The OCCAM project
An innovative Italian approach to an old problem

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Research into occupational cancers is important for cancer prevention and the safety of the population as a whole (1). The European Union (EU) recently urged Member States to implement a reporting system for occupational diseases (2). Italian law requires cancer cases due to occupational exposure to be identified and referred for compensation. However, only a tiny fraction of occupational cancers is identified (3), not simply because of long disease latency and multiplicity of causes, but because occupational histories are almost never taken from cancer patients, even for cancers potentially of occupational origin (e.g. bladder and lung cancer), and treating physicians in general are not "tuned in" to the issue of work-related causes of cancer (4)(5). However, it has been estimated that in the early 1990s, a substantial proportion of workers in the EU were exposed to carcinogens (6).

The Italian Occupational Safety Act (legislative decree 626/94) provides for the establishment of a nation-wide occupational cancer registry, under the auspices of the National Institute for Occupational Health (ISPESL), tasked with identifying both activities associated with a risk of cancer, and cancer cases likely to be of occupational origin. With a view to setting-up such a system, the National Cancer Institute of Milan and ISPESL began working together in 2000 to evaluate the potential of using the computerized past employment database kept since 1974 by the Italian National Institute for Social Security (INPS). This stores the name of the employing firm and industry sector in which Italian private sector workers are employed for each year of employment.

Why are many occupational cancers not recognized?

- Occupational history is never collected at the bedside.
- Patients are often unaware of their past exposures to carcinogens.
- Treating physicians often overlook the occupational causes of cancer.
- Occupational cancers are not different from "spontaneously-presenting" cases.
- The carcinogenic potential of many substances is often a matter of debate.

There are several sources of population-based cancer case data: cancer registries (CRs), regional death registers, and regional hospital discharge records. Appropriate controls can be sampled from electronic population files, also available for many regions. It is therefore possible to carry out population-based case-control studies in different areas in order to estimate the risk of cancer by site in relation to industry sector, by linking cases and controls with their employment histories.

Moreover, it is possible to identify cancer cases that are probably attributable to occupational exposures by using area-specific risk estimates or, simply, by looking at cancer sufferers with an employment history in industries where there is a known increased cancer risk, e.g. bladder cancer sufferers who worked in the leather and shoe industry, or lung cancer sufferers who worked in iron and steel foundries.

This innovative information system on occupational cancers is based on an automatic linkage of cancer cases (and controls) with the information available in the Social Security archives. The name – OCCAM – is the acronym of Occupational Cancer Monitoring. The project's aims are estimating the burden of occupational cancer, the prevention of occupational cancers and identifying occupational cancers. The OCCAM approach is three-pronged:

1. Estimating the occupational cancer risk by area;
2. Actively searching for occupational cancer cases;
3. Searching for and classifying the available evidence on occupational cancer.

Estimating the occupational cancer risk by area

Occupational cancer risk estimation is done by a series of population-based case-control studies in areas where available electronic archives allow for new (incident) case identification and source population sampling. Two sources of cancer cases are used: incident cases from cancer registries (CRs) and incident cases identified by Hospital Discharge (HD) records.

Cases obtained from CRs are all cases occurring in a defined population, and are characterised by a diagnosis of high reliability. Therefore, as controls are sampled in the source population and occupational histories are collected automatically regardless of case-control status, the only bias in these studies comes from the lack of sensitivity and specificity of occupational histories available in the Social Security archives. Further details on study design and methods used and a discussion of the limitations of this approach are available in an article recently published in the *American Journal of Industrial Medicine* (7). The use of CR data makes it possible to evaluate the burden of the known risk factors in the area covered by the CR. Moreover, as cancers from all sites are examined, new hypotheses can be formulated

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How the OCCAM system works

For cancer mapping and to improve knowledge about occupational carcinogenesis

- A series of population-based, area-specific case-control studies is carried out.
- Incident cases are obtained from cancer registries and hospital discharge records. Controls are sampled from NHS records.
- The occupational history (past employers and their business activity) of cases and controls is automatically searched for in social security records.
- Cases and controls are considered as "exposed" to a business activity if it is the prevalent economic sector of the firms in which they worked.
- Cases and controls who worked exclusively in the trade and retail sectors are classed as "non-exposed".
- Relative risk by area and business activity are estimated.
- Elevated risks for "known" carcinogenic activities (e.g., elevated lung cancer risk for steel foundries) should impel action to eliminate suspected risks if they are still present.

To locate occupational cancer victims

- Newly-diagnosed cases of lung, larynx, bladder cancer and leukaemia * are identified from hospital discharge records.
- The occupational history of these cases is automatically searched for in social security records.
- Cases with a history of working in high-risk sectors (e.g., lung cancer patients who worked in steel foundries) are notified to Local Health Units' Occupational Health Services, and the list of past employers is supplied.
- Using prior knowledge of existing risks in these employing firms, coupled to a face-to-face interview, local services will identify subjects whose cancer may be attributable to past carcinogenic exposures.
- These cases are notified to the Insurance Board and, if appropriate, legal proceedings are brought.

