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Commission of the European Communities

“Europe Against Cancer” Programme

European School of Oncology Advisory Report

Cancer Treatment in the Elderly

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Within the EC approximately one million cases of cancer are diagnosed every year. At present, more than 55% of cancers occur in subjects aged over 65 years. There has been little clinical attention to the problem of neoplasia in the elderly. They are not receiving the same standard of specialised oncological care as younger patients. Other diseases (co-morbidity conditions) associated with cancer, and influencing its treatment and outcomes are not being properly considered. Information on surgery, radiotherapy and chemotherapy in younger patients exists for all cancers and could be adapted for the elderly. Controversial aspects of neoplasia in the elderly concern the intensity of chemotherapy, extent of surgery and the relative roles of specialised cancer centres, community hospitals and primary care providers. Future research should aim to replace subjective opinions on presence of frailty with objective instruments such as the multidimensional geriatric assessment scale. New trials could then seek to improve treatment in well-defined populations in terms of both efficacy and quality of life. Funding priorities should firstly consider that clinical trials for tumours in the elderly must be organised from cancer institutes and specialised referral centres in collaboration with geriatricians, primary care and community hospital physicians. Continuing education of doctors should be supported. A document such as this with appropriate modifications might be used as an initial message on neoplasia in the elderly to be published for information to clinicians and the public throughout Europe. Specific measures of quality assurance need financial support to evaluate the improvements in patterns of care. The 10 points of the ‘Europe Against Cancer Guidelines’ need re-emphasising.

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INTRODUCTION

This document has been prepared for the EC Medical Commission to provide information on the problem of cancer in the elderly, with present and future needs for treatment and education, in order for the EC to provide recommendations to the Member States. The main object of this document is to

underline that chronological age is not a reliable indicator of frailty and thus cannot be used for selecting the most appropriate therapeutic strategy for cancer in the elderly. Concomitantly, this report has been conceived for parallel dissemination to European public health officers and possibly to all medical doctors.

Table 1. Estimated number of new cases per year of the 10 commonest cancers in the European Community (O.M. Jensen, 1990)

Women				Men			
Cancer sites	n	% of cases in elderly ≥ 65*	≥ 70†	Cancer sites	n	% of cases in elderly ≥ 65*	≥ 70†
Breast	135 000	42	34	Lung	135 000	51	36
Colon	51 000	69	60	Prostate	85 000	81	68
Stomach	38 000	77	70	Stomach	55 000	64	53
Liver	27 000	76	64	Colon	42 000	61	48
Ovary	26 000	40	33	Bladder	41 000	57	43
Uterus	24 000	47	33	Liver	31 000	63	47
Lung	23 000	67	55	Oropharynx	27 000	36	22
Cervix	22 000	37	27	Larynx	25 000	37	24
Rectum	20 000	69	59	Rectum	24 000	58	45
Brain	17 000	43	37	Leukemia	17 000	51	42

* Including those over 70 years. † Based on incidence data from the Varese Cancer Registry, Northern Italy (Zanetti and Crosignani).

DEFINITION OF THE PROBLEM

Within the EC approximately one million cases of cancer are diagnosed every year. At present, approximately only 15% of the population in Europe is over 65 (Cancer Incidence in Five Continents, IARC, 1987), yet over 55% of cancers occur in this age group. The numbers of older men and women with common malignancies are shown in Table 1, according to the proportions aged ≥ 65 and also ≥ 70 years.

The risk of cancer increases as age advances. However, in spite of the social and economic costs of this burden, there is still a considerable lack of clinical attention to the problem of the elderly (65–75 years and over 75 years). There is a large proportion of unstaged or unknown stage neoplasms in the older age groups. Older people are not receiving the same high standard of specialised oncological care as younger adults. Recent data suggest that the medical approach to cancer patients is strongly related to their chronological age. This does not in fact necessarily coincide with physiological or biological age. Prior attitudes have led to the exclusion from clinical trials. For example, older people in their 70s are more likely to be undertreated for their cancer or, to a lesser extent, even to be overtreated. There are no differences between the behaviour of cancers in elderly and adult patients. The lack of solid data on some aspects of cancer treatment for older patients is the cause for these inconsistencies. The aging process increases the complexity of the therapeutic approach and the evaluation of its efficacy. Clinical investigation on multiple domains, such as health status, co-morbidity, disability, cognition, parameters influencing drug pharmacokinetic and anaesthesiologic risk is needed. A higher standard of oncological care and research can be obtained with the joint effort of clinical oncologists in cancer

institutes, geriatricians, primary care physicians, and other physicians of community hospitals and universities.

