The Incurable Cancer Patient at the End of Life

Medical Care Utilization, Quality of Life and the Additive Analgesic Effect of Paracetamol in Concurrent Morphine Therapy

BY

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ABSTRACT


Optimal quality of life and health care utilization are objectives of all palliative services. The aim of this study was to present background data on health care utilization and quality of life, explore potential outcome variables of health care utilization, evaluate a hospital-based palliative support service, provide a quality of life tool specially designed for incurable patients at the end of life and to establish whether paracetamol has an additive analgesic effect to morphine.

Only 12% of the patients died at home. When the period between diagnosis and death was less than one month, every patient died in an institution. Younger patients, married patients, and those living within a 40 km radius of the hospital utilized more hospital days. The "length of terminal hospitalization" and the "proportion of days at home/total inclusion days" seemed to be feasible outcome variables when evaluating a palliative support service. The hospital-based palliative support service in this study defrayed its own costs thanks to a median saving of 10 hospital days/patient, compared with matched historical controls.

A 19-item quality of life questionnaire (AQEL) was developed which evidenced good signs of reliability and validity. The item most closely correlated to global quality of life was the sense of meaningfulness. This was true for both patients and their spouses. Patients‘ levels of pain and anxiety did not increase at the end of life.

In this study we could not find any convincing evidence of an additive analgesic effect of paracetamol in morphine therapy of pain in cancer patients.

Keywords: palliative, cancer, place of death, health care utilization, quality of life, morphine, paracetamol, pain

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Look to this day,
   for it is life,
   the very life of life.
In its brief course lie all
the realities and verities of existence,
   the bliss of growth,
   the splendour of action,
   the glory of power.

For yesterday is but a dream,
   and tomorrow is only a vision.
But today, well lived,
makes every yesterday a dream of happiness
   and every tomorrow a vision of hope.

Look well, therefore, to this day.

*Sanskrit proverb*
ABBREVIATIONS

AQEL Assessment of Quality of life at the End of Life
CIPS Cancer Inventory of Problem Situations
DGS Department of General Surgery, Östersund
EORTC European Organization for Research and Treatment of Cancer
GP General Practitioner
KPS Karnofsky Performance Score
NH– Health care centre without a nursing home attached
NH+ Health care centre with a nursing home attached
NRS Numerical Rating Scale
PSS Palliative Support Service
QUALY Quality Adjusted Life Year
QoL Quality of Life
RT Radiotherapy
S.D. Standard Deviation
Sw.kr Swedish kronor
U.S. United States
VAS Visual Analogue Scale
WHO World Health Organization
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This thesis is based on the following papers which will be referred to by their Roman numerals:

I  Place of death correlated to socio-demographic factors
A study of 203 patients dying of cancer in a rural Swedish county in 1990

Bertil Axelsson & Svend Borup Christensen

II  Medical care utilization by incurable cancer patients in a Swedish county

Bertil Axelsson & Svend Borup Christensen

III  Evaluation of a hospital-based palliative support service
with special reference to financial outcome measures

Bertil Axelsson & Svend Borup Christensen

IV  Assessment of quality of life in palliative care
Psychometric properties of a brief questionnaire

Bertil Axelsson & Per-Olow Sjödén

V  Quality of life of cancer patients and their spouses in palliative home care

Bertil Axelsson & Per-Olow Sjödén

VI  The additive analgesic effect of paracetamol in morphine therapy of pain in cancer patients - A double-blind randomized study

Bertil Axelsson & Svend Borup Christensen
Submitted to Palliative Medicine

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INTRODUCTION

Death is an inevitable part of all life. Mortality has always been, and will always be, 100%. Once in every life, the time comes for dying and death. We do not know when or how, but we all know that one day it will be our turn to leave this life. Care of the dying, sooner or later, concerns us all. Care of the dying is an unceasing responsibility for the medical profession and for society at large.

Daniel Callahan (1) states that "no moral impulse seems more deeply embedded than the need to relieve suffering...... It has become a foundation stone for the practice of medicine, and it is at the core of the social and welfare programs of all civilized nations".

For a couple of decades during the 20th century (1950-70), when medical progress astonished everyone, one almost got the impression that very soon the day of total cure would arrive. Historically, doctors have never been able to do much more than palliate and comfort. This aspect of medicine was almost neglected during an optimistic era of newly introduced antibiotics, vaccines, chemotherapy, and transplantations. Every disease could be cured, if not today, then probably tomorrow. This line of thought seemed to be unconsciously extended to: "Without diseases there may be no death and dying".

In striving for immortality, increasing funds were allocated to medical care and modern hospitals were erected all over Sweden. A feeling of "a right to be cured" grew and those not cured were very reluctant to be discharged from hospital. Many a death was regarded as a failure. Hardly anyone died outside of an institution. Knowledge of how to care properly for the dying was almost forgotten. Advances in the science of medicine appeared to lead to a decline in the art of medicine (2).

Starting in England, Dame Cicely Saunders and a few health professionals came to the realization that the needs of incurably ill and dying were persistently neglected. They therefore opened the first hospice in modern times, St Christopher’s, in 1967 (3). Gradually, palliation and palliative medicine emerged as a distinct branch on the tree of medical science, focusing on optimal quality of life by controlling symptoms, by using a holistic approach including psychological, social, existential as well as the physical aspects, and by involving the family in the patient’s care (4). This approach is nowadays called the hospice philosophy and forms the basis of all palliative care. Palliative medicine is today recognized as a specialty of its own in the Great Britain,
Australia, Hong Kong and Singapore, a specialty with scientific standards as strict as any other.

In the *Oxford Textbook of Palliative Medicine* it is stated: "Palliative medicine seeks to relieve suffering and to increase the meaning and quality of life in the face of death. Several concepts, including rigorous symptom analysis and treatment, care for the whole person, patient-centered communication, ethical decision-making, interdisciplinary team work, dealing with patients and families as a whole unit, and creation of therapeutic environments, have found a secure home in palliative medicine" (5).

In Sweden, Barbro Beck-Friis has been the pioneer of palliative medicine, developing a hospital-based form of home care called the Motala Model (6). Drawing on her work as a source of inspiration, many other initiatives have been launched all over Sweden during the recent decades. Today there are numerous variations on this given theme, with organizations varying from hospices to single-handed specialist nurses.

In an era of financial restraint, decision makers, palliative care professionals and patients are all interested in how to choose the optimal palliative care model for each setting. To facilitate this choice we need ways and means to evaluate costs and effects of different programs. Unfortunately there is so far no consensus in the palliative field (7-11), which specific measures to apply in these evaluations.

Besides the lack of established measures, a specific problem in many parts of Sweden is the sparse population scattered over a vast area. Many existing services offer hospital-based home care, usually covering a radius of 20 to 40 km, round-the-clock with nurses and doctors on call. This kind of service is obviously unsuitable in a region such as the county of Jämtland, covering a geographical area with maximum radii from the hospital ranging from 85 up to 250 km, depending on the cardinal point. There have to be other solutions, based on the present medical care structure.

To try to develop such a palliative support program, feasible for sparsely populated areas, and to devise ways to evaluate it in comparison with conventional care, has been the prime aim behind the studies comprising this dissertation. As these studies emerge from a surgical department at a county hospital, 400 km from the nearest department of oncology, many patients with incurable cancer disease have been cared for by surgeons until death supervened. The extent of this palliative work at
the surgical department in Östersund is illustrated by such facts as: 412 of 642 (64%) new cancer cases annually in our catchment area (the County of Jämtland) occur in the domain of general surgery (12); almost 20% of all in-patient days per year at the Department of General Surgery (DGS) at Östersund are utilized by cancer patients who die of their disease within 6 months.

Despite the size of this patient group, surgeons generally have little or no specific education in palliative medicine, have little knowledge of recent advances in palliative treatments, and of how we can provide palliative care in a way that enables dying cancer patients to enjoy an optimal quality of life. The work behind this thesis has placed the needs of the incurable cancer patients in focus at DGS, Östersund, thereby hopefully contributing to general improvements in the palliative care provided.

**Palliative support**

Incurable cancer patients who prefer to stay at home - and their families - need readily accessible medical expertise, moral support and the security of a continuing contact with medical care.

Of tradition incurable cancer patients had to be admitted to hospital in order to obtain such support. Where hospital-based domiciliary care teams are now established, patients can be tended at home and provided with all necessary care. When patients live too far away, this way of providing palliative care is very time consuming and, as the distance increases, it gradually becomes impracticable. Nevertheless, every citizen in Sweden, regardless of place of residence, has the legal right to demand an equal provision of medical care (13). It is a challenge to try to fulfil this right, even for patients living far away from the nearest hospital.

In an area with long distances between patient and hospital, a palliative support program has to be based on existing staff resources, such as district nurses, assistant nurses, and general practitioners (GPs) working on the location. Now and then these professionals may need to consult colleagues for advice. This consultative expertise may consist of a doctor and a nurse, both with a broad knowledge and experience of palliation, who occasionally travel to the patient’s home to make a joint assessment of the patient, together with the local GP and district nurse. Apart from this, support and expert advice may be readily obtained by telephone.
Thanks to a benevolent grant from the Swedish Cancer Society in 1990 we were able to initiate a palliative support program in 1991, staffed by one full-time nurse and one surgeon (the author) participating 4 hours per week. Five other surgeons were involved intermittently. The target population consisted of incurably ill cancer patients who wished to stay at home as long as possible.

The nurse’s task was to act as a link between home and hospital, to give support to the patient, the principal carer and the district nurse, to instruct the district nurse in the care of infusers, epidural catheters, central venous catheters and other technical devices, and to give blood transfusions, low-dose chemotherapy and parenteral nutrition at home, when needed. She was based at the DGS and was equipped with a leasing car and a mobile telephone.

A prerequisite for functional collaboration between hospital staff and representatives from primary health care, is that accurate medical information is readily available whenever medical assessment of a patient is needed. This is seldom the case in ordinary care when many different professions are involved. The common factor in all assessment situations is the patient himself. Why then not equip the patient with the essential medical information?

To improve communication between the DGS and primary health care, the patient, on discharge from hospital, was given a folder with copies of the essential information from the medical records, complemented by three specific fact sheets. One listed the names and telephone numbers of all the staff involved. Another contained all the prescribed drugs, information on their effects and instructions how to administer them. The third sheet contained the precise information given by the doctor to the patient on the disease and its course. This folder was kept continuously up to date by regularly adding nursing documentation and copies of medical records from new consultations.

**Evaluation**

When the organization of the palliative support program was ready, the next question was how to evaluate it. The aim of the program was to improve quality of life at a cost not exceeding conventional care. How do we measure costs and savings in palliative care? How do we measure quality of life?
Economic evaluation

Economic comparisons in the National Hospice Study (14) and other American studies (7-10) have been facilitated by the existence of the Medicare system. All costs generated by a patient can be accounted for by checking the bills to the insurance system. The Swedish welfare system of today does not allow such distinct individual accounting of costs, which makes any economic evaluation more difficult. In spite of the availability of the Medicare costs per patient, there is so far no American consensus that palliative care saves money. The same conclusion was drawn by the Swedish Council on Technology Assessment in Health Care who sifted the world literature on palliative domiciliary care in 1999 (15). The only convincing difference was that patients and their spouses were more satisfied with palliative domiciliary care than with conventional care.

Place of death has been used in some studies as an outcome measure with economic connotations. The drawback is that the place of death only informs us about the last hour of life, saying nothing about the time prior to that. It does not say anything about the number of days spent at home or in hospital during the terminal phase. Using "place of death" may convey an impression that death at home is to be preferred to death in hospital. This is unfortunate, as some studies (16, 17) report that about 40-45% of dying cancer patients do not want to die at home.

Beck-Friis (18) has compared the costs of hospital-based home care with conventional care, by dividing the total costs of the home care program by the total number of patient days in the program. This calculation is based on the assumption that all patients in the program would spend all days from the inclusion day to death in a conventional institution if not supported by the program. If this assumption were to prove erroneous, this way of comparing costs would be unduly advantageous to the home care program.

A need for basic data on the utilization of standard medical care by incurable cancer patients arises. Long et al. (9) report that the average cancer patient spent 48 days in hospital during the last year of life. Is that true in Sweden as well?

The next step is to define one’s study population. How weak are the patients and how long before death are they admitted to the program? The bulk of care expenses accrues during the last 2 months of life (9,10,14). Obviously one can reduce the daily
costs of a palliative service by enrolling relatively strong patients early in the disease course.

It is also important to include all kind of costs regardless of account. In Sweden, some parts of medical care are defrayed by the County Council (hospitals and GPs) and other parts by the local municipalities (nursing homes, district nurses, and home-care assistants), whereas the great work done by the relatives is usually not a charge on society. It is not a justifiable achievement merely to shift costs from one account to another. Besides, any financial analysis requires readily registered variables that denote the utilization of palliative care and conventional medical care in a comprehensible way. This is a prerequisite for comparisons between different programs, whether nationally or internationally.

The traditional types of health economic evaluation unfortunately appear inappropriate for financial assessment of palliative care programs. The four standard evaluations are (19):

1. **Cost minimization.** This method assumes that the consequences of two compared programs will be alike. We then compare the costs and choose the less expensive program. Even though all terminally ill patients ultimately die, we cannot guarantee equality of care between any two palliative programs. Thus this method is difficult to apply for such a comparison. If, on the other hand, we have reason/facts to assume that the quality of care is comparable in two different programs, it would be fair to compare the costs by applying this method.

2. **Cost effectiveness.** This method takes costs as well as consequences into consideration when comparing different treatments. The consequences are traditionally measured as years of life gained. The therapy entailing the lowest cost per life-year gained is supposed to be most economical.

In palliative care it is hard to identify an outcome measure to be regarded as equivalent to years of life gained. Palliative care is not supposed to either prolong or shorten life. Whether extra days at home are a useful alternative to life-years gained can be discussed. Without doubt, a mere counting of days but excluding the quality aspect would be far from satisfactory.

3. **Cost utility.** In this method the consequences are adjusted according to quality of life. The only example so far is quality-adjusted life-years (QUALYs), in which each
health status is given a weighting. Full health is given the weight 1.0 and death 0. The problem is to find a way to determine these weights in a proper way. Usually, healthy people have been asked to grade different degrees of handicap and suffering. These gradings do not correlate well with gradings made by ill people. Inter-individual variability is also substantial, and what seems to make sense at first glance is actually no better than a crude guess.

4. Cost benefit. In this analysis costs and consequences are both expressed in money terms. The crucial point is to attach a value to the consequences, but in the palliative field there are no such calculations available.

Of the traditional health economic analyses, the cost-effectiveness approach is the most attractive. However, there are several difficulties in applying this technique in real life. The hardest task is to measure the outcome. In studies where hospice care (home care or hospital based) and conventional care have been compared, no difference in symptom control has been reported, but greater care satisfaction in the hospice group (7, 8, 20). This may permit us to assume that most palliative care programs provide care of at least the same quality as conventional care. If this is true it would be warranted to compare a palliative program with conventional care by calculating the costs for each program, i.e. using the cost-minimization technique.

Whynes (21) emphasizes that, in order to compare costs, even work provided by volunteers and staff paid for by an external agency has to be included. In Sweden, volunteers were not used at the time of this study. District nurses and assistant nurses were all employed by the municipalities and their costs were taken into account.

In home care, the most substantial workload usually is borne by the spouse and/or other family members. In most cases, this strenuous work is unpaid, usually because the spouse is retired, or sometimes because they have not been informed of their right to financial support. Each terminally ill Swedish citizen can use 60 workdays to enable a family member or a friend to stay at home to assist, with financial compensation identical to sick leave. We can register work done by spouses, but it is hard to estimate the cost of their support.

When you, as a customer, decide which of two seemingly identical products you want to buy, you want to know both the price and what you get. You may prefer a more expensive product as long as the quality is better, but if the quality is identical
it is self-evident to choose the less expensive item. This crude principle is also applicable when deciding on the organization of palliative care. The discussion in palliative care, though, is complicated by a few other considerations: 1. What size of geographical area is the palliative support service supposed to cover? 2. Will this program be equally available to all county inhabitants regardless of place of residence? 3. What degree of infirmity and what kind of family support is essential to become eligible? 4. How much of the care provided by the program is indispensable and how much is an overutilization induced by increased availability? 5. To what extent is it reasonable to offer a round-a-clock service?

The size of the area to be covered obviously influences the options. Most palliative care services have been launched in rather densely populated areas where the operating radius seldom exceeds 20-40 km. To adopt such a program in the county of Jämtland with vast distances and few inhabitants would feel inappropriate, as it would cover only a minor part of the county. Vast distances also preclude a round-the-clock service from a central base.

