A SURVEY OF THE AVAILABILITY OF PALLIATIVE CARE DRUGS TO PATIENTS SERVED BY THE PUBLIC SECTOR IN THE KNYSNA HEALTH SUB-DISTRICT.

MINI-DISSERTATION (In partial fulfilment of the requirement for the degree of M Phil in Palliative Medicine)

COURSE: M Phil (Palliative Medicine) (PPH747W)

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DECLARATION:

I, Janet Alice Stanford, declare that this dissertation embodies only my original work, except where acknowledgement indicates otherwise and that no part of it has been, or is being submitted for another degree at this or any other university.

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ACKNOWLEDGEMENTS

The list of people who assisted in this research project is long. Some of them are named below, but the list is by no means exhaustive.

Special thanks go to the following:

John Stanwix, my husband, for infinite support and insightful advice.

John and Josephine Stanford, my parents, for willing and loving grandparenting.

Emily, Ben and Louisa Stanwix for patience and understanding of many family activities deferred.

Karin Cohen and Liz Gwyther for supervision of my research, in addition to the rest of their very busy working lives.

Laurel Spies, Cathy Purdon and Pat Cuthbert, the pharmacist respondents who showed patience and interest while answering my questionnaire.

Fareed Abdullah, who intervened in the lengthy process of obtaining research permission from the Western Cape Health Department.

The MESAB Bursary Fund, without which this course of study would have been deferred until all my children were educated.

DEFINITION OF PALLIATIVE CARE

WHO (World Health Organisation) definition of Palliative Care:

Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

Palliative care:

- provides relief from pain and other distressing symptoms,
- affirms life and regards dying as a normal process,
- intends neither to hasten nor postpone death,
- integrates the psychological and spiritual care of the patient,
- offers a support system to help patients live as actively as possible until death,
- offers a support system to help the family cope during the patient's illness and in their own bereavement,
- uses a team approach to address the needs of patients and their families, including bereavement counselling if indicated,
- will enhance quality of life and may also positively influence the course of illness,
- is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.

Revised 2002. Sepulveda et al. JPSM 2000, vol. 24 pp. 91-96.

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ABSTRACT

Introduction

The research aimed to assess the availability of palliative care drugs to patients served by the public sector in the Knysna Health district. The population of approximately 50 000 is served by a Hospice organisation which offers home-based care (it has no residential component), 4 Municipal Clinics, the 96 bed Knysna Provincial District Hospital and a regional referral centre 65km away, viz. the George Provincial Hospital. Tertiary referral is to Cape Town 600km away. The need for palliative care services has increased with the HIV/AIDS epidemic. Drugs on the hospital level EDLs are collected from the Knysna Provincial Hospital by the Hospice staff and given to their patients.

Literature review

A literature review was undertaken in order to compile a list of palliative care drugs which would include drugs to treat most common palliative care conditions. Taking into account the large palliative care burden of patients with HIV/AIDS and the fact that HAART constitutes the most effective palliation for AIDS, drugs to treat opportunistic infections and ARVs were included in the list.

Methods and research design

A questionnaire was then compiled to administer to the Regional Hospital, District Hospital and Municipal Clinics pharmacists. This determined whether the drugs on the list were available, had been out of stock and the level of health worker permitted to prescribe each drug.

Results

The findings were that most drugs on the list were stocked at the appropriate level, although paediatric and injectable formulations were not always available. The provincial code list was used by the hospital in ordering, with the EDLs not being used. At the time of administering the questionnaire, only the George Provincial Hospital ran an ARV clinic, with the availability of ARVs reflecting this. However drugs for PEP and the PMTCT programme were available as appropriate at the other service levels. Pack sizes were aimed at short term treatment and not always appropriate to the needs of palliative care patients.

The implementation of the new Medicines Act from June 2005 was an issue of concern to the pharmacists interviewed, as it prohibits manufacturing and repacking from bulk supplies. This is of concern for the supply of mist morphine, dermatological preparations and the cost of tablets, which are significantly more costly in prepacked form.

Medical officers are permitted to prescribe most drugs on the list, with a few being restricted to specialists. However the palliative care drugs which clinical nurse practitioners may prescribe are limited (nine out of thirty eight). The legislation guiding the prescription by clinical nurse practitioners is also unclear.

Recommendations

The recommendations arising from the research include health systems issues such as the increased use of EDLs for ordering and therapeutic decision making, accompanied by training. With respect to drugs, the supply of drugs in formulations and pack sizes appropriate to the needs of palliative care patients would improve the ability to relieve their symptoms in keeping with the principles of palliative care. Further research into the knowledge, attitudes and practice of health care workers with respect to palliative care is recommended, followed by appropriate training.

CHAPTER ONE

INTRODUCTION

The study was carried out in the setting of the Knysna Public Health Service, where the researcher works for the Local Authority Primary Health Care Service. Knysna is a town of approximately 50 000, served by a 96-bed District Hospital. There is an active Hospice organisation, which employs a medical practitioner for a weekly clinic, 4 registered nurses and 8 home-based carers. The Hospice cares for patients in their homes and does not have an inpatient unit. There are four primary health care clinics, which serve ambulant patients. The three levels of care (home, clinic and hospital) take joint responsibility for public sector patients. Referral for secondary level care is to George (65km away) and for tertiary referral patients go to Cape Town (600km away). The resources for adequate palliative care should therefore be located within the district.

The needs of palliative care patients with cancer have historically been met by referral from the clinics and hospital to the Knysna-Sedgefield Hospice. The Hospice has a weekly clinic, at which the doctor prescribes medication, which is then obtained from the Knysna Provincial Hospital. The Hospice does not have its own pharmacy, is dependent on donations, with no financial support from government and is therefore dependent on the pharmacy of the provincial hospital to meet the medication needs of patients. However the HIV/AIDS epidemic has increased the number of people needing palliative care. It is therefore timely to examine the availability of palliative care drugs in the public sector health services.

Some local figures will bear out the observation that palliative care needs have increased. Figures from the cemetery in Knysna for the 12 months from 1 September 2003 to 31 August 2004 show that 19% of all burials were of people aged 20 to 40 years. (Sarie Hills, personal communication).
The number of patients cared for by the Knysna-Sedgefield Hospice has increased as follows (Fiona

Simpson, personal communication):

Table 1 : Patients cared for by the Knysna-Sedgefield Hospice

Year	Cancer patients	HIV/AIDS patients
2001	120	12
2002	128	24
2003	133	53
2004	142	61 (up to April)

The HIV positive prevalence among mothers offered HIV tests as part of the Prevention of Mother to Child Transmission (PMTCT) Programme for 2003 was 15.6% (Gail Holton, personal communication). This is the highest in the rural Western Cape Province. The antenatal HIV prevalence can be divided by 2.5 in order to obtain the population prevalence. (Dr Peter Bock, UCT public health dept, personal communication). With a population of 50 000, this calculation gives a prevalence of 6.4% or 3 200 HIV infected people. With a newly launched antiretroviral treatment site at the Knysna Provincial Hospital in September 2004, it is not possible to estimate the number of HIV infected people who will require hospice care.

As discussed by Zwarenstein and Bachmann (1997, pp. 147-157), Health Systems research works towards moving from assumptions about health care to evaluation. The problem with an evolving health system is that evaluation requires a standard for comparison that is not always in place with explicitly defined goals. The writers define quality health care as follows: "Quality health care is safe, contributes to good health, meets user expectations, and is the best use of finite health care resources." The standards for quality palliative care appropriate to the resources in South Africa are defined by the Hospice Palliative Care Association.This includes standards for handling medicines and symptom management, without listing individual drugs.*(Standards for the Provision of Palliative Clinical Care in Hospice* 1998) Zwarenstein and Bachmann point out that "promoting improvements in the health system is seldom a

single one-off event - it is an ongoing, long-term process which should be flexible enough to respond to changing needs in the population." With the roll-out of a public sector antiretroviral treatment programme, the maturing AIDS epidemic, and with more HIV infected people reaching the terminal stage, it is timely to examine the changing palliative care needs of the population. Good quality palliative care, with an adequate supply of appropriate drugs accessible to users of the public sector health care service, seems to deserve scrutiny.

The WHO defined essential drugs in 1975 as " indispensable and necessary for the health needs of the population. They should be available at all times, in the proper dosage forms, to all segments of society." (Managing Drug Supply, 1997, p.19).

The first WHO essential drug list was published in 1977 and has been revised every 2 to 3 years. Following the discovery of effective drugs, well-resourced areas were flooded with many products about which there was no reliable information, and poor countries had few drugs, many of which were unreliable and outdated. This led to the essential drugs concept. This was accompanied by the expiry of patents of some drugs and the manufacture of drugs in countries where the patents were not recognised. With the expiry of patents, the concept of high quality generic drugs allowed countries with limited budgets to acquire an adequate selection of effective drugs.

The WHO publication entitled *How to investigate drug use in health facilities* (1993) recommends a retrospective period of a year for drug supply surveys, but points out that data elements may be missing and accuracy may be difficult to verify. The stages of investigation include assessment, introduction of protocols and improvement of supplies of EDL drugs, then measurement of the impact of the interventions. This study will comprise only the first step in a cycle, with the findings being handed over to service providers to follow up. Other questions the WHO document recommends investigating are who makes decisions about which drugs are ordered for a health facility and whether the list is based on the

EDL or a list of previously consumed drugs. This is a useful distinction, which may serve to highlight needs which are not being adequately served within the resources available.

The need for pain and symptom control is motivated by the recognition that for the foreseeable future "in the absence both of totally effective measures for prevention, early diagnosis and curative treatment of cancer, and of sufficient health care workers, active supportive care will be the only realistic humane approach for many patients." (*Cancer pain relief and palliative care*, 1990, p.11) A multi-disciplinary meeting of experts in the management of cancer pain met in Milan in 1984. This meeting resulted in the publication in 1986 of *Cancer Pain Relief*, which disseminated the notion that, through the use of a limited number of drugs, pain relief was a realistic target for most cancer patients. This has been followed by the adoption of policies for the care of the terminally ill by several countries and the increase in research, with the publication of a number of palliative care journals. The definition of palliative care in this report was "palliative care is the active total care of patients whose disease is not responsive to curative treatment." (*Cancer pain relief and palliative care*, 1990, p.11)

A treaty governing the control of narcotics, including opioids is known as the *Single Convention on Narcotic Drugs, 1961*. Signatory countries (of which South Africa is one (*Medicines and Related Substances Act* , Section 22A, Para. (12)(a)(iii)1965)) are required to control all aspects of opioid use internally and across borders, providing reports on production, manufacture, imports, exports and consumption to the International Narcotics Control Board (INCB). The INCB and WHO have addressed the medical use of opioids and recommend that countries have a national policy for drug supply and utilisation which covers safety, efficacy, licensing, allocation of drugs to different categories, labelling and surveillance. The WHO report (*Cancer pain relief and palliative care*, 1990, p.37) quotes a study of 12 000 patients receiving at least one opioid for moderate to severe pain, in whom only 4 well-documented cases of drug dependence were found. It recommends that the control measures should not be of such an onerous nature that they inhibit the use of opioids for medical purposes. It also recommends that an opioid

antagonist should be available in case of hyper-responsiveness or overdose. Other common symptoms of cancer patients are discussed and it is pointed out that the same problems occur in patients with AIDS. AIDS palliative care training should therefore follow the same protocols for integrated palliative care as for other diseases. Guidelines are given in the WHO report on implementation of national palliative care policy, with the ultimate indicator of success being the application of palliative care at rural health clinics. (*Cancer pain relief and palliative care*, 1990, p. 61) Currently, palliative care is only provided by hospices.

CHAPTER TWO

LITERATURE REVIEW

In the literature review I will look at the history and theory of essential drug lists (EDLs), the process of EDL compilation and management, the ethics and reasoning behind including palliative care drugs in an EDL, and the situation in South Africa with respect to drug management. I will then review various publications for a list of essential palliative care drugs against which to measure what is available in the study area.

O'Neill and Fallon (1998) list the essential components of palliative care as effective control of symptoms, effective communication with patients and their families, rehabilitation, continuity of care, terminal care, support in bereavement, education and research. They emphasise that without research, advances in the science of symptom control and quality of care will stagnate.

Ronald O'Connor, in the preface to the publication *Managing Drug Supply* (1997, p.x), writes as follows. "The worst tragedies in public health are the avoidable ones: those problems for which solutions are known and that local resources are available to deal with on a sustainable basis, but which remain inadequately addressed. ...Essential drugs are critical to the success of health programs" and "The challenge for policy-makers in public health revolves around making choices: deciding which problems to address and organising the resources to solve them."

Managing Drug Supply (1997, pp. 9-11)gives a history of the development of drug management concepts, which started in the 1950's and comprise:

- A national drug policy
- Wise drug selection

- Effective management
- Rational drug use
- Systematic assessment and monitoring

The N*inth report of the WHO expert committee on the use of essential drugs* (2000, p.1) reports that model lists have been invaluable in improving the quality of health care and reducing costs. Quality of care is improved when the EDL is linked to evidence-based treatment guidelines. Exactly which drugs are regarded as essential is a national responsibility. It is recognised that the EDL contains drugs requiring a high degree of expertise for safe and effective use and that their availability should be linked to the required level of practitioner.

The manual *Managing Drug Supply* (1997 p. 608) points out that implementation of rational drug use is influenced by an adequate understanding of the factors which influence prescribing, and patient perceptions. The package on offer in a health service is also influenced by the financing model, which is shaped by a number of factors among which are public financing, user fees, health insurance and donor support. The rationale for governments being involved in essential drugs programmes is that drugs are expensive and without government involvement, the poor would be denied access to drugs. The consumer is also unable to assess the quality, safety or efficacy of drugs. A regulatory function must come from the government.

The drug selection process recommended in the above document (*Managing Drug Supply* , 1997 p. 122-136) is as follows:

- review prevalent health problems
- identify treatments of choice
- choose individual drugs and dosage forms
- decide on which drugs will be available at each level of care

The manual *Managing Drug Supply* (1997, p. 41) outlines the requirements for an assessment as:

a. Government commitment to the process
b. A qualified assessment team
c. A clear definition of objectives and procedures
d. An unbiased approach.

Chirac (2003) comments on the process of reviewing the WHO EDL, recommending that price should *not* be a criterion for excluding drugs from the list and the EDL concept should assist countries in gaining access to the treatments on the EDL. He also recommends that the selection should be evidence-based, with the evidence being submitted to the selection panel timeously.

Levy et al (2003) conducted an assessment of the impact of the essential drugs concept. It was found that although many countries have adopted the concept, fewer than a third of these have developed national drug policies. The newest WHO EDL was published in 2002 and includes antiretroviral drugs. The authors discuss the difficult issue of patents and the rights of countries to manufacture or import generic drugs. They suggest that evaluations of EDL programs be carried out regularly and published in peer-reviewed journals, so that strengths and weaknesses become known to a wider professional audience.

