PALLIATIVE SEDATION:

The development of a policy and guidelines for the use of Palliative Sedation for refractory symptoms in dying patients at Sungardens Hospice, Pretoria.

Mini-dissertation presented as part requirement for the degree of Master of Philosophy (Palliative Medicine), Department of Public Health and Primary Care, University of Cape Town.

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GLOSSARY

Domiciliary service	a service provided to patients in their homes by a registered, palliative care trained nurse.
Euthanasia	the intentional, active termination of life.
Existential distress	suffering caused by a sense of the meaninglessness of life.
Hospice Association of South Africa	an association of about 40 South African hospices who provide care to dying patients on the basis of need and not the ability to pay.
Informal settlement	an area consisting of dwellings without formally developed infrastructure and amenities.
Nursing assistant	a person trained to do certain nursing functions under the supervision of a registered nurse.
Opioid induced Neurotoxicity	the occurrence of myoclonic jerking, confusion and hyperaesthesia caused by high dose opioids, especially in the presence of dehydration and poor renal function.
Palliative care	a multidisciplinary approach to the care of dying patients, focused on relief of symptoms.
Palliative sedation	the use of sedative medication to relieve refractory symptoms by reduction in patient consciousness.
Parenteral	by injection.
Quality Improvement Cycle	a method of bringing about improvement through the use of a recurring cycle of observing-planning-acting and the observing again.

Refractory symptoms	severe symptoms which have failed to respond to the usual accepted palliative care remedies.
Registered nurse	a fully trained professional nurse registered with the South African Nursing Council.
Sanctity of life	the belief that human beings are made in the image of an infinite personal God and thus of inestimable value.
Short Course in Palliative Nursing Care	six month course registered with the South African Nursing Council which covers palliative care and includes a short research component.
Volunteer caregiver	a non-paid volunteer, who has received a basic course of training in patient care and who assists the nursing staff.

ABBREVIATIONS

Alp.	Alprazolam
Benzo	Benzodiazepam
CAM	Confusion Assessment Method
GIT	Gastro-intestinal tract
Halo	Haloperidol
IMI	Intra-muscular injection
IPU	In Patient Unit
IV	Intravenous
Lor.	lorazepam
mg/d	milligram per day
mg/hr	milligrams per hour
mg/kg	milligram per kilogram
Mid.	midazolam
OIN	Opioid induced neurotoxicity
P-C-D	Primary-Constant-Deep
P-I-M	Primary-Intermittent-Mild
PME	Parenteral Morphine Equivalent (mg/day)
P.O.	Per os
PPI	Palliative Prognostic Index
PPS	Palliative Performance Scale
PR	Per Rectum
SC	Subcutaneous
S-C-D	Secondary-Constant-Deep
S-C-M	Secondary-Constant-Mild
SL	Sublingual

1. PREFACE

Sedation in the context of terminal care has been a hotly debated topic for many years. There are two main reasons for this. Firstly, the wide variation in its reported use[1] leads to doubts about the appropriateness of the care available in areas with a high percentage of sedation, and secondly, there is the suspicion that terminal sedation is actually a euphemism for euthanasia.[2,3,4] Ventafridda's report[5] in 1990 that 52% of moribund patients required sleep-inducing sedation to control physical suffering, stimulated a lot of discussion in palliative care circles with many physicians being surprised at the apparent high percentage of patients needing terminal sedation. This was followed by the publication of studies from various centres throughout the world in an effort to determine current international practice. A meta-analysis of 13 studies showed that the incidence of sedation varied from 1-72%.[1] This wide variation needs an explanation. It can be attributed in part to differences in the terminology used.[1,6,7] However, there appear to be other reasons, including cultural differences in the application of palliative care in different parts of the world and possibly varying standards and criteria for the use of sedation.[8] To add to the concern of many, there was the accusation that, in reality, terminal sedation is the equivalent of "slow euthanasia."[2] While many authors feel that terminal sedation is a legitimate option for refractory physical symptoms, its use for severe existential distress is less well accepted.[9]

It is thus apparent that there is a need to clearly define the terms used and to develop guidelines that have international recognition and acceptance by staff and patients. Such developments would help to encourage improved standards of care. The development of such guidelines is thus an urgent need.

2. PURPOSE OF THIS STUDY

2.1. Develop guidelines for the use of palliative sedation at Sungardens Hospice.

2.2. Evaluate the current use of palliative sedation at Sungardens Hospice against these guidelines.

2.3. Use the guidelines and the results of this survey to develop a policy for the use of palliative sedation at Sungardens Hospice which acknowledges the ethical principle of respect for the sanctity of human life and which uses the most effective means of modern palliative medicine to manage refractory symptoms.

3. THE STRUCTURE OF THE REPORT.

It was decided to use a quality improvement cycle to effect change as the study progressed.[10] For this reason the report of this project will be presented in a different way from the usual descriptive study.

The traditional structure of a scientific article (IMRAD: Introduction, Methods, Results and Discussion) is not suitable for a quality improvement report because Quality Improvement usually involves a continuous cycle of measurement and change. Often as much can be learnt from what does not work as from what does. The editors of the journal *Quality in Health Care*[11] suggest the following structure:

- Brief description of context
- Outline of problem: what were the participants trying to accomplish?
- Key measures for improvement

- Methods used to assess the problems
- Analysis and interpretation: how did this information change the understanding of the problem?
- Strategy for change: what actual changes were made, how were they implemented, and who was involved in the change process?
- Effects of change: did this lead to improvement for patients? How does one know that an improvement took place?
- Next steps: what has been learnt and/or achieved, and how will this be taken forward

This type of strategy is more suitable for complex situations where the answers are not straightforward and where it is important for those involved to be active participants in the resulting process of change. The major drawback is that it requires an extended period of time to effect the whole cycle of change.[12] As far as possible this approach will be used for the structure of this project.

4. A BRIEF DESCRIPTION OF THE CONTEXT.

4.1. Sungardens Hospice

Sungardens Hospice originated in 1987 as a nurse lead domiciliary service providing care for dying patients in the greater Pretoria area (Population 1.48 million, 1996 Census). It was based on the principles of the modern hospice movement that had developed in England during the 1960s under Dame Cecily Saunders at St Christopher's Hospice, London.

From the beginning Sungardens has been an independent, non-government organization supported by its own fund raising efforts. Patients are cared for according to their need and not their ability to pay. Thus no-one in need of terminal care is turned away. Although there are oncology units at a number of private hospitals and at the Pretoria Academic Hospital, Sungardens Hospice is the only hospice specifically catering for terminal patients in Pretoria.

The first In Patient Unit (IPU) was opened in a converted house in the eastern suburbs of Pretoria in 1990 and the present specially designed IPU was opened in November 1997. The IPU has 7 beds and provides short stay care for a wide range of terminal patients. In addition to terminal care, patients are also admitted for symptom control and family respite.

4.2. Dual Ethos

The modern hospice movement was founded on a firm Christian faith and an acknowledgement of the sanctity of life.[13] It was the desire to integrate a strong compassion for the dying with the scientific means to relieve pain and suffering that lead Cecily Saunders to open St Christophers Hospice in 1967. At Sungardens Hospice most of the staff still subscribe to this dual ethos. Many nurses feel that in the shift from the concept of hospice to the broader, more mainstream concept of Palliative Medicine, there has been a degree of secularization. There has been a cutting loose of medical care from its firm spiritual foundation. The controversy around terminal sedation has heightened the suspicions of some that this shift has reached a degree where their personal faith and ethical standards are being challenged and that the sanctity of human life is no longer respected. The effective teamwork of hospice would be adversely affected if there were serious misgivings and disagreements amongst the staff about such an important aspect of current management. Thus there is a need not only to develop guidelines, but also to attempt to resolve these dilemmas as far as possible by ensuring a firm commitment to the principle of the sanctity of life in the use of palliative sedation. It was also felt that, by involving the staff of the IPU in the process of formulating these guidelines, their ideas and concerns could be incorporated. One of the main problems of all guidelines is that they are difficult to implement if those involved in implementing them do not have a sense of ownership of the guidelines.[14]

4.3. Staffing and work load

At present the domiciliary service consists of 12 registered nurses and 8 nursing assistants, who together care for an average of 310 patients at any one time. The area served includes several large periurban informal settlements. Patients referred for domiciliary care, have an average survival of 3 months and during this time they will receive an average of 60 nursing contacts. The domicilary nurse liaises with the patient's own doctor if there are problems. Occasionally one of the hospice doctors will do a home visit. At this stage the hospice cannot afford to provide a full medical service to all patients in their homes. Admission to the IPU is arranged by the domiciliary nurse in charge of the patient or by direct transfer of patients from local hospitals.

On average 218 patients are admitted to the IPU each year. (See Tables 1&2) The majority (76%) of these patients are suffering from advanced cancer. Over the last few years the number of AIDS patients has been steadily increasing. (At present AIDS makes up 12% of admissions and 33% of domiciliary patients.) The average length of stay in the IPU is 15 days and the Unit has a bed occupancy rate of 82%. A third of the patients admitted can be discharged to domiciliary care again once their symptoms have been controlled.

Table 1: Total number of admissions to the In Patient Unit of Sungardens Hospice, 1998 – 2001 and the number of AIDS patients admitted each year.

YEAR	Total Admissions	No. of AIDS patients
1998	217	22
1999	223	30
2000	212	28
2001	223	28

The IPU is staffed by 2 registered nurses and 2 nursing assistants during each morning shift and by 1 registered nurse plus 2 assistants during the afternoon and again during the night shifts. There is an additional community volunteer caregiver during the day shifts. A total of 20 different staff members work in the IPU. The 9 registered nurses do various shifts of between 6 to 120 hours per month. This flexibility of working hours does create some problems with continuity of patient care, but it is popular with the nurses and has contributed to the stability of the staff. Twelve of the IPU staff are presently in their 10^{th} year of service at Sungardens.

Most of the registered nurses employed by Sungardens Hospice, have completed the Hospice Association of South Africa's Short Course in Palliative Nursing Care, accredited by the South African Nursing Council.

Sungardens has the services of a part time chaplain but because of limited finances, does not have a social worker or psychologist on the staff. Various staff members spend a good deal of their time counseling patients and their families. If a need arises that the nursing and medical staff cannot handle, outside professional help is obtained.

The medical care is provided by 3 general practitioners. Two of these doctors are in private practice while the third is a senior consultant in the Department of Family Medicine at the University of Pretoria. They have been involved with Sungardens Hospice for 2, 5 and 15 years respectively. For a period of 7 days at a time, they take it in turn to look after the patients in the IPU. They are responsible for doing a daily

ward round and are available for any new admissions or problems that may arise before the next ward round.

In South Africa there are no registered specialists in Palliative Medicine. Four South African doctors have completed the Diploma in Palliative Medicine through the University of Wales while about 20 more are currently registered for either a Diploma or an M.Phil.(Palliative Medicine) degree through the University of Cape Town.

5. OUTLINE OF THE PROBLEM

Although it is possible to adequately control the symptoms of the majority of terminal patients, there are some whose symptoms remain refractory. For a symptom to be labeled refractory, it must be persistent and severe despite the use of established palliative care remedies. One of the options available for the relief of intractable suffering in such patients, is the use of terminal or palliative sedation. A review of the international medical literature (see below) revealed a number of problems surrounding the use of sedation for refractory symptoms. These problems included the wide variation in the reported use of terminal sedation, the inconsistency in the definition of terminal or palliative sedation, the ethical problem of whether terminal sedation was a form of "slow euthanasia" and the concern that a difficult symptom may be declared refractory because of ignorance of modern means of palliative care. There are, as yet, no widely accepted guidelines for the use of sedation in terminal patients and also no internationally accepted definition of terminal or palliative sedation.

A retrospective audit of the last 200 admissions to Sungardens Hospice during 2001 (See Table 2), revealed a number of concerns. It was often unclear from the written notes why sedation was being used and whether there had been proper consultation with the patient and/or the family. In a number of cases, sedation was prescribed but it appeared from the nursing records that this was not very effective, especially in cases of agitated delirium.

Table 2: A retrospective audit of the reasons for the use of sedation in 42 patients out of 200 admissions to Sungardens Hospice during 2001.

REASON FOR SEDATION	Number sedated	%
Restlessness/Delirium	25	59
Anxiety	4	10
Dyspnoea	3	7
Convulsions/Twitching	2	5
Nausea	2	5
Not swallowing	1	2
Not stated	5	12
TOTAL	42	100

Following this audit, it was decided to do a prospective study of the first 100 admissions from 1 January 2002 where the use of sedation would be carefully documented. During this time, an attempt would be made to clarify a definition of palliative sedation, establish clear guidelines and a policy for the use of palliative sedation, and develop a means of carefully monitoring the effectiveness of sedation at Sungardens Hospice. The opinions of overseas experts would be sought, to see if these guidelines were in accordance with the standards of modern palliative care. In addition a literature review would be done so that the results of this study can be compared with work already published. This comparison, together with the documents produced by this study, would form the key measures for its evaluation.

6. LITERATURE REVIEW:

6.1. Introduction

A Medline search using the key terms "terminal sedation" and "palliative sedation" was carried out. In addition, references of articles were also obtained from overseas colleagues interested in the subject, as a number of specialised palliative care journals are not listed on Medline. A number of other articles were also collected on related topics such as prognosis, prognostic scores, intractable or refractory symptoms, delirium, euthanasia, terminal suffering, physician assisted suicide, the principle of double effect and guidelines. Special attention was paid to articles by Morita and colleagues from Japan who have written extensively on terminal sedation and related topics.

