Eur J Cancer, Vol. 27, No. 2, pp. 201–207, 1991.
Printed in Great Britain

0277–5379/91 $3.00 + 0.00

Feature Articles

EORTC Joint Ventures in Quality Control: Treatment-related Variables and Data Acquisition in Chemotherapy Trials

K. Vantongelen, W. Steward, G. Blackledge, J. Verweij and A. Van Oosterom

In multicentre studies, non-compliance with the protocol may limit the chances of reaching a correct conclusion. A procedure to examine the administration of chemotherapy in multicentre EORTC protocols has been developed. General aspects are covered in a mailed questionnaire on the prescription of drugs with rounding up or down of dosages, local facilities for preparation and the procedure for preparation and administration. More detail is collected during a quality control site visit. Ten centres have been visited and there was significant variation between centres in the organisation of chemotherapy administration. However, more striking differences were noted between the type and quality of hospital files. The lack of systematic recording of sequence, timing and doses of chemotherapy and, in particular, treatment related toxicity, is a major difficulty limiting the effectiveness of quality control. These shortcomings emphasise the need for standardisation of some aspects of case records and a suggested check-list has been drafted.
Eur J Cancer, Vol. 27, No. 2, pp. 201–207, 1991.

INTRODUCTION

CLINICAL STUDIES in oncology are aimed at improving the quality of management of the patient. In multicentre studies, differences in the way that protocols are adhered to in the various centres may limit the chances of reaching a correct conclusion [1]. Concern for quality control procedures should therefore begin in the early stages of planning and continue until the final study report is written. In chemotherapy trials, how should quality be controlled and to what extent [2]? The answers are not readily available. However, it is very important to monitor the most vulnerable steps of a multicentre trial and to integrate the different steps in a collaborative approach.

In recent years, the need for a systematic comparison of the quality of the work in each centre has been discerned from government organisations. The existing structure of the co-operative groups in the European Organization for Research and Treatment of Cancer (EORTC), in which different clinical centres have collaborated for many years and thus have built up a strong relationship, is the ideal basis to start projects in quality control at the institutional level. Because site visits, which are expensive, are needed, a programme could only be started after a grant was obtained from the European Community.

The EORTC Radiotherapy Group has done a pioneering job in this field. From 1982, independent experts in radiation therapy and radiation physics audited quality in participating centres. Initially, the team evaluated the hospital facilities, equipment, staffing and workload. They later compared the calibration procedures of radiation beams, mechanical stability and beam alignment devices on all therapy units as well as on radiotherapy simulators [3–7]. Their efforts have developed continuously and have since become integrated in the group's protocols. In the new breast cancer trial (22881/10882), quality control even goes one step further to the investigation of the possibility of not only doing controls in irradiated volumes in individual patients, but also doing *in vivo* dosimetry in a number of patients.

Since 1988, the EORTC Study Group on Data Management has piloted a method for data quality control in clinical trials [8]. Twenty site-visits have been made to the largest centres entering patients in EORTC trials. Several important aspects have been highlighted, including the need for better recording of data within the hospital case record, better documentation of toxicity and closer adherence to the protocol. The visits have proved useful, stimulating interaction between physician and data manager and improving, where necessary, the organisation of local data collection. The quality control programme has expanded and, after radiotherapy, programmes in surgery and medical oncology have been planned, and a procedure to examine the administration of chemotherapy to patients in multicentre protocols has been developed. A search of the medical literature did not reveal any procedure for the assessment of the technical aspects of drug administration and preparation in oncology trials. Indeed, quality control studies concentrate on tumour response, rarely on toxicity and never on administration [9–11].

