



**INTERNATIONAL AGENCY  
FOR RESEARCH ON CANCER**



**EUROPEAN COMMISSION  
C4-HEALTH DETERMINANTS**

**EUROPEAN NETWORK OF CANCER REGISTRIES**

**WORKSHOPS AND GENERAL MEETING**

European Commission  
Luxembourg, 26-27 October 2004

**REPORT**

## INTRODUCTION

A meeting of the European Network of Cancer Registries (ENCR) was held on 26-27 October 2004 in Luxembourg, organised jointly by the European Commission (EC) and ENCR. The meeting was financed largely by the EC (C4 - Health Determinants), with additional support from the Federation of European Cancer Societies (FECS).

The meeting consisted of four workshops and a short general meeting. The topics of the workshops were: evaluation of clinical care, childhood cancer, automated cancer registration and molecular pathology. The Chairman responsible for each workshop decided on the content and structure of the workshop, as well as on the speakers to be invited. Participants from the cancer registries were also invited to make short communications on the respective topics.

Letters of invitation were sent to all ENCR members, as well as to national and other cancer associations. Staff from the EC were also invited. Some 75 people attended the meeting.

K. Freese (C4 - Health Determinants) opened the meeting on behalf of the European Commission. He considers ENCR to be one of the more important projects which has been established within the Cancer Programme, being a cornerstone from which many other activities can be successfully developed and implemented. Without figures which allow comparisons between member states, one of the important sources of motivation to increase and improve cancer prevention and cancer therapy would be lacking. K. Freese has been the EC representative on the ENCR Steering Committee since 1999.

This report contains the programme of the meeting, the abstracts of the presentations, some comments on the presentations, a summary of the general meeting and the list of participants.

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## PROGRAMME

### TUESDAY, 26 OCTOBER 2004

**08.00 – 09.00** Registration

**09.00 – 09.15** Opening of the meeting

Karl Freese, EC

#### **09.15 – 13.00 Workshop on Evaluation of Clinical Care by Cancer Registries**

Chairman: Dr Risto Sankila, Finnish Cancer Registry

09.15 – 09.30 Introduction

Risto Sankila

09.30 – 09.55 Quality or population-based registers?

Jarle Norstein

09.55 – 10.20 Repeated studies on quality of colorectal cancer care in France - did they have an impact?

Jean Faivre

*10.20 – 10.50 Coffee break/Poster viewing*

10.50 – 11.15 Cancer registries' contribution to planning cancer services in Scotland

Roger Black

11.15 – 11.40 FECS and clinical epidemiology of cancer in Europe

Jan-Willem Coebergh

11.40 – 12.10 Oral communications by participants:

- *Prognostic factors in breast cancer survival*
- *Registry-based evaluation of radio- and chemotherapy using current data*
- *Regional and inter-hospital variations in the use of breast-conserving surgery in the Netherlands*

*David Forman  
Eugenio Paci*

*Sabine Siesling*

12.10 – 12.30 Population based cancer registries: catalysts and partners in improving the quality of cancer care in Europe

Ian Kunkler

12.30 – 13.00 Discussion

*13.00 – 14.00 Lunch*

#### **14.00 – 17.30**

#### **Workshop on Childhood Cancer**

Chairman: Dr Eva Šteliarová -Foucher, IARC

14.00 – 14.15 Introduction

Eva Šteliarová-Foucher

14.15 – 14.40 International variation in childhood cancer incidence

Charles Stiller

14.40 – 15.05 The ACCIS project

Eva Šteliarová-Foucher

15.05 – 15.30 Use of period analysis for timely disclosure of progress in childhood cancer survival

Hermann Brenner

*15.30 – 16.00 Coffee break/Poster viewing*

16.00 – 16.25	The UK Childhood Cancer Study	Eve Roman
16.25 – 16.55	Oral communications by participants: <ul style="list-style-type: none"> <li>▪ <i>Second malignant neoplasms after childhood cancer - epidemiological data from the German Childhood Cancer Registry</i> Peter Kaatsch</li> <li>▪ <i>Actual problems in the registration of cancer in childhood: experiences in Slovakia</i> Ivan Plesko</li> <li>▪ <i>Childhood acute lymphoblastic leukaemia incidence trend: a steady increase?</i> Luisa Zuccolo</li> </ul>	
16.55 – 17.30	Discussion	

**WEDNESDAY, 27 OCTOBER 2004**

**08.00 - 10.00**

**GENERAL MEETING**

Chairman: Dr D.M. Parkin, IARC

- |   |                                |
|---|--------------------------------|
| 1. Opening  | <i>K. Freese</i>               |
| 2. Introduction   | <i>D. Brewster</i>             |
| 3. ENCR – 15 years' service to European cancer registries | <i>D.M. Parkin</i>             |
| 4. European cancer projects                               |                                |
| - <i>EUNICE</i>   | <i>D.M. Parkin</i>             |
| - <i>European Cancer Observatory</i>                      | <i>E. Šteliarová-Foucher</i>   |
| - <i>CaMon</i>  | <i>F. Bray</i>                 |
| - <i>EUROCARE</i>   | <i>H. Møller</i>               |
| - <i>EUROCADET</i>  | <i>J.W. Coebergh</i>           |
| - <i>EUROCHIP</i>   | <i>F. Bray</i>                 |
| - <i>Cervical cancer screening</i>                        | <i>M. Arbyn</i>                |
| - <i>Breast cancer screening</i>                          | <i>L. von Karsa</i>            |
| 5. Future of the ENCR                                     | <i>D.M. Parkin/D. Brewster</i> |
| - <i>Activities</i>                                       |                                |
| - <i>Funding</i>  |                                |
| 6. Any other business                                     |                                |
| 7. Closing session  | <i>D. Brewster</i>             |

*10.00-10.30 Coffee break/Poster viewing*

**10.30 – 13.00**

**Workshop on Automated Cancer Registration**

Chairman: Dr Lorenzo Simonato, University of Padova, Italy

10.30 – 10.45	Introduction and background	Lorenzo Simonato
10.45 – 11.10	The Cancer Registration Dataset and Messaging Project in England	Chris Carrigan
11.10 – 11.35	Automated cancer registration: Reliability measurements	Richard Middleton
11.35 – 12.00	Automated record consolidation efforts in the United States: National projects and a case study	Wendy Scharber
12.00 – 13.00	Oral communications by participants: <ul style="list-style-type: none"><li>• <i>Comparison between manual and automatic registration. An application of the SITE software to the Tuscany Cancer Registry</i> Emanuele Crocetti</li><li>• <i>Automated cancer registration within a data warehouse system: an example of use for cancer risk investigation</i> Margherita De Dottori</li><li>• <i>The Danish progress with automated cancer coding</i> Henrik Mulvad Hansen</li><li>• <i>Automated cancer registration - pilot project for the Holycross Region in Poland</i> Ryszard Mezyk</li><li>• <i>Reliability of record linkage with pseudonymised identity data</i> Irene Schmidtman</li><li>• <i>Automated cancer registration: Quality control of automatically defined cancer cases</i> Sandro Tognazzo</li></ul>	
13.00 – 14.00	Lunch	

**14.00 – 17.30**

**Workshop on Molecular Pathology and Cancer Registries**

Chairman: Dr Joakim Dillner, Malmö General Hospital, Sweden

14.00 – 14.15	Introduction	Joakim Dillner
14.15 – 14.45	Molecular tools for molecular medicine: Analyzing genes, transcripts, and proteins	Ulf Landegren
14.45 – 15.15	Modern infectious disease epidemiology: Exploiting population-based cancer registries, vaccination registries and biobanks	Mads Melbye
15.15 – 15.45	Genetic epidemiology of cancer exploiting registries	Kari Hemminki
15.45 – 16.15	<i>Coffee break/Poster viewing</i>	
16.15 – 16.45	Should cancer registration include biobank registration? The Swedish example	Joakim Dillner
16.45 – 17.10	Oral presentations by participants: <ul style="list-style-type: none"><li>• <i>The role of cancer registries in cytogenetic biomarker research</i> Ariana Znaor</li><li>• <i>The creation of a new national cancer registration system in Belgium, including linkage to biosamples and pap smears</i> Marc Arbyn</li></ul>	
17.10 – 17.30	Discussion	

## WORKSHOP ON EVALUATION OF CLINICAL CARE BY CANCER REGISTRIES

**Chairman:** Risto Sankila (Finnish Cancer Registry).

**Commentator:** Ian Kunkler (University of Edinburgh, UK)

**Invited speakers:** Jarle Norstein (Cancer Registry of Norway); Jean Faivre (Burgundy Digestive Cancer Registry, France); Roger Black (Scottish Cancer Registry, UK); Jan-Willem Coebergh (Eindhoven Cancer Registry, the Netherlands)

**Communications:** David Forman (Northern and Yorkshire Cancer Registry, UK); Eugenio Paci (Tuscany Cancer Registry, Italy); Sabine Siesling (IKST, the Netherlands).

### Introduction

The Chairman introduced the session by giving a short presentation on the regional survival differences in Finland. Survival rates in five university districts in Finland were compared. The regions are fairly similar and there should be no differences in survival rates. H. Brenner's period survival method was used, using the latest available information in terms of survival rates. Striking differences were observed in ovarian carcinoma, with the highest excess mortality in the Kuopio region. These results were presented to the oncologists and the gynaecologists in the five regions and again in Kuopio to the Gynaecological Oncology Society. When they saw these rates and the fact that they also had a problem with corpus uteri, which is a fairly treatable cancer, they realised something was going on in their region that needed improvement. They had already some plans to centralise treatment. There are three smaller hospitals in the region and they asked themselves, if something different was being done in these smaller hospitals. Two of them agreed to pass their patients on to the university hospital to be operated. The university hospital is now operating more proportionally and in numbers than they used to. A survey in 1999 will show the impact of bigger units or the volume by surgeon, or the qualifications of the surgeon. We are now ready for 5-years survival analyses and will see if it makes any difference. The regional analysis will be repeated in a few years to see if there still are differences, and if improvements have taken place.

### Presentation 1. QUALITY OR POPULATION-BASED REGISTERS?

#### Abstract

*Jarle NORSTEIN and Frøydis Langmark, Cancer Registry of Norway, Oslo, Norway*

Population-based cancer registries have traditionally focused on registration of cancer incidence and calculation of survival rates. Combination of information on incidence rates and information on exposures to possible carcinogens has contributed to etiological research, providing insight into risk factors for cancer. Some of these have been modifiable, but in practice the potential of cancer prevention may be limited. Although prevention of cancer is the ultimate goal, prevention of cancer death may be a less remote aim. In order to contribute to prevention of cancer death, cancer registries must expand the data sets they record towards variables influencing cancer survival, i. e. information on early diagnosis (staging information) and information on treatment. Such detailed data must be of high quality to be useful. Feedback to clinicians, health administrators, and politicians is instrumental in implementing evidence-based changes in healthcare policy and cancer treatment. Relevant information on treatment and treatment results make clinicians more interested in cancer registry activities and improves compliance and data quality, in spite of the increased burden imposed by more detailed reporting. However, a strong legal basis and patient identifiable information are prerequisites for population-based quality registries.

The Cancer Registry of Norway contains staging and treatment information from the start of the registry in 1953. These data have been extracted from pathology forms and clinical notifications. Lately, these sources have been supplemented with electronic data sources, like patient administrative

data with treatment codes (billing data) from hospitals and radiotherapy data from the verification systems of radiotherapy treatment machines. Information on chemotherapy represents a problem, due to the protracted delivery of such therapy. Follow-up data with regard to recurrences and metastases that are not verified by histopathology also demand special efforts from the cancer registry in order to achieve complete information.

At present, the Cancer Registry of Norway holds information on surgical treatment on about 370.000 patients and detailed information on radiotherapy of more than 100.000 patients. The proportion of all cancer patients receiving surgical therapy has increased from 24.5% in men and 44.4% in women in 1954-58 to 36.1% and 62.9% in 1994-98. The relative survival rates for men and women have increased from 25.2% and 36.6% in the first period to 53.1% and 61.7% in the last, for patients having had a resection from 42.6% and 58.8% in 1954-58 to 68.9% and 78.7% in 1994-98.

In conclusion, there is no contradiction between quality of information in cancer registries and their function as population-based registries. The two aspects, quality and a population base, are mutually beneficial.

## Questions

R. Sankila: Incredible progress has been made in Norway. In 1999, the conclusion of the meeting in Veldhoven was that, rather than collecting everything in the clinical database, we should do *ad hoc* studies and then collect the specific data items that we need in a population-based cancer registry. What has been done in Norway is an example that you can do this kind of operation on a population-base and collect a large number of more detailed clinical items, when you have enough resources. Can you tell us a bit about the problems you faced?

J. Norstein: The problems related mainly to resources, but the Norwegian government has recently found out that resources can be saved by standardising treatment and giving patients the correct treatment at the correct time. There is currently substantial funding for the development of these activities, because the government thinks it is an investment and will save money in the short and long term. There were no problems with clinicians or pathologists who were very co-operative.

J.W. Coebergh: What are the resources for using the data. Who is using the data? Only people in the registry, or across the country? Are universities involved?

J. Norstein: Data are being collected now and the point is obviously to use all the data in a decent manner. Clinicians and laboratory people from all of Norway are invited to use data from the cancer registry and this is increasingly being done. At present several clinicians come to the cancer registry, take off the cohorts and use the data, go home and produce articles from the data. The Norwegian Cancer Registry has a very open attitude towards the outside world, making the data accessible to those who produce and provide the data. This has been the policy of the cancer registry for many years and it is a very successful policy.

D.M. Parkin: The cancer registries have had difficulties in collecting quality data on the clinical aspects. In Norway, can you capture most of this from the clinical data sources and laboratories or are your registry staff involved in checking and looking at the quality of the data from these sources?

J. Norstein: The registry staff is deeply involved in checking the quality of the data. As the quality of the data is variable, this check is absolutely necessary. Currently we try to define systems to be used by all hospitals to check the data before they are dispatched to the cancer registry and the hospitals which are now introducing electronic patient record systems, can build check routing systems into the patient record systems. As the legal basis for collecting data makes the procedure very long, we can request high quality data. We owe the patients to record correct data. Notification of cancer is compulsory. We tried to have the hospitals deprived of the payment if they did not report to us, but the Ministry of Health did not want that solution. If not adhered to, the hospital director will be fined after one year, or sentenced to prison, or both. The cancer registry did not like this solution, but it is effective.

L. Simonato: What is the difference between the information available at hospital level and the information sent to the registry? What do you mean by semi-automatic control?

J. Norstein: The registry receives more information than is stored in the hospital; both the coded information and the original information (operative reports in original text, pathology reports in original text, etc.). The attempt was to design a system to retain in the hospital also the information sent to the cancer registry, so that each hospital could make their own database. The semi-automated procedure consists of an automatic quality check on codes and inconsistency of codes to ensure that all the information is there. In addition, there is a manual check of all errors to avoid repeated clarifications with the hospital, with possible misunderstandings. The reason the process is not totally automated is that very clever coders are needed to process the information.

F. Langmark: The real basis for the success of the registry today is the legal basis that the cancer registry now has, namely, that informed consent is not needed, and the clinicians now understand the importance of population-based research. In addition, organ-specific project groups (breast, cervix, colorectal) have been established in the registry with clinical and laboratory medicine reference groups which are geographically dispersed all over the country so that they feel they have a proportion of the cancer registry as their own data base. Finally, when research is done using the registry data, clinicians are invited, not only from Oslo, but from other parts of the country, so that people living in the outskirts also have the possibility to come to the registry and do research. A system has been set up to practically and economically arrange these visits.

G. Meledandri: I think it is very important to have a multidisciplinary team and the registry should be part of it. You mention the surgical margins which is very important too for the clinician, and very important for radiotherapy. However, as far as codes for the surgical margin are concerned, only specialist groups in surgery can make these definitions. You have international definitions regarding surgical margins for different tumour types, and my suggestion is that you really should make an investigation by tumour type. In head and neck cancer, for example, it is not only the total radiation dose which is important, but also the target volume and it is nice that you are inviting the clinician to co-operate with the registry.

S. Siesling: Some data about the local recurrence were shown, but how did you get the notification for them?

J. Norstein: Notifications of all histopathological verified recurrences are received. In these cases, lists of patients they have treated are returned to the hospital with questions about local recurrence in any of these patients. They have to go to the patient records and look. It is a huge task to do this type of study and you need very good co-operation with the clinicians. An attempt is being made to design a system which can do this more or less automatically with electronic patient records in the hospital. Funding for this is currently being investigated.

R. Tumino: Collecting clinical data is a lot of work. For example, you mentioned that you tried to have the text of the histological report, but when we collect this kind of information, we should be aware that we are not collecting a homogeneous set of data. I also think that not all pathologists in Norway write their report in the same way. As you may know, there are some guidelines on pathological reporting and I think that collecting histological reports is good in order to evaluate the compliance to these guidelines. It could be a good feedback to pathologists. What do you think?

J. Norstein: This is exactly what is being done – standardise reporting with the pathologists and reinforce the standards we have agreed upon. At meetings with the pathologists, standardisation for some locations, especially rectal cancer, have been agreed upon. Rectal cancer is described uniformly all over Norway and if the information obtained is not what we should have, the pathologist is being contacted and asked to comply with the regulations. This will be done for specific cancer sites, but it is a huge task to monitor all cancer locations all the time.

D. Forman: (1) In Norway you have a legislative basis that some of us can only dream about. Has there been any reaction to the legislation from the privacy lobby, a group that is very vocal in the UK, for example? (2) I did not quite understand the theme of pathology reporting. You say you are getting electronic downloads of the full text. At the moment, is it cancer registry staff who then take out the various fields of that text for coding – that is a very resource-intensive process - and are you planning to move away from that with your boxes and millimetres? How successful do you think you are going to be in getting pathologists to report in terms of ticking boxes and writing millimetres?



J. Norstein: (1) There has been a strong lobby in Norway some 10 years ago but Froydis Langmark stood up and fought back that lobby. It was a tremendous task and very strong struggle but she and the cancer registry actually won. That is the reason why we now have such good relations that have helped us so much. (2) The pathologists like long and very detailed descriptions. That is why we have been very interested in standardising reporting. We have some very important points which should be in database format and should be transmitted electronically. The pathologists have agreed to make them and I believe they will.

K. Freese: Is there nation-wide screening for breast cancer, cervical cancer and colorectal cancer by FOBT in Norway and is the registry involved in the evaluation and assessment of those screening programmes?

J. Norstein: A country-wide cervical cancer screening programme has been going on for a long time and is located in the cancer registry. The breast cancer screening programme has been fully implemented in Norway in 2004 and is also located in the cancer registry. All data comes to the registry and are processed there. The data are also available in the screening units for own use.

R. Sankila: Do clinical geneticists have access to your database in order to evaluate the pedigrees?

J. Norstein: This is in process. Permission to do this was obtained about 2 years ago, but so far we have only informed the geneticists. We have not received any hereditary information from them yet, because it is also a question of resources. There is a problem with the relatives – while the cancer patient cannot object to be registered, the relatives can, and we do not know how to deal with for the moment.

R. Sankila: You have electronic interactive reporting where you can request specific examinations or data on those examinations. Can you ask the clinicians to take a blood sample from this patient?

J. Norstein: This is not possible yet, but we will design projects together with the clinicians, so that they agree to participate in projects. It is fully possible to make this system work and there is a great interest in biobanking in Norway at the moment, however, the regulations are very strict and you need to have informed patient consent before you take specimens for biobanking. It is therefore very important to make sure that this informed consent is given before the tissue or blood is taken.

F. Langmark: We also have the Polyposis Registry. In that particular cohort we do actually send suggestions to the clinicians and geneticists to do control colonoscopy examinations as an invasive procedure.

K. Freese: It appears that the derogation from the informed consent for registration of medical data according to the data protection directive of the EC (95/46/EC, article 8.3), has been fully implemented in Norway. I think those member states which did not fully implement this should consider following the Norwegian example.

R. Sankila: This was a world-class presentation about a world-class registry that has been integrated into the clinical process. This obviously makes it much easier for the registry to function, because there is full support from the clinicians, they get immediate feedback and see the results of their own work. This is what we should all aim at.

The conclusion is that there is no contradiction between quality of information in cancer registries and their function as population based registries. The two aspects, quality and a population base, are mutually beneficial – and should be combined.

## **Presentation 2. REPEATED STUDIES ON QUALITY OF COLORECTAL CANCER IN FRANCE – DID THEY HAVE AN IMPACT?**

### **Abstract**

*J. FAIVRE, A.M. Bouvier and the FRANCIM Network, Registre Bourguignon des Cancers Digestifs, Dijon, France*

Over the past 20 years, numerous developments have taken place in the management of colorectal cancer. Initialised in specialised centres these advances have progressively spread, but their impact at a population level is not well known. In the French health care system, the management of colorectal cancer is decentralised among multiple places of treatment and various specialists. Population-based studies recording all cases diagnosed in a well-defined population represent the only way to assess real changes in the management of this cancer. In this context, special surveys were conducted by cancer registries in France in 1990, 1995 and 2000. Data was collected on diagnostic assessment, preoperative work-up, surgical and medical treatments and stage at diagnosis.

The proportion of patients having a first intention diagnostic colonoscopy alone, as recommended by the Consensus Conference, increased over time, while the proportion of patients having a colonoscopy and a barium enema or a barium enema alone decreased. CEA dosage is no more recommended by the Consensus Conference. However its use only slightly decreased. Echoendoscopy, which is indicated in rectal cancers to distinguish T1/T2 tumours, not requiring preoperative radiotherapy from T3/T4, has not reached its full development. There was an increased use over time of abdominal computed tomography.

