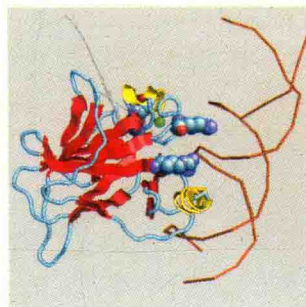
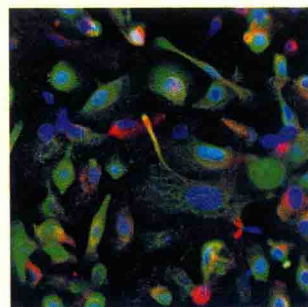
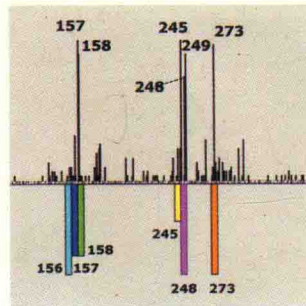
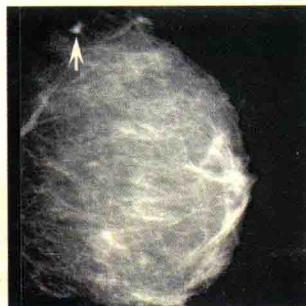
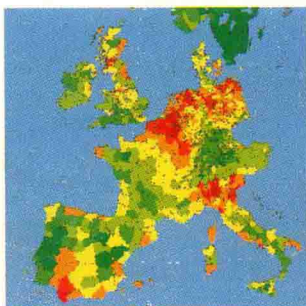
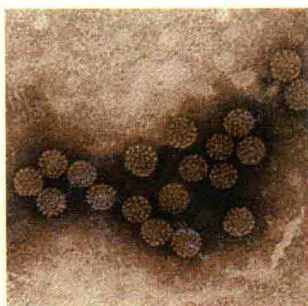


WORLD HEALTH ORGANIZATION



International Agency for Research on Cancer



**Biennial Report  
2002/2003**

WORLD HEALTH ORGANIZATION



INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

# BIENNIAL REPORT

2002–2003

International Agency for Research on Cancer  
Lyon, France

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# Introduction

This biennial report covers the period from January 2002 to December 2003 and provides detailed information on current and newly initiated projects. It reflects the wide range of IARC scientific activities, ranging from basic molecular biology and genetics to major studies on cancer prevention.

IARC scientists have an enviable record of publications in major scientific and medical journals, with 570 articles published or accepted for publication during the biennium under review, mostly in peer-reviewed journals. In addition, many chapters were included in books and IARC staff were editors of 18 books.

## Cancer registration

IARC continues to provide extensive support for cancer registration activities by giving practical and financial help to countries lacking the necessary indigenous resources, by promoting the optimization and standardization of registration procedures and by offering courses for training of personnel. The IARC-generated Can-Reg software for computerized registration is now installed in over 120 registries throughout the world, with versions in languages such as Arabic, Chinese and Thai.

## Cancer occurrence

The highlight of the descriptive epidemiology programme is the quinquennial publication of *Cancer Incidence in Five Continents*, of which the eighth volume appeared early in 2003. Some registries now have data series extending over 40 years. The sets of data from these volumes being assembled as an electronic publication will provide an incomparable resource for monitoring trends and progress in cancer control at the national and international levels.

Another unique recent publication from this programme is *Cancer in Africa*, which brings together information from all reported studies of cancer occurrence and etiology from the continent.

## IARC Monographs

The IARC Monographs programme has revisited a number of agents for which there is new evidence. The reconsideration of tobacco smoking was a major undertaking in view of the volume of published literature, but confirmed the carcinogenicity of both passive and active smoking, extending the list of sites at which tobacco causes cancer to include nasal cavities and sinuses, oesophagus (adenocarcinoma), stomach, liver, kidney (renal-cell), cervix and myeloid leukaemia. Re-evaluations of agents have usually strengthened the evidence of their carcinogenicity to humans. For some exposures, lack of epidemiological evidence and/or the assumption that tumours in experimental animals were caused through mechanisms not operative in humans, have led to a downgrading to a lower hazard level. This has been criticized by activist groups, but the Agency is confident that these evaluations will stand the test of time.

## Diet and nutrition

Uncertainties about the role of dietary factors in carcinogenesis remain considerable, but the first data on some 20 000 cancers among over 500 000 subjects in the EPIC cohorts, across 10 European countries, have mainly provided support for existing hypotheses, with regard to, for example, protective effects of higher consumption of fruit, vegetables and fibre against colorectal cancer and of fruit against lung and stomach cancer. In view of the increasing evidence of the importance of hormonal factors in the dysregulation of cellular development that leads to cancer, a new research group has been established, under the leadership of Dr Rudolf Kaaks, that is conducting mainly epidemiological studies of these effects. The main foci of these studies are insulin and related molecules and the steroid sex hormones, in relation to cancers of, for example, the breast, endometrium, ovary and prostate, for which known environ-

mental carcinogens do not seem to be major etiological factors. During the biennium, the capacity for high-throughput genetic analyses has been greatly expanded. For several major cancer types, DNA polymorphisms of the genes involved in hormonal pathways are being explored.

## Infectious agents

Viral agents are now believed to participate in the etiology of many cancers, and many epidemiological studies are in progress to refine our understanding of these. To enhance the in-house capacity for work with these agents, a new unit has been created, headed by Dr Massimo Tommasino, and a new high-containment P3 laboratory has been installed.

Two infectious agents now clearly established as causes of cancer are human papillomavirus as an essential factor in cervical cancer, and the bacterium *Helicobacter pylori*, which is involved in stomach carcinogenesis. Infections with both agents are much more common in human populations than the corresponding cancers, so detailed work is under way to define what co-factors (environmental, metabolic or genetic) lead certain infected tissues to progress to a malignant state. It appears that certain forms of some HPV proteins may be associated with persistence of the viral infection, with consequently increased risk of cancer. Inflammation and oxidative stress are also involved in the effects of *H. pylori* in relation to stomach cancer, and the mechanisms of the interactions between these effects are being analysed in detail.

## Lung cancer

Although tobacco smokers run a high risk of cancer, as well as of many other diseases, many smokers somehow escape the harmful effects of their habit. This could be due to compensatory beneficial lifestyle aspects, such as high consumption of protective fruit and vegetables, or to genetic variations in the enzymes involved in the



activation and detoxification of the carcinogens known to be present in tobacco smoke. Epidemiological studies are exploring these issues, including detailed genetic analyses using newly developed microarray techniques to evaluate the roles of many different polymorphisms.

### Breast cancer

Breast cancer has a clearly genetic component in its etiology. The two major genes identified to date (*BRCA1* and *BRCA2*) account a significant part of the heritable fraction of the disease. Work is in progress to assess the role of other genes such as *ATM* and others involved in the repair of DNA damage, as well as to identify hitherto unknown genes. In parallel, the significance of specific polymorphisms or mutations in the known breast cancer genes is being examined using new analytical and statistical techniques, to assess which variants are particularly deleterious. With the spread of genetic analysis in clinical evaluation, this work is becoming of direct relevance to patient care and counselling.