To define adequate utilization of care is virtually impossible. As optimal quality of life, a strictly subjective measure, is the main objective of all palliative care, the patient is probably the only one able to define adequate care utilization. We also have to be aware that no economic analysis so far has been able to set a price on patient autonomy. To the individual, incurably ill with cancer, the ability to stay in command, to have the right to decide how long to stay at home and when to go into hospital, and to decide when to discontinue treatment, is invaluable.

The lack of base-line economic data from the conventional care setting complicates attempts at evaluation. The lack of established variables for measuring medical utilization further increases the difficulties. The potential obstacles to completing a randomized controlled trial with terminally ill patients are numerous: huge numbers would be needed to make the groups comparable, many patients would probably refuse the random allocation procedure or withdraw (22), a spread-over effect between study group and control group is likely as they will be cared for by the same staff.

These considerations constitute the background to the methodological compromises and decisions involved in the economic evaluations in this dissertation.
Quality of life of patients with incurable cancer

As morbidity and mortality have been felt inadequate as the sole outcome measure in many comparative evaluations of different treatment modalities, quality of life has emerged as an appropriate complement. The parallel development over time of palliative care and the concept of quality of life (QoL) is remarkable. QoL as a value is self-evident. Naturally everyone is interested in enjoying optimal QoL. Optimization of QoL is the ultimate aim of all palliative endeavour. Unfortunately there is no generally accepted definition of QoL.

When approaching the concept, several questions emerge: How do we define QoL? Who should define it? Is there a single definition covering all situations? Does the definition of QoL remain stable over time, historically and throughout the span of an incurable disease? Is the definition identical for two different individuals, from two different cultures?

The World Health Organization states that health is not merely the absence of disease or infirmity but also physical, mental and social well-being (23). This statement has promoted the development of the QoL concept towards a multidimensional definition.

In the literature we find many attempts to define QoL. The angle of approach differs. Some authors emphasize normality, stating that QoL can be "viewed as fulfillment, the ability to lead a normal life" (24), or "the ability to use one’s mental abilities, to think clearly, to see, to love and be loved, to make decisions for oneself, to maintain contact with family and friends, to live at home and to walk" (25). Some focus on satisfaction by claiming that QoL is "the degree of need satisfaction" (26) or that it is "the extent to which pleasure and satisfaction characterize human existence" (27). Other authors emphasize individuality when defining QoL as "the capacity of the individual to realize his life plans"(28) or "the perception of personal meaning" (29).

The most prevailing definition involves a comparison between the current status and the one desired (30, 31). Cella and Tulsky (32) suggest that QoL should be defined as "patients’ appraisal of and satisfaction with their current level of functioning compared with what they perceive to be possible or ideal"; the narrower the gap between the two, the better the QoL (33).
In this study, QoL is perceived as an individual experience as private as the experience of pain and happiness. Only the individual himself can state whether his present QoL is high or low. There is no thermometer with which we, as staff, can objectively measure the QoL of a patient in digital numbers. But by asking the individual, we can obtain a measurement (34). We now know that there are major disparities between patients’ ratings and the ratings of family members, though the latter still correlate better to patients’ ratings than do those made by staff (34, 35).

QoL contains a relative judgement. The individual has to compare present circumstances with an imaginary status of maximal QoL, completely freely chosen by the individual. When making this comparison between the present and the imagined, the individual also is completely free to give different weightings to different dimensions of the QoL concept. This accounts for many of the surprising differences in QoL between two persons with seemingly the same physical conditions, and also explains how seriously ill and handicapped persons can claim a surprisingly high QoL.

If we stick to the point that QoL is strictly a personal experience that is based on a comparison between the present and an imaginary status, the implication is that an ability to imagine is a prerequisite to the experience of QoL. But what about the confused cancer patient and/or the one with impaired short-term memory? Can they not experience QoL or a suboptimal QoL at all? A definition of the QoL concept ought to include every patient, regardless of mental capacity.

A possible way to tackle this problem is to include suffering. Someone lacking the ability to imagine the future or to remember the past is still able to suffer in the present situation - to suffer from thirst, hunger, cold, pain, or lack of physical contact at this very moment. When all these instant sufferings are abolished, the individual lacking all imaginative ability experiences his or her optimal quality of life. Once basic needs are fulfilled the individual does not suffer, unless he/she is able to imagine some other condition than the present, and actually suffers from the disparity between the actual and the ideal.

By this rationale QoL may be defined as the degree of freedom from suffering - suffering being used in a broad sense, including a suboptimal physical status as well as a suboptimal psychological, social, or existential state of being as defined by the individual.
Researchers during the last two decades have gradually arrived at some kind of consensus about the multidimensional properties of the QoL concept (36-38). Physical, psychological, and social aspects are generally accepted as vital components of QoL (32, 38-41).

In palliative care, another mandatory dimension is the existential (42-44). Questions about meaning, guilt, religion, and what happens after death, are some of the issues that frequently preoccupy the minds of incurably ill patients. Many of these thoughts may be completely new to the patient. The novelty makes it hard to find appropriate words to express these very private thoughts. This difficulty may even add to the suffering of the dying person.

The definition of QoL should be independent of diagnosis or stage of the disease. The instruments with which we measure QoL have to be appropriately adapted to specific diagnoses and/or stages of disease. Otherwise they are unlikely to detect relevant problem areas and significant changes in QoL associated with that specific disease or stage of disease.

The perceived QoL on the individual level is dependent on both the historical and the cultural settings. History and culture both influence the image of the ideal. The image of the ideal state in the mind of a 19th century farmer is likely to be a world apart from that of a yuppie in the 1990s. In the same way, the image of the ideal will differ between a north European atheist and a Buddhist monk. As long as basic needs are provided for, it is not self-evident that the QoL of one should surpass the other. It all depends on the degree of suffering caused by disparities between the actual and the ideal.

**Quality of life measurement**

Who should measure? Referring to the arguments above, that QoL is a very private experience, it is self-evident that the most honest way to measure it is by letting the patients themselves rate their own QoL. Slevin et al. (34) reported a poor correlation between patients’ and doctors’ ratings and also a wide variability between doctors’ and other health professionals’ ratings concerning the same patient.

How should we measure? Questionnaires are suited to repeated administration to large numbers of patients. In routine praxis, interviews are too time-consuming and expensive, but are a necessary complement in some research situations.
What should we measure? Items from the physical, psychological, social, and existential dimensions seem the most appropriate in palliative care, according to the present consensus. When selecting items from different dimensions, the situation of the presumptive target population has to be borne in mind. The items have to be regarded as relevant by the respondents (44). They have to focus on an appropriate capacity level. Thus it is not feasible to use exactly the same items for a healthy population, a cancer population during potentially curative surgery, and a group of incurable cancer patients involved in a palliative care program (42, 44).

What scale should we use? Two main traditions dominate the existing questionnaires: Likert scales and visual analogue scales (VAS). Likert scales consist of given answer options with verbally described distinct steps such as never, seldom, sometimes, often, always. A VAS is a 10 cm long line with a verbal anchor at each end, defining the two extremes. The most classic is the VAS for pain. The advantage with the VAS is that it has innumerable answer options, it is sensitive to change, and does not force any `in between´ answers into any given alternative. Drawbacks are a more time-consuming registration of the answers and that some patients may find it intellectually hard to grasp the continuum of a specific item. In reality the recorded millimetre registrations on the VAS are grouped in 10 or fewer units to facilitate the result analysis, thus in some ways reminiscent of a category scale such as Likert scales.

A methodological problem with Likert scales is that the verbal options are converted into numbers during the analysis. This assumes that there is an identical difference in experience between each one of the answer options - otherwise comparisons of means, etc, will be meaningless.

**Quality of life instruments**

A vast number of QoL instruments exist today. To measure QoL in a certain population, it is crucial to select an instrument appropriate to that specific group of patients. Development over the last 50 years started with the Karnofsky Performance Status (= KPS; 45), which was created by two oncologists in 1949 to determine nursing requirements on an oncological ward. It is observer based, and strictly physical, with 10 steps ranging from 100 (normal, no complaints) to 0 (dead). It is widely used in research to categorize the patients included. Its lack of multidimensionality disqualifies it from being a QoL measure in the modern sense of the word, though it can be regarded as a pioneer and is still widely used.
Some of the existing QoL instruments are of a general nature, rather than disease specific. Examples of these general instruments are the General Health Questionnaire (GHQ; 46), the Sickness Impact Profile (SIP; 47), the Nottingham Health Profile (NHP; 48), and the Short Form 36 (SF-36; 49).

LASA (= Linear Analogue Self-Assessment; 50) from 1976, was the first QoL questionnaire devised specifically for cancer patients. It was developed to measure the impact of breast cancer and its treatment on QoL. The 25 items, each with a VAS, considered physical, psychological and social domains.

Examples of other cancer-specific QoL instruments designed for clinical trials in oncology are Selby’s LASA (51), the Functional Living Index: Cancer (FLIC; 52), the Rotterdam Symptom Checklist (53), the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30; 38), the Functional Assessment of Cancer Therapy Scale (FACT; 54), and the Cancer Inventory of Problem Situations (CIPS; 55).

The FLIC (52) was the first to introduce a graded linear analogue scale, i.e. a line marked with integers between 1 and 7 and with a verbal anchor at each end. At the time when we initiated the studies comprising this thesis, the only cancer-specific instruments available in Swedish were the CIPS and the EORTC QLQ C-30.

The CIPS has 131 items where the patient is asked to grade the appropriateness of a statement between 0 (= no problem) and 4 (= severe problem). The purpose is to detect disease-related problem areas in everyday life for cancer patients and to be able to assess these areas again after certain attempts at rehabilitation. The length of this instrument limits repeated use, as it takes some 20 minutes to complete. Its strength is that more than one question explores each problem area, thus increasing its reliability.

The EORTC QLQ C-30 is a core questionnaire consisting of 30 items concerning physical, emotional, social and economic dimensions. Tremendous efforts have been invested in the process of developing this questionnaire available in most European languages. Besides this core questionnaire, the EORTC has developed many disease-specific modules which one can use to suit most major cancer diagnoses. Unfortunately, no palliative module is available so far, which makes EORTC QLQ C-30 appear too healthy. The current core questionnaire unfortunately lacks items tapping the existential domain.
QoL instruments specifically developed for cancer patients in the palliative setting are the MacAdam assessment of suffering in terminal illness (56), the McMaster Quality of Life Scale (MQLS; 35), and The McGill Quality of Life Questionnaire (MQOL; 58).

MacAdam (56) has developed a shorter 20-item version from the initial questionnaire with 43 items asking incurably ill cancer patients to consider their past week and to use a 5-point Likert scale. The original aim was to use the scale during initial assessment by a member of any profession in the hospice/palliative care team, i.e. not self-administered.

The MQLS (35), developed in 1995, consists of 17 items covering physical, psychological and existential domains. In 3 of the items the patient is first asked to identify one of the most troublesome physical symptoms and to grade it on a 7-point scale with a verbal anchor at either end. The patient is asked to consider the past 2 days.

The MQOL (58) was devised in 1996 by a team that decided on 32 relevant items covering physical, psychological, social, and existential domains. It asks the patient to consider the previous day and to indicate on a 7-point Likert scale any change attributable to the illness.

Unfortunately none of these three assessment instruments was available in Swedish back in 1991, when this study commenced. As mentioned above, the CIPS appeared too time-consuming for repeated use, while the EORTC QLQ C-30 appeared to be devised for healthier patients as well as having no items tapping the existential domain. This urged us to devise a new QoL instrument specifically designed for Swedish cancer patients within palliative care.

**Paracetamol**

Pain relief is crucial for optimal QoL. For the treatment of nociceptive cancer-related pain, the WHO devised the analgesic ladder of 1986 (59). Its didactic stepwise strategy has gained world-wide recognition. The ladder recommends the use of non-opioids through all steps. In Sweden, paracetamol has been the non-opioid analgetic used most frequently during the last decade. The third step of the ladder has been synonymous with slow-release morphine and paracetamol (60, 61). The underlying rationale was a theoretically additive effect of the centrally acting morphine and the
peripherally acting paracetamol. We have searched the literature in vain for scientific evidence to support this routine.

Many severely ill cancer patients underline the importance of convenient drug administration. Many have difficulty in swallowing and each extra tablet is burdensome. The paracetamol tablets - normally prescribed 2 tablets 4 times a day - are among the largest and most frequently questioned. Do they really improve the pain control during concurrent morphine therapy? If ‘yes indeed’, we have to inform our patients more carefully, because many patients reduce the dose or quit by themselves. If not, the QoL of many would improve merely by not having to swallow these tablets.

Paracetamol (acetaminophen) was introduced into clinical medicine by von Mering in 1893 (62). Since the 1950s it has been extensively used for the treatment of pain and fever. Paracetamol’s mechanism of action is still unclear (63, 64). Traditionally it has been regarded as an analgesic having a peripheral action. Its effect on prostaglandins in peripheral tissue is weak (65) and paracetamol does not have any anti-inflammatory effect at clinically relevant doses in humans (66). Recent experimental (67-70) as well as clinical investigations (71-73) strongly favour a direct action on the central nervous system.

Paracetamol has pharmacokinetic properties, such as liposolubility and weak binding to plasma proteins, which enable it to cross the blood–brain barrier (68). Its antipyretic effect as such, mediated by inhibiting prostaglandin synthetase in the brain, signifies paracetamol’s central action. Another sign is the 2–hour latency between the peak plasma level of paracetamol and its maximum analgesic effect, which probably reflects the distribution kinetics of paracetamol within the central nervous system (71, 74). Animal experiments have provided indicia for a central effect involving serotonergic pathways in a way reminiscent of morphine (68, 70, 71).
THE AIMS OF THE STUDY

1. to ascertain the impact of socio-demographic factors on the place of death of incurable cancer patients (Paper I);

2. to elicit baseline data on health care utilization by incurable cancer patients (Paper II);

3. to explore the potential use of economic outcome measures such as duration of the terminal hospitalization, proportion of days spent at home/total inclusion days, and days at home during the last 2 months of life (Papers II, III).

4. to evaluate the economy in a hospital-based palliative support program compared with that in conventional care (Paper III);

5. to develop a brief QoL instrument adapted specifically to the palliative care setting and to describe its psychometric properties (Paper IV);

6. to explore how the QoL of incurable cancer patients and their spouses changes at the end of life (Paper V);

7. to ascertain whether paracetamol has an additive analgesic effect during concurrent morphine therapy (Paper VI).
Figure 1. County of Jämtland with County Hospital of Östersund (▼), and primary health care centres with (▲) and without (●) nursing home attached. The circle marks the area within 40 km radius of Östersund.
MATERIAL AND METHODS

Geographical characteristics

Sweden is a country with 8.7 million inhabitants spread over an area of 449,000 square kilometres. The county of Jämtland is relatively sparsely populated, with 130,000 inhabitants spread over 49,443 square kilometres (1.5% of the population on 11% of the area of Sweden). Jämtland has only one hospital - situated in the city of Östersund. Primary care was at the time of the investigation provided by 27 health care centres spread throughout the county (Fig. 1). In 12 cases, the centre had a nursing home attached. No palliative care programs were available before the present study; no private care either, but two GPs, two orthopaedic surgeons, and one gynaecologist in Östersund.

Jämtland is an inland county situated in central Sweden, adjoining the Norwegian border. The western part of the county, close to the border, is mountainous and mainly uninhabited with the exception of a couple of river valleys and ski resorts. East of the mountains, vast areas of sparsely inhabited afforested areas predominate. Along numerous lakes and rivers, there is some agricultural activity, based mainly on dairy production. The population centre is Östersund and its hinterland along the shores of Lake Storsjön, holding approximately half of the county’s population. Östersund is the main service centre, with hospital, education, governmental services and military garrison. Tourism and forestry dominate the economy in the rural parts.

The Department of General Surgery (DGS) in Östersund had 104 beds in 1990 and offered specialist care in urology, vascular surgery, gastrointestinal surgery and endocrine surgery. Today there are 68 beds within general surgery. The nearest university hospital and oncological department is at Umeå, 400 km away. A medical oncologist from Umeå visits Östersund once a week.

Patients

I+II. All patients (n=203) in Jämtland who died in 1990 of a carcinomatous disease affecting the gastrointestinal tract, the urogenital organs, skin, breast, or thyroid were included in the study. These diagnoses represented the panorama customarily treated at a department of general surgery.
The patients were traced by the death certificates issued by the DGS, and complemented with information on vital statistics from all 38 parish registries in the county, thus also including patients who died outside the DGS.