There was no significant change over time in the resection rate of colon and rectal cancers. It was not far from an optimum for colon cancer, being 92% in 2000. It was lower for rectal cancer (84%). The proportion of continence preserving operations in patients undergoing a resection slightly increased from 60% in 1990 to 74% in 2000.

Results concerning pathological examination of the resection specimen were partly satisfactory. Data concerning the TNM status and the number of examined nodes was provided for nearly all cases. However, the number of cases with the recommended harvested lymph nodes was insufficient, being 53% in 1995 and 57% in 2000. Pathologists must be made aware that the decision to perform adjuvant chemotherapy must be based on reliable staging.

Results concerning adjuvant chemotherapy and radiotherapy are particularly striking. The efficacy of adjuvant chemotherapy for stage 3 colon cancer was demonstrated in the 1990's, while its worth for stage 2 is still controversial. The proportion of patients receiving chemotherapy increased both for stage 3 and stage 2. In this latter situation, there is clear evidence of over practice. It would have been better if these patients had been included in clinical trials than being treated without proof of treatment effectiveness. In 2000, 3.5 % of colon cancers and 5.5% of rectal cancers were included in clinical trials. Age played a major role in the practice of adjuvant chemotherapy. It is mostly offered to patients under 75. Concerning adjuvant radiotherapy in rectal cancer, evidence-based medicine indicates that preoperative radiotherapy is superior to post operative radiotherapy and that it reduces local recurrences and increase survival. Comparing the three studied periods there was only a slight increase in the proportion of patients receiving adjuvant radiotherapy. However there was a shift from postoperative radiotherapy to preoperative radiotherapy.

It can be concluded that adherence to recommendations varies from one recommendation to another. For certain important guidelines (resection whenever possible, precise pathology report in order to classify patients according to the TNM classification, chemotherapy in stage 3 colon cancer under 75) physician's adherence is good. The main divergence with recommendations appear to be related to inertia due to previous practices (CEA measurement), difficulty to perform a recommended behaviour (examination of a sufficient number of lymph nodes) to a lack of familiarity (chemotherapy in the elderly, radiotherapy in rectal cancer) and to overpractice (stage 2 colon cancers).

## Questions

R. Sankila: This was a special service done every 5 years. Was it active data collection?

J. Faivre: Data are actively collected, with a very precise protocol in order to try to collect comparable data in the different areas.

R. Sankila: Is the change in practices a direct result of the recommendations of the consensus statements or is it just the natural evolution of the treatment practices?

J. Faivre: It is difficult to say. Consensus data are very much publicised and these cancer registry data are also often presented at gastroenterology or surgical meetings. Clinicians are interested in knowing and these repeated oral presentations at major meetings of surgery and gastroenterology in France probably have some influence. It is difficult to know exactly what can be related to the recommendations and what to the presentations of the data.

I. Kunkler: Concerning preoperative radiotherapy for rectal cancer, in the UK there is a shortage of radiotherapy resources, and one might explain the differences on the basis of lack of radiotherapy resources. Is that the case in France? In addition, how does the French National Cancer Plan plan to address the delivery of non-evidence based therapy?

J. Faivre: It is not a problem of number of radiotherapists and access to radiotherapy. There is no waiting list for radiotherapy at the moment in France. Unfortunately the health authorities are not very interested in publicising these data, because they think it will not be very popular. In principle, there should be some control of what is done, but in practice there is none, in particular in chemotherapy. You can treat what you want with whatever drugs you want. There is some improvement in the relationship with the Cancer Plan. It has now been decided that hospitals and practitioners have to be accredited, and the hospitals which are treating too few patients, or even the surgeon not treating enough rectal cancers, will not be accredited any more. This is a big change, but because it will be implemented in the near future, there is a trend towards a multidisciplinary approach to treatment and probably the treatment will be more in relation to the recommendations of this multidisciplinary approach. You cannot be accredited if you are not involved in a network of treatment of cancer. There are some improvements, but the health authorities should be acting more strongly.

I. Kunkler: The impact in the UK of the multidisciplinary team in this setting has been enormously important. For example, it is not possible to recommend a non-evidence based treatment in a group of peer-reviewed professionals who know that this is not appropriate treatment.

J.W. Coebergh: If everyone in France and Europe would treat colorectal cancer as they should, and if there were a reasonable screening programme for familial cancer or high-risk cancers, would you think there is still a great benefit to be gained from colorectal screening?

J. Faivre: The proportion of colorectal cancer found in high-risk families - that is the genetic group of colorectal cancer which is a very small proportion when you look at population-based data - is between 2-3% of all colorectal cancer. You have also an increased risk when you have a third-degree relative with colorectal cancer, but we know this risk is increasing only when your parents were affected before age 60-65. Screening programmes limited to this high-risk population will not change much the problem of colorectal cancer, because it represents too small a portion.

K. Freese: What is your mean follow-up lag time between screen-detected lesion or another clinically diagnosed lesion and the time of operation?

J. Faivre: I do not have very precise figures but in general the delay between the screening and surgery is in the range of 1-2 months.

### **Presentation 3. CANCER REGISTRIES' CONTRIBUTION TO PLANNING CANCER SERVICES IN SCOTLAND**

#### **Abstract**

*Roger BLACK, Epidemiology and Statistics Group, NHS National Services Scotland, Edinburgh*

The Scottish Cancer Registry is represented on the senior committee advising the Scottish Executive Health Department on policy-making and planning of cancer services: the Scottish Cancer Group. Accepting evidence of very large variations in outcomes of cancer treatment socially and geographically in Scotland, and indications of poor survival compared to other countries, the group asked the registry to undertake an analysis of trends in cancer incidence and mortality, in anticipation of a major investment in service improvement from 2001.

Age-period-cohort models of historical data from 1960-1997, and population projections, were used to estimate incidence and mortality in the five-year time periods up to 2011-2015. We then asked leading experts in cancer prevention, screening, treatment and palliative care to review results for the major cancer sites and indicate (a) which interventions could be considered which could be of potential benefit and (b) what the magnitude of that benefit might be. For example, it was thought that extending the breast screening programme to age 69 would reduce mortality from breast cancer by 3% overall. The projections for incidence and mortality were then recalculated, permitting presentation of two 'scenarios': one with no further interventions; the other with all proposed interventions included. These results were used to inform discussions on priorities for expenditure plans from 2001-2004 and beyond.

More recently, the registry was asked to support an investment programme in radiotherapy equipment and staffing. This was done using projected incidence rates from the scenarios exercise to estimate overall requirements, and a Geographical Information System (GIS) to optimise the siting of these resources with regard to patient travel times. The geography of Scotland presents a particular challenge in providing health services both to the densely populated 'central belt' and the highly dispersed rural population of the Highlands and Islands.

#### **Questions**

R. Sankila: The data presented is not entirely registry-based. It has been collected from other sources than the cancer registry alone. Are you going to monitor the developments?

R. Black: Yes. We put a lot of work into the initial scenario exercise, but we have also been closely involved in following up the implementation of the policy document 'Cancer in Scotland, Action for Change' and Dr Brewster is a member of the Scottish Cancer Group, which is the senior policy-making committee advising the Health Department about this sort of investment. We are also involved in follow-up in different ways, for example, in the implementation of a colorectal screening programme. The registry has been identified as the place which will be in charge of the monitoring and the evaluation of that programme and we have been given the task of designing an information system to do that evaluation and to propose indicators that will be examined to assess that.

D. Brewster: One of the causes of instability of these estimates or projections is when the government actuaries change their population projections, because between the first iteration of the scenarios project and the subsequent one, the proportion of people in age-group +75 had changed quite substantially. It made quite a difference to the projections.

R. Black: They got it wrong by about 10%.

K. Freese: You have mentioned that part of these projections halts the expectation that more and more interdisciplinary work will be introduced into the services. How do you bring this interdisciplinary concept into this kind of sector planning for investment?

R. Black: We are in a situation where it is not a zero-based funding outlook for the next 5-10 years, but some very substantial increases in funding for cancer services in the UK as a whole. In fact in

Scotland we are spending much more, but proportionally less than the investment in England, so the fact that we are spending a lot on radiotherapy does not mean that other things are being neglected. Everything is being enhanced and there is the example of the colorectal screening programme. Some advocates of that were suggesting we should just implement it right now, but when you look at what has to be put in place – the colonoscopists, the equipment, the clinics, the nurses – it is going to take 5 years to build that up. We are approaching it in a rational way, which means that things do not get overlooked, because there is a strong lobby for radiotherapy.

G. Meledandri: The provided care in the Scottish isles is quite poor. Does this depend on demographic reasons, political reasons or epidemiological reasons? In the past the British Isles were very important to build models for epidemiology – as an example I am referring to child psychiatry. Why do you not take into account the possibility of developing a scenario on the Hebrides or Orcades. Are the populations very small?

R. Black: The Western Isles has a population of 20,000 people. These are very sparsely populated areas. The patients in the Western Isles would tend to be treated in Glasgow and there is an air ambulance service for emergencies to take people to the mainland.

#### **Presentation 4. FECS AND CLINICAL EPIDEMIOLOGY OF CANCER IN EUROPE: THE IMPORTANCE OF CANCER REGISTRIES**

##### **Abstract**

*Jan Willem COEBERGH, Eindhoven Cancer registry, Comprehensive Cancer Centre South (IKZ) Eindhoven; and Erasmus University Medical Centre, Rotterdam, The Netherlands*

The Federation of European Cancer Societies (FECS) coordinates 17 groups of oncological professionals and researchers, representing about 18,000 European cancer specialists, among whom no epidemiologists (yet). It organises the biannual ECCO and is also stakeholder in the European Journal of Cancer and the European School of Oncology (ESO). The FECS board is a spokesperson for the European Commission and increasingly also for the Parliament. Despite the absence of organised epidemiology within FECS, the board co-sponsored this ENCR meeting, because of great interest in cancer registries as tools for European comparative analyses of incidence, patterns of care and survival. It would also welcome an organised representation of cancer epidemiologists for which proposals are being developed.

What does epidemiology have to offer the European cancer scene? There are at least five major domains:

1. Of course its major contribution to cancer prevention is both by scientific etiological research, but also by exhibiting the huge variation in incidence across Europe, the latter also an indicator of preventive potential. The board of FECS deems cancer registries extremely important in this respect and we know that we offer more reliable information than the data on cause-of-death from, unfortunately, increasingly less reliable mortality statistics. Except for tumours that are amenable to (mass) screening, trends in cancer incidence are much more reliable than mortality. For the decline of mortality statistics structural developments are responsible like less autopsies, application of more effective treatments with all sorts of – sometimes lethal - side effects including second cancers, and involvement of more doctors (who know less of dying patients) outside office hours. Cancer mortality statistics may thus be less valid for estimating trends.
2. Another essentially useful epidemiological approach is its marketing research potential to feed scenarios with incidence data, e.g. for prevention of or investment decisions for diagnostic or therapeutic equipment. This is relevant for all the FECS constituent societies that are mostly confronted with increasing numbers of patients with higher expectations, improved technologies and the usual tight budgets that do not allow for investments. Such scenarios are on the one

hand based on the meticulous work of registries and science (of the past) and are on the other hand, by definition, future oriented and thus speculative. But they are about access to care (in the future) and as such vital to the quality assessment process. What use is there in determining bad quality of clinical care, when the available resources or skills were badly planned or trained in the past. It is clear that scenarios for oncological care (prevalence) in the future across Europe need to take into account the consequences of demographic changes, both in relation to care demand as to supply of caring and curing (wo)manpower, potentially in short supply. The latter would be crucial for quality of clinical care.

3. The use of cancer registries in the evaluation of mass screening has already been dealt with in 1999 and does not get attention now. But without cancer registries mass screening would really become an irresponsible act.
4. Cancer registries have become active in clinical care evaluation since the 80's and deliver a large amount of population-based studies on adequacy and outcome of care. This increasingly also happens at European scale since the early 90's, when the Eurocare study group started to gain steam. Albeit being novel, their comparative survival analyses confirmed already existing notions on inferior outcomes in Denmark (where the surgical profession had been demoralised during the 70's), the UK (where under-investment was the rule since the 60's) and Eastern Europe (where no investment could be generated any more since the 60's). Although it has taken a very long time, the data of patients diagnosed during the 80's changed the outcomes for patients diagnosed almost 20 years later; the formula worked and needs continuity, also because it only covers less than one third of Europe. Is it reasonable to assume that cancer survival is worse in areas uncovered by registries? Can this be proved otherwise than by random sampling or is a registry needed?. However, building a reliable database with truly comparable data is a long term process; quite a few problems with accurate and complete data collection and complete active follow-up of vital status need to be solved. How to be sure? The higher the expectations become of precise comparisons across Europe and the stronger the media- and policy-culture of punishing league table fetishism, the more important comparability is and the urge to know the determinants of variation. It is clear that FECS will do everything to promote the availability of resources for reliable European databases, that serve as magnet and truly support the European oncological community, to carry out European studies of detection, staging, treatment and treatment outcome. The search for a gold standard will start. Patients will increasingly want to have true insight and demand investments instead of run to the best clinic. But the registries themselves need to guarantee that the survival and patterns of care comparisons truly pertain to all incident cases, for which the control mechanisms exist through acceptance, either or not with an asterisk, by the editors of Cancer Incidence in 5 Continents. Registries with suboptimal quality or with specific peculiarities should always be indicated in these league tables. Otherwise the good registries (and the doctors that serve them) will suffer from the bad ones.
5. From the FECS point of view some clinical studies might be in particular attractive based on the following – global- study questions:
  - a. Provide rapid feed back on the speed of spreading of evidence-based oncological care. Would there still be a large variation?
  - b. What is the impact in Europe from phase III EORTC-and possibly other trials?
  - c. What is the survival rate of patients some time after the diagnosis ? This would come down to estimation of conditional survival.
  - d. What is the incidence and survival of unusual, uncommon malignant disorders, especially in the young ?
  - e. What are optimal treatments for cancer in the very elderly and in those (e.g. with co-morbidity) who are seldom enrolled in clinical trials?
  - f. Provide systematic feed-back on quality of life from short- and especially long-term survivors
  - g. Does the variation in care (detection, staging, treatment) become smaller and which are the determinants ?
  - h. Do certain types of regionalisation work better than others?
  - i. What is the incidence of long-term side effects that most often are relatively rare?

It is clear that the interaction with the various clinical groups should improve in order to have more and better studies. By doing more studies more presentations could become possible at the various congresses.

## Questions

R. Sankila: Has the Federation of European Cancer Societies given some tasks for the European cancer registries or is this still at discussion level?

J.W. Coebergh: Most of the time they would think about us when they need some figures and they would call people or look at EUCAN or GLOBOCAN. I have talked to some of the Board members and they would rather be involved in a more strategic way, in particular they would like to involve epidemiology and the cancer registry in a more strategic way.

R. Sankila: This sounds as if there would be a place on their Board for either a well trained clinician also trained in epidemiology, or an epidemiologist who understands the clinical world.

D.M. Parkin: I do not wish to reopen the debate about the relative merits of incidence, survival and mortality. I think you are wrong to imply that cancer mortality is not a valid endpoint. After all, we know the difficulties in attributing cause of death, and there is a problem now, particularly trying to use survival data, where there is a bigger emphasis on earlier diagnosis. I looked the other day at the SEER website and noticed that for some subgroups of patients, survival from prostate cancer in the US is over 100%. That is impossible to interpret, unless you know something about the incidence and mortality. Otherwise, the lesson you would draw is that prostate cancer treatment has been so successful that you have better to have it than not. This is clearly nonsense, if this is the only data we are going to look at as a measure of progress.

J.W. Coebergh: I only said "don't do it unless you have certain reasons to do it". And then do it in a very conscious way. I indicated on the slide that, in tumours that are screened, you have to do it, but if you now take the example of prostate cancer, the cause of death statistics are tricky, because there are millions of men in the US whose prostates have been taken out, they all have prostate cancer, so there is a tendency to attribute cause of death to the tumour, when people do not know, because often in very old men it is rather difficult to find out.

R. Sankila: Some of the registries are able to link individual data on incidence and mortality and they do not have any problems with this. It is a question of whether you attribute the death to the cancer in question or not. But that is the solution and all registries should try to get to that point.

K. Freese: I am grateful for you mentioning that making data comparable, developing the underlying standards which, from my point of view at a European level, has been the biggest impact of ENCR over these 15 years, is a tedious task and if you look back from where you started, I think you have reached a wonderful level. Colleagues in other areas of health always say that cancer statistics are light-years ahead of any other epidemiological statistics, having registries and having all these types of standardisation. From a European point of view it is important that we get comparable data. We have still some areas of concern like mortality data. As you know, there is a Working Group on Mortality for all kinds of health outcomes. I would expect that the ENCR, with its body of practical experience and theoretical insight in the deficits of the system in various member states, would do more in explaining what should be done to obtain sufficient quality of cancer death statistics and reporting. Some of these areas only relates to technical reporting. If you take prostate cancer as an example, the reasons why you are here is that you have been doing this type of work, you have obtained excellent results and we want more of this to happen in the future. This should also include your particular experience with the various ways of collecting and interpreting mortality data in the member states, with feedback to EUROSTAT and other actors in the field.

## **Presentation 5. PROGNOSTIC FACTORS IN BREAST CANCER SURVIVAL**

### **Abstract**

*David FORMAN<sup>1,2</sup>, Jasmina Stefoski<sup>3</sup>, Cheryl Craigs<sup>1</sup>, Keerthi Prakash<sup>2</sup>*

*(1) Northern & Yorkshire Cancer Registry and Information Service, UK, (2) University of Leeds and (3) Cancer Research, UK*

### Background

In the U.K., among the major cancers, breast cancer has one of the largest survival differences between affluent and deprived patients. In the Northern and Yorkshire region, the gap in 5-year survival between the most affluent and the most deprived patients has widened from 8% for 1990-93 to 11% for 1994-97 diagnoses. This study aimed to identify possible health care factors that may contribute to such differences in survival after adjustment for case-mix factors.

### Methods

Female breast cancer patients (n=12,880) diagnosed during 1998-2000 and registered with the Northern and Yorkshire Cancer Registry, were grouped into SES quartiles using the Townsend deprivation index, a census based measure. Percentage distributions for each SES quartile were calculated and multiple logistic regression analyses were undertaken in relation to patients' age and stage at diagnosis, treatment received and the time taken to receive the first hospital appointment and start treatment.

### Results

Statistically significant differences between SES quartiles of patients were found in relation to tumour stage with 38.6% of the most affluent diagnosed at stage I compared to 32.7% in the most deprived and age at diagnosis where 35.9% of the most affluent were older than 65 years compared to 45.4% of the most deprived. After adjusting for both age and stage, the odds ratios (ORs) for having to wait for more than 14 days for a first hospital appointment and the start of treatment were significantly elevated in the most deprived SES quartile to 1.20 (95% CI 1.07-1.36) and 1.16 (95% CI 1.05-1.29) respectively. Patients from the most deprived areas were significantly less likely to have surgical treatment (OR 0.62, 95% CI 0.50-0.76), and, if they had surgery, they were more likely to have mastectomy (OR 1.16, 95% CI 1.04-1.29) and less likely to have breast conservation surgery (OR 0.78, 95% CI 0.70-0.88). Socially deprived women also received significantly less radiotherapy (OR 0.82, 95% CI 0.72-0.93) after adjustment for other factors including the type of surgery received.

### Conclusions

Even after adjustment for age and stage, important SES-related differences remain in both the time taken to commence treatment and the treatment received. As these factors can be managed by the health service, this study has important implications for the reduction of such differences. The extent to which these factors directly influence survival will be the subject of future research.

### **Questions**

**D. Brewster:** Have you the ability to split your cases into screen detected and non-screen detected and if so, would you consider introducing that as a variable as well?

**D. Forman:** We have not got sufficiently complete information on screen detection, however, we have been able to stratify and look separately at the age-group of women who are eligible for screening, which is not quite the analysis you want, but quite close to it. For some of those effects, although you see a stronger effect in the screening-age related group, you certainly see the same effects and they still achieve statistical significance in women younger or older than those being offered screening.

**R. Sankila:** How did the Health Service react to these results? Is there a selective way of improving some of the indicator outcomes in terms of the deprived areas more than in general terms?

**D. Forman:** As yet these results are unpublished, so we have not been able to assess their impact in terms of the Health Service. The deprivation-related data have been published several times



previously and always have an incredibly high profile. Michel Coleman's group have published deprivation-related survival outcomes for the whole of England and Wales and this has generated enormous amounts of media publicity and these socio-economic differentials in terms of cancer care are a major political issue within the UK.

## **Presentation 6. THE LINK OF CANCER REGISTRY AND HOSPITAL DISCHARGE DATA TO IDENTIFY THE CHEMOTHERAPY USE. AN EVALUATION IN THE TUSCANY TUMOUR REGISTRY**

### **Abstract**

*Eugenio PACI, G. Miccinesi, F. Giusti, E. Crocetti, Clinical and Descriptive Epidemiology Unit, CSPO- Research Institute of the Tuscany Region, Florence, Italy*

Adjuvant chemotherapy is today considered standard of care in several cancers and monitoring the practice patterns is considered important in order to assess the quality of the therapeutic protocols. Variations in the use of chemotherapy over time and between areas or hospitals is important to monitor the adherence to evidence-based guidelines. Population-based evaluation of chemotherapy use started to be possible using Hospital Discharge data, which report the episodes of hospitalisation for chemotherapy in treating hospitals. The relevance of the link of cancer registry data with the Hospital discharge data as source of information on chemotherapy use and the implications for monitoring pattern of care will be discussed.