### Carcinogenesis

A population-based study on more than 900 glioma cases revealed excellent survival of patients with pilocytic astrocytoma, but also very poor prognosis associated with glioblastoma: only about 1% were still alive three years after diagnosis. The only significant predictors of particularly poor prognosis were old age and loss of heterozygosity on the long arm of chromosome 10, whereas other genetic alterations had no influence on survival.

Genetic analysis of oesophageal carcinomas from Iran, a country with a very high burden of this disease, revealed a high prevalence of G:C to A:T transitions at CpG dinucleotides, strongly suggesting an endogenous origin, probably reflecting chronic inflammatory tissue damage. The habit of drinking very hot tea remains a possible etiologic factor.

Inflammation activates a variety of inflammatory cells, which induce and activate several oxidant-generating enzymes. These enzymes produce high concentrations of diverse free radicals and oxidants, which

react with each other to generate other more potent reactive oxygen and nitrogen species such as peroxynitrite. These species can damage DNA, RNA, lipids, and proteins, leading to increased mutations and altered functions of enzymes and proteins, thereby contributing to the multistage carcinogenesis process.

### Cancer prevention

Work on primary prevention of cancer, aiming at reducing the burden of disease by preventing the initial causes, is particularly focused on vaccination programmes against viral infections. The Gambia Hepatitis Intervention Study has now been running for more than 15 years. The principal activity of following up the vaccinated cohort is in a long-term routine phase through the national cancer registry, although improvements in registry coverage and in identification of cohort members are always being sought. Meanwhile, ancillary studies, for example of aflatoxin-related *TP53* mutations, continue to benefit from the infrastructure now in place for the main study.

A second vaccination project, still in the planning phase in collaboration with WHO, is designed to test the reduction in human papillomavirus infection, with the aim of diminishing the incidence of cervical cancer, one of the commonest cancers of women in developing countries. Another prong of the attack on this disease is the major project in 10 African and Asian countries, with the generous support of the Bill and Melinda Gates Foundation, for early detection of cervical lesions and their treatment, by methods adapted to use in countries with limited resources. Various detection techniques are being tested, in parallel with programmes to train health care personnel. Randomized trials in India and Nepal are comparing cryotherapy and loop electrosurgical excision procedures for removal of pre-invasive cervical cancer.

The *IARC Handbooks of Cancer Prevention* have evaluated the cancer-preventive effects of breast-cancer screening and of consumption of fruit and vegetables. The book on breast cancer screening has had a great impact on discussions in several IARC member states which are consi-

dering the introduction of population-based screening programmes.

### IARCPress

The Agency's own book publication programme has continued to produce many important volumes, as demonstrated by the ever-increasing sales figures achieved by IARCPress. In the series WHO Classification of Tumours (WHO Blue Books), five volumes have been published and the sixth, on *Tumours of the Urinary System and Male Genital Organs*, went to press in December 2003. It is anticipated that the entire series of 10 volumes will be published by the end of 2004. These Blue Books now have an initial print run of 15 000 copies each. One exceptional project was the *World Cancer Report*, published in early 2003, which reviews the whole field of cancer, covering its occurrence, causes, mechanisms of carcinogenesis, treatment and prevention and national cancer control programmes. A first in the Agency's history, the book was well received, with 20 000 copies already printed and a French edition in preparation.

### Fellowships and training

In the present biennium, 15 fellowships were awarded in each year to young scientists of exceptional merit, to pursue their research careers either at IARC or in other institutions, mainly in Europe or the United States. Eight training courses were held in the core programme, hosting over 300 participants, and in addition the Unit of Descriptive Epidemiology was particularly active in organizing courses on cancer registration and on coding and computer software, as well as several on various aspects of cancer epidemiology.

### Staff and visitors

At the end of the biennium, a total of 326 people were working at the Agency, of whom 143 were fixed-term staff members, 72 short-term staff members, and the other 111 special training awardees, fellows, visiting scientists and trainees. While budgetary constraints have limited the recruitment of long-term staff, an increasing number of doctoral students and postdoctoral fellows contribute to the



work of the Agency. In addition, the Agency has become increasingly attractive for visiting scientists, who often bring new ideas and frequently initiate collaborations that continue long after their departure.

During 2002–2003, the IARC Visiting Scientist Awards were held by Dr John Witte, from the Department of Epidemiology and Biostatistics at Case Western Reserve University, Cleveland, Ohio, and Dr Tony Fletcher, from the Environmental Epidemiology Unit, Department of Public Health and Policy at the London School of Hygiene and Tropical Medicine.

Dr Paola Pisani, from the Unit of Descriptive Epidemiology, went on special leave for training purposes to Leeds University in the UK, and Mr Ebrima Bah (The Gambia) went on study leave to Tampere University in Finland.

In June 2002, Dr Giovanni Romeo, Chief of the Unit of Genetic Cancer Susceptibility, retired to become Professor of Genetics at the University of Bologna, Italy. To succeed him, the Agency recruited Dr Sean Tavtigian, who previously worked at Myriad Genetics in Salt Lake City, Utah, where he was part of the team that identified and sequenced the *BRCA1* gene.

Following the retirement of Ms Helis Miido in October 2002, Ms Sharon Grant, previously at McGill University, Montreal, Canada, was appointed head of the Library, which is now part of the Unit of Communications.

Dr Jerry Rice also retired in 2002 and was succeeded as Chief of the Unit of Carcinogen Identification and Evaluation by Dr Vincent Coglianò, previously at the United States Environmental Protection Agency, Washington, DC. In the same Unit, Dr Nikolai Mironov took early retirement in March 2002, and Mrs Christiane Partensky retired, after more than 30 years of service to the Monographs programme, at the end of January 2003.

Dr Paolo Boffetta, Chief of the Unit of Environmental Cancer Epidemiology accepted an offer from the German Cancer Research Centre (DKFZ) in Heidelberg, to become Chief Epidemiologist and Professor of Epidemiology at the University of Heidelberg.



Visit to IARC of the French Minister of Health, Professor Jean-François Mattei (centre) on 8 December 2003, with Dr Paul Kleihues (left) and Dr Gilbert Lenoir, the French delegate to the Governing Council (right)

Dr Harri Vainio, Chief of the Unit of Chemoprevention, left IARC in December 2003 to take up the position of director of the Finnish Institute of Occupational Health in Helsinki.

New professional staff members at IARC in 2002–2003 include: Dr Wael Al-Delaimy in the Unit of Nutrition and Cancer, Dr Deepika de Silva in the Unit of Genetic Cancer Susceptibility, Dr Isabelle Deltour in the Unit of Radiation and Cancer, Dr Yann Grosse in the Unit of Carcinogen Identification and Evaluation, Dr Zdenko Herceg and Dr Wei-Min Tong in the Unit of Gene–Environment Interactions, Dr Hervé Huang in the Unit of Molecular Pathology, Dr Cédric Mahé in the Unit of Descriptive Epidemiology and Dr Tomohiro Sawa in the Unit of Endogenous Cancer Risk Factors.

Two new Research Units were created in 2002. The Unit of Infection and Cancer is headed by Dr Massimo Tommasino, previously at the German Cancer Research Centre (DKFZ) in Heidelberg, who is continuing his work on mechanisms of HPV-associated carcinogenesis, particularly in the development of skin tumours. Dr Emmanuel Lazaridis, previously at the University of Tampa, Florida, USA, was appointed Chief of the Unit of Bioinformatics and Biostatistics.