6.2. Terminology

Mild sedation, especially with benzodiazepines, is commonly used in palliative care to relieve insomnia and mild anxiety unresponsive to non-drug measures. Patients with severe symptoms such as confusion, dyspnoea, nausea, vomiting, agitation, convulsions and pain may require large doses of a variety of drugs, including the phenothiazines, opioids, barbiturates and even anaesthetic agents such as ketamine, all of which may cause some degree of sedation as a side effect.[15,16] Deep sedation, enough to induce complete loss of consciousness, is occasionally needed in extreme situations in advanced cancer patients when massive haemorrhage, massive pulmonary embolism or complete airway obstruction occurs.[16,17,18,19] There is probably little disagreement about the use of sedation in any of the above situations.

There is tremendous pressure on physicians to help their patients to die well. A number of studies, which have been summarized by Bruera, have shown that negative

perceptions of patient comfort by the surviving family, during the dying period, can complicate the grieving process.[20] The agitation and restlessness of some dying patients can be very distressing to all concerned. Nursing becomes a nightmare and families are overwhelmed.

There are many reasons for terminal restlessness.[7,16] Although an attempt should be made to correct the underlying cause, this is often not possible. While it may be relatively easy to correct problems such as urinary retention and faecal impaction, and while it may some times be possible to improve matters by eliminating drug toxicity, in the vast majority of patients terminal restlessness is multi-factorial and irreversible. In such situations, sedation seems the only option. This is where the difficulty and controversy arise. Is sedation being used because of lack of skill in controlling terminal symptoms? Is sedation being used for problems such as existential distress or emotional suffering, problems that may be difficult to quantify? Many physicians have reservations about the use of deep sedation in such cases. Is such sedation merely euthanasia in disguise?[19,21] Is "terminal sedation" a self fulfilling prophesy as the normal means of sustaining life, such as food and water have been withdrawn at the same time as sedation has been introduced?
Concern about these issues has prompted some to propose new terms to replace terminal sedation. After conducting a survey of 61 international experts in 1998, Chater proposed that the phrase 'sedation for intractable distress in the dying' be used in place of terminal sedation.[22] Morita has suggested that the term 'palliative sedation therapy' be used.[23] This he defines as '*the use of sedative medications to relieve intractable and refractory distress by reduction in patient consciousness'*.

This suggestion is I believe a good one. It removes the stigma associated with terminal sedation and places the emphasis on the purpose of the sedation rather than on the outcome. It sets out clearly the aim and the means.

Morita has also proposed a system of classifying sedation that may help to minimize misunderstanding. Sedation can be classed as mild or deep depending on the degree of sedation, intermittent or continuous according to the duration of the sedation, and primary or secondary according to the drug's pharmacological properties. Primary sedation refers to the relieving of the distress by sedation rather than the pharmacological treatment of the distressing symptom. Secondary sedation is where there is reduced consciousness in addition to treatment directed at the underlying symptom. The target symptom, such as delirium, for which sedation is being used, must be classified according to its severity. In addition, Morita proposes that the presence or absence of vital organ failure be noted or that a standardized prognostic rating index be used. Thus one has a set of five descriptions, which will clarify the reason and type of sedation being prescribed. If consensus could be reached, these proposals would help to clarify matters and allow better comparison between different centres. Clarity on this aspect of sedation would help universal guidelines of good practice to be developed.

6.3. Ethical Dilemmas

In 1996 the article entitled "Slow euthanasia" by Billings and Block created quite a stir amongst palliative care physicians.[2] Billings and Block defined slow euthanasia as *"the clinical practice of treating a terminal patient in a fashion that will assuredly lead to a comfortable death, but not too quickly."* They went on to state, *"Such practices seem to indicate a tacit acceptance by the medical community of voluntary*

euthanasia under particular circumstances, but they also reflect professional reasoning that may be ethically muddled." They dismissed the principle of double effect as *"an unconvincing rationalization"*. They questioned the claim that intent to sedate and not to cause death could be differentiated from active euthanasia, as the outcome was the same. It was only duration that differentiated the two practices. The fact that other supportive measures such as hydration and nutrition were also usually withdrawn was a clear indication that death in fact was intended, rather than just foreseen. Justifying the practice by means of the principle of double effect was, in fact, just clouding the issue. In addition, it was allowing some undesirable practices to occur. In some instances, patients and their families were not fully informed of the implications of the practice of "*hanging a morphine drip*". Involuntary euthanasia was thus being practiced. Taking things a step further they questioned for whose benefit this process was being used. On the one hand, "*drawing out death*" was being used as "*an inappropriate substitute for comprehensive palliative care*" while on the other hand, it was a smoke screen to cover the hastening of death when all else had failed. It was thus more for the benefit of the doctor rather than the patient. Billings and Block could, with some apparent justification, claim that "*slow euthanasia puts an acceptable face on an otherwise forbidden practice*".

This paper evoked a vigorous response especially from Mount [24] and from Portenoy [25] both of whom pointed out that Billings and Block's article presented no formal data. It was based on anecdote and opinion. Both Mount and Portenoy defended the principle of double effect. Mount correctly pointed out that the principle of double effect did not only apply to end of life care but was involved in every therapeutic decision. Side effects or complications were possible with any treatment. Although

side effects could be foreseen they were not intended. Without the principle of double effect, it would be difficult to practice medicine. Discarding it here does more than just speed up dying; it may endanger the whole of medical practice, as we now know it.

Far from being only a subtle difference of no consequence, euthanasia and terminal sedation intended for good symptom relief, are vastly different. By creating a new meaning for the term slow euthanasia, Billings and Block were actually adding to the confusion of terms.

6.4. Variation in the reported frequency of terminal sedation.

When comparing the results of the studies that have been done on sedation in terminal care, one of the main differences is the wide range in the frequency of its use. In a review of all the clinical studies published in the previous 10 years, Sales[1] reported a range of 1-72% in the use of sedation. This difference was due to a number of factors. Firstly there was no uniformity in what was meant by the term "sedation". In some cases it referred to the use of anxiolytics as an adjunct in the control of major symptoms, while in others, it referred to the rendering of the patient deeply unconscious. There is thus a need for clarity in the use of the term, so that valid comparisons can be made in the future and so that proper guidelines can be drawn up.

Retrospective studies report a lower average frequency (21%) than prospective ones (38%). The studies also look at different phases of the terminal period. While Peruseli [26] looked at the last 12 hours of life, Ventafridda[5] followed up patients from their discharge from hospital until they died (average of 41 days).

In a more recent study, not included in the ones analyzed by Sales, Fainsinger[27] has been able to show that the need for sedation can be kept low (7%) by means of intensive palliative care. He also suggests that some of the variation reported in the international literature may be due to "cultural differences". In an earlier joint international study[8], 22% of patients in Spain had to be sedated. The need in Spain for sedation for "existential or family distress" was 9%. A possible contributing factor is that a considerably lower percentage of Spanish patients are informed of their diagnosis as compared to their North American counterparts. The implication is that there was more patient and family distress because of Spanish society's approach to disclosure of the terminal diagnosis. However, before one can jump to that conclusion, one needs to be sure that the same definition of sedation is being used in both countries. This is not clear from the article. Stone[28] reported an average of 26% of patients requiring sedation in a survey done in London. This difference from Fainsinger's Canadian figures can surely not be explained by major differences in culture or palliative care skill.

In France, a same day poll was taken of 42 centres. It showed a prevalence of 9.9% out of 413 patients were receiving deep sedation.[29]

Reporting bias could be another important factor contributing to the variation in reported rates of sedation[6]. Wanting to prove that good palliative care reduces the need for sedation may influence which definition of sedation is used, as well as the decision about whether or not to use sedation.

It seems that before the apparent variation in the use of sedation is attributed to lack of skill or cultural differences, greater clarity of terms and indications is needed. The difference may be more apparent than real. Progress in palliative care in this area will only occur when clarity replaces ambiguity.

6.5. Further Ethical Dilemmas

As has been mentioned this topic has stimulated a lot of heated debate. There are two main issues that need to be decided if one is going to get beyond accusation and counter-accusation. The first key issue is the legal and ethical difference between "*allowing to die*", and killing.[24] Closely related to this is the second key issue, namely the validity of the principle of double effect.

If one accepts euthanasia or physician assisted suicide, then Billings and Block have a case and there is no real ethical distinction between 'fast' and 'slow' euthanasia. It is then purely a matter of duration. If this is so, their very pointed question needs to be considered carefully. They ask, *"Why should a patient who requests a quick death be subjected to a prolonged dying?"*[2] In an attempt to answer this, Mount has tried to argue that, *"with sedation the patient benefits from palliative care that is guided by the same consistent treatment aim that has guided care throughout the disease trajectory, i.e. enhanced quality of life."*[24] The difficulty is that there are occasional patients who despite the best possible care, feel that life has no purpose and that continued existence is intolerable for them. In a recent paper, Morita and colleagues discuss terminal sedation for existential distress and are able to show how the principles of good palliative care and the appropriate use of sedation can deal with even the most difficult of cases, without the need for euthanasia.[30]

The real difference, from a legal perspective, is the issue of intent. Culpability is, to a large extent, determined by intent. However, it is as well to note that this distinction is not as clear-cut as one would imagine. If a harmful effect is foreseen as a virtually certain consequence of one's actions, claiming that it was not intended will be difficult to defend. If this were not so, many genuine criminals would go unpunished. The courts are at present assessing the actions of a doctor, who acted in good faith, in a different way to the ordinary citizen, claims Morris.[31] Thus, intent remains a valid defense for the doctor acting in good faith. From a legal perspective, Morris finds this inconsistency unsatisfactory and claims that "*to do justice, the law needs to be certain, expedient and consistent.*" He suggests that "*the current law is not adequately equipped to deal with issues posed by modern palliative medicine.*" This is an important warning and should motivate all involved in palliative care to see that as far as possible, ambiguities and confusing terms are eliminated. Justice must not only be done, it must be seen to be done.

Perhaps a more disturbing development was brought to the fore by the decision of two US Federal Courts of Appeal in 1996, that there was "*no ethical or legal difference of importance between death by treatment withdrawal and death by euthanasia.*" This is a denial of the validity of the principle of double effect and, as Brody[32] suggests "*in so doing the court eliminated the ethical justification for many of the best and most compassionate practices of palliative care.*" It is indeed fortunate that the Supreme Court subsequently invalidated this ruling.[33] This may, however, be but a temporary reprieve.

As has been mentioned on several occasions, the principle of double effect is crucial to an understanding of palliative care and indeed all good medical practice. It allows for an action, which although intended to do good, may have possible negative effects.[34,35,36] Such an action may be morally permitted if it meets the following conditions: -

(i) The action is not in itself immoral.

(ii) If only the good effect is intended, although the bad effect may be foreseen.

(iii) The bad effect may not be the means to the good effect.

(iv) The good effect must outweigh the bad effect.

The appropriate use of palliative sedation meets all four criteria.[37]

As has also been mentioned, this principle is intrinsic to all medical care but even experienced doctors seem to have difficulty understanding this. Hunt for example states that it only applies to situations where death is hastened.[38] He goes on to claim that it has an exclusive focus on the doctor's agenda and that it could be used to justify terminal sedation against a patient's wishes. This is obviously a gross misrepresentation of the principle, which is design to encourage good not evil. It appears that his real reason for discrediting this principle is that it stands in the way of euthanasia. Other supporters of euthanasia also attack it, for the same reason.[39]

The principle is also not just a convenient instrument to determine whether an action is right or wrong by first looking at its outcome, and then arguing its moral value in a consequentialist manner. As Sulmasy points out, "*one sets out initially to do a*

morally good action, taking full account of the foreseeable consequences." It is not simply a matter of choosing the lesser of two evils.[36]

Morita and colleagues have also highlighted the need for proper communication with patients and their families.[40] They need to understand the extent of the disease and the likely prognosis, the alternatives available and the effects and outcome of the proposed sedation.

6.6. Quality of Life

Let us briefly return to the argument of quality of life. There are a number of practical and ethical difficulties involved in trying to measure quality of life in situations where lives have been judged to have no quality. Farsides and Dunlop suggest the following problems.[41] Firstly, there are no quality of life measures that have been shown to reliably identify patients who feel that life is not worth living. Caution is needed because of the fluctuating nature of patients' assessment of life and their desire for death. The effect of depression and of symptoms that may as yet not be under control, may also create uncertainty as to the real wishes of the patient. While some may assess the quality of life of a dying person as abysmal, the dying person may find some quality.[42] In the case of non-competent patients, the use of proxies compounds the difficulties, because of the possible differences in assessment that there may be between the proxy and the real wishes of the non-competent patient. For the competent person, some may say that personal autonomy should be the determining principle. They would claim that if a competent person wishes to end his life, that should be enough cause for him to be allowed to do so.[9,43] The real argument is not about quality of life as much as it is about whether the principle of

personal autonomy is absolute. The American Supreme Court has ruled that the fact that the individual views his or her life as not worth living does not give him or her a fundamental right to physician assisted suicide.[33]

The fundamental worth of human life is something that most societies still hold supreme. The palliative care movement has to a large extent developed out of a concern for the worth of the lives of dying patients. Even in our increasingly secular society, for many people that worth stems from their belief that human life is God given and an expression of God's image. Thus the worth of the individual goes beyond the value that even that individual places on his or her own life. Whatever the personal belief system of the doctor, he or she needs to be aware of the spiritual dilemmas of dying people and of the nursing staff who have to care for them in their final moments. Nurses are often the ones who have to administer the sedation ordered by the doctor. Thus any guideline or policy has the very difficult task of addressing all these concerns. The opposite may also apply, it may be the doctor who is struggling with his or her conscience and a desire to respect the sanctity of life while the patient or the nursing staff may feel it is time to "end things."