Public policy interventions aimed to change this lack of clinical attention are strongly needed. In fact, at best, not only the available information on cancer treatment in the elderly should be used but also evidence that cancer treatment could be as safe and possibly effective in the older as in the younger patients, taking into account the presence of significant co-morbidities and other functional parameters.

Additionally, there needs to be widespread public education of the entire population and particularly of the elderly themselves and their families.

STATE OF THE ART

Surgery for most common cancers can be part of curative treatment, or used to relieve symptoms if the disease is advanced. Many older people are not referred to hospital or are given sub-optimal treatment. Unwarranted fears exist that they are more likely to die because of a result of general anaesthesia or may develop postoperative complications that will prolong their hospital stay. There is substantial evidence that non-emergency surgery can be performed with low mortality, minimal morbidity and without protracted bed occupancy.

Radiotherapy plays a central role in the curative treatment and palliation of patients with cancer but is underused in the elderly. It can be given as external treatment or by an implant (interstitial), to form part of the curative therapy of certain malignant lymphomas, breast cancer and other solid tumours. Palliative treatment can reduce the bulk of tumour, and promote the healing of malignant ulcers. Pain from bone metastases or inoperable lung cancer can be successfully relieved with radiotherapy.

Chemotherapy can be effectively employed in older patients. However, because there is general belief that elderly patients are less tolerant of chemotherapy, its use requires intensive research. Chemotherapy administration in the elderly needs to take into account the possible degree of toxicity, the estimated efficacy, and the patient's preferences for active treatment.

Therapeutic approach by disease types

Mortality statistics of older patients indicate that lung, prostatic, colorectal, liver and bladder cancer are the leading causes

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of death from malignancy in males (two thirds of cases). In female patients, breast, colon, stomach, ovary and pancreas are the primary sites of the majority of elderly cases. The present situation with regard to more common cancers in the elderly is as follows.

Of the common solid tumours, breast cancer is the only malignancy in which several controlled clinical trials have been conducted. For the majority of patients adjuvant treatment with hormones (and occasionally chemotherapy) can be offered after local control by surgery and/or radiotherapy. It has been found that tamoxifen reduces mortality in women aged 70 and older by 21%. In order to avoid mastectomy, tamoxifen has been given in the place of surgery. However, recent results suggest that tamoxifen alone constitutes inadequate treatment for breast cancer in the elderly who are fit for surgery.

Patients suffering from metastatic breast cancer should be offered palliative therapy including radiotherapy, hormonal manipulation and, where appropriate, correctly dosed chemotherapy. Studies examining quality of life of elderly breast cancer patients have yet to be completed. In younger patients the benefit of symptom-free life outweighs the time spent under chemotherapy.

Lung cancer is often diagnosed late, as its symptoms, like coughing and shortness of breath, are common in old people. Small cell carcinoma of the lung may effectively be palliated with chemotherapy (sometimes combined with radiotherapy). Because the prognosis is dismal for most of these patients, emphasis should be put on prevention. Curbing the usage of tobacco in adults will lead to a decreased incidence of cancer and other diseases in the elderly.

Gastrointestinal tract cancers (oesophagus, stomach, colon, rectum). Radical surgery can be curative but in selected cases less extensive resection can be combined with postoperative radiotherapy and/or chemotherapy. These data need confirmation in elderly patients. Good palliation of oesophageal cancer may be achieved using endoscopically directed laser treatment to clear the obstructed gullet. Pancreatic cancers are rarely operable but can sometimes be palliated by radiation, with or without chemotherapy. Except for the rare patients who can benefit from surgery, other therapeutic approaches at present remain investigational.

Gynaecological cancers usually present at late stages in elderly people, because they do not seek the same specialised gynaecological attention as younger persons. Surgery and chemotherapy can offer long-term palliation and even cure to patients with ovarian cancer, especially if early diagnosis is possible. Surgery and palliative or curative radiation are effective methods for local control of uterine or cervical cancer; hormonal treatment may be offered to selected cases of metastatic uterine carcinoma.

Genito-urinary tract cancers in the elderly are prostate and bladder cancer. In advanced cases removal of the bladder (radical cystectomy) may be replaced by radical radiotherapy, or by local excision followed by radiotherapy and chemotherapy to spare the bladder. Prostatic cancer is a common incidental autopsy finding in elderly patients dying of other diseases and carefully designed screening studies are underway. Cancer of the prostate is often dependent on male hormones and prolonged remissions can occur after bilateral orchidectomy or monthly injections of hormone blocking drugs (LH-RH antagonists) along with anti-hormones. No data exist to show that they are any more effective nor that there is any improvement in quality of life when compared with the less expensive operation of orchidectomy.