All medical records were analysed to ascertain the main cause of death, the place of death, socio-demographic factors, and data on health care utilization. The latter was divided into two arbitrary groups: last 6 months of life and the preceding period.

**III. Study group:** All 57 patients who received support from the palliative support team from February 1991 to August 1993. Criteria were: 1. A symptomatic, incurable cancer disease. 2. The cancer disease had to be within the field of general surgery. 3. The patient had to live within 40 km of the County Hospital. 4. The patient had to express a wish to stay at home. 5. A principal carer had to be ready to support the patient at home. All study patients carried a folder where all home care utilization was recorded in a diary, both profession and time spent (travel time included).

**Control group:** Of the 203 patients who died in 1990 in Jämtland of carcinomatous disease, 41 were matched with study patients older than 57 years, regarding age, diagnosis, place of residence, and as far as possible even for sex and marital status. Their overall health care utilization was compared with that of the study group. Particular attention was paid to the period during which the study patient in each pair received support from the palliative support program. The same number of days before death were analysed regarding institutional utilization by the matched control patient, in order to calculate the ratio between days at home/ total inclusion days.

**Reference group:** 15 consecutive patients with symptomatic, incurable carcinomatous disease who fulfilled the same criteria as the study group, but who lived beyond the 40-km radius from the hospital. All reference patients were equipped with a folder for regular registration of home care utilization.

**IV. Group A:** 30 consecutive patients with symptomatic, incurable carcinomatous disease treated at the DGS.
**Group B:** 28 patients who received support from the hospital-based palliative support team and who were willing to answer QoL questionnaires.
**Group C:** 13 patients eligible for support from the palliative support team but who lived too far away (>40 km from the hospital) and were willing to answer QoL questionnaires.
Reliability was analysed by asking patients in group A to complete the questionnaire twice, with a 3-day interval. Correlation values between the two registrations were calculated.

Validity. Patients in group B completed one AQEL questionnaire and one CIPS questionnaire within 2 weeks. Correlations between corresponding items in these two registrations were calculated (= concurrent validity). Correlations were also computed between Karnofsky Performance Status (KPS) and the strength item and the total score of the AQEL.

Construct validity was examined by factor analysis and the extent to which the instrument yielded factors with a logical composition. The criteria for inclusion of an item in a factor were a factor score of >0.50 and a correlation within a factor between the included items of >0.30. Registrations from patients in groups A, B, and C were included in the factor analysis, i.e. 71 patients in all.

The ability of the instrument to detect change over time was investigated by asking group B patients to complete a questionnaire every month until they died, or withdrew from participation.

V. 37 patients treated by the palliative support service and who agreed to complete one or more QoL questionnaires (the AQEL) and had a spouse agreeing to do likewise were included in this study.

On 84 occasions, patient and spouse completed QoL questionnaires, within the same week, at most 30 weeks before the patient’s death. Questionnaires were analysed in groups according to how many weeks before death they were completed, thus forming a 1–2-week group (n=10), a 3–6-week group (n=13), a 7–10-week group (n=18), a 11–14-week group (n=11), a 15–20-week group (n=14), and a 21–30-week group (n=18). Mean values were compared over time, 23 observations from 1-6 weeks were compared with 23 observations from 7-12 weeks for statistically significant changes, and patient-spouse paired observations were compared over time.

VI. Incurably ill cancer patients with ongoing medication with slow-release morphine and paracetamol were invited to participate. To avoid confounding effects of other therapeutic measures on the pain level during the 2-week study period, we excluded patients having had chemotherapy, radiotherapy or strontium therapy during the preceding 2 months. Also excluded were patients who had commenced amitryptiline
treatment during the last month, and patients started taking corticosteroids or NSAIDs during the previous fortnight. The numerical scale rating for pain should be 3 or less at inclusion.

We approached 49 incurably ill cancer patients. Seven of these declined to participate for personal reasons, and 42 patients accepted after receiving informed consent.

Twelve patients dropped out after a median of 2 days (range 0–9 days) due to: rapid deterioration (n = 3), septicemia (2), nausea (2), difficulty in swallowing the capsules (2), acute paraplegia (1), sudden pain from the liver (1), and diarrhea (1). These 12 patients did not differ significantly from the study group concerning gender, age, diagnosis, site of pain, type of pain, Karnofsky, NRS for pain, dose of slow-release morphine, or treatment arm.

The remaining study group consisted of 30 patients. We chose a double-blind randomized placebo-controlled crossover design for this study. The patients were randomized to receive 1000 mg of paracetamol or placebo four times a day for one week. The following week, patients crossed over to receive the other modality, thus serving as their own control.

The patients were asked to record daily their average pain level on a numerical rating scale (NRS; 0–10) and the amount of extra morphine consumed. On days 0, 7, and 14 they filled in the QoL questionnaire (AQEL, Fig. 8) concerning the preceding week. One item was "How much pain have you had last week?" and another "How has your quality of life been last week?".

On days 4 and 11 a blood sample was taken to check the serum level of paracetamol. The intention was to take the blood sample 1-3 hours after ingestion. The analyses were run on an Abbott ADx instrument using fluorescence polarization immunoassay (FPIA, 75). The therapeutic interval was considered to be 65–130 µmol/litre and the half-time 2-3 hours (63, 74). The results were stored separately until the conclusion of the study.

On day 15 the patients were asked to state in which week they had felt most pain, which week their quality of life was best, and whether their health had improved or worsened. These three questions had one answer alternative, which implied no change/no difference.
Statistics

Chi-2 analysis and non-parametric tests such as Mann-Whitney U, Kruskal Wallis, and Wilcoxon signed rank test were used when comparing groups. The non-parametric analyses were chosen because of small numbers and frequently skewed distributions (76). Factor analysis (orthogonal varimax transformation) and correlation values were used when devising and describing the new QoL questionnaire.

In paper VI the probability of an analgesic effect of paracetamol was determined to 0.2, which implied that of 30 evaluable patients, 10 had to experience a positive effect to get a significant result on the 5% level. This study design may discount a significant paracetamol effect if the probability for this effect is set to 0.15 or less. We decided that the probability of a paracetamol effect ought to be at least 0.3 or more in order to warrant a routine prescribing together with slow-release morphine.
RESULTS AND COMMENTS

I. Place of death in relation to socio-demographic factors.

Of the 203 patients who died of cancer diseases (treated by DGS) in 1990 in Jämtland, 129 (64%) died in hospital, 49 (24%) in local nursing homes and 25 (12%) at home. Of the 129 patients dying in hospital, 110 died at the DGS, 14 in other departments (Internal Medicine or Geriatric Rehabilitation), while 5 died at University Hospital, Umeå. Twelve of the 49 patients dying in local nursing homes had lived there due to other diseases before the diagnosis of cancer was established.

Comment: Thus, 88% of the patients died in an institution. This confirms the impression of relatively few cancer patients dying at home.

Sex, diagnosis, age, and marital status

The place of death did not differ significantly according to sex. Of the 109 male patients, 11 (10%) died at home, 29 (27%) in nursing homes and 69 (63%) in hospital. Of the 94 women, 14 (15%) died at home, 20 (21%) in nursing homes and 60 (64%) in hospital.

The diagnoses were representative of the surgical panorama (Table 1).

<table>
<thead>
<tr>
<th>Cancer of</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Breast</td>
<td>23</td>
<td>11</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>7</td>
<td>3.5</td>
</tr>
<tr>
<td>Ventricle</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Pancreas</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Bile ducts/liver</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Colorectal</td>
<td>37</td>
<td>18</td>
</tr>
<tr>
<td>Kidney</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Bladder</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Prostate</td>
<td>39</td>
<td>19</td>
</tr>
<tr>
<td>Melanoma</td>
<td>3</td>
<td>1.5</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>203</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 1. Diagnoses in 203 patients who died in 1990

The place of death did not differ significantly according to diagnosis. This was equally true whether the diagnoses were analysed individually or in diagnostic groups (Fig.2).

The proportion of home deaths was found to be unrelated to marital status. We regarded anyone living with a life companion of the opposite sex as married, whether they were formally married or not. Of 87 singles, 11 (13%) died at home and of 107 married, 13 (12%) died at home. Of the 107 married patients, 76 (71%) died in hospital, which was significantly more than the 46 (53%) of the 87 who lived alone (p< 0.02). Excluding the 12 who had
lived in a nursing home before the cancer diagnosis, the difference between married and unmarried with respect to place of death was no longer significant, as all of these 12 patients were unmarried and all died in a nursing home.

The proportion of home deaths was not significantly correlated to age. Four of 22 (18%) patients younger than 60 years died at home, compared with 21 of 181 (12%) patients older than 60 years (Fig. 3, \( p=0.07 \)).

**Comment:** Neither sex, diagnosis, age, nor marital status was correlated to the proportion of home deaths in this study. Apparently these socio-demographic factors are less predictive than one might believe. Frequently, older and single persons can depend on extensive support from other family members such as children or sisters and brothers.

**Death in hospital versus nursing home**

With advancing age, fewer patients died in hospital, while more died in nursing homes (Fig. 3). Thus, 94 of 133 patients (72%) younger than 80 years died in hospital, compared with 35 of 72 patients (49%) 80 years and older \( (p = 0.0001) \). This difference was significant \( (p<0.02) \) even when we excluded the 12 patients who had lived in a nursing home before the cancer diagnosis was established. Eleven of these 12 patients were 80 years old or older.
Sixty-three of 118 patients (53%) who lived more than 40 km from the County Hospital, died in hospital, i.e. a proportion significantly smaller than for those living within the 40-km radius, where 66 of 85 patients (78%) died in hospital (Fig. 4, p< 0.001). There was no difference between the two areas regarding the proportion of patients who died at home, but more patients from beyond the 40-km radius died in nursing homes (39 of 118 = 33%), than from within the 40-km radius (10 of 85 =12%; p< 0.001).

In the area beyond 40 km from Östersund, 9 of 18 health care centres had a nursing home attached (NH+) where the local GP was responsible and where trained nurses were on duty round the clock. Nine other centres had no nursing home attached (NH–) and had to rely for admissions on a nursing home located in a neighbouring district. The proportion of hospital deaths was significantly higher in districts without a nursing home attached (29 of 44 patients = 66%) than in districts with such a nursing home (27 of 65 patients = 42%, p<0.05, Fig. 5). The reason for this was obviously that significantly fewer patients in the NH– areas died in nursing homes (20%) compared with patients from the NH+ areas (43%, p<0.05). All the 9 patients from NH– who died in a nursing home lived in that home before the cancer disease was diagnosed. Thus all other patients from the NH– areas were referred to hospital for terminal care.
Of the 85 patients who lived within 40 km of the County Hospital, 66 died in hospital, 10 in nursing homes and 9 at home. This distribution did not vary significantly from the pattern found in the NH−, i.e. the health care centres beyond the 40-km radius without a nursing home attached (Fig 5).

Comment: The proportion of deaths in nursing homes increased with advancing age, and when the patient lived further than 40 km from the County Hospital, at least when the local medical care centre had an attached nursing home. Within the 40 km radius from the hospital, despite the nearness to a nursing home, 75% of the patients preferred to die in the hospital. Obviously distances and the level of care available both influenced patients’ preference.

**Interval between diagnosis and death**

Of the 27 patients who died within one month of diagnosis, none died at home, i.e. all 27 died in an institution. In 11 of these 27 cases the cancer diagnosis was an autopsy finding. When the interval between diagnosis and death exceeded one month, a significantly greater proportion died at home (25 of 176 =14%, *p* < 0.005, Fig. 6). An increasing interval from diagnosis to death after the first month was not significantly correlated to place of death.

Comment: This is the only factor analysed in this study that was found to be related to the proportion of home deaths. Other authors report similar findings (93, 96). Obviously patients and their families - and the medical authorities and staff - need some time between diagnosis and death to be able to make arrangements for a death to take place at home.
II. Medical care utilization by incurable cancer patients in a Swedish county

Throughout the course of their cancer disease, from diagnosis to death, 208 patients utilized 12,276 institutional days in hospitals and nursing homes. The median was 44 days/patient (range 0–409 days). Of the total, 7,570 days (62%) were utilized at the DGS. During the last 6 months of life, patients spent significantly more days in nursing homes and fewer days at the University Hospital, compared with the period preceding the last 6 months (Table 2). The proportion of days at the DGS remained constant during both these periods.

<table>
<thead>
<tr>
<th></th>
<th>Last 6 months</th>
<th>From diagnosis to 6 months before death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>days</td>
<td>%</td>
</tr>
<tr>
<td>University hospital</td>
<td>485</td>
<td>6</td>
</tr>
<tr>
<td>Dept of surgery, County Hospital</td>
<td>5002</td>
<td>61</td>
</tr>
<tr>
<td>Other County Hospital departments</td>
<td>271</td>
<td>3</td>
</tr>
<tr>
<td>Nursing homes</td>
<td>2470</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>8228</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2. Type of institutional care utilized during different periods of the disease

Of the total number of institutional days, 8,228 (67%) were utilized during the last 6 months before death (median = 28.5 days).

Comment: As there was neither a palliative unit nor a department of oncology or geriatrics in the county of Jämtland at the time of this study, the DGS had to provide most of the institutional care throughout the disease course, including both the palliative and terminal phases. Patients spent only about one month (median) in institutions during the last 6 months of life. This was a valuable piece of information in the evaluation of different organizations for palliative care. It is often assumed that incurable cancer patients who do not get support from a palliative organization will spend every remaining day in an institution.

Terminal hospitalization

The terminal hospitalization, i.e. the period of continuous institutional care ending with the patient’s death (days admitted to hospital and/or nursing home), accounted for a total of 4,814 days (39% of all institutional days). The median was a terminal hospitalization of 10 days (0–365 days; interquartile interval = 23) and a mean of 23.5 days (S.D. = 44). The duration of terminal hospitalization did not vary significantly
according to diagnosis, age, sex, marital status, or distance to hospital (within or beyond 40 km).

The median number of hospital admissions during the last 6 months of life was 2 (0–11). Only 37 (18%) of the patients were admitted four times or more. These 37 were considerably younger, more often married, lived closer to the hospital, survived longer from diagnosis to death, received cytotoxic treatment more frequently, and fewer died in a nursing home, than the patients with at most three admissions.

Comment: These findings highlight the increased utilization of care toward the end of life. Obviously the duration of the terminal hospitalization varies a lot on an individual basis, as emphasized by the difference between the median value and the mean. None of the variables analysed seems to relate to the duration of the terminal hospitalization, which may qualify it as a reliable outcome measure in future evaluations of palliative measures.

**Diagnosis**

The number of days of institutional care throughout the course of the cancer disease varied significantly between different diagnoses \((p < 0.01; \text{Table 3})\). Patients with breast cancer required most institutional care (median = 80 days), followed by patients with prostatic cancer (median = 63 days). Low consumers were those with cancer of the bile ducts, liver, and miscellaneous (melanoma, thyroid cancer, and unknown primary) with median values of approximately 20 institutional days.

The greater number of institutional days utilized by breast cancer patients was concentrated to the period preceding the last 6 months of life, as neither the medical care utilization during the last 6 months before death, nor the duration of terminal hospitalization varied significantly between different diagnoses (Table 3). Nor did the number of admissions, time spent in a nursing home, or the number of days at the DGS during the last 6 months before death vary between patients with different diagnoses. The main contribution to the high total utilization of institutional days by breast cancer patients was significantly more days at the University Hospital.

The relationship between length of survival from diagnosis to death (all patients) and total medical care utilization was very weak (correlation coefficient = 0.257). There was no significant difference between patients with different diagnoses regarding days spent in a nursing home.
<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>n</th>
<th>Total institutional days (median)</th>
<th>Days at University Hospital (median)</th>
<th>Days at Dept of Surgery (median)</th>
<th>Days in nursing home (median)</th>
<th>Months from diagnosis to death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>23</td>
<td>80</td>
<td>10</td>
<td>37</td>
<td>0</td>
<td>53</td>
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<tr>
<td>Gastrointestinal</td>
<td>99</td>
<td>34</td>
<td>0</td>
<td>29</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Urological</td>
<td>67</td>
<td>59</td>
<td>0</td>
<td>33</td>
<td>0</td>
<td>22</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>19</td>
<td>17</td>
<td>0</td>
<td>15</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 3. Utilization of institutional days in subgroups of diagnoses.**

**Comment:** The results could imply that patients with incurable cancer, regardless of diagnosis, converge more toward a similar pattern of medical care utilization as death approaches. Patients with breast cancer stand out as high consumers of care, but the difference almost disappears in the terminal phase. The cause for high utilization of institutional days by breast cancer patients was not analysed specifically in this study. To some extent it may be due to care routines during periods of radiotherapy, when more patients were admitted to hospital wards earlier than is the case today. Survival time from diagnosis to death has a very marginal influence on the utilization of care.