Laing et al (2003), reviewed 25 years of WHO essential medicines lists. The revised, 2002 definition of essential medicines is given as: "Those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations;

exactly which medicines are regarded as essential remains a national responsibility." The authors point out that the name has changed from essential drugs lists to essential medicines lists. In view of the fact that the current South African publications still refer to EDLs, I will continue to use this term.
They give a chronology of the World Trade Organisation meetings at which the ethics of access to drugs versus the protection of intellectual property rights was extensively debated. This thorny issue resulted in the mandate of the WHO being extended to work on trade-related issues affecting the availability of medicines. The WHO group has also been mandated to address the problem of inadequate research and development into health needs of developing countries. Laing et al point out that only 1% of medicines developed in the past 25 years have been aimed at addressing developing country needs.

In making the difficult decisions about resource allocation, it may be considered that palliative care is yet another "single issue advocacy initiative", as pointed out in the chapter on ethics in the *Oxford Text book of Palliative Medicine*. (Roy and Macdonald, 1998, pp. 97-138). However the authors also quote Daniel Callahan "No moral impulse seems more deeply embedded than the need to relieve suffering...it has become a foundation stone for the practice of medicine, and it is at the core of the social and welfare programmes of all civilised nations." (p. 107) The writers argue that palliative care should inform all patient care across specialities and is fundamental to good medical practice. They recognise that wasteful spending does occur in attempting cure where symptom control would be more appropriate. It is also argued that the lack of resources for palliative care stems not from ethical shortcomings of policy makers, but lack of clear guidelines of what it is that good palliative care requires, and that in a climate where research is driven by pharmaceutical companies, this area is under-researched.

South Africa does have a National Drug Policy which was developed in 1996 and an essential drugs list committee has published 3 guidelines comprising standard treatment guidelines and essential drugs lists for primary care, hospital level for adults and hospital level for paediatrics. Whether the other components of the drug management concept outlined in the manual *Managing Drug Supply* (1997, pp.9-11) are in

place, such as effective management, rational drug use and systematic assessment and monitoring, is likely to be dependent on local infrastructure and capacity. The EDLs contain motivation forms for addition of new drugs, which allows health care workers at all levels to participate in the review of the EDLs.

The outline of the essential drugs concept in the The South African *Standard Treatment Guidelines and Essential Drugs List: Primary Health Care* (1998, p. iii) specifies the following working principle for the competence of the prescriber: "treatment for the conditions will be initiated at primary level, will be competency-based and not restricted to specific occupations". It does not address who will assess this competency or take responsibility for maintaining it. A more detailed protocol for assessing the competence of each level of health worker to prescribe, and the legal regulation of drugs would be useful. The *Nursing Amendment Act* of 1981 states that a registered nurse may administer or prescribe medicines provided the services of a pharmacist or a doctor are not available. The South African Nursing Council in 1984 allowed registered nurses to prescribe drugs up to schedule 4, on condition that authorisation is given by the South African Nursing Council and consultation with the South African Pharmacy Council is included in the process. The *Medicines and Related Substances Act* 1965 states that " no nurse.. may prescribe a medicine or scheduled substance unless he or she has been authorised to do so by his or her professional council". This leaves the situation rather unclear, as the EDL preface would like to see prescription of any drugs being competency based, while the South African Nursing Council allows prescription of drugs up to schedule 4. It is anticipated that the new EDLs will address prescriber levels (Laing et al, 2003, pp. 1723-29). The first EDL committee was dissolved after publishing, which resulted in a poor monitoring and review process. The EDL concept has yet to gain full acceptance, with 160 items on the primary care EDL and 1 600 different medicines still being procured by the public sector (Laing et al, 2003, pp.1723-29). In a discussion document entitled *Towards compliance with the legislation applicable to the supply of medicines in public sector facilities in the Western Cape (work in progress)(* May 2004), there is still a great deal of uncertainty and speculation about how the newly amended *Medicines and Related Substances Act* (Act 101of 1965) (published in May 2003, but

applicable to the public sector from July 2005) will affect the supply of drugs to the public sector. The stringent standards of Good Manufacturing Practice will limit small-scale manufacturing and bulk compounding of morphine and dermatological compounds and the pre-packing of medicines to facilities which are licensed and recorded as manufacturing pharmacies. This will result in the need for careful planning in order to meet the needs of patients in the Southern Cape if such manufacturing facilities are in Cape Town.

From the general principles of drug management and the principle of EDLs, to the specifics of palliative care. the WHO produced a report *(Cancer pain relief and palliative care*, 1990, WHO Technical Report Series 804) on cancer pain relief and palliative care.

The report recommends that nurses should be allowed to adjust doses to meet the needs of patients. The obstacles to implementation are explored and include absence of national policies, lack of education among policy makers, professionals and the public, fear of addiction to some of the drugs and financial constraints. The argument is made that resources spent on ineffective attempts at curing cancer could be better spent on effective palliative care, with the point being made that the two are not mutually exclusive. The nature of cancer pain is described, with the multi-factorial causation of "total pain", which has to be understood and treated with an insight into the various contributing factors.

The WHO monitors the consumption of morphine as an indicator of the commitment of countries to palliative care, as described in *Cancer pain relief and palliative care (*1990, WHO Technical Report Series 804, pp. 23-41). Global consumption has increased since the 1984 Milan meeting, where orally administered morphine was accepted as the mainstay of cancer pain management.

On the African continent, a study by Jitta et al (2003) on availability of drugs in Ugandan primary care was carried out in 1996. The drugs were supplied in kits deemed to be appropriate for the various levels of facility. The basic kit contained antimalarials, antibiotics and analgesics (paracetamol and acetylsalicylic

acid tablets). The problem with the kit system is that drugs in the kit are not used up at the same rate and a new kit could not be ordered until the old one was finished. The perceptions of users and prescribers were related to availability of drugs, but not to the possibility that irrational use could be negatively influencing availability. The shortages were augmented by supplies from the private sector, thus undermining rational drug use. The importance of taking into account the perceptions of policy makers, coal-face health care workers and patients is illustrated in this study.

A list of minimum drugs required for pain and symptom control was compiled by the Ugandan Hospice (Benson and Merriman, 2002 pp. 118-9). This comprises 22 drugs and includes doses and formulations.

Susan Beck (1999) reviews cancer pain management in South Africa in a field study, which finds strengths, including protocols for pain management, inclusion of morphine and codeine on the primary health care EDL and universal primary care. The problems discussed include poor access in rural areas and inequity as a result of the parallel private and public health systems.

A publication entitled *Palliative care for adults: a guide for health professionals in South Africa* (2003) published by the Department of Health outlines the drug therapy for pain and other common symptoms in terminal illness.

Dickerson (1999) conducted a survey of 50 palliative care physicians (selected on the basis of their individual contributions to the discipline of palliative care), in order to establish a list of essential drugs in palliative care. He compiled a list of core symptoms for which he sought the respondents' management recommendations. He also asked for suggested additional symptoms and management protocols. None of the palliative care experts surveyed was from Africa or Asia, and drugs and symptoms specific to palliative care in HIV/AIDS were not considered.

Cameron, Bridge and Blitz-Lindeque (2004) examined the use of sedation to relieve refractory symptoms in dying patients in a Pretoria hospice. Their use of sedation for refractory symptoms was comparable to international practice.

The National Health System (NHS) in Britain has commissioned a *Palliative Care Formulary* (Twycross, 1998). This is a comprehensive 254 page book which is appropriate to the resources of the NHS. It is an excellent guide to the use of the drugs listed, but too comprehensive for the purposes of compiling a list of drugs to be surveyed in this study where Dickerson's list may be more useful.

The *Handbook of HIV Medicine*, (Wilson et al. 2002, pp. 375-382) includes a list of essential drugs for primary care facilities. These include treatments for opportunistic infections and antiretroviral drugs in addition to general palliative care drugs.

The *South African Medicines Formulary* (SAMF) (Gibbon, 2003, pp. 8-10) includes an introductory section on prescribing in palliative care. There are 13 conditions listed compared with Dickerson's 14.

The South African *Standard Treatment Guidelines and Essential Drugs List: Primary Health Care* (1998) includes treatment guidelines for mouth ulcers, abdominal pain/dyspepsia, constipation, diarrhoea, nausea and vomiting, delirium, depression, cough, insomnia and pain in cancer.
The South African *Standard Treatment Guidelines and Essential Drugs List: Hospital Level, Paediatriccs* (1998)), gives recommendations for post-operative analgesia, but does not deal at all with other types of pain or the WHO pain treatment ladder.
The South African *Standard Treatment Guidelines and Essential Drugs List: Hospital Level, Adults* (1998) gives guidelines for constipation and impaction, delirium, depression, anxiety and HIV/AIDS. The list of drugs available is slightly longer than the primary care EDL.

CHAPTER THREE

AIMS AND OBJECTIVES

AIM:

To determine the availability of palliative care drugs to public sector health facilities and patients within the Knysna Health District.

OBJECTIVES:

1. Review literature to determine an effective essential drug list for palliative care
2. Compare the list of essential drugs in the literature with those available on the South African primary and hospital Essential Drug Lists
3. Determine whether the essential drugs on the EDL are available at health facilities in the District
4. Determine the level of health worker who may prescribe the essential drugs
5. Make recommendations to provincial, regional and local level on availability of essential drugs and training if necessary

LIMITATIONS:

The scope of this study will not include the knowledge, attitudes and practice of local public sector health care providers with respect to management of palliative care patients and their families. There is scope for a further study to explore these issues and make recommendations about training needs and legislative changes in order to facilitate optimal palliative care, which is accessible to patients being cared for at home or in a primary care setting.

CHAPTER FOUR

METHOD

The research is a Health Systems Research project, presented as a descriptive, observational situation analysis to determine the availability of Palliative Care drugs to patients served by the public sector in the Knysna health sub-district. It will provide recommendations to ensure that management of these patients can be improved through the secure access to essential Palliative Care drugs.

The question of validity and reliability has been taken into account in that no sampling was necessary: all 3 pharmacists supplying drugs to the public sector were interviewed by the same researcher, using the same questionnaire in each interview. The interviews were all conducted in English, which is the home language of the researcher and the respondents. The recall periods of 3 months and 12 months were discussed with a pharmacological researcher at the University of Cape Town Pharmacology Department, Dr Karen Barnes, and decided upon on the basis of her recommendations and the WHO document *How to investigate drug use in health facilities* (1993, p.11). The 12 month recall period aims to control for seasonal variations, and the 3 month recall period is aimed at validating the 12 month recall by making it easier to recollect episodes of drugs shortage over a shorter period.

The questionnaire was piloted with the Knysna Municipality pharmacist in order to estimate the time it would take to administer before making appointments with the other pharmacists and also to determine any changes needed. She suggested a few changes in format which were implemented.

The research comprised two phases which are elaborated below.

1. **Compilation of a List of Palliative Care Drugs**.

Firstly a list of essential palliative care drugs was compiled from a literature review and compared with the

South African essential drug lists to determine any discrepancies. This selection process is described in the results chapter.

2. **Compile a questionnaire and administer to respondents**.

   A. **A Regional hospital pharmacy** (This is part of the George regional hospital, which is the specialist referral centre for the surrounding region and has specialists on its staff who are able to prescribe some drugs which are on "specialist only" code. Patients on these drugs need to be under the care of a specialist whom they see in George on a regular basis.)

   B. **A District Hospital Pharmacy** (This is part of the Knysna district hospital, staffed by medical officers and community service doctors, who have access to a more limited drug list)

   C **A Local Authority Pharmacy** (This supplies 4 clinics in the Knysna Municipality and stocks drugs on the primary care EDL which can be prescribed by a clinical nurse practitioner, the single medical practitioner who visits each clinic twice a week and the psychiatric nurse practitioner who visits each clinic monthly. The clinics offer ambulant care only.)

The questionnaire (Appendix Three p.64) lists the essential drugs identified in the literature review, which are available on the South African EDLs and asks:

a. Do you have the drugs on the list (each formulation listed)?
b. List the pack sizes available
c. Have you run out of the drugs in the last 3 months or 12 months?
d. Which level of health worker can prescribe each drug on the list (choice of specialist, medical officer or clinical nurse practitioner)?
e. Do you order drugs from the EDL or from a list of previously consumed drugs?
f. Are there drugs which you would like to order which are not on the EDL.? If so, please list.

g. Are there drugs for which you have had requests, which are not on the EDL? If so, please list.

It was considered important to determine pack sizes, as these are predetermined by level of facility on the provincial code list and the short course treatments appropriate for most conditions are not always appropriate for palliative care patients. The method of ordering by EDL or previously consumed drugs was explored in order to highlight needs that are not being met with the available resources and that would benefit from staff training and the implementation of treatment protocols.

ETHICAL CONSIDERATIONS:

Permission has been obtained from the University of Cape Town Medical School's research Ethics Committee to conduct the research.

Permission has also been obtained from the Health Department of the Provincial Administration of the Western Cape to conduct research in public health facilities.

Permission has been obtained from the Knysna Municipality to conduct research in their facilities.

No patient records are to be used therefore patient confidentiality is not an issue.

Feedback will be given to the Regional health department, George hospital, Knysna hospital and Knysna Municipality on findings and recommendations at the completion of the research.

There are no conflicts of interest in the conducting of this research.

It is hoped that this study will bring to light the existence of any deficiencies in the availability of palliative care drugs, and consequently patient care, at the primary, district hospital and secondary hospital which could be addressed with the EDL currently in place. The questions concerning drugs not on the EDL may also serve to prompt discussion about drugs to be included on the EDL when the current list is reviewed. These outcomes are intended to impact positively on health care delivery and to address distributive justice in access to care.

CHAPTER FIVE

RESULTS

LIST OF DRUGS FOR AN EFFECTIVE PALLIATIVE CARE SERVICE

Following a review of the literature, Dickerson's list (1999) was selected as the reference list for the study. Furthermore, in view of the fact that a large proportion of palliative care in the Knysna health care district as well as in Southern Africa is comprised of patients with AIDS, it was decided to add the antiretroviral drugs which are on the protocol of the *National Antiretroviral Treatment Guidelines* (2004). This list was then compared with local guidelines comprising the EDLs, the *Handbook of HIV Medicine (2002)* and the *South African Medicines Formulary (Gibbon,* 2003). The final list on the questionnaire comprised only drugs on the EDLs and the *National Antiretroviral Treatment Guidelines* (2004). The items listed by Dickerson (1999) that do not appear on this list are methadone, megestrol acetate and tramadol. (The antiretrovirals will presumably be listed in the yet-to-be-published second edition of the hospital level EDLs).