The scope of the chemotherapy quality control programme is to develop a procedure that is reproducible and valid for most

Correspondence to K. Vantongelen.
K. Vantongelen is at U.H. St. Rafaël, Radiotherapy Department, Capucijnenvoer 33, 3000 Leuven, Belgium; W. Steward is at Beatson Oncology Centre, Western Infirmary, Glasgow, U.K.; G. Blackledge is at the Queen Elisabeth Hospital, Birmingham, U.K.; J. Verweij is at the Dr. Daniel den Hoed Cancer Centre, AE Rotterdam, The Netherlands; and A. Van Oosterom is at U.H. Antwerp, Department of Oncology, Wilrijkstraat, Edegem, Belgium.
Revised 22 Oct. 1990; accepted 24 Oct. 1990.

chemotherapy regimens. The quality assessment should cover the main steps from drug prescription to preparation and administration. It should further highlight the weak points in multicentre chemotherapy trials, promote standardisation of therapeutic practice and finally, in the long term, improve chemotherapy practice in oncology in general.

Two EORTC Co-operative Groups (the Soft Tissue and Bone Sarcoma Group and the Gynecological Group) agreed to include a pilot test on the technical aspects of chemotherapy administration during the site visits they have planned for data quality control in two of their ongoing studies. The first is a phase II study of the use of granulocyte–macrophage colony-stimulating factor (GM-CSF) with doxorubicin and ifosfamide in advanced soft tissue sarcomas in adults. The second is a randomised phase III trial of vindesine, cisplatin, bleomycin and mitomycin vs. cisplatin in disseminated squamous cell carcinoma of the uterine cervix. We describe here the procedure and the organisational aspects and summarise the first results.

METHODS

Several items representative of the total treatment have been carefully selected. Regardless of the regimen, the exercise should give information on precision, systematic deviations from the protocol, procedure and errors in specific patients. Thus a list was written, including the different steps and the main aspects of the chemotherapy prescription, preparation and reconstitution of drugs, administration and toxicity evaluation. We split this list into points that could be checked by sending out a questionnaire and those which needed to be checked on-site.

Questionnaire

The general information, collected by a mailed questionnaire, should guide the first site-visits and the further development of the procedure (Fig. 1). The questionnaire was sent to the centres participating in one of the two protocols under study and completed before site visit, which was planned for the major contributors to the two protocols. The questions assess general technical aspects of drug preparation and administration. Information on prescription procedure, persons responsible at this stage, check of the calculated dose and the administered dose (rounding up or down of the prescribed dose), local facilities for preparation of the drug(s) and the environment and procedure for preparation and administration of the chemotherapy is compiled in detail.

The questionnaire also has a protocol-specific section (Fig. 2). This information should enable the study co-ordinator to evaluate whether the centres follow strictly the protocol guidelines about the use of the products: for instance, the reconstitution, sequence, timing and mode of administration. Details on antiemetic policy and the local organisation for recording side-effects complete this list. The completed questionnaire is discussed during the quality control visit.

Site visit

Besides the mailed questionnaire, which already provides interesting and, thus far, unknown information, some aspects need to be checked on-site. The procedure can easily be combined in one visit.

Dose calculation in individual patients. Depending on the availability of information in the local hospital file, a check on the calculated dose per cycle compared with the protocol dose is made. A 100% protocol dose is recalculated, based on the weight and height of the patient at onset and adapted to the weight before each cycle. The actual dose is noted on the quality control forms. The reason for reduction of treatment, if any, is also coded. Deviations from the intended 100%, 75% or 50% dose are calculated by computer and presented as percentages. This part also includes the interval between cycles, with reference to the exact interval in the protocol. If the hospital file is complete and well documented, the results of this exerise should give a fairly good view of theoretical protocol adherence.

Chemotherapy data on case report forms. Because information has been transferred from the hospital file onto the case report forms, and is thus available at the central Data Center for review, the check described above also assesses the accuracy of data collection and the reliability of the data transfer related to the dose of each drug given, the days of drug administration, concomitant treatments, side-effects and performance status of the patient during treatment. The evaluation of the quality of the data on the treatment forms is doubly coded and is based on the slightly modified procedure used in the data quality control programme (Table 1). From the data quality control site visits, it was known that for some centres, the information coded on the forms was not always available in the hospital file. Our procedure was therefore adapted to document local data collection and transfer in the centre. The codes for causes therefore further differentiate the two major situations encountered (Table 2).