**Distance between place of residence and the County Hospital**

Patients living close to the County Hospital (<40 km) required more admissions (median 2) during the last 6 months, than those who lived more than 40 km distant (median 1; p<0.0001). Patients within the 40 km radius spent more days at the DGS during the last 6 months of life (24 days), but fewer days in a nursing home (median 0 days, mean 8.4) compared with patients living further afield (hospital days 15; p = 0.0002; nursing home days median 0 days, mean 15.6; p < 0.02). In all other respects, also including age, diagnoses, survival time, marital status, there were no significant differences between the two groups.

**Comment:** Obviously patients living close to the County Hospital relied more on the DGS for institutional care, whereas patients further afield used the local nursing home more. Availability again appears to influence the pattern of care utilization.
Age, sex and marital status

Duration of terminal hospitalization and the total number of institutional days throughout the disease course did not vary significantly with age. However, admissions were more frequent among patients younger than 70 years during the last 6 months of life (median = 3), compared with those older than 70 years (median = 1; \( p = 0.0001 \)). Number of days at the DGS and total number of institutional days during the last 6 months varied significantly with age group (\( p < 0.005 \)). Both parameters peaked in the age interval 60-69 years, with median values of 38 days at the DGS (Fig. 6) and 47 institutional days during the last 6 months. There was no significant difference between men and women regarding the outcome measures analysed.

Marital status was significantly correlated to the number of admissions during the terminal 6 months; thus married patients had a median of 2 admissions and those living alone 1 admission (\( p = 0.0001 \)). Married patients differed from unmarried by spending more time at the county hospital during the last 6 months of life (23 days versus 15.5; \( p < 0.01 \)), and requiring more university care throughout the course of the disease (median 0, mean 10.7 days versus median 0, mean 3.1; \( p = 0.0012 \)). However, there was no significant difference in diagnosis, duration of survival, or duration of terminal hospitalization, between married and unmarried patients.

Comment: Contrary to what one might spontaneously assume, increasing age did not automatically imply more days in an institution. The peak in this study was in the age interval 60–69. As home care depends mainly on the presence of a caring family member, it is frequently assumed that male cancer patients would spend less time in an institution than females, as they are tended at home by their wives. This study did not support this assumption, as we found no difference in medical care utilization between the sexes.
Married patients utilized more admissions, spent more days at the DGS during the last 6 months of life and required more university care throughout the disease course. Whether this is the result of an anxious spouse still searching for a cure, or an incurably ill cancer patient needing a healthy spokesman to arrange the appropriate care in our medical system, is hard to say.

Palliation with surgery, radiotherapy and chemotherapy

During the last 6 months of life, 86 patients (41%) underwent surgery. The most common procedure was laparotomy (23 patients), other procedures being intestinal stoma or resection (n=18), external stoma (n=4), and gastric resection (n=3). Six orthopaedic operations were performed, three of them being laminectomy for medullary compression. Four patients underwent nephrectomy for renal cancer. Nine patients had a bilateral orchidectomy for prostatic cancer. Twelve transurethral resections were performed on patients with prostatic cancer (n=6) or bladder cancer (n=6). Other surgical interventions during the last 6 months of life were biliary endoprosthesis (n=8), esophageal dilatation (n=5), pyelostomy/stent for ureteral obstruction (n=4).

Fifty-one of the patients with gastrointestinal cancer (51%) underwent surgery during the terminal 6 months. In most of those with breast cancer and urological cancers, the surgery was performed prior to the terminal 6 months (Table 4).

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>n</th>
<th>Patients operated on during terminal 6 months (n/%)</th>
<th>Patients operated on prior to terminal 6 months (n/%)</th>
<th>Not operated on (n/%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>23</td>
<td>3 (13)</td>
<td>19 (83)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>99</td>
<td>51 (51)</td>
<td>43 (43)</td>
<td>25 (25)</td>
</tr>
<tr>
<td>Urological</td>
<td>67</td>
<td>25 (36)</td>
<td>46 (69)</td>
<td>4 (6)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>19</td>
<td>7 (29)</td>
<td>5 (22)</td>
<td>10 (56)</td>
</tr>
</tbody>
</table>

Table 4. Distribution of surgical procedures over time in different subgroups of diagnoses

Twenty-one (10%) of the patients received one (n=17) or two (n=4) courses of radiotherapy (RT) during the terminal 6 months. Target area for the treatment was in most cases painful bone metastases (n=16).

When we consider the whole course of the disease, 42 of the patients (20%) received RT for palliation. RT was most frequently given to patients with breast cancer, of
whom 16 of 23 (70%) were treated. Thirteen of 42 patients (31%) with prostatic cancer and 4 of 15 (27%) with bladder cancer received radiotherapy. Three of 10 patients with renal carcinoma (30%) were treated, as were 6 of 37 colorectal cancer patients (16%). The reason for RT of renal carcinoma was metastases to the brain and to the thoracic and lumbar vertebrae. The median age of those who received RT was 70 years, which was significantly lower than the median of 78 for those who did not (p = 0.0001).

Forty-four patients (21%) received palliative chemotherapy at some time during the disease course. Their median age was 64 years, also significantly lower than for those who did not have chemotherapy (median age=78; p=0.0001). Thirty-one of the patients receiving chemotherapy were treated during the last 6 months of life. The main indication for chemotherapy was breast cancer, where 15 of 23 (65%) patients were treated at least twice (range 2-18) during the disease course.

Of 99 patients with gastrointestinal cancer, 10 patients (10%; 7 colorectal and 3 pancreatic) received chemotherapy, as did 8 of 67 patients with urological cancer (12%; 7 prostatic and 1 bladder). Of 10 patients with renal carcinoma, 6 were given Interferons/interleukines.

One group of 39 patients (19%) were neither operated on nor received radiotherapy or chemotherapy. They were characterized by significantly higher age (median = 82, p= 0.0001) and shorter survival time from diagnosis (mean = 4.9 months, median=1, p= 0.0001) than patients who had received some kind of palliative antitumoral treatment. They were significantly more often single (25 of 39 versus 62 of 169, p < 0.001) and female (25 of 39 versus 69 of 169, p < 0.05). As we found only 3 breast cancers in this group, tamoxifen-treated breast cancer cannot explain the sex difference. The main diagnoses were the gastrointestinal cancers (25 of the 39 patients). Eight patients had miscellaneous tumours, 3 had breast cancer and 2 had urological cancers. Accordingly 25% (25 of 101) of patients dying from gastrointestinal cancers did not receive any antitumoral treatment for palliation.

Seventeen of the 39 patients (44%) who did not receive any antitumoral treatment died in nursing homes; this was significantly more than in the treated group of patients (32 of 164 = 20%, p< 0.01). The duration of terminal hospitalization did not vary between the groups.
Comment: In this study we found that 41% of the patients were treated with surgery, 10% with radiation and 15% with chemotherapy, during the last 6 months of life. Those patients who did not receive any antitumoral therapy were older, more often female and single than those actively treated.

III. Evaluation of a hospital-based palliative support service - with particular regard to financial outcome measures.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study group (n)</th>
<th>Control group (n)</th>
<th>Reference group (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>41</td>
<td>41</td>
<td>15</td>
</tr>
<tr>
<td>Male</td>
<td>24</td>
<td>19</td>
<td>9</td>
</tr>
<tr>
<td>Female</td>
<td>17</td>
<td>22</td>
<td>6</td>
</tr>
<tr>
<td>Single</td>
<td>7</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>Married</td>
<td>34</td>
<td>29</td>
<td>13</td>
</tr>
<tr>
<td>Living &lt;40 km from DGS</td>
<td>41</td>
<td>41</td>
<td>0</td>
</tr>
<tr>
<td>Living &gt;40 km from DGS</td>
<td>0</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>Median age</td>
<td>72 years</td>
<td>70 years</td>
<td>71 years</td>
</tr>
<tr>
<td>Age range</td>
<td>58 - 87</td>
<td>52 - 86</td>
<td>49 - 88</td>
</tr>
<tr>
<td>Karnofsky index (median at enrolment)</td>
<td>60 (10 - 90)</td>
<td>-</td>
<td>70 (40 - 80)</td>
</tr>
<tr>
<td>Median survival time from diagnosis to death</td>
<td>23 months</td>
<td>12 months</td>
<td>6 months</td>
</tr>
</tbody>
</table>

Table 5. Background characteristics of the three populations studied

<table>
<thead>
<tr>
<th>Primary cancer site</th>
<th>Study group (n)</th>
<th>Control group (n)</th>
<th>Reference group (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>5</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Stomach</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Pancreas</td>
<td>5</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Bile ducts</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Colorectum</td>
<td>8</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Kidney</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Prostate</td>
<td>10</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>4</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 6: Diagnoses in the three groups studied

Characteristics of the three groups studied are presented in Tables 5 and 6.

Comment: Characteristics correspond between the study group and the control group. The reference group had fewer patients with breast cancer and prostatic cancer and a shorter survival time from diagnosis to death.
Duration of the terminal hospitalization

The median duration of the terminal hospitalization for the study group (supported by the palliative support service, PSS) was 3 days (mean=9.6 days), which was significantly shorter than for the control group (10 days; mean 22.7 days; \( p = 0.017 \); Table 7). If we exclude those who died at home in both groups, this difference in duration of terminal hospitalization was not significant (study =11 days, control = 14 days; \( p = 0.090 \)). When comparing the study group with the control group we found no significant difference regarding place of death (\( p = 0.16 \)) as 20 of 57 (35%) patients in the study group and 7 of 41 (17%) patients in the control group died at home.

Proportion of days spent at home during the enrolment period

The study group patients spent 46 days (median) at home, from the date of enrolment with the PSS to death, i.e. significantly more days than the control patients during the same period of time (median 23 days; \( p = 0.0001 \)). Expressed in percentages, the study patients spent 85% of the days at home between enrolment and death, compared with 58% for control patients (Table 7), during the same period.

Days spent at home during the last 2 months of life

During the last 2 months of life, study group patients spent 44 days (median) at home, i.e. significantly more than the 38.5 days (median) for the control group patients (\( p < 0.01 \); Table 7).

Comment: The duration of terminal hospitalization, proportion of days spent at home during the enrolment period, and days spent at home during the last 2 months of life are outcome variables that focus on the last 2 months of life. All three measures showed significantly less medical care utilization by the study group, which may be an effect of the intervention by the hospital-based palliative support team.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Study group (n = 41)</th>
<th>Control group (n = 41)</th>
<th>Reference group (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days within service</td>
<td>64 (5-548)</td>
<td>64 (5-548)</td>
<td>55 (5-186)</td>
</tr>
<tr>
<td>Total institutional days from diagnosis to death</td>
<td>52.5 (0-299)</td>
<td>68 (5-409)</td>
<td>53,5 (8-107)</td>
</tr>
<tr>
<td>Institutional days prior to last 6 months</td>
<td>15 (0-280)</td>
<td>12 (0-246)</td>
<td>8,5 (0-71)</td>
</tr>
<tr>
<td>Institutional days last 6 months</td>
<td>31 (0-94)</td>
<td>37 (5-163)</td>
<td>25 (0-97)</td>
</tr>
<tr>
<td>Admissions last 6 months</td>
<td>3 (0-12)</td>
<td>3 (0-7)</td>
<td>3 (0-8)</td>
</tr>
<tr>
<td>Duration of terminal hospitalization</td>
<td>3 (0-85)</td>
<td>10 * (0-163)</td>
<td>12 (0-47)</td>
</tr>
<tr>
<td>Days spent at home after enrolment</td>
<td>46 (5-295)</td>
<td>23 *** (0-325)</td>
<td>29 a (0-184)</td>
</tr>
<tr>
<td>Ratio of days at home/inclusion days</td>
<td>85% (0-100%)</td>
<td>58% *** (0-100%)</td>
<td>72% a (0-100%)</td>
</tr>
<tr>
<td>Days spent at home during last 2 months of life</td>
<td>44 (0-60)</td>
<td>38.5 ** (0-59)</td>
<td>39 (15-60)</td>
</tr>
</tbody>
</table>

Table 7. Outcome measures referring to health care utilization

All values are median values (range). * = p< 0.05, ** = p< 0.01, *** = p< 0.001, a = p= 0.07

Other medical care utilization variables

Neither the total number of days in institutional care from diagnosis to death, the number of institutional days during the last 6 months, nor the number of days during the period following diagnosis prior to the last 6 months differed significantly between the study group and the control group (Table 7).

We found no significant differences in health care utilization when we compared the study group with the reference group (Table 7), nor was there any significant difference in the utilization of resources at home outside the PSS, such as district nurses, or domiciliary service, etc. (Table 8). The patients in the reference group did not in any case use ’night sitters’ or their legal right for next of kin to stay at home from work to nurse the patient. The extensive use of auxiliary nurses and domiciliary service staff by some study patients had no counterpart among the reference group patients. The resources utilized at home by control group patients could not be retrieved.
The median number of admissions to hospital during the last 6 months of life was three in all three groups. The median duration of support from the PSS was 64 days (range 5–548 days) for the study group.

Comment: The median time of enrolment of 64 days assures us that the PSS approached the patients during a relevant period. It is also evident that comparisons between the groups outside these last 2 months of life did not produce any significant differences.

That the study group did not use more alternative support resources (e.g. district nurses and domiciliary service) outside the hospital than did the reference group may come as a surprise. We interpret this as caused either by the very substantial workload borne by the PSS nurse, or that these services are readily available to anyone who needs them, regardless of further professional support.

**Economic analysis**

By subtracting the number of institutional days utilized by a patient in the study group during the period supported by the PSS, from the institutional days utilized by the matched patient in the control group during an identical period of time before death, we obtained the 41 values plotted in Fig. 7. A positive value means that the study patient utilized fewer institutional days than his/her matched control. The study patient utilized 10 (median) fewer institutional days (range = -118–80 days; \( p = 0.012 \)) than the matched control patient. The sum of all negative and positive values (Fig. 7) gave a net saving of 435 institutional days for the study group.

<table>
<thead>
<tr>
<th>Resource at home</th>
<th>Study (median; range)</th>
<th>Reference (median; range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant nurse</td>
<td>14.5 hours (2-157)</td>
<td>-</td>
</tr>
<tr>
<td>Surgeon</td>
<td>2 h (0-11)</td>
<td>-</td>
</tr>
<tr>
<td>District nurse</td>
<td>2.25 h (0 - 81)</td>
<td>4.5 hours (0 - 33.5)</td>
</tr>
<tr>
<td>Assistant nurse</td>
<td>0 h (0 - 79.5)</td>
<td>0 h (0 - 1.5)</td>
</tr>
<tr>
<td>General practitioner</td>
<td>0 h (0 - 3)</td>
<td>0 h (0 - 3)</td>
</tr>
<tr>
<td>Domiciliary service</td>
<td>0 h (0 - 435)</td>
<td>0 h (0 - 12)</td>
</tr>
<tr>
<td>Night sitting</td>
<td>0 h (0 - 96)</td>
<td>0 h (0 - 0)</td>
</tr>
<tr>
<td>Next of kin off work</td>
<td>0 days (0 - 12)</td>
<td>0 days (0 -0)</td>
</tr>
</tbody>
</table>

**Table 8. Resources utilized at home**
One day in a department of general surgery in a county hospital in Sweden cost 3,600 Sw. kr in 1991 (77), (100 Sw.kr. = 13.7 U.S. dollars). Thus, the cost of hospitalization was 1,566,000 Sw.kr less for the 41 patients in the study group, compared with the control group (435 x 3,600 Sw.kr).

This saving of 1,566,000 Sw.kr must of course be set in relation to the cost of running the PSS. The annual budget for this development project was 475,000 Sw.kr/year over 3 years. In 2.5 active years, 57 patients died and 12 were still alive at the end of August 1993. The costs expended on the 41 matched study patients can thus be calculated as follows: 2.5 years x 475,000 Sw.kr x 41 / 57 = 854,170 Sw.kr.