6.7. Sedation and life expectancy

It is interesting to note that so called 'terminal sedation' does not necessarily mean the shortening of life. Several authors[5,6,28,44] have documented no difference in survival of both sedated and non-sedated terminal patients. In addition, Bercovitch and colleagues have shown no difference in survival of patients on low or high doses of morphine.[45] These are important findings and they go a long way to establishing

the legitimacy of palliative sedation. It is by no means certain that the patient will actually die. Three cases in the present study improved and were able to be discharged. Both Morita and Fainsinger relate similar cases[40,46]

6.8. Legislation or Clinical Guidelines?

Even in the advanced palliative care units, there are going to be cases where the best symptom control is not completely effective. The symptoms for which sedation has been needed include delirium, pain, dyspnoea, nausea and vomiting, haemorrhage and extreme anxiety[1,5,6,8,27,46] The symptom that seems to remain most refractory, is severe delirium. Varying degrees of sedation may be needed to control agitation, hallucinations and restlessness. The primary goal must, however, remain relief of distress not shortening of life. The need for sedation in the rare extreme emergencies, such as massive haemorrhage or suffocation, is also well accepted.

We have seen ample evidence of the complexity of this topic. Will more regulation help or will it perhaps need to be so convoluted and complex that it clouds the issue further? This will ironically allow more 'wiggle room' for the very practices such regulations are designed to curb.[32] I would suggest that even before we think of legislation we need consensus on the clinical terminology so that there can be valid comparison of practice and straightforward, clear clinical guidelines.

6.9. Conclusion

The real issue then appears to be not whether sedation is used but rather how it is used. Are the indications correct, are patients/families fully informed, are appropriate drugs and dosages used and is the patient appropriately cared for until death?

7. THE PROCESS

7.1. Review of the use of sedation at Sungardens Hospice

In order to assess current practice, a retrospective survey of the clinical records of 200 consecutive admissions prior to 31 December 2001 was carried out. (See Table 2) Some form of sedation was used in 42 patients (21%). The main reason was for terminal restlessness/delirium (25 patients, 59%). In 3 patients the main refractory symptom was anxiety. It was uncertain from the records if these patients had other features of delirium. The other reasons included convulsions (2 patients), dyspnoea (3 patients) and severe nausea (2 patients). In 5 patients the reason was not clearly stated in the notes. There was a lack of standardization of the recording of observations. It was difficult to judge if appropriate action had been taken as a result of the observations, so that the refractory symptom was controlled satisfactorily.

7.2. Initial Guidelines & Recording Forms

The next step was to draw up the preliminary guidelines for the IPU staff. (See Appendix 1.) These guidelines were derived from the literature review, discussion with the staff and comments from palliative medicine colleagues in other countries. These guidelines were expanded to included an introduction, a brief literature review, instructions on assessment, communication, consent and monitoring (See Appendix 2).

The second document developed was a form for recording sedation. (See Appendix 3) This contained the various items that had to be checked before starting sedation.

The main reason for using sedation was to be stated and an estimation of the likely prognosis was to be made. In addition there was a sheet for recording at 6 hourly intervals the drugs prescribed, the level of sedation and the effect of the sedation on the refractory symptom (this was later modified to hourly observation and recording). Finally there was the information to be completed after the death of the patient and an assessment of the process by the staff and the researcher. (Not many of the staff made written suggestions for improvements to the guidelines or forms. It was found to be much more useful to speak to individual nurses and get their suggestions directly.)

A copy of the full research protocol, the guidelines and an example of a completed recording form, were placed in a folder in the IPU duty room. All the staff working in the IPU were informed about the research and instructed on how to complete the recording form. They were encouraged to suggest improvements to the guidelines and the recording forms.

7.3. Strategies for keeping staff informed

Making sure that everyone understood the process and the forms proved to be more difficult than was first anticipated. Initially this was done on an individual basis. However, as the project proceeded, various alterations were made. It was very difficult to keep everyone informed of the changes. Staff meetings were arranged but not everyone could attend. A regular staff newsletter outlining the developments was produced and distributed (See Appendix 4). This was a far more practical solution. Apart from outlining the changes, various other problems such as the difficulty of diagnosing delirium, the management of Opioid Induced Neurotoxicity and the estimation of prognosis, were also dealt with in these newsletters.

As can be expected, numerous difficulties were encountered in the beginning. The recurrent changes that were made created some confusion and uncertainty amongst the staff. To prevent them from becoming frustrated with this process, it was then decided only to make changes that most people felt were essential. Eventually there were five major revisions of the guidelines and four of the recording form.

7.4. Selection of patients

Because of the difficulty that the nursing staff experienced in differentiating between ordinary mild sedation and palliative sedation for refractory symptoms, it was decided to include all patients for whom sedating drugs were prescribed. This can be criticized as being too broad, however, the aim of this project was mainly to develop a policy rather than just to describe a practice. Patients who only required a normal sleeping tablet at night were excluded. No patients or their families refused to participate in this research project.

The study was completed once there had been 100 admissions to the IPU from 1 January 2002. Of these 100 admissions, sedation was used in 22 patients between 1 January and 15 June 2002. One patient (No16) was discharged and readmitted later (No 19). (See Table 2.)

8. ANALYSIS AND INTERPRETATION.

In this section the results of this survey will be analyzed and interpreted. Where necessary, comparisons will be made with similar surveys from the international literature.

8.1. Patient Profile

Of the 22 patients who required sedation, 8 (36%) were men and 22 (64%) women and their average age was 68.8 years (range 49 – 88 years). (See Table 3) This is very similar to the gender ratio and average age of whole group of patients admitted during this period (See Tables 4&5).

8.2. Diagnosis

In this period sedation was only needed for patients with cancer. The frequency of the various types of cancer is also similar in both the sedated and in the whole group (See Table 4). The 3 most frequent types of cancer, found in the group of patients that were sedated, were colon (4), pancreas (4) and ovary (3). The terminal phases of these cancers are often associated with intestinal obstruction and delirium.

8.3. Reason for Sedation

The main refractory symptoms requiring sedation were delirium (41%), nausea & vomiting (23%), convulsions (14%), dyspnoea (9%) and pain (4%). In the remaining 2 patients, the first had advanced squamous cancer of the neck and requested increased sedation at night and the other, who had an astrocytoma, was semi-conscious and having difficulty swallowing, necessitating a syringe driver for medication (morphine sulphate and haloperidol). Neither of these would qualify as refractory symptoms if one applied the definition strictly. (See 7.4)

Table 3 : Patients requiring sedation who were admitted to Sungardens Hospice between 01/01/2002&15/06/2002

No.	Sex	Age	Diagnosis	Clinical Problems	Refractory Symptoms	PPS	PPI	Prog. est. by staff	Actual Survival (hrs)	Feeding	Classif..	Delay till Effective (hrs)	PME* mgs /24hrs	Benzo mgs /24hrs	Halo mgs /24hrs
1	M	49	Ca Pancr.	Pulmon.Oedema	Dyspnoea		15		*20 min*	P.O.	P-C-D	*20 min*	85	Mid 7.5	
2	M	69	Ca Colon	Intest.Obstruct.	Delirium		10.5	>72hrs	105	Spray	P-C-D	48	180	Mid 30	10
3	F	74	Ca Lung	GIT Bleed	Delirium		14	<48hrs	38	Spray	P-C-D	4	167	Mid 30	
4	M	77	C.U.P.		Delirium		9	<48hrs	50	Spray	P-C-D	2	26.3	Mid 15	10
5	F	69	Ca Ovary		Delirium		8.5	>72hrs	106	Spray	P-C-D	13	41.3	Mid 15	10
6	F	88	Ca Pancr.		Vomiting		6	>72hrs	33	Spray	S-C-M	10	15		10
7	M	55	Ca Kidney	Lung metastases	Dyspnoea		7.5	>72hrs		P.O.	S-C-D	16	85		5
8	F	65	Ca Colon	Intest.Obstruct.	Vomiting		4.5	>72hrs	169	Spray	P-C-D	25	260	Mid 40	10
9	F	88	Ca Pancr.		Delirium		7.5	>72hrs	191	Spray	P-I-M	96	47	Mid 10	5
10	F	68	Ca Brain	Comatosed	Dysphagia		10.5	>72hrs	80	Spray	S-C-D	6	15		5
11	M	81	Sq Ca Neck	Insomnia	Patient's request		8	>72hrs	67	Spray	P-I-M	10	15	Lor 1	5
12	F	72	Ca Bladder	Convulsion	Convulsions		11	<48hrs	44	Spray	P-C-D	2	60	Mid 15	
13	F	60	Ca Lung	Gangrene of feet	Delir.& Pain		11	<48hrs	110	P.O.	P-C-D	24	105		10
14	F	63	Ca Pancr.	GIT Bleed	Delirium		7.5	>72hrs	30	IV	P-C-D	14	23.7		5
15	F	62	Ca Bladder	OIN ?	Convulsions		10	<72hrs	6	SC	P-C-D	8	15		5
16	F	63	Ca Colon	Jaundice	Vomiting		2.5	>72 hrs		P.O.	P-I-M	14	45	Alp 0.25	5
17	F	71	Ca Ovary	Intest.Obstruct.	Vomiting		5	>72 hrs	74	Spray	P-C-D	6	45		10
18	F	45	Ca Breast	Intest.Obstruct.	Vomiting	30%	3.5	3-7days	104	S.C	P-I-M	11	45	Lor 1	10
19	F	63	Ca Colon	Jaundice	Delirium	30%	8	49-72hrs	369	Spray	P-I-M	86	45	Mid 15	
20	M	77	Ca Prost.	Bone metastases.	Convulsions	30%		3-7days	86	Spray	P-C-D	1	90	Mid 15	
21	M	73	Ca Breast	Brain metastases	Delirium	?	?	49-72hrs	75	IV	P-C-D	12	60	Mid 15	
22	F	77	Ca Ovary	Intest.Obstruct.	Vomiting	50%	9	3-7days	60	Spray	P-C-D	2	15		5
23	M	74	Ca Colon	Bone metastases.	Delirium	30%	7.5	7d-2w		P.O.	P-I-M	5	120	Mid 15	

(See p vii for abbreviations.)

* Mean daily dose of morphine: 70 mgs (range 15-260 mgs)

Table 4: The diagnoses and the use of sedation in the patients admitted to the IPU between 31/01/2001 and 15/06/2002 in 3 groups of 100.

Group	Group 1		Group 2		Group 3		Total	
Dates	31/01/01 to 23/07/01		24/07/01 to 31/12/01		01/01/02 to 15/06/02			
Diagnosis	Admitted	Sedated	Admitted	Sedated	Admitted	Sedated	Admitted	Sedated
TOTAL AIDS	**13**	**2**	**14**	**1**	**15**	**0**	**42**	**3**
Cancers								
Ca Breast	6	2	10	0	17	2	33	4
Ca Colon	7	2	14	0	10	4	31	6
Ca Lung	13	4	7	1	9	2	29	7
Ca Brain	5	3	10	3	2	1	17	7
Ca Prostate	4	1	7	2	5	1	16	4
Ca Pancreas	5	2	2	1	8	4	15	7
Ca Mouth	4	0	7	2	0	0	11	2
Ca Ovary	4	2	2	1	3	3	9	6
Ca Cervix	4	1	2	0	3	0	9	1
Ca Liver	2	0	4	1	1	0	7	1
Ca Bladder	2	1	0	0	4	2	6	3
Ca Uterus	1	0	3	1	2	0	6	1
Ca Stomach	4	0	1	1	1	0	6	1
Melanoma	2	0	2	0	2	0	6	0
Ca Oesophagus	3	0	0	0	2	0	5	0
Myeloma	2	1	1	0	1	0	4	1
Lymphoma	1	0	0	0	3	0	4	0
Ca Larynx	0	0	1	0	2	0	3	0
Mesothelioma	2	1	1	0	0	0	3	1
Sq.Cell Ca	0	0	1	0	2	1	3	1
Ca Kidney	2	0	0	0	2	1	3	1
Ca Anus	0	0	0	0	2	0	2	0
Ca Penis	1	0	0	0	0	0	1	0
Ca Max. Sinus	1	0	0	0	0	0	1	0
TOTAL CANCER	**76**	**20**	**76**	**13**	**82**	**22**	**226**	**55**
Non-Malignancies								
COPD	7	2	3	0	0	0	10	2
Chr. Renal Failure	1	0	1	1	1	0	3	1
Mult. Sclerosis	1	0	1	0	0	0	2	0
MND	0	0	2	2	0	0	2	2
CVA	0	0	1	0	1	0	2	0
Cirrhosis	1	1	0	0	0	0	1	1
Parkinson's Dis.	1	0	0	0	0	0	1	0
Scleroderma	0	0	1	0	0	0	1	0
Alzheimer's Dis.	0	0	1	0	0	0	1	0
TOTAL NON-MALIGNANCIES	**11**	**3**	**10**	**3**	**2**	**0**	**23**	**6**
GRAND TOTAL	**100**	**25**	**100**	**17**	**100**	**22**	**300**	**64**

Table 5: The gender and the use of sedation in the patients admitted to the IPU between 31/01/2001 and 15/06/2002 in groups of 100.

Group	Group 1		Group 2		Group 3		Total	
Dates	31/01/01 to 23/07/01		24/07/01 to 31/12/01		01/01/02 to 15/06/02			
	Admitted	Sedated	Admitted	Sedated	Admitted	Sedated	Admitted	Sedated
Gender								
Male	53	14	41	10	34	8	128	32
Female	47	11	59	7	66	15	172	33
Total	100	25	100	17	100	23	300	65

Malignant intestinal obstruction was present in 5 patients, 2 other patients had extensive bony metastases, 1 patient had severe jaundice, 1 had brain metastases, 2 patients had GIT bleeding and 1 developed opioid induced neurotoxicity.