### Background and methods

The Tuscany Tumour Registry (RTT) covers about one third of the Tuscany Region (3.500.000 residents) and all incident cancer cases from 1998 onwards have been linked to the regional Hospital Discharge database. Three local authorities are covered by the Registry (Firenze, Prato, Empoli), whereas for the others the RTT provides each year an estimate of the expected number of cases ([www.cspo.it](http://www.cspo.it), Colonna method) at least for major cancer sites. Chemotherapy practice in the Tuscany Region is not allowed as outpatient or at home. We selected the first chemotherapy episode for each incident cancer case in the period 1998-2003. In order to estimate the variation in the use of chemotherapy also in the areas and years not covered by the registry (incident data are at 2001) we proposed indicators of chemotherapy use using estimate of incident and prevalent number of cases.

### Results

From 1998 to 2003 about 12,000/year episodes of first chemotherapy were registered in residents who received the treatment in the hospitals of the regional health service. About the 70% of the chemotherapies were performed as day hospitals. The proportion of subjects receiving chemotherapy varies by age, with a strong decreasing rate for older people (75+). In more than the 95% of the cases it was possible to define a cancer site using diagnoses as reported in the hospital discharge note. In 2000-2003 variation in the pattern of use of chemotherapy was evident across the 12 local health authorities of the region. In the area covered by the RTT the pattern of care of each cancer case was available on the basis of the cancer site defined by the registry and the incidence date. The 30% of the chemotherapy episodes for all tumours occurred within 3 months since the diagnosis and the 57% within 1 year. The ratio of the chemotherapy episodes to the 0-74 years old incident cases (year 2000) was the 36.8% for all cancer sites (excluding skin) with a 58.0% for colorectal cancer and 50.7% for breast cancer. In Breast cancer cases we related the occurrence of chemotherapy with the node status at diagnosis. Node positive breast cancer cases (less than 75 years of age) received chemotherapy in the 75.6% of cases, whereas node negative breast cases were treated in the 26.7%.

### Conclusion

In recent years there has been growing interest in the linking of routinely collected data, as hospital discharge episodes, and cancer registry data. High-resolution studies have provided information on the use of chemotherapy in several registries in Europe but the data are occasional and trends are not easily available. Routinely collected hospital discharge data are today easily available and quite

reliable. So the goal is to set up a common set of standards and to develop co-operative research in order to share criteria for the evaluation of the pattern of care and identification of false positive and false negative results. The goal is to provide further link with chemotherapeutic agent databases and possibly on a sample basis to evaluate the relationship between prescriptions and guidelines.

## No questions

### **Presentation 7. REGIONAL AND INTER-HOSPITAL VARIATIONS IN THE USE OF BREAST-CONSERVING SURGERY IN THE NETHERLANDS**

#### **Abstract**

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#### Background

Breast-conserving surgery (BCS) is generally considered to be a safe treatment option for the majority of patients with T1 breast tumours (i.e.,  $\leq 2$  cm) and a substantial part of those with T2 tumours (i.e., 2-5 cm).

#### Materials and methods

We used data of two cancer registries to study the trends in the use of BCS in 10,514 patients with T1 (i.e.,  $\leq 2.0$  cm) and 6,961 with T2 (i.e., 2.1-5.0 cm) breast cancer, treated in general hospitals in the southern and eastern part of the Netherlands in the period 1990-2000.

#### Results

Between 1990 and 2000, the proportion of patients undergoing BCS in the eastern and southern part of the country was 51 and 66% for pT1 cancers and 25% and 37% for pT2 cancers, respectively. In both regions a significant increase was observed in the use of BCS for patients of 70 years or older with T1-tumours; in the early nineties around 30% underwent BCS, whereas in 2000 64% underwent BCS in the southern part of the country and 46% of those in the eastern part. A decrease in the use of BCS was observed in patients <50 years of age, especially for those with T1-tumours in the eastern part of the country (from 71% to 57%). Only in the eastern part of the Netherlands, the use of BCS increased from 50% to 60% for patients of 50 to 70 years (screened age group) of age with T1 breast cancer and from 20% to more than 35% for those with T2 breast cancer. Inter-hospital variation within regions appeared to be larger than the differences between regions. In the period 1996-2000 the use of BCS for patients with T1 tumours varied between 42% (95% CI: 36-48) and 82% (95% CI: 77-86) in the hospitals in the southern part and between 43% (95% CI: 37-49) and 61% (95% CI: 53-68) in the eastern part of the Netherlands. For T2 tumours these proportions were 16% (95% CI: 11-21) versus 63% (95% CI: 56-71) and 24% (95% CI: 18-29) versus 38% (95% CI: 29-46), respectively.

#### Conclusion

More than 20 years after the introduction of BCS in the Netherlands, large variations still exist between hospitals and regions in the use of this treatment. Differences can be partly explained by the patient's wish, specialist's belief in the treatment and favourable or unfavourable experiences with local recurrence after BCS. More specific guidelines and regular evaluation of adherence to these guidelines and the local recurrence rate in each hospital are needed to attain acceptable variations in the surgical treatment of breast cancer.

(The big discussion is what is the optimal percentage of BCS. It depends on the change in local occurrence and what is the patient's risk is expected cosmetically. The specialists believe in the treatments and therefore .... experiences with local recurrences after BCS and the guidelines are pointing out towards for tumours less than 2cm BCS, it's where the BCS is not possible and larger tumours 50% could be possible. The recommendation is we should obtain local recurrence rate pro hospital and get survival rates, more specific guidelines and better implementation of these guidelines and of course better evaluation).

## Questions

R. Sankila: You also need to take into account the adjuvant radiotherapy given to the BCS patients. I think we do not yet know the long-term outcome of BCS; there are very few studies with extremely long follow-up. We will probably change our view of the optimal percentage or the types of tumours that can be treated.

S. Siesling: You cannot say what is the best percentage at this moment.

G. Meledandri: The T2 is quite a large category, so when there is screening, within the T2 category you will probably have a shift towards more tumours of 2cm than 5cm.

S. Siesling: You mean that in the pT2 tumours in 2000, for instance, because of biennial screening, there will be more tumours towards the size 2 cm than to 5 cm? We need to look at the centimetres of the tumour as well. We have those data and have to look at those numbers. It is a good suggestion.

## **Presentation 8. POPULATION-BASED CANCER REGISTRIES : CATALYSTS AND PARTNERS IN IMPROVING THE QUALITY OF CANCER CARE IN EUROPE**

### **Abstract**

*Ian KUNKLER, University Department of Clinical Oncology,  
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Quality of care may be considered as the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge.

In response to the increasing accountability internationally of health care providers and cancer professionals to both government, purchasers and consumers, information is being increasingly sought on the quality of cancer care. Examples are the National Initiative on Cancer Care Quality of the American Society of Clinical Oncology and the Clinical Standards Board for Scotland. Additional drivers are the establishment of national cancer plans, which have set targets for the improvement of cancer services. In 1995 the Calman Hine report on cancer services recommended use of UK cancer registries to monitor the quality of cancer treatment and specialisation. The interdependency of high quality cancer services and high quality population cancer registries cannot be overemphasised.

Population-based cancer registries from 12 European countries in the first EUROCARE-2 report, covering the period 1985-1989, showed significantly poorer survival in England, Scotland and Denmark for common cancers (e.g. lung, breast, large bowel and prostate). For breast cancer these data were corroborated by other UK studies showing wide inter- and intra-regional variations in outcomes related to access to specialist care. However, the continuing wide variation in the extent of coverage of cancer registration in continental Europe threatens to undermine confidence among some oncologists in the validity of the differences in survival found in the EUROCARE studies. National coverage of cancer registration remains an important priority. Nonetheless the poor performance of the UK against western continental comparators proved pivotal in persuading the UK government that

major action to improve the organisation and delivery of diagnostic and treatment services was needed. This resulted in the establishment of National Cancer Plans for England in 2000 and equivalents in Scotland, Wales and Northern Ireland. National cancer plans have now also been developed in other European countries including Denmark, France and Spain. Policy makers are in general very sensitive to their performance against international benchmarks of cancer care.

Among western European countries (Denmark, England, Scotland, Wales, Malta and Portugal) the EURO CARE-3 study, covering the period 1990-1994, showed that survival was generally below the European average. In Denmark and the UK however survival for Hodgkin's Disease, melanoma of the skin and testicular cancer was not below the European average. This probably reflects the concentration of the management of these patients in centres of excellence.

Differences in survival identified by cancer registries flag up to policy makers that careful study of the pathways in diagnosis and treatment is needed. The relationship between process and outcome is complex and has been examined in high resolution studies (e.g. for breast cancer). Where EURO CARE identifies significant differences in survival between countries, prospective European cohort studies are needed using population-based registries to identify critical elements of the diagnostic and treatment process, which impact on outcomes. Factors may include provision of specialist staff, multidisciplinary organisation and prompt access to diagnosis and therapy.

In the EU funded EUROCHIP-1 project European cancer registries have taken a leading role in establishing with clinicians internationally agreed benchmarks for cancer care in Europe. These key indicators include aspects of lifestyle, cancer prevention, early diagnosis and treatment. In EUROCHIP-2 the feasibility of collecting of these key indicators in the expanded European Union will be examined.

In planning cancer services in Europe, the application of the evidence base for effective treatment needs to be linked to the burden of cancer in individual countries. Already the EU funded QUARTS study (**QU**Antification of Radiation **T**herapy **I**nfrastucture and **S**taffing Needs) under the auspices of the European Society of Therapeutic Radiology and Oncology (ESTRO) is developing such a service model for radiotherapy in Europe. This is to be linked to European cancer registration data to estimate radiotherapy and staffing requirements against a common standard. Similar models will be needed for surgery and systemic therapy. Cancer registries will be central to the success of this endeavour.

## **Comment**

I. Kunkler: What do we need to do? What are the take home messages? Firstly, we need to agree international benchmarks of cancer care and a start has been made through the EUROCHIP project. We need to create new collaborative networks and we have already heard this morning of suggestions of collaboration with FECS – and I would endorse that – particularly with ESTRO with projects looking at radiotherapy uses. What they want to do is link the provision of radiotherapy staffing and equipment to the burden of cancer in those individual countries and develop models that are doing that. Thirdly, we need to develop projects which are aimed to improve the quality of care in defined areas, where there are difficulties, so that we understand the relationship between process and outcome. Finally, we need to identify the resources. A cancer service without cancer registration is like a clinical trial without a statistician.

## **Comments on the previous presentations**

I. Kunkler: J. Norstein indicated that the quality of rectal cancer care is critically dependent on surgery and we saw that total rectal incision is generalised. What we have seen in the UK is that surgeons and pathologists have got together, they have organised training workshops and videos to make sure that this kind of technique is generalised into every District General Hospital setting. What we were hearing from Dr Faivre in relation to the provision of chemotherapy is that, despite evidence-based guidelines there is still the widespread provision of non-evidence based chemotherapy and the cost of

delivery of chemotherapy is rising at an exponential rate. We could make calculations that the cost of delivering cancer care will exceed the gross national product of many individual countries unless the resource is used widely. What was also interesting was that if you look at the guidelines that were developed, these were very high-quality guidelines. If you look at the FNLCC on the treatment of breast cancer, they are very strongly evidence-based and yet there seems to be a disparity for example in the application of pre-operative radiotherapy for rectal cancer. If you look at the application of CEA in the treatment of colorectal cancer, despite the evidence that it is of no value, he has already showed evidence that substantial numbers of patients are continuing to have this measured and I am not sure if that relates to either the fact that the guidelines are not really owned at a local level by the individuals who are practising them.

The main message that comes out of the talks is that the application of known knowledge is absolutely critical. The continuing practice of non-evidence based medicine is no longer acceptable and is not affordable and as J. Faivre was indicating, the proportion of patients in France going into randomised trials still remains relatively small. In the UK, one of the targets was to double the recruitment into randomised trials to 8% and that target was met last year. There is a similar target in Scotland. In areas of uncertainty, we must be putting patients into clinical trials. Those are the main take-home messages.

R. Sankila: Since this is a European workshop and the second of its kind, we should start thinking about what we really need to do. The sad part obviously is that with ENCR not being funded by the Commission any more, the framework within which we could continue is a little more vague.

I. Kunkler: What Roger Black has shown is that the cancer epidemiology community is a key resource in scenario planning and the kind of template that David and Roger and their colleagues have developed in Scotland could be the kind of template that other countries could develop. The difficulty is that if cancer registries are remote from the decision-making process, they are remote from the resources. A collaborative network, in which cancer registries are embedded within the clinical community, is the way to actually direct resources to what is needed to improve the quality of care. This is a kind of structural and professional change which is perhaps difficult to achieve, but some kind of agreement is needed that this is the goal we are working for. If you bring the clinical community along with you, they have enormous influence with governments, and many of the difficulties you have in funding are related to the fact that you are not as closely-knitted into the decision-making process and policy as you could and should be.

R. Sankila: Currently the population-based cancer registries are in a very heterogeneous situation in terms of serving the clinical community. In many areas there has been no demand, because it was not clear that they could actually be players in the field. This is now changing, and changing rapidly. We should move forward and start working more closely with the clinical community. Maybe around this table there is time for some formal activity, take certain indicators that are available and maybe produce some kind of standard scenario for every country in terms of what would be a feasible number of radiotherapy machines in the next 10 years. That would be some kind of standard which could be given to the political decision makers, as guidelines for what to expect and many of the politicians do not realise that in the next 10-15 years the ageing population will cause an explosion in number of patients, even if there is no change in risk and that will require extensive resource allocation by that time.

I. Kunkler: Governments will be extremely grateful in 10-15 years time, if the kind of scenario planning has enabled the appropriate reinvestment to be made, so that we actually get the delivery of evidence-based timely care for a rising cancer burden. From the Commission's point of view, that must be the absolute priority and any kind of structure that facilitates that must clearly be supported.

K. Freese: Although the ENCR contract came to an end as the Europe against Cancer Programme also came to an end, there is a new project, EUNICE, which has been selected, but the contract not yet established. There is also the so-called European Cancer Network which main task is to take forward the Council recommendations on cancer screening and which has already developed EU guidelines. In the case of breast cancer, it also includes a section of management and follow-up of screen-detected lesions. The epidemiological work that has been done in the past in the different cancer screening

networks has to be integrated in the EUNICE project. One of the recommendations from the Council is that screening programmes should be followed up, monitored and evaluated by independent cancer registries. In many member states this may help to extend the cancer registry services for the whole of the country. There is a non-legal and non-binding pledge from the member states that, if you introduce population-wide screening, you should have cancer registries for follow-up. There will be calls for proposals every year, the next one for the Public Health Programme will come up in January 2005 most likely, but we will have to see what is in there for cancer registration. There are also very intense, and from the level of funding much higher efforts which have been implemented under the cancer research programme by my colleagues from DG Research.

## WORKSHOP ON CHILDHOOD CANCER

**Chairman:** Eva Šteliarová-Foucher (IARC)

**Co-chairman:** Max Parkin (IARC)

**Invited speakers:** Charles Stiller (National Registry of Childhood Tumours, UK); Eva Šteliarová-Foucher (IARC); Hermann Brenner (German Centre for Research on Ageing); Eve Roman (University of York, UK)

**Communications:** Luisa Zuccolo (Childhood Cancer Registry of Piedmont, Italy); Peter Kaatsch (German Childhood Cancer Registry); Ivan Plesko (National Cancer Registry of Slovakia).

### Introduction

Childhood cancer is an important public health problem, although only about 1% of cancer cases occur in children. About 1 in 600 children will develop cancer before the age of 16, cancer is the second most common cause of death in children and incidence rates are increasing. At the same time childhood cancer is difficult to study, because it is a rare disease and in order to analyse the data in a meaningful way, long time series or large areas are needed to collect enough cases.

Childhood cancer is not a single disease, but a variety of diseases and probably comprises more histological types than in adults. In addition, the causes of cancer in children are less well known than those in adults. Further methods should be developed for early detection of cases, which would permit earlier treatment and better outcome and, although there has been considerable improvement in survival of these childhood cancers, treatment can still be improved. The improvement of quality of life in survivors should also be taken into account.

How can the cancer registries contribute to this? First of all through collection of high quality data. This requires joint efforts between the cancer registries, based on standardisation, to enable good comparability of the data. Further developing the ACCIS database with more data from the cancer registries is another possibility, which would permit more detailed analysis on the population level. It would also permit looking into the possibilities of linking cancer registries' data with other databases, as for example databases of biological samples or congenital anomalies.

### **Presentation 1. INTERNATIONAL VARIATION IN CHILDHOOD CANCER INCIDENCE**

#### **Abstract**

*Charles STILLER, Childhood Cancer Research Group, University of Oxford, UK*

Age-standardised annual incidence rates for cancer among children aged 0-14 in registries with good quality data are usually between 80 and 180 per million in boys and between 60 and 150 per million in girls. Greater variation is seen between populations for some specific diagnostic subgroups. Some of the largest variations are geographical. In some instances, such as Burkitt's lymphoma, Kaposi's sarcoma and differentiated thyroid carcinoma in regions of exceptionally high incidence, these can be attributed to environmental factors. Variation mainly on ethnic lines seems likely to be a marker of genetic predisposition. For example, Wilms' tumour and Ewing's sarcoma have low incidence in East Asian populations, and genetic differences in both these tumours have recently been found between Japanese and Caucasian patients. Weak predisposition may also be important in some childhood cancers, including acute lymphoblastic leukaemia, though results so far have only limited consistency with patterns of incidence. Finally, variations in medical practice and availability of facilities can influence recorded incidence of certain cancers, notably neuroblastoma and central nervous system tumours.

## Questions

E. Šteliarová-Foucher: What is your opinion about the low incidence rates of leukaemias in Africa?

C. Stiller: That is a very complex picture. The natural history of childhood leukaemia is overwhelmingly an acute disease and, if untreated, is fatal. There is still a lot of controversy in Britain and elsewhere as to how much the trend in incidence going back to the 1950s was due to greater recognition of leukaemia rather than overwhelming infections, which took a fatal hold on children who in fact had an underlying leukaemia that was undiagnosed. I suspect that it is partly a matter of competing causes, partly a matter of medical and diagnostic facilities, but there is an element of a real difference. Some of the international studies that have been done, looking at the immunophenotypes of ALL, have found a higher proportion of T cell rather than precursor B cell disease among sub-Saharan African children with ALL and yet both of these diseases would have a very poor prognosis and that argues quite strongly in favour of some of the difference being real.

R. Sankila: M. Parkin might have an idea of how the urban area might increase the possibility of diagnosing leukaemia in Kampala. Elsewhere in Africa when children die, they just die and therefore we will always see low rates for this acute disease. My point is that, now that neuroblastoma screening is not being recommended anywhere any more - even last year in Japan some kind of consensus was made to quit the population-based screening there - we still see these immense differences in Europe. Is there some spontaneous screening going on?

C. Stiller: There was a fairly large study of screening carried out in Germany, and two very small studies carried out in the UK over rather shorter times, but mostly it is a matter of incidental diagnosis of an abdominal or thoracic mass in an infant, either when they go for a routine early childhood health check or, for example, in some instances we find there was a greater percentage of cases incidentally diagnosed, when children had attended a physician with some other unrelated complaint and the neuroblastoma was discovered during the examination. I think that is more likely to explain any persistent differences and indeed differences in countries which had never even in the spirit of studying rather than providing a national service had ever got involved in biochemical screening.

D.M. Parkin: Concerning leukaemia in Africa, these low rates is rather a consistent finding. You do not see this big scatter as for the CNS tumours. I think Charles has given a very judicious reply, some of it is artefact, but I think probably there is a chance that some of that low incidence in Africa is a genuine effect, not just missed in diagnosis as it such a consistent finding in every dataset.

K. Hemminki: I have a comment on these data that you had on methylenetetrahydrofolate, that polymorphism explains some of the high incidence rates. If that were true, if that kind of polymorphism would be related to risk of ALL, that would mean one should be able to see a sibling risk, and if you remove monozygotic twins, I don't think there is very much of a sibling risk for ALL, so I am quite doubtful whether that kind of polymorphism can explain incidence rates.

G. Meledandri: In your experience, are there any simple rules to assume that a low incidence is not due to a type 1 error?

C. Stiller: Where there is consistently low incidence of a particular tumour type across a wide range of populations that share a certain characteristic (whether geographical, regional or ethnical), and where at the same time you find in the same groups that they have consistently higher rates for certain other cancers, which could hardly be confused with them as a matter of differential diagnosis, I think this would indicate that there is a true difference.

## **Presentation 2. THE ACCIS PROJECT**

### **Abstract**

*Eva STELIAROVA-FOUCHER, International Agency for Research on Cancer, Lyon, France*

Automated Childhood Cancer Information System (ACCIS) is a collaborative project of European Cancer registries, co-ordinated from IARC. It aims at collection and interpretation of data on cancer in



children and adolescents. The ACCIS database contains data on some 160,000 cancer cases, arising in 1.3 billion person-years and data collection continues.

Collected data are centrally verified and evaluated for international comparability. Those considered comparable are included in studies of incidence and survival. Presently, a series of descriptive studies are under preparation and are planned for publication in 2005 in a special issue of European Journal of Cancer.

These studies show that the overall incidence rate of cancer in children (standardised to world standard population 0-14) for the period 1988-1997 was 138 per million. Significant differences were observed between the five geographical regions: British Isles (131), West (136), East (141), South (148) and North (160).

The incidence rates of childhood cancer have increased significantly since 1973 by about 1% per year: the age-standardised incidence rates for the five consecutive periods were 119 (1973-77), 119 (1978-82), 127 (1983-87), 134 (1988-92) and 141 (1993-97).

Survival of children with cancer has improved markedly and significantly in all regions since 1973. 5-year survival of children diagnosed in 1988-1997 attained 62% in East, 71% in British Isles, 72% in South, 75% in West and 77% in North.