As the systematic registration of conventional domiciliary nursing by district nurses and others did not reveal any significant differences between the study group and the reference group (Table 8), no extra costs have been added in this analysis when comparing the costs of the palliative service vis-à-vis conventional care. The overall financial gain from this service will thus be the savings generated minus the costs: 1,566,000 – 854,170 Sw.kr = 711,830 Sw.kr. This means a saving of 17,360 Sw.kr/patient (711,830 Sw.kr/ 41 patients), or 2,378 U.S.dollars/patient.

Another way to make a financial assessment is to try to answer how many institutional days we had to save per patient in order to defray the costs of the PSS. Expenses of 854,170 Sw.kr divided by 41 patients give 20,833 Sw.kr/ patient. The number of non-utilized institutional days/patient needed to cover the costs of running the PSS was: 20,833 / 3600 Sw.kr/day = 5.8 days/patient.

Comment: The results of the present study indicate that the palliative support program was self-financing, provided that the study group and the control group
were comparable. However, our findings can be interpreted even more favourably, in financial terms, showing a saving of 17,000 Sw.kr per patient.

IV. Assessment of quality of life in palliative care - psychometric properties of a short questionnaire.

**Development of the AQEL (Assessment of Quality of Life at End of Life)**

The questionnaire consists of 19 quality-of-life questions and three complementary questions. The time frame chosen for all questions was the preceding week. This choice was based on the literature (37, 38, 78) and the clinical experience that these cancer patients nearing the end of life may have ‘good’ days and ‘bad’ days alternately but that the overall trend is deterioration. Thus, a time frame of one or a few days may by chance cover only one extreme.

The response format of the QoL questions was a modified visual analogue scale, the modification being that the line was interrupted by all integers between 1 and 10. The patients were asked to encircle the figure that best expressed their answer (Fig. 8). The extreme values were defined verbally, e.g. regarding pain, 1 was defined as ‘no pain’ and 10 as the ‘worst possible pain’. This particular modification

Last week:

1. Approximately how many hours per day (8 a.m. to 8 p.m.) have you been lying down?
   - 1 = One hour at the most
   - 10 = 10 hours or more

2. How much help have you needed with dressing and hygiene?
   - 1 = No help at all
   - 10 = Help with everything

3. How has your bodily strength been?
   - 1 = None
   - 10 = As healthy persons of the same age

4. How much pain have you had last week?
   - 1 = Painfree
   - 10 = Worst possible pain

5. How much nausea have you had?
   - 1 = None
   - 10 = Worst possible nausea

6. Have you had any trouble with your bowel movements?
   - 1 = None
   - 10 = Worst possible

7. Have you been able to do what you would like to do last week?
   - 1 = Not at all
   - 10 = Yes, completely
8. How has your memory been for things happening lately?
   1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
   Have had great difficulty in remembering
   No problems in remembering

9. Have you felt worried?
   1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
   Not worried at all
   Very worried

10. Have you had difficulty sleeping?
    1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
    None at all
    Very difficult

11. How has your ability to concentrate been?
    1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
    Very bad
    Very good

12. Have you felt depressed/low in mood?
    1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
    Not at all
    Very depressed/low in mood

13. How much of your worries have you shared with any member of your family?
    1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
    Nothing
    Everything

14. Have you been reckoned with by your friends as usual?
    1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
    Not at all
    Completely as usual

15. Has your day felt meaningful?
    1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
    Not at all
    Completely

16. Has anything made you happy last week?
    1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
    Nothing
    A lot

17. How easy/hard has it been to get hold of medical staff who know you when it has been needed?
    1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
    Very easy
    Very hard

18. Have you received the medical care you have needed?
    1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
    Not at all
    Completely

19. How has your quality of life been last week?
    1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10
    Very poor
    Best possible

20. How many days during the past week have you spent in a hospital/nursing home?
    _ None, _one day, _two days, _three to six days, _the whole week.

21. Are you at home or in hospital when you answer this questionnaire? _At home _In hospital.

22. Has anything especially pleasant or unpleasant happened during the past week? In your family? Among your friends? With your disease? Write a couple of lines to explain.
__________________________________________________________________________________________
__________________________________________________________________________________________

Figure 8. The AQEL questionnaire for assessment of patient’s quality of life in palliative care
of the VAS was recommended by Cohen and Mount (79) as the ideal for palliative care. It combines a high sensitivity to change with the facility of occasional assisted completion, e.g. when the patient is too weak to hold the pencil, a spouse or a member of staff can read out the questions and the patient can answer with a number.

Depending on how the question was formulated, good quality of life corresponded to a high or a low number. This format was chosen to counteract any tendency to response bias.

The items were selected to represent the physical, psychological, social, existential, and global aspects of QoL (78) as well as an estimation of the accessibility of medical care. The QoL questions were classified as follows on the basis of their content: 6 physical items (hours recumbent during the day, need for help with hygiene and dressing/undressing, physical strength, pain, nausea, trouble with bowel movements), 5 psychological items (memory, anxiety, insomnia, depression, ability to concentrate), 2 social items (sharing worries with any family member, reckoned with by friends), 3 existential items (ability to do what one wants, meaningfulness, ability to feel joy), 2 medical care items (possibility to contact staff, to receive adequate care) and one global item (How has your quality of life been the past week?). The choice of items within each domain was guided by recommendations in the literature (38, 40, 51, 80) and our clinical experience with this specific group of cancer patients at the end of life.

A brief discussion of some of the items follows.

**Physical items.** The item ´Hours recumbent during the day´ deviates from the rest by focusing on the number of hours rather than the grading of a symptom or an experience. We included it as a reflection of the deterioration of bodily functions toward the end of life which may be expressed by the amount of time spent reclining. This assumption is probably more valid in the home care setting than in institutional care. ´Need for assistance with hygiene and dressing/undressing´ is an attempt to condense an ADL assessment (39) into a single item. ´Trouble with bowel movements´ is a fusion of questions on diarrhea and constipation, but also avoids the problem of defining these concepts (39, 81).

**Psychological items.** ´Insomnia´ (Have you had difficulty sleeping?) tries to summarize different sleep disturbances in one item. ´Memory´ and ´Ability to concentrate´ were used to capture cognitive functions.
Social items. Serious illness often leads to a shrinking sphere of social interaction. The interactions with family or friends that most strongly affect QoL are insufficiently studied at the end of life. The items ‘How much of your worries have you shared with any member of your family’ and ‘Have you been reckoned with by your friends as usual’ are attempts to capture dimensions of these interactions.

Existential items. In many review articles on QoL instruments for cancer patients, the authors have stressed the need to include existential items when dealing with incurable cancer (43, 44, 79, 82). They have also pointed out that most of the available comprehensive instruments do not have even a single item representing this dimension. The item that has been most frequently suggested is the one of ‘meaning’ (43, 79, 83), which we expressed as ‘Has your day felt meaningful?’ (“Not at all” to ”completely”). ‘Ability to feel joy’ (39) and ‘Ability to do what one would like to do’ (39) try to capture other aspects of the existential dimension.

Medical care items. Items of this kind are not included in traditional questionnaires, but have been proposed by Cella (54) and Aaronson (38). In palliative care, where patients have very frequent contacts with staff, even when at home, quality of care received and ability to reach different members of staff are both essential.

Global item. Some authors highlight the importance of a global question to get an idea of the patient’s own estimation of all the different aspects of QoL. This item may reflect the impact of other factors not covered by specific questions in the instrument (38, 84). The inclusion of a global item makes it possible to identify the specific items that are most strongly related to the global dimension.

Complementary questions. Three general questions were included at the end of the questionnaire as a complement that may help to explain sudden variations in the QoL scores. Such variations may be caused by co-morbidity or factors outside the patient-carer relationship that usually remain unknown to researchers. Wenger (85) has stressed this as an important entity when interpreting QoL data in clinical studies. No existing instrument seems to gather this kind of information systematically.

Before we introduce a new questionnaire in everyday practice, it is essential to evaluate its psychometric properties, i.e. reliability and validity. Reliability can be explained as the degree of precision in measuring. A reliable thermometer shows +10 Celsius every time you measure the temperature of water 10 degrees warm. Validity
shows that the questionnaire measures what it is supposed to measure, i.e. quality of life and not only say, anxiety. A valid thermometer measures temperature, not humidity, wind, or precipitation.

**Reliability**

The test–retest correlations ranged between 0.51 and 0.97 for each of the 19 questions and 14 values were >0.70. Exact values are shown in Table 9. Factor analysis yielded seven independent factors. Test–retest correlations for the factors were computed on the basis of data from group A. These correlations ranged between 0.63 and 0.94 (Table 10).

**Comment:** Test–retest correlation values >0.70 are recommended by Selby et al. (51) as strong indicators of adequate reliability. The 0.70 cut-off was reached or exceeded by 14/19 items. In five of the items, test–retest values ranged between 0.50 and 0.70. The 0.70 cut-off was exceeded by 5/7 factors, the remaining two being fairly close, viz. 0.68 and 0.63 (Table 10).

<table>
<thead>
<tr>
<th></th>
<th>Test–retest correlation</th>
<th>Correlation to KPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hours recumbent during the day</td>
<td>0.72</td>
<td>0.49</td>
</tr>
<tr>
<td>Need for help with hygiene/dressing</td>
<td>0.84</td>
<td>0.33</td>
</tr>
<tr>
<td>Physical strength</td>
<td>0.78</td>
<td>0.66</td>
</tr>
<tr>
<td>Pain</td>
<td>0.65</td>
<td>0.23</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.73</td>
<td>0.36</td>
</tr>
<tr>
<td>Trouble with bowel movements</td>
<td>0.75</td>
<td>0.38</td>
</tr>
<tr>
<td>Ability to do what one wants</td>
<td>0.52</td>
<td>0.22</td>
</tr>
<tr>
<td>Memory</td>
<td>0.86</td>
<td>0.46</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.67</td>
<td>0.09</td>
</tr>
<tr>
<td>Insomnia</td>
<td>0.70</td>
<td>0.05</td>
</tr>
<tr>
<td>Ability to concentrate</td>
<td>0.69</td>
<td>0.46</td>
</tr>
<tr>
<td>Depression</td>
<td>0.80</td>
<td>0.34</td>
</tr>
<tr>
<td>Sharing worries with any member of family</td>
<td>0.90</td>
<td>-0.09</td>
</tr>
<tr>
<td>Reckoned with by friends</td>
<td>0.83</td>
<td>0.08</td>
</tr>
<tr>
<td>Meaningfulness</td>
<td>0.74</td>
<td>0.56</td>
</tr>
<tr>
<td>Ability to feel joy</td>
<td>0.64</td>
<td>0.53</td>
</tr>
<tr>
<td>Ability to reach staff</td>
<td>0.81</td>
<td>0.53</td>
</tr>
<tr>
<td>Obtain appropriate care</td>
<td>0.68</td>
<td>0.24</td>
</tr>
<tr>
<td>Global quality of life</td>
<td>0.75</td>
<td>0.61</td>
</tr>
<tr>
<td>Total score</td>
<td>0.78</td>
<td>0.63</td>
</tr>
</tbody>
</table>

*Table 9. Test–retest correlations and correlations with Karnofsky scores (KPS) for all AQEL items (n = 30)*
These slightly higher figures for factor reliability compared with individual items are in line with expectations. However, the fact that 5/19 items did not exceed 0.70 is no reason to dismiss them, as there are 10 options with which to answer each item. Ware (86) emphasized that the greater the number of response alternatives, the harder it is to attain high test–retest correlation values. However, the test–retest interval was as short as 3 days, which may have inflated the values. The choice of such a short period is, however, motivated by possible rapid changes in patient status.

Validity

Correlations were calculated between selected CIPS statements and corresponding AQEL items (Table 11). In general, there were moderate to strong correlations in the areas of physical and psychological problems. For the social aspects of QoL, the correlation was weak. The CIPS does not contain any questions concerning existential aspects, quality of medical care, or global quality of life. It is noteworthy that the sum total of the questionnaires correlated strongly (0.80).

<table>
<thead>
<tr>
<th>CIPS item (number)</th>
<th>AQEL item</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting/lying (1)</td>
<td>Hours recumbent</td>
<td>0.66</td>
</tr>
<tr>
<td>Eat, dress, wash independent (9-12)</td>
<td>Ass. with hygiene/dressing</td>
<td>0.79</td>
</tr>
<tr>
<td>Pain (51-52)</td>
<td>Pain</td>
<td>0.78</td>
</tr>
<tr>
<td>Leisure difficulties (20-21)</td>
<td>Ability to do what one wants</td>
<td>0.64</td>
</tr>
<tr>
<td>Memory (50)</td>
<td>Memory</td>
<td>0.62</td>
</tr>
<tr>
<td>Insomnia (22-24)</td>
<td>Insomnia</td>
<td>0.81</td>
</tr>
<tr>
<td>Concentration (49)</td>
<td>Ability to concentrate</td>
<td>0.63</td>
</tr>
<tr>
<td>Depressed (44,47,48)</td>
<td>Depression</td>
<td>0.54</td>
</tr>
<tr>
<td>Talk with partner about feelings, future, illness (113-115)</td>
<td>Share worries with family</td>
<td>0.07</td>
</tr>
</tbody>
</table>

All (questions included above) Total score 0.80

Table 11. Correlations between selected CIPS items and corresponding AQEL items (n = 28)

Further validation was performed by computing correlations between AQEL items and the KPS (Table 9). The item ‘physical strength’ had a correlation of 0.66, and the total QoL score 0.63 with the KPS, thus illustrating adequate convergent validity. Other items such as ‘anxiety’, ‘insomnia’, ‘pain’, and ‘sharing worries with family’ had low correlations (0.05–0.23) suggesting adequate discriminant validity.
<table>
<thead>
<tr>
<th>Item</th>
<th>Symptoms</th>
<th>Life content</th>
<th>Friends</th>
<th>Cognitive</th>
<th>Family</th>
<th>Medical care</th>
<th>Existential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hours recumbent during the day</td>
<td>0.54</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Help with hygiene/dressing</td>
<td>0.61</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical strength</td>
<td></td>
<td>0.79</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>0.75</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>0.72</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trouble with bowel movements</td>
<td>0.62</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ability to do what one wants</td>
<td></td>
<td>0.86</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memory</td>
<td>0.86</td>
<td>0.89</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.86</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>0.86</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ability to concentrate</td>
<td></td>
<td>0.84</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>0.87</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Share worries with family</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reckoned with by friends</td>
<td></td>
<td></td>
<td>0.63</td>
<td>(0.43)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meaningfulness</td>
<td>(0.59)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ability to feel joy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reach staff</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obtain appropriate care</td>
<td></td>
<td></td>
<td>(0.54)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global quality of life</td>
<td>0.65</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test-retest correlations (n=30)</td>
<td>0.85</td>
<td>0.86</td>
<td>0.77</td>
<td>0.81</td>
<td>0.94</td>
<td>0.68</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Table 10. Factor analysis (orthogonal varimax transformation; n=71). All positive values > 0.40 are shown. Loadings in parentheses indicate that items are not included in the respective factor.
Sensitivity to change was investigated by testing the extent to which scores declined when approaching death. Figure 9 illustrates the distinct decrease in mean total score (sum of 19 items) over time.

**Comment:** The finding that factor analysis yielded factors with a logical composition strengthens the validity of the questionnaire. Most items loaded on only one factor and in a reasonable pattern. The fact that the items ‘meaning’ and ‘global quality of life’ loaded on both ‘Life content’ and ‘Existential’ is understandable. The item ‘obtain appropriate care’ loaded on ‘Friends’ and ‘Medical care’, while ‘reckoned with by friends’ loaded on ‘Friends’ and ‘Cognitive’. This is harder to explain. However, these four items were the only ones that loaded on more than one factor.

V. Quality of life of cancer patients and their spouses in palliative home care

**Patient - correlations to global quality of life**

To ascertain which items contributed most to the patient’s score for the global quality-of-life item (‘How has your quality of life been last week?’), we analysed the correlations between the global item and the other items. All items had similar variances and no curvilinear relations were found in the scattergrams. The top five correlations were: ‘meaningfulness’ 0.79, ‘ability to do what one wants’ 0.71, ‘physical strength’ 0.58, ‘hours recumbent’ 0.58, and ‘ability to feel joy’ 0.57. Next, in descending order were: ‘ability to concentrate’, ‘anxiety’, ‘nausea’, ‘depression’, and ‘assistance with hygiene and dressing/undressing’ - all items with a correlation of approximately 0.45. The lowest correlations with global QoL were obtained for: ‘reckoned with by friends’ 0.21, ‘pain’ 0.19, ‘defecation problems’ 0.06, and ‘sharing worries with family’ 0.003.