In the studies reviewed by Sales[1], delirium (39%) and dyspnoea (38%) were the main refractory symptoms for which sedation was used. Nausea and vomiting were refractory in 6%. The reason for the high incidence of vomiting at Sungardens was that there were 5 patients with intestinal obstruction in a relatively small total number (22) of patients.

Lack of uniform diagnostic criteria and the reporting of more than one refractory symptom, makes comparison of these results with other surveys difficult.

In this group of patients, no patients with AIDS or non-malignant diseases required sedation. Small numbers of patients from these categories did require sedation during 2001. (See Table 4) In all cases, this sedation was for terminal restlessness.

8.4. Response and Outcome of Sedation

It took an average of 18 hours (range 20 minutes to 96 hours) for the sedation to be fully effective (reasons for this apparent delay are outlined below). Patients survived an average of 90 hours (range 20 minutes to 369 hours) after sedation was started. The review of 13 surveys by Sales[1] showed survivals of between 1.5 –3.9 days after beginning sedation.

8.5. Estimation of Prognosis

The staff's estimation of prognosis was accurate in 13 cases (59%). In 3 cases the patients improved and were able to be discharged. One of these (No 16) was subsequently readmitted for terminal care (No 19).

The Palliative Prognostic Index (PPI) was scored in 20 patients. Their mean score was 8.7 points. A score of 6 or more indicates a prognosis of less than 3 weeks. (See Appendix 5) Only 2 patients had a score below 6. These patients had scores of 3.5 and 5, and both had malignant intestinal obstruction. The first survived for 104 hours and the second for 74 hours. Towards the end of the project the Palliative Performance Score (PPS) was tried out.[47] Although this score appears useful for predicting periods shorter than 3 weeks, the change from the PPI to the PPS caused some confusion as the staff were just getting used to the PPI. There was insufficient time to adequately teach everyone to use the PPS before the project ended. Morita reported an average PPI of 11 and all but 1 patient had a score of 6 or above.[6]

8.6. Medication Used

Morphine sulphate and transdermal fentanyl were the only opioids used. The fentanyl dose was converted, according to the manufacturer's table (See Appendix 6), to

parenteral morphine equivalents for ease of comparison. The mean parenteral morphine equivalent used was 70 mg per 24 hours (range 15 – 260). (See Table 6.)

Alternative opioids such as hydromorphone, diamorphine and oxycodone are not available in South Africa. Methadone is difficult to obtain and is only available in a liquid form with a concentration of 2mg/5ml.

For sedation, midazolam and haloperidol were the main drugs used. In all but 1 case these drugs were give by SC route by means of a syringe driver. Occasionally either 1 mg sublingual lorazepam or 0.25 mg alprazelam was added. In the 12 cases where midazolam was used, the mean dose was 18.5 mg / 24 hours (range 7.5 – 40). Haloperidol was used in 16 cases with a mean dose of 7.5 mg / 24 hours (range 5-10).

The above figures are very similar to the average daily dosage of 66.2 mg of parenteral morphine and a dose range of midazolam of 2.5 to 47 mg during the last 3 days of life in the series of patients reported by Turner.[48] Thorns & Sykes report a mean daily dose of 55.5 mg of parenteral morphine.[49] Morita reported using a mean dose of 26 mg/day of midazolam and a range of 0.8 – 25 mg of haloperidol /day.[50] (See Table 6)

Table 6: The mean dosage of morphine, midazolam & haloperidol used at Sungardens, compared with 3 other studies.

	Mean Parenteral Morphine Equivalent	Mean dose of Midazolam	Mean dose of Haloperidol
Sungardens	70mg/24hrs (range 15-260) n22	18.5 mg/24hrs (range 7.5-40) n12	7.5mg/24hrs (range5-10) n16
Turner[48]	66.5/24hrs		
Thorns[49]	55.5mg/24hrs		
Morita[50]	68/24hrs	26mg/24hrs (range3-240)	5mg (range 5-24)

Only one patient required IV midazolam for sudden acute severe dyspnoea due to suspected acute pulmonary oedema unresponsive to oxygen, IV furosemide and fentanyl. He had been vomiting and then developed acute respiratory distress, dyspnoea and frothy pink sputum. Prior to this he had been extremely ill (PPI of 15) with partial intestinal obstruction, severe jaundice and a left sided pleural effusion. Following the failure of the above measures, he was given midazolam slowly intravenously, with a brief delay between increments. A total dose of 7.5mg was eventually given before his distress subsided. The patient died 10 minutes later. This dose is much higher than the usual recommended loading dose of 0.5 – 1.5 mg in normal circumstances.[9,15] However, in such emergencies, an anaesthetizing dose of a rapidly acting sedative should be given.[37]

(See Table 7 for the drugs and dosages recommended in the literature.)

Table 7: Drugs and dosages recommended for palliative sedation therapy[9,15].

Drug	Type	Starting dose	Maintenance dose	Route
Midazolam	Rapid, short-acting benzodiazepine.	0.5-1.5 mg/h	30-100 mg/d	IV or SC
Lorazepam	Benzodiazepine	1-4 mg 4-6 h(SL) 0.5-1 mg/h(IV)	4-40 mg/d	Sublingual, SCor IV
Diazepam	Benzodiazepine	10 mg	10-20 mg/6h	IV or PR
Haloperidol	Neuroleptics	0.5-20 mg	5-40 mg/d	PO,IMI or SC
Thiopental	Ultrashort-acting barbiturate	5-7 mg/kg	20-180 mg/h	IV
Phenobarbital	Long-acting barbiturate	200mg loading dose, repeated every 10-15 minutes prn	600-1200 mg/d	SC or IV
Propofol	Ultrashort-acting anaesthetic	5-10mg/h bolus:20-50 mg	10-200 mg/h	IV

The dosages are very variable and will need to be individualized and adjusted. Macleod [19] calls for caution in the use of the last three drugs without a system of life support as they are considered anaesthetics. He maintains that their use would be legally unacceptable and a form of active euthanasia. This is not an opinion shared by all. Propofol is not available at Sungardens Hospice because of cost. Only the first four drugs are currently used at Sungardens Hospice.

8.7. Hydration

Four patients were receiving IV or SC fluids at the time sedation was started. These fluids were not discontinued. The possible use of IV or SC fluids was, however, discussed with all patients and their families prior to sedation. Their wishes were the main determining factor in deciding what should be done about hydration. During this project, parenteral fluids were not commenced after sedation had begun. Four patients were able to continue some oral fluids, while the remainder received mouth spraying and routine mouth care only.

Parenteral fluids are seldom used at Sungardens Hospice. Most terminally ill patients stop eating and drinking during the last few days of life. Comfort is maintained by good mouth care and mouth spraying.

8.8. Classification

Using the classification suggested by Morita and colleagues[23,51] the 22 cases can be divided into the following sub-groups:-

Primary – Constant – Deep: 13 (59%)

Primary – Intermittent – Mild : 5 (23%)

Secondary – Constant – Deep : 2 (9%)

Secondary – Constant – Mild : 1 (4%)

The main difference is that Morita and colleagues[51] initially use mild intermittent sedation more often (See Table 8). Mean daily doses of drugs are very similar (See Table 6).

Table 8: A comparison of the classification of the sedation used for patients with refractory symptoms in Sungardens Hospice, South Africa and Seirei Hospice, Japan.

	South Africa	Japan
Numbers	22	87
Percentage	22%	47%
Percentage of males	36%	61%
Survival	90 hrs	72 hrs
Primary	86%	61%
Secondary	14%	39%
Intermittent	22%	67%
Continuous	88%	33%
Mild	32%	51%
Deep	68%	49%
Primary-intermittent-mild	23%	8%
Primary-intermittent-deep		38%
Primary-continuous-mild		15%
Primary-continuous-deep	63.5%	
Secondary-inter.-mild		21%
Secondary-inter-deep		
Secondary-cont-mild	9%	16%
Secondary-cont-deep	4.5%	2%
REFRACTORY SYMPTOM(S)*		
Restlessness/delirium	41%	67%
Dyspnoea	9%	40%
Pain	4%	18%
Nausea/vomiting	23%	6%
Convulsions	14%	1%
Other**	9%	

*Some patients had more than one refractory symptom.

**See 8.3

8.9.Communication

All patients and/or their families were fully informed and consented to the use of sedation. In the case of the delirious patients, the closest family member gave consent on their behalf.

9. PROBLEMS ENCOUNTERED DURING THE PROJECT

9.1. Recording the Effect of Sedation

The staff was asked to measure two aspects of the use of sedation. Firstly, they had to measure the level of sedation, using the score described by Rudkin.[52] (See Table 10)

Table 10: Sedation Scale: The scale suggested by Rudkin[52] has been slightly modified for the sake of clarity.

Observation of patient	Score
Fully conscious	1
Drowsy but wakes up if spoken to	2
Eyes closed but can be woken by gently pulling on ear	3
Eyes closed and does not wake up when ear is gently pulled	4

This was well understood and the recording of these observations was correctly carried out. The second aspect was to measure the effect of the sedation on the refractory symptom. They were required to fill in whether the sedation was fully effective, partially effective or not effective at all. This was not well understood and some staff thought that if the patient was not deeply sedated, the sedation was not effective. As the researcher did not personally see many of the patients, this misunderstanding was also not detected for some time. It may explain why it appears from the completed Recording Forms that it took a long time (average of 18 hours) for some patient's symptoms to be effectively controlled. The Recording Form was changed and a place was made to fill in the reason for sedation, just below the heading, Effect of Sedation. This change improved the assessment of the effect of sedation. The average time for a patient's sedation to be fully effective was reduced to an average of 5 hours. This is still a relatively long period of time. In some areas

sedation is given intravenously and the patient is immediately sedated.[2] The fact that there is no resident doctor, makes this approach difficult at present at Sungardens Hospice.

9.2. Recognition of Delirium

Delirium is a common clinical disorder in terminal patients. Its presentation can be subtle and often the signs fluctuate in severity. Unless patients are specifically assessed for its presence, abnormal behaviour may be attributed to anxiety, the effect of medication, senility or the expected deterioration of the terminal cancer patient.

As Sungardens Hospice is not attached to a public hospital, and as most of the patients cannot afford to pay for diagnostic investigations, patients are mainly assessed on clinical grounds. A specific clinical examination for delirium is not done routinely on all patients.

A doctor sees all the patients in the IPU on a daily basis and prescribes the necessary medication. However, as there is no resident doctor, the assessment of a change in the condition of a patient, is initially made by the nursing staff. (The nursing staff completed 15 out of the 22 Recording Forms for this project.) The first staff newsletter tried to give guidance about the recognition of delirium (see Appendix 4.1). This did not, however, appear to have much effect as, in a number of subsequent cases, the reason for sedation was recorded as anxiety. On review of the clinical records there were definite clinical features of delirium in each of these cases.

The introduction of a specifically designed assessment tool such as the Confusion Assessment Method (CAM) may have been more effective.[53] The CAM has been shown to enable non-psychiatric clinicians to detect delirium quickly. Specific training of the IPU nursing staff, followed by a trial of this method, should be undertaken in future. (See Appendix 7)

9.3. Opioid Induced Neurotoxicity (OIN).

Myoclonic jerking, confusion, hyperaesthesia and even convulsions are well known complications of high dose morphine in terminal cancer especially in the presence of dehydration and poor renal function.[54] Opioid rotation and parenteral rehydration are not common practices at Sungardens Hospice.

A patient (No 8), with a large pelvic tumour and partial intestinal obstruction, developed OIN. She had been on a syringe driver with 120 mg of morphine sulphate and 5 mg of haloperidol for 4 days. As she then began to experience severe pain, her morphine was rapidly increased. She then became confused at times. It was only 2 days later when she developed myoclonic jerking that OIN was diagnosed. The morphine was stopped and the twitching was controlled with midazolam. The patient died peacefully the next day.

Another patient (No 15), who was admitted in a coma following convulsions at home, may also have had OIN. She was suffering from advanced bladder cancer. There was uncertainty about the dosage of the morphine given at home. She died a few hours after admission.

These rather dramatic complications of morphine provided a very useful learning opportunity for the staff, especially with regard to the recognition of this complication. The issue was also addressed in a staff newsletter and stimulated much discussion. (See Appendix 4.2.)

9.4. Participation by staff

Attitudes to research may vary as it usually involves extra work. Protocols have to be understood. Extra observations have to be done. Forms have to be completed. The changes that are introduced to established routines, may lead to uncertainty and stress. In addition some may perceive the research process as a threat, as if someone is spying on one's work.

No apparent staff resistance was encountered at Sungardens. All the nurses were very co-operative right from the beginning. Several nurses remarked on how interesting they had found it, and one of the senior nurses even asked when the next project could be started.

In the last staff newsletter (See Appendix 4.5), the 9 registered nurses working in the IPU, were asked the following question:

"Finally, could you comment on whether you think this project has affected the standard of medical and nursing management of our dying patients needing sedation?" Eight written replies were received. All felt that the project had had a positive effect on the standard of nursing and medical care. Two respondents also made the comment that midazolam (Dormicum) was much more effective in sedating

restless patients than haloperidol (Serenace). It was also felt that patients were more restful and died more peacefully. There was a request to continue the staff newsletters so that the staff could keep up to date.