A part of the observed geographical differences and time trends may be explained by different diagnostic and registration techniques, which vary by region and over time. However, some of the findings provide a good basis for further studies into the possible causes of some cancers (incidence of lymphoid leukaemia), as well as for setting-up public health policies on European level (differences in survival).

## Questions

I. Kunkler: Paediatric malignancies, the model of clinical trial recruitment and multidisciplinary management – are you able to tease out the impact of patients either treated on trial protocols or off trial protocols in terms of your outcomes?

E. Šteliarová-Foucher: Currently this information only comes from the registries themselves, and it is true that it is not always possible to have it for all the participating countries. This would be yet another item to collect.

R. Sankila: There is a very nice example from the Nordic countries of the effect of standardising treatment and including all the paediatric cancer patients in trials –that is the NORPHO collaboration (the five Nordic countries' paediatric oncology groups working together), because we see clear differences in survival rates. In the 1960s Finland and Denmark had much lower rates than Sweden and Norway, but by the late 1970s, when the NORPHO collaboration was very active and treatment was standardised over the 5 countries and patients entered trials, the differences completely disappear in the 1980s and 1990s and now they are in the top 5 world-wide. This is a very good example of how you can achieve very high survival rates with this type of operation in this specific group of patients.

J.W. Coebergh: We may also have a problem because the registry data are both in the EURO CARE study and in the ACCIS study, and we will see publications coming out from one or the other with sometimes different survival rates. Registries should be aware that the level of checks and controls are not the same. Personally, being involved in both these studies, I would prefer that the childhood cancer data, including those in the EURO CARE study, go through all the controls and checks which have been done in the ACCIS study. Currently this is not the case. We should change this as soon as possible, because the political and psychological impact of rates and data is great.

K. Freese: The public is usually very much moved by claims of clustering of childhood cancers. At the Budapest Conference on Environmental Health, childhood cancer was singled out as one of the

priorities for environmentally-linked negative health outcome. It shows that childhood cancer has a very high priority in the public eye. Can anything be done with the data density already available?

E. Šteliarová-Foucher: At the moment it would be difficult or impossible to do it in ACCIS, because for clustering you would need more detailed information on population-at-risk. For the moment we only have population for the total registration area. The EUROCLUS study tried to deal with this problem, but they were not able to include all the countries in the study, because the population data are not available in enough detail in all the countries.

### **Presentation 3. USE OF PERIOD ANALYSIS FOR TIMELY DISCLOSURE OF PROGRESS IN CHILDHOOD CANCER SURVIVAL**

#### **Abstract**

*Hermann BRENNER, The German Centre for Research on Ageing (DZFA), Heidelberg, Germany*

#### Background

For many forms of childhood cancer, there has been major improvement in prognosis in recent decades. However, improvement in long-term survival was disclosed with substantial delay, partly because of the methods used for survival analysis. A couple of years ago, the "period survival" method was introduced, which gives more weight to the most recent observations, to derive more up-to-date survival estimates.

#### Methods

The period survival method was thoroughly evaluated and compared to traditional cohort based survival analysis for childhood cancer, using the database of the Automated Childhood Cancer Information System (ACCIS).

#### Results

Using the follow-up data available in 1989, 10-year survival for all cancers combined calculated by traditional cohort life-table analysis was 50%, while it was 58% when calculated by the period survival method. The latter was much closer to the true 10-year survival of 61%, observed in 1999 for the patients diagnosed 10 years earlier. A similar range of differences was observed for survival of patients with selected groups of common neoplasms.

#### Conclusion

The period survival method is especially useful for up-to-date monitoring of children with cancer, as it more timely discloses the rapid progress in management of these patients seen in the last decades.

#### **Questions**

E. Šteliarová-Foucher: What would you suggest to cancer registries? Can they ever use the life-table method again or should they all switch to period survival method?

H. Brenner: I think the traditional methods have their value. My conclusions were relating to the situation where one tries to get the most up-to-date estimates possible. Sometimes it is of clear interest to look at it retrospectively to see in which time periods the survival estimates have improved and to what extent. It is often easier to link these changes to the introduction of specific therapy and try to explain what happened in different time periods. I think these traditional methods, especially the cohort method, would be the method of choice, but if the goal is to have up-to-date survival estimates, it is a case for period analysis.

R. Sankila: One can perfectly well use the traditional methods when doing trend analysis of, say, 5-year survival over long periods of time, because those rates do not change. The real value of the period method is when you take a look at the most recent data and predict survival of today's patients based on the most recent data.

H. Møller: The main attraction of Hermann's method, and the reason most of us have started using it, is that it has the possibility of giving long-term estimates of survival based on as current data as possible. The trouble is that the parameter of interest often should not be long-term survival but short-term survival. All the international variation in childhood cancer survival occurs in the very short term, so the parameter of interest here is actually rather 2-year survival, to elucidate the international variations.

G. Meledandri: To look at childhood survival you can use any method, it does not really matter. But for many of these patients, what one really wants to know is what are the perspectives to survive in the long term. If you look at the survival curves, not all of them are flat after 2 or 3 years. Many go down for many years, so it is not sufficient to look at 1, 2 or 3 years survival for childhood cancer, at least for many forms of childhood cancer.

J. Norstein: We have only seen examples of survival improving. How does this method perform when survival is actually decreasing, as we now see for gastric cancer, for example, because of getting older?

H. Brenner: You would also see this change earlier with the period analysis than with the traditional methods. There are examples for cervical cancer in some countries, where survival decreased over time, not because therapies became worse, but it was a selection effect due to the otherwise very successful screening. In these countries, if one applies the period analysis on these lower rates following the introduction of screening, then with the other rates, you see these changes earlier than you would have seen with the traditional methods.

K. Freese: If you now have this wonderful improvement in survival, the problem of secondary cancer becomes important. Did you have a chance to look in the dataset for the same group of patients in the ACCIS database and in the ENCR adult database to compare?

H. Brenner: This has not been done so far. There is always a concern with secondary cancers but I think, especially from the Nordic cancer registries, there is work showing that even the occurrence of secondary cancers has decreased or, in the long run, excess mortality from secondary cancers has decreased.

R. Sankila: The second malignancies are not such a big problem. There is an increased risk compared to the general population, but it is not so big and it is not increasing any more.

#### **Presentation 4. UNITED KINGDOM CHILDHOOD CANCER STUDY**

##### **Abstract**

*Eve ROMAN, Epidemiology & Genetics Unit, University of York, UK*

##### **Background**

Pre-natal and early life exposures have long been thought to be important determinants of cancer in children and young adults; and sufficient evidence had accrued by the time the United Kingdom Childhood Cancer Study (UKCCS) began in the early 1990s to suggest that the aetiological role of four main exposures, acting at different time periods, were worth testing: -

	<b>Time period</b>		
	Pre-conception	In-utero	Post-natal
<b>Ionising radiation</b>	X	X	X
<b>Chemicals &amp; drugs</b>	X	X	X
<b>Infections</b>		X	X
<b>ELF-EMF</b>			X

### Design and data sources

The United Kingdom Childhood Cancer Study (UKCCS) is a collaborative multi-centre case-control study covering the whole of England, Wales and Scotland. Children diagnosed in England & Wales between 1992-96, and in Scotland between 1991-96, were potentially eligible for inclusion. Control children, matched on sex, date of birth and area of residence were selected at random from population registers. Information about both groups was obtained from a wide range of sources including parental interviews, primary care records, obstetric and neonatal records, household electric and magnetic field measurements and household gamma and radon measurements.

For cases, pre-treatment and remission blood samples were also obtained and stored. Detailed diagnostic information was obtained from multiple sources including treatment trials, the UK Children's Cancer Study Group (UKCCSG), cytogenetic laboratories, and individual clinicians. For leukaemias, the principal diagnostic sources were treatment trials, but for cancers other than leukaemia, a histopathology review database was specially created for the study.

At the start of the study, a common protocol was agreed by the management Committee and, for the purposes of study management, ten regions were created; the conduct of the study within each region being the responsibility of a single epidemiological centre. Each regional centre was responsible for ensuring the completeness of ascertainment of cases diagnosed within their boundaries. The majority of cases were ascertained directly by treating hospitals; and cross-checks against regional and national cancer registries were also conducted

### **Questions**

E. Šteliarová-Foucher: I think it will be a long time before this sort of study could be done on a European level, but maybe we could start thinking about it and get some ideas for using the precious data that cancer registries are collecting.

K. Freese: Childhood cancers are rare diseases. We have a couple of European databases and there is co-operation. I do not see that there is an obstacle against having something on the European level which might be linked to other rare disease efforts already going on.

E. Roman: The initiative to set up something more permanent would be a very good one.

K. Freese: You mentioned electromagnetic fields, radon and x-ray. Did you also look for the effect of tobacco consumption of the parents?

E. Roman: We have looked at that and not found anything. The findings from the recent German and UK and US case-control studies are presently being pooled.

J.W. Coebergh: You have not presented any data, but if you had the opportunity to redo this study, whether in the UK or elsewhere, what would you try to study?

E. Roman: I would not put so much effort into the interview. One of the interesting things we have been able to do is to look at the medical records in conjunction with what is reported at interview. At times there are serious discrepancies between them, even in terms of serious illnesses like measles. The parent may say yes and when you look back the child has not and vice versa. I would concentrate much more on obtaining people's consent to access routinely compiled medical data

J.W. Coebergh: Which are the hypotheses?

E. Roman: I certainly think immunological factors for leukaemia are very appealing, but doubt, that it is simply a question of exposure to infections. It is clearly more complicated than that. Leukaemia itself is a heterogeneous disease; and for certain other cancers aetiology may be even more complicated. A fundamental tenant of epidemiology is that disease does not necessarily occur at random, but I wonder sometimes whether in fact it does!

R. Sankila: One of the principal rules in use of biological samples that have been collected for scientific purposes is that they can only be used for the specific purpose stated in the consent.

E. Roman: We went to every single ethics committee in the country in the early 1990s, as the study was conducted before the introduction of large national ethics committees in the UK. We obtained

signed consent from all participants in the study to use biological samples for research purposes. Nowadays, in the UK, you would have to specify much more carefully which genetic tests you are going to do.

R. Middleton: We did a similar study in Northern Ireland linking leukaemias only with something called the 'Child Health Record', which was collected by midwives by and large. I am wondering if anyone else in Europe has similar types of data, like birth weight, whether the mother smoked, was it breast fed, etc? There may be other types of data like that people could use. The point is to make people aware that there could be databases out there we could be linked to cancer registries.

E. Roman: This is good ideas, but I think smoking is not necessarily very well recorded in paediatric records. That is one thing you might have to actually ask people – and then they do not tell the truth.

## **Presentation 5. CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA INCIDENCE TREND: A STEADY INCREASE?**

### **Abstract**

*Milena Maria Maule<sup>1</sup>, Luisa ZUCCOLO<sup>1</sup>, Corrado Magnani<sup>1,2</sup>, Guido Pastore<sup>1,3</sup>, Franco Merletti<sup>1</sup>, Dario Gregori<sup>1,4</sup>*

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Temporal variations in the incidence of childhood leukaemia have been the focus of several studies in the past decade. There is wide variation both in the estimates provided and in the methods of analysis, and the resulting world-wide scenario is heterogeneous: whether incidence is currently increasing or moving towards stability is not completely clear. Childhood Cancer Registry of Piedmont (Italy) data on the temporal variation of acute lymphoblastic leukaemia incidence (688 cases recorded in the period 1975-2001) are analysed through two different approaches: standard Poisson regression and a Bayesian approach including an autoregressive component. The two models fit the data equally well; yet, they lead to different and partly conflicting interpretations. The first predicts ever increasing rates while the latter suggests a non-monotonic behaviour of rates and therefore a change in the sign of time trend in the last few years.

### **Questions**

R. Sankila: Did you actually 'predict' or did you just fit your models into the existing data and expect that it would continue in the direction of your fitted line?

L. Zuccolo: This is an exercise I did about 2 months ago. We started implementing this sort of models and learning about them, so we have not validated models in terms of predictions. The intention is to fit observed data until, say, 1994 and see how the predictions for the two models fit the observed data in the same validation process done by Brenner for survival analysis. We cannot interpret predictions yet, so we do not know what to expect for 2002.

J.W. Coebergh: Did you also look at these data by birth cohort or year of birth?

L. Zuccolo: We did not. We just adjusted for age at diagnosis. Data were too sparse to allow further classification.

J.W. Coebergh: Because if there are changes in vaccination strategies or other patterns in pregnancy, or after that, sometimes you may see a pattern.

L. Zuccolo: That is a good suggestion.

L. Zuccolo: One of the two models, the Bayesian approach, is taking into account and correcting for the extra variability of rare diseases. The Poisson model is not suitable for these rare data, because it underestimates the intrinsic variability.

## **Presentation 6. SECOND MALIGNANT NEOPLASMS AFTER CHILDHOOD CANCER – EPIDEMIOLOGICAL DATA FROM THE GERMAN CHILDHOOD CANCER REGISTRY**

### **Abstract**

*Peter KAATSCH, Irene Reinisch, Birgit Schulz, Claudia Spix, German Childhood Cancer Registry, IMBEI, 55101 Mainz, Germany*

The relevance of secondary malignant neoplasms (SMN) increases with the improvement of the survival of childhood cancer in the last decades. Since 1980, all malignancies in Germany below 15 years of age are systematically reported to the German Childhood Cancer Registry (GCCR) (over 36,000 cases, completeness 95%). We currently know about 26,000 surviving cases. About 8,000 of these are currently older than 18 years and have a follow-up of at least 5 years. A reliable long-term follow-up leads to a high completeness of registration of SMN. To estimate risks for developing SMN until age 30, the base risk in the general population was determined using data of the GCCR (until age 15) and of two of the population-based general German cancer registries (from age 15).

389 cases with SMN are currently known at the GCCR (1.1% of all patients). Most of these occurred after lymphoid leukaemias (n=139) or cerebral primitive neuroectodermal tumours (n=34). Most common SMN are MDS and acute non-lymphocytic leukaemias (n=98). The most common combinations were lymphoid leukaemias followed by acute non-lymphocytic leukaemias (36) and by astrocytomas (22). The median time interval between primary and secondary malignancy is currently 5 8/12 years. The Standardized Incidence Ratio of developing an SMN up to age 30 compared to the risk of a primary malignancy is 15.7 (95%-confidence interval: 14.2 - 17.3). The cumulative risk of developing an SMN within 10 years after the primary neoplasm is 1.8%. This risk is expected to increase further along with the probability of survival.

Our epidemiological data on SMN are representative for the German population. Thus a current study of the GCCR, evaluating the effects of therapy and genetic factors on the risk of developing an SMN, will yield particularly relevant results.

The work was supported by the 'Competence Network Pediatric Oncology and Hematology' sponsored by the German Federal Ministry of Science and Education (funding number: 01GI9967/3).

### **Questions**

**C. Stiller:** Clearly one would not be surprised if the patterns changed with increasing follow-up, not least because the survivors will be entering the age range when most cancers occur anyway. Do you have any evidence that the pattern of second cancers has been changing between different time periods of diagnosis as treatment has changed?

**P. Kaatsch:** We think that the rates of solid tumours after the first malignancy are too low. We see that the solid tumours occur relatively late so that the patterns will move. What we do not see in Germany, because of lack of follow-up data, is the well-known combination of retinoblastoma followed by osteosarcoma.

**R. Sankila:** Your relative risk was very high compared to many other international studies. One of the reasons may be that once you follow up paediatric patients until they are up to 50 years old, you see a diluting effect of the rapidly increasing number of expected cases. With the very young population here, your expected number is very small and therefore every case will increase the risk proportionately very much.

**P. Kaatsch:** It may be that it is not so good only to have the expected number of cases based on two registries. I think we have a very complete long-term follow-up also in adulthood. The completeness is very high, so we have perhaps a higher relative risk compared to other series. I do not know how exact the number of expected cases is in Germany.

H. Møller: Even if we accept your guesstimate as close to the truth, it might be misleading to communicate what seems to be a twenty-fold increased risk. It would be much more useful to communicate the absolute risk or absolute increases in risk. I think they are much easier to absorb by our colleagues and by other members of the public.

P. Kaatsch: You are right, it is a question of the risk communication. We are looking for other parameters which we can communicate to people. When I show these data to the parents, they are very angry.

K. Freese: Does ACCIS include or exclude secondary cancers?

E. Šteliarová-Foucher: Normally we are collecting them, but for now we did not attempt to analyse them, because we think that this collection is not complete.

## **Presentation 7. ACTUAL PROBLEMS IN THE REGISTRATION OF CANCER IN CHILDHOOD - EXPERIENCES IN SLOVAKIA**

### **Abstract**

*Ivan PLESKO, National Cancer Registry of Slovakia, Bratislava, Slovak Republic*

Since the establishment of the National Cancer Registry in Slovakia in 1976, considerable effort has been directed toward the collection and completion of detailed data on malignant neoplasms in children aged 0 to 15 years. The first step in preparing a comprehensive list of malignancies in childhood in Slovakia comprised the collection and analysis of all available sources of information on cancer patients and deaths which occurred in this country from 1968. Histological confirmation of tumours in children was relatively high from the start of the registry. All the DCO cases - about 2.5% of cases - were detected or confirmed at necropsy, which was obligatory in children who died under the age of 15 years. In the last 10 years the quality of registration has gradually decreased, not only of children but also of adults. Autopsy rates showed a dramatic decrease and the obligatory autopsy of children is no more respected.

The introduction of the law on the protection of personal data in 2003 makes registration of cancer patients more and more difficult, particularly with respect to date of deaths, despite the fact that notification of cancer remained compulsory. The establishment of common and adequate rules applicable to all population-based registries in EU seems necessary. Even temporary breaks or restrictions in registration may have a negative impact on the registration of cancer patients including children.

### **Comments**

Childhood registration in Slovakia was good in the past, because from the 60s-80s all childhood cancers were concentrated in one hospital and from the middle of the 80s in three different hospitals. The childhood cancer incidence data were complete and we had almost 100% of cases microscopically confirmed. Autopsy was obligatory for all children dying before the age of 15. Currently, autopsy is not obligatory and from 100% in 1989 it decreased to 4% today. Also in adults autopsy in cancer patients was 50%, now it is only 2.7%. It has also become a big problem to have complete microscopical confirmation of cases.

What is a real problem is the protection of personal data. In eastern or central Europe there are now very strong data protection laws. The 'Guidelines for confidentiality in population-based registries' published two years ago by ENCR has been translated into Slovak. It is being used in the Ministry of Health and the Ministry of Interior, because mortality data are under the Ministry of Interior. However, it would be good to publish these guidelines once more, because some policy makers in public health say that these guidelines were published before Slovakia's membership in the European Union. For example, automated cancer registration according to this law is absolutely impossible.

## Questions

E. Šteliarová-Foucher: Thank you for bringing up this important problem, namely, that the new EU countries which had no laws for data confidentiality now are creating them based on the most stringent of those existing in Europe. Maybe we can get some help from the EC to improve access to data and improve cancer registration.

I. Plesko: For instance, in the Czech Republic, oncological registration is allowed by parliamentary law, but the law was presented to the Parliament by the President of the Republic. After 6 months it once again had to be confirmed in the Parliament. It was quite a long way to go to allow registration.

J. Norstein: I would like to comment on the situation in Norway. Data protection is very strict in Norway, in particular in the Cancer Registry of Norway. This is the reason why we do not have problems. The data protection is extreme by most standards and data are much more protected than in hospitals. It is very important that everyone knows that data in a cancer registry is more protected than in hospitals. For example, insurance companies can get permission from patients to get data from hospitals, but it is not possible from the cancer registry. It is specifically forbidden to give information to insurance companies, even if the patient agrees.

I. Plesko: All registry employees must make declaration. All visitors, even the electrician, must sign a document. Until now we did not have any problems with data protection. No information was allowed to leave the registry. But the new law may be so strict that cancer registration is no longer possible.

T. Aareleid: The situation in Estonia is similar and we are currently fighting to continue cancer registration. Our new data protection law does not require informed consent on cancer registration yet, but we are blocked from the other side, i.e., we cannot receive death data, because the statistical office cannot collect personal data any more at the moment. We have not received any data for two years already, which means that we have no completeness for incidence. We cannot link death certificates, trace them back, or follow up our patients. We have to withdraw from survival studies where we have been included (in EURO CARE for 12 years). It is a very big problem in Estonia, and in Latvia as well. Maybe EC or IARC or FECS can help us with a message to our governments.

D.M. Parkin: As you may know, a set of guidelines for confidentiality in Europe was produced two years ago. These have now been generalised to general international recommendations from the IACR and IARC. Maybe these can form a basis for an approach. Of course, these are rather specific to registries and the problem in Estonia is a more general one. If now even vital statistics departments are being forced to have informed consent, this is reaching heights of absurdity. Some years ago there was a plea signed by a number of eminent epidemiologists, including Sir Richard Doll, about the importance of databases for epidemiological research and the importance of such research to public health. Maybe it is timely to do something like that again.

K. Freese: In the past, the ENCR has developed very good advice to governments and to those who developed the EC data protection directive. In 1994 H. Storm was leading the ENCR Working Group on Confidentiality. It might be of interest if your governments could invite them as experts. They can also explain the possibilities of implementation of the European Data Protection Directive. The EU only checked for the community acquit, if the primary transposition of the data protection directive was correct, but they do not check, if all the secondary legislation coming up is in agreement with it. The best way might be support from ENCR in the future under this new contract, or by other means, some kind of consultation mechanism, particularly for the new member states or those member states which are lagging behind in dealing with this problem.

C. Martínez: This is not only a problem of Slovakia or Estonia, it is also a problem in Spain and in France. What I want to say is that this is still a problem for cancer registries.

