

This innovative monitoring system can potentially be transferred to all EU countries, thereby strengthening European public health and cancer prevention policies. It is not expensive, as the system relies on information available in electronic archives. However, data handling needs to be in the hands of a stable organization and the organization in charge of the system needs to be authorised to manage and process identifiable health records. It is a good idea to establish a specific data flow to preserve confidentiality by storing all identifiable health information at source (e.g. in the Cancer Registry, at the Health Authority responsible for the management of Hospital Discharge Records).

According to our experience, this system is a very effective way of detecting low-incidence tumours of occupational origin without incurring major costs.

Last but not least, the OCCAM approach can also be used for monitoring diseases other than cancer. Encouraging results were obtained for neurodegenerative diseases, in particular for multiple sclerosis (Oddone *et al.* 2013).

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