9.5. Opinions of colleagues

The initial guidelines were circulated for comment on the international Palliative Medicine e-mail discussion list during June 2002. Some of the suggested improvements were incorporated into the revised guidelines. The policy document from the Carl T. Hayden Medical Center, Phoenix, Arizona, was particularly helpful. With Dr Paul Rousseau's permission we have based our own policy on this document. (See Appendix 8)

10. STRATEGY FOR CHANGE

The strategy of using a quality improvement cycle proved very successful despite the inexperience of everyone in its formal use. The nursing staff were enthusiastic and actively contributed valuable suggestions that resulted the development of the guidelines, recording forms and policy. While it was initially difficult to keep everyone informed of the changes as they occurred, the staff remained enthusiastic throughout. In the end the nurses felt that significant improvements had been made, especially as the restless delirious patients were being more effectively sedated.

11. EFFECTS OF THE CHANGES

Change is a complex process. The real effects of even small changes can take time to become apparent. The following are some of the developments and changes that have come out of this project.

1. It was gratifying to see that the results of this study compare favourably with international standards with regards to the indications for sedation, percentage of patients sedated, the drugs & dosages used.

2. Within the very limited time available, clear guidelines, a policy statement and a practical recording form were developed.

3.The recommendations of Morita and colleagues[6,23] with regard to a definition of palliative sedation, the classification of sedation and the use of the Palliative Prognostic Index were tested and found to be very helpful.

4. The sedation scale proposed by Rudkin[52] was also found to be very practical.

5. There was greater clarity about the objective of palliative sedation, what observations were appropriate and what the responsibilities of each of the staff involved was.
6. The concerns of staff about several ethical issues were addressed.

There are, however, a number of limitations of this study. The number of patients involved was relatively small. Caution should be exercised in extrapolating these findings. The guidelines are specifically designed for use at Sungardens Hospice, Pretoria and they would have to be carefully adapted to other contexts. A simple example would be the need for written 'Do Not Resuscitate' orders that are required in North America.

Refinements are still needed, especially with regards to the Recording Form. Ideally, the monitoring of sedation should be incorporated into the normal daily charts.
In retrospect perhaps the main weakness of this study is that too many different aspects of palliative sedation were tackled simultaneously. This caused confusion regarding the use of the PPI and the PPS.

12. NEXT STEPS

Palliative sedation has been confirmed as an ethically sound option for the very difficult problem of refractory symptoms in dying patients. It is also a practical solution that makes for better nursing care of patients, who can otherwise be very difficult to manage.

The following steps are still needed.

1. The Recording Form needs refining.

2. The guidelines should be translated into Afrikaans, Tswana and Zulu and then discussions should be held with all the staff to ensure that everyone understands and accepts them.

3. Any remaining dilemmas surrounding the use of parenteral fluids need to be addressed.

4. The guidelines should be tested in other South African hospices.

5. A co-ordinated international study across a diverse range of cultural settings, should be undertaken.

13. GUIDELINES FOR THE USE OF PALLIATIVE SEDATION AT SUNGARDENS HOSPICE, PRETORIA.

The Guideline should be read in conjunction with the Policy Document: THE USE OF PALLITIVE SEDATION (AUGUST 2002) when palliative sedation is being considered for a dying patient with intolerable, refractory symptoms.

ASSESSMENT:

1. Have all symptoms been treated according to the **latest palliative care principles**? Will no further available and acceptable treatment relieve the suffering of the patient, within his or her estimated life expectancy, without a high risk of aggravating this suffering?
2. Have **urine retention** and **faecal impaction** been excluded?
3. Has the patient's current prescription been carefully reviewed, to exclude **side effects** and **drug interactions** as a possible reason for the patient's distress?
4. Is **parenteral hydration** inappropriate?
5. Would any further **investigations** be unlikely to clarify why the symptom is refractory and thus lead to an improvement in the patient's condition?
6. If the answer to all these questions is **"Yes"**, proceed to the next step. If the answer is **"No"**, carry out the appropriate intervention.

PROGNOSIS:

1. Is the patient's **Palliative Prognostic Index** greater than 6? (See Recording Form)
2. Is any **life threatening complication** present?
3. Do you consider the patient's **life expectancy** to be days rather than weeks?

4. If the answer to the above questions is **"Yes"**, proceed to the next step. If the answer is **"No"**, ask an experienced colleague to review the options with you.

COMMUNICATION:

1. Is the patient **fully conscious** and **well orientated** with no features suggestive of delirium?? (See the Confusion Assessment Method.)
2. Is the present level of symptoms **intolerable** to the patient?
3. Does the patient accept the need for sedation?
4. Does the **family** understand the patient's present condition and do they accept the need for sedation?
5. If the patient is incapable of understanding the use of sedation, is the closest family member willing to give **consent** for the use of sedation?
6. Are all the **staff** in agreement with the need for sedation?
7. Has the reason for sedation and the patient's or family's consent been recorded in the medical records?
8. If the answer to these questions is **"Yes"**, proceed to the next step. If the answer is **"No"**, arrange an urgent case conference.

PROCESS:

1. If mild or intermittent sedation is required, use lorazepam 1mg sublingually, repeated 4-6 hourly as required. The dose can be gradually increased to 4mg, if needed.
2. For delirious patients that are not very restless, haloperidol 0.5-5 mg can be given by mouth at night. This can be gradually increased to 20 mg, if necessary. A syringe driver can also be used for patients with difficulty swallowing.

3. If the patient is very restless or severely distressed, midazolam can be given in a syringe driver at an initial rate of 0.5-1.5 mg/hr. The usual maintenance dose is 30-100 mg/day.
4. In exceptional circumstances, such as a massive haemorrhage, acute airway obstruction, status epilepticus or severe agitation, midazolam 2.5 –5 mg can be given slowly IV by a doctor and repeated every 5 minutes until the patient is no longer distressed. In the absence of a doctor, an intra-muscular injection can be given by a nurse.
5. The medication should be increased, at an appropriate rate, so that an acceptable level of comfort is achieved, within a reasonably short period of time. It should be possible to achieve this, in most patients, in less than 5-6 hours.
6. If a satisfactory response is not achieved, consult with an experienced colleague.
7. It would, however, be inappropriate for the continued escalation of the dose of the medication, once an acceptable level of comfort was achieved.

NURSING CARE:

1. Normal nursing care should be continued, with special care being taken of the patient's mouth and pressure points.
2. The level of sedation and the level of comfort must be monitored and recorded at least 4 hourly. More frequent observations may be needed, until the patient's level of comfort is satisfactory.
3. Where the prescribed dose of medication does not appear to be controlling the patient's symptoms satisfactorily, the doctor on duty should be consulted (See point 6 of Process above).

REVIEW OF RECORDS:

The Ethical Committee will review the records of all patients requiring palliative sedation. Please make the records available to the Committee as soon as possible after the patient has died.

DATE OF COMMENCEMENT: August 2002.

DATE OF REVIEW: August 2003.

DR DAVID CAMERON, Medical Adviser, Sungardens Hospice, Pretoria.

MRS BRIGET DYER-SMITH, Matron, IPU, Sungardens Hospice, Pretoria.

14. POLICY DOCUMENT: THE USE OF PALLITIVE SEDATION SUNGARDENS HOSPICE, PRETORIA.

1. PURPOSE: This policy document has been drawn up to clarify the use of palliative sedation in terminally ill patients at Sungardens Hospice, Pretoria, so that the highest ethical and medical standards are maintained.

2. POLICY: To provide palliative sedation to dying patients at Sungardens Hospice, when their symptoms are intolerable and have not responded to standard palliative therapies.

3. BACKGROUND:

3.1. Care of dying patients needs a comprehensive, multidisciplinary approach, which is directed at relieving suffering caused by physical, emotional, social and spiritual problems. Despite good palliative care, some patients have persisting, severe symptoms that will not respond to any available remedies without a significant risk of increased suffering, and with little chance of benefit to the dying person. Such symptoms are labeled refractory. In such difficult situations, as a last resort, careful consideration needs to be given to the possible use of palliative sedation.

3.2.In considering the need for sedation, two issues are of crucial importance. Firstly, a symptom can only be regarded as refractory when all available, reasonable measures apart from sedation, have been tried. Secondly, palliative sedation therapy means the use of sedative medications to relieve intolerable and refractory distress by deliberately reducing the person's level of consciousness.

3.3.Before palliative sedation is used, the patient and/or the patient's immediate family must have been fully informed and must have given consent. Such consent must be documented in the patient's medical records, including the symptom for which palliative sedation is being used.

3.4.The intent of such sedation is to relieve severe, refractory, intolerable symptoms and not to hasten death. This is in agreement with the ethical principle of double effect. The degree of sedation must be in proportion to the severity of the refractory symptom. Sedation may be given intermittently or continuously.

3.5.One of the main difficulties about the use of sedation in dying patients has been the suspicion that this is a form of euthanasia. It has been suggested that the lives of such patients are being artificially shortened. For many years there has been well-documented evidence to demonstrate that adequate dosages of pain relieving drugs, can relieve the pain of most people without the danger of artificially shortening their lives. This has meant that we are able to give enough strong analgesics without the fear of causing our patients harm. Reports published recently have shown that the same is true for the most commonly used drugs for palliative sedation. When used in appropriate dosages, patients can be made more comfortable without their lives being endangered.

4. PROCEDURES:

Indications for palliative sedation include, but are not limited to:

4.1.1. Terminal agitation and restlessness, refractory to benzodiazepines and neuroleptics in dosages that do not reduce consciousness.

4.1.2.Pain refractory to high dose opioids and adjuvant analgesics.

4.1.3.Vomiting refractory to aggressive anti-emetic therapy.

4.1.4.Dyspnoea refractory to oxygen, bronchodilators, corticosteroids and opioids.

4.1.5.Status epilepticus and severe myoclonic jerking refractory to standard dose benzodiazepines, or other anti-epileptics.

4.2.Consultation: The doctor and at least 2 senior nurses must be in agreement about the need for sedation. All documentation must be completed prior to starting palliative sedation.

5. RESONSIBILTIES:

5.1.The doctor on duty has the responsibility to make the decision about the appropriateness and the instituting of palliative sedation.

5.2.The nursing staff has the responsibility of regularly observing the level and effect of sedation, of recording these observations and of adjusting the sedation in consultation with the doctor.

5.3.The Ethics Committee of Sungardens Hospice will review all patients receiving palliative sedation. This committee has the responsibility of implementing and reviewing this policy in consultation with the medical and nursing staff of Sungardens Hospice. It is also responsible for resolving any disputes amongst staff regarding sedation.

6. REFERENCES:

1.Cherny N & Portenoy RK. Sedation in the management of refractory symptoms: Guidelines for evaluation and treatment. J Palliat Care 1994;10:31-38.

2. Rousseau PC. Terminal Sedation in the care of dying patients. Arch Intern Med 1996;156:1785-1786.

3. Hallenbeck J. Terminal Sedation for intractable distress. Not slow euthanasia but prompt response to suffering. West J Med 1999;171:222-223.

4. Morita T, Tsunoda J, Inoue S & Chihara S. Do hospice clinicians sedate patients to hasten death? J Palliat Care 1999;15:20-23.

7. DATE OF COMMENCEMENT: August 2002

8. DATE OF REVIEW: August 2003

DR DAVID CAMERON Medical Advisor, Sungardens Hospice, Pretoria.

MRS BRIGET DYER-SMITH Matron, IPU, Sungardens Hospice, Pretoria

15. POSTSCRIPT: GUIDELINES – SOME COMMENTS

15.1. Good or bad?

While it is well accepted that guidelines are helpful to encourage improved standards and best practice, it is also sadly true that they have seldom had the impact on clinical practice that their authors had wished.[14] Some authors have been openly hostile to the introduction of guidelines. Anbar maintains that guidelines promote 'cookbook medicine', are suitable for paramedics and not doctors, stifle judgment, are impossible to keep up to date and are even "*paving a fast road to hell!*"[55] Is there a way that guidelines can become 'food for thought' that can assist medical staff and their patients to make appropriate decisions in difficult circumstances? Can they become 'power-lines' that liberate and encourage good care, rather than 'tram-lines' that only ensure rigid conformity?

15.2. Legal implications

Schwarts and colleagues raise an additional concern regarding the legal implications of medical guidelines.[56] Once guidelines have been produced, will those who do not follow them be guilty of negligence? In answering this question, it is important to have a clear definition of what a guideline is. A helpful understanding is given by the US Institute of Medicine.[57] Guidelines should be viewed as '*systematically developed statements to assist practitioners and patient decisions about appropriate healthcare for specific clinical circumstances.*' They are tools that aid decision making and not hand-cuffs to restrict clinical freedom. Guidelines are usually produced by individuals or groups that have no specific legal authority. Therefore, they cannot be seen as binding on all, in every situation. Good guidelines represent the state-of-the-art, something to be aimed at, rather than a law that must be blindly obeyed.

However, if they are up to date and well researched, they may be used as an indication of good practice and this may have legal implications for a doctor who decides to deviate from the established standard. Where such a deviation occurs, the doctor concerned should be able to justify such an action.

In a similar way, the question arises as to whether adherence to guidelines would protect a doctor from liability? It is important to state that adherence to guidelines does not give absolute indemnity as no guidelines can be expected to address all the circumstances of a specific case. A doctor is still expected to use good clinical judgement in handling each patient and always to act in the patient's best interest.

This does pose a significant problem in situations of limited resources. In such circumstances, the needs of the majority may restrict the freedom of the individual. Although one could go on, endlessly thinking up difficult situations and exceptional circumstances, in reality all care is a delicate process of negotiation between patients and health professionals. As stated above, guidelines are there to assist this process.