Quality control of key data. The programme also checks supportive data for each protocol: eligibility of the patient, previous treatment, diagnosis, initial tumour indices and evaluation of the tumour response. The procedure to assess the quality of these data is the same as detailed above (Tables 1 and 2).

Other points. The specific structure of the local data management support, if any, is part of the general quality control assessment. Information is collected on who is filling in and who is supervising the case report forms. After each site visit a confidential report is sent to the study co-ordinator, the central Data Center data manager and to the visited team. To guarantee anonymity, each centre is assigned a number.

Centralised organisation

From the start it was obvious that, to collect all information in a standardised way, administrative support from a central office would be essential for co-ordination. Thus, the different co-operative groups could be advised on how to set up the quality control study for their protocol and to do the site visits based on the experience in the EORTC so far.

One important aspect for the proper functioning of the programme is the organisation of the site visits. Preferably the date for the visit should be agreed at least six weeks ahead. The people involved from both sides should then receive all relevant information, including details on time, place and the patient files, randomly chosen, that should be prepared for the review.

The first site visit for a specific protocol is done in collaboration with the representative of the central structure. During this visit the study co-ordinator is trained to become familiar with the procedure. The central office further provides the groups with computerised check-lists, designed for each study, of the items that the study co-ordinator wishes to include in the review. Thus, each protocol has a specific set of quality control forms designed according to the original case report form and the treatment regimen involved.

Name : .....

Institute : .....

PLEASE COMPLETE THIS FORM BEFORE THE PLANNED SITE VISIT (Write number in box, tick or fill in blanks or circle as appropriate) – THE TOPICS WILL BE DISCUSSED DURING THE VISIT.

I. CHEMOTHERAPY PRESCRIPTION (usual procedure)

1. Chemotherapy prescription written by :

☐ 1 = Junior doctor
2 = Specialist
3 = Other (detail : .....
.....)

2. Prescription is checked : Y/N

If Y, by whom ?.....

3. Is dose, at prescription : rounded up ? Y/N
rounded down ? Y/N

General rule :

II. CHEMOTHERAPY PREPARATION AND ADMINISTRATION

PLEASE DESCRIBE HOW THERAPY FOR A TYPICAL ADMISSION IS CALCULATED AND PRESCRIBED

4. In your hospital, is chemotherapy prepared by :

1= Pharmacist 2 = Nurse 3 = Doctor

Always	over 80% of prescriptions	50 – 80% of prescriptions	Never
☐	☐	☐	☐

5. Where is chemotherapy prepared ?

☐ 1 = in pharmacy on ordinary worktop
2 = in pharmacy with exhaust canopy/laminar flow
3 = on ward on ordinary worktop
4 = on ward with exhaust canopy/laminar flow
5 = other

6. When chemotherapy is prepared, is any protective clothing worn ?

☐ 1 = always 3 = 50 – 80% of instances
2 = over 80% of instances 4 = never

7. If protective clothing worn, does it include :

glasses Y/N mask Y/N
gloves Y/N gown Y/N

8. When chemotherapy is prepared, is prescribed dose:

rounded up ? Y/N rounded down ? Y/N

General rule :

9. Chemotherapy residue is :

☐ 1 = used 2 = thrown out
3 = other (specify).....

10. Chemotherapy is given by :

☐ 1 = specialist nurse 4 = combination
2 = other nurse 5 = no general rule
3 = doctor

Fig. 1. Quality control of technical aspects of drug administration and preparation.

To meet these requirements, the central office is well equipped with the related computer facilities which include the development of the data base for each protocol under study, data entry of the site visit results and the analysis and reporting of the results.

PRELIMINARY RESULTS

The programme started in early 1990 and so far 10 centres have been visited. During these visits, the files of an average of 7 patients per centre have been completely reviewed. The two co-operative groups will report detailed analyses of the chemotherapy quality control findings when the programmes are complete. It is already apparent, however, that for both groups there was significiant variation between centres in the organisation of chemotherapy administration.