The list of symptoms in Dickerson's (1999) survey were asthenia (defined as "lack or loss of strength and energy; weakness" (*Dorland's illustrated medical dictionary* 2003, p.168)), anorexia/cachexia, anxiety, constipation, delirium, depression, nausea/vomiting and pain. Additional symptoms from his respondents included cough, diarrhoea, dyspnoea, dysphagia, oedema, fever, hyperacidity, insomnia, malodour and oral candidiasis. Respondents were asked to list 20 essential drugs in palliative care. Of the 20 drugs, 14 therapeutic drug classes were included, with recognition of the variations needed to tailor therapy to the needs of individuals by having a choice within a class. Nine of the selected drugs were on the WHO EDL. The following were the 20 selected by the respondents:

morphine (normal release)
haloperidol

metoclopramide
dexamethasone
morphine (sustained release)
amitryptiline
midazolam
lactulose
acetaminophen (paracetamol)
methadone
hyoscine butylbromide
transdermal fentanyl
senna
diclofenac
clonazepam
megestrol acetate
diazepam
codeine
nystatin
tramadol.

Dickerson concludes that seven drugs (morphine, haloperidol, metoclopramide, dexamethasone, amitryptiline, midazolam and lactulose) can be used to treat twelve common symptoms (asthenia, anorexia/cachexia, anxiety, constipation, cough, delirium, depression, dyspnoea, dysphagia, nausea/vomiting and pain) and that therefore a simple formulary, with global application could improve the management of palliative care.

The South African Medicines Formulary (Gibbon 2003, pp. 8-10) includes an introductory section on prescribing in palliative care. There are thirteen conditions listed, compared with Dickerson's fourteen. They are pain, depression, anxiety, insomnia, peripheral neuropathy, delirium, nausea and vomiting, constipation, diarrhoea, malignant bowel obstruction, anorexia, dyspnoea and hiccups. There is a large number of items on the list which overlap, but asthenia, oedema, fever, hyperacidity, malodour and oral candidiasis are only on Dickerson's (1999) list and peripheral neuropathy, malignant bowel obstruction and hiccups are only on the SAMF (2003) list.

A list of minimum drugs required for pain and symptom control was compiled by the Ugandan Hospice. (Benson and Merriman 2002, p. 118-9) This comprises 22 drugs and includes doses and formulations.

Benson and Merriman's list comprises amitryptiline, phenytoin, acetylsalycilic acid, diclofenac, codeine, morphine, chlorpromazine, thioridazine, haloperidol, dexamethazone, diazepam, furosemide, spironolactone, ketoconazole, nystatin, magnesium trisilicate, metoclopramide, metronidazole, amoxycillin, bisacodyl, hysocine butylbromide and chlorpheniramine. A second list comprises nineteen items including those for opportunistic infections.

However, three South African publications examine palliative care issues locally. Norval (2004) collected data from 103 AIDS patients in Johannesburg who were asked to identify their ten most common symptoms and five most common sites of pain. This is helpful in informing the compilation of a list of palliative care drugs that are relevant to patients with AIDS. The ten most common symptoms were found to be **pain, weight loss, loss of appetite, low mood, weakness, dry skin, diarrhoea, nausea and vomiting, cough and fatigue**. The most common sites of pain **were lower limb pain, mouth pain, headache, throat pain and chest pain**, with patients experiencing an average of 2.91 different pains. Norval emphasises that antiretroviral drugs are the most effective palliation for many AIDS symptoms. This survey will therefore include the limited list of antiretroviral drugs that comprise the *National Antiretroviral Treatment Guidelines* (2004) and treatments for selected opportunistic infections. However, antibiotics and drugs used in the treatment of tuberculosis form part of general medical care and the National TB Control programme respectively, and will therefore not be included in the survey. The survey questionnaire was compiled on the assumption that palliative care is delivered within a functioning health system in which other drugs are available for the care of conditions which occur in any patients.

Cameron, Bridge and Blitz-Lindeque (2004) examined the use of sedation to relieve refractory symptoms in dying patients in a Pretoria hospice. Their use of sedation for refractory symptoms was comparable to international practice. Haloperidol and midazolam via syringe driver were the most commonly used sedatives. The conditions for which sedation was needed were agitated delirium, intractable vomiting, convulsions and myoclonic jerking, severe dyspnoea and pain.

The National Department of Health publication: *Palliative care for adults: a guide for health professionals in South Africa* (2003) gives guidelines for management of pain, anorexia, dysphagia, abdominal cramps, diarrhoea, nausea and vomiting, constipation oral thrush, common skin conditions, pruritis, peripheral neuropathy, incontinence, dyspnoea, cough, anxiety, sleep disturbances, asthenia, confusion and terminal restlessness..

The Handbook of HIV Medicine (2002, pp. 375-382) includes a list of essential drugs for primary care facilities. These include treatments for opportunistic infections and antiretroviral drugs, in addition to general palliative care drugs. The general palliative care drugs are:
codeine phosphate (tablets and syrup), ibuprofen (tablets and suspension), morphine (injection and oral solution), paracetamol (tablets and solution), carbamazepine (tablets and suspension, valproic acid (capsules and syrup), amitryptiline (tablets and suspension), fluoxetine (capsules/tablet and suspension), fluconazole (capsule/tablet and suspension), griseofulvin (tablet), cyclizine (tablet, suppository, syrup and injection), promethazine (tablet and syrup), haloperidol (tablet and injection), thioridazine (tablets), diazepam (tablets), lorazepam (injection), oxazepam (tablets), dexamethasone (tablets), prednisone (tablets), hyoscine butylbromide (tablets and injection), loperamide (tablets/capsules), metoclopramide (tablets), senna (tablets).

The South African *Standard Treatment Guidelines and Essential Drugs List: Primary Health Care* (1998) includes treatment guidelines for mouth ulcers, abdominal pain/dyspepsia, constipation, diarrhoea, nausea and vomiting, delirium, depression, cough, insomnia and pain in cancer. The drugs available are senna, amitryptiline, chlorpromazine, fluoxetine, fluphenazine decanoate, haloperidol, lorazepam, paracetamol, ibuprofen, morphine (oral and injectable), codeine phosphate. The 3 step approach to pain is described, but with no adjuvants in the 1998 edition. The 2003 edition includes ibuprofen as an adjuvant. For constipation, senna and 70% sorbitol are available. For diarrhoea, only rehydration solutions, no loperamide in the 1998 edition and for nausea and vomiting, oral metoclopramide. The 2003

edition of *Standard Treatment Guidelines and Essential Drugs List: Primary Health Care* , does include loperamide. No mention is made of bowel obstruction and the need for an agent which acts on the vomiting centre , such as cyclizine. However, haloperidol does appear on the EDL. There is a difficulty with drugs appearing on the EDL for purposes other than palliative care, as one cannot assume the legality or knowledge of using them for other indications than those enumerated in the EDL. For delirium, lorazepam, diazepam and haloperidol are available. For depression, amitryptiline is the first choice, with fluoxetine for prescrption only by those with psychiatric training. Codeine phosphate is not recommended for cough, which is only managed by looking for a cause to treat. Insomnia is managed by non-drug measures. Naloxone is on the EDL, as recommended by the WHO.

The South African *Standard Treatment Guidelines and Essential Drugs List: Hospital Level, Paediatriccs* (1998) gives recommendations for post-operative analgesia, but does not deal at all with other types of pain or the WHO ladder. The drugs listed are paracetamol, ibuprofen, diclofenac suppositories, codeine phosphate, fentanyl, morphine, pethidine and tilidine. There are treatment guidelines for constipation for which phosphate-containing enemas, ispaghula husk sachets and lactulose are available. Depression can be treated with amitryptiline or fluoxetine. Haloperidol is suggested for chorea in rheumatic fever. Diazepam is listed for convulsions.

The South African *Standard Treatment Guidelines and Essential Drugs List: Hospital Level, Adults* (1998) gives guidelines for constipation and impaction, delirium, depression, anxiety and HIV/AIDS. The list of drugs available is slightly longer than the *Standard Treatment Guidelines and Essential Drugs List: Primary Health Care* , (2003). The items listed by Dickerson, which do not appear on this list are methadone, megestrol acetate and tramadol. Fentanyl is listed, but the patches are not specifically itemised. Morphine injection and tablets are listed, but the sustained release formulation is not. The hospital level EDLs have not yet been published in second editions. The 1998 editions only list antiretrovirals used for prevention of mother to child transmission and post exposure prophylaxis, not long-

term treatment regimens.

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A Western Cape Provincial Health Department Circular dated 2002 gives guidelines for paediatric pain management and outlines a stepwise pain management protocol. This progresses from paracetamol to codeine (which is not on code, therefore a paracetamol/codeine preparation is suggested) to a non-steroidal anti-inflammatory drug (NSAID) (a choice of ibuprofen, diclofenac suppository or mefenamic acid) to tilidine drops.

The items on Dickerson's (1999) list which are not on the South African EDLs are tramadol and rantidine. However, cimetidine is on the South African Hospital EDL. Antiretroviral drugs are on the WHO EDL, but not on the current South African EDLs, though there are national ARV treatment guidelines. One therefore assumes that ARVs will be included on the next edition of the South African EDLs. Whether ARVs will be available at clinic or hospital level remains unclear.

The personal experience of the researcher (working in the primary care setting in the local authority clinics) with respect to the availability of palliative care drugs is that the limited pack sizes available at the clinics (for instance, ibuprofen 15, senna 10, loperamide 6) do not meet the needs of palliative care patients. These pack sizes are prescribed by the provincial code list for clinic level. The removal of cyclizine from the list of available drugs leaves metoclopramide and haloperidol for the management of nausea and vomiting. Amphotericin B lozenges not being available tempts one to prescribe fluconazole in oral candidiasis, while the donor programme indicates that fluconazole should only be for oesophageal candidiasis and cryptococcal meningitis. This holds a risk for the emergence of resistance and threatens the long- term efficacy of fluconazole. The lack of paediatric formulations for drugs such as fluconazole and acyclovir result in inaccurate dosing with tablets.

The list of drugs included in the questionnaire is thus compiled from the published literature, both locally and internationally, in order to give a reasonable choice of drug to treat most conditions encountered in palliative care, but finally is limited to those drugs on the South African EDLs. The questionnaire explores both availability and the level of health worker who may prescribe, thereby meeting the aim of the research, which is to determine the availability of palliative care drugs to patients in the public sector within the Knysna Health District. The compilation of a list of essential drugs for palliative care relied to a large extent on literature that focussed exclusively on cancer and did not take HIV/AIDS into account. Although the palliation for both conditions is similar, it was considered appropriate to investigate the availability of treatment for some opportunistic infections and antiretrovirals (ARVs) as the best form of palliative care for HIV/AIDS. The question then arose as to where to draw the line in the treatment of opportunistic infections. The decision was made bearing in mind that palliative care is offered in the context of a functioning public health service, with clear protocols for the management of tuberculosis and other infections.

The list is compiled from the following publications discussed in the literature review: (Most lists do not specify formulations)

South African Medicines Formulary (2003)

Handbook of HIV Medicine (2002)

Dickerson D. 1999 '*The 20 essential drugs in palliative care*'

Benson TF, Merriman A. 2000 *Palliative Medicine: Pain and Symptom Control in the Cancer and/or AIDS Patient in Uganda and other African Countries*. 3rd edn, Hospice Africa Uganda, Kampala.

Standard Treatment Guidelines and essential Drugs List: Primary Health Care (2003)

Standard Treatment Guidelines and essential Drugs List: Hospital Level Adults(1998)

Standard Treatment Guidelines and essential Drugs List: Hospital Level Paediatrics(1998)

National Antiretroviral Treatment Guidelines , 2004, National Department of Health, South Africa

A table (Table Two) showing the drugs included in the questionnaire, with those on the South African

EDLs indicated in bold, appears below:

TABLE TWO

LIST OF DRUGS FOR AN EFFECTIVE PALLIATIVE CARE SERVICE

(Drugs appearing on the South African EDLs are highlighted)

CLASS	*DRUG*	*FORMULATION*	*LIST*
ANALGESIC (OPIOID)	**MORPHINE**	INJECTION 10mg/ml 15mg/ml	WHO [1] DICKERSON[2](100 %)[3] **SA PHC**[4]
		ORAL SOLUTION	WHO DICKERSON(100% **SA PHC**
	CODEINE	TABLET 30 mg	WHO DICKERSON (39%) **SAHOSP ADULT**[4]
		SYRUP 25mg/5ml	**SA PHC**
	TILIDINE	DROPS 50mg/0.5ml	**SAHOSP PAED**[5]
	TRAMADOL	TABLET	DICKERSON (37%)
		INJECTION	DICKERSON (37%)
ANALGESIC (NON-OPIOID)	**PARACETAMOL**	TABLET500mg	WHO DICKERSON(58%) **SA PHC**
		SYRUP 120mg/5ml	WHO DICKERSON(58%) **SA PHC**
	IBUPROFEN	TABLET 200 mg	**SA PHC**
		SYRUP 100mg/5mL	**SA PHC**
ANTIEMETICS	**METOCLOPRAMIDE**	TABLET 10 mg	WHO DICKERSON(95%) **SA PHC**
		SYRUP 5mg/5ml	**SA PHC**
		INJECTION 10mg/2ml	**SA HOSP ADULT**
ANXIOLYTIC	**MIDAZOLAM**	INJECTION15mg/3ml 5mg/5ml	DICKERSON(63%) **SA HOSP ADULT**
	DIAZEPAM	TABLET 2 mg 5 mg 10 mg	WHO DICKERSON (42%) **SA PHC**
		INJECTION 10mg/2ml	WHO DICKERSON (42%) **SA PHC**
	LORAZEPAM	TABLET 1 mg	**SA PHC**
		INJECTION 4 mg/ml	**SA PHC**
CORTICOSTEROID	**DEXAMETHASONE**	TABLET 0.5mg	WHO DICKERSON (92%) **SA HOSP ADULT**
		INJECTION 4 mg/ml	WHO DICKERSON (92%) **SA HOSP ADULT**
LAXATIVES	**LACTULOSE**	SYRUP 3.3g/5ml	DICKERSON (63%) **SA PHC**
	SENNA	TABLET 7.5 mg	WHO DICKERSON (45%) **SA PHC**