D.M. Parkin: The European Directive is not a problem now. That battle was fought 5 or 6 years ago. In fact, the European Directive does not require informed consent for collecting patient data, if it is for



public health purposes. What has gone wrong is that it sets a minimum threshold and now several countries compete against each other to be more stringent than the other, to show that somehow they are more virtuous in protecting the public from being entered into databases. We explained very carefully to the EC and the Parliament why it is important for cancer registries to have access to named data. We were not simply interested in generating a lot of statistics, the issues were those we started the day with, the great value of being able to link together databases and expand the utility in that way.

## WORKSHOP ON AUTOMATED CANCER REGISTRATION

**Chairman:** Lorenzo Simonato, University of Padova, Italy.

**Invited speakers:** Chris Carrigan (National Cancer Action Team, UK); Richard Middleton (Northern Ireland Cancer Registry, UK); Wendy Scharber (Minnesota Cancer Surveillance System, USA)

**Communications:** Emanuele Crocetti (Tuscany Cancer Registry, Italy); Henrik Mulvad Hansen (Danish Cancer Registry); Ryszard Mezyk (Holycross Cancer Registry, Poland); Irene Schmidtman (Rheinland-Pfalz Cancer Registry, Germany); Sandro Tognazzo (Veneto Cancer Registry, Italy)

### Introduction

*Lorenzo SIMONATO, University of Padova, Italy*

Automated cancer registration could be defined as 'the process through which a proportion (variable depending on cancer registry and quality of source information) of incident cases are registered without any intervention by registry personnel'. Using electronic transfer from data sources does not mean that a registry is automated; the key aspect of automated registration is the process, not the data sources. The automated process should be considered as an alternative to the traditional cancer registration and very few registries (mainly in UK and Italy) are fully using such a process. The key question that registries will face from now onwards is "why should humans code and register incident cases which can be registered by a software?"

The Working Group on Automated Cancer Registration has been operating within the framework of ENCR. It is planned to hold a workshop in the summer of 2005, which will be a follow-up of the course on automated cancer registration in 2003. This time it will focus on some specific steps of the process, e.g. the problem of record linkage, how you prepare the data sources for cancer registration, etc. Even if very few registries are using the process, several are testing the methodology, and some are planning to move from manual to automated. If registries do not use the same algorithm or the same quality control, problems of comparability will occur. Therefore, there is an urgent need for comparability between registries.

### **Presentation 1. THE CANCER REGISTRATION DATASET AND MESSAGING PROJECT IN ENGLAND**

#### **Abstract**

*Chris CARRIGAN, National Coordinator for Cancer Registration, London, England*

#### Objectives

To produce, agree and implement a robust mechanism by which information can be recorded, transferred, linked, consolidated and aggregated for the purpose of cancer registration.

#### Methods

The National Health System (NHS) in England is on a pathway of the most significant investment in IT in its history. This will eventually (2010 and beyond) deliver integrated health records based on clinical events and messages.

The cancer registries in England are in the process of implementing or upgrading their internal processing systems to a multi-sourced, rules-based approach in readiness for the receipt of structured source data. Pilot projects ran across 2 cancer registries, 2 cancer networks and 6 large acute trusts to test and prove the extraction, production, transmission and subsequent usage of cancer "messages" within an overall XML schema for cancer. All existing clinical data sources were examined and utilised where possible to identify potential "gaps" in key data items, and to examine changes in process or technology which would fill these gaps.

## Results

Both pilots reported success in most areas. The availability of structured and coded pathology data was, as expected, low. However the design of the XML schema enabled the transfer of textual data which could then be retrospectively coded within the schema by the registry as required. The project results have been taken forward and have been submitted to the NHS Information Standards Board for approval as an operational standard. If this approval is gained, the NHS local providers of IT are contacted to implement this standard.

## Conclusions

The XML schema is fit for purpose. Electronic notification using cancer messages can be used to deliver data from healthcare providers. The registry rules-based systems can be used to produce cancer registrations from these source data, augmented by manual intervention.

## **Questions**

R. Sankila: How do you identify the patients?

C. Carrigan: By NHS number. The whole national programme forces the use of NHS number, it imposes it on the NHS. There is a government edict that says that every bit of information on health care that flows around the NHS has to use the NHS number. That will have to include the private providers as well.

G. Meledandri: Could you tell something more about the collaboration with the National Health Service Information Authority you mentioned?

C. Carrigan: The NHS Information Authority (NHSIA) is a national body that the NHS has established to make sure that information, governance and standards and best practice are adopted. What we could not do, was to impose data standards on people. That would not have been our job, so the registries was working with us. We defined what we needed and worked with them as they developed the standards, the schemes, the datasets, the definitions and the validation rules to be part of the whole NHS data dictionary.

J.W. Coebergh: Are private hospitals involved in this system?

C. Carrigan: Registries at the moment get varying levels of data from private hospitals. In some areas of the country it is very easy, in other areas it is very difficult, and the usual problem has been confidentiality. In this pilot, the private hospitals were not involved because most of them were not connected to the NHS net. What we have done is to design a project that will work with what we have got now, so if the private hospitals want to be involved they can. In the future we know they will be part of the whole national programme for IT and we are ready for when that actually happens. They were not involved in the pilot as it stands now. For the moment we take whatever information we can get from private hospitals.

J. Norstein: I am very impressed with what you have been doing in England, but I am a little confused, firstly about the legal basis of what you are doing and secondly when do patients lose their NHS ID number in this system and where are the records pseudonymised?

C. Carrigan: At the moment the registries are protected by law with a Health and Social Care Act. There is a section in there, which says that cancer registration can continue using identifiable data. So the feed of data within the pilot still used identifiable data, but with NHS number as well. We designed the messages so it could do both. When the NHS is ready to send an NHS number, they click the switch and send the NHS number within the message. If you have to rely on other information, then you can include the personal details as well. The pilot tested both, but did actually carry some personal data as well as the NHS number. In the longer term the NHS wants to move to pseudonymisation, but they have difficulties in defining how it is going to work, so it is not working at the moment. There are lots of good things about it, but there are moments when you have to use some level of identifiable data, for example postcode, for cluster analysis for instance. We are looking for other ways to take forward the legal situation in the country to give us the protection to do that.

## **Presentation 2. AUTOMATED CANCER REGISTRATION: RELIABILITY MEASUREMENTS**

### **Abstract**

*Richard J. MIDDLETON, Northern Ireland Cancer Registry, Belfast, UK*

#### Introduction

Automated cancer registration has been in operation in Europe since the early 1990's. It is now possible to make comparisons with the data obtained from registries which operate using automated cancer registration techniques with registries using more traditional methods.

#### Methods

Information on data quality indicators was extracted from "Cancer in Five Continents" from a number of cancer registries in the United Kingdom and Italy. However, the quality of cancer registry data can only really be assessed when it is used for specific projects and studies. With this in mind the results from survival analysis were looked at. Where possible survival rates for certain cancer sites were compared using data published from selected comparable studies.

#### Results

The data quality measures carried out in our own registry will be described and the implications for this on cancer registry resources. Comparisons between automated registries in both the UK and Italy show that in the area of data quality measurements, the automated registries perform at least as good, and sometimes better than traditional registries.

Recent pooled registry data from studies in Italy<sup>1</sup> and comparisons within the UK have been used to calculate survival of patients with cancer. The work in both countries show that the data from automated cancer registries are of a comparable quality with more traditional registries and can be used in survival estimates and other studies.

#### Conclusion

The quality of data from registries which use automation as part of their registration process can produce data of a high quality.

### **Questions**

**A. Znaor:** Can you tell us, or estimate from your experience, how much time it took to train the staff? Did you use any systematic procedure like a textbook, or were they just trained by working? Do you think it merits a textbook or guidelines? This is a situation which we will all meet sooner or later, we will have to train our data entry staff to become quality assurance staff.

**R. Middleton:** In Northern Ireland wherever you recruit – we have just recruited two quality assurance staff – you are really talking about a year at the absolute minimum to get people up to the standard you need to be happy to send them out on their own to work. We run a course ourselves which is based on the UKACR training course. We had to supplement it to our own needs and that is probably what everybody will have to do. Inevitably, there are some local variations in the way people present data and the way notes are handled etc., that will be unique to your own registry, but certainly there are training materials there. There is also the SEER training materials which we have used some parts of. The other thing I would like to see is that at some stage, somewhere along the line, there could be some kind of qualification that registry staff could avail themselves of, and there could be several levels of that, e.g., a data entry qualification, a quality assurance qualification, etc.

**D. Brewster:** How many source records does your computer process to end up with your 6,000 or 6,500 registrations? If you did not check the single source registrations, what would your incidence be?

**R. Middleton:** It is difficult for me to give you an answer, because certainly we found that our source records are increasing. The reason for that is that there has been a shift in the national health service, particularly in hospital discharge information, and we are getting a lot more of those than we used to.

There are on average three pieces of hospital discharge information for each registration; you would have at least one pathology information for 80% of them, plus a third of them will have a radiotherapy information. Certainly the move from having shorter spells in hospital results in having more hospital discharge information. If we did not look at our single sources, I would say roughly about 5% of them would be totally wrong, they would not be the right site, they would not be the correct behaviour, etc.

L. Simonato: Concerning the unique source - within this category you have very different types of records, of different quality. Have you been trying to explore this? You may have just the unique record, for which the risk of being unreliable is as high as for the others, while you can test the full consistency within the sources, because you may have five pathology records which are consistent with one diagnosis. This would make a difference in how to treat this problem.

R. Middleton: Some are better than others. We have experienced that lung cancer can be a difficult one, because you get patients who are discharged and it says 'lung cancer' and when you go and you look at the notes you find out that actually it was not lung cancer. They had a shadow on their lung and what went out on the discharge letter was 'possible lung cancer' and the clinical coder put that down as 'lung cancer'. But other ones would be actually quite reliable, multiple myeloma for example is not one that clinical coders mix up.

### **Presentation 3. AUTOMATED RECORD CONSOLIDATION EFFORTS IN THE UNITED STATES: NATIONAL PROJECTS AND A CASE STUDY**

#### **Abstract**

*Wendy SCHARBER, RHIT, CTR, Minneapolis, Minnesota, USA*

Central cancer registries in the United States and Canada have had ongoing activities in the area of automated tumor linkage and consolidation (record consolidation) since 1997. Information regarding current levels and methods of performing consolidation have been published as technical reports from the North American Association of Central Registries –NAACCR ([www.naacr.org](http://www.naacr.org)).

#### NAACCR Record Consolidation Report, 1999<sup>1</sup>:

Documented the principles and processes of record consolidation. A comparative test was performed by seven central registries on a file of 86 source records from 67 patients. It showed good agreement among the registries in counting the number of tumors, but had several limitations, including small sample size, the small number of primary sites involved and the need to perform patient linkage on the source record prior to performing tumor linkage and consolidation.

#### NAACCR Record Consolidation Report, 2000<sup>2</sup>:

Evaluated the feasibility of producing a test file of source records to measure the consistency and accuracy of determining the number of tumors, and determine the process for creating, testing and implementing it. The subcommittee determined that a test file was feasible and would produce meaningful results.

#### NAACCR Record Consolidation Report, 2003<sup>3</sup>:

Discussion and results of the creation of a diverse test file containing multiple source records on a large group of patients. The test file was "designed for use by member registries to test their record consolidation procedures, and to determine whether different registries are consolidating reports consistently in terms of tumor counts." Nine member registries and one fully automated system took part in the testing of the source file; results are included in the report.

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<sup>1</sup> Report of the Record Consolidation Committee to the Board of Directors of NAACCR, 1999.

<sup>2</sup> Report of the Record Consolidation Committee to the Board of Directors of NAACCR, Submitted March 1, 2000.

<sup>3</sup> Braun JE, Ross FE, Capron JE (eds). Creation of a Record Consolidation Test File: Report to the NAACCR Board. Springfield (IL): North American Association of Central Cancer Registries, December 2003.

NAACCR has three record consolidation projects in progress. The Record Consolidation Test Project Test is available on the NAACCR website. Its objectives are to measure the differences between registries and the gold standard in applying the SEER multiple primary rules; measure the difference between registries in counting tumors; evaluate the potential for developing standard, best practices algorithms and/or rules for performing tumor linkage; and to measure consistency in determining the consolidated values for five major data items (diagnosis date, site, laterality, histology, behavior). The website includes instructions for running the test, a simulated followback website, the test records, the expert panel answers, and tools to analyze a registry's performance.

NAACCR also has two best practices workgroups: Tumor *Linkage*: developing rules for automating the determination of number of primaries; and *Data Item Consolidation*: developing rules for choosing the best value for data items included in a consolidated record.

#### A Case Study in Automated Tumor Linkage and Consolidation: Minnesota Cancer Surveillance System

The Minnesota Cancer Surveillance System has had an automated record consolidation system in place since 1989. Its current software, MN-Patient and Tumor Resolution Algorithms (MN-PATRL) has been operational for 5 years. The lessons learned from developing, implementing, monitoring and upgrading this system have been translated into a new model for performing record consolidation and both the lessons learned and the new model will be presented.

### **Questions**

L. Simonato: There was a project to circulate a test file, to compare the test files between European registries and your registry.

W. Scharber: We did that with UK and Minnesota and we have the results. We could try it again with MN-PATRL and see how it works.

C. Carrigan: The test file we developed within the UK and within Europe was sent to America. The test results for the UK, European and Minnesota registries have been on our website for over a year. R. Middleton has also looked at the US test file.

H. Møller: What are the risks involved in running the system along the lines you do, i.e. how big is the problem when your programmer leaves? What would be the impact on your running of the organisation, despite your carefully documented system, if you lost the critical programme person tomorrow?

W. Scharber: It would be difficult. It would probably give us a delay, if we needed to correct something in the current system. It would probably take somebody about a month to get into the set of programme and figure out how it was set out and how it works. What we would lose is the ability of that person to fully test and upgrade. I would have to do the testing myself. Writing it in Perl would be a much bigger improvement, because we would eliminate all the computer entanglements that we have got ourselves into.

D. Forman: What is the federal or the NAACCR strategy in this? Is this very sophisticated wheel you have been developing going to be reinvented by other registries within the US or is the philosophy really to have one system as in the English model, which all the registries will then adopt?

W. Scharber: We are very independent in the US. We will all have our own systems and what we are hoping for is that we could stay with our system. That is part of the reason why we all started at different times. The newer registries have been able to chose from one of the older systems and that has helped some. What we are hoping for are the resources for the standard references, the standard rules that can be put into the computer system. The next version of our system will be built so it can run on PCs or on Unix and it will be totally outside whatever database environment that you have, so that you can connect in or not. Someone who will take our new system and put it into their system would need to write how the data are going to get to the program, and whether they are going to use the reference tables as a database lockup or pull them into the program. We decided we will pull them into the program, as it is so much faster, but it will be an option.

## **Presentation 4. COMPARISON BETWEEN MANUAL AND AUTOMATIC REGISTRATION. AN APPLICATION OF THE SITE SOFTWARE TO THE TUSCANY CANCER REGISTRY**

### **Abstract**

*Emanuele CROCETTI, Alessandra Benvenuti, Gianfranco Manneschi, Claudio Sacchetti, Eugenio Paci, Tuscany Cancer Registry, Florence, Italy*

#### Aim

A software ("Site") for the automatic definition of incident cases has been presented and distributed during the course on cancer automation held in Lyon (July 2003). The aim of the present study was to evaluate how many cases traditionally defined in the Tuscany Cancer Registry (RTT) as incident in 2001 would be attributed by the automatic "Site" procedure. The Site software defines only basic variables (date of incidence, site, morphology, base of diagnosis), we evaluated the possibility of harvesting further variables from the pathological reports by means of an automatic search of strings of text.

#### Methods

The Tuscany Cancer Registry is a traditional population-based cancer registry active in the provinces of Florence and Prato, central Italy (1,200,000 inhabitants) since 1985. Hospital discharge notes are available for all the public Italian hospitals on an electronic media since 1997, death certificates for all the residents in the Tuscany region since 1985 and, in more recent time, also the Pathologic Departments have moved towards electronic archives.

A backward procedure was carried out to the 2001 RTT incident cases to identify the related basic electronic sources of information. These sources were introduced into the Site procedure for the automatic definition of cases.

In addition, for 6291 cases (incidence 2001) with electronic pathology reports we compared the manual definition of several pathology variables with the corresponding ones from the automatic search of strings of text in the pathology report. The Cohen's kappa was computed to estimate the agreement out of chance.

#### Results

Among 9381 cancer patients (9496 cases) incident (malignant and non malignant) during 2001 according to the 'manual' RTT procedure, 9080 subjects were linked with at least one of the main electronic sources of information. The Site simulation created 5389 automatically defined cases (62.9%) and 3176 cases for manual solving (37.1%), moreover 781 not malignant cases, and 81 poorly documented skin cancers were excluded.

The observed concordance of automatic cases with the RTT traditional definition for behaviour (malignant/ non malignant) was 98.1% and for site (3 digit ICD9) was 84.9%.

As far as strings reading is concerned, the comparison between manual and automatic definition of pathologic variables showed very high values of Cohen's kappa, e.g. pT (96.2%), pN (98.7%), Gleason (96.2%), Clark (91.2%), grading (90.3%).

#### Conclusions

This preliminary test on the application of the "Site" software to the RTT case-series seems encouraging for a future possible use. This procedure defines a relevant part of the case-series although the concordance with traditional coding needs evaluation. The automatic search of strings of text in the pathologic report allows to collect a huge number of information.

### **Questions**

L. Simonato: It is interesting to see how, whatever method we use, there are always some historical problems. How to influence the pathologists not to miscode? Bladder cancer is one of the most long-

standing difficulties within the ENCR. There is an unwritten rule which is that we do some manual checking on most of the bladder cancer cases, because this is a problem that is difficult to deal with.

A. Znaor: Is the coding of strings manual or automated?

E. Crocetti: It is automated. You have to build up a 'situation' table. For example, if the medical record contains the word 'infiltrating', behaviour cannot be lower than 3, unless the medical record in fact says "NOT infiltrating", etc. Building up such a table involves a lot of manual work, but allows automation afterwards.

## **Presentation 5. THE DANISH PROGRESS WITH AUTOMATED CANCER CODING**

### **Abstract**

*Henrik MULVAD HANSEN, Danish Cancer Registry, Copenhagen, Denmark*

#### Preface

The Danish Cancer Registry is at the moment undergoing one of the most significant reconstructions in many years. In the constant effort to provide better and more accurate data, the update process of the Register has been accelerated. Furthermore the method for assembling the data and even more important the way of comparing the incoming data with the existing is changing from a purely manual process to a fully automated process.

#### More updated information

In the effort to provide useful data for researchers and the political decision makers, the Danish National Board of Health have taken initiative to shorten the lag from data is created until the information reaches the Danish Cancer Registry. In the past year many resources has been invested in this project and the result is, that the Danish National Board of Health shortly can publish preliminary data for the year 2003. As such the Danish Cancer Registry is now up to date. The updated information in the Danish Cancer Registry will, among many other purposes, be the foundation for the revision of the National Cancer Plan, which will be published ultimo November 2004. This significant result marks the end of the way of collecting and processing the Danish Cancer data, as we know it.

#### Modernising the Danish Cancer Registry

In order to comply with the demands for rapid updates of the Danish Health Registers, The Danish National Board of Health has the recent year been working on a large-scale modernisation project. One of the results of this project is that all health-related data from the secondary care level since January 2004 have been reported electronically directly to the Danish National Board of Health – including data to the Danish Cancer Registry. From January 2005 the same rules will apply for the primary care sector.

Simultaneously with the modernisation of the data-flow the processing of the incoming data has also been modified. Until 2004 all the incoming cancer-related data was treated manually by the Danish National Board of Health. From January 2004 the majority of the incoming data will be processed automatically untouched by human interference. This is made possible by converting all of the manual process into structured logical routines understandable by computers. This process has resulted in the "Danish Automated Cancer Logic" which is implemented as the backbone of the Danish Cancer Registry. The Cancer Logic is a clinical conversion of the manual rules for cancer coding and much emphasise has been laid on the continuity of the Danish Cancer Time-line.

The testing of the new workflow is estimated to begin in September and by the end of year 2004 the Danish Automated Cancer logic will be ready to go into production. The result is that the Danish Cancer Registry from now on will be updated in real-time and that the lag from data creation until the register is updated is minimised.



## Questions

C. Carrigan: Is your automated cancer logic published? Can we see it and, more importantly, can we try it? We have the tools to try it out now.

H. Mulvad Hansen: You can get the document and run your own data through it. I think that would be possible.

C. Carrigan: That is what we should do. We should test it out and give you a comparison of how it performs against how others perform.

K. Freese: With this decentralised coding, how did you ensure consistency among the different inputs and how do you manage the quality problems?

H. Mulvad Hansen: We rely on the decentralised coding in Denmark, and the doctors are used to putting the codes on the registration themselves back to 1997. There is a long tradition of coding, so we believe they are able to do this in the cancer area too. Of course we will run some quality studies. We are going to compare the incoming data with the actual medical journals from time to time. We are going to monitor if some cancer incidences are increasing rapidly. We will try to find out the reason why they are doing that, so we are going to follow the quality very closely.

J. Norstein: What do you do about stage in this system? Is it totally dependent on automatic coding as well?

H. Mulvad Hansen: Yes, stage is also a part of the automatic coding.

J. Norstein: Will that be TNM staging in all cases?

H. Mulvad Hansen: It will be TNM for the relevant cases and other staging where we cannot use TNM.

C. Carrigan: What has automatic cancer registration done to your staffing structure? Have you had to change the way people work?

H. Mulvad Hansen: We had to upgrade the people just sitting and feeding the data into the system earlier. I also think we have to recruit or upgrade, and maybe use another kind of staff in the quality control area.

R. Middleton: How much do you think this will improve the timeliness of Danish data? Do you think it will make it cheaper to run the cancer registry?