15.3. Validity

In judging the validity and authority of guidelines, the following criteria, suggested by Schwartz and colleagues,[56] can be applied to the guidelines for Sungardens Hospice:

Face credibility: Will these guidelines be accorded credibility by the staff of Sungardens Hospice? Will they be put into practice? Are they relevant and workable? Can the staff see a benefit for themselves and their patients? The participation of the

staff in drawing up the guidelines, and their assessment that there had been an improvement in the handling of these difficult situations, should make the acceptance of these guidelines easier.

Validity: Will these guidelines lead to improved standards of care? Further research will obviously be needed to answer this question. As mentioned above some improvement has already been noted.

Reproducibility: Will other similar hospices be able to apply these guidelines? To avoid the confusion of multiple guidelines emerging, there is a need to encourage other hospices in South Africa, and perhaps elsewhere, to try these guidelines out. Until a reasonable degree of consensus can be found, it will continue to be difficult to compare results from different centres.

Representativeness: Although the staff of Sungardens were involved in drawing up the guidelines and the comments of some international experts have been saught, the opinions of the doctors and nurses working in other hospices will be needed before they could be introduced elsewhere.

Flexibility: There needs to be room for variation. Valid exceptions need to be identified, and suggestions for the management of such circumstances may be needed. An obvious problem that needs to be addressed, is the patient who requests sedation or even euthanasia for existential distress without the presence of refractory physical symptoms. Although this is not a common situation at Sungardens Hospice, there is ample evidence in the international literature of such requests. Both Morita[30] and Rousseau[58] have addressed this issue. Mild intermittent sedation, or respite sedation for short periods, appears to be an appropriate option that will be ethically acceptable to most people. This type of sedation is not without risk and further research is needed.

Clarity: This is obviously essential. However, as English is not the first language for some staff and patients, it will be necessary to check that all understand the meaning of these documents. The translation of these documents into Afrikaans, Tswana and Zulu should be considered.

Reliability: Despite attempts to clarify issues, differences of interpretation were still present during this project especially in the assessment of the response to sedation and the diagnosis of delirium. Further training and follow-up will be needed, to ensure that all staff understand these aspects.

Transparency: This was achieved by encouraging the involvement of all the staff in the process of drawing up these guidelines.

Scheduled review: This is clearly stated on the documents. This is very important as further evaluation of these guidelines needs to take place. The staff need to feel that their new suggestions will be considered and possibly incorporated.

15.4. Implementation

The reasons guidelines have been so difficult to implement in the past also need to be addressed. One of these reasons is the way experienced doctors reach decisions in their daily practice. Greenhalgh discussed this issue in a fascinating article, 'Intution and evidence – uneasy bedfellows?'[59] She has summarized the work of a number of researchers, such as Hubert & Stuart Dreyfus[60] and Kathryn Montgomery Hunter[61] While novices are inclined to adhere to rules and guidelines, the expert practitioner has an intuitive grasp of situations based on deep, tacit understanding from years of experience. How does this intuition work? If one asks experts they will have some difficulty explaining how they arrived at a certain decision. Like Sherlock Holmes they may reply, "*From long habit the train of thoughts ran so swiftly though my mind*

that I arrived at the conclusion without being conscious of intermediate steps."[62] In familiar situations, experts do not solve problems, they do not make decisions, they do what normally works. There is a selective application of general rules to particular patients and situations. As each patient is unique and different, a rigid rule-based guideline will not work. Knowledge, by itself, also does not influence clinicians' behaviour. The knowledge of best practice must be combined with a change in motivation, structural barriers must be overcome and the new behaviour must be encouraged and reinforced.

The introduction of guidelines may need even more thought, planning and enthusiasm than it took to formulate the guidelines themselves. The presentation will need to be clear, challenging and aimed at the right level. For the nursing staff, the tangible benefit of easier nursing care of patients whose symptoms are well controlled, should be evident to all. Helping 'old docs learn new tricks' will need a different approach. Allowing flexibility within a broad framework, regular review and feedback to encourage participation will help to sustain interest. The fact that the Ethics Committee will review the records of all patients sedated, may also encourage staff to ensure best practice. Sungardens Hospice is small enough for this 'part carrot, part stick' approach to work.

16 ADDENDUM

Recent work by Chochinov and colleagues in Canada[63-66], has greatly helped to clarify the concept of dignity especially from the dying patient's perspective. A very practical model has been developed that can help medical and nursing staff to support, in an appropriate way, the patient's sense of dignity and 'will to live'. As two of these articles were only published after this review was originally completed, they did not influence this project. However, it will be interesting to test and validate this model in settings that are culturally different from Canada and to see if it can be used to assist in dealing with patients who are suffering from existential distress.

17. APPENDICES

Appendix 1: Initial Suggested Guidelines for the use of Palliative Sedation at Sungardens Hospice.

In reaching a decision to sedate a terminally ill patient, the following issues should be carefully considered:

1.All symptoms should have been treated according to the latest international standards.

2. Exclude all easily reversible conditions such as drug interaction, full bladder or faecal impaction.

3.Consider the pros and cons of rehydration if dehydration appears to be the source of delirium or distress.

4.Document performance score, presence of vital organ failure and estimate of prognosis according to the Palliative Prognosis Index.

5.The decision should be taken after adequate consultation with a multidisciplinary team including the doctor on duty and two senior nurses. If the patient is unable to give consent because of confusion or if there is disagreement amongst the family or staff, a "family" conference must be called to consider available options.

6.The patient and the family should be fully informed of the situation and of the possible alternatives and consequences.

7.The indications and aims of sedation should be clearly recorded.

8.All normal measures of care should be maintained.

9.The level of sedation should be measured and recorded at hourly intervals according to a standard sedation scale such as the one suggested by Rudkin.

10.The level of sedation should be the minimum needed to achieve the objective of comfort from the distressing symptom.

11. Regular review must be continued.

Appendix 2: Guidelines for the Use of Sedation at Sungardens Hospice. (Draft 3)

A. Introduction:

Despite good palliative care, some patients have persisting distressing symptoms such as pain, delirium, dyspnoea or vomiting. As a last resort in these patients, it is sometimes necessary to use sedation to relieve suffering. At present there are no widely accepted guidelines for the use of sedation in terminal patients. This project has been designed to assist Sungardens Hospice to develop its own guidelines in a way that is in agreement with the recommendations of international experts in Palliative Medicine.

B. Literature Review:

The medical literature on sedation in terminal patients has been reviewed to find out the views of international experts. A copy of this review is available in the duty room. One of the main difficulties about the use of sedation in dying patients has been the suspicion by some that this is a form of euthanasia. It has been suggested that the lives of such patients are being artificially shortened.

For many years there has been well documented evidence to demonstrate that adequate dosages of pain relieving drugs, can relieve the pain of most people without the danger of artificially shortening that their lives. This has meant that we are able to give enough strong analgesics without the fear of causing our patients harm. Reports published recently have shown that the same is true for sedating drugs. When used in appropriate dosages, patients can be made more comfortable without their lives being endangered.

See the Research Protocol for a more complete discussion of these issues as well as the references.

C. Proper Assessment Before Sedation:

1. First make sure that the patient is not uncomfortable because of a full bladder or an impacted rectum.
2. Review the current prescription to make sure that there are no drug interactions causing confusion or restlessness.
3. Estimate the patient's prognosis by considering the following factors:-
   - What can the patient still do for her/himself?
   - What is the patient's fluid intake?
   - Is oedema of the feet or hands present?
   - Is the patient dyspnoeic at rest?
   - Are there signs or symptoms of delirium?
   - Is there any evidence of vital organ failure (e.g. kidney, liver, lung or heart)?

   Look at the scoring charts, calculate the Palliative Prognostic Index and then give your assessment of the patient's prognosis.

Calculation of the Palliative Prognostic Index

Criteria	OBSERVATION	SCORE
1. Performance	Moribund or very sick	4
	Needs assistance with everything	2.5
	Needs only occasional help	0
2. Oral fluid intake	Mouthfuls or less	2.5
	Reduced	1
	Normal	0
3. Oedema	Present	1
	Absent	0
4.Dyspnoea	Present	3.5
	Absent	0
5. Delirium	Present	4
	Absent	0

The total score is out of 15.

A score of more than 4 indicates a prognosis of less than 6 weeks.

A score of more than 6 indicates a prognosis of less than 3 weeks.

The presence of vital organ failure will affect this estimate.

The prognosis should be recorded as: -

a) Less than 24 hours; b) 25-48 hours; c) 49-72 hours, d) greater than 72 hours.

D. Communication with the patient and the family.

After every effort has been made to relieve distressing symptoms, it is important for the medical and nursing staff to discuss the option of sedation with the patient and/or the family.

The following points need to be discussed: -

1. The seriousness of the current stage of the illness, the degree of suffering and the lack of other options.
2. The possibility of reducing the patient's level of consciousness sufficiently to relieve the current distressing symptoms.
3. Explain carefully that the aim of sedation is to relieve suffering and not to shorten the patient's life.
4. The route of administration and whether the drugs would need to be given continuously or intermittently.
5. The possibility of unwanted side effects. (E.g. tremor, twitching, amnesia, etc.)
6. The appropriate means of continued nutrition and hydration.
7. Where possible a family member should remain with the patient while he/she is sedated.

E. Agreement:

In addition to the consent of the patient and the family, the doctor and at least 2 senior nurses must be in agreement about the need for sedation. If the patient is unable to give consent because of confusion or if there is disagreement amongst the family or staff, a "family conference" must be called to consider available options.

F. Monitoring:

The level of sedation should be measured according to the Sedation Scale and recorded 6 hourly. All normal means of care should be maintained.

Sedation Scale:

Level of consciousness of patient	Score
Fully conscious	1
Drowsy but wakes up if spoken to	2
Eyes closed but can be woken by gently pulling on ear	3
Eyes closed and does not wake up when ear is gently pulled	4

F. Data Collection:

This project is an attempt to improve the quality of care at Sungardens Hospice so that we are in line with the best international standards. Please complete the data sheet as indicated and let me know when a patient is started on sedation. We would value your advice about any improvements to the guidelines. Each case will be carefully reviewed and you will be kept up to date with developments. The project will continue until we are all happy that the guidelines are working well and that our care is in line with the best standards. We think it will take until the end of April to complete this process.

F. Ethical Approval:
The Ethics Committee and Management of Sungardens Hospice have approved this project. I will be submitting a report on it to the University of Cape Town, as part of the course I am doing in Palliative Medicine. No names of patients or their personal particulars will be mentioned in the report. Thank you for assisting in this project.

David Cameron December 2001

Appendix 3: Recording of Sedation (Draft 4).

1. Patient Number:.....(write this number on the top right hand corner of the IPU file)
   Age: Gender: F/M Diagnosis:
   Problems:.....
2. **Reason for Sedation**: (Circle the main reason for reducing patient's level of sedation)

a)**Pain**; b)**Delirium**; c)**Vomiting**; d) **Dyspnoea**; e) **Convulsions**; f)Other .....
(Is a syringe driver only being used because the patient cannot swallow? Yes/No)

3. Has a full bladder, faecal impaction, drug side effects been excluded? Yes/No.

4. Measure the **Palliative Performance Score(PPS)** (See separate sheet)

At 40% the average patient will usually survive less than 11 days.
At 30% ----------ditto---------- 7 days.
At 20% ----------ditto---------- 3 days.
At 10% ----------ditto---------- 2 days.
Using the PPS and your **clinical judgement**, estimate the patient's prognosis :-

a) less than 24 hours
b) 25-48 hours,
c) 49-72 hours,
d) greater than 72 hrs but less than 7 days
e) between 7 days and 2 weeks
f) greater than 3 weeks.

Estimated by doctor/nurse. (Initials.....)

5. Has the patient/family been fully informed about the option of sedation? Yes/ No
6. Give reason(s) if not done.....

7. **Recording of Sedation:**

Enter the patient's name in the register and write the register number on the recording form.
Enter the date and time sedation was started.....
In the drug column, only enter strong opioids (e.g.morphine and fentanyl(Duragesic), etc.) and sedating medication (e.g. haloperidol (Serenase); midazolam(Dormicum); lorazepam(Ativan), etc.).

8. Record the patient's **level of consciousness** hourly

Observation of patient	Score
Fully conscious	1
Drowsy but wakes up if spoken to	2
Eyes closed but can be woken by gently pulling on ear	3
Eyes closed and does not wake up when ear is gently pulled	4

9. Record the **effectiveness** of the sedation hourly in relieving the **symptom** for which it was originally prescribed (See 2).

Effectiveness	Score
Fully	F
Partially	P
No effect	N

Postmortem Assessment (to be completed by the duty nurse or doctor)

10. Record the date and time of death. Duration of sedation:
11. Method of **feeding** during the last 24 hours: IV/ S.cut/ N.G./ P.O./ Nil
12. Do the **guidelines** need to be improved? Yes/No
13. Does **this form** need to be improved? Yes/No
14. Do you have any comments or recommendations?.....

Thank you for your assistance. Please notify David Cameron whenever a patient is put on sedation.

Classification of sedation: Primary/secondary, Constant or intermittent, Deep or mild

Sedation Recording Form

Patient No……

Date……..

Time																								
Drug, dosage & route																								
Level of Sedation																								
Effect of Sedation																								
Reason for Sedation																								
Comments																								

Appendix 4.1: Staff Letter No 1: Palliative Sedation Research Project.

Thank you to all those who have helped so far with this project. We have used palliative sedation on 3 patients so far and I think it has been a very interesting experience trying to grapple with the difficulties of caring for this type of patient and for doing this type of research. I would particularly like to thank those of you who have helped to fill in the forms and who have given me such useful advice.