**Comment:** The importance of existential and physical activity items on the global QoL stands out, meaningfulness having the highest correlation to global QoL of all
items. Psychological items trail behind and social items and pain seemed to be entirely without impact. The result regarding pain should not be interpreted, however as indicating that severity of pain has no effect on patients’ QoL. Ferrel et al. (39), who compared 50 cancer patients in pain with 50 pain-free cancer patients in the same disease state, found that the former group had significantly poorer QoL in all dimensions.

**What was worst?**

Table 12 provides information on which items deviated most from 10 (= maximum QoL) during the terminal phase. We found the lowest mean values for the following items: ‘ability to do what one wants’, ‘physical strength’, ‘global quality of life’, and ‘meaningfulness’. ‘To contact staff’ and ‘get appropriate care’ seemed to be least problematical. During the last 6 weeks of life, the worst two scores were reported by approximately 74% of the patients regarding ‘ability to do what one wants’, 56% for ‘physical strength’, 52% for ‘global QoL’, 48% for ‘meaningfulness’, and 26% for ‘ability to feel joy’.

<table>
<thead>
<tr>
<th>Item</th>
<th>Mean 7-12 weeks (n = 23)</th>
<th>Mean 1-6 weeks (n = 23)</th>
<th>Signif. (P= )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability to do what one wants</td>
<td>3.2</td>
<td>2.1</td>
<td>n.s. (0.27)</td>
</tr>
<tr>
<td>Physical strength</td>
<td>3.1</td>
<td>2.5</td>
<td>n.s. (0.45)</td>
</tr>
<tr>
<td>Global quality of life</td>
<td>5.3</td>
<td>3.3</td>
<td>0.017</td>
</tr>
<tr>
<td>Meaningfulness</td>
<td>4.9</td>
<td>3.5</td>
<td>n.s. (0.13)</td>
</tr>
<tr>
<td>Ability to feel joy</td>
<td>6.0</td>
<td>4.7</td>
<td>n.s. (0.061)</td>
</tr>
<tr>
<td>Concentration</td>
<td>7.3</td>
<td>5.5</td>
<td>0.023</td>
</tr>
<tr>
<td>Depression</td>
<td>6.8</td>
<td>5.9</td>
<td>n.s. (0.23)</td>
</tr>
<tr>
<td>Hours recumbent</td>
<td>6.5</td>
<td>5.9</td>
<td>n.s. (0.44)</td>
</tr>
<tr>
<td>Help with hygiene/dressing</td>
<td>8.2</td>
<td>6.0</td>
<td>0.020</td>
</tr>
<tr>
<td>Nausea</td>
<td>7.6</td>
<td>6.3</td>
<td>n.s. (0.053)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>7.0</td>
<td>6.4</td>
<td>n.s. (0.27)</td>
</tr>
<tr>
<td>Defecation problems</td>
<td>7.8</td>
<td>6.7</td>
<td>0.031</td>
</tr>
<tr>
<td>Pain</td>
<td>7.0</td>
<td>6.7</td>
<td>n.s. (0.71)</td>
</tr>
<tr>
<td>Memory</td>
<td>7.9</td>
<td>6.7</td>
<td>n.s. (0.33)</td>
</tr>
<tr>
<td>Sharing worries with family</td>
<td>6.6</td>
<td>7.1</td>
<td>n.s. (0.72)</td>
</tr>
<tr>
<td>Reckoned with by friends</td>
<td>8.8</td>
<td>7.4</td>
<td>0.043</td>
</tr>
<tr>
<td>Insomnia</td>
<td>8.7</td>
<td>7.5</td>
<td>n.s. (0.12)</td>
</tr>
<tr>
<td>Reach staff</td>
<td>9.2</td>
<td>9.6</td>
<td>n.s. (0.64)</td>
</tr>
<tr>
<td>Get appropriate care</td>
<td>9.7</td>
<td>9.6</td>
<td>n.s. (0.96)</td>
</tr>
</tbody>
</table>

Table 12. Changes in patients’ quality of life when comparing the period less than 6 weeks before death with the period 7 - 12 weeks before death
Comment: Obviously, patients’ QoL was generally not most negatively affected by lack of symptom control, the only exception being fatigue.

Areas of most pronounced deterioration terminally

First we analysed the mean in each time-group for each of the 19 items in the patient’s questionnaire and found that QoL deteriorated over time according to most parameters. The most manifest deterioration during the last month of life affected the following items: need for assistance with hygiene and dressing/undressing, memory, ability to concentrate, ability to feel joy, meaningfulness, and global quality of life (Fig. 10).

To identify which items deteriorated significantly over time, we compared the means of all 23 assessments during the period 7-12 weeks prior to death versus the means of all 23 assessments during the period 1-6 weeks before death. There was a significant deterioration for five items: ‘help with hygiene and dressing/undressing’, ‘defecation problems’, ‘ability to concentrate’, ‘reckoned with by friends’, and ‘global QoL’. Changes over time regarding ‘nausea’ and ‘ability to feel joy’ approached statistical significance (Table 12).

Comment: The present study confirms the general downward trend of most patient QoL items when approaching death. Seventeen of 19 patient items showed a decrease in mean scores, though only five of these decreases reached significance. The finding of an accelerated deterioration in QoL items during the terminal 2-3 weeks tallies closely with results presented by other authors (35, 87, 88).
What was least bad?

For five parameters (pain, anxiety and sharing worries with family, contacting staff, getting appropriate care), the mean values remained stable over time, without any tendency to decrease close to death. The items gaining the highest scores throughout were: ´contacting staff´ and ´getting appropriate care´. The distribution of pain scores was stable over time (Fig. 11). At each point in time, approximately 60% of the patients reported one of the four lowest pain scores, i.e. they felt no pain or very little. No patient reported either of the worst two pain scores during the last 10 weeks of life. In 11 of 19 items, more than 25% of the observations yielded either of best two scores during the last 6 weeks of life.

Comment: The stability over time of the ´pain´ and ´anxiety´ items challenges the accepted picture of the dying cancer patient as being tormented by agonizing pain and anxiety. Fig. 11 shows that the distributions of pain scores are roughly as stable over time as are the mean values. Both Morris et al. (87) and Hinton (89) have reported similar stability in pain scores over time.

Figure 11. Pain item versus time for patient

Spouse - correlations to global quality of life

To ascertain which items contributed most to the spouses´ global QoL we studied the correlations between the global QoL item and all other items. The five highest correlations were: ´meaningfulness´ 0.70, ´feeling of security´ 0.57, ´reckoned by friends´ 0.48, ´depression´ 0.48, ´hours to leave the patient alone´ 0.40. It is noteworthy that ´anxiety´ with the second lowest mean value (4.2) was weakly correlated (0.36) to the spouses´ global QoL.

Comment: Meaningfulness is again the top correlate to global QoL, as with the patients. It highlights the impact of existential matters when a family member is incurably ill and dying.
What was worst?

The lowest mean scores during the terminal 6 weeks were found for the items: ‘ability to leave the patient during daytime’, ‘anxiety’, ‘global quality of life’, ‘depression’ and ‘security’ (Table 13).

The largest proportions of the worst ratings (scores 1 and 2) during the last 6 weeks before the patient died were found for ‘ability to leave the patient alone’ (44%), ‘assistance with hygiene/dressing’ (26%), and ‘anxiety’ (26%).

Comment: Obviously the physical constraints on the principal carer of a dying person are immense. Interestingly, these items do not correlate appreciably with the global QoL. Nevertheless it illustrates the need of physical assistance on behalf of the principal carer as the patient approaches death.

<table>
<thead>
<tr>
<th>Item</th>
<th>Mean 7-12 weeks (n = 23)</th>
<th>Mean 1-6 weeks (n = 23)</th>
<th>Signif. (P= )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability to leave patient</td>
<td>4.6</td>
<td>4.1</td>
<td>n.s. (0.74)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>5.7</td>
<td>4.2</td>
<td>n.s. (0.070)</td>
</tr>
<tr>
<td>Global quality of life</td>
<td>6.0</td>
<td>5.2</td>
<td>n.s (0.27)</td>
</tr>
<tr>
<td>Depression</td>
<td>6.5</td>
<td>5.6</td>
<td>n.s. (0.17)</td>
</tr>
<tr>
<td>Feeling of security</td>
<td>6.0</td>
<td>5.9</td>
<td>n.s. (0.93)</td>
</tr>
<tr>
<td>Support from friends</td>
<td>6.3</td>
<td>6.0</td>
<td>n.s. (0.60)</td>
</tr>
<tr>
<td>Sharing worries with patient</td>
<td>7.6</td>
<td>6.1</td>
<td>n.s. (0.17)</td>
</tr>
<tr>
<td>Need for assist. w. hygiene/dress</td>
<td>8.1</td>
<td>6.2</td>
<td>0.049</td>
</tr>
<tr>
<td>Insomnia</td>
<td>7.7</td>
<td>6.2</td>
<td>0.047</td>
</tr>
<tr>
<td>Sense of meaning</td>
<td>6.5</td>
<td>6.2</td>
<td>n.s. (0.72)</td>
</tr>
<tr>
<td>Support from care</td>
<td>6.1</td>
<td>6.4</td>
<td>n.s. (0.64)</td>
</tr>
<tr>
<td>Responsibility</td>
<td>6.9</td>
<td>6.8</td>
<td>n.s. (0.91)</td>
</tr>
<tr>
<td>Need to assist at night</td>
<td>9.4</td>
<td>8.2</td>
<td>n.s. (0.27)</td>
</tr>
<tr>
<td>Quality of care</td>
<td>9.2</td>
<td>9.4</td>
<td>n.s. (0.48)</td>
</tr>
</tbody>
</table>

Table 13. Changes in spouses’ quality of life when comparing the period less than 6 weeks before patient’s death, with the period 7 - 12 weeks before death

Areas of most pronounced deterioration terminally

Deterioration over time in the 14 items in the spouse’s questionnaire (Fig. 12) was not as prominent as in the patient’s. The worsening during the last month of the patient’s life was most pronounced for the three items concerned with the need for
physical assistance (hours to leave the patient alone, assistance with hygiene/dressing, and assistance at night; Fig. 13).

Statistically significant worsening was found for two items only: 'need for help with hygiene/dressing', and 'insomnia'. The item concerned with anxiety was almost significant (Table 13).

Comment: Findings concerning spouse’s quality of life highlight the importance of both psychological and physical assistance of spouses. Hinton (90), in his study of which patients with terminal cancer are admitted to hospital from home care, noted increasing fatigue, anxiety and depression among the spouses prior to the admission. The present results strengthen the impression that, especially during the terminal 2 weeks, the extent of the physical burden warrants extra staff, such as night sitters. Without this support, physical exhaustion of the spouse is most likely to necessitate admission of the patient to an institution. The need for occasional or regular relief for the spouse is also evident from the fact that they are unable to leave the patient alone at home for any length of time.

What was best?

Items such as ‘care quality’, ‘reckoned by friends’, ‘meaningfulness’, feelings of ‘security’ and ‘responsibility’, and ‘care support’ were fairly stable over time. Best were the mean scores for ‘need for assistance at night’ and ‘quality of care’. The largest proportion of the best ratings (scores 9 and 10) during the same period was found for ‘quality of care’ (83%), ‘assistance at night’ (65%), and ‘assistance with hygiene/dress’ (44%).
During the last week:

1. How many hours per day (8 a.m. to 8 p.m.) have you at the most been able to leave your ill spouse unattended?

At the most 1 hour 10 hours or more

2. How much have you assisted with hygiene and dressing/undressing?

Not at all Completely

3. How frequently do you need to help during nights?

Never Many times every night

4. Have you had sleeping difficulties?

Not at all Very much

5. Have you felt worried?

Not at all Very worried

6. Have you felt depressed/low in mood?

Not at all Very depressed

7. Have your days felt meaningful last week?

Not at all Completely

8. How much of your worries have you shared with your ill spouse?

Nothing Everything

9. How has the contact with your friends been?

None Very lively

10. What do you think of the support from the medical care?

Completely insufficient Too much

11. What do you think of the quality of care your spouse has received?

Very poor Best possible

12. How have you experienced your responsibility for your ill spouse?

Too little Too much

13. How secure/insecure have you felt last week?

Very insecure Completely secure

14. How has your own quality of life been last week?

Very poor Best possible

Figure 12. Spouse’s questionnaire
The patient’s and spouse’s questionnaires had seven corresponding items, of which meaningfulness, and global QoL differed significantly between patients and their spouses at simultaneous points in time. Spouses had better scores for meaningfulness and global QoL (Figs. 14, 15). Patients tended to be less anxious than spouses \((p = 0.057)\). In about 10% of the observations concerning anxiety, meaningfulness, and global QoL, the scores of the patient and spouse within a couple differed by 3 or more points counter to the direction of mean difference. For the items ‘assistance with hygiene/dressing’, ‘depression’, ‘insomnia’, and ‘sharing worries with family’, there were no mean differences between patients and their spouses. Further analysis of the distribution of score differences between patient and spouse within couples at simultaneous times, evidenced good agreement for the item ‘assistance with hygiene/dressing’, with no differences between patient and spouse exceeding 2 points. In the case of ‘depression’, ‘insomnia’ and ‘sharing of worries’, approximately 25% of the patient–spouse score differences exceeded 2 points (ranging between 3 and 9) and were equally frequent in favour of patient and spouse.

\[\text{Comment: The finding that spouses tended to be more anxious than patients confirms earlier results reported by Hinton (89), who also claimed that depression was more common among spouses than among patients, something that we could not confirm. This difference may be}\]
due in part to different assessment techniques. Hinton used skilled psychiatric observation.

The comparisons of global quality of life and meaningfulness, between spouse and patient, showed lower values for the patients throughout. One hypothesis is that the experience of meaningfulness is for the spouse to some extent heightened by the responsibility of caring for the patient and this in turn augments the spouse’s overall QoL.

VI. Is there an additive analgesic effect of paracetamol in morphine therapy of pain in cancer patients?

The 30 study patients could not detect any difference in pain level between the week with paracetamol and the week with placebo (p = 0.22). Thirteen patients could not distinguish any difference in pain level between the two weeks, 9 felt that they had less pain during the week with paracetamol and 8 felt that they had less pain with placebo.

Comment: The distribution of preferences resembles closely pure chance.

The pain question in the AQEL questionnaire did not differ significantly between the week with paracetamol and the week with placebo (median = 3 during both weeks).

Sixteen patients had not felt any difference in QoL between the two weeks; 10 experienced better quality of life during the week with paracetamol and 4 during the week with placebo (n.s.). According to the AQEL questionnaire the global QoL gave a median of 7 during the paracetamol week and a median of 5.5 during the placebo week (n.s.).

Comment: The patients as a group did not notice any significant difference between paracetamol and placebo, either on direct comparison or in QoL assessment.

Using Wilcoxon’s signed rank test, we compared the total of daily pain scores/week and found a significantly (p= 0.04) lower total score for the week with paracetamol (median = 11) compared with placebo (median = 15). To make a clinical difference we decided that pain had to differ at least one step per day and the amount of extra morphine per day by at least half a tablet (i.e. 5 mg). The total amount of extra morphine/week did not differ significantly (p= 0.06; median 30 mg extra with
paracetamol, 50 mg extra with placebo). When sorting the totals of daily painscores/week according to the clinical criterion of an at least 7-step difference, we found no significant difference between paracetamol and placebo (Chi-2 = 3.6; p > 0.05). We had previously decided that a daily pain difference of at least 1 scale step (of a 10-step scale) was needed to reach clinically significance. Accordingly a 7–unit difference was a minimum on a weekly basis. The total of extra morphine doses/week, according to the criterion of an at least 35 mg difference to be of clinical importance (i.e. half a 10 mg tablet of morphine/day), did not differ significantly either (Chi-2 = 3.6; p > 0.05). The distribution of observations is shown in Table 16.

<table>
<thead>
<tr>
<th>Total daily pain scores/week</th>
<th>Patients (n)</th>
<th>Total extra morphine/week</th>
<th>Patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No difference (&lt;7-unit difference)</td>
<td>20</td>
<td>No difference (&lt;35 mg difference)</td>
<td>20</td>
</tr>
<tr>
<td>Better on paracetamol (&gt;7-unit difference)</td>
<td>8</td>
<td>Better on paracetamol (&gt;35 mg difference)</td>
<td>8</td>
</tr>
<tr>
<td>Better on placebo (&gt;7-unit difference)</td>
<td>2</td>
<td>Better on placebo (&gt;35 mg difference)</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 16. Total daily pain scores/week and total extra morphine/week grouped according to criteria of clinical relevance

Comment: Even when the total daily pain scores/week resulted in a statistical difference favouring paracetamol, this difference was evidently not detected by the patients as clinically significant.