In February 2002, a new research group was created: Hormones and Cancer,

headed by Dr Rudolf Kaaks. In July 2002, Dr Pierre Hainaut was promoted to Chief of the Unit of Molecular Carcinogenesis.

On behalf of the Agency and its member states, I should like to express my gratitude and appreciation for the excellent work of the outgoing staff members, together with best wishes for their future activities.

### Relations with the City of Lyon

After some intensive negotiating, the Convention with the City of Lyon regarding the lease of the tower building was renewed and signed by the Mayor, Mr Gérard Collomb, and the Director on the occasion of IARC Day in May 2002. This reflects the excellent relationship and the continuous support that the Agency has received from the City of Lyon, ever since its creation in 1965.

### Visit of the French Minister of Health

In December 2003, Professor Jean-François Mattei, the French Minister of Health, visited the Agency and signed an agreement for an extra-budgetary donation of !1 000 000 from the French Government to extend the Agency's scientific programme. These funds will be mainly used for research on tobacco and cancer.

### IARC Day

This traditional event is held in conjunction with the Governing Council



meeting and is important since it strengthens the Agency's interactions with the scientific, diplomatic and political communities of Lyon. The Professor Roger Sohler Lecture 2002 was delivered by Dr J. Koplan (previously Director, Centers for Disease Control, Atlanta, Georgia, USA), who impressively documented the dramatic changes in lifestyle in developed countries and their adverse effects on public health. Another highlight of IARC Day 2002 was the musical performance of Dr Gottfried Thiers, Chairman of the WHO Executive Board, who is an accomplished singer and was greatly applauded for his programme of classical songs.

IARC Day 2003 was the last for the outgoing Director, who presented the Sohler Lecture on Poverty, Affluence and the Global Burden of Cancer and who also acted as guest conductor of the IARC chamber orchestra.

### Scientific Council

Members of the Scientific Council are elected on the basis of their expertise in areas of cancer research relevant to the work of the Agency. In addition to critically reviewing the work of IARC scientists, they give valuable advice on future research strategies. Our sincere thanks go to the Chairmen and Vice-Chairmen of the Scientific Council, Dr M. Aguet (Switzerland), Dr L. Borysiewicz (United Kingdom) and Dr A.L. Børresen-Dale (Norway). At the same time, we wish to thank those members who left the Council during the past biennium: Dr L. Aaltonen (Finland), Dr M. Aguet (Switzerland), Dr D. Bootsma (The Netherlands), Dr J. Olsen (Denmark), Dr F. Berrino (Italy), Dr A.L. Børresen-Dale



Dr Kleihues conducts the IARC chamber orchestra, in a performance of a Handel organ concerto with the solo part played on the piano by Dr Hiroko Ohgaki



Dr J.M. Martin-Moreno (Spain) with the Chairman of the Governing Council, Dr J. Larivière, at the admission of Spain as a Participating State of IARC on 15 May 2003

(Norway), Dr K. Hemminki (Sweden), and Dr H. Rabes (Germany). Newly elected to the Council were Dr H. Autrup (Denmark), Dr J. Jiricny (Switzerland), Dr F. van Leeuwen (The Netherlands), Dr P. Pietinen (Finland), Dr J.D. Potter (USA – re-elected), Dr W. Boecker (Germany), Dr E. Lund (Norway), Dr M. Pierotti (Italy), and Dr R. Toftgard (Sweden).

### Election of IARC Director

At the Governing Council meeting in May 2003, Dr Peter Boyle, Director of the Department of Epidemiology and Biostatistics at the European Institute of Oncology, Milan, Italy, was elected Director of IARC for the period 2004–2008. He will take office on 1 January 2004. Since his election, he has been in frequent contact with the current Director and the Administration to ensure a smooth and effective transition.

### Spain joins the Agency

At the May 2003 meeting of the Governing Council, Spain was admitted as the 16th Participating State of the Agency. All delegates and IARC staff warmly welcomed this event, and look forward to increasing collaboration with the Spanish cancer research community.

### Governing Council

At the Governing Council in 2003, the budget for the biennium 2004–2005 was approved with a 4.43% increase in the programme budget. This will enable IARC to maintain its current level of scientific activities and will enable the new Director to expand into some new research domains.

### Interaction with WHO Headquarters

The relationships with WHO Headquarters have been further strengthened at both the technical and administrative levels. We wish to thank Dr Gro Harlem Brundtland, Director-General, WHO, for her continuous support and advice. The new Director-General of WHO, Dr J.-W. Lee, has shown a strong interest in the work of the Agency and plans a visit to Lyon early in 2004.

On behalf of the Agency and its staff, I would like to thank the Governing Council for its support during my term as Director over the past 10 years.

Paul Kleihues, M.D.  
Director



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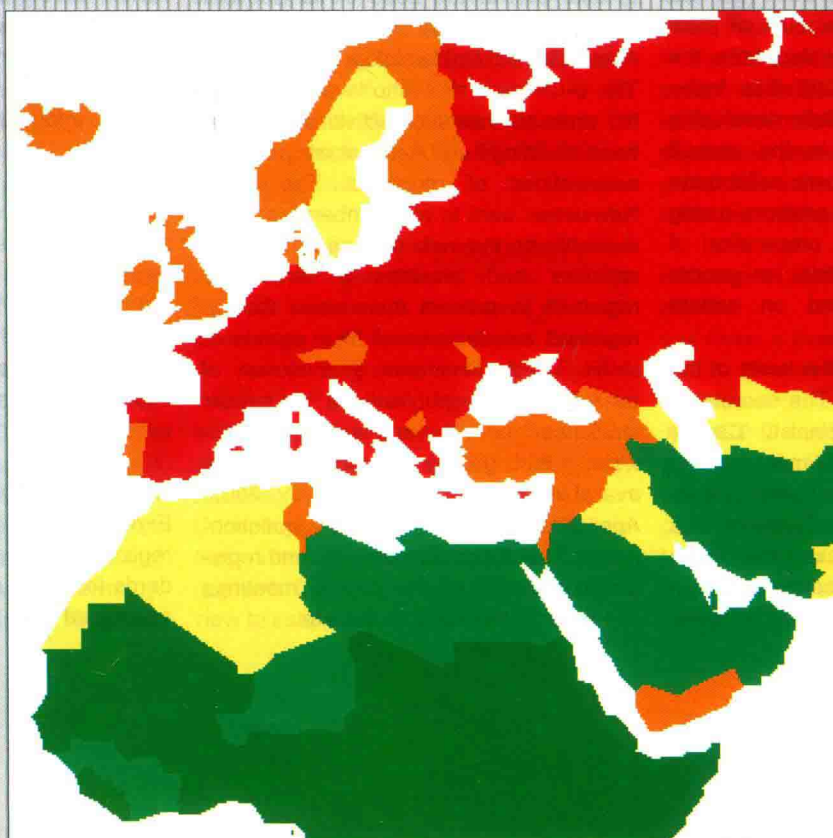


## Part 1

# Cancer occurrence and outcome

IARC provides support for cancer registries in all regions of the world. These registries constitute an essential public health resource for national cancer control programmes and a key activity of the Agency is to ensure that registries use common methods and definitions, so as to ensure comparability of their data. Many studies of cancer causes such as environmental and genetic factors in specific populations are built upon data on incidence and outcomes from the cancer registries, as are a range of primary and secondary prevention studies.