CLASS	*DRUG*	*FORMULATION*	*LIST*
ANTIPSYCHOTICS	**HALOPERIDOL**	TABLET 0.5 mg	WHO DICKERSON (95%) **SA PHC**
		INJECTION 20 mg/2ml	WHO DICKERSON (95%) **SA PHC**
	CHLORPROMAZINE	TABLET 10 25 50 100 mg	WHO **SA PHC**
		INJECTION 50mg/2ml	WHO **SA PHC**
	FLUPHENAZINE DECANOATE	INJECTION 25mg/10ml	WHO **SA PHC**
ANTIDEPRESSANTS	**AMITRYPTILINE**	TABLET 10mg 25mg	WHO DICKERSON ((82%) **SA PHC**
	FLUOXETINE	TABLET 20mg	**SA PHC**
ANTICONVULSANTS	**CLONAZEPAM**	DROP 2.5mg/ml	WHO (comp group)[7] DICKERSON (42%) **SA HOSP ADULT**
		TABLET 0.5mg 2mg	WHO (comp group) DICKERSON (42%) **SA HOSP ADULT**
		INJECTION 1 mg/ml	WHO (comp group) DICKERSON (42%) **SA HOSP ADULT**
	DIAZEPAM	INJECTION 10mg 2ml	WHO (ess group)[8] DICKERSON (42%) **SA PHC**
		TABLET 10mg 5mg 2mg	WHO (ess group) DICKERSON (42%) **SA PHC**
ANTISPASMODICS	**HYOSCINE BUTYLBROMIDE**	INJECTION 20mg/ml	DICKERSON (55%) **SA HOSP ADULT**
		TABLET 10mg	DICKERSON (55%) **SA HOSP ADULT**
ANTIFUNGALS	**NYSTATIN**	SUSPENSION 100 000U/ml	WHO DICKERSON (37%) **SA PHC**
		TOPICAL CREAM 100 000 U/G	WHO DICKERSON (37%) **SA PHC**
		VAGINAL TABLETS 100 000U	WHO DICKERSON (37%) **SA PHC**
	FLUCONAZOLE	TABLET 200mg	**SA PHC**
		SUSPENSION 50mg/5ml	**SA PHC**
	AMPHOTERICIN B	LOZENGES 10mg	**SA HOSP ADULT**

CLASS	*DRUG*	*FORMULATION*	*LIST*
PROGESTINS	**MEGESTROL ACETATE**	TABLETS 40mg	DICKERSON (42%)
	MEDROXYPROGESTERONE	TABLET100mg 500mg	WHO (COMP) **SA HOSP ADULT**
H2 ANTAGONISTS	RANTIDINE	TABLET 75mg 150mg 300mg	DICKERSON
	CIMETIDINE	INJECTION200mg/2ml	WHO **SA HOSP ADULT**
		SYRUP 200mg/5ml	WHO **SA HOSP ADULT**
		TABLET 200mg 400mg	WHO **SA HOSP ADULT**
ANTIDIARRHOEALS	**LOPERAMIDE**	TABLET 2mg	**SA PHC**
ANTIBIOTICS	**TRIMETHOPRIM/SULPHAMET HOXAZLOE**	TABLET 80/400mg	**SA PHC** WHO
		SYRUP 40/200mg	**SA PHC** WHO
ANTIVIRAL	**ACYCLOVIR**	TABLET 200mg	**SA PHC** WHO
		SYRUP 200mg/5ml	**SA PHC** WHO
ANTIRETROVIRALS	STAVUDINE	CAPSULES 15, 20, 30, 40 mg	WHO
		POWDER 1mg/ml	WHO
	LAMIVUDINE	TABLETS 150mg	WHO **SA PHC**
		SOLUTION 10mg/5ml	WHO
	ABACAVIR	TABLET 300mg	WHO
		SOLUTION 20mg/ml	WHO
	DIDANOSINE	TABLETS 25, 50, 100, 150mg	WHO
		SUSPENSION 10 mg/5ml	WHO
	ZIDOVUDINE	CAPSULES 100 250mg TABLETS 300mg	WHO **SA PHC**
		SYRUP 50mg/5ml	WHO
	EFAVIRENZ	CAPSULES 50, 200mg	WHO
	NEVIRAPINE	TABLETS 200mg	WHO
		SUSPENSION 50mg/5ml	WHO
	RITONAVIR	CAPSULE 100mg	WHO
		SOLUTION 80mg/ml	WHO
	LOPINAVIR/RITONAVIR	CAPSULE 133.3/33.3	
		SOLUTION 80/20mg/ml	
	NELFINAVIR	TABLET 250 mg	WHO
		POWDER 50mg/g	WHO

1 World Health Organisation Essential drugs, as listed in the *South African Medicines Formulary* (2003)

2 Dickerson (2003) list of *The 20 Essential drugs in palliative care*

3 Percentage of Dickerson's respondents who considered the drug an essential palliative care drug.

4 *Standard Treatment Guidelines and Essential Drugs List: Primary Health Care* (2003)

5 *Standard Treatment Guidelines and Essential Drugs List. Hospital Level, Adults* (1998)

6 *Standard Treatment Guidelines and Essential Drugs List: Hospital Level, Paediatrics* (1998)

7 WHO complementary group as listed in the *South African Medical Formulary* (2003)

8 WHO essential therapeutic group as listed in the *South African Medical Formulary* (2003)

2. The Interviews

The interviews were conducted in person, with the pharmacist interviewees able to check their shelves and records for the validity of the responses. All of the interviewees were first language English speakers, so the need for translation of the questionnaires did not arise. The process of interviewing, as opposed to sending the questionnaires to be filled in was very useful, as it enabled the interviewer to check how the respondent verified information. The interview was also accompanied by an informal running commentary, which illuminated many practical concerns and problems that would not have been elicited from the questionnaire alone. The interviews were conducted between 25 August 2004 and 2 September 2004 by the researcher. All interviews were conducted at the workplace of the respondent by appointment. All three respondents were willing to be interviewed and were able to make time for the process.

The 3 levels of pharmacist interviewed all use the provincial code list, a regularly updated stock list, which describes the items, their formulation and pack size, as well as the level of practitioner who may prescribe each item. The items on this list far exceed those listed in the EDLs.

Although the respondents verified their answers by referring to current stock and records, the possibility of bias does exist, in that items out of stock could reflect badly on their management, unless the problem was clearly with another level in the supply chain or with policy guidelines.

As there were only three pharmacists involved in responding to the questionnaires, no sampling was necessary. The information could be obtained from one pharmacist at each level, as the information relates to the institution, not to the individual pharmacist. The local authority has only one half-day pharmacist who serves all 4 clinics. Therefore the questionnaires were administered to the pharmacist in charge of each institution. Each level has access to different drugs (clinics to the primary care EDL, district hospital to the Hospital EDLs and regional hospital to the Hospital level EDLs, including some specialist

only items which may not be available to the district hospital staff). Thus, the responses to each questionnaire reflect the situation at that level of service and are descriptive in nature. The analysis takes the form of a description of the drugs on the list, which are and are not available at each level. The question about how the re-ordering is done is used to shed light on the availability of the drugs at each level.

Table Three shows the drugs surveyed by level of health professional permitted to prescribe (specialist, medical officer or clinical nurse practitioner) and EDL level (primary care or hospital). This information was elicited from the questionnaires and verified in the EDLs.

TABLE THREE

PALLIATIVE CARE DRUGS BY EDL LEVEL AND PRESCRIBER LEVEL

DRUG	EDL LEVEL 1. Clinic 2. Hospital	LEVEL OF HEALTH CARE WORKER WHO MAY PRESCRIBE 1. Specialist 2. Medical Officer 3. Clinical Nurse Practitioner
ANALGESIC (OPIOID)		
Morphine	1,2	1,2
Codeine	2	1,2
Tilidine	2	1,2
ANALGESIC (NON-OPIOID)		
Paracetamol	1,2	1,2,3
Ibuprofen	1,2	1,2,3
ANTIEMETIC		
Metoclopramide	1,2	1,2,3
Haloperidol	1,2	1,2
ANXIOLYTIC		
Midazolam	2	1,2
Diazepam	1,2	1,2
Lorazepam	1,2	1,2
CORTICOSTEROID		
Dexamethasone	2	1,2
LAXATIVE		
Lactulose	1,2	1,2,3
Senna	1,2	1,2,3
ANTIPSYCHOTIC		
Haloperidol	1,2	1,2
Chlorpromazine	1,2	1,2
Fluphenazine decanoate	1,2	1,2
ANTIDEPRESSANT		
Amitryptiline	1,2	1,2
Fluoxetine	1,2	1,2
ANTICONVULSANT		
Diazepam	1,2	1,2
Clonazepam	1,2	1,2
ANTISPASMODIC		
Hyoscine butyl bromide	1,2	1,2,3
ANTIFUNGAL		
Nystatin	1,2	1,2,3
Fluconazole	1,2	1,2
Amphotericin B lozenge	2	1,2
PROGESTIN		
Medroxyprogesterone	2	1
H2 ANTAGONIST		
Cimetidine	2	1

DRUG	EDL LEVEL 1Clinic 2 Hospital	LEVEL OF HEALTH CARE WORKER WHO MAY PRESCRIBE 1.Specialist 2. Medical Officer 3 Clinical Nurse Practitioner
ANTIDIARRHOEAL		
Loperamide	1,2	1,2,3
ANTIBIOTIC		
Trimethoprim/sulphamethoxazole	1,2	1,2,3
ANTIVIRAL		
Acyclovir	1,2	1,2
ANTIRETROVIRAL		
Stavudine	2	1,2
Lamivudine	1,2	1,2
Abacavir	2	1,2
Didanosine	2	1,2
Zidovudine	1,2	1,2
Efavirenz	2	1,2
Nevirapine	2	1,2
Ritonavir	2	1,2
Lopinavir/Ritonavir	2	1,2
Nelfinavir	2	1,2

The EDLs are published for hospital and primary health care levels of service. In practice there is a difference between George and Knysna Provincial hospitals, as specialists are available in more disciplines in the George Provincial Hospital and this allows the prescription of drugs that are limited to specialist only prescriptions. Thus although there are only two EDL levels, in effect there are three tiers with respect to availability of drugs: George Provincial Hospital (regional), Knysna Provincial Hospital (district) and the Knysna Municipal Clinics.

The conditions which can be treated by a clinical nurse practitioner at clinic level is limited, as they may only prescribe non-opioid analgesics, metoclopramide, laxatives, hyoscine butylbromide, loperamide and trimethoprim/sulphamethoxazole.

The interviews revealed that most of the drugs on the list were available. Problems that were experienced with specific drugs or formulations are discussed below and the results of the interviews are presented in Table Four below.

TABLE FOUR

PALLIATIVE CARE DRUGS AND FORMULATIONS AVAILABLE AT GEORGE PROVINCIAL HOSPITAL

DRUG	FORMULATION	PACK SIZE/VOLUME	IN STOCK	IN STOCK	IN STOCK	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 12 MONTHS	OUT OF STOCK IN PAST 12 MONTHS	OUT OF STOCK IN PAST 12 MONTHS
ANALGESIC (OPIOD)			George H	Knysna H	Knysna Cl	George H	Knysna H	Knysna Cl	George H	Knysna H	Knysna Cl
Morphine	Injection 10mg/ml	10amps	Yes	Yes	Not St	No	No		No	***Yes***	
	Oral solution 20,40,80mg/5ml	Any	Yes	Yes	Not St	No	No		No	No	
Codeine	Tablet 30mg	100	Yes	Yes	Not St	No	No		No	No	
	Syrup 25mg/5ml	100ml	Yes (Quality problem)	Avialable on request	Not St	No	Yes		No	Yes	
Tilidine	Drops50mg/0.5ml	10ml	Yes	Yes	Not St	No	No		No	No	
ANALGESIC (NON OPIOD)											
Paracetamol	Tablet 500mg	Any	Yes	Yes	Yes	No	No	No	No	No	No
	Syrup 120mg/5ml	50/100ml	Yes	Yes	Yes	No	No	No	No	No	No
Ibuprofen	Tablet 200mg	15/84/bulk	Yes	Yes	Yes 15s	No	No	No	No	No	No
	Syrup 100mg/5ml	100ml	Yes	Yes	Not St	No	No		No	No	
ANTIEMETIC											
Metoclopramide	Tablet 10mg	10/1000	Yes	Yes	Yes	No	No		No	No	No
	Injection 10mg/ml	10amps	Yes	Yes	Yes	No	No		No	No	No
	Syrup 5mg/5ml	100ml	No	Yes	Yes		No	No		No	No
ANXIOLYTIC											
Midazolam	Injection 15mg/3ml 5mg/5ml	 5amps 5amps	 Yes Yes	 No Yes	Not St	 No No	 Yes No		 No No	 Yes No	
	Tablet 7.5/15mg		No	No	Not St						
Diazepam	Injection 10mg/2ml	10 amps	Yes	Yes	Yes	No	No	No	No	No	No
	2mg 5mg	14/500 14/500	Yes Yes	Yes Yes	Yes Yes	No No	No No	No No	No No	No No	No No

DRUG	FORMULATION	PACK SIZE/VOLUME	IN STOCK	IN STOCK	IN STOCK	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 12 MONTHS	OUT OF STOCK IN PAST 12 MONTHS	OUT OF STOCK IN PAST 12 MONTHS
			George H	Knys H	Knys C	George H	Knys H	Knys C	George H	Knys H	Knys C
Lorazepam	Injection 4mg/ml	5 amps	Yes	Yes	Yes	No	No	No	No	No	No
	Tablet 1 mg	100	Yes	Yes	Yes	No	No	No	No	No	No
CORTICOSTEROID											
Dexamethasone	Injection 4mg/ml	2ml	Yes	Yes	Not St	No	No		No	No	
	Tablet 0.5mg	100	Yes	Yes	Not St	No	No		No	No	
LAXATIVE											
Lactulose	Syrup 3.3mg/5ml	500ml	Yes	Yes	Not St	No	No		No	No	
Senna	Tablet 7.5mg	12/200/1000	Yes	Yes	Yes(12s)	No	No	No	No	No	No
ANTIPSYCHOTIC											
Haloperidol	Injection 20mg/5ml	5 amps	Yes	Off code	Not St	No	Yes		No	Yes	
	Tablet 0.5mg	60	Yes	Yes	Yes	No	No	No	No	No	No
Chlorpromazine	Tablets 25/50/100mg	500	Yes	Yes	Yes	No	No	No	No	No	No
Fluphenazine decanoate	Injection 25mg/10ml	2/10ml	Yes	Yes	Yes	No	No	No	No	No	No
ANTIDEPRESSANT											
Amitryptiline	Tablet 10/25mg	28/84/500	Yes	Yes	Yes	No	No	No	No	No	No
Fluoxetine	Capsule/tablet 20mg	100	Yes	Yes	Yes	No	No	No	No	No	No
ANTICONVULSANT											
Clonazepam	Injection 1mg/ml	5 amps	Yes	Not Stocked	Not St	No			No		
	Tablet 0.5/2mg	90	Yes	Yes	Yes	No	No	No	No	No	No
ANTISPASMODIC											
Hyoscine butylbromide	Injection 20mg/ml	10 amps	Yes	Yes	Yes	No	No	No	No	No	No
	Tablet 10mg	10/100/500	Yes	Yes	Yes 10s	No	No	No	No	No	No
	Syrup		Not Stocked	Not St	Not St						