Head and neck carcinomas can be treated with surgery and

radiotherapy in older patients but careful attention has to be paid to rehabilitation.

Haematological malignancies

Multiple myeloma represents a typical neoplastic disease of advanced age. The effect of age on response to treatment remains controversial, as a large proportion of patients over the age of 70 die of intercurrent conditions like infection. The major improvements in supportive therapy and infection prophylaxis have now allowed the inclusion of elderly patients in intensive therapy protocols. Similar problems are seen when treating chronic lymphocytic leukaemia.

Malignant lymphomas: 25–35% of non-Hodgkin's lymphoma (NHL) cases occur in patients who are aged 70 years or older. Old age represents the main negative prognostic factor in aggressive NHL. Approximately 70% of NHL in patients aged over 70 years require chemotherapeutic treatment. Some elderly patients affected by NHL die because of complications due to chemotherapy but dose reduction to lower the percentage of toxic deaths reduces the percentage of responses.

The prognosis of acute myeloid leukaemia (AML) in adults has greatly improved in recent years. About 60–80% of patients treated with conventional drugs usually achieve a complete response. Patients more than 60 years of age suffer a high percentage rate of treatment-related deaths, although, in spite of this risk, therapy cannot be withheld.

In Europe, the EORTC Leukaemia Group studied the effects of withholding therapy in older AML. Therapy was needed within a short time in the majority of patients randomised to deferred palliative chemotherapy.

CONTROVERSIAL ASPECTS

Intensity of chemotherapy

Adequate dosage of chemotherapy is fundamental to achieve a response in patients with advanced cancer. Administration of more intensive and multiple drug regimens has further restricted older patients' inclusion in protocols without any corresponding improvement in alternative treatment options, particularly in haematological malignancies. In general, treatments considered optimal set an age limit ranging between 55 (AML) and 70 years of age (myeloma), which excludes from treatment at least 30–40% of patients (the median age at diagnosis being, respectively, 63 years in AML, 65 in NHL and 68 in myeloma). This overestimates the real efficacy of such regimens in the whole age range of patients.

At present, evaluation of kidney and liver function together with nutritional status (albumin level and relative increases in body fat) are primary determinants for dose adaptation of many chemotherapeutic agents. Probably by paying due attention to drug metabolism, some of these toxicities can be decreased. Pharmacokinetic studies may help to define particular patterns of drug disposition in elderly patients and thus provide guidelines for adequate drug dosing. Minimal sampling techniques are available allowing studies in elderly patients.

Results from prospective studies on the intensity of the dose of chemotherapy administered to elderly patients are not available. However, at present the use of haematopoietic growth factors such as granulocyte colony-stimulating factor (G-CSF) could probably increase intensity, and should be restricted to life-threatening granulocytopenia after chemotherapy.

Community hospitals and cancer centres

The pattern of care of elderly cancer patients in EC countries has not been adequately studied. Presently, both specialised

consultation and referral centres are not available in many areas. Thus, the large majority of patients are generally treated in a non-specialised environment such as community hospitals. However, it should be recognised that, due to the interaction between age- and cancer-related pathophysiological modifications, cancer treatment in elderly patients needs a range of expertise and knowledge which is available only in specialised cancer centres. For example, palliation should include not only pain and psychological management but also surgical approaches, endoscopic treatments, hormonal and cytotoxic and radiation therapy. Thus, a major task of the referral centres will be to inform physicians in community hospitals and primary care providers on the use of correct referral and proper palliative approaches to elderly cancer patients.

NEED FOR FUTURE RESEARCH

Introduction

Extrapolation from the results of trials on patients in their fifties and early sixties to the older patients is not acceptable. Ways can be found to organise prospective studies that focus on the elderly as a target group and make age group comparisons. In these studies, due to the reduced life expectancy of some of the population addressed, attention should be devoted to quality as opposed to length of life.

Functional measures should be used to identify those in whom the physiological condition is more vulnerable to stressful events such as surgical procedures or therapies with cytotoxic agents. Therefore, results of multidimensional evaluation and, in particular, of functional status should be regarded as a primary concern in the choice of the most appropriate therapeutic strategies.