Analysis of geographic variation in cancer incidence, trends and outcomes depends on the development of suitable software packages. A major preoccupation is the dissemination of the results through the publication of *Cancer Incidence in Five Continents* and a range of other printed and electronic outputs.





## 1.1 Support to cancer registries

Cancer registries are the source of information on incidence of cancer in defined populations, as well as on outcome, in terms of survival. They also provide a framework for conducting epidemiological studies into the cause of different cancers. In many parts of the world, cancer registries provide the only available information on the nature and evolution of the local cancer problem. The comparative value of the statistics which cancer registries produce depends upon the use of common methods and definitions, so that international collaboration in this area is essential.

### International Association of Cancer Registries (IACR)

D.M. Parkin, S.L. Whelan, S. Haver; in collaboration with D. Forman, Leeds, UK; H.H. Storm, Copenhagen, Denmark

IARC provides administrative facilities to the International Association of Cancer Registries (IACR). The IACR is a non-governmental organization in official relations with WHO, and in 2003 had 463 members in 123 countries, 80% of them cancer registries. Membership fees are used to fund Association activities, including support to members from developing countries to participate in the annual scientific meetings. Members collaborate actively with IARC in projects using cancer registry data, the preparation of publications presenting data on cancer occurrence worldwide and on cancer registration methodology.

Assistance is provided to the hosts of the annual scientific meeting. The secretariat collaborated with the Finnish Cancer Society to organize the 2002 meeting, held in Tampere in June. The overall theme was *Registries in Cancer Research* and the programme encompassed the health effects of the Chernobyl accident, evaluation of prevention strategies, biological

and genetic data banks, survival and ethics. In 2003, the subject of *Cancer Registration and Surveillance around the World* was the focus of a meeting in Hawaii, including sessions on Pacific islanders and indigenous populations, physical activity, diet, migrants and cervical cancer with special reference to human papillomavirus and vaccines. Preparations are now being made for the 2004 meeting, to take place in Beijing, China.

The Association provided support for African registry members to attend a meeting of the African Organization for Research and Training in Cancer, held in Accra, Ghana, in October 2003. The African Regional Representative of IACR, Dr Henry Wabinga, took the opportunity to organize a meeting of the African group of IACR cancer registries.

A Calum Muir Memorial Fellowship (to help personnel working in cancer registries to spend time in institutions which offer learning opportunities not available in their home institute) was awarded to Dr Chu Hoang Hanh from Hanoi, Viet Nam to take part in the 2003 IARC Summer School on Cancer Registration and Applications in Epidemiology.

The IACR web site (<http://www.iacr.com.fr/>) presents news of activities, publications, meetings and national and regional associations of registries. The IACR Newsletter, sent to all members and also available on the web site, gives news of activities and provides a forum for registries to present their work. Cancer registries send copies of their reports to IACR, which maintains a collection of over 2300 such publications on cancer incidence, mortality and survival worldwide, a bibliography of which was made available on the web site in 2003. Applications for membership, questionnaires for collaborative projects and registration material for the annual meetings can be downloaded from the site.

### European Network of Cancer Registries

D.M. Parkin, J.E. Tyczynski, F. Bray, E. Démaret, J. Ferlay, E. Riboli; in collaboration with L. Barlow, Stockholm, Sweden; U. Batzler, Stuttgart, Germany; D. Brewster, Edinburgh, UK; J.W.W. Coebergh, Eindhoven, Netherlands; J. Faivre, Dijon, France; I. Izarzugaza, Spain; H. Møller, London, UK; L. Simonato, Padua, Italy

Supported by the Public Health Directorate of the European Commission

The aims of the European Network of Cancer Registries (ENCR) are to improve the quality, comparability and availability of data from cancer registries in Europe, and to promote the use of these data in research and cancer control activities. The ENCR has 184 member registries in 43 European countries (97 member registries in countries of the European Union (EU)). A steering committee, comprising elected members and nominees of cancer registry associations, guides and advises the secretariat provided by IARC. An ENCR Scientific and General Meeting was held in Tampere (Finland) in 2002 to review ENCR activities and to present registries' research projects.

The ENCR Internet home page at <http://www.encr.com.fr> provides comprehensive information on the activities of the ENCR.

#### *Automated cancer registration*

A specific web site for automated cancer registration was launched in spring 2003 (<http://150.92.82.173/encr>), to provide information on the principles and benefits of automated registration, definitions, an interactive test site and related publications.

#### *Establishing standards and definitions*

Expert working groups review aspects of registration practice and propose standards for the European registries. Issues addressed in 2002 and 2003 were

## 2 Support to cancer registries



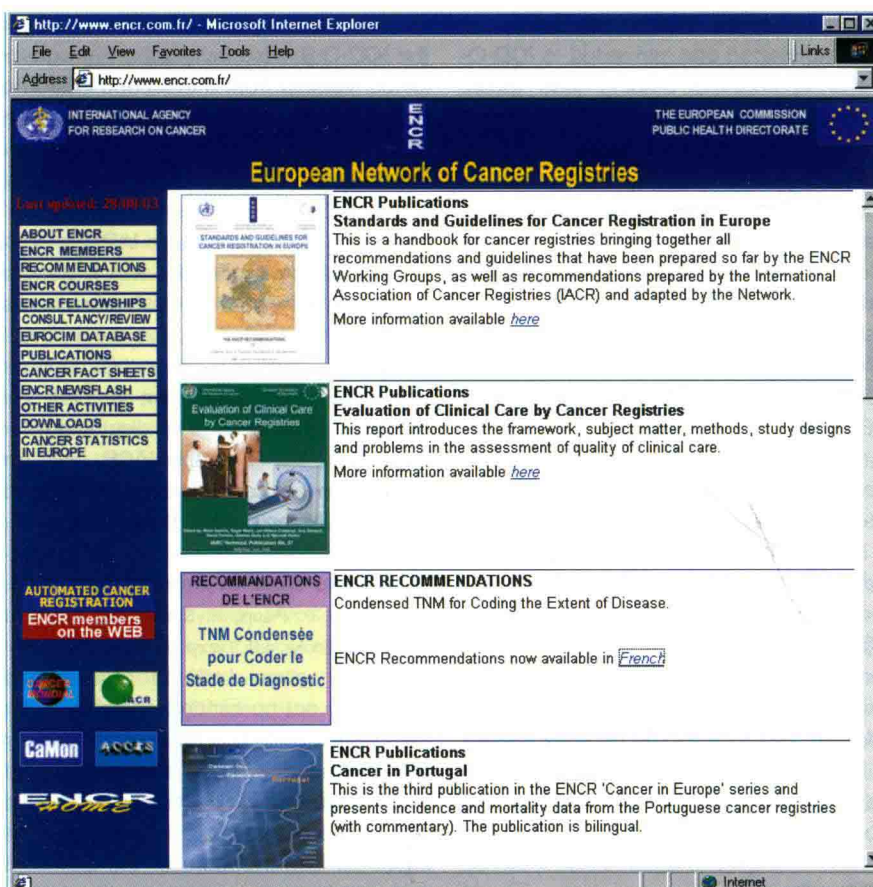


Figure 1. The ENCR home page

confidentiality in cancer registration (March 2002) and coding extent of disease (May 2002), and work on coding of bladder cancers and on completeness of registration was initiated. The working group on automated cancer registration met three times in 2002 and in 2003.