H. Mulvad Hansen: We hope to publish the 2004 data in early 2005. When it comes to costs, we do not know yet. It would be nice to save some money, but I am not sure we will.

J. Norstein: What is the budget?

H. Mulvad Hansen: I think the total budget for this project has been approximately 5 million Danish Kroner (~ 670 000 €).

## **Presentation 6. RELIABILITY OF RECORD LINKAGE WITH PSEUDONYMISED IDENTITY DATA**

### **Abstract**

*Irene SCHMIDTMANN, Krebsregister Rheinland-Pfalz, Mainz, Germany*

Data privacy concerns in Germany have led to cancer registration models involving the encryption of patient identity data. These models aim to reconcile high standards for data privacy and usability of data for scientific purposes.

The cancer registry in Rhineland-Palatinate consists of two units: the confidential office handles notifications and communicates with doctors. It performs encryption and forwards epidemiological data and encrypted identity data to the registration office. After completion of record linkage in the registration office the plain text data are deleted. The encryption scheme ensures that record linkage is feasible. However, re-identification is only possible after special permission and involves obtaining a secret key, which is stored outside the cancer registry.

During an extensive pilot phase we investigated the reliability of record linkage with pseudonymised identity data using several fairly large data sets. In our investigations we used automatic stochastic record linkage with varying cut off points. We found in these settings that record linkage errors below 1% are possible. We also demonstrated that homonym error rates increase with the size of the database if the number of items used in record linkage and the values they can have remain constant. However, taking additional medical and administrative information into account can balance this. We now have seven years experience with this scheme in routine work. We use semi-automatic stochastic record linkage in which all potential links are reviewed. In routine, about 10% of potential links require querying with the confidential office; approximately 1% of potential links needs to be checked with one of the notifying physicians.

In our experience, cancer registration with encrypted identity data is feasible. The scheme is accepted by data protection officials, doctors, and patients. However, it has to be borne in mind, that it entails extra-work and is therefore more costly. High quality data entry is necessary in order to ensure high data quality and correct record linkage.

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#### **No questions**

### **Presentation 7. AUTOMATED CANCER REGISTRATION - PILOT PROJECT FOR THE HOLYCROSS REGION IN POLAND**

#### **Abstract**

*Stanisław Gozdz, Ryszard MEZYK Holycross Cancer Registry, Kielce, Poland*

The Polish Ministry of Health requires physicians to report all cases of cancer to the regional registry using a standardised form. The information required is: name, national ID, address, date of birth, sex, social and professional category, site, TNM, morphological code, methods of treatment, date of diagnosis, date of death. Holycross Cancer Registry is one of the sixteen regional cancer registries in Poland. The registration process is carried out by hand and based on paper records delivered by mail.

The information provided at the ENCR training course on „Automated Cancer Registration” made us interested in automatic registration of cancer cases. The rapidly developing IT infrastructure in Kielce Province, and in Poland as a whole, opened new opportunities and possibilities of taking advantage of IT technology in medicine and cancer case registration.

Plans for automatisisation (using IT technology) of the cancer registration process have been worked out based on:

- on-going project “e-świątokrzyskie” concerning the creation of an information community of the Kielce Province;
- electronic reimbursement system in public health care in Poland;
- pressure for electronic data exchange from private health insurance funds;
- analysis and studies in data processing in the health care system.

It is planned in the pilot project that:

- each cancer case will be submitted electronically;
- HL7 standards will be used as the basis for definition of messages;
- advantage will be taken of experience in developed countries.

## **No questions**

### **Presentation 8. RELIABILITY OF AUTOMATIC CANCER CASES REGISTRATION MADE BY THE VENETIAN TUMOUR REGISTRY**

#### **Abstract**

*S. TOGNAZZO<sup>1</sup>, A. Andolfo<sup>1</sup>, A.R. Fiore<sup>1</sup>, A. Greco<sup>1</sup>, S. Guzzinati<sup>1</sup>, D. Monetti<sup>1</sup>, C.F. Stocco<sup>1</sup> and P. Zamboni<sup>2</sup>: <sup>1</sup>Registro Tumori del Veneto, Azienda Ospedaliera di Padova, Padua, Italy, <sup>2</sup>Dipartimento Scienze Oncologiche e Chirurgiche, Università di Padova, Padua, Italy*

#### Background

The registration system developed by the Venetian Tumour Registry is based on coded data extracted from computer files relating to hospital discharge (H), pathology records (P) and death certificates (DC). A procedure for automatic processing of diagnosis has been implemented, by which 55% of the total number of primary cancer registered (non melanotic skin cancer excluded) has been accepted without any manual decision. A reabstraction study was conducted to assess the reliability of the information produced in this way.

#### Methods

The study put a stratified sample of 1,539 automatically accepted cases (out of 25,477 incident in the 1990-94 period) through a double-blind manual revision. The universe of automatically accepted cases with a diagnosis of primary cancer (ICD IX 173 excluded) was partitioned in eight strata, characterised by different diagnostic evidence, under the rationale that different evidence brings about different probabilities of incorrect decision. The analysis of results was conducted using ordinary measures of association for contingency tables, logits and cumulative logits models.

#### Results

The proportions of "false positive" (i.e. not cancer) and prevalent subjects, with regard to the universe of "automatic" cases, were estimated to be 1.6% and 2%, respectively. A significantly higher proportion of prevalent cases were found among breast, prostate and larynx cancer cases without microscopic confirmation (8.5% against 1.1% for subjects with pathology record), while there is a clear strong inverse relationship between the number of concordant diagnostic sources and the proportions of discordant diagnoses: cases based only on a single cytology record are particularly unreliable. A small quota of unreported multiple cancers (0.9%) has been detected, too: most of them have not been registered because of one of the rules applied by the diagnosis evaluation routine.

#### Conclusion

The overall proportion of incorrect decisions is not high and similar to those reported by other registries, but errors are correlated to the diagnostic evidence pattern. The outlined results led to modify the automatic decision program. In particular, clinical cases for the three sites mentioned are now manually revised, in order to reduce the proportion of prevalent cases, as well are cytology-based diagnoses, so as to reduce the number of "false positives". Coverage of hospital discharge source has been extended in order to decrease the proportion of cases based only on pathology records.

## **No questions**

**Chairman:** Joakim Dillner (Malmö University Hospital, Sweden)

**Invited speakers:** Ulf Landegren (Rudbeck Laboratory, Sweden); Mads Melbye (Statens Serum Institut, Denmark); Kari Hemminki (DKFZ, Germany); Joakim Dillner (Malmö University Hospital, Sweden)

**Communications:** Ariana Znaor (Croatian National Cancer Registry); Marc Arbyn (Scientific Institute of Public Health, Belgium)

The Chairman introduced the workshop with an overview of the biobanking system in Sweden.

### **Presentation 1. MOLECULAR TOOLS FOR MOLECULAR MEDICINE: ANALYSING GENES, TRANSCRIPTS, AND PROTEIN**

#### **Abstract**

*Ulf LANDEGREN, Mats Nilsson, Johan Banér, Tom Conze, Fredrik Dahl, Olle Ericsson, Simon Fredriksson, Mats Gullberg, Sigrun Gustafsdottir, Jenny Göransson, Mathias Howell, Jonas Jarvius, Henrik Johansson, Masood Kamali, Chatarina Larsson, Jonas Melin, Edith Schallmeiner, Lena Spångberg, Johan Stenberg, Ola Söderberg  
Rudbeck Laboratory, Uppsala University, Sweden*

The availability of total genome sequence information provides the basis for a molecular perspective on medicine. Extensive molecular epidemiological analyses can now be considered as a means to select smaller numbers of molecules for development as diagnostic or therapeutic target molecules. However, such studies crucially depend on the availability of a combination of large, well-characterized patient sample collections, and on highly resolving, high-throughput molecular tools.

Our group has established a series of molecular procedures that allow detected DNA, RNA, or protein molecules to be represented as short strings of DNA, for highly specific analysis of large sets of molecules, in solution or *in situ*.

Padlock probes are linear oligonucleotide probes, that are converted to DNA circles when they recognize their target nucleic acid sequences. After amplification of the DNA circles, the products are identified, for example by hybridization to universal tag microarrays. In this manner tens of thousands of DNA sequence variants (SNPs) can be typed in a single reaction. Similar assays can be used for global measurements of gene or transcript copy numbers.

In proximity ligation, pairs of antibody reagents that can bind a target protein are equipped with DNA strands that are joined by ligation when the reagents have bound the same target protein molecule. The process effectively reverse translates target proteins into signature DNA molecules that can then be amplified to large numbers and identified for highly sensitive, precise protein detection in homogenous or solid-phase assays. The procedure is suitable for parallel analyses of very large sets of proteins, with read-out on tag-arrays. The method also provides unique opportunities to demonstrate interactions between pairs of target proteins.

Both reacted padlock and proximity probes can be amplified via rolling circle replication reactions. The method is ideal for precise amplification of large sets of reacted probes. The same mechanism also permits *in situ* detection of individual reacted padlock or proximity probes for detection of even single target molecules in cells and tissues.

Taken together these methods represent a toolbox that will permit extensive analyses of the molecular basis of disease by investigating biobanked samples using universal arrays for DNA, RNA and protein detection, and they will allow the functional involvement of molecules to be demonstrated *in situ*.

## Questions

R. Sankila: Most of the old samples are cancer blocks. Can you use them?

U. Landegren: We do not know yet. This is fairly recent and I imagine we will have about the same problems that one has with the regular antibodies *in situ*. If you talk about *in situ* detection of the protein, the difficulties will be similar but not necessarily worse, and possibly better, as we do not need as many proteins intact, having determinants that can be recognised. If you can use antibodies for *in situ* detection currently, we should be able to do it in this format. So far we have no experience of that. Everything has been done with frozen tissue sections and mostly with cells that are grown on slides.

K. Freese: I was very impressed by the elegant technologies you presented. Have the prices also gone down so that you could collect complementary data on population genetics for a fair price?

U. Landegren: The protein methods are relatively recent and not yet available commercially. In gene typing techniques worldwide there has been a tremendous drop in price and there is fierce competition. Part of the reason is that for association studies, there is the feeling we will probably need to look at some 100,000 markers or more per sample, so it is unthinkable to pay the previous prices. Prices are approaching the cent per genotype, but if you are going to look at that many samples, it is still a tremendous cost. I think we can expect further reduction in cost.

## **Presentation 2. MODERN INFECTIOUS DISEASE EPIDEMIOLOGY: EXPLOITING POPULATION-BASED CANCER REGISTRIES, VACCINATION REGISTRIES AND BIOBANKS**

### **Abstract**

*Mads MELBYE, Statens Serum Institut, Copenhagen, Denmark*

In a recent article in the American journal "Science", Danish epidemiological research was described under the title "When an entire country is a cohort". In contrast to most epidemiologists around the world Scandinavian researchers are fortunate to have enormous data materials at their disposal thanks to a long tradition of making registration of a wide variety of information on all residents. Linkage of the information recorded in the different registries is made possible by a person specific identification number given to all Danish residents. Examples of how research on our national registries is performed and used in combination with information from biobanks will be given. In particular, focus will be on the study of early life exposures, e.g. infections, and their association with chronic disease development. Another is on the long-term consequences of our vaccination policy. In recent years an increasing number of serious conditions have been hypothesized associated with childhood vaccination. Vaccine trials deal with short term consequences but prior to our studies few had been set up to specifically address the possible existence of long-term non-intended effects. Recently, the Danish parliament passed a legislation regarding the future use of the millions of biological specimens kept in biobanks in the hospital sector and elsewhere. The conditions set down will provide Danish researchers with unique future possibilities for research. These will also shortly be mentioned in the presentation

## Questions

K. Freese: What about the recent reports that hepatitis B vaccination might be linked to multiple sclerosis later in life.

M. Melbye: I would have liked to address that, but unfortunately we do not have hepatitis data in Denmark. We do not vaccinate against hepatitis.

J.W. Coebergh: Could you tell a bit more about this opt out registration? Does it mean that patients are informed somehow, and does it really work? Have you been able to include it in brochures in hospitals, etc.?

M. Melbye: This means heavy information, but this initiative just started one month ago. We have just developed all the brochures and all that is needed, but you have to inform the public. There will also be television programmes. It is much better than to have to ask for permission.

D. Forman: Can we clarify what we all understand by a 'biobank'. In the UK, 'biobank' has developed a very specific meaning, representing the 'biobank project', which is a large-scale epidemiological cohort, where blood samples will be banked from cohort members. It is an epidemiological study and there is a whole set of ethical issues around that. I take it from the Chairman's introduction and your presentation, that when you are talking about biobanks, you are talking about any biological material from any source that is laid down. I do not know if large scale cohort investigations, equivalent to the UK biobank project, are under way in either Denmark or Sweden. The question is, in those cohort studies, is it the same sort of ethical constraints you identified in terms of what I understood to be routine pathological material, whereby essentially as long as the project is approved by an ethics committee, the patient cannot exercise unless he or she earlier on opts out, they cannot then opt out of a specific research study. Is that the ethical paradigm in which you are operating?

M. Melbye: The problem is basically for all the patients in the hospital sector or somewhere in the healthcare system and they do not think of these specimens being used for research purposes. It is much easier to control and follow problems related to study participants, people who study a specific research project, whereas you heard yesterday another study where you actually got permission to use the various specimens for whatever purpose. This is not the case today, as we all know. So there may be problems with the old studies. The biggest collection of specimens we have in Denmark covers the entire population of Denmark born since 1978. Then we have the 100,000 cohort, but we have nothing like the UK biobank initiative, however, both we and the Swedes are thinking seriously about that.

### **Presentation 3. GENETIC EPIDEMIOLOGY OF CANCER EXPLOITING REGISTRIES**

#### **Abstract**

*Kari HEMMINKI, German Cancer Research Center (DKFZ), Heidelberg, Germany, and Department of Biosciences, Novum, Karolinska Institute, Huddinge, Sweden*

Reporting of cancer in relatives is unreliable particularly for internal cancers, which causes bias in the obtained familial risk estimates. The preferable way of obtaining information is to use medically verified data on complete families, which is feasible on population-based family datasets, such as those in Utah, and recently, in all the Nordic countries.

As to the Swedish example, Statistics Sweden created a family database, "Second Generation Register" in 1995 and it was later renamed to "Multigeneration Register", because it covers up to 5 generations. We have linked this register to the Swedish Cancer Registry (started in 1958) to make the Family-Cancer Database in several updated versions, most recently in year 2004. The number of cancers in the second generation increased from 20 000 in 1996 to 190 000 in 2002; in the parental generation the increase was from 500 000 to 700 000 first invasive cancers. Parents have been registered at the time of birth of the child. Thus it is possible to track "biological" parents in spite of divorce and remarriage. The national personal identification code (personnummer) has been deleted from the Database. This code is the key for the construction of families, and year 1947, introduction of the code in Sweden, is an important landmark for possibilities of linking family members. Those who were age 15 or younger in 1947 were registered with their parents; thus, year 1932 was the first year of recording of the second generation. The Database has been used in some 160 studies so far, and examples are taken on some recent analyses addressing the questions about environmental and heritable causation of cancer and the mode of inheritance of cancer. The availability of reliable data on familial risks on almost all types of cancer is a challenge to clinical counselling: some familial risks are very high and most cancers lack guidelines for clinical counselling and action level.

## Questions

R. Sankila: We usually see these elevated risks. Did you see any general pattern, where there would be a protective effect of a cancer pair, or healthy pair, or that a healthy sibling would be a protective effect?

K. Hemminki: No, we have only been comparing increased risks, so if there is a decreased risk we have not paid attention to that.

K. Freese: One slide listed all the different sites and some genes involved, like breast, but you did not mention Li-Fraumeni.

K. Hemminki: p53 was listed among breast cancer, but it is so rare that it does not really contribute anything.

## **Presentation 4. SHOULD CANCER REGISTRATION INCLUDE BIOBANK REGISTRATION? THE SWEDISH EXAMPLE**

### **Abstract**

*Joakim DILLNER, Lund University, Dept of Medical Microbiology, Malmö, Sweden*

The use of biobanks in research allows studies to be designed to produce more reliable results in a more efficient way. Biobanks allows large epidemiological studies to be performed in clearly defined populations in a relatively short time. Techniques commonly used in biobank based studies include molecular genetics, proteomics, seroepidemiology, and comparable genomics.

However, it must be realised that there are major bottlenecks and potential risks regarding biobank-based research. Design of sufficiently large studies very often involves collaboration of many biobanks in different countries. For the scientist wishing to design an important study, it is difficult to obtain a comprehensive overview over which types of studies that would actually be possible as information on the content and quality of different biobanks is not widely available. Furthermore, rules for obtaining access to samples are commonly unclear and highly variable between different countries and even between biobanks in a single country. The accessory information available may be incomplete and/or not quality controlled and not standardised between countries. Large-scale studies entail large logistic efforts in retrieval of samples, sample refinement (e.g. DNA extraction or sectioning of tissues) as well as in the actual testing of samples. Lastly, and most importantly, handling of the comprehensive, personally identifiable information from health data registries as well as handling of the possibly sensitive information that is contained in the biological samples entails substantial risks. There may be violation of the integrity of the individual if personally identifiable information is released or if substantial numbers of researchers have access to the information. Both comprehensive health data registries and comprehensive clinical biobanking systems are built on public trust. Since these systems are essential not only for research, but for the routine evaluation and continuous improvement of health care, decline in public confidence may result in damage on the health care system and thus on society. There has been an increasing awareness of this potential problem over the past few years, that has e.g. resulted in special biobank legislation in a number of EU countries.

To develop systems for biobank-based research that minimise the risks to the individuals and to society, while simultaneously improving quality and usefulness of biobanks and registries for cancer research is therefore important. The Southern Sweden Regional Biobank Registry is a part of the Regional Cancer Registry that has been assigned the task by the four county councils in Southern Sweden to register all biobank samples being stored (both in health care and research) in the catchment region (Southern Sweden).

The registry is registering all biobank samples stored, as well as their informed consent status. Individuals who wish to know exactly which samples have been stored and/or wish to change their informed consent can turn to the registry to change the consent status in all biobanks. Furthermore,

the registry is developing a secure format for maintaining the database and is providing service to researchers by building of study files, coding of samples and identities and maintaining codes.

## Questions

J.W. Coebergh: Are there any discussions on what type of research can be done with this secondary use material. We often say we do research, but what aims does the quality of care serve? Is what you do scientific? Maybe it is not research.

J. Dillner: Previously, when the type of quality development as part of clinical care was being carried out, it was not classified a research. It did not have ethical committee approval, but as of last year that type of clinical development also needs an ethical committee approval. That is a major change. When it comes to the standards for new consent, when you have a specific project, this is also up to the ethical committee to decide that the patient has said yes, you can store the sample, you can use it for research. That does not mean you can use it for anything. Each new project needs a new ethical committee approval and they may say that you need to write to everybody, including their descendants, if the patient is dead. They may also say that it is not necessary to obtain new informed consent because the issue is entirely non-controversial, or they can say that we need to advertise in the newspapers, and so on. In the instance where we do have already consent for clinical storage, at least we know that we have it and research has helped in dealing with the ethical committees.

J.W. Coebergh: I think it would be useful if the decisions that such ethical commissions take were also published in one form or another, because ad hoc commissions can have very different criteria.

J. Dillner: There are a lot of complaints that some of the commissions are more positive, some more scared of biobank research in different areas of Sweden. We are just starting to exchange typical cases, so we are working towards having a policy of what is considered typically controversial and non-controversial. It would be useful to have such studies even on a European level.

J. Norstein: I react to some statements to the great potential of breaches to integrity and confidentiality. I am a little reluctant to stress it too much, because we in the cancer registry in the Nordic countries have not had a single example of breaches of confidentiality. It is a very theoretical possibility. Another thing is the anonymisation of test results. That would mean that if you want to study the effect of the Epstein Barr virus, for example, you need to draw new controls from these very valuable specimens. Sooner or later you have nothing left of the specimen. I think it is an enormous resource they have got here and you should safeguard it as much as possible and especially not reanalyse, if you have done a reliable analysis on standard things like Epstein Barr virus antibodies already.

J. Dillner: The first thing is that a lot of people are worried about what information can be achieved from all these samples. We are not aware of a single case where all these biobank samples that are being stored have actually been misused. Still we have to talk to the public and the ethical committee and maximise the benefits and minimise the risks. As to the other issue – getting a new code if they get new specimens - of course a registry can decide to reveal to the investigators that the samples were the same, if they decide to do that. However, it is a matter of principle that different investigators should not be able to compare samples from different studies freely, because the accessory information may be combined and may make the study basis identifiable, in particular if you have a lot of accessory information.



## **Presentation 5. THE ROLE OF CANCER REGISTRIES IN CYTOGENETIC BIOMARKER RESEARCH**

### **Abstract**

*A. ZNAOR<sup>1</sup>, S. Bonassi<sup>2</sup>, M. Ceppi<sup>2</sup>, H. Norppa<sup>3</sup>, 1) Croatian National Cancer Registry; 2) National Cancer Institute Genova, Italy, 3) Finnish Institute of Occupational Health*

The frequency of chromosome aberrations (CA) in peripheral blood lymphocytes has been used since 1960s for biomonitoring of workers occupationally exposed to genotoxic agents. It was long assumed that genome damage could be associated with cancer development, but until the end of 1980s, there were no epidemiological studies to directly support this hypothesis, due to a lack of cohorts large enough for a reliable risk assessment. The first international effort to suggest that CA level is a cancer risk biomarker was based on a Nordic cohort in early 1990s, followed by a confirming Italian study. Nordic-Italian collaboration subsequently showed that CA predicts cancer independently of exposure to genotoxic agents.