Table 17 illustrates the absence of ‘period difference’, as the distribution of turnouts is similar whether the active substance was introduced during the first or the second week. It is worth noting that the randomization code for the 42 patients originally included contained 16 patients given paracetamol during week 1 and 26 patients with paracetamol week 2.

The serum concentration of paracetamol was 66 µmol/l (median; 0–166 µmol/l) in patients taking active substance and 0 µmol/l (0–22 µmol/l) in patients taking placebo. Two patients had 0 µmol/l during the paracetamol week, the rest had more
than 30 µmol/l. Five patients had serum levels exceeding zero (8, 9, 10, 13, and 22 µmol/l) during the placebo week.

<table>
<thead>
<tr>
<th>Total extra morphine/ week</th>
<th>Paracet. week 1</th>
<th>Paracet. week 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No difference (&lt;35 mg difference)</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Better on paracetamol (&gt;35 mg difference)</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Better on placebo (&gt;35 mg difference)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Figure 17. The effect of paracetamol according to whether paracetamol was given during the first or second week in the study**
GENERAL DISCUSSION

The original purpose of this work was to find ways to evaluate a palliative service. Input (i.e. medical care utilization), and effects (i.e. QoL), had to be measured to accomplish this. Unfortunately the lack of generally accepted evaluation tools and the absence of baseline data considerably complicated the task. Thus, compilation of baseline data and ways to assess medical care utilization and QoL constitute the core of this thesis.

We found that 12% of the incurably ill cancer patients died at home. Two earlier Swedish studies, from 1990 (91, 92), reported that 7% of all cancer patients within a certain geographical area died at home. A factor contributing to this difference might be that patients with lymphoma and leukaemia were excluded from the present study. Both McCusker (93) and Constantini et al. (94) reported that significantly fewer patients with lymphoma and leukaemia died at home, than patients with cancer of the breast, prostate, or colo-rectum.

In the international literature we find a wide variety of figures concerning the proportions of cancer patients dying at home (7, 14, 16, 93-96). The frequencies range from 3% to 7% in a Californian material (7), to 18% in Australia (96), 27% overall in Great Britain (16, 95) and 33% in Genoa, Italy (94).

The 12% rate of home deaths found in the present study is still far lower than the proportion of patients with incurable cancer disease who wished to die at home, according to studies in Great Britain by Dunlop et al. (17) and Townsend et al. (16). Those authors reported that 53–58% of patients with incurable cancer preferred to die at home. Hinton (89) reported that 100% of patients referred to a Hospice Home Care Service initially preferred home, but that the proportion gradually diminished over time, being 54% the week before death.

The fact that not all patients with incurable cancer want to die at home is important to remember. It must not be regarded as a failure when a patient decides to be admitted to hospital. The possibility of obtaining palliative home care should enhance the freedom of choice, but not be an obligation.

We found that neither gender, diagnosis, age, nor marital status was correlated to the proportion of home deaths. Similar results regarding gender and age has been reported in previous studies (93, 96-98). Patients with diagnoses such as leukaemia
and lymphoma has been less likely to die at home (as stated above). Some authors have found that married persons are more likely to die at home (94, 97, 98), while others, like us, have found no difference (96, 99). The explanation is probably that social support factors other than marriage are of great importance to patients with terminal disease. The extent of support from children, other relatives, and friends was not documented in the medical records analysed in this study.

The optimal proportion of home deaths from cancer in the county of Jämtland is hard to determine. A doubled proportion, i.e. 20–25%, in 5–10 years time does not feel unrealistic, thus approaching the level in Great Britain (100). Well organized palliative support from different levels of the medical care system will most likely shorten terminal hospitalization and give more days at home prior to death. In the Swedish county of Östergötland, where a comprehensive round-the-clock hospital-based palliative support organization has been operating for 25 years, 37% of all cancer deaths in 1995 occurred at home (101). The achievements in the Spanish region of Catalonia (102) are impressive. By organizing palliative support services throughout the region and on different levels within the health care system, the proportion of cancer patients dying in hospitals decreased from 60% to 15% over a period of 8 years. In that study factors such as availability and travel distances appeared to affect where patients preferred to die. We found no differences in home deaths according to these variables, but that more people died in nursing homes if they lived further than 40 km from the hospital and if the local village had a nursing home. Similar findings were recently reported from England by Thorne et al. (103) who found that the availability of general practitioner community hospitals significantly reduced the proportion of cancer deaths at the specialist service units.

Why dying cancer patients at primary health care centres without an attached nursing home, and situated 40–230 km from the County Hospital, preferred terminal care in distant Östersund to local alternatives could not be established in this study. These patients may have given higher priority to the standard of care at the hospital than to travelling time. Patients who lived near the County Hospital were favoured in all respects if they chose the hospital. By preferring the hospital they maintained continuity with the hospital staff, they obtained a higher medical standard of care, yet they did not lose the nearness to their home and family. If they chose the local nursing home in the city, they had to decide more proactively against hospital care. The reasons why patients and their family members choose different types of institutional care need to be investigated in further studies.
Similar differences between groups were found regarding medical care utilization. Patients living further than 40 km from the hospital accounted for fewer admissions and fewer days at the DGS than patients living near the hospital. Patients living further afield spent more days in local nursing homes.

Married patients required more admissions and hospital days than did unmarried patients. One might have assumed the opposite, as the support of a spouse could facilitate earlier discharge from hospital and more support at home. Maybe the anxiety and the worries of the spouse increased the urge for institutional care.

Overall, breast cancer patients utilized more hospital days throughout the disease course than any other diagnosis. One explanation was that these patients spent more days at the university hospital prior to the last 6 months of life. As death approached, regardless of diagnosis, medical care utilization seemed to converge, as we could not find any significant differences between different diagnoses at the end of life.

According to Riley et al. (10), who analysed Medicare expenditure during the last year of life of more than 50,000 deceased, this convergence may apply even to diagnoses outside oncology. They found that cancer patients, heart patients and cerebrovascular patients accounted for about half of the last year’s expenditure during the terminal 2 months, regardless of diagnosis. As regards total costs, cancer care was still the most expensive.

This convergence between different diagnoses, as death approached, is further illustrated by the fact that the duration of terminal hospitalization did not vary significantly with any sociodemographic variable or diagnosis. Terminal hospitalization accounted for an impressive 39% of all institutional days of the cancer disease, from diagnosis to death. Adequate support during this difficult period in life seems to have a substantial potential to save institutional days in an era when the number of hospital beds is being reduced.

The importance of concentrating on the last 2 months in life when trying to reduce medical care utilization was further emphasized by Greer et al. (14) who concluded in their investigation, which was part of the National Hospice Study in the U.S.A., that home care programs were less expensive than conventional care, but only during the final 2 months. They, as well as Long et al. (9), conclude that the utilization of
hospital care, and its attendant costs, increases substantially during the final 2 months of life.

At the same time we have to be well aware that some patients live with a symptomatic, incurable cancer disease, and a need for palliative support, for much longer than 2 months. One example was a patient in this study who received our support for 548 days before death supervened. A reasonable inclusion criterion for any palliative support ought to be a symptomatic, incurable disease necessitating frequent contacts with the medical services. Whether the needs are physical, psychological, social or existential, they should qualify equally for support.

In the search for useful outcome measures depicting medical care utilization, it was clear that reliance solely on ‘place of death’ was too blunt an instrument. The results in this dissertation suggest that outcome measures such as ‘duration of the terminal hospitalization’ and ‘proportion of days at home during the enrolment period’ serve as good complements to ascertain the potential effect on medical care utilization of a specific palliative intervention during the most care-intensive period (i.e. the last 2 months of life).

The optimal utilization of surgery, radiation and chemotherapy by patients with incurable cancer disease is not known. It will no doubt change in the future due to the constant development of new, less invasive and less side-effect-provoking treatment modalities. In this study we found that 81% of the patients had received some kind of active anti-cancer therapy throughout the disease course. During the last 6 months of life 41% of the patients required surgery, 10 % radiation and 15% chemotherapy. Kane et al. (7) studied 247 male war veterans with terminal cancer. During their last 4 months, 18% of those treated with conventional care required surgery, 48% radiation and 16% chemotherapy. Bearing in mind the majority of lung patients (36%) in the Kane study and our completely surgical panorama, the figures are not surprising when compared, radiotherapy being an established palliative treatment for late-stage lung cancer. The relatively low proportion given radiation therapy in this study may also be indicative of relative underutilization of palliative radiotherapy (104).

The financial evaluation of the hospital-based palliative support service encountered the notorious difficulty within palliative care of finding an appropriate control group. As we would not be able to randomize patients for either extra support or nothing, we settled for what we regarded as second best, i.e. a matched historical
control group combined with a contemporary reference group from another geographical area.

The comparison between the study group and the control group had three potential biases. The first could be that recorded differences may not have been caused by the intervention, but be the result of changing routines within health care, commencing 1990. The fact that we could not detect any significant differences between the groups in overall health care utilization, such as number of admissions or total number of institutional days, reduces the probability of policy changes having occasioned a substantial bias.

The second bias could be that patients in the study group had a stronger wish to stay at home and could reckon with more support from family members or friends than was the case for control patients. Information on available support by family and friends in the control group, besides marital status, could not be retrieved from the medical records. The impression gained from our daily work with incurable cancer patients is that those patients who completely lack support and have no wish to stay at home are few. On the other hand, an integrated part of the study group intervention was to encourage the spouse and other members of the family to actively participate in tending the patient. Whether this should be regarded as a bias can be doubted.

The third bias could be that the surgeons deliberately selected patients most likely to benefit by support from the palliative service to the study group, and excluded patients with a more symptomatic disease. The impression was that more symptomatic patients were rather selected for the study group as their need of support was more pronounced.

To analyse whether any biases might have had a substantial impact on the results of the present study, we found it valuable to include the results of the reference group. If policy changes within health care had substantially reduced health care utilization by incurably ill cancer patients from 1990 to 1992-93, if there had been markedly less family support and less wish to stay at home among the patients in the control group than in the other two groups, and if the control group was burdened by more symptomatic patients than were the other two groups, then we ought to have seen more health care utilization by the control group than by the reference group.
The finding that the reference group was more compatible with the control group than with the study group regarding such parameters as duration of terminal hospitalization, days spent at home after enrolment and days spent at home during the last 2 months of life, implies that these differences between the study group on the one hand and the control group and the reference group on the other were due to the intervention in the study group rather than selection bias.

The absence of significant differences between the study group and the control group in the proportion of home deaths is not demoralizing. Place of death is a measure only reflecting the last hour of life. The work of a palliative service may be successful in symptom control and in saving days of institutional care even if the patient decides to spend his/her last 2 or 3 days in an institution.

In the present study the duration of terminal hospitalization was 3 days (= median, mean = 9.6 days) for the study group and 10 days (= median, mean = 22.7 days) for the controls. We interpret this difference as a result of the support given by the PSS. These findings are fairly consistent with previously published results. Woo et al. (99) in their study of 69 terminally ill patients with colorectal cancer who had been treated with conventional care in Concord, Australia, found a median terminal hospitalization of 7 days. Chan & Woodruff (105) found a median terminal hospitalization of 7.5 days for 56 patients dying of cancer at the Austin Hospital, Australia. Flynn & Stewart (106) studied 33 consecutive cancer patients dying in an emergency care hospital in Ohio, U.S.A., and found a mean terminal hospitalization of 20.1 days. Apparently there are great similarities in the need for institutional care of terminally ill cancer patients, regardless of nationality and health care system.

The number of admissions during the terminal year was reported by Doyle (107) to be two or three, on average; we found a median of two during the last 6 months of life. The number of admissions during the terminal 6 months appears to be unsuitable as an outcome measure in palliative care, due to small absolute numbers, and a time frame extending beyond the most care-intensive period (the last 2 months).

The study patients spent 85% (median) of their days at home during a enrolment time of 64 days (median). A similar result was reported by Maltoni et al. (11) in a home care program in Romagna province, Italy. This program was similar to the service described in this study in aspects such as: the service was based at the local hospital (Dept of Oncology), it was not a 24-hour service, and was relatively sparingly staffed. Maltoni found that included patients spent 81.8% of the
enrolment days at home; mean duration of care was 68.1 days. By reporting the enrolment period, we can also be assured that the palliative program in question dealt with the appropriate period in the lives of these terminally ill patients. By early inclusion of patients, resulting in long total inclusion periods, it ought to be possible to improve the ratio days at home to total inclusion days, without improving the palliative care. Control patients only spent 58% of the days at home during an identical period of time. The difference between the study group (85%) and the control group in this respect seems to express a significant impact of the PSS, which was not obvious when comparing place of death.

The financial evaluation in this study implies that palliative home care is no more expensive than conventional institutional care. Depending on the way of calculating, even substantial savings can be found. Regardless of the analysis chosen, the "hotel costs" of the hospitals disappear with domiciliary care and there is always an immense unpaid workload borne by family members and friends. As long as the spouse and other family members are willing and able to help, the patient can stay at home. Therefore the support of the family is essential and should be considered an integral part of any palliative support program (108). We have not in this study included any costs for this unpaid work undertaken by family members. If we did, the potential saving of 17,360 Sw.kr/patient found in paper III, would probably disappear. Hjortsberg and Svarvar (109) included costs of housing and of family members’ work and concluded that domiciliary care is just as expensive as hospital care, when taking all costs into account. But even if the costs were identical, the quality of care and the QoL for the incurable cancer patient are likely to have been better in the study group. No one has so far been able to put a price tag on an extra day at home, and as long as the costs are the same, it is natural to prefer the alternative offering the best quality.

In this study we have registered costs both within and outside institutions. Even so, we have not found anything to gainsay the general impression of a financially effective care coordinated by the hospital-based PSS.

A financial analysis such as that in paper III does not justify every kind of palliative service. We believe that there is a danger of ‘over-doing’, i.e. allocating too much to patients coping perfectly well by themselves or with support from the conventional health care system. The support service ought to be the "glue" holding the different parts of the health care system together in an appropriate way and supplying support (knowledge, experience and technical know-how) when there is a need for it.
Conclusions from non-randomized trials must always be drawn with caution. Another reason for caution in this study is that occasionally a patient with extraordinary needs will generate exceptionally high costs for the service. For instance, a widow in the study group, with ulcerating anal cancer, was enabled to live alone at home thanks to intensive round-the-clock nursing by the home help service. She alone was the source of the extremely high figures reported in Table 8 for domiciliary services, including assistant nurses and night sitters.

A good QoL until death supervenes is the primary aim for all incurable patients and all palliative care effort. Accordingly, assessment of QoL ought to be mandatory in all palliation regardless of setting. In clinical research as the primary outcome measure, and in routine clinical work to identify the individual patient’s area(s) of major concern and then to evaluate the potential success of the treatment. In both settings an appropriate QoL instrument has to be comprehensive, adjusted to the palliative care setting, easily completed, and validated in the appropriate language.

When we were about to start this study we could not find any QoL instrument which fulfilled the criteria above. So we developed the AQEL instrument to suit our purposes. The results available so far strengthen our impression of the AQEL instrument as being both reliable and valid. More extensive evaluations with greater numbers of patients are needed to confirm this.

The validation process contains an innate problem. There is no gold standard available. Is an instrument more valid if it correlates well with an older instrument which in turn was validated with another instrument which in turn was the first of its kind? The answer can be both yes and no. Yes, if it correlates well with another more accepted instrument one can be fairly sure that the two measure something similar. No, it does not assure you that the new instrument really does measure QoL. But lacking an acknowledged prototype, this is the best we can do.

We regard factor analysis as a complementary way of assessing validity. The factor analysis yielded in the case of the AQEL instrument logical groups of items, which we interpret as strengthening the validity. Others question this technique.

Interestingly the factors emerging from the factor analysis were not identical with the postulated dimensions of QoL. ‘Insomnia’, ‘anxiety’ and ‘depression’, assumed to be from the psychological domain, loaded on the same factor as the physical
symptoms. This finding could raise questions about the validity of the questionnaire. But as covariation between physical symptoms and psychological items seem rational (a patient with pain is more likely to have problems with anxiety and insomnia than a patient who is pain free), and that earlier studies report similar findings (110), we rather interpret it as an expression of a debatable validity of the strict conceptual separation between the traditional dimensions within QoL. ‘Physical strength’ did not load on the symptom factor but on a separate factor together with ‘ability to do what one wants’ and ‘global quality of life’. Intellectually this connection of ‘physical strength’ to life content variables rather than symptoms seems reasonable.