A handbook on *Standards and Guidelines for Cancer Registration in Europe* (IARC Technical Publication No. 40) [518] was published in 2003.

#### Training and fellowships

Cancer registration courses were held in Lyon, France in April 2002 and in Cluj, Romania in August 2003. Courses on statistical analysis methods are held annually; the topic in 2002 was geographical analysis, and in 2003 time trends analysis. Four courses on coding using ICD-O-3 were organized, in Germany, Norway, Spain and the United Kingdom.

Courses on the use of the new EUROCIM software (version 4.0) were held in Spain and in Italy (see Section 7.3).

ENCR provides support to registry personnel to attend ENCR courses or to exchange skills through working visits to other registries. In 2002–03, 30 fellowships were awarded.

#### Consultancy and structured reviews

In 2002, an audit programme to provide in-depth reviews was introduced. Reviews took place in Hungary (National Paediatric Cancer Registry, Budapest), Poland (Holycross Cancer Registry, Kielce), Ireland (National Cancer Registry, Cork) and Germany (Regional Cancer Registry, Bremen).

Consultancy visits were made to Bosnia and Herzegovina (R. Sankila) and northern Cyprus (J.E. Tyczynski), with a view to establishing cancer registries.

### Provision of information on cancer in Europe

Information on the burden of cancer in European populations is provided through traditional and, increasingly, electronic publications. Work included updating the EUROCIM databases and software, developing the new EUCAN dynamic database and software package and providing data for new projects (see Section 1.2). Work on the series "Cancer in Europe" continued, with the publication of an analysis of cancer incidence and mortality in Portugal (IARC Technical Publication No. 38) [372]. Analyses of time trends in melanoma, mesothelioma, breast cancer and lung cancer in Europe were published [75,81,134,314]. Three ENCR Cancer Fact Sheets were produced (on lung, breast, and bladder cancer in Europe).

### Reliability and validity of registry data

#### International Classification of Diseases

D.M. Parkin, S.L. Whelan; in collaboration with A. Jack, Leeds, UK; C. Percy, A. Fritz, Bethesda, MD, USA; K. Shanmugaratnam, Singapore; L. Sobin, Washington, DC, USA

IARC is responsible for producing the neoplasms chapter of the International Classification of Diseases (ICD) and the International Classification of Diseases for Oncology (ICD-O). The extensive revision of the haematological morphology rubrics in the third edition of ICD-O (ICD-O-3), published in 2000, led to inconsistencies in the international rules for the counting of multiple primary diagnoses. A working group was convened in 2003 and revised rules are to be published.

#### Histological groups for comparative studies

D.M. Parkin, J. Ferlay, S.L. Whelan; in collaboration with K. Shanmugaratnam, Singapore; L. Sobin, Washington, DC, USA

The ICD-O histology codes are grouped into classes for studies of etiology and survival. *Histological Groups for Comparative Studies* (Parkin *et al.*, 1998, IARC Technical Report No. 31) provided a description of recognized histological subtypes of selected cancers. In 2002 a



scheme for presenting histological data on one further site, cancer of the anus, and groupings for the tabulation of the major types of sarcoma and for mesotheliomas by site, were produced and published in Volume VIII of *Cancer Incidence in Five Continents*.

### International Classification of Childhood Cancer

E. Šteliarová-Foucher, D.M. Parkin, N. Mitton; in collaboration with P. Kaatsch, Mainz, Germany; B. Lacour, Nancy, France; C.A. Stiller, Oxford, UK

Publication of the third edition of the ICD-O (see above) necessitated a revision to the existing International Classification of Childhood Cancer (ICCC). In order to preserve the capacity for comparison with older data, the new edition (ICCC-3) is, as before, classified into twelve main diagnostic groups: leukaemias, lymphomas, central nervous system tumours, neuroblastoma, retinoblastoma, renal tumours, hepatic tumours, bone tumours, soft-tissue sarcomas, germ-cell tumours, epithelial tumours and other and unspecified tumours. All these groups except retinoblastoma are further classified into more homogeneous diagnostic subgroups. The overall content of the different diagnostic groups is similar to that in the previous edition of ICCC, but newly recognized entities are included. The most important change is the inclusion of myelodysplastic syndrome and other myeloproliferative diseases, now considered to be malignant. Another new feature is the capacity to divide selected diagnostic subgroups into 2–11 subdivisions.

ICCC-3 was submitted for publication during 2003 and an automatic conversion program is in preparation.

### Computer software for cancer registries

#### CanReg

D.M. Parkin, A. Cooke

CanReg is a configurable computer program designed for cancer registration in population-based registries. Over the last two years, all users of version 3 have been upgraded to the Windows version, CanReg4 (Figures 2 and 3). This was accomplished by organizing regional

courses in which the users' databases were transferred and converted to ICD-O-3 and appropriate training was given. Over 120 registries are now using the program in about 60 countries.

The data-entry module provides consistency checking for impossible/rare cases, searching for duplicate records and multiple primaries using probability matching and conversion from one classification system to another. Easy-to-use analysis options include frequency distributions, reports, incidence tables and an interface to EpiInfo.

CanReg4 allows full integration into a Windows-based network environment and extends the language-swapping capability to languages such as Arabic, Chinese, and Thai.

Special versions have been developed in collaboration with the Middle East Cancer Consortium and installed in the participating countries (Egypt, Jordan, Cyprus, Palestine). The project is partially funded by the Bill and Melinda Gates foundation through the Alliance for Cervical Cancer Prevention and Control.

#### IARCcrgTools

IARCcrgTools is a Windows®-based package providing various batch programs to convert data from ICD versions 9 or 10 or

the first and second editions of ICD-O, to the ICD-O-3. Also included are programs for conversion from the second edition of ICD-O to ICD versions 9 and 10, and from ICD-O-3 to ICD version 10 and to the International Classification of Childhood Cancer (ICCC).

The IARC-CHECK and the IARC multiple primary check programs, which perform various validity and consistency checks, have been updated to use the ICD-O-3 codes. In particular, new histology/site validation rules have been defined. The IARCcrgTools package is distributed free from the Internet at the IACR web site (<http://www.iacr.com.fr/iarcrcrgtools.htm>) or on CD-ROM (on request).

#### Support to specific cancer registries

D.M. Parkin, P. Pisani, R. Sankaranarayanan, S.L. Whelan, A. Cooke, J.E. Tyczynski

Advice is given both to organizations wishing to set up cancer registries and to established registries on the methodology of registration and the analysis of data. Staff of the Unit of Descriptive Epidemiology have made visits to many cancer registries in the course of the biennium, and individuals working in cancer registries have visited IARC for training or discussion. A structured course in cancer registration and applications in epidemio-

Figure 2. CanReg4; example of data-entry screen



logy is held every May in Lyon and 10 courses on coding and use of CanReg were held during the biennium (see Section 7.3). In May 2003, a course was held in Buenos Aires jointly with the country programme (VIGIA) of the World Bank, for new registries recently established in Argentina.

In September 2003, 26 cancer registries in developing countries were receiving direct support in the form of a collaborative research agreement, to enable them to start activities or to purchase equipment. Several commonly used computer programs are provided to registries (see above). Aid with analyses often leads to joint publications (see Section 1.2).