More striking differences were noted between the type and quality of hospital files that are kept in different centres. The major difficulty limiting the effectiveness of quality control is the lack in many centres of systematic recording of timings and doses of chemotherapy administration and, in particular, treatment related toxicity. In addition, many hospital files are complicated and poorly organised, and the information is difficult to find.

The correct dosing and scheduling of cytotoxic agents which may have a profound impact on outcome, and the monitoring of toxicity, particularly for regimens that will not be curative, are critical aspects and it is therefore imperative that they are clearly documented. There are probably a few more important pieces of information that should be clearly detailed in a patient's case notes. Sadly it is just such information which is the most difficult

III. 62883 PROTOCOL

11. Origin of products used in protocol 62883(Firm)

☐ Doxorubicin
1 = Farmitalia 2 = other (.....)

☐ Ifosfamide
1 = Asta Degussa 2 = other (.....)

☐ GM - CSF
1 = Behringwerke 2 = other (.....)

12. Reconstitution of protocol products

☐ Doxorubicin
☐ Ifosfamide
☐ Mesna
☐ Mesna + ifosfamide

1 = glucose 5%
2 = saline
3 = combination
4 = other

13. Sequence of drug administration

☐
1 = mesna, doxorubicin, ifosfamide + mesna, mesna
2 = doxorubicin, mesna, ifosfamide + mesna, mesna
3 = mesna, ifosfamide + mesna, mesna, doxorubicin
4 = other (specify:.....)

14. Timing of drugs

☐ Doxorubicin
1 = push within 5 min
2 = slow push within 15 min
3 = prolonged over .....min

☐ Ifosfamide / mesna
1 = exactly 24 h
2 = shorter (.....h)
3 = longer (..... h)

☐ Mesna before
1 = over 15 min
2 = shorter (..... min)
3 = longer (..... min)

☐ Mesna after
1 = exactly 12 h
2 = shorter (..... h)
3 = longer (..... h)

15. Mode of administration

☐ Doxorubicin
☐ Ifosfamide
☐ Mesna
☐ Mesna + ifosfamide

1 = IV, peripheral
2 = IV, peripheral catheter
3 = IV, central catheter
4 = IV, via Portacath
5 = subcutaneous

16. Approximate time delay (min) between preparation to administration of drugs in protocol 62883

☐ for doxorubicin ☐ Ifosfamide

17. General anti - emetic policy for first - line chemotherapy patients ? Y/N
If yes, detail anti - emetics
.....
.....
.....

Dexamethasone/other steroids as anti - antiemetics Y/N

18. Toxicity : are side - effects recorded in hospital files ?

Y/N If yes, Is a special form used ? Y/N

Are data recorded as descriptive/coded/both ?
(please enclose a copy of any form used)

IV. GM - CSF SPECIFIC

19. Who gave injections ?

☐ 1 = patient 2 = doctor 3 = nurse
4 = combination 5 = other :.....

20. Was the patient given written instructions about how to reconstitute and store GM - CSF ?

Y/N If so, please enclose an example

21. Who records toxicity ?

☐ 1 = doctor 2 = nurse 3 = patient

Are data recorded as descriptive/coded/both ?

Is a special form used for this ? Y/N
(if yes, include example)

How frequently is toxicity checked ? every.....days

Date..... Signature.....

Fig. 2. Protocol-specific section.

Table 1. Coding for quality of data

Code A (quality of data)	
1 =	correct
2 =	incorrect
3 =	data missing on treatment form
4 =	data on form, but not in hospital file
Code B (causes for deviations)	
1 =	incorrect transfer of information
2 =	information missing in hospital file
3 =	related to unclear and/or ambiguous instructions on study protocol and/or study forms

Table 2. Coding for causes of data on form, not in hospital file

5 =	data directly coded on study forms by physician without delay in filling in forms
6 =	data are coded more than one month later by physician or data manager and without available notes in hospital file
7 =	data are not available for other reasons (specify)

to find during quality control site visits. In both groups an important percentage (mean 20%) of the data could not be checked (range 0.7–45.6%) (Fig. 3). This mainly reflects the lack of documentation on treatment dose, time and toxicity.