Inclusion of the elderly in clinical research on cancer, and trials specifically addressed to the elderly should be promoted in the following areas.

Radiotherapy

At present curative radiation treatment is usually given as daily treatments (fractions) over 6–7 weeks. This can provide logistical problems and can also be physically tiring for the patient, particularly the elderly. Trials are needed to examine whether a reduced number of treatment fractions can be given.

Surgery

Anaesthesiological guidelines for the exclusion of elderly people at high risk from surgical procedures should be developed.

Many elderly patients are receiving sub-optimal surgery leading to increased risk of recurrence. Quality assurance studies need to be conducted to determine the appropriateness of exclusion criteria and also to measure the outcome of surgical procedures. Further work should examine the effectiveness of a combination of less extensive surgery with radiotherapy, together with the role of adjuvant drug therapy for a variety of patients with solid tumours.

Chemotherapy

Older patients should be offered the opportunity to enter prospective controlled trials since this is usually accompanied by well monitored quality of care and conducted with specifically devised protocols. However, participation and adherence to therapy in older patients do need special monitoring. It is particularly important to ensure that alternative options for treatment are fully explained to older patients and to their

relatives. The opinion of the patient should be taken into account in the choice of therapeutic interventions.

Multidimensional geriatric assessment for elderly cancer patients

The use of multidimensional assessment and measure of comorbidity opens new prospects for the management of cancer in older patients. Calendar age has in the past been considered as an exclusion criteria from clinical trials, although a large proportion of people reach old age without substantial loss of function. Therefore, older patients with a diagnosis of cancer should not be excluded *a priori* from potentially curable surgical procedures or full-dose chemo- and radiotherapy treatments. On the other hand, special consideration should be devoted toward elderly patients in whom the burden of cancer is likely to be superimposed on the effect of other diseases and disabilities.

Thus, the identification of a comprehensive functional assessment, specifically created and validated for the elderly patients with cancer, should be a primary concern. Geriatric assessment comprises the following basic dimensions: physical health, activities of daily living and mental health. Socioeconomic status and level of informal care are also important. There is a need of comparable data within the EC. Considering the diversities among different countries, the identification of reliable instruments for measuring these aspects should be a topic for future research.

Physical health. Oncologists and geriatricians have become more aware that the general health status and prognosis of older cancer patients are related both to the extent of the cancers as well as to comorbid conditions. In comparison, in young adults, the neoplasm is often the only disease present. Since measures of comorbidity have not been included in studies on cancer in the elderly, the reliability of the scarce information available is questionable. In fact, comorbidity is likely to influence not only the impact of the cancer on health status but also clinical evolution and response to treatment.

For future research, a simple evaluation of comorbidity can be obtained by examining the presence of specific pathological conditions most relevant to the elderly patients (e.g. hearing impairment, congestive heart failure . . .). Statistical reports on the most prevalent chronic conditions in the population over 65 years of age are available in many countries.

Assessment of the relative importance of each pathological condition in the process of health deterioration is a function of its severity. Thus methods to classify severity based on observable anatomical and physiological measures should be clearly stated.

Activities of daily living. Cancer, like the other chronic conditions in the elderly, is frequently associated with the development of disability. The most frequently used approaches for the measurement of disability are the self-report and the performance methods. In the former, the patient is asked specific questions concerning his/her autonomy in several activities which are considered to be essential for maintenance of an independent life. In the performance method, physical/cognitive capacities are measured, asking a subject to perform a standardised task and evaluating his/her performance using predetermined criteria. Since different types of cancer affect specific aspects of physical function, the proper tool to be selected in each situation should be identified in future research.

Mental status. Relevant components of the health-related quality of life in the elderly are cognitive status and depression.

Cognitive functioning (*a measure of intellectual performance*). The incidence of both cognitive impairment and cancer increase with age, so in the elderly co-existence of the two is not a rare event. Hospitalisation and treatment for cancer may influence cognitive performance in the frail elderly, thus assessment of cognitive performance is mandatory to establish the effect of therapy both in terms of efficacy as well as toxicity. Complete evaluation is very time consuming and it is reasonable to rely on measures which simply allow the distinction between poor and normal cognitive function, such as the Folstein's Mini Mental State.