DRUG	FORMULATION	PACK SIZE/VOLUME	IN STOCK AT	IN STOCK AT	IN STOCK AT	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 12 MONTHS	OUT OF STOCK IN PAST 12 MONTHS	OUT OF STOCK IN PAST 12 MONTHS
ANTIFUNGAL			George H	Knys H	Knys cl	George H	Knys H	Knys cl	George H	Knys H	Knys cl
Nystatin	Oral suspension 100 000 U/ml	20ml	Yes	Yes	Yes	No	No	No	No	No	No
	Vaginal Tablet 100 000U/ml		Not stocked	Not st	Not St						
	Topical ointment	15g	Yes	Yes	Yes	No	No	No	No	No	No
Fluconazole	Tablet 200mg	28	Yes	Yes	Yes	No	No	No	No	No	No
	Supension 50mg/5ml		Not Stocked	Not St	Not St						
Amphotericin B	Lozenge 10mg	20	Yes	No	Not St	No			No		
PROGESTIN											
Medroxyprogesterone	Tablet 100mg	100	Yes	Yes	Not St	No	No		No	No	
H2 ANTAGONIST											
Cimetidine	Tablet 200/400mg	150/60	Yes	Yes	Not St	No	No		No	No	
	Syrup		Not Stocked	Not St	Not St						
ANTIDIARRHOEL											
Loperamide	Tablet 2mg	6	Yes	Yes	Yes	No	No	No	No	No	No
ANTIBIOTIC											
Trimethoprim/sulphamethoxazole	Tablet 80/400	Up to 1000/28	Yes	Yes	Yes 28s	No	No	No	No	No	No
	Syrup 40/200per5ml	50/100ml	Yes	Yes		No	No	No	No	No	No
ANTIVIRAL											
Acyclovir	Tablet 200mg	25	Yes	Yes	Yes	No	No	No	No	No	No
	Suspension 200mg/5ml		Not Stocked	Not St	Not St						

DRUG	FORMULATION	PACK SIZE/VOLUME	IN STOCK	IN STOCK	IN STOCK	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 3 MONTHS	OUT OF STOCK IN PAST 12 MONTHS	OUT OF STOCK IN PAST 12 MONTHS	OUT OF STOCK IN PAST 12 MONTHS
ANTIRETROVIRAL			George H	Knys H	Knys cl	George H	Knys H	Knys cl	George H	Knys H	Knys cl
Stavudine	Capsule 20/30/40mg	60	Yes	Not St	Not St	No			No		
	Suspension 1mg/ml		Not Stocked	Not St	Not St						
Lamivudine	Tablet 150mg	60	Yes	Yes	Yes	No	No	No	No	No	No
	Solutiion 10mg/5ml	240ml	Yes	Yes	Not St	No	No		No	No	
Abacavir	Tablet 300mg	60	Yes	Not St	Not St	No			No		
	Solution 20mg/ml		Not stocked	Not St	Not St						
Didanosine	Tablet 10/150mg	60	Yes	Not St	Not St	No			No		
	Suspension 10mg/5ml	2g	Yes	Not St	Not St	No			No		
Zidovudine	Capsule 100/300mg	100/60	Yes	Yes	Yes	No	No	No	No	No	No
	Syrup 50mg/5ml	200ml	Yes	Yes	Not St	No	No		No	No	
Efavirenz	Capsule 50/200/600mg	30/90/30	Yes	Not St	Not St	No			No		
Nevirapine	Tablet 200mg	60	Yes	Yes	Not St	No	No		No	No	
	Suspension50mg/5ml	240ml	Yes	Yes	Not St	No	No		No	No	
Ritonavir	Capsule 100mg	84	Yes	Not St	Not St	No			No		
	Solution 80mg/ml	90ml	Yes	Not St	Not St	No			No		
Lopinavir/ritonavir	Capsule 133.3/33.3mg	180	Yes	Not St	Not St	No			No		
	Solution 80/20mg/ml	5X60ml	Yes	Not St	Not St	No			No		
Nelfinavir			NotStocked	Not St	Not St						

Analgesics:

Morphine is not stocked at the Knysna Municipal clinics as there is only one itinerant, half-day pharmacist for all four clinics and the Hospice gets its prescriptions filled at the Knysna Provincial Hospital.

There was a period during the twelve month recall period when morphine injection was out of stock at the Knysna Hospital.

Codeine syrup is only stocked by the George hospital. The product in stock (*Resmed*) had a precipitate at the bottom of all the bottles, making accurate dosing impossible. The pharmacist was willing to use it as a cough suppressant, but not as an analgesic. He did, however, follow the procdure for reporting the problem on the adverse event and product quality problem report form and return the consignment to the supplier.

Tilidine, a hospital EDL drug, was not stocked at the Knysna Hospital, because there was seldom a call for it.

Ibuprofen syrup is not in stock at the clinic level. It was not on the 1998 Primary care EDL but has been added to the 2003 edition, which was only distributed in June 2004. The tablets are in bulk or prepacks at the hospitals and only in prepacks of 15 at the clinics.

Paracetamol tablets and syrup are available at all three levels. Only the hospitals have bulk packs, the clinics only have packs of 10 tablets.

Antiemetics:

All three levels have **metoclopramide** injection and tablets. The hospitals stock in bulk, the clinics only in 10s. The Knysna Hospital and clinics stock metoclopramide syrup, but George Hospital does not.

Haloperidol injection is available at the George hospital and tablets are available at all three levels.

Cyclizine was not included in the questionnaire as it is not on the EDLs.

Anxiolytics:

Midazolam injection, a hospital EDL item, is stocked in 5mg/5ml strength by Knysna Provincial Hospital, but in 15mg/3ml and 5mg/5ml by George Provincial Hospital. Its use is permitted by trained paramedics in addition to doctors.

Midazolam tablets were not stocked at any of the 3 service levels.

Diazepam injection, as well as 2mg and 5mg tablets were available at all service levels, but 10mg tablets were not stocked.

Lorazepam injection, as well as 1mg tablets were stocked at all three service levels.

Corticosteroids:

Dexamethasone injection and tablets were available at both hospitals. The Hospice prescriptions were filled from the Knysna Provincial Hospital.

Laxatives:

Lactulose syrup was not stocked at the clinics. It was not on the 1998 primary care EDL, but is on the 2003 edition.

Senna was available at all sites, but only in 12 tablets prepacks at the clinics, with both bulk and prepacks at the hospitals.

Antipsychotics:

Haloperidol injection was only available at the George Provincial Hospital. The Knysna Provincial Hospital chief pharmacist believes it is "off-code" and has received requests from the Hospice, which she cannot fill. **Haloperidol tablets** are available at all three levels.

Chlorpromazine injection is not stocked at any level. The tablets are available at all three levels.

Fluphenazine decanoate injection is available at all three levels.

Antidepressants:

Amitryptiline is available in all three services, but with only prepacks of 28 at the clinics and several pack sizes at the hospitals.

Fluoxetine tablets are available at all three levels.

Anticonvulsants:

Clonazepam tablets are available at all three levels. The drops are not stocked at all and the injection only at the George Provincial Hospital.

Diazepam is listed under anxiolytics, injection and tablets being available at all three levels.

Antispasmodics:

Hyoscine butylbromide injection is a hospital EDL item, which is in stock at both hospitals. The tablets are available at all three levels, but with only prepacks of 10 at the clinics and bulk stock at the hospitals. The syrup is not stocked at any level.

Antifungals:

Nystatin oral suspension and ointment is available at all levels. The vaginal tablets are not stocked, with clotrimazole being substituted on the primary care EDL.

Fluconazole 200mg tablets are available at all three levels on the Pfizer donor programme. The suspension is not available at all, resulting in the pharmacists making a suspension from the tablets on request, although they comment that they are uncertain of the stability of this.

Amphotericin B lozenges. These are available at the George Provincial Hospital. The 2003 Primary care EDL recommends antifungal lozenges, without naming a specific one.

Progestins:

Medroxyprogesterone tablets are hospital level items and are available at both hospitals.

H2 antagonsts:

Cimetidine is a hospital level item. The tablets are stocked at both hospitals, but the syrup is not stocked.

Antidiarrhoeals:

Loperamide tablets are stocked at all three levels in prepacks of 6.

Antibiotics:

Trimethoprim/sulphamethoxazole tablets and syrup are available at all three levels. At George Provincial Hospital, bulk stock (1000) is available, but the other facilities have only packs of 28.

Antivirals:

Acyclovir tablets are stocked at all three levels, but none has the suspension.

Antiretrovirals:

Stavudine tablets are available in tablets of 20, 30 and 40 mg at George Provincial Hospital. The suspension is not stocked.

Lamivudine tablets are available at all three levels and the solution at the two hospitals.

Abacavir tablets are available at the George Provincial Hospital. However, the solution is not stocked.

Didanosine is stocked in 100mg and 150mg tablets, as well as suspension at the George Provincial Hospital.

Zidovudine capsules are available at all three levels and syrup at the two hospitals.

Efavirenz is available in 50mg, 200mg and 600mg capsules at the George Provincial Hospital.

Nevirapine tablets and suspension are available at the two hospitals.

Ritonavir capsules and solution are stocked at George Provincial Hospital.

Lopinavir/ritonavir capsules and solution are stocked at the George Provincial Hospital.

Nelfinavir is not stocked at any of the service points.

The additional information elicited during the interviews with the three pharmacists was useful and is discussed in further detail:

Interview with Chief Pharmacist, George Provincial Hospital.

a. The Codeine phosphate syrup supplied by *Resmed* had a sugar precipitate on the bottom of bottles, therefore it was theoretically in stock, but the pharmacist was not able to use it for accurate dosing requirements, such as analgesia. This raises concern about quality control by the Western Cape Pharmaceutical Services.

b. The interviewee was concerned about the *Medicines and Related Substances Act* (Act 101 of 1965 amended May 2003 (effective in the public sector from July 2005), which will not allow repacking (which will result in increased costs) or manufacturing. This is of concern for morphine solution, 190 litres per month of which is used at present. In total, 39 items are manufactured at the hospital, all of which will no longer be available under the new legislation. Many of these are dermatological preparations made up on request. The specific needs of palliative care patients for larger than usual quantities of drugs will be a problem if repacking by a hospital pharmacist is no longer permitted. In the discussion document *Towards compliance with the legislation applicable to the supply of medicines in public sector facilities in the Western Cape (work in progress)* (May 2004), it is observed that "no specific provision is made in the legislation for bulk compounding in hospitals/clinics - this does not, however, prevent a pharmacist from compounding extemporaneous preparations per patient (refer Section 14(4) of the *Medicines Act*)". The logistics of compounding per patient instead of in bulk would have implications for efficiency. The same document refers to Regulation 33 of the *Medicines Act*

- " pre-packing must be done under the direct personal supervision of a pharmacist"
- "pre-packing can only be done in compliance with stringent standards of Good

manufacturing Practice (GMP)"

- "no specific provision is made in the legislation for pre-packing in hospitals/clinics" .
- "draft proposed amendments to the General Regulations to be published in terms of of the Medicines Act, suggest that pre-packing can only be done in a facility which is licensed and recorded with the SAPC as a manufacturing pharmacy and licensed as a manufacturer with the MCC in terms of Section 22c of the *Medicines Act*."

As with the compounding legislation, it is therefore possible to dispense per patient, but pre-packing at hospitals may become difficult.

c. Although it is listed on the Pfizer donor programme, fluconazole suspension is not available. On request, the tablet is made into a solution, but the pharmacist warns that he has no knowledge of the stability of this preparation. In the light of the debilitating nature of severe candidiasis, it is necessary to make fluconazole available to children, despite the innovative preparation method.
d. Verification of responses to the questionnaire was by referring to the provincial code list and physically checking on the shelves, which he did at least five times. This is an indication that he did not guess.

Interview with the Chief Pharmacist of Knysna Provincial Hospital, which is a district hospital, in contrast with the status of George Provincial Hospital as a secondary, referral hospital:

a. Verification was by checking on the shelves. She does not use EDL at all, only provincial code list and used the provincial guideline to ascertain which items can be prescribed by clinical nurse practitioners. This list is updated by the Provincial Pharmacy staff regularly and contains the ordering codes and is therefore easier to use for stock control and ordering than the EDLs.

b. An average volume of 8 litres per month of morphine is made up, with the strength according to request, the strongest having been 240mg/5ml. It is not considered necessary to add preservative if the supply is for less than a month. The episode during which morphine injection was out of stock lasted 3 weeks, during which the provincial store could not supply, but she managed to borrow stock from the George Provincial Hospital pharmacy, so the supply to patients was not disrupted and the supply arrived before George depleted their reserves. The Hospice staff collect morphine (prescribed by the Hospice medical practitioner, the Knysna Provincial Hospital medical practitioners or the oncologist at the George Provincial Hospital) and either deliver it to their patients at home or at the weekly Hospice clinic.

c. There is a problem with the Hospice prescriptions for oxazepam, because the rules only allow a supply for 14 days per month, whereas the Hospice patients need to be kept on a sedative for longer.

d. Haloperidol injection is requested by the Hospice for subcutaneous infusion, but it is "off code" and the hospital is therefore unable to supply it.

e. Fluconazole tablets are dissolved for paediatric use, as the suspension is not available. As with the George Provincial Hospital pharmacist, she was unable to comment on the stability of this preparation.

f. The Medical Superintendent has to sign approval for the prescription of acyclovir, although medical officers may prescribe it.

g. Midazolam injection is intermittently supplied in the 15mg/3ml or 5mg/5ml strength.

Interview with the Knysna Municipal clinic pharmacist:

a. Although she uses the provincial code list for ordering from the Western Cape Pharmaceutical depot, she uses the primary care EDL in deciding upon which drugs to stock, with other items on the provincial code list by request.

CHAPTER SIX

DISCUSSION

In general, a choice of drugs appropriate to the treatment of palliative care patients and used internationally was found to be available on the South African EDLs and the three facilities surveyed had a reliable supply of most drugs on the list compiled for the questionnaire.