‘Reckoned with by friends’ and ‘sharing worries with family’ were assumed to be from the same social dimension, but loaded singularly on separate factors. Whether this finding should be interpreted as if the item is unclearly worded or if it illustrates the complexity of the social dimension, is hard to decide. Other authors have reported similar difficulties in grasping the social dimension (78). Further work is necessary.

Concurrent validity in relation to corresponding CIPS items was moderate to strong in all cases but one, namely ‘sharing worries with family’ compared with ‘talk with partner about feelings, future, and illness’. A possible explanation may be that many patients preferred to share their worries with another family member rather than with their partner, or that ‘sharing worries with family’ is too difficult as one may think of persons outside the core family as well.

Comparisons with the KPS revealed a pattern of correlations supporting both convergent and discriminant validity. Correlation values between the KPS and the item concerned with physical strength were in the same range as has been reported for items in the Functional Living Index - Cancer (52) and by Selby et al. (51). The KPS did not correlate at all with ‘anxiety’, ‘insomnia’, ‘sharing worries with family’, or ‘reckoned with by friends’ thus expressing discriminant validity.

The decline in QoL scores during the terminal 3 weeks has been described earlier by Morris et al. (87), Higginson & McCarthy (88) and Hinton (89). Our results agree closely with their findings and show that the questionnaire is sensitive enough to detect change over time, at least in the terminal phase. The number of patients assessed varied between different observation points in Figure 9. The impact of this on the results is probably an underestimation of the terminal decline in AQEL scores.
Arguments in favour of this assumption are that we found a general decline in AQEL scores as individual patients approached death, and that it is conceivable that the drop-outs were patients with the poorest quality of life.

The results of our QoL assessments of incurable cancer patients at the end of life, and their spouses, emphasize the importance of the existential dimension and fatigue. They also illustrate how pronouncedly the spouse’s QoL is affected by caring for an incurably ill wife or husband.

The importance of assessing existential items is strongly emphasized by the fact that the items ‘meaningfulness’, ‘ability to do what one wants’, and ‘ability to feel joy’ ranked as numbers 1, 2, and 5 among the five items with the strongest correlations to the global QoL rating. This suggests that as the physical condition deteriorates, existential issues gain in importance as determinants of global QoL. Cohen et al. (58), using the McGill Quality of life Questionnaire, and Fowlie et al. (111) found that global QoL correlated the most closely with the spiritual factor in a palliative care setting.

Whether or not such existential problems could be alleviated by some kind of intervention was beyond the scope of this study. However, we suggest that it will be difficult to substantially improve the overall QoL of these patients unless the existential domain is considered.

‘Physical strength’ and ‘hours recumbent’ were ranked third and fourth with respect to patient’s global QoL. These items both reflect the concept of fatigue. Gough et al. (80) asked 115 patients with metastatic cancer to identify and rank which QoL items, from the physical, psychological and social domains, were most important to them at the time. Fatigue was ranked as the most important concern, thus underlining physical capacity per se rather than specific bodily symptoms as determinants of the global sense of QoL.

A potential explanation for the lack of correlation between global QoL and most physical symptoms may be that nowadays we are relatively good at alleviating pain, nausea, etc. Interestingly, a notorious exception is fatigue, for which very little can be done once anaemia is corrected and treatment with corticosteroids fails.

The relative importance of ‘physical strength’ and ‘ability to do what one wants’ for the sense of global QoL also highlights the importance of autonomy. Without
sufficient physical strength it is impossible to do what one wants, and as self-value in western societies of today is intrinsically connected with what one does, it is a natural deduction that when you are unable to do anything you are worthless. All patients struck by incurable cancer disease pass slowly through the transition from a healthy ‘do-er’ to a dependent ‘be-er’. The loss of abilities and individual independence has a detrimental affect on the experienced meaningfulness and QoL.

Contrary to most expectations, not all items got worse when approaching death. ‘Pain’, ‘anxiety’, ‘sharing worries with family’, ‘contacting staff’ and ‘getting appropriate care’ did not get worse closer to death but remained stable over time.

It is important to realize that approximately 35% of the patients were pain-free during their terminal month. This figure should be compared with those from the National Hospice Study in the U.S.A. (112) reporting 16% pain-free during the last week according to the primary care person, and Higginson & McCarthy (113) who reported complete pain control for about half of their patients throughout the last 2 months, according to staff reports.

Caring for a dying family member is without doubt a most substantial burden on and stress for the principal carer, as the mean value of spouses’ global QoL sinks as low as 4.6 out of a maximum of 10 during the terminal 2 weeks. Nor should we forget that this mean value hides a spectrum of experiences of which some implied an even worse QoL, though others were better. Nor should we interpret the two linear plots of means over time (Figures 14, 15) as if patients in all patient–spouse couples experienced a worse QoL than their spouse at all times. Therefore, it is important to apply an unprejudiced QoL assessment to each individual in each patient–spouse couple encountered.

In paper VI we found very little to support the routine use of 4 g paracetamol per day with concurrent morphine therapy. All but one statistical analysis supported the null hypothesis, i.e. no significant analgesic difference between paracetamol and placebo when combined with morphine therapy. The only statistically significant finding was a lower total of daily pain scores/week during paracetamol therapy than with placebo. The difference between the median values was 4 units. It seems as if the patients in this study were unable to detect this slight difference in pain level of approximately half a scale step per day, as the week with most pain was not detected as the placebo week, in either the AQEL questionnaire or on direct questioning.
Even though the study design avoided selection biases, the results may not be suitable for generalization. This study only included patients with fairly stable pain levels and a pain of 3 or less on the numerical rating scale. Thus the results do not say anything about the clinical effects of paracetamol in patients with worse pain. Bjune et al. (114) in a single-dose study of postoperative pain detected a significant effect of paracetamol and paracetamol + codeine, compared with placebo, but only in patients with pain intensity more than VAS = 6.

All patients spent the study period at home, thus excluding the hospitalized patients. The study patients were closely supervised and given detailed instructions how to take their prescribed drugs in a way that most ordinary patients do not. Whether the analgesic effect of paracetamol depends on the intensity of pain or other individual characteristics was not analysed in this study.

The mechanism behind the finding that the addition of the non-opioid paracetamol did not increase the analgesic effect of morphine is not known. It may be a result of some common pathway within the central nervous system for both paracetamol and morphine. Whatever the mechanism is, it may be involved in the explanation of why many studies and reviews (72, 73) have had great difficulty in demonstrating a substantial additional analgesic effect of the weak opioids (codeine and dextropropoxiphene) on single drug paracetamol.

Even if the routine use of paracetamol with morphine can be questioned, occasional patients may benefit, especially when the pain intensity is rather severe. We recommend an individual approach and welcome further investigations of paracetamol’s analgesic effects.
SUMMARY

Referring to the aims of this study, the following conclusions have been drawn:

1. Neither sex, diagnosis, age, nor marital status did correlate to the proportion of home deaths. Only when the period between diagnosis and death was less than one month did no patient die at home. The proportion of deaths in nursing homes increased with age and when the patient lived further than 40 km from the hospital with a local nursing home nearby.

2. Incurable cancer patients spent approximately one month (median) in institutions during the last 6 months of life. The terminal hospitalization (median = 10 days) accounted for 39% of all institutional days generated by the cancer disease, from diagnosis to death, and did not vary significantly according to any socio-demographic factor or diagnosis.

Patients with breast cancer utilized most institutional days throughout the duration of the cancer disease, followed by patients with prostatic cancer. This difference between diagnoses disappeared during the last 6 months in life.

Patients living close to the hospital and married patients had more hospital admissions and spent more days at the Department of General Surgery during the last 6 months in life than those who lived further away and those who were unmarried.

During the last 6 months of life, 41% of the patients underwent surgery, 15% received palliative chemotherapy, and 10% radiotherapy.

3. Measures such as "length of terminal hospitalization", "proportion of days at home/total inclusion days", and "days at home during the last 2 months of life" reflect the most care-intensive period, i.e. the last months of life. They all appear as potentially valuable complementary measures of institutional utilization when evaluating palliative support measures.

4. The results indicate that the palliative support program was self-financing and may have generated a saving of 17,000 Sw.kr per patient.
5. A short quality of life instrument (AQEL = Assessment of Quality of life at the End of Life) with 19 items has been developed specifically for the palliative care setting. It contains items from physical, psychological, social and existential dimensions as well as items addressing global quality of life and medical care issues.

A test–retest procedure produced fair signs of reliability. Validation by factor analysis and comparisons with concurrent KPS and CIPS scores produced values suggesting adequate validity.

6. The item having the closest correlation with the global quality-of-life item was ´meaningfulness´ for both patient and spouse. ´Ability to do what one wants´ and ´physical strength´ ranked second and third for patients. Pain seemed to be without impact. The distribution of pain scores was stable over time without any obvious deterioration terminally.

For spouses, the lowest scores during the terminal 6 weeks were for ´ability to leave the patient during daytime´ and ´anxiety´. As a group, spouses tended to be even more anxious than the patients at the same point in time.

7. This study does not offer any definitive corroborative evidence of a clinically relevant additive analgesic effect of paracetamol in addition to morphine for the treatment of pain in incurable cancer. Routine use of paracetamol in these patients may therefore be strongly questioned.
SVENSK SAMMANFATTNING

Vården av obotligt sjuka cancerpatienter har genomgått stora organisatoriska förändringar under 80- och 90-talet. Framväxten av den palliativa medicinen har syftat till att optimera såväl livskvalitet som vårdutnyttjande. Problemet i början av 90-talet, då detta arbete startade, var avsaknaden av svenska bakgrundsdata, överenskomna utvärderingsvariabler och kortfattade livskvalitetsinstrument avsedda för den svårt sjuke cancerpatienten.

I denna avhandling har jag försökt belysa olika delar av detta problemkomplex. Patientunderlaget är hämtat från Jämtlands län där jag successivt sedan 1991 varit med om att bygga upp ett palliativt resursteam (Storsjögläntan) som utgår från Östersunds sjukhus och stöttar obotligt sjuka cancerpatienter i Jämtland och Härjedalen som helst vill vårdas hemma. 130 000 länsbor är utspridda över en yta som motsvarar drygt 10% av Sveriges, vilket innebär reseavstånd vid hembesök upp till 80-250 kilometer enkel (beroende på väderstreck).

I delarbete I+II analyserades journaluppgifter på alla patienter som dog 1990 av kirurgisk cancer i Jämtlands län (n=203). Dödsplatsen är ett ofta använt, men trubbigt, mått på den palliativa vårdens effektivitet. 129 patienter (64%) dog på sjukhus, 49 (24%) på sjukhem och 25 (12%) i det egna hemmet. Varken kön, diagnos, ålder eller civilstånd korrelerade till andelen som dog hemma. Endast när tiden mellan diagnos och död var kortare än en månad noterades en signifikant minskning av antalet som dog hemma. Andelen som dog på sjukhem ökade med stigande ålder och om avståndet från bostadsorten till sjukhuset översteg 40 km.

Medianpatienten tillbringade 28,5 vårddagar på institution (sjukhus och/eller sjukhem) under det sista levnadshalvåret och det terminala vårdtillfället var 10 dagar. Längden på detta var inte beroende av diagnos, ålder, kön, civilstånd eller avstånd till sjukhus, vilket gör det terminala vårdtillfället till en intressant variabel vid organisationsförändringar.

Utnyttjandet av sjukhusvård var större för vissa cancerdiagnoser (bröstcancer och prostatacancer), de som bodde nära sjukhuset och de som var gifta (eller sammanboende).

I delarbete III jämfördes alla 57 patienter som fick stöd från det palliativa resursteamet under dess första 30 månader (9101-9308) med matchade (ålder, kön,
diagnos och avstånd till sjukhus) historiska kontroller från 1990 beträffande vårdutnyttjande. Såväl andelen dagar i hemmet (85% jämfört med 58%) som längden på det terminala vårdtillfället (3 dagar jämfört med 10 dagar) utföll till studiegruppens fördel.

Vid jämförelse av de matchade parens institutionsdagar visade det sig att medianstudiepatienten sparade 10 dagar och det sammanlagda nettot var 435 dagar färre i studiegruppen. Med en vårddagskostnad på 3600 kr innebar det att besparingen av 435 vård dagar betalade det palliativa resursteamets kostnader och dessutom gav en besparing på 17 360 kr/patient.

I delarbete IV redovisades de psykometriska egenskaperna hos det livskvalitetsinstrument med 19 frågor som vi specifikt utvecklat för att användas av palliativa patienter i livets slutskede. Frågorna berör fysiska, psykiska, sociala och existentiella dimensioner. Framför allt den sista dimensionen saknas fortfarande hos de flesta instrument som kommit fram till dags dato. Varje fråga besvaras med en siffra mellan 1 och 10 där ytterlägena förklaras med text, exv "smärtfri" respektive "värsta tänkbara smärta".

Reliabiliteten testades med test-retestförfarande på 30 patienter med tre dagars intervall. Korrelationerna låg mellan 0,51 och 0,97 och 14 frågor hade mer än 0,70. Validiteten testades genom samtlig applikation av CIPS-formuläret (ett formulär med 131 frågor som översattes till svenska och användes i samband med omvårdnadsprojektet i Uppsala; n=28), korrelation till Karnofskyvärdet (n=30) och genom faktoranalys (n=71). Korrelationerna mellan de åtta frågor som hade motsvarigheter i CIPS-formuläret låg i sju fall av åtta mellan 0,54 och 0,81. Karnofskyvärdets korrelation till frågan om fysisk ork var 0,66 och faktoranalysen gav faktorer med logisk sammansättning. Sammantaget gav detta information om att det framtagna livskvalitetsinstrumentet (AQEL = Assessment of Quality of life at the End of Life) uppvisade tecken till god reliabilitet och validitet.

I delarbete V applicerades detta livskvalitetsinstrument på obotligt sjuka cancerpatienter en gång per månad. Samtidigt fyllde en anhörig i en modifierad anhörigversion av livskvalitetsformuläret med 14 frågor. 84 parvisa observationer analyserades. Patienterna hade en tendens att vara mindre oroliga än sina anhöriga men hade sämre känsla av meningsfullhet och total livskvalitet. Frågan om den totala livskvaliteten hade allra bäst korrelation till frågan om meningsfullhet (0,79 patient; 0,70 anhörig) för både patient och anhörig. Notabelt var att smärta endast hade 0,19 i
korrelation till den totala livskvaliteten och inte visade någon tendens till att öka ju närmare döden patienten kom. För anhöriga var framför allt svårigheter att lämna den sjuke ensam, ett allt större behov av hjälp med hygien och på- och avklädning, oro samt tilltagande sömnpårar svårigheter i slutskedet.

I delarbete VI användes livskvalitetsinstrumentet som ett av flera effektmått i en dubbel blind placebokontrollerad cross-over studie av paracetamols additiva analgetiska effekt vid samtidig morfinbehandling på 30 patienter. Sedan WHO:s analgetikastege lanserades 1986 har det i Sverige varit rutin att alla cancerpatienter som behandlas med morfin också har stått på regelbunden paracetamolmedicinering 1 g x 4. Denna rekommendation bygger troligtvis på antagandet att paracetamols förmodade perifera effekt skulle adderas till morfinets centrala analgetiska effekt. Då vi inte kunnat finna några vetenskapliga belägg för denna hypotes och många patienter är besvärade av att svälja 8 stora tabletter/dag kändes det viktigt att genomföra studien.

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Det går genom tiden en säregen fläkt,
en sjukdom som allmänt benämnes jäkt.
Och bannlyst är stunden av ro och av frid.
Man hör bara ständigt: Jag har inte tid.

Du äger kanhända en sjuklig vän,
det sista besöket var länge sen.
Du säger en ursäkt, blir öm och blid,
men tröstar dig med: Jag har inte tid!

Kanske har du en mor, som är gammal nu,
vars enda ljuspunkt i livet är du.
Att glömma henne, är du på glid?
Ditt samvete kväves med: Jag har inte tid.

Så lever du livet i stora drag,
hur skall jag hinna allting idag?
Jäktet förvandlat ditt liv till en strid,
Din slogan har blivit: Jag har inte tid.

Men när du har levat ditt antal år.
När döden på tröskeln väntande står.
När man dig kallar från livets id,
skall du då svara: Jag har inte tid...

Torsten Palmqvist