These shortcomings emphasised the need for standardisation of some aspects of case records. This could be done with a check-list of chemotherapy data, study variables and treatment related toxicities. The check-list can be adapted according to the special needs of certain trials. A suggested form has now been drafted and will be tested in these co-operative groups during the next months (Appendix). It resembles check-lists already in use in several hospitals in Europe that have also been collected by the quality control members.

DISCUSSION

Quality control visits to monitor the progress of studies in different centres involved in co-operative studies have two major drawbacks. These are the cost in terms of travel expenses and administration and the time involved for reviewers and those who are reviewed. Properly conducted, the cost for a single site visit covering assessment of 6–8 patients is approximately US$800. This does not include the salaries that are lost through time taken from regular duties. Although this might seem an expensive exercise, with increasing experience of the results of such site visits, the benefits appear to outweigh the costs greatly. It is usual for local physicians, data managers and nurses to be unaware of shortcomings in their organisation and problems were inevitably highlighted during the visit. Although this is a stressful experience for those visited at the time, subsequent improvements in organisation are inevitably made and adherence with the protocol increases considerably. This is perhaps one of the most important results of such a site visit and is becoming increasingly useful as clinical trials become more complex and difficult to run well in a collaborative group. This is particularly the case in trials organised by the drug industry where adherence to Food and Drug Administration and good clinical practice guidelines is essential.

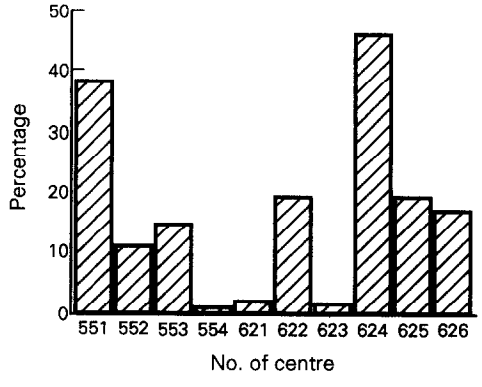


Fig. 3. Proportion of data that could not be checked.

A further benefit which accrues from visits to individual members of a multicentre study is that a better informed analysis of the results of the protocol treatment can be formulated. Responses can be assessed and follow-up treatments reviewed. Extra data, which are missing from flow sheets sent into a central Data Center, are frequently obtained from hospital files. A final, and most important, result of the site visits is the checking of accuracy of submitted data. With increasing devolvement of the responsibility for abstracting data from hospital notes to non-medical personnel, mainly to data managers, it is essential that future trials are carefully monitored for data accuracy. Without such external monitoring, the results of clinical trials must be viewed with some scepticism.

The contacts which have been established between study co-ordinator, quality control team and local responsible physicians in both the multicentre studies that have been monitored to date have already increased the accuracy of adherence with protocol treatments. The impact that these visits will make on future studies should be a positive one which should not only improve the smooth running of the study but will also improve the care of individual patients.