While the CA assay only detects genome damage caused by clastogenic agents, the micronucleus assay, introduced in the 1970s, also reveals aneugenic effects. Early attempts to assess the cancer risk predictivity of micronuclei (MN) were compromised by small cohorts, short follow-up times, and variable methods to assess MN. The aim of the present study was to estimate cancer risk predictivity of MN in peripheral lymphocytes based on the cytokinesis-block method, which avoids the influence of cell proliferation on MN frequency. In scope of EC research programme "Cytogenetic biomarkers and human cancer risk" (QLK4-2000-00628), a cohort of 6587 subjects monitored for micronuclei in peripheral blood lymphocytes between years 1985 and 2000 has been assembled from nine countries. Follow-up for cancer incidence was performed through cancer registries or, where not available, national mortality registries. The preliminary results show a borderline significant increase of cancer risk by 30% for subjects in the highest tertile of the frequency of micronucleated lymphocytes when compared with those in the lowest tertile. Due to the formation of large databases of cytogenetic data and the possibility of their linkage with cancer registry databases, a new role of cancer registries in assessment of cancer risk predictivity of cytogenetic biomarkers has emerged. The results of cytogenetic biomarker studies should be implemented for creating policies to protect populations exposed to environmental and occupational genotoxic agents.

### **Questions**

**J. Dillner:** Is it possible to measure cytogenetic markers in stored samples, like in a biobank for example?

**A. Znaor:** Yes, they could be measured in samples, but there are more sophisticated methods to measure genome damage. The great advantage of studying chromosome aberrations and micronuclei is precisely because these methods are quite old, so we have test results from the 80s, 70s, 60s, that can yield enough person years for validation of markers in terms of cancer risk. Because although there was an hypothesis, which was the most biologically plausible, in fact the hypothesis was not, the markers could not be validated until sufficient follow-up had been done. It happened in practice that chromosome aberrations that were used for 30 years as biomarkers of exposure were actually proven to be biomarkers of cancer risk.

## **Presentation 6. A NEW NATIONWIDE CANCER REGISTRATION SYSTEM IN BELGIUM: PILOT TESTING OF GENERATION OF ANONYMISED LINKAGE TO BIOSPECIMENS**

### **Abstract**

*Marc ARBYN, Scientific Institute of Public Health, Brussels, Belgium*

It is planned that, in 2005, a new nation-wide cancer registration system will be started up in Belgium. Data collection from newly diagnosed cancers will be managed by a registration network set up by the health insurance agencies, which will be fed by two pathways. A first clinical pathway will canalise data from all patients receiving a *multi-disciplinary oncologic consult* (MOC); a second pathway will drive information from cyto-pathological and haematological laboratories pertaining to cyto-pathological diagnoses related to cancer. A legislative basis is being established for making these registrations mandatory. The unique national register number will be used for patient identification and data-linkage. After control of data-quality and ID-anonymisation, cancer data will be transmitted to the Scientific Institute of Public Health in Brussels for statistical analysis, epidemiological interpretation and reporting. An additional step will be the pilot testing of a *Biobank Information Management System*, developed in collaboration with the Southern Sweden Cancer Registry, in the framework of a joint EU sixth framework project. The aim is to establish an anonymous link between the bio-samples in the laboratories and the cancer register allowing and facilitating further research, assuring the integrity of the patient concerned and in full respect of ethical and scientific rules.

### **Questions**

K. Freese: I would like to ask a slightly provocative question and do not express any view of the European Commission. One could look at the specimen or biobank sample as an extension of the old cardboard that we used to keep to record the patient data. The patient record is just extended with some material, blood or tissue or whatever. Only if you apply a test to this kind of sample, does it become meaningful and generates data that are then recorded, either in written form on the cardboard or in the computer stored as an electronic record. If a biological sample would just be an extension of the information file of the personal record, then it is subject to the European Data Protection Directive and the national transposition into national law, and again, derogation as per article 8.3 on the need for informed consent would apply. You do not have to ask for informed consent to generate this data, if you make sure everything is kept under medical secret and it is only for medical research or public health purposes or for medical care directly serving the patient. Probably it would simplify the matter and, on the other hand, it would be subject to harmonising legislation, not minimal standards. That would mean that co-operation in the European networks would be very much facilitated.

J. Dillner: The work we are doing, we are more or less obliged to by law and, personally, I think that the approach that was taken by Denmark on classifying the biobanks as registries really solves many problems. It would be very interesting to see the outcome of their experience. I think sooner or later we will have legislation in a lot of countries, perhaps even at the European Union level. We have experience on active informed consent for collecting samples even in the clinic and we have data on what it costs, the total amount of informed consent, etc. There are rumours that we will be turning to more opt out like registration like you have in the near future. When we look at the costs and logistics involved, it appears that the legislative bodies are less enthusiastic about individual informed consent for this.

J.W. Coebergh: I think it is extremely important that studies are being done to show how big the burden is of the legislation and in many countries there is also political pressure to reduce the pressure of regulation in general.

K. Freese: From my point of view it is clear that the use of the data, the non-medical, non-public health use of the data, is the real issue for regulation. Instead of stop-gapping the creation of the data, or breaking it, or slowing it down by this kind of process, I think it is much more important - and I have learned that it already exists in Sweden - to have a regulation for the use of data and in particular genetic data. In Germany, there is a legislation on its way to the Parliament where such

issues are taken up and probably, if the use of the data is really tightly regulated, there is hope that all dealings with data and creation of databases will become easier in the future.

J. Dillner: It is unlikely that a European standard will be established with active individual informed consent the way we are doing. I still think it is a very big advantage with the overview of the samples and to register them as approved public bodies for overview of the type we are doing. In Denmark they are also doing this with all the pathology samples in one registry at the National Board of Health and Welfare. This is a very important process that I think we should try and speed up. There has not been any misuses so far, but we should prevent them from ever happening.

D. Forman: Tactically, I think the suggestion of K. Freese is something that we should avoid at all costs, certainly in the context of the UK. At the moment in the UK, and I suspect in other countries as well, we are trying to make a very clear border between registry information, the medical record and biological information as collected through pathology specimens or blood samples. There is no doubt that there is going to be extraordinarily strict parliamentary legislation relating to tissue samples and genetic testing of blood samples coming into force, and we are doing all we can to distance ourselves in the registration community from that legislative drive. There are those within the privacy lobby that say that any information about an individual should be treated to the same confidentiality and privacy constraints as DNA from that individual, or a pathology specimen from that individual. Our tactic is that in terms of the registration information we obtain, we must obtain that without informed consent, because of our absolute obligation for public health monitoring and surveillance, and if we were to try and blur the distinction between that and genetic information and pathology information, certainly in the UK it would be the end of cancer registration.

## POSTER PRESENTATIONS

### **Abstract 1. SENTINEL NODE BIOPSY INCREASES DETECTION OF POSITIVE LYMPH NODES**

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**Objective:** Every year, approximately 11,000 women are diagnosed with invasive breast cancer in the Netherlands. Standard treatment for patients with early breast cancer formerly consisted of local tumour resection, followed by axillary lymph node dissection (ALND). Based on the presence or absence of tumour tissue in the axillary nodes, patient groups are selected for adjuvant therapy. The sentinel node biopsy (SNB) replaces the ALND in lymphatic staging. The aim of this study is to investigate whether the introduction of SNB leads to a shift in staging of breast cancer, due to the more thorough examination of lymph nodes.

**Methods:** We retrospectively retrieved all breast cancer patients from the Regional Cancer Registry Middle Netherlands over the period 1997-2002. All patients with primary mamma carcinoma stage T1-3 were included. Patients with clinically diagnosed metastasis in regional lymph nodes or distant metastasis were excluded, as well as patients without surgical treatment. We compared the proportion of patients with positive nodes treated with or without SNB.

**Results:** 3825 patients were selected from the Regional Cancer registry. Most patients had relatively small tumours (70% stage T1, 28% stage T2, 2% stage T3). The data show the gradual introduction of the SNB; in 1997 no SNB's were performed, whereas in 2002 70% underwent a SNB. The percentage of node positive patients varied from 31.1% (95%CI 29.4-32.8) in patients with only ALND and 40.8% (95%CI 37.7-43.9) in patients with SNB. The proportion of micro metastasis in these groups was 4.3% (95%CI 3.0-5.6) and 20.2% (95%CI 16.2-24.2) respectively.

**Conclusion:** Data from the Regional Cancer Registry Middle Netherlands confirm that the introduction of SNB has led to a higher detection rate of positive lymph nodes.

### **Abstract 2. MORBIDITY AND MORTALITY OF PATIENTS WITH PANCREAS TUMOURS IN THE REGION STEDENDRIEHOEK**

*S. SIESLING<sup>1</sup>, S. Koopa<sup>2</sup>, .E.J. Hesselink<sup>3</sup>, .J.M. Smit<sup>4</sup>, M. van der Aa<sup>1</sup>, F. ter Borg<sup>5</sup>, M. Eeftinck Schattenkerk<sup>2</sup>, E.H. Eddes<sup>2</sup>*

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Diagnosis and treatment of pancreas tumours by means of a Whipple procedure have an accepted morbidity of 40% and a mortality of 3%. It is shown that these percentages can only be achieved by large hospitals.

The aim of this study was to reveal whether it is possible to achieve a mortality and morbidity, comparable with the large volume centres, by centralisation within the region of the Stedendriehoek. The Stedendriehoek is a region with 430.000 inhabitants. The cities Apeldoorn, Zutphen and Deventer have their own hospital. The study period was from 1 May 2001 to 1 May 2002. All patients who had the diagnosis pancreas tumour in one of the three hospitals were included and followed until 1

January 2004.

All patients were referred to the same two surgeons, who performed the PPPD and had the responsibility for the readjustment. The data collection and the analysis were carried out by the Comprehensive Cancer Centre (CCCST).

During the study period 55 patients (M:F=33:22) were diagnosed with a pancreas tumour. Mean age at onset was 70 years (44-92 years). The tumours were localized as follows: Ampulla of Vater (n=6), body (n=4), head (n=29), overlapping (n=3), tail (n=8), extrahepatic bile ducts (n=3) and not otherwise specified (n=2). 41 patients had contra-indications for a Whipple procedure (15 had distant metastasis, 21 vascular encasement, 5 other reasons). These patients were treated with chemotherapy, a stent and pain treatment. A Whipple procedure was performed in 14 patients. During the surgery distant metastasis were found in 9 of these patients. In only 5 patients the Whipple procedure was curative. In one of these patients an intra-abdominal abscess was developed, which was drained (morbidity 20%). None of the patients died caused by the Whipple procedure (mortality 0%). The median survival after the curative Whipple procedure was 12.8 months (95% CI 6.8-18.8).

Centralisation within one region can achieve the general accepted mortality and morbidity of a treatment of rare diseases. Results of treatment of the pancreas (and other rare cancers) should be evaluated regularly.

### **Abstract 3. CERVICAL CANCER: SCREENING PROGRAMME VERSUS "MEDICAL INDICATION"**

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Since several years a national screening programme for cervical cancer has been implemented in the Netherlands. The goal of this screening programme is early detection of premalignancies of invasive cervical cancer by women aged 30 to 60 years. The problem is that also invasive tumours are being detected. The aim of this study was to determine differences between invasive tumours detected by means of the screening programme (SP) and detection based on medical indication (MI) in the region of the Comprehensive Cancer Centre Stedendriehoek Twente (CCCST).

In the period 1992 to 2001, women aged 30 to 60 years with invasive cervical tumours were selected from the regional cancer registry of the CCCST. Way of detection was registered besides the standard collected data. Postal code was taken to determine the kind of neighbourhood and urbanisation (source: RIVM). Tumours diagnosed in the period between 1992 and 1998 had a minimal follow-up time of 5 years.

287 invasive cervical tumours were diagnosed in the region of the CCCST in the period 1992-2001. 106 women (37%) were diagnosed by means of the screening programme and 181 women (63%) were diagnosed based on medical indication. The SP tumours were diagnosed in lower stages than the MI tumours; 75% (66-83 95% CI) versus 50% (43-58 95% CI) stage I tumours. For MI tumours the histological differentiation was described more often; 66% (60-74 95% CI) versus 43% (34-53 95% CI) in the SP group. In comparison with normal neighbourhoods, deprived neighbourhoods had less tumours detected by SP; 27% (4-49 95% CI) versus 38% (32-43 95% CI). SP tumours had a significant better prognosis than MI tumours (HR 2,7, 1,4-5,5 95% CI, p=0,004).

SP tumours have more favourable characteristics than MI tumours and therefore a better prognosis. Future research should find out whether there are more differences, for example in KOPAC and PAP scores of the smears and treatment.

#### **Abstract 4. INCIDENCE AND SURVIVAL OF CHILDREN WITH SOLID TUMOURS IN SPAIN, 1990-1999**

R. PERIS-BONET<sup>1,2,3</sup>, P. García-Miguel<sup>2,3</sup>, J. Sánchez de Toledo<sup>2,3</sup>, O. Cruz<sup>2,3</sup>, A. Navajas<sup>2,3</sup>, C. Calvo<sup>3</sup>, L. Sierrasesumaga<sup>3</sup>, N. Pardo<sup>3</sup>, F.J. Molina<sup>3</sup>, F. Guerrero<sup>3</sup>, M. Guibelalde<sup>3</sup>, J.M. Indiano<sup>3</sup>, M. Melo<sup>3</sup>, G. Javier<sup>3</sup>, J.L. Fuster<sup>3</sup>, B. Giner<sup>1,2</sup>.

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<sup>3</sup> Spanish Society of Paediatric Oncology

#### **Objectives**

To document the incidence and survival of solid tumours in Spain during 1990-1999 in children resident in the areas where the National Childhood Cancer Registry shows population-based coverage.

#### **Background**

Incidence of childhood cancer in Spain is 143 cases per 10<sup>6</sup> children aged 0-14 years (world-age standardized rate (ASR)). Cancer is the first cause of death in children, excluding infants. Solid tumours are 58% and the cause of 70% of cancer deaths in Spanish children. In 1980 the Spanish Society of Paediatric Oncology promoted the National Childhood Cancer Registry to evaluate the progresses of care in terms of survival and to contribute to childhood cancer epidemiology.

#### **Patients and methods**

**Setting:** The study included five Autonomous Communities (Aragon, Balear Islands, Basque Country, Catalonia and Navarra) and 24% of Spanish children. **Period:** 1990-1999. **Subjects:** Solid tumours were defined as groups III to XI of the *ICCC-1996*. In total, 1226 children were included. **Completeness of registration.-** Ratio of observed-to-expected cases. **Incidence:** Incidence rates were calculated as the average annual number of cases per million person years. World standard population was used for standardization. **Survival:** 5-year survival estimated by the Kaplan-Meier's method for cohorts diagnosed during 1990-98, 1990-92; 1993-95 and 1996-98. Follow-up was active. **Source of data:** National Childhood Tumour Registry.

#### **Results**

**Completeness:** Ratio of observed-to-expected cases was 1.03 (95% CI: 0.99-1.07). **%MV** was > 90% except for CNS (82%), hepatic (84%) and retinoblastoma (62%). **Incidence:** Main groups were tumours of CNS (ASR=31.2), of sympathetic nervous system (14.3), kidney (8.2), bone (8.5) and soft tissues (9.6). ASR for hepatic tumours was 1.3. For retinoblastoma, germ cell and epithelial tumours was between 3 and 4. **Survival:** 5-year follow-up was 94%. Survival for tumours of CNS was 67%; for sympathetic tumours: 69%; retinoblastoma: 98%; kidney: 88%; hepatic: 49%; bone; 64%; soft tissues: 69%; germ cells: 85%; carcinomas and epithelial neoplasms: 84%. In CNS, the highest survival was for astrocytoma, overall survival rise from 69% until 76% and for PNET increased from 47% until 64%. Survival for sympathetic tumours improved from 66% to 76%; in kidney from 82% to 93%; and for carcinomas and epithelial neoplasms, from 76% to 92%. No increases were observed for other groups.

#### **Discussion**

Completeness of registration is estimated to be close to 100%. Our population-based survival results refer to 24% of the Spanish childhood population and are the expression of the care in the paediatric oncology units relevant for the geographical area. These results are within the upper half of the range observed in western European countries (EUROCARE, 1990-94) and similar to those in the SEER program (1985-99).

## **Abstract 5. WEB-BASED SPANISH CHILDHOOD CANCER REGISTRY (RNTI-SEOP)**

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### **The Registry**

In 1980 the Spanish Society of Paediatric Oncology (SEOP) promoted the RNTI-SEOP to evaluate the progresses of care in terms of survival and to contribute to childhood cancer epidemiology. The RNTI-SEOP is based in a network of all the hospital paediatric oncology units of Spain, on a voluntary basis. It includes 41 units, which do notification and active follow-up under the supervision of a paediatric oncologist responsible to the registry. All cases of childhood cancer (behaviour code, 3) and of any behaviour for CNS are registered. IARC/IARC recommendations, including rules for multiple tumours, are followed.

The RNTI-SEOP was conceived as hospital-based. Presently, it is also population-based for some geographical areas. While current average completeness for Spain is 85%, since 1990, five Autonomous Communities (Aragon, Balear Islands, Basque Country, Catalonia and Navarra) show a ratio of observed-to-expected cases statistically  $\geq 1$ . These areas are believed to be in practice population-based and include 24% of Spanish children.

**Cases registered:** 14,853 (May 2004). **MV:** 92%. **5-year follow-up:** 96% (cases diagnosed until 1997). **Incidence:** ASR (0-14 years, in population-based areas): 145 per million. **5-year survival:** 73%.

### **Web-based system**

The system allows notification of new cases, follow-up and death, as well as updating by means of appropriate forms and interaction with the registry's web with a standard browser. Each paediatric oncologist may consult own patients and data only. With this restriction, retrieval and counts may be made by each user. New cases or updates are checked centrally before going into the data base. Access to the system requires authentication by means of a personal user name and password only known by each individually authorised paediatric oncologist. User names and passwords are produced centrally. The list of authorised users is kept and updated in accordance with the oncologists responsible to the registry.

The central system is composed of two servers with operative system UNIX. Both, are at the Computing Department of the University of Valencia, under the protection of a firewall. The SQL database for the registry is sited in one of the servers. The web programme, made in PHP language is in the other server. Thus no direct access from internet is possible to the server where the registry data base is. Protection against possible data losses is achieved by means of a RAID1 (Redundant Arrays of Inexpensive Disks) in each of the servers, as well as systematic backups that include a daily incremental backup and a weekly full backup. The communications between the users and the server are encrypted in 128 bits under SSL protocol.

## **Abstract 6. QUALITY OF DATA ON MORPHOLOGY CODES FROM PATHOLOGY REPORTS IN MURCIA, SPAIN**

*Dolores CHIRLAQUE LÓPEZ, Murcia Cancer Registry, Murcia, Spain*

### **Introduction**

The automation of cancer registration allows to obtain a high benefit of the codified information and reduce manual time to complete cancer cases. As a previous step to an automatic process is necessary to know the validity of codified and stored information in magnetic support because the automatic process does not have to decrease the quality of data, quite the opposite, it will have to improve.

### **Objective**

To measure the agreement in morphology codes of malignant neoplasms between pathological reports and those registered at the population-based cancer registry.

### **Methods**

The information of pathological reports comes from the Pathological Department of the main hospital in Murcia Region, south-east Spain, whereas incident tumours have been obtained from Murcia Cancer Registry. Both have been selected from year 1998. The pathological reports included in the study have been those with morphology codes malignant primary site (5<sup>th</sup> digit /3), in one or several reports but with the same morphology codes. Reports that show more than one morphology code of different invasive tumour (except 8000/3) have been excluded.

We analyse the agreement in SNOMED (Systematized Nomenclature of Medicine) morphology codes at first three digits level that for neoplasms range from 8000 to 9989. Agreement has been measured for all morphological groups and by specific morphological groups (epithelial, squamous cell and basall cell neoplasms (801-811), transitional cell papillomas and carcinomas (812-813), adenocarcinomas (814-855), complex epithelial and specialised gonadal neoplasms (856-867), paragangliomas and glomus tumours, nevi and melanomas (868-879), soft tissue tumours and sarcomas (880-958), lymphomas and leukaemias (959-998)) by means of the Kappa index and a 95% confidence interval.

### **Results**

1405 incident cases have been included in the analysis. The percentage in overall agreement between the two sources of information has been 78.7%, Kappa index 0.75 (IC 0.73-0.77). By morphology groups, epithelial, squamous cell and basall cell neoplasms (801-811), which represents 51% of total cases, show the highest agreement (Kappa index 0.87 (CI 0.81-0.92), whereas lymphomas and leukemias, which represents 3% of total of cases, offer the lowest agreement with a percentage of 25%, Kappa 0.20 (CI 0.14-0.27). The lack of agreement normally takes place within next morphology groups.

**Conclusions:** A high overall agreement is observed. For some morphology groups the future automated process could be implemented maintaining the current quality indicators in the cancer registry. Other groups will require a manual examination before being stored.



## ENCR GENERAL MEETING

**Opening:** Karl Freese (EC)

**Chairman:** David Brewster (Scottish Cancer Registry, UK)

**Speakers:** Max Parkin (IARC); Eva Šteliarová-Foucher (IARC); Freddie Bray (IARC); Henrik Møller (Thames Cancer Registry, UK); Jan-Willem Coebergh (Eindhoven Cancer Registry, The Netherlands); Marc Arbyn (Scientific Institute of Public Health, Belgium); Larry von Karsa (EBCN, Germany)

### **Presentation 1. ENCR – 15 YEARS' SERVICE TO AND BY EUROPEAN CANCER REGISTRIES**

*Max PARKIN, International Agency for Research on Cancer, Lyon, France*

ENCR was established in 1989 within the 'Europe Against Cancer' Programme and has been funded for 15 years by the European Commission, first DGV (1989-1999), then SANCO (1999-2004). The original aim of ENCR was to provide information on the burden of cancer in Europe, the patterns of cancer incidence and mortality and on the variation of these patterns within and between EU member states, with the objective to improve planning of cancer prevention and treatment services in the EU.