* Most Italian regions have a specific registry for mesothelioma and nose cancer.

about the potential role of employment in causing neoplasms other than those already known.

Although population-based CRs are an important and unbiased source of cancer cases, they have only limited national coverage (i.e., about 20% of the total Italian population), and their incidence data only become available at the soonest two years (and often more) after case occurrence. This means that not all areas are suitable for CR-based cancer monitoring. Moreover, the lag in record availability means that emerging occupational hazards are not detected early enough to conduct in-depth investigations (e.g., interviews with cancer patients before they die) to verify working conditions and whether exposures are ongoing.

Another source of cancer cases are the hospital discharge (HD) records. In most Italian regions these records are used as the basis for making payments (from Regional funds) to public and private hospitals for patient diagnosis and treatment. As a result, they are virtually complete. Discharge records contain the patient identification code, municipality of residence, diagnostic codes, and date of discharge. They are archived in Regional databases and are available only after six months. The identification of new (incident) cases is simply carried out using diagnostic codes and defining as a period-specific incident case a subject with no previous discharge with the same disease. The information in these records is less reliable than CR data. Nevertheless, the use of these records has proved effective in identifying "known" risks in parts of Lombardy (e.g., bladder cancer associated with shoe manufacturing in the province of Pavia) where hazardous manufacturing operations were carried on.

Actively searching for occupational cancer cases

Cancer of some sites found among workers in "known" cancer risk jobs are suitable cases for detailed investigation to ascertain their potential occupational origin. Relevant sites are the nose, larynx, lung, pleura (even though a mesothelioma CR operates in many Italian regions), bladder and leukaemia. For exploration purposes, non Hodgkin's lymphomas, pancreas and soft tissue sarcomas are also considered.

For these purposes, the OCCAM system provides local Occupational Health Services (OHS) with the following information for each case:

- personal data: name, surname, date of birth, address;
- clinical data: diagnosis, date(s) and hospital(s) of discharge, clinical records reference, general practitioner;
- occupational data: employer firm(s), employment commencement and termination date(s).

Using this information, and their knowledge of production cycles and firms in their area, OHS staff are able to determine a subset of subjects apt to be affected by an occupational cancer. General practitioners will be enlisted to help contact these subjects for interview and possibly referral for occupational disease compensation. If the firms where these subjects worked are still operating, a detailed investigation into the presence of carcinogens in the workplace will be carried out. The pilot project, run in the Lombardy region, identified 102 cases as being of occupational origin out of 271 initially considered as potentially work-related.

Does OCCAM work?

- 102 new work-related cancer cases were identified in Lombardy in the first two years of operation.
- 271 occupational histories were looked at to identify these cases.
- These cases had never been considered as work-related.
- The system will be rolled out in other Italian regions.
- The main obstacles are lack of resources for Local Occupational Medicine Units and the lack of stable funding for coordination activities.

A matrix of available evidence has been devised (see below) to help identify the types of business operation that present a carcinogenic risk. Moreover, clusters of cases occurring in (sufficiently large) firms can be searched for.

Searching for and classifying the available evidence

To improve the recognition of occupational cancers and interpret the findings generated by the OCCAM project, we performed an extensive bibliographic search of scientific literature on occupational cancers.

We built an on-line "literature matrix" (available at www.occam.it) containing "positive" results from 685 (January 2008) cohort, case control and cross sectional, occupational cancer epidemiologic published studies. IARC monographs were also included. Papers were systematically scrutinized and results were classified by cancer site and production cycle or type (e.g., iron foundry, leather and shoe manufacturing, etc.). The matrix currently includes 1870 citations of results of epidemiologic studies from the 1960s to the present day, and is updated on an ongoing basis.

The matrix can be viewed as a tool for ascertaining whether a cancer case may be attributed to a worker's past work in a firm or business sector. It has been designed for ease of use by practitioners with little or no background in occupational medicine. The only information needed to use our data set are cancer site and business sector.

The matrix can also be used to interpret the findings of occupational cancer surveys, like the OCCAM project (7) where several associations are to be evaluated. This tool can provide prima facie evidence of the plausibility of the association of interest without the need for a formal literature search.

An interactive system (OCCAM-Medici di Medicina Generale) has been devised to allow general and hospital practitioners to ascertain the possibility of a cancer case being work-related. The system runs on an ordinary desktop computer under Windows and can be downloaded from the OCCAM web site.

Hopefully, the system we have devised will be taken up in other countries; we will gladly share our experience and tools to improve the recognition of occupational hazards and the active search for occupational cancer cases. ■

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