1. Arriagada R, De The H, Le Chevalier T, *et al.* Limited small cell lung cancer: possible prognostic impact of initial chemotherapy doses. *Bull Cancer* 1989, **76**, 605–615.
2. Knatterud G. Methods of quality control and of continuous audit procedures for controlled clinical trials. *Control Clin Trials* 1981, **1**, 327–332.
3. Suntharalingham N, Johansson KA, Quality assurance/physics/dosimetry. *Int J Radiat Oncol Biol Phys* 1988, **14**, S21–S24.
4. Horiot JC, Johansson KA, Gonzalez DG, van der Schueren E, Van den Bogaert W, Notter G. Quality assurance control in the EORTC Cooperative Group of Radiotherapy. 1. Assessment of radiotherapy staff and equipment. *Radiother Oncol* 1986, **6**, 275–284.
5. Johanson KA, Horiot JC, Van Dam J, Lepinoy D, Sentenac I, Sernbo G. Quality assurance control in the EORTC Cooperative Group of Radiotherapy. 2. Dosimetric intercomparison. *Radiother Oncol* 1986, **7**, 269–279.
6. Johansson KA, Horiot JC, van der Schueren E. Quality assurance control in the EORTC Cooperative Group of Radiotherapy. 3. Intercomparison in an anatomical phantom. *Radiother Oncol* 1987, **9**, 289–298.
7. Johansson KA, Hanson WF, Horiot JC. Workshop of the EORTC Radiotherapy Group on quality assurance in cooperative trials of radiotherapy: a recommendation for EORTC Cooperative Group. *Radiother Oncol* 1988, **11**, 201–203.
8. Vantongelen K, Rotmensz N, van der Schueren E. Quality control of validity of data collected in clinical trials. *Eur J Cancer Clin Oncol* 1989, **8**, 1241–1247.
9. Frei E. III and Canellos GP. Dose: a critical factor in cancer chemotherapy. *Am J Med* 1980, **69**, 585–594.
10. Gehan EA. Dose-response relationship in clinical oncology. *Cancer* 1984, **54**, 1204–1207.
11. White JE, Chen T. McCracken J, *et al.* The influence of radiation

APPENDIX

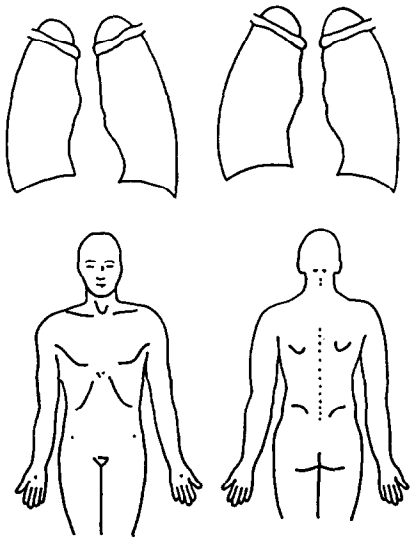
Patient's name

SYSTEMIC THERAPY CHECKLIST

Height (cm) ☐☐☐

Hospital no. .....
Diagnosis .....
Protocol no. .....
Reason excluded.....
.....

MEDICATIONS							Remarks* Refer to cycle
Tumour therapy							
Year Date							
Cycle no.							
Doctor (initials)							
Co-medication							1. Toxic related
1.							2. Other (relevant)
2.							
SIGNS / SYMPTOMS / ADVERSE EFFECTS(WHO grades)							*Detail disease or drug related WHO grades (see overleaf)
Performance status							
Weight							
Surface area							
Nausea / vomiting							
Oral							
Defecation / diarrhoea							
Cutaneous							
Alopecia							
Neurological							
Respiratory							
Cardiac							
Other							
TUMOUR SIZE (mm x mm)							
A							
B							
C							
D							
E							
INVESTIGATIONS							
Response (WHO)							
X-ray							
Bone scintigraphy							
Computed tomography							
Ultrasound							
EF							
Other							
LABORATORY VALUES							
Haemoglobin							
Leucocytes							
Other							
Platelets							
Creatinine							
Alkaline phosphate							
Lactate dehydrogenase							
Other							
Markers							



11. White JE, Chen T. McCracken J, *et al.* The influence of radiation therapy quality control on survival, response and sites of relapse in oat cell carcinoma of the lung. *Cancer* 1982, **50**, 1084–1090.

Acknowledgements—We thank the following participants in the quality control study whose contribution made this report possible: G. Favalli (Brescia), J. Vermorken (Amsterdam), M.E.L. van der Burg (Rotterdam), J. Renard (EORTC Data Center) and D. Thomas (EORTC Data Center). We also thank Mrs L. Minnen and E. Boyen for their skilful typing.