The compilation of a list of essential drugs for palliative care relied to a large extent on literature which focussed exclusively on cancer and did not take HIV/AIDS into account. Although the palliation for both conditions is similar, it was considered appropriate to investigate the availability of treatment for some opportunistic infections which occur in HIV infected patients and ARVs as the best form of palliative care for HIV/AIDS. Any palliative care physician would consider management of opportunistic infections (especially in the absence of ARVs) as the prime intervention in symptom control and improving quality of life. The comment is often made that ARVs are the most effective palliative measure in managing HIV illness. The question then arose as to where to draw the line in the treatment of opportunistic infections. The decision on drugs to be included in the questionnaire was made bearing in mind that palliative care is offered in the context of a functioning public health service, with clear protocols for the management of tuberculosis and other infections.

It is encouraging to note that, as recommended by Chirac (2003), the South African government has not used the price of drugs (such as antiretrovirals), as an exclusion criterion, but has explored ways around the intellectual property rights of drug companies, such as local generic manufacturing and import of generic drugs.

Zwarenstein and Bachmann (1997, pp. 147-157) point out that "promoting improvements in the health

system is seldom a single one-off event - it is an ongoing, long-term process which should be flexible enough to respond to changing needs in the population." It is important to ensure that this process is structured into the health system. This needs international input from the WHO, national policy and local evaluation and feedback. A WHO report *The use of Essential drugs 2000, Ninth report of the WHO expert committee* (pp. 2-4) reports that model lists have been invaluable in improving the quality of health care and reducing costs. Quality of care is improved when the EDL is linked to evidence-based treatment guidelines. In acknowledging the benefits of model lists linked to evidence- based guidelines, the promotion of these to all relevant health care workers is a vital component of their implementation. Although a survey of health worker knowledge, attitudes and practice was not part of this research project, it is the impression of the researcher that promotion of and training in use of the essential drug concept has not accompanied the distribution of the EDLs at a local level. In addition, the National Department of Health publication *Palliative care for adults: a guide for health professionals in South Africa* (2003) was not available at the Regional office of the Department of Health in George, nor was it on the National Department of Health website.

The concept of palliative care as "active total care" emphasises the importance of *actively* planning, implementing and evaluating the integration of palliative care into the health services. The need for this aspect of care to be given priority is reflected in the extent of the increased palliative care demand as a consequence of the HIV/AIDS epidemic and the moral impulse to relieve suffering as discussed in the literature review. . "The challenge for policy-makers in public health revolves around making choices: deciding which problems to address and organising the resources to solve them." (WHO 1997, pp 130-5)

With respect to **health systems problems** which came to light, the following was observed:

1. The mechanism of disseminating the changes in newer editions of the EDLs needs to be examined.

The books are sent from Cape Town whenever anyone attending a meeting there has space in their vehicle and they are distributed in a fairly random manner. It would help to bring changes to the attention of the pharmacists and prescribers if the new or deleted items were listed and circulated. As highlighted in the WHO publication *How to investigate drug use in health facilities* (1993, p.23), the availability of an up to date EDL is one of the measures used to evaluate rational drug use. In addition "Examples of interventions likely to fail include....standard treatment manuals without an active orientation" (*Managing Drug Supply* 1997, pp. 130-135.)

2. The South African *Standard Treatment Guidelines and Essential Drugs List: Primary Health Care*, 2003 edition became available while compiling the list of drugs to be surveyed, but the Hospital level EDLs are still 1998 editions, making for inconsistency. For example, the ARVs listed are only those used for PMTCT (prevention of mother to child transmission) and PEP (Post-exposure prophylaxis) for sexual assault and occupational injury. No highly active antiretroviral treatment (HAART) regimens are included in the EDLs. In the rapidly changing field of policies and treatment for HIV/AIDS, it is difficult to maintain consistency in all publications relating to essential drugs and treatment guidelines. This highlights the need for maintaining communication with health care practitioners by means of dated and numbered circulars and focused, active approaches to changing drug use practises as discussed in *Managing Drug Supply* (1997 p.11) The same publication also emphasises that implementation of rational drug use is influenced by an understanding of the factors which influence prescribing and patient perceptions.

3 Pack size is understandably limited at a clinic level, but the availability of some bulk items for palliative care patients needs to considered e.g paracetamol, ibuprofen, senna and loperamide. The pack sizes for clinic level are specified in the *Provincial Code List* , not in the primary health care EDL. There is therefore scope for regional flexibility with respect to pack sizes which clinics may stock. The dose of prophylactic trimethoprim/sulphamethoxazole is 2 tablets daily and the pharmacists commented that a pack of 56 would simplify dispensing for HIV positive patients. However, as discussed in the Handbook of HIV Medicine (2002, p. 91), one single strength tablet daily is probably as effective and

causes fewer side effects. The guidelines should ideally be standardised.

Paediatric formulations are useful for the elderly, weak and those with swallowing difficulties, as well as for children. There were number of instances in which drugs were not available in paediatric formulations (Codeine syrup, ibuprofen at the clinics, metoclopramide at George Provincial Hospital, fluconazole, cimetidine, hyoscine butylbromide, acyclovir, stavudine and abacavir generally).This contradicts a principle of the essential drugs concept, namely that essential drugs "should be available at all times, in the proper dosage forms (*Managing Drug Supply* 1997, p.19).

4. The sensitivity to Haloperidol and other drugs in AIDS is not specifically addressed in the EDLs and is a problem which clinical training in the management of HIV/AIDS will need to bring to the attention of practitioners. As discussed by Wilson et al in the *Handbook of HIV Medicine* (2002, p.193), " HIV infection in the CNS can make patients vulnerable to the side-effects of medication, which should be started at a low dose and increased very slowly." The EDLs are also standard treatment guidelines, which are intended to be used in all public health care settings by health care practitioners, and would therefore be the appropriate medium by which to disseminate warnings about problems related to using drugs in HIV infected patients. The use of Medicines Safety Alerts or "Dear Health Care Professional" letters to alert practioners to special sensitivites to drugs in HIV infected patients can be used by drug manufacturing companies.
5. The limited number of drugs on the list compiled for the survey that can presently be prescribed by a clinical nurse practitioner is of concern for patients where there are few medical practitioners and referral involves transport over long distances. In introducing the essential drugs concept, the *Standard Treatment Guidelines and Essential Drugs List: Primary Health Care* (2003, p.ii) notes that "provincial and local Pharmacy and Therapeutics Committees may provide additional drugs from the Hospital level EDL based on the services offered and the competency of the staff at each facility."
6. With respect to antiemetics, there is inconsistency between the National Department of Health's *Palliative care for adults a guide for health professionals in South Africa* (2003) and the EDLs in that the EDLs do not include cyclizine, which is listed as one of the three first line antiemetics in the

palliative care publication (metoclopramide, haloperidol and cyclizine). However, the guideline also cautions that this drug will require special motivation. The logistics of obtaining a first line drug by special motivation in a rural clinic or hospital mean that this will seldom arrive in time to be of use for a patient.

7. The inconsistent strength of midazolam ampoules supplied to the Knysna Provincial Hospital is potentially hazardous if users become accustomed to one strength and it changes without warning.

With respect to **specific drugs**, Amphotericin B lozenges or equivalent are important to have in stock in order to spare fluconazole for the indications of the donor programme (oesophageal candida and cryptococcal meningitis) and minimise the risk of developing resistance. Tilidine is not stocked in the Knysna Provincial Hospital because it is not prescribed. On enquiry from a principal medical officer at the hospital, it seems that paracetamol only is used for paediatric pain management. (Dr L Giddy, personal communication)

The roll-out of antiretroviral clinics is a fairly new service in the region and it is understandable that some of the problems observed were related to this service. The only facility running an antiretroviral clinic at the time that the survey was conducted was the George Provincial Hospital. An antiretroviral clinic started at the Knysna Provincial Hospital in September 2004, with the first patient receiving ARVs in October 2004. The Knysna Provincial Hospital's maternity ward follows the protocol PMTCT and also offers PEP to staff for occupational injuries and to patients who have suffered sexual abuse. The clinics supply zidovidine for the initiation of PMTCT and post-exposure prophylaxis to staff. The antiretrovirals stocked at each level reflect the programmes offered at each facility.

Stavudine suspension is on both the first-line regimens for children under six months of age and over six months of age where a fridge is available. The suspension is not available at the George Provincial Hospital although paediatric patients are cared for at the ARV clinic.

Lamivudine tablets are available at all 3 levels as part of post-exposure prophylaxis. The solution is only

available at the hospitals because this is where children are treated following sexual assault.

Abacavir solution is not available at the George Provincial Hospital, despite being part of the second line regimen for children with no fridge.

Zidovudine capsules are available at all 3 levels as part of the PMTCT and post-exposure prophylaxis regimens. The syrup is only used at the hospitals as part of the paediatric HAART regimen and for post exposure prophylaxis in sexual assault.

Nevirapine is used for the PMTCT regimen for mothers and babies as well as for HAART and is therefore available at both hospitals. It is no longer stocked in the clinics since the PMTCT regimen was changed from the mother taking a tablet as she goes into labour at home to only taking the nevirapine once she is in hospital.

Nelfinavir is recommended in the paediatric regimen of HAART as a substitute for ritonavir or lopinavir/ritonavir if intolerance develops. *National Antiretroviral Treatment Guidelines* (2004, p.36). However it is not available at the George Provincial Hospital ARV clinic.

Of concern for the fostering of research in the public sector in general and in palliative care specifically, was the period taken for approval of this research proposal by the Western Cape Health Department. This process took 9 months. In view of that fact that research is an essential component of palliative care, as discussed by O'Neill and Fallon (1998), this is a significant barrier to the fulfilment of this component of palliative care in the local setting.

CHAPTER SEVEN

RECOMMENDATIONS

The research study has prompted the following recommendations:

Health system:

1. The provincial mechanism for authorising research conducted in public health facilities should be reviewed and streamlined to accommodate ethically acceptable research.
2. The changes in a new edition of the EDL should be listed and distributed in a circular to all users and an effective and timeous method of distributing the EDLs should be implemented. Training workshops around changes in the EDLs would also help to keep users in the field up to date and elicit useful feedback for the compilers of the EDLs on barriers to their use or other problems.
3. The use of EDLs should be encouraged as the initial therapeutic decision-making guide. Reliance on the Cape Medical Depot drugs which do not appear on the EDLs should be discouraged or the process of having these drugs on the EDLs should be motivated.
4. The level of health care practitioner who may prescribe palliative care drugs needs to take into account the access to other levels of care, the risks involved in the prescription of the drug and the knowledge of the various levels of health care practitioner. The present lack of clarity with respect to prescribing by clinical nurse practitioners needs to be reviewed taking local resources into account. The registration of health professionals trained in pallliative care with the Health Professions Council of South Africa, with the right to prescribe restricted drugs may help to overcome this problem.
5. The establishment of a Regional Pharmacy and Therapeutics Committee (it is assumed that such committees exist in the *Standard Treatment Guidelines and Essential Drugs List: Primary Health Care*, 2003, p. ii) would serve the purpose of monitoring and evaluating drug use in the Region. This would be useful for ensuring cost-effective prescribing, setting training priorities and

motivating changes to the currently available list of drugs in order to best meet the needs of the population served.

6. The wider promotion and distribution of the Department of Health publication *Palliative care for adults: a guide for health professionals in South Africa* (2003), would guide health care practitioners in caring for patients requiring palliative care. It is simply written in forty five pages of A5 format and would be a helpful pocket guide.

Drugs:

1. The availability of paediatric formulations of drugs should be reviewed. A reliable supplier needs to supply codeine phosphate. Ibuprofen is now on the primary care EDL and should become available at the clinics. Metoclopramide syrup is not available at George Provincial Hospital, where there is an oncology clinic, a specialist paediatric service and an ARV clinic, so this should be in stock. The Pfizer donor programme educational material implies that both tablets and syrup are available - the terms of the donation need to be clarified and fluconazole suspension sourced from another manufacturer if necessary. Acyclovir, hyoscine butylbromide and cimetidine should be available in the paediatric formulation. Paediatric formulations of stavudine and abacavir are part of the first and second line regimens respectively and therefore should be available at the George Provincial Hospital ARV site. Nelfinavir, as an alternative protease inhibitor in the case of adverse reactions, should also be available in a paediatric suspension.
2. Tilidine is not stocked by Knysna Provincial Hospital because it is not prescribed. There is scope for an investigation into the current paediatric pain control protocols and training in paediatric pain management.
3. Cyclizine is considered a first-line antiemetic in the guidelines published by the National Department of Health (*Palliative care for adults: a guide for health professionals in South Africa, 2003*), but restricted to special motivation and not listed on the EDLs. Since the drug is the only antiemetic of its class (antiemetics working on the vomiting centre), it is recommended that it be

more freely available.

4. The new legislation affecting the ability of hospital pharmacies to manufacture and repack will need to be addressed, with appropriate planning and budgeting for the supply of morphine and the other items currently manufactured and repacked at George and Knysna Provincial Hospitals.
5. The supply of drugs to the clinics in prepacks is generally appropriate, but exceptions need to be accommodated for palliative care patients. For example, paracetamol, ibuprofen, loperamide and senna should be available in larger packs in order to meet the needs of pallaitive care patients.
6. The *Handbook of HIV Medicine* (2002, p.108) recommends cotrimoxazole 2 tablets daily for pneumocystis carinii pneumonia prophylaxis, although the case is also made for 1 tablet daily (p.91). In order to provide secondary prophylaxis, the current prepacks of 28 tablets therefore need to be supplemented with 56 tablets in order to supply patients for a month, as is the practice with other chronic medication.
7. The potentially confusing and hazardous situation regarding unpredictable changing of the strength of Midazolam injection supplied to the Knysna Provincial Hospital needs to be reviewed and standardised in order to decrease the risk of dosing errors.
8. The non-availability of haloperidol injection at the Knysna Provincial Hospital needs to be clarified. Dickerson's (1999) survey of palliative care specialists indicated that 95% of respondents considered haloperidol to be in the top 20 essential palliative care drugs and the Knysna Provincial Hospital pharmacist indicated that it was frequently requested by the hospice team. It is therefore important to ensure its availability.
9. Amphotericin B lozenges should be made available at the Knysna Provincial Hospital and clinics in order to spare Fluconazole for the specific conditions of the donor programme (oesophageal and disseminated candidiasis and cryptococcal meningitis)
10. The problem of a benzodiazepine sedative (oxazepam) only being available for a 14 day course needs to be reviewed for palliative care sedation.
11. The special needs of palliative care patients differ from those of other patients with similar

symptoms in that the medication is continued for longer and by routes specific to the needs of these patients. In order to render an appropriate and humane service in keeping with palliative care principles, these special needs must be accommodated within the drug supply policy. This would entail a review of maximum pack size, availability of paediatric formulations, and drugs to be administered by continuous subcutaneous infusion (such as haloperidol for nausea and vomiting or delirium).