ENCR is a joint effort of the International Association of Cancer Registries, the International Agency for Research on Cancer, the Group for Epidemiology and Cancer Registration in the Latin Language Speaking Countries (GRELL) and the Association of Nordic Cancer Registries. The Steering Committee is composed of representatives of these four associations, and three members elected by the ENCR member registries. Today ENCR has 175 member registries in 42 European countries, of which 144 are in the 25 EU countries. The number of members has doubled since the ENCR was initiated.

The major ENCR activities are (1) harmonisation of cancer registry data (Working Groups); (2) consultancies and structured reviews; (3) courses; (4) registry surveys; (5) workshops and symposia; (6) dissemination of information; (7) databases; (8) publications.

ENCR is not only a service to the cancer registries, but an important service to Europe, providing data on the burden of cancer to facilitate monitoring of the cancer problem in Europe; the EUCAN data are incorporated in the EU databases (EUPHIN-HIEMS); statistical data on cancer incidence, mortality, prevalence, survival, time trends and projections are available on internet; data are available to health administrators, medical profession, politicians and the public. The project has been running for 15 years thanks to the European cancer registries (providing data, collaborating, participating), the European Commission and IARC (funding, disseminating), the Steering Committee (guiding, planning, co-ordinating, supporting) and the Secretariat at IARC.

### **Presentation 2. EUNICE**

*Max PARKIN, International Agency for Research on Cancer, Lyon, France*

In April 2004 an application for funding of an "EU Network for Information on Cancer" (EUNICE) was submitted to the European Commission. The project builds on the achievements of former projects supported under the Europe Against Cancer Programme, e.g. ENCR and the screening networks. It continues the work of ECHI and EUROCHIP to complete agreed and relevant indicators, analysing and interpreting these indicators and making them widely available.

EUNICE is based on the work of 120 population-based cancer registries and the results of the following European projects: ENCR, EUROCARE, ACCIS, CaMon, EBCN, ECCSN, OEI, EUROCHIP and ECHI. The partners have experience in data collection, quality control and interpretation of data on cancer: International Agency for Research on Cancer (Lyon, France), Centre for Cancer Epidemiology and Prevention (Torino, Italy), Scientific Institute of Public Health (Brussels, Belgium), Cancer Society of Finland (Helsinki, Finland), Karolinska Institutet (Stockholm, Sweden), International Atomic Energy

Agency (Vienna, Austria), and the German Institute for Ageing, Heidelberg, Germany). The benefits to the European Public Health Programme are: European cancer database, standard methodologies, quality and comparability, involvement of the new member states, monitoring and planning.

EUNICE will be a sort of portal compiling and analysing health indicators for cancer, on the burden of cancer, a bit like ENCR was doing, but expanding its activities into areas other than the traditional indicators of incidence and mortality. EUNICE is a collaborative project involving 7 institutes, but ENCR is still the heart of the application.

## **Comments**

The question was raised whether we could somehow influence the people preparing the work programmes or those who distribute the EU funds. It was felt that it would also be useful to the EU system if, when the call for proposals are being prepared, those concerned would have an input. This could only be done by asking the government in each member state to instruct their delegate to the programme committee or working groups which can deliver input from a majority of countries. As ENCR is a network covering all of Europe, it should be possible at least to get some clarifications before the programme is finalised. The Commission has to balance many different priorities listed in the Public Health Programme and the legal decision about the budget of the programme also has to be taken into account. The problem in 2003 was that cancer was no longer a priority. There are two possible reasons for that: (1) there was a lot of jealousy because cancer got its own programme in the old Public Health Programme - "Europe against Cancer", whereas other diseases did not; (2) there is a cyclical wave in all organisations moving from disease orientation to integrated horizontal programmes.

## **Presentation 3. EUROPEAN CANCER OBSERVATORY**

*E. Šteliarová-Foucher, International Agency for Research on Cancer, Lyon*

An application for funding of a European Cancer Observatory was sent to Canceropole Rhone-Alpes, a new French regional cancer research programme. This project builds on several successful international projects: ENCR, CaMon and ACCIS and also includes automated cancer registration and CanReg. The objectives are to: expand existing databases on cancer in Europe, promote standard registration methodology, analyse and interpret collected data (geographical differences, time trends and predictions of incidence, mortality, survival, prevalence), disseminate data collected and knowledge (training courses, software development, publications, internet resources, collaborative projects, evaluation of data and impact on public health politics). The specific tasks cover: organisation of training courses (cancer registration, statistical, automated cancer registration, EUROCIM, CanReg), consultancy/audits, working groups (standards, childhood, predictions, survival, time trends, automated cancer registration, CanReg), updating of databases (EUROCIM, ACCIS, survival), development of software (EUROCAN, childhood), analysis and interpretation.

## **Comments**

Some participants were surprised that this application had been prepared without any information to the cancer registries and felt that there could be a risk that cancer registries do not want to participate in the project. Unfortunately, the possibility of applying to Canceropole Rhone-Alpes for a project which would cover ENCR activities came up rather unexpectedly and had to be submitted within a very short time, hence no consultation with the Steering Committee or the cancer registries was possible in advance. While it was agreed that IARC should react when opportunities for funding occur, it was stressed that the network of cancer registries must be informed as they are the fundamental audience for these activities and providers of the data.

## **Presentation 4. CAMON**

*Freddie Bray, International Agency for Research on Cancer, Lyon*

The CaMon (Comprehensive Cancer Monitoring in Europe) was a 2-year project supported by the Health Monitoring Programme (Health and Consumer Protection Directorate-General) of the European Commission (EC). When the "Europe Against Cancer" programme came to an end, some of the activities related to the output of ENCR were put into the CaMon project, essentially to monitor the incidence and mortality in the European Union (EU) and greater Europe. The aims of the CaMon project were (1) to develop a cancer surveillance system for cancer occurrence and outcome (incidence, mortality, survival, prevalence), permitting situation analysis and monitoring of cancer burden in the EU member and applicant states (2) to disseminate such information within EU and world-wide and to make it available for incorporation into the health monitoring system of the EU Public Health Programme.

The tasks covered: compilation, update and maintenance of a database of indicators of cancer burden and outcome for Europe; analysis of time trends and provision of short-term projections of cancer incidence and mortality for Europe; dissemination of information; provision of data to other health monitoring programmes. EUCAN was updated and two interesting workshops held, one on prevalence, one on time trends. The Prevalence Workshop in Paris, organised jointly with the French Cancer League, brought together methodologists and users to discuss what is meant by prevalence and what we use it for. The Time Trends Workshop was held in Lyon with a small group of specialists on temporal variations to plan a comprehensive and systematic analysis of time trends of incidence and mortality of 23 cancers in Europe. Experts in the field were identified for each cancer site and invited to collaborate in the project as interpreters of the trend analyses and predictions, and to act as lead authors of a series of cancer-specific scientific papers. Some articles have been published. There has been close collaboration between CaMon and EUROCHIP-1 and 2. The EUCAN data are included in the New Cronos database of EUROSTAT.

## **Presentation 5. EUROCHIP-2**

*Freddie Bray, International Agency for Research on Cancer, Lyon*

EUROCHIP-1 started in 2001, also funded by the EC Health Monitoring Programme, with the major aim to draw up a comprehensive list of health indicators useful for monitoring cancer in the countries of the European Union, to help the development of the European Health Information System and to promote actions within the context of cancer control. The EUROCHIP team has been working with five domains: prevention; epidemiology and cancer registration; screening; treatment; and macrosocial and economic variables. A series of meetings have been held on the national or regional level to decide which indicators were important on a high priority, medium priority and low priority list.

The aims of EUROCHIP-2, which started in 2004, are to (1) extend the collaboration of networks on cancer (new participating countries); (2) establish multidisciplinary working groups in each country; (3) analyse the behaviour of various indicators in relation to their utility as determinants of clinical outcomes, possibly leading to modifications (permanent consensus conference); (4) promote at least one important initiative in each country (to improve the system of cancer information); (5) establish/strengthen a health information system in co-operation with other chronic disease networks as for common risk factor or morbidity indicators.

EUROCHIP-2 will contribute to setting up a cancer health indicator system at three different levels in each country depending on the particular indicator: (1) Knowledge of indicator: finding source of data, what is available, data collection, improvement/standardisation of data collection; (2) Choice: analysing data, comparing data, finding relations, finding major deficiencies; (3) Action: to design, validate and finance an action which promotes a choice or the knowledge behind it, or, directly reduces cancer disparities. These phases should be looked at as part of an iterative process. The execution of EUROCHIP-2 can be described by a "process" approach, represented on three axes: (a) cancer health indicators, (b) the phases of execution and (c) countries. For every given health

indicator, EUROCHIP-2 may be promoting a certain phase (or phases) in certain countries, and another phase (or phases), in other countries. The "module" may therefore vary for each indicator. What is referred to as "process" is the simultaneous vision of all phases. All participating countries will be able to benefit from both data comparison and experience of others. EUROCHIP will be useful mostly if you have already a national or regional cancer plan.

#### **Presentation 6. EUROCARE-4**

*Henrik Møller, Thames Cancer Registry, London, UK*

The core output of EUROCARE-3 was published in 2003. Subsequently, the EUROCARE Steering Committee met and decided to continue the project and update the data, with the aim to publish another monograph in a few years time. The EUROCARE Working Group met in Ragusa in September 2004. Two options were discussed: update the project with incident cases up to 1999 or 2000 (would involve ~60 cancer registries) or update the project with incident cases up to 2002 (would involve ~30 cancer registries). The first option based on maximum inclusiveness was agreed on, but there were diverging views between the large group of cancer registry collaborators and the small group of professionals working on EUROCARE in Rome. A further problem is funding, as the fairly generous European level funding in the past is no longer available. Applications for EU support to the Working Group are pending, but the outcome is unknown and the likelihood of further European funding small. In the interim, funding is provided by INT (Milan) and ISS (Rome) to sustain a minimum level of activity. For EUROCARE-4 the proposed date for data submission is mid-2005. The publication of the monograph is planned for late 2006, including special articles on selected cancers, methods development, and high resolution studies. A number of items will have to be provided by the participating registries, some compulsory, some optional, and this may be the right moment to try again to go in the direction of a common database to which the cancer registries can submit their data for several projects at the same time (EUROCARE-4, EUROCIM, CI5, etc.).

#### **Presentation 7. EUROCADET**

*Jan Willem Coebergh, Eindhoven Cancer Registry, The Netherlands*

Eurocadet (European Cancer Determinants) is a co-ordination action within the 6th Framework Programme of the EU, that aims to develop scenarios for primary prevention of cancer across Europe for the period 2010-2040. It will concentrate on potential short- and long-term effects of smoking prevention and cessation, lowering alcohol intake, raising healthy dieting and physical exercise. This would affect substantially the incidence of 12 major cancers with more than 60% of all new cases. The aim of scenarios is to involve policy makers so that they cannot escape their responsibilities for long-term prevention. The project received a favourable expert evaluation but is still under negotiation; it aims to start in 2005 and would take 4 years to complete. It will strongly stimulate the use of registry data by extending the CAMON-project of trends up till 2020. It will also make use of data and experience, present at IARC concerning the estimation of population-attributable risks. Furthermore, attention will be paid to socio-economic and educational determinants of exposures (Anton Kunst) and - with some lag time also - incidence rates. Logically, effects on other relevant chronic diseases will also be (roughly) estimated, a.o. based on co-morbidity data.

A simulation model, Prevent, developed at Erasmus University Medical Centre Rotterdam, Dept of Public Health, (Jan Barendregt and Johan Mackenbach) will develop the various scenarios based on more or less optimistic assessments and systematic literature reviews of effects of preventive interventions (carried out by Hans Brug at Erasmus MC) and systematic (political and societal) barriers by Knud Inge Klepp (Norway), in collaboration with various exposure experts, in particular from the EPIC group.

The scenario development process will focus on 5 regions of Europe (north, west, middle, south and east, each with overlapping areas), but the Prevent model allows for do-it your self feeding by researchers in individual countries or regions. Four training workshops will be held at the end of the

project. Currently, about 10 people from the registries are involved, but this will increase towards the end of the project.

Co-ordinators will be Jan Willem Coebergh, with Esther de Vries, at Erasmus MC Rotterdam and Eindhoven Cancer Registry (also because of the co-morbidity data) and IARC and ENCR will be involved in work packages (Freddie Bray and Paola Pisani). Eurocadet will also contribute to Eurochip (Andrea Micheli) with suggestions for indicators for primary prevention. Special attention will be given to web-based communication, storage of documents, and scenarios, which would need to be continued after the project finishes end of 2008.

## **Presentation 8. CERVICAL CANCER SCREENING**

*Marc Arbyn, Institute of Public Health, Brussels, Belgium*

The EU policy in cancer screening was defined about 5 years ago in Vienna, where experts reached consensus that screening can reduce mortality for three sites: breast, cervix and colorectum. For cervix, a pap smear should be offered to women starting between 20-30 years of age and continuing until age 60 and later if resources are available. At 3-5 year intervals cost effective screening can be carried out. This scientific consensus was further developed and agreed upon at a political level. At the end of 2003 the Council agreed on a Council recommendation on cancer screening which was based on the Vienna consensus. Screening should only be offered in organised settings with monitoring and quality assurance at all levels. Screening need to be done in accordance with scientifically based evidence and guidelines should be evidence-based as much as possible. It was stressed in the Council recommendations that research should be carried out on new screening methods, using randomised control trials as the preferred method and targeting public health relevant outcomes. Normally, the outcome for cancer screening is mortality. For cervical cancer screening, reduced incidence can also be accepted as evidence for effectiveness of a new method.

The European Cervical Cancer Screening Network (ECCSN) had a contract with EC which ended in December 2003. Guidelines were developed but only in draft form. The second draft is available on internet and a third draft is under preparation. In September 2004, ECCSN was invited to continue the work to reach a publishable version of the guidelines. The Director of IARC has agreed to contribute to that process.

A further activity of the ECCSN is a questionnaire survey on screening among key persons in Europe. One of the inclusion criterion was to be a country or a region where high quality data are available for cervical cancer mortality trends and/or for cervical incidence trends, so it was limited to a selection of countries. Wide variation in policy, screening coverage, quality etc. was observed. In some countries with opportunistic screening there was a tremendous amount of over-screening. Currently, the European recommendations are only met in a few countries and one could say that they are insufficiently binding being only recommendations, not directives.

A lot of work has been done on new methods via systematic reviews and meta-analyses: HPV triage, HPV follow-up after treatment of CIN, liquid-based cytology, HPV vaccination. Within the EUNICE application the trend studies will be continued, screening indicators will be monitored and guidelines on confidentiality of screening registration prepared. Within the new European Cancer Network (co-ordinator: L. von Karsa), work will be done on the health technology assessment of new screening and treatment methods and HPV vaccination, and this information will be used for development of future guidelines. Cervical cancer is a special problem in some new member states and guidelines will not be enough to tackle that problem. More action and European support is needed.

## **Presentation 9. BREAST CANCER SCREENING**

*Larry von Karsa, European Breast Cancer Network, Bergisch-Gladbach, Germany*

The European Breast Cancer Network started about 15 years ago with the "Europe Against Cancer" Programme with the countries experienced in organised population-based breast cancer screening. In the beginning, focus was more on the organisation of a screening programme, how to set up an invitation system, special quality assurance, etc., and over the years the network has continued with a motor that got all people involved in setting up organised screening programmes (administrators, policy makers, advocates) together, to help setting up these programmes in their own country. Setting up an organised population-based screening programme is a very challenging management endeavour and you can lose the effectiveness of screening at any step in the process. It is almost impossible for one single country by itself to tackle this management job in a short period of time. By co-operating internationally it was possible to learn from the mistakes, but also from the successes of other countries. All the people involved in this network are convinced that international co-operation and exchange of experience have been very instrumental in setting up high quality screening programmes through Europe. Before the new 10 countries entered the EU, there were, as a result of these activities, national and regional breast cancer screening programmes based on mammography in all of the member states. Around 2000, the scope of the network was expanded to not just address screening and management of screen-detected lesions, but also the entire range of breast cancer care. It was widely recognised that introduction of population-based organised screening programmes has had a considerable spin-off in improving the quality of the overall breast cancer care in these countries. There has been an increasing emphasis on developing databases and instruments to have a uniform data collection across Europe, to be able to see how effective breast cancer care is in the different member states.

An application for a European Cancer Network was submitted in 2004, with major focus on screening, but also addressing the full scope of symptomatic care and not only covering breast but also the other screening interventions which are recognised by the Council. The general goals of the European Cancer Network are to: (1) integrate the new Member States into the mainstream of European efforts toward continuous improvement of best practice in secondary cancer prevention; (2) assist the new Member States in implementation of the evidence-based screening tests for breast, cervical and colorectal cancer; (3) establish framework for continuation and consolidation of best practice efforts of the cancer screening networks of the previous European Public Health programmes; and (4) promote pan-European exchange of information and expertise on the development and implementation of best practice in secondary cancer prevention. The main objectives are to: (a) develop a strategy for improving best practice in cancer screening in Europe, taking new Member States into account (structured, pan-European workshops); (b) establish network of partners previously participating in the European Networks for Breast Cancer, Cervical Cancer and Cancer Registries, as well as Colorectal Cancer screening experts and administrators cooperating with professionals and authorities in the new Member States; (c) review programme performance and evidence of effectiveness and cost-effectiveness of cancer screening; (d) reduce variation between Member States in achieving the recommended high standards; and integrate advocacy training in dissemination of results.

## **Presentation 10. DIRECTORATE GENERAL OF SCIENCE AND TECHNOLOGY**

*Joanna Namorado, European Commission, Luxembourg*

FP6 and cancer research opportunities within FP6 were described, in particular the forthcoming calls for proposals. The next calls will include prevention, detection and treatment of familial cancers, such as cancer of the prostate, ovary, breast, colon and skin. A future call may include a topic centred on childhood cancer and the organisation of a workshop on childhood cancer.

## **GENERAL DISCUSSION**

### Funding of ENCR

Currently, the funding situation of ENCR is very precarious and the attempts in the last years to write applications have been frustrating. The ENCR Steering Committee has discussed several times over the last couple of years about possible alternative sources of funding. One more radical proposal has been to try and move away from the dependency on grant giving bodies, whether EC or others, and consider the possibility of becoming self-funded, at least partly. One way of doing this would be to ask cancer registries for a contribution or annual subscription. To explore this possibility, the registries have to be formally consulted and it was decided to carry out a survey among the registries. A contribution of 500-1000 EUR seemed reasonable, or a small percentage of each registry's annual budget.

However, it was recognised that what cancer registries can contribute would not be enough to run the organisation as it has been run in the last years. Funding by the registries would only be an emergency solution. However, it seemed obvious that a project like ENCR should be funded by the European Union.

So far, the registries have collaborated with a lot of organisations for free, giving data and participating in projects. If there was a registry organisation that was strong and in regular contact with its members, and was the portal for supplying data to the people regularly asking for it, including EU, then one would be entitled to ask for a fee for doing that, or to be a partner in a project that receives money.

For comparison, the North American Association of Central Cancer Registries (NAACCR) is financed through a flat rate for each central registry. The Association has also sustaining members such as CDC, SEER, and NCI which are charged more. Registration fees are being charged for conferences. The NAACCR employs an Executive Director, a web programmer and 3-4 assistants/tumour registrars.

Consideration should be given to approaching some of the European cancer research charities and organisations, either individually or collectively, in the attempt to raise funding. There is an initiative from IARC to try to organise some networking between the various cancer charities in Europe with a view to extracting some European level financing. It might also be easier to apply for funding if ENCR were a legal entity and this possibility will be further investigated.

An application for a network for the study of rare tumours, involving the cancer registries, is being submitted to FP6 mid-November. It will concern data analysis with EURO CIM, ACCIS and EURO CARE data. A further call for proposals within SANCO will be advertised end January beginning of February and consideration should be given to submitting a further application.

### Common centralised database

The establishment of a co-ordinated, quality controlled data submission process with simultaneous submission to all the European projects (CI5, EURO CIM, EURO CARE-4, etc.) was discussed. There was an overall feeling that time has now come to work towards the creation of such a quality controlled gateway. The idea would be to have a central service, owned by the registries but managed through ENCR, which could provide a facility for cancer registries for submitting data to ensure uniform and consistent processing of data. These could then be fed into the collaborative projects and other agreed uses of the data. ENCR would be the focal point which would gather all the registries.

### Confidentiality

The problem of confidentiality was also raised, in particular with respect to the new member states. While there is no formal monitoring process within ENCR, it was felt that it would be useful to monitor the current situation in relation to privacy legislation. However, it was agreed that it is very difficult to follow what every country's parliament is doing. In the past, when data protection problems arose in a particular country, action was taken by ENCR, IACR or IARC, usually all three, by writing to ministries.

This, of course, is a reactive process rather than keeping up-to-date with how things are evolving. The problem will be discussed with J. Ryan at the Steering Committee meeting.

Closure

D. Brewster closed the meeting. He thanked the cancer registries for attending and supporting the ENCR. Special thanks for contributing went to those not directly associated with ENCR. The contribution of Max Parkin to ENCR over the years was specifically acknowledged in view of his imminent retirement. He also thanked the European Commission and FECS for financing the meeting.

K. Freese thanked the speakers and the ENCR Secretariat and, in particular, the registry people who had helped the Commission services to better understand the impressive work cancer registries are doing.



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