Close collaboration is maintained with regional offices of WHO with respect to cancer registry activities. IARC staff provided consultancies on cancer registration and cancer control in several countries.

*Algeria:* Three registries received assistance: in Mascara (H. Hamdali), Oran (L. Mokhtari and N. Midoun) and Sétif (M. Hamdi-Chérif).

*Argentina:* Three registries are supported, Bahia Blanca (E. Laura and N. Arias Ondicol), Buenos Aires (R. Pradier) and Concordia (M.A. Price). A consultant visit was made on behalf of IARC to Mendoza and Bahia Blanca.

*Bahrain:* (J. Al-Sayyad): Progress was reviewed during a visit in 2003.

*Burkina Faso:* (B. Sakande and R.B. Soudré): Registration for the city of Ouagadougou commenced in 1998. A review visit by a staff member was made in March 2003.

*Cambodia:* (P. Piseth Raingsey and Khuon Eng Mony): The registry was visited in 2002 and a consultant visit arranged in 2003, to assist the staff with abstraction and coding of data and with the use of CanReg.

*China:* (Li Lian-di, Yang Ling, Zhang Si-wei): During the biennium, a special programme was established to enhance cancer registration and availability of cancer data from China. A visiting fellow from the National Office of Cancer Prevention and Control assisted with a review of existing data sources (both

mortality and incidence) and carried out a survey of cancer registries nationwide, and training courses were held for registry staff, in collaboration with the National Office of Cancer Prevention and Control. A version of CanReg was developed using Chinese characters and a special training course was held (see Section 7.3).

*Congo:* (C. Gombe-Mbalawa and S. Moubie): Support continues for the Brazzaville registry.

*Côte d'Ivoire:* (A. Echimane): Support to the registry continues.

*Cuba:* The central registry in Havana (L. Fernandez and Y. Galan) is being decentralized to regional registries, and assistance is being provided in developing computer systems.

*Gabon:* (E. Belembagao and P. Nsi-Obame): A consultant visit took place in March 2002, and recommendations were made for development of the national registry in two locations.

*The Gambia:* (E. Bah): The cancer registry is an integral part of the Gambia Hepatitis Intervention Study (see Section 5.1) and the registry collaborates in the study of cancer survival (Section 1.4).

*Guam:* (R.L. Haddock): Population coverage has been completed with the inclusion of information from private clinics. A consultant visited on behalf of IARC in June 2003.

*Guinea:* (M. Koulibaly and I. Kabba): Support to the registry continues.

*Honduras:* The registry supervisor in Tegucigalpa (J. Figueroa) took part in a training course in Lyon

*India:* Numerous registries participate actively in research projects on cervical cancer screening (Ambilikkai: J. Cherian and R. Rajkumar; Barshi: B. Nene, K. Jayant and A. Budukh; Kolkata (Calcutta): M. Siddiqi and U. Sen), cancer survival (Bhopal: S. Khanere and R. Dikshit; Mumbai (Bombay): B.B. Yeole; Chennai (Madras): V. Shanta and C. Swaminathan), oral cancer screening (Trivandrum: K. Nair and A. Mathew) (Section 5.3) and a cohort study focusing on the risks of tobacco use (Mumbai and Trivandrum) (Section 2.4). IARC staff act as advisers to the National Cancer

Registry Project (A. Nandakumar) and to a WHO-sponsored project to develop a national cancer atlas for India (A. Nandakumar). Technical support was provided for development of pathology-based and population-based cancer registries in various regions of India.

*Iran:* The registry in Teheran (A. Mohagheghi and A. Mosavi) now covers the entire metropolitan population. New registries have been established by the Digestive Diseases Research Centre (R. Malekzadeh and A. Sadjadi) in the Caspian region, for studies on oesophageal cancer (Golestan) (see Section 3.1) and stomach cancer (Ardabil). There are plans to reactivate the cancer registry in Shiraz (M.J. Saalabian and J. Shamsnia). *Kenya:* Progress at the recently established cancer registry in Eldoret (N. Buziba), western Kenya, was evaluated at a visit during 2002, and a staff member assisted with renewal of the computer system in 2003.

*Lao People's Democratic Republic:* (B. Phouthone and P. Alongkone): A visit to evaluate the success of this registry project was made in 2002.

*Malawi:* (C. Dzamalala and N.G. Liomba): Dr Dzamalala attended a training course on CanReg4 in Lyon in September 2002.

*Mali:* (S. Bayo and S. Kané): The registry is actively collaborating in the studies of cervical cancer screening (see Section 5.3). A visit was made in March 2003 to evaluate progress.

*Mauritania:* (M.H. Diop): A consultant visit was made in 2002 to discuss setting up a cancer registry. Dr Diop attended a training course in Lyon in 2002.

*Mozambique:* (J. Ferro): A consultant visit on behalf of WHO in April 2003 recommended delay in the implementation of a regional registry until the issue of the scientific direction could be clarified.

*Niger:* (H. Nouhou): Support to the registry continues.

*Nigeria:* The Ibadan registry (J.O. Thomas) provides the framework for a study of non-Hodgkin lymphoma related to human immunodeficiency virus (HIV) and surveillance of temporal trends in HIV-related related cancers (Section 2.7). A consul-



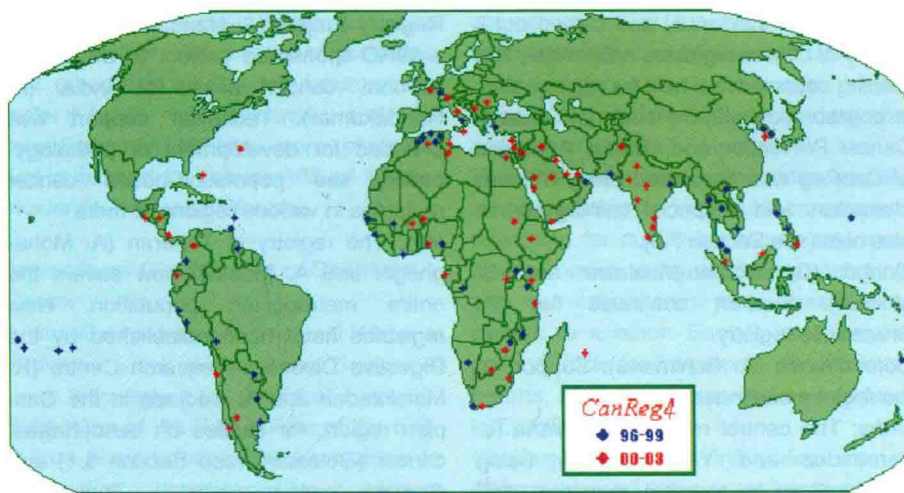


Figure 3. Locations of CanReg4 installations

tant visit was made in 2003, to advise how to support the development of registry projects in Ife-Ijesha (S. Ojo), Calabar (I.O. Ekanem) and Maiduguri (M.I. Khalil).

**Oman** (J. Al Lawati): Registry results for 1993–97 were published in volume VIII of *Cancer Incidence in Five Continents*. Progress was reviewed during a visit in 2003.

**Pakistan**: A population-based registry (Y. Bhurri) covering the population of the southern part of Karachi is supported. A new registry is planned for the city of Lahore, with the support of the International Network for Cancer Treatment and Research (INCTR). A consultant visit was made during 2003.