Depressive symptoms. The relationship between cancer and depressive symptoms in the elderly is very complex. For example, depression may be a symptom clinically evident before a conclusive diagnosis of cancer is made, a reaction to the diagnosis or a side-effect of treatment. The severity of depressive symptoms in the elderly is often the result of the growing burden of disease and disabilities rather than a 'physiological effect' of aging. Instruments for the evaluation of depressive symptoms have been used in several trials comparing different therapeutic approaches to severe chronic disease. To be used reliably in the elderly these instruments should be independent by the direct effect of somatic symptoms such as the Yesavage's Geriatric Depression Scale.

Quality of life. With regard to multidimensional geriatric assessment, instruments which are intended to measure the quality of life as a single contrast should be considered as complementary and not as substitutive. Quality of life is a reference concept as well as an important outcome variable. The effectiveness of the comprehensive geriatric assessment in cancer patients can be assessed only in clinical trials in which the ideal outcome is quality of life.

A two-pronged effect within the context of the European School of Oncology effort on cancer treatment in the elderly is suggested. This involves (1) using expertise gained within the EORTC Quality of Life Group during the last 8 years and (2) addressing the practical problems of implementing quality of life study techniques in clinical settings and outpatient clinics for elderly cancer patients in particular.

The EORTC Quality of Life Study Group method is very well regarded since it consists of a core instrument and tumour-specific questions and methods may be adapted for older cancer patients.

SUGGESTED FUNDING PRIORITIES

- A.
 1. Continuing education programs must provide valuable and valid information on cancer in the elderly and age-associated conditions.
 2. Special efforts must be made to encourage primary care physicians to attend the complex clinical problems that are likely to exist in older patients diagnosed of cancer.
 3. A variety of educational materials should be organised to address the major aspects of cancer in the elderly. This document, with appropriate modifications, can be the first step in distribution to medical health professionals and the public. For example, it has been shown that cancer registry data have made considerable contributions in sensitising the clinical community. The role of cancer registries should be emphasised for this purpose.
- B. Quality of care must be assured and demonstrated. Therefore, appropriate support should be provided for evaluation

of patterns of care studies for different tumours and in various medical care settings.

- C. The expertise of geriatricians, primary care physicians and physicians in community hospitals must be linked with the expertise of clinical oncology specialists for improving cancer treatment and care of older age patients. Special needs of older patients may create unique situations or contexts that only a team approach can provide. Clinical oncology must take advantage of the body of information that has already been developed by gerontologists for geriatric assessment. Development of information in other disciplines (e.g. epidemiology, pathology, etc.) that pursue the objective of improving cancer treatment and care of older cancer patients should be supported.
- D. Clinical trials to research tumours that occur primarily in older persons must be organised to demonstrate the efficacy and the effectiveness of treatment in the presence of the influence of the aging process. It must be emphasised that one of the major outcome parameters in this type of study must include quality of life assessment pertinent to the tumour under study.

MESSAGE FOR THE PUBLIC

Cancer in the elderly is treatable

— Age of individuals and their risk of getting cancer are closely related. As more European people are living longer, so the total number of cancer patients is likely to increase.

— Provided that the right treatment is given, those aged over 70 are just as likely to be cured as younger adults. Treatment may involve surgery, radiotherapy, drugs or a combination of these.

— Treatment of cancer patients gives them the chance to regain their sense of well-being and continue living their life as before.

— This Advisory Group endorses the European Code against Cancer (see Appendix) The following two specific priorities should be added:

1

If you are an older person you should ask for a specialist's opinion if it is suspected that you have a cancer. Treatments that can either cure or improve symptoms are available to all regardless of age.

2

Age is not itself a barrier to the successful treatment of cancer. Don't hold back because of fear! Your life is too important!

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APPENDIX

EUROPEAN CODE AGAINST CANCER CERTAIN CANCERS MAY BE AVOIDED:

1. Do Not Smoke
Smokers, stop quickly as possible and do not smoke in the presence of others.
2. Moderate your consumption of alcoholic drinks, beers, wines or spirits
3. Avoid excessive exposure to the sun.

4. Follow health and safety instructions especially in the working environment concerning production, handling or use of any substance which may cause cancer.

Your general health will benefit from the following two commandments which may also reduce the risks of some cancers.

5. Frequently eat fresh fruit and vegetables and cereals with a high fibre content.
6. Avoid becoming overweight and limit your intake of fatty foods.

7. See a doctor if you notice a lump or observe a change in a mole or abnormal bleeding.

8. See a doctor if you have persistent problems, such as a persistent cough, a persistent hoarseness, a change in bowel habits or an unexplained weight loss.

For women:

9. Have a cervical smear regularly
10. Check your breasts regularly and, if possible, undergo mammography at regular intervals above the age of 50.