12. As indicated in Chapter Three, the findings and recommendations will be forwarded to the institutions in which the research was conducted and other relevant bodies. The follow-up of the subsequent responses and action will be documented by the researcher. Further research could arise from this process.

CHAPTER EIGHT

CONCLUSION

The research aimed to undertake an examination of the drug supply to palliative care patients within the Knysna Health District. This was considered to be one of the components of evaluating the capacity of the public health sector in the Knysna Health District to meet the needs of palliative care patients. Palliative care is considered to be "fundamental to good medical practice" *(Oxford Text book of Palliative Medicine,* Roy and Macdonald 1998, pp 97-138). It is also argued that the lack of resources for palliative care stems not from ethical shortcomings of policy makers, but lack of clear guidelines of what it is that good palliative care requires. This research therefore examined international and local literature in order to determine an economically sustainable list of palliative care drugs as one of the components of clear guidelines for quality palliative care. The availability of these drugs was then evaluated in the setting of the public sector facilities serving patients in the Knysna health district.

The supply of palliative care drugs to public sector patients has taken on added urgency with the HIV/AIDS epidemic in Southern Africa. This is also the case in the Knysna Health District, as can be seen from the trend in the workload of the Knysna-Sedgefield Hospice (Table One, p 2).

The Essential Drugs concept is useful in examining a list of appropriate drugs for palliative care. South Africa does have a National Drug Policy, which was developed in 1996 and an essential drugs list committee has published 3 guidelines comprising standard treatment guidelines and essential drugs lists for primary care, hospital level for adults and hospital level for paediatrics. However, it was found that the EDLs are not used for ordering drugs at the hospital level. A provincial code list is used, which contains a considerably more drugs. The EDLs were found to be underutilised as the guideline for drug use. This is in part because the Hospital level EDLs are 1998 editions and do not contain the ARVs for HAART and are no longer consistent with the 2003 edition of the primary care EDL.

Within the scope of the current EDLs (*Standard Treatment Guidelines and Essential Drugs List: Primary Health Care*, 2003 , *Standard Treatment Guidelines and Essential Drugs List: Hospital Level, Paediatrics*, 1998 and *Standard Treatment Guidelines and Essential Drugs List: Hospital Level, Adults*, 1998), it is possible to treat most of the palliative care problems discussed in the literature reviewed. However, the special needs of palliative care patients with respect to route of administration are not taken into account when stocking of particular formulations is decided upon. Paediatric formulations are important in palliative care patients with swallowing difficulties and children. Injectable formulations of relevant drugs for continuous subcutaneous infusion should also be available. Addressing this would go a long way to making an adequate supply of palliative care drugs in appropriate formulations available. This is in keeping with the WHO definition of essential drugs in 1975 as " indispensable and necessary for the health needs of the population. They should be available at all times, in the proper dosage forms, to all segments of society." (*Managing Drug Supply* 1997, p 19).

The scope of the research did not include knowledge, attitudes or practice of health care workers in the area. The use of only paracetamol for pain management in children at the Knysna Provincial Hospital indicates that further investigation of the training needs of health care workers in palliative care is warranted. This would create a demand for drugs which are currently available, but not used (for example, tilidine at the Knysna Provincial Hospital). The level of health care worker permitted to prescribe palliative care drugs merits further examination in order to achieve the aim of effective palliative health care for all, including those served by rural clinics.

The outline of the essential drugs concept in the South African *Standard Treatment Guidelines and Essential Drugs List: Primary Health Care* (2003, p. iii) specifies the following working principle for the competence of the prescriber "treatment for the conditions will be initiated at primary level, will be

competency-based and not restricted to specific occupations". It does not address who will assess this competency or take responsibility for maintaining it. A more detailed protocol for assessing the competence of each level of health care worker to prescribe, and the legal regulation of drugs would be useful.

The scope of the current EDLs includes most of the drugs used internationally by palliative care experts surveyed by Dickerson (1999). The availability of these drugs to all palliative care patients, even in rural clinics, is dependent on a realistic recognition that the of the level of health care worker caring for many patients is a clinical nurse practitioner, appropriate legislation to define the scope of practice of clinical nurse practitioners, training and support of health care workers caring for patients requiring palliation and attention to detail, such as the formuations available in facilities. The WHO principle: "They should be available at all times, in the proper dosage forms, to all segments of society."(*Managing Drug Supply* 1997, p.19), makes a significant difference to the ability to care properly for a patient. Given the tiered nature of the EDLs (primary care and hospital level), it is also essential for the proper care of patients that the referral system works efficiently, with affordable, efficient transport, willing accommodation of patients referred and a system of making appropriate drugs available when patients are referred back to the primary care level.

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Sarie Hills (Secretary in the Knysna Municipal Health Department dealing with burial orders)

Gail Holton (Professional Nurse in the Knysna Health District in charge of Prevention of Mother To Child Transmission and Voluntary testing and Counselling)

Fiona Simpson (Professional Nurse with Knysna-Sedgefield Hospice)

Peter Bock (Researcher, School of Public Health and Primary health Care, UCT)

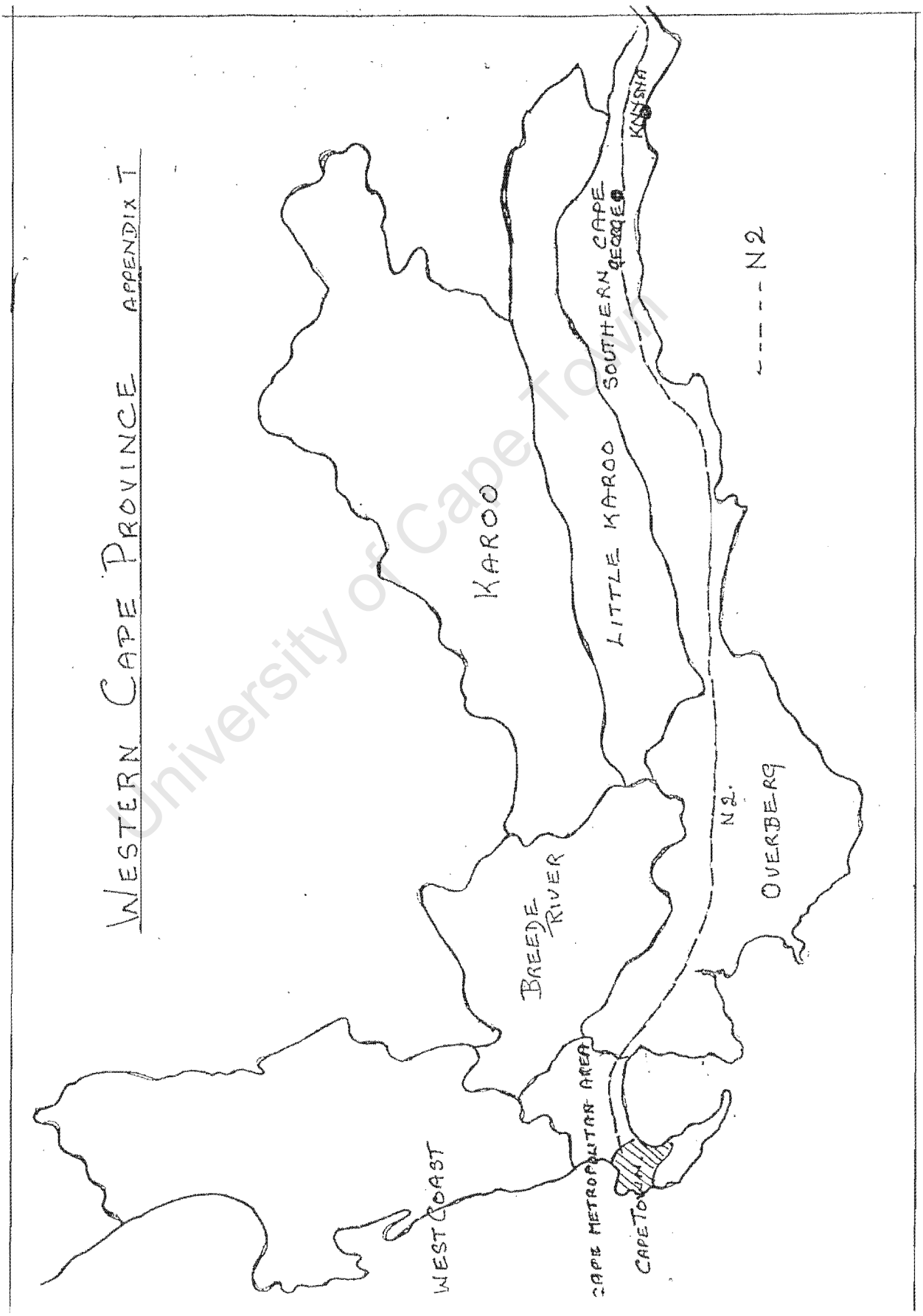
Laurel Giddy (Principal Medical Officer, Knysna Provincial Hospital)

APPENDICES:

1. Map of Western Cape province
2. Map of South Africa
3. Questionnaire to pharmacists
4. Draft Letters
   a. Chairperson, ethics research committee
   b. Director, Pharmaceutical Services
   c. Director, Human Resources Development
5. Permission to conduct research from
   a. Provincial Authority (Health Department of the Western Cape Province)
   b Knysna Provincial Hospital
   c. Local (Knysna Municipal Health Department)
   d. University of Cape Town Ethics Committee
6. Work plan

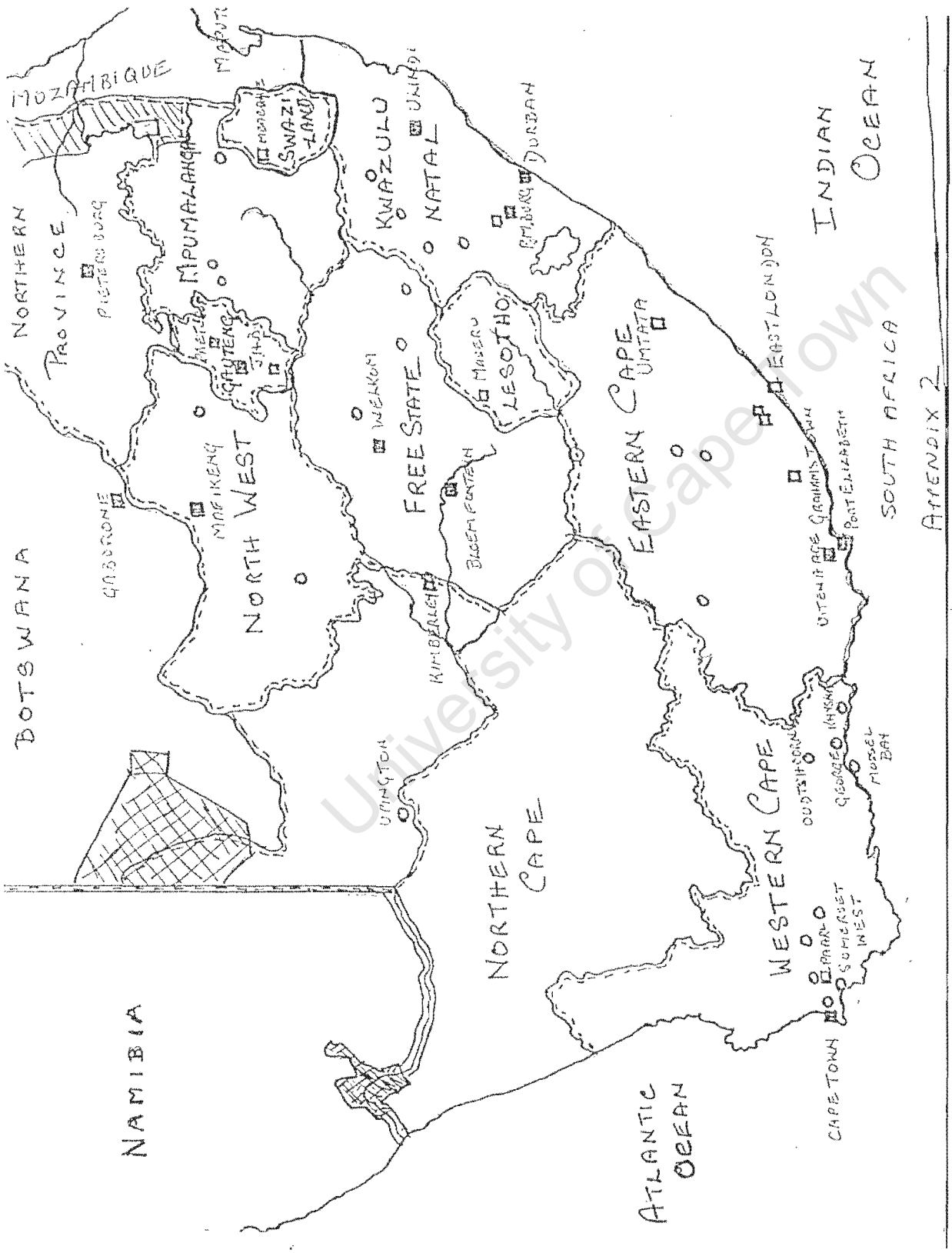
APPENDIX ONE

MAP SHOWING THE WESTERN CAPE PROVONCE



APPENDIX TWO

MAP SHOWING THE REPUBLIC OF SOUTH AFRICA



APPENDIX THREE

QUESTIONNAIRE FOR PHARMACISTS

Respondent:

Institution: Date:

DRUG	FORMULATION	PACK SIZE/ VOLUME	EDL LEVEL 1. Clinic 2. Hospital	IN STOCK (YES/NO/EQUIVALENT)	LEVEL OF HCW WHO MAY PRESCRIBE 1.Specialist 2. Medical officer 3 Clinical nurse practitioner	OUT OF STOCK IN PAST 3 MONTHS? YES/NO	OUT OF STOCK IN PAST 12 MONTHS ?
Morphine	Injection 10mg/ml						
	Oral solution						
Codeine	Tablet 30mg						
	Syrup 25mg/5ml						
Tilidine	Drops 50mg/0.5ml						
Paracetamol	Tablet 500mg						
	Syrup 120mg/5ml						
Ibuprofen	Tablet 200mg						
	Syrup 100mg/5ml						
Metoclopramide	Tablet 10mg Injection 10mg/ml						
	Syrup 5mg/5ml						

DRUG	FORMULATION	PACK SIZE/ VOLUME	EDL LEVEL 1. Clinic 2. Hospital	IN STOCK (YES/NO/EQUIVALENT)	LEVEL OF HCW WHO MAY PRESCRIBE 1.Specialist 2. Medical officer 3. Clinical nurse practitioner	OUT OF STOCK IN PAST 3 MONTHS? YES/NO	OUT OF STOCK IN PAST 12 MONTHS ?
Midazolam	Injection 15mg/3ml 5mg/5ml						
	Tablet 7.5mg 15mg						
Diazepam	Injection10mg /2ml						
	Tablet 2mg 5mg 10mg						
Lorazepam	Injection 4mg/ml						
	Tablet 0.5mg 1mg 2.5mg						
Dexamethasone	Injection 4mg/ml						
	Tablet 0.5mg						
Lactulose	Syrup 3.3g/5ml						
Senna	Tablet 7.5mg						
Haloperidol	Injection 20mg/5ml						
	Tablet 0.5mg						