**The Philippines**: The two registries in greater Manila (D. Esteban and A. Laudico) are active in the follow-up of the breast cancer screening project (Section 5.3). The data of the Manila registry are being used for studies of survival.

**Romania**: Cancer registration (C. Chiotan, D. Coza and N. Ghilezan) is being developed through initiatives in the Ministry of Health and in several provinces. The regional cancer registry in Cluj-Napoca hosted a course in cancer registration and CanReg4 for the ENCR in August 2003 (see Section 7.3). The Ministry of Health plans to develop five regional cancer registries (with support of the ENCR and the European Commission's PHARE programme), to cover the whole population

of Romania. A special version of the CanReg4 software has been prepared.

**Saudi Arabia**: The national registry (N. Al Hamdan) provides a resource centre for the other registries in the countries of the Gulf Cooperation Council. A visit was made in 2003 to discuss how to coordinate support to the latter group.

**Senegal**: One of the first population-based registries in Africa was located in Dakar. The situation seems favourable to its reactivation, which was discussed during a consultant visit, and the director of the project (J.-M. Dangou) attended the training course in Lyon in 2003.

**South Africa**: Currently, the only population-based registries are in the Transkei regions of the Eastern Cape, supported by the PROMEC programme of the South African Medical Research Council (four districts: N. Somdyala, W. Marasas and W. Gelderblom) and the University of Transkei (Umtata district, D. Mugwanya). A visit was made to make recommendations for future development.

**Swaziland** (S. Okonda): A visit was made to review progress with the national cancer registry in April 2002.

**Tanzania**: A registry in Moshi (E. Moshi) has operated since 1998, covering four surrounding districts of the north of Tanzania. A hospital-based cancer registry has been set up in the Ocean Road Cancer Institute (T. Ngoma and F. Temu-Mbaga), as a first step to population-

based registration in the Dar es Salaam area. A staff member received training in Lyon.

**Thailand**: Five population-based registries (Lampang, Chiang Mai, Khon Kaen, Bangkok and Songkhla) (S. Deerasamee, P. Srivatanakul, S. Srisukho, S. Sontipong, S. Sriamporn, H. Sriplung and N. Martin) are collaborating in the preparation of a third monograph on cancer in Thailand. Khon Kaen registry provides follow-up for a population-based study (Section 3.3) and together with Chiang Mai participates in the studies of cancer survival (Section 1.4).

**Turkey** (M. Tuncer, C. Fidaner and S. Eser): Registration for Izmir province is now complete. The registry is providing a model for the development of a network of regional registries. A consultative visit was made in January 2003.

**Uganda** (H. Wabinga and S. Namboozee): The registry continues to act as a resource for training in east Africa. It is one of the centres monitoring temporal trends in HIV-related cancers (Section 2.7) and collaborates in the study of survival in Africa (Section 1.4). The registry also provides a resource for other collaborative studies with IARC (see Section 2.7).

**Viet Nam**: The registries in Hanoi (Pham Hoang Anh) and Ho Chi Minh City (Nguyen Chan Hung and Nguyen Manh Quoc) have been supported for some time, and are active in supporting the development of several new registries in the country. A visit to review needs for training and technical support was made in November 2003.

**Yemen**: The registry in Aden (A. Bawazir) continues to receive support and has prepared a first report of results for 1997–2001. A new registry is being started in Sana'a (N. Nagi), with the establishment of a cancer treatment centre.

**Zimbabwe**: The registry in Harare (M. Bassett, M. Borok, E. Chokunonga and B. Mauchaza) continues to act as a resource for training and consultancy in southern Africa. It is one of the centres monitoring temporal trends in HIV-related cancers (Section 2.7) and collaborates in the study of cancer survival (Section 1.4).



## 1.2 Geographical variation in cancer occurrence

Documenting the enormous range in incidence and mortality from diseases in different populations has been a powerful stimulus to research into the underlying causes. The presence or absence of environmental exposures, or differing susceptibility of the populations may contribute to the observed variations, to varying degrees. Therefore the collation, processing, analysis and presentation of cancer data are important activities. It is also possible to estimate how much of the cancer burden in different parts of the world can reasonably be ascribed to environmental exposures susceptible to modification; this provides a quantitative indication of priorities for public health intervention.

### Cancer Incidence in Five Continents

#### *Cancer Incidence in Five Continents Volume VIII*

D.M. Parkin, S.L. Whelan; J. Ferlay; in collaboration with L. Teppo, Helsinki, Finland; D. Thomas, Seattle, USA

The eighth volume in the *Cancer Incidence in Five Continents* series, published in 2002, presents comprehensive data on cancer incidence for over 200 populations worldwide. The period covered is 1993–97, making information available on patterns and trends of cancer for over 40 years for the older-established cancer registries. The book follows the traditional format, with background chapters and descriptions of the areas and populations presented, as well as data on incidence by site and by histological type. The printed tables are, however, less numerous than previously, the detail of age-specific incidence now being presented as PDF files on an accompanying compact disc. This disc includes the entire database (as text files), with cases tabulated by population (registry), age group, sex and diagnosis (252 units defined by site and histology) that can be extracted for analysis. It also

contains software to analyse and present these data in a tabulated or graphic format: the usual summary rates (crude, cumulative, world and European age-standardized) can be calculated over any chosen age range. The software also performs some elementary statistical tests, e.g., for homogeneity, trend and significance of the ratio of age-specific rates from two populations.

#### *Cancer Incidence in Five Continents, Volumes I–VIII*

D.M. Parkin, S.L. Whelan, J. Ferlay; in collaboration with N. Al-Hamdan, Riyadh, Saudi Arabia; H.H. Storm, Copenhagen, Denmark

The data from the eight volumes of *Cancer Incidence in Five Continents* are being prepared for publication in electronic format. At an editorial meeting held in April 2003, it was decided to prepare three databases. The first will provide the basic published data, so giving access to data from earlier volumes that are no longer readily available. A second database will present time-trend data for registries with three or more time-periods in the volumes. For these data, the denominators and the data will be updated and, where necessary, corrected and years will be re-grouped to correspond to standard five-year periods. The third database will provide annual incidence and mortality rates, and graphs based upon them. Registries contributing data to Volume VIII and registries with 15 years or more of recent data have been invited to send an updated database.

### Cancer in Europe

#### *Cancer Monitoring in Europe (CaMon)*

F. Bray, E. Démaret, J. Ferlay, P. Pisani, D.M. Parkin; in collaboration with F. Berrino, Milan, Italy; L. Cherie-Challine, St Maurice, France; M. Colonna, Grenoble, France; M. Diaz, Paris, France; T. Hakulinen, Helsinki, Finland; Y. Le Cam, P. Mouroug, Paris, France; M. Guerra Yi, Havana, Cuba; C. Mathers, Geneva, Switzerland; A. Micheli, Milan, Italy; F.

Pignatti, London, UK; G. de Pourville, Villejuif, France; M. Stenbeck, Stockholm, Sweden

Supported by the Health Monitoring Programme (Health and Consumer Protection Directorate-General) of the European Commission

The CaMon (Comprehensive Cancer Monitoring in Europe) project was set up with the objectives of (i) developing a cancer surveillance system for cancer occurrence and outcome (incidence, mortality, prevalence and survival), permitting situation analysis and monitoring of the cancer burden in the Member States of the EU and its applicant states; and (ii) disseminating such information within the EU and worldwide, and making it available for incorporation into the health-monitoring system of the European Commission.