Eur J Cancer, Vol. 27, No. 2, pp. 207–209, 1991.
Printed in Great Britain

0277-5379/91 $3.00 + 0.00

Cancer Incidence Registration and Trends in the Canton of Vaud, Switzerland

Fabio Levi, Van-Cong Te, Lalao Randimbison and Carlo La Vecchia

THE VAUD Cancer Registry collects data concerning incidence, mortality and survival of malignant neoplasms in the resident population of the Canton, whose population in 1980 was about 530 000. It began operation in January 1972, and the registration scheme was progressively implemented during the first few years after its inception. Thus, reliable data have been available since the late 1970s, and have been published from volume IV of *Cancer Incidence in Five Continents* onwards [1–2].

Information routinely collected includes sociodemographic characteristics, primary site and histological type of the tumour according to the International Classification of Diseases (ICD) for Oncology [3] and time of diagnostic confirmation. Passive and active follow-up are undertaken, and each subsequent item of information is used to complete the individual record. Thus, this is one of the few European cancer registration schemes that produces population-based survival data [4]. Information from death certificates is routinely integrated in the data file: cases known only through death certificate contribute to less than 5% of the average number of new cases registered per year. Overall, histological confirmation exceeds 90%.

Data for the period 1984–1988 are now available and will be published, as for previous five-year calendar periods [5, 6], in a standard report (available from F.L.). Here we summarise the main findings. Furthermore, the whole data set for the decade 1979–1988 (including 27 694 registered cancers, 14 548 males and 13 146 females) has been used for analyses of trends over two five-year calendar periods (1979–1983 and 1984–1988). This updates a previous analysis based on two consecutive issues of *Cancer Incidence in Five Continents* [7].

In Fig. 1, overall age-standardised rates (to the world standard population) are presented, although they provide only summary information and may obscure heterogeneous or diverging age-specific patterns [8]. The whole pattern of age and cohort specific rates is published in the registry report.

In males, lung cancer was the commonest form of malignancy,

Table 1. Percentage rate of change of overall age-standardised (world) incidence rates from selected cancers or groups of cancers (Vaud, Switzerland, 1984–1988 vs. 1979–1983)

Site	ICD-9	Percent change in: Males	Females
Mouth or pharynx	140–9	+14.0	−14.2
Oesophagus	150	−15.0	−11.8
Stomach	151	−16.6	+ 3.5
Colon	153	− 0.2	+ 1.1
Rectum	154	−15.4	−17.5
Intestine, total	152–4	− 6.6	− 3.9
Liver	155.0	+12.1	− 9.6
Gallbladder	156	− 8.5	−19.6
Pancreas	157	− 6.2	+29.4
Larynx	161	− 4.0	− 4.9
Trachea, bronchus and lung	162	− 1.4	+48.1
Skin melanoma	172	+46.3	+42.3
Skin non-melanoma	173	+21.7	+33.4)
Breast	174	—	+ 9.2
Cervix uteri	180	—	−28.4
Corpus uteri	182	—	−14.8
Ovary	183	—	+ 0.7
Prostate	185	+ 3.5	—
Testis	186	− 0.6	—
Bladder (infiltrating)	188	+ 2.6	+22.2
Kidney, other urinary	189	+13.9	+19.9
Brain and nerve	191–2	+16.4	+36.0
Thyroid	193	−32.0	−15.5
Hodgkin's disease	201	−14.7	−17.0
Other lymphomas	200, 202	+ 5.6	− 7.5
Multiple myeloma	203	+ 4.0	+40.6
Leukaemias	204–8	− 2.4	+ 2.9
Total, all sites	140–208	+ 5.4	+ 9.4
All sites except skin non-melanoma	All − 173	+ 1.1	+ 3.6

Correspondence to F. Levi.
F. Levi, V.-C. Te and L. Randimbison are at the Registre Vaudois des Tumeurs, Institut Universitaire de Médecine Sociale et Préventive, CHUV Falaises 1, 1011 Lausanne, Switzerland; C. La Vecchia is at the Institut Universitaire de Médecine Sociale et Préventive, Bugnon 17, 1005 Lausanne, Switzerland and the Istituto di Ricerche Farmacologiche "Mario Negri", Milan, Italy.
Received and accepted 5 Nov. 1990.