We are still having difficulty designing a recording form that is easy to use and which accurately records the effect and the level of sedation. I would appreciate it if you could let me have any further suggestions. Another difficulty I am experiencing is being able to meet with everyone whenever a change is made. Unfortunately, the process of allowing improvements to the guidelines and the recording form, means that there will be changes. In future I will only make the changes when you have all had a chance to comment. To improve communication, I will put everything in writing in a staff letter.

One of the main reasons for sedation is delirium or confusion. This is a common problem in dying patients. Delirium is not always easy to diagnose. The following are some indications of the presence of delirium:-

Sudden onset and fluctuating severity.

Disorientation.

Hallucinations.

Rambling or incoherent speech.

Anxiety especially if the patient is aware that he/she is confused.

Poor concentration and short-term memory.

Misinterpretations or delusions or paranoid ideas.

Restless, aggressive or noisy behaviour.

Drowsiness.

There appears to be some confusion (I hope no-one is delirious!) about when the Sedation Recording Form should be filled in. I would greatly appreciate it could be done as soon as there is a decision to used palliative sedation to relieve a symptom by reducing a patient's level of consciousness. This means the doctor or the nurse doing the ward round and making the decision to use sedation should immediately fill in the form. Please indicate clearly the main reason why the sedation is being used. All subsequent assessments depend on everyone clearly knowing the reason for sedation. In addition please notify me whenever a patient is put on sedation and then again when they die.

Thank you all once again for your help.

Kind regards,

David.

03/02/2002

Appendix 4.2: Staff Newsletter No 2: Palliative Sedation Research Project

Thank you all once again for you help with this project. It is a challenge to deal with this very difficult situation but I believe we will all be much better at handling these difficulties when we have finished this project.

I would like to highlight a difficulty we encountered recently with 2 of our patients. Both presented with twitching or myoclonic jerking. Both patients were on fairly high doses of morphine (One by mouth and the other via a syringe driver), both had tumours involving the pelvic area. Neither patient had a catheter. One patient had a recto-vaginal fistula and the other had oedema of both legs. In such situations it is difficult to determine exact urine output and, in the absence of laboratoy tests, to determine kidney function. Obstruction to the ureters is common in patients with tumours in the pelvic region. This can lead to a deterioration in renal function.

Morphine is an excellent, safe analgesic even in high doses, especially in our advanced cancer patients. There is, however, one situation where it can cause problems and that is where a patient on high doses develops renal failure or obstruction to the ureters. The main way that the body gets rid of morphine once it has been used and broken down (or metabolised) is by excreting it in the urine. It is obvious therefore that blocked ureters or kidney failure will prevent this happening and the metabolites (breakdown products) of morphine will begin to rise in the blood stream. Poor intake of fluids and a low blood pressure will obviously aggravate this by further impairing kidney function.

Morphine has 3 different metabolites: morphine-3-glucuronide (M-3-G), morphine-6-glucuronide (M-6-G), and normorphine (NM). What is very interesting is that M-6-G acts like morphine, it binds to the opioid receptors and relieves pain. M-3-G on the other hand does not bind to the opioid receptors and so it does not relieve pain. In fact it is thought to block the effect of morphine and M-6-G and so the patient will start experiencing more pain. In addition, M-3-G can also stimulate the brain and the nervous system. This can lead to confusion, hallucinations, tingling sensations, twitching or myoclonic jerking and even convulsions. NM is also thought to cause brain stimulation[53].

Thus the patient on morphine who develops renal failure can present with various different clinical pictures. If there is mainly M-6-G build-up, the patient will present with progressive sedation, small pupils, sweating and respiratory depression. In those patients where there is mainly a build up of M-3-G or NM , there may be hallucinations, a tingling sensation, myoclonic jerking, pain on being touched or convulsions. In such patients the pupils may be normal sized.

Well now, what do we do when we recognise these symptoms? The obvious first point is that we must **recognise** them! Having done that we must take immediate acting to prevent the situation from getting worse. In the milder case, one can reduce the dose of morphine but in the more severe case, especially if the patient is experiencing significant pain, we will need to change to another strong analgesic which has different breakdown products, such as Duragesic (fentanyl) transdermal patches. If rapid pain relief is needed, one can give a Sublimase injection (this is also fentanyl). The twitching and other side effects may take up to a week to disappear completely. Obviously, the same problem can occur with the new drug that is being

used and it may be necessary to keep changing or rotating the opioids in the patients with kidney failure.

A further tricky question is whether such patients would benefit from IV fluids? In the absence of ureteric obstruction this may be a good idea. Should we be preventing this from happening by using IV or SC fluids in patients on palliative sedation? I would be interested in your comments.

Now I know most people don't like learning pharmàcology, but you will have to admit that this is fascinating information. Please let me have any suggestions and keep up the good work. We will be having a staff meeting on Thursday 7th March where we can sit down and make any further changes you think necessary.

Kind regards,

David 15/02/2002

P.S.: Please sign this letter to indicate you have read it.

Appendix 4.3: Staff Newsletter No 3: Palliative Sedation Research Project. To measure or not to measure… that is the question.

There has been a lot of debate in hospices throughout the world, on the value of 'measuring' our patients more objectively. The Hospice Movement grew out of concern for the poor care that dying patients received in general hospitals. What a terminal patient needs is good symptom control and good nursing care. They do not need a lot of the routine observations that take up so much of the time of a nurse in a busy general ward.

However, good symptom control needs assessment, active management and good communication between staff. One of the problems we face is that symptoms are not as easy to 'measure' as for instance, a temperature. This may make it difficult to decide on the condition and degree of comfort of a dying patient. Different ways of recording may also make it difficult to evaluate progress especially when different members of staff are involved in assessing comfort. What we need is a simple measure which we can all learn to use, which is easy to complete, which is standardised so that we all mean the same thing and which will save time in explaining and recording.

A question frequently asked by patients and especially by relatives, is "How long?" We all know how often we are wrong when we try to answer that question, yet it would be nice if we had a reasonably accurate way of calculating a patient's prognosis. This would help families to plan and prepare for the end. It would also help us to manage our resources, such as staffing levels, more effectively.

The **Palliative Performance Scale (PPS)**[47] is a standardised way of measuring the condition of a dying patient. It can also help us to estimate prognosis more accurately and gives an objective indication of the amount of nursing care that is needed for the patient. We have been using an abbreviated version of this scale, but I would like to suggest we try the full scale for a short while to see if it can help us to manage our patients better. I'm sure that your immediate thought is that this will just mean more administrative work and less time for good care. You may be right, but on the other hand if it helps us, we will all be pleased.

The way to use the PPS is to start with the Ambulation column. Choose the description that best fits the patient. Then do the same for the Activity column and then the other columns from left to right. The performance of the patient is the % level that most closely fits the patient. Some judgement may be needed if one of the levels doesn't fit with all the others. In that case the columns on the left, Ambulation, Activity and Self-Care, should count more than the others.

I suggest we try it out on all patients on admission to the IPU. Initial research showed that at a PPS level of 10% patients survived less than 2 days, at 20% less than 3 days, at 30% less than 7 days and at 40% less than 11 days.

This will help to fill the gap we have now with the Palliative Prognostic Index (PPI), which gives us an estimate of 3 to 6 weeks. Please read the full article in the Guideline file.

David Cameron 16/03/2002

Appendix 4.4: Staff Newsletter No 4: Palliative Sedation Research Project.
New Recording Form

I believe the time is now right to do a major revision of the recording form. I would like to recommend the following changes that I hope will make things simpler.

1. **Patient details.** I have included a few more details a) Gender ; b) Age ; c) Diagnosis ; d) Complications/Problems (This takes the place of the section on vital organ failure)
2. **Reason for sedation.** Please separate patients who are put on a Syringe Driver because they **cannot swallow** from those in whom the purpose is to deliberately reduce the **level of consciousness** because all other measures are not effective. This distinction is most important so that we can see just how often we are deliberately **sedating** patients. This is a very important aspect of this project.
3. **Item 3.** This is sometimes not being filled in. Remember to check for a full bladder, faecal impaction and drug side effects.
4. **Prognosis.** Many of the patients admitted to the IPU do not live more than 3 weeks. I would therefore suggest we change from the Palliative Prognostic Index (PPI) to the Palliative Performance Scale (PPS)[47] to measure prognosis. This gives an estimate of this shorter period. It doesn't take long to learn how to use it and it will be a useful tool to use on **all** our patients on admission. Please have a careful look at Newsletter No 3 for details of the PPS.
5. **Effectiveness.** I have made the changes to this item as were suggested at our last meeting. Please remember that effectiveness is judged by the relief of the primary symptom (See item 2). To help remind you, I have added this to the daily recording form. Please enter it there after circling it in item 2.

6. **Informed Consent.** Do you think a written consent form that explains the use of sedation, the syringe driver and the options for hydration & nutrition would help?
7. **The Recording Form.** We have been charting the level of sedation and its effect on an hourly basis. Is it necessary to do this so often? Would it be adequate to do it once every 3 or 4 hours? I'm not sure the way we are charting the medication is clear. Are there any suggestions as to how we can improve this?
8. **Results of the Project.** Some interesting results have come from our research so far. Although 15 forms have been completed, not all fit the definition of Palliative Sedation. One patient with dyspnoea was put on mild sedation. His condition improved enough for him to be discharged. A syringe driver was used in a brain tumour patient because of difficulty with swallowing and not because there was any need to reduce the patient's level of consciousness. In a 3rd patient, Serenace was used to treat vomiting, and not primarily as a sedative. A 4th patient only required intermittent mild sedation mainly at night (his own request). The survival of the remaining 11 cases was very variable (20 minutes to 191 hours). The first patient developed acute pulmonary oedema and was clearly dying in great distress. He was sedated and died shortly afterwards. The remaining 10 patients survived for an average of 85 hours which is slightly longer than other studies in which patients on sedation only survived an average of 72 hours. (The PPI of all our patients was 6 or more.) In most cases our estimate of prognosis was reasonably accurate. In 3 cases we overestimated survival, while in one case we underestimated survival. The main reason for the use of sedation, is in the management of delirium (6/10). The other reasons were for vomiting, convulsions and severe dyspnoea.

Thank you all once again for you help with this project. If possible, please try to be at the staff meeting on Thursday, 4th April at 08h00.

David Cameron 31/03/2002

Appendix 4.5: Staff Newsletter No 5: Palliative Sedation Research Project.

This research project has now been completed and I would like to thank you all for your help. Over the next few days I will be analysing the data we have collected. I would appreciate it if we could arrange a short staff meeting so that we can discuss the results. I am sure you will find the results very interesting.

As you will remember the aim of the project was to develop guidelines to help us to provide good palliative care in the difficult situation where sedation is thought to be the only remaining option. I would greatly appreciate your comments on the proposed final guidelines. Are there any improvements necessary? Please feel free to make any comments on the attached copy of the guidelines.

Finally, could you comment on whether you think this project has affected the standard of medical and nursing management of our dying patients needing sedation? Please feel free to say as much or as little as you like. I would also like to hear about any interesting or challenging incidents that may have happened with any of the patients that we have had to sedate this year. (You do not need to write your name, so you can feel free to say whatever you like. Skryf in Afrikaans as nodig.) Please return your comments to me by Friday, 28th June 2002.

Comments:

Appendix 5: The Palliative Prognostic Index[6].

Criteria	OBSERVATION	SCORE
1. Performance	Moribund or very sick	4
	Needs assistance with everything	2.5
	Needs only occasional help	0
2. Oral fluid intake	Mouthfuls or less	2.5
	Reduced	1
	Normal	0
3. Oedema	Present	1
	Absent	0
4.Dyspnoea	Present	3.5
	Absent	0
5. Delirium	Present	4
	Absent	0

The total score is out of 15.

A score of more than 4 indicates a prognosis of less than 6 weeks.

A score of more than 6 indicates a prognosis of less than 3 weeks.

The presence of vital organ failure will affect this estimate.

Appendix 6: Duragesic (Fentanyl) Dosage Conversion Reference Guide.

Fentanyl ug/hr	25	50	75	100	125	150
Morphine PO mg/d	<-135	135-224	225-314	315-404	405-494	495-584
Morphine IM mg/d	8-22	23-37	38-52	53-67	68-82	83-97

Appendix 7: The Confusion Assessment Method (CAM) Diagnostic Algorithm.[52]

Feature 1. **Acute Onset and Fluctuating Course**

This feature is usually obtained from a family member or nurse and is shown by positive responses to the following questions:

- Is there evidence of an acute change in mental state from the patient's baseline?
- Did the (abnormal) behaviour fluctuate during the day, that is tend to come and go, or increase and decrease in severity?

Feature 2. **Inattention**

This feature is shown by a positive response to the following question:

- Did the patient have difficulty focusing attention, for example, being easilydistractible, or having difficulty keeping track of what was being said?

Feature 3. **Disorganized Thinking**

This feature is shown by positive response to the following question:

- Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

Feature 4. **Altered Level of Consciousness**

This feature is shown by the answer other than "alert" to the following question:

- Overall, how would you rate this patient's level of consciousness? (alert [normal], vigilant [hyperalert], lethargic [drowsy, easily aroused], stupor [difficult to arouse], or coma [unarousable])

The diagnosis of delirium by CAM requires the presence of features 1 and 2 and either 3 or 4.

Appendix 8: Dr Rousseau's guidelines

CARL T. HAYDEN VA MEDICAL CENTER
PHOENIX, ARIZONA NURSING HOME CARE UNIT
USE OF PALLIATIVE SEDATION

1. **PURPOSE:** To establish policy and procedures to address the use of palliative sedation in terminally ill veterans in the NHCU.