DRUG	FORMULATION	PACK SIZE/ VOLUME	EDL LEVEL 1. Clinic 2. Hospital	IN STOCK (YES/NO/EQUIVALENT)	LEVEL OF HCW WHO MAY PRESCRIBE 1.Specialist 2. Medical officer 3. Clinical nurse practitioner	OUT OF STOCK IN PAST 3 MONTHS? YES/NO	OUT OF STOCK IN PAST 12 MONTHS ?
Chlorpromazine	Injection 50mg/2ml						
	Tablet 10mg 25mg 50mg 100mg						
Fluphenazine Decanoate	Injection 25mg/10ml						
Amitryptiline	Tablet 10mg 25mg						
Fluoxetine	Capsule/tablet 20mg						
Clonazepam	Tablet 0,5mg 2.0mg						
	Drop 2.5mg/5ml						
	Injection 1mg/ml						
Hyoscine butylbromide	Injection 20mg/ml						
	Tablet 10mg						
	Syrup 5mg/5ml						

DRUG	FORMULATION	PACK SIZE/ VOLUME	EDL LEVEL 1. Clinic 2. Hospital	IN STOCK (YES/NO/EQUIVALENT)	LEVEL OF HCW WHO MAY PRESCRIBE 1.Specialist 2. Medical officer 3. Clinical nurse practitioner	OUT OF STOCK IN PAST 3 MONTHS? YES/NO	OUT OF STOCK IN PAST 12 MONTHS ?
Nystatin	Oral suspension 100 000U/ml						
	Vaginal tablet 100 000						
	Topical cream 100 000u/g						
Fluconazole	Tablet 200mg						
	Suspension 50mg/5ml						
Amphtericin B	Lozenge 10mg						
Medroxyprogesterone	Tablet 100mg 500mg						
Cimetidine	Tablet 200mg 400mg						
	Syrup 200mg/5ml						
Loperamide	Tablet 2mg						

DRUG	FORMULATION	PACK SIZE/ VOLUME	EDL LEVEL 1. Clinic 2. Hospital	IN STOCK (YES/NO/EQUIVALENT)	LEVEL OF HCW WHO MAY PRESCRIBE 1.Specialist 2. Medical officer 3. Clinical nurse practitioner	OUT OF STOCK IN PAST 3 MONTHS? YES/NO	OUT OF STOCK IN PAST 12 MONTHS ?
Trimethoprim/sulphamethoxazole	Tablet 80/400						
	Syrup 40/200per 5ml						
Acyclovir	Tablet 200mg						
	Suspension 200mg/5ml						
Stavudine	Capsule 15mg 20mg 30mg 40mg						
	Suspension 1mg/ml						
Lamivudine	Tablet 150mg						
	Solution 10mg/5ml						

DRUG	FORMULATION	PACK SIZE/ VOLUME	EDL LEVEL 1. Clinic 2. Hospital	IN STOCK (YES/NO/EQUIVALENT)	LEVEL OF HCW WHO MAY PRESCRIBE 1.Specialist 2. Medical officer 3. Clinical nurse practitioner	OUT OF STOCK IN PAST 3 MONTHS? YES/NO	OUT OF STOCK IN PAST 12 MONTHS ?
Abacavir	Tablet 300mg						
	Solution 20mg/ml						
Didanosine	Tablet 25mg 50mg 100mg 150mg						
	Suspension 10mg/5ml						
Zidovudine	Capsule 100mg 250mg Tablet 300mg						
	Syrup 50mg/5ml						
Efavirenz	Capsule 50mg 200mg						
Nevirapine	Tablet 200mg						
	Suspension 50mg/5ml						

DRUG	FORMULATION	PACK SIZE/ VOLUME	EDL LEVEL 1. Clinic 2. Hospital	IN STOCK (YES/NO/EQUIVALENT)	LEVEL OF HCW WHO MAY PRESCRIBE 1.Specialist 2. Medical officer 3. Clinical nurse practitioner	OUT OF STOCK IN PAST 3 MONTHS? YES/NO	OUT OF STOCK IN PAST 12 MONTHS ?
Ritonavir	Capsule 100mg						
	Solution 80mg/ml						
Lopinavir/ Ritonavir	Capsule 133.3/33.3mg						
	Solution 80/20mg/ml						
Nelfinavir	Tablet 250mg						
	Powder 50mg/g						

Question d: Do you order your drugs from

(i) the Essential Drugs lists (Yes/no)

(ii) from the list of drugs previously prescribed? (Yes/no)

Question e. Are there drugs which you would like to order which are not on the EDL? If so, please list.

Question f. Are there drugs for which you have had requests which are not on the EDL? If so, please list.

APPENDIX FOUR

DRAFT LETTER a

Chairperson
Research Ethics Committee
Department of Health
Provincial Administration of the Western Cape

cc Regional Director of Health, George Office, Provincial Governent of the Western Cape

Dear Sir/ Madam,

Re: Ethical approval for research conducted in Provincial Health Facilities

I have recently been involved in seeking approval to conduct research in Provincial Health facilities in order to fulfill the requirements of a M Phil degree in Palliative Care through the University of Capre Town.

In the course of my reading, it has become clear to me that health systems research is an essential component of ongoing evaluation and improvement of the health service. It is for this reason that I am bringing to your attention a serious obstacle to this research within the Western Cape Province.

My leter requesting ethics approval to conduct research into the availability of pallaitive care drugs in the Knysna health district was submitted to the Regional office of the health department in October 2003. After repeated e-mail enquiries, I had not received an answer by July 2004. At this point, I asked my supervisor, Dr Karen Cohen to intervene. This resulted in a single sentence e-mail from Dr Fareed Abdulla, giving me permission to conduct the research.

In order that the health service may benefit from the findings of research projects conducted within the health facilites (not just the academic centres), I ask you to review the process whereby research ethics permission is granted.

Yours faithfully,
JA Stanford (Head of Department, Primary Health Care Service, Knysna Municipality)

DRAFT LETTER b

Director
Pharmaceutical Services
Department of Health
Provincial Government of the Western Cape

cc Regional Director of Health, George Office, Provincial Goverment of the Western Cape

Dear Sir/Madam,

Re: Palliative care research

I have recently been involved in conducting research into the availability of palliative care drugs to public sector patients in Knysna as part of a post graduate degree (M Phil in Palliative Care, UCT). I undertook, as part of the conditions of ethics approval, to report my findings to the appropriate policy making bodies.

A survey was conducted at the George Provincial Hospital, Knysna Provincial Hospital and Knysna Municipal Clinics in which the availability of a list of palliative care drugs based on the primary care and hospital level EDLs was investigated.

The following were some of the findings:

1. In general, a choice of drugs appropriate to the needs of palliative care patients and used internationally was found to be available on the South African EDLs and the three facilities surveyed had a reliable supply of most drugs on the list compiled for the questionnaire (List attached).

2. The EDLs were available in the facilities, but the Provincial Code list was used by the pharmacists at the 2 hospitals for guiding re-ordering and level of health worker who may prescibe. Training of all levels of health care workers on the principles and practical use of EDLs would be helpful. The fact that the Primary care EDL is a 2003 edition and the Hospital level EDLs are 1998 editions led to some discrepancies. The launch of a new EDL should ideally be accompanied by training. As discussed in the publication *Managing Drug Supply* 1997 (2nd edn, Kumarian Press, Connecticut no. 4 pp.130-135) "Examples of interventions likely to fail include ... standard treatment manuals without an active orientation".

3. Pack size is understandably limited at clinic level, but the availability of some bulk items for palliative care patients would be helpful, eg. Paracetamol, ibuprofen, senna and loperamide. The pack sizes are specfied in the *Provincial Code List*, not in the EDLs. It is therefore to be hoped that there is scope for flexibility with respect to pack sizes which clinics may stock.

4. Paediatric formulations are useful for the elderly, weak and those with swallowing difficulties as well as for children. There were a number of instances in which drugs were not available in paediatric formulations. These were codeine syrup and ibuprofen syrup at the clinics, metoclopramide at George provicial hospital, fluconazole, hysoscine butylbromide, acyclovir at all three levels of service and antiretroviral drugs which are listed in the *National Antiretroviral Treatment Guidelines (*2004): stavudine and abacavir in the paediatric formulations.

5. The sensitivity to Haloperidol and other drugs in AIDS is not specifically addressed. It is suggested that

this could be included in the treatment guidelines of the EDLs, clinical training of health care practitioners or added to package inserts or "Dear Health Care Practitioner" letters circulated by drug manufacturers.

6. The limited number of drugs on the list compiled for the survey that can presently be prescribed by a clinical nurse practitioner is of concern for patients where there are few medical practitioners and referral involves transport over long distances. In introducing the essential drugs concept, the *Standard Treatment Guidelines and Essential Drugs List: Primary Health Care* (2003, p.ii) notes that "provincial and local Pharmacy and Therapeutics committees may provide additional drugs from the Hospital level EDL based on the services offered and the competency of staff at each facility". An extended list for clinical nurse practitioners with advanced training in palliative care might be considered.

7. With respect to antiemetics, there is inconsistency between the National Department of Health's *Palliative care for adults: a guide for health professional in South Africa* (2003) and the EDLs in that the EDLs do not include cyclizine, which is listed as one of the three first line antiemetics in palliative care. However, the guideline also cautions that this drug requires special motivation. The logisitcs of obtaining a first line drug by special motivation in a rural clinic or hospital would need to be examined in order to balance safety with effective care of palliative care patients.

8. In the supply of Midazolam injection to Knysna Provincial Hospital, there is reported to be an intermittent supply of either 15mg/3ml or 5mg/5ml. This could result in dosing errors.

9. Amphotericin B lozenges were only available at the George Provincial Hospital .Antifungal lozenges are listed in the primary care EDL. Without them, there will be the risk of overuse of fluconazole outside of conditions of the donor programme and the risk of developing resistance to fluconazole.

10. Tilidine is not stocked at the Knysna Provincial Hospital because it is not prescribed. With the staffing of the hospital by a few senior doctors and a majority of community service medical officers, it is suggested that paediatric pain management be included in the continuing medical education program.

11. At the Knysna Provincial Hospital, haloperidol injection was reported as "off code" by the Pharmacist in charge. The use of haloperidol by continuous subcutaneous infusion is frequently required by palliative care practitioners. The restriction of oxazapam to a 14 day supply per month is also an obstacle to sedation of palliative care patients. The review of the availability of these drugs in appropriate dosage forms and quantities would assist in providing palliative care to patients in Knysna.

12. The establishment of a Regional Pharmacy and Therapeutics Committee would serve the purpose of monitoring and evaluating drug use in the region. This would be useful for ensuring cost-effective prescribing, setting training priorities and motivating changes to the currently available list of drugs in order to best meet the needs of the population served.

Yours faithfully,

JA Stanford (Head of Department, Primary Health Care Service, Knysna Municipality)

DRAFT LETTER c

Director
Human Resource Development
Department of Health
Provincial Administration of the Western Cape

cc Regional Director of Health, George Office, Provincial Governent of the Western Cape

Dear Sir/Madam

Re: Palliative Care Research

I have recently been involved in conducting research into the availability of palliative care drugs to public sector patients in Knysna as part of a post graduate degree (M Phil in Palliative Care, UCT). I undertook, as part of the conditions of ethics approval, to report my findings to the appropriate policy making bodies.

The following were findings with implications for training of health care workers:

1. The Department of Health publication *Palliative care for adults: a guide for health professional in South Africa* (2003) was not available through the Regional office of the Department of Health in George, nor was it listed on the website of the department under the publications. The wider distribution of this publication as a pocket guide to health care practitioners would be useful in improving palliative care in the study area and more generally.
2. The Knysna Provincial Hospital Chief Pharamcist reported that tilidine is not stocked because it is not prescribed. This may indicate a need to offer further training in paediatric pain management.

3. The EDLs were found to be in stock at the 3 facilities surveyed, but training did not accompany the distribution of the EDLs or the publication of the 2003 edition of the primary care EDL. As discussed in the publication *Managing Drug Supply* 1997 (2nd edn, Kumarian Press, Connecticut no. 4 pp.130-135) "Examples of interventions likely to fail include ... standard treatment manuals without an active orientation".

4. The limited list of palliative care drugs which can be prescribed by a clinical nurse practitioner (list of drugs and level of health worker permitted to prescribe attached) could be a factor limiting access to these drugs by patients who would benefit from them. Futher training of clinical nurse practitioners in palliative care, with recognition of this training by the Nursing Council and permission to prescribe a wider list of drugs is suggested as a method of making access to palliative care a reality for all users of the health services.

Yours faithfully,

JA Stanford (Head of Department, Primary Health Care Service, Knysna Municipality)

APPENDIX FIVE a

PERMISSION TO CONDUCT RESEARCH FROM THE PROVINCIAL GOVERNMENT OF THE WESTERN CAPE

J Stanford

From: "Fareed Abdullah" <Fabdulla@pgwc.gov.za>
To: <jstanford@knysna.gov.za>; "Eugene Reynolds" <Ereynold@pawc.wcape.gov.za>
Sent: Thursday, March 18, 2004 6:27 PM
Subject: Re: Fw: Research permission

This study has my support

Fareed Abdullah

>>> "J Stanford" <jstanford@knysna.gov.za> 15/03/2004 08:51:31 >>>

----- Original Message -----
From:
To:
Cc:
Sent: Wednesday, March 10, 2004 10:17 AM
Subject: Research permission

Dear Mr Reynolds
I attach my more detailed research proposal for the degree M Phil in palliative care for which I am registered at UCT. The submission date for this is 15 August 2004. The permission from the UCT ethics and scientific research committees takes about a month. I am therefore urgently requesting you to let me know how my application to conduct research in Provincial Administration facilities is progressing.
Regards Janet stanford

APPENDIX FIVE b
PERMISSION TO CONDUCT RESEARCH FROM THE KNYSNA PROVINCIAL HOSPITAL

Ethics committee
Medical school
University of Cape Town

Re: PERMISSION TO CONDUCT RESEARCH

I.....ANTON....MATTHYS..... (NAME)

In my capacity as.....CHIEF...MEDICAL...OFFICER..... (POSITION)

In .....KNYSNA....PROVINCIAL...HOSPITAL.....(INSTITUTION)