The tasks included the compilation and maintenance of an updatable database of indicators of cancer burden and outcome for EU countries and applicant states. This was achieved by expanding the EUCAN database with estimates for other European countries, supplementing the incidence, mortality and prevalence data with recent estimates of survival from EUROCARE.

A workshop on time trends in November 2002 reviewed the methodological aspects of systematic time trend analyses (see below). A second workshop, in February 2003 (in collaboration with the French Cancer League), brought together methodologists, users and potential users of cancer prevalence data. It focused on the usefulness of prevalence, and on the problems encountered in defining, measuring and estimating this indicator.

Recent and future trends in lung cancer mortality (in relation to current smoking patterns) in the 15 EU Member States have been examined in detail [81]. The CaMon project has been described in relation to the role of the key indicators specific to cancer monitoring and the most recent estimates of the burden of the disease in the EU and Europe [78].



## European cancer incidence and mortality databases

J. Ferlay, F. Bray, D.M. Parkin, J.E. Tyczynski

EUROCIM is a powerful software package allowing statistical analyses of cancer incidence and mortality data contributed by ENCR members (see Section 1.1). In addition to the set of standard statistical tools (age standardization, log linear model-fitting), the latest EUROCIM software (Version 4.1) contains a time trends analysis module that allows the user to fit age-period-cohort models to the registry incidence and mortality data (Figure 4). New databases (Version 2.4) containing data from over 140 European cancer registries covering the period 1953 to 2000 have been distributed to ENCR members via a secure FTP web site. New versions of EUROCIM are made available periodically, with further software enhancements, as well as the most recent cancer registry data. The software and database are managed and maintained at IARC, while an external contractor is responsible for the development of the program.

EUCAN is a Windows®-based package which provides access to the most up-to-date information on cancer incidence, mortality, prevalence and survival in the 15 Member States of the EU for 24 major cancer sites. Various descriptive statistics such as the numbers of cases or deaths, the age-standardized rate and the cumulative risk can be displayed in a conventional tabular format, graphically as line plots, bar or pie charts, or as maps. The presentations can be easily printed or exported to other packages. In addition, the countries and cancer sites can be grouped, allowing users flexibility in specifying their own requirements. The EUCAN database is updated annually to incorporate the latest incidence and mortality data. The user can download new versions of the database directly from the ENCR Internet home page (<http://www.enccr.com.fr/>). The latest estimates for 1998 were made available online in 2002. A new version of the software (EUCAN 2000) is under deve-

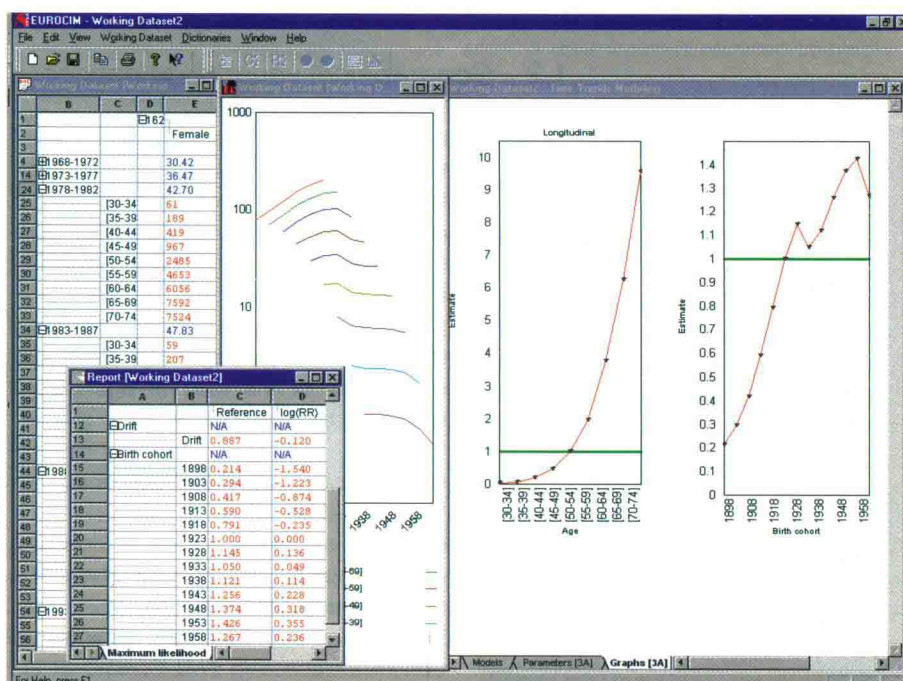


Figure 4. EUROCIM version 4: evaluating the effects of age, period and cohort on lung cancer rates over time

lopment (Figure 5). The user interface and the online help have been extensively revised to enhance ease of use. This new version takes into account the forthcoming inclusion of ten new Member States

and three associated countries (Iceland, Norway and Switzerland) and provides estimates of cancer incidence, mortality and prevalence for the year 2000. A simplified version of the EUCAN soft-

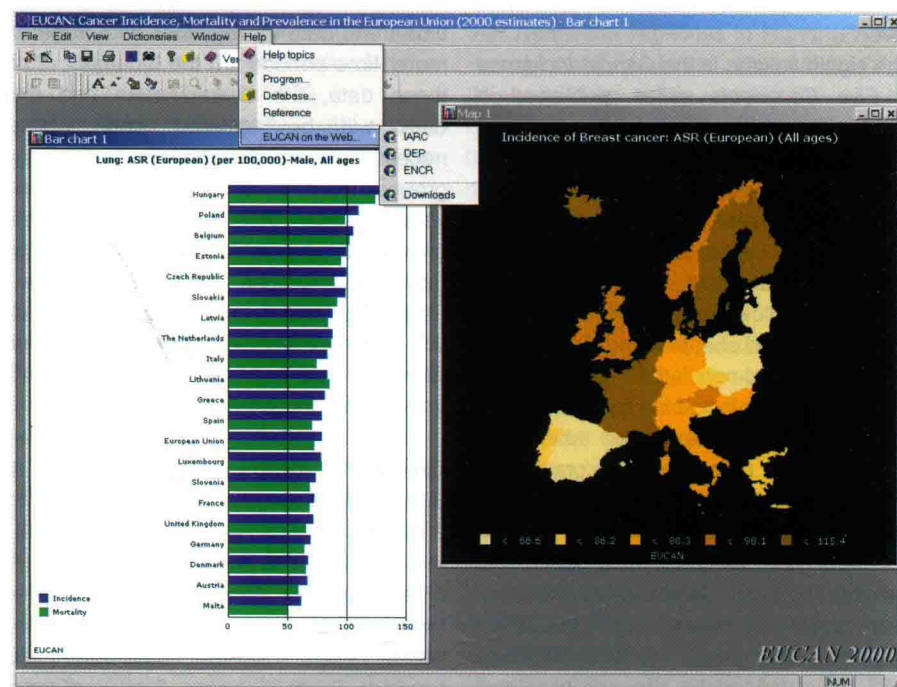


Figure 5. EUCAN screen display of lung cancer data

## 8 Geographic variation in cancer occurrence