2. **POLICY:** To provide palliative sedation to appropriate veterans with a terminal diagnosis and symptoms that are refractory to standard palliative therapies.

3. **BACKGROUND:**

a. Palliative care of terminally ill individuals acknowledges as a cardinal tenet the control of physical, spiritual, and psychosocial symptoms. Although symptoms are often ameliorated with standard palliative therapies, they may become refractory and require aggressive intervention, including palliative sedation.

b. In ascertaining the need for sedation, two definitions are crucial: refractory symptom and palliative sedation. A refractory symptom is defined as a symptom that cannot be adequately controlled despite aggressive efforts to identify a tolerable invasive or noninvasive therapy that does not compromise consciousness. Palliative sedation is defined as the intention of deliberately inducing and maintaining deep sleep, but not causing death in specific intractable and refractory circumstances.

c. The decision to provide palliative sedation is predicated upon the presence of refractory symptoms and informed consent by the patient or the patient's surrogate. However, once a decision is made to provide palliative sedation, every effort should be taken to provide a comfortable level of sedation adequate for mitigation of symptom(s). The ethical principle of double effect provides the basis for the use of palliative sedation wherein the intent of palliative sedation is to relieve symptoms, not hasten death.

4. **PROCEDURES**

a. The health care provider should consider instituting palliative sedation when indicated. Indications for palliative sedation include but are not limited to:

(1) terminal agitation and restlessness refractory to benzodiazepines and neuroleptics;
(2) pain refractory to opioids and adjuvant analgesics;
(3) vomiting refractory to aggressive anti-emetic therapy;
(4) dyspnea refractory to oxygen, bronchodilators, corticosteroids, and opioids; and
(5) psychological and/or existential distress refractory to appropriate interventions including but not limited to psychological and/or psychiatric

modalities, pharmacologic agents (i.e. antidepressants), and religious or spiritual support

b. Consultations:

(1) At the discretion of the health care provider, a psychiatric consult directed at the terminally ill individual may be obtained to ascertain the influence of psychiatric condition(s) in the request for palliative sedation. In addition, an Ethics Advisory Committee consult may be obtained in cases where ethical concerns arise regarding proposed initiation of palliative sedation.

c. Instituting Palliative Sedation:

(1) Once a symptom is deemed refractory to standard palliative therapies and reversible causes have been excluded that if treated may alleviate the symptom(s), palliative sedation is appropriate. Informed consent must be obtained from the patient and/or the patient's surrogate, and such consent must be documented in the patient's medical record, including the symptom(s) for which palliative sedation is indicated. In addition, a Do Not Resuscitate (DNR) order must be in effect. The choice of a sedating agent(s) is based on the health care provider's decision as to which is most appropriate and may include but is not limited to benzodiazepine, neuroleptic, opioid, barbiturate, or anesthetic medication.

5. RESPONSIBILITIES:

a. The designated health care provider, in conjunction with the attending physician, is responsible for evaluating appropriateness and instituting palliative sedation where indicated.

b. All cases of palliative sedation will be reviewed by the ACOS for Geriatrics and Extended Care who has overall responsibility for the implementation of this policy.

6. REFERENCES: Cherny N., Portenoy R.K. Sedation in the Management of Refractory Symptoms: Guidelines for Evaluation and Treatment, J. Palliat Med 1994; 10 (2): 31-38; Quill TE, Dresser R, Brock DW. The Rule of Double Effect-A Critique of Its Role in End-Of-Life Decision Making, N Engl J Med 1997; 337 (24): 1768-1771; Rousseau, PC. Terminal Sedation in the Care of Dying Patients. Arch Intern Med 1996; 156:1785-1786; Hallenbeck J. Terminal Sedation for Intractable Distress. Not Slow Euthanasia but a Prompt Response to Suffering. West J Med 1999; 171: 222-223

7. EXPIRATION DATE: February, 2002

PAUL ROUSSEAU, MD
ACOS, Geriatrics & Extended Care Services

EUGENE ROSS, MD
Chief of Staff

REFERENCES:

1.Sales JP. Sedation and terminal care. Euro J Palliat Care 2001; 8:97-100.

2. Billings JA & Block SD. Slow Euthanasia. J Palliat Care 1996;12:21-30.

3. Yanow ML. Responding to terminal suffering. Ann Intern Med 2000;135:560.

4. Krakauer EL. Responding to terminal suffering. Ann Intern Med 2000;135:560.

5. Ventafridda V, Ripamonti C, de Conno F & Tamburini M. Symptom prevalence and control during cancer patients' last days of life. J Palliat Care 1990;6:7-11.

6. Morita T, Tsunoda J, Inoue S & Chihara S. Do hospice clinicians sedate patients to hasten death? J Palliat Care 1999;15:20-23.

7. Hardy J. Sedation in terminally ill patients. Lancet 2000;356:1866-7.

8. Fainsinger RL, Waller A, Bercovici M, Bengtson K, Landman W, Hosking M, Nunez-Olarte JM & de Moissac D. A multicentre international study of sedation for uncontrolled symptoms in terminally ill patients. Pall Med 2000;14:257-65.

9. Quill TE & Byock IR. Responding to intractable terminal suffering: the role of terminal sedation and voluntary refusal of food and fluids. Ann Intern Med 2000;132:408-14.

10. Miller Franco L, Newman J, Murphy G & Mariani E. Achieving Quality Through Problem Solving and Process Improvement. 2nd ed. Bethesda: Quality Assurance Project; 1997.

11. Moss F, Thompson R. A new structure for quality improvement reports. Qual Health Care 1999;8:76.

12. Zuber-Skerritt O. Improving learning and teaching through action learning and action research. Higher Education Research and Development. 1993;12:45-58.

13. Bradshaw A. The Spiritual Demension of Hospice: The secularization of an Ideal. Soc Sci Med 1996; 43: 409-419.

14. Rosser WW, Davis D & Gilbart E. Promoting effective guideline use in Ontario. CMAJ 2001;165:181-182.

15. Swarm RA & Cousins MJ. The management of intractable pain. In: Doyle D, Hanks GWC & MacDonald N. (eds) Oxford Textbook of Palliative Medicine 2nd ed. Oxford: Oxford University Press; 1997.p.406-408.

16. Twycross R. Symptom Management in Advanced Cancer. 2nd ed. Oxon:Radcliff Medical Press;1997.p.111-5.

17. Fowell A & Stuart N. Emergencies in Palliative Medicine. Medicine 2000:15-19.

18. Jones DK & Davies RJ. Massive Haemoptysis. BMJ1990;300:889-90.

19. Macleod AD. The management of delirium in hospice practice. Euro J Palliat Care 1997;4:116-20.

20. Bruera E, Martinez-Garcia M, Sweeney C & Palmer L. Perception of discomfort among relatives of unresponsive terminally ill patients. J Palliat Care 2001;16:59-60.

21. Orentlicher D. The Supreme Court and Physician Assisted Suicide. NEJM 1997;337:1236-9.

22. Chater S, Viola R, Paterson J & Jarvis V. Sedation for intractable distress in the dying: a survey for experts. Palliat Med 1998;12:255-69.

23. Morita T, Tsuneto S & Shima Y. Proposed definitions for terminal sedation. Lancet 2001;358:335-6.

24. Mount B. Morphine drips, terminal sedation, and slow euthanasia: Definitions and facts, not anecdotes. J Palliat Care 1996;12:31-37.

25. Portenoy R. Morphine infusions at the end of life: the pitfalls in reasoning from anecdote. J Palliat Care 1996; 12:44-45.

26. Peruselli C, di Giulio P, Toscani F et al. Home palliative care for terminal cancer patients: a survey on the final week of life. Palliat Med 1999;13:233-241.

27. Fainsinger R, Miller MJ, Bruera E, Hanson J & Maceachern T. Symptom control during the last week of life on a palliative care unit. J Palliat Care 1991;7: 5-11.

28. Stone P, Phillips C, Spruyt O & Waight C. A comparison of the use of sedatives in a hospital support team and in a hospice. Palliat Med 1997;11:493-4.

29. Lassauniere JM. Guidelines for use of sedatives in terminal agitation. palliative-medicine@mailbase.ac.uk. 17 June 2001.

30. Morita T, Tsunuda J, Inoue S & Chihara S. Terminal sedation for existential distress. Am J Hospice Palliat Care 2000;17: 189-195.

31. Morris C. Concept of intent being defined inconsistently by courts. BMJ 1999;319:639.

32. Brody H. Commentary on Billings and Block's "Slow Euthanasia". J Palliat Care 1996;12:38-41.

33. Churchill LR & King NMP. Physician assisted suicide, euthanasia or withdrawal of treatment. BMJ 1997;315:137-8.

34. Thorns A. A review of the doctrine of double effect. Euro J Palliat Care 1998;5:117-120.

35. Hawryluck LA & Harvey WRC. Analgesia, Virtue and the Principle of Double Effect. J Palliat Care 2000;16:S24-S30.

36. Sulmasy DP. The Rule of Double Effect. Arch Intern Med 1999;159:545-50.

37. Cherny NI & Portenoy RK. Sedation in the management of Refractory Symptoms: Guidelines for Evaluation & Treatment. J Palliat Care 1994;10:31-38.

38. Hunt R. Taking responsibility for affecting the time of death. Pallit Med 1999;13:439-41.

39. Quill TE, Dresser R & Brock DW. The rule of double effect- a critique of its role in end-of-life decision making. NEJM 1997;337:1768-71.

40. Morita T, Inoue S, Chihara S. Sedation for symptom control in Japan: The importance of intermittent use and communication with family members. J Pain Sympt Manage 1996; 12: 32-38.

41. Farsides R & Dunlop RJ. Is there such a thing as a life not worth living? BMJ 2001;322:1481-83.

42. Twycross R. Pain Relief in Advanced Cancer. Oxon: Radcliffe Medical Press, 1994.p. 553-555.

43. Quill TE, Coombs Lee B & Nunn S. Palliative treatments of last resort: choosing the least harmful alternative. Ann Intern Med 2000;132:488-93.

44. Fainsinger RL, de Moissac D, Mancini I & Oneschuk D. Sedation for delirium and other symptoms in terminally ill patients in Edmonton. J Palliat Care 2000;16: 5-10.

45. Bercovitch M, Waller A & Adunsky A. High dose morphine in the hospice setting; a database survey of patient characteristics and effect on life expectancy. Cancer 1999; 86 : 871-877.

46. Fainsinger RL. Use of sedation by a hospital palliative care support team. J Palliat Care 1998;14:51-54.

47. Anderson F, Downing GM, Hill J. Palliative Performance Scale (PPS): a new tool. J Palliat Care 1996;12: 5-11.

48. Turner K, Chye R, Aggarwal G, Philip J, Skeels A & Lickiss JN. Dignity in Dying: A preliminary study of patients in the last three days of life. J Palliat Care 1996;12:7-13.

49. Thorns A & Sykes N. Opioid use in the last week of life and implications for end of life decision-making. The Lancet 2000; 356:398-399.

50. Morita T, Tsunoda J, Inoue S & Chihara S. Effects of high dose opioids and sedatives on survival in terminally ill cancer patients. J Pain Sympt Manage 2001; 21: 282-289.

51. Morita T, Tsunoda J, Inoue S & Chihara S. The decision-making process in sedation for symptom control in Japan. Palliat Med 1999;13:262-4.

52. Rudkin GE, Osborne GA, Finn BP, Jarvis DA & Vickers D. Intra-operative patient-controlled sedation. Anaesthesia 1992;47:376-81.

53. Inouye S, van Dyck CH, Alessi CA, Balkin S, Siegal AP & Horwitz RI. Clarifying Confusion: The Confusion Assessment Method 1990;113:941-948.

54. Vanegas G, Ripamonti C, Sbontto & DeConno F. Side effects of morphine administration in cancer patients. Cancer Nursing 1998; 21: 289-297.

55. Anbar M. Guidelines for Medical Practice and the Future of Medicine. Arch Intern Med 1992;152:266-7.

56. Schwartz PJ, Breithardt G, Howards AJ, Julian DG & Rehnqvist Ahlberg N. The legal implications of medical guidelines- a Task Force of the European Society of Cardiology. Euro Heart J 1999;20:1152-7.

57. Field MJ, Lohr KN, eds. Institute of Medical Guidelines for Clinical Practice: from development to use. Washington,DC: National Academy Press; 1992.

58. Rousseau PC. Existential suffering and palliative sedation: A brief commentary with a proposal for clinical guidelines. Am J Hospice Palliat Care 2001;18:226-8.

59. Greenhalgh T. Intuition and evidence – uneasy bedfellows? Br J Gen Prac 2002;52:395-400.

60. Dreyfus HL, Dreyfus SE. Mind over machine: The power of human intuition and expertise in the era of the computer. Oxford:Blackwell; 1986.

61. Hunter K. 'Don't think zebras': uncertainty, interpretation, and the place of paradox in clinical education. Theor Med 1996;17:225-41.

62. Conan Doyle A. Silver Blaze. London: Methuen; 1892.

63. Chochinov HM, Wilson KG, Enns M, Mowchun N Lander S et al. Desire for death in the terminally ill. Am J Psychiatry 1995;152:1185-91.

64. Chochinov HM, Tataryn D, Clinch JJ, Dudgeon D. Will to live in the terminally ill. Lancet 1999;354:816-19.

65. Chochinov HM, Hack T, McClement S Kristjanson L & Harlos M. Dignity in the terminally ill; a developing empirical model. Soc Sci Med 2002;54:433-43.

66. Chochinov HM. Dignity conserving care – a new model for palliative care: helping the patient feel valued. JAMA 2002;287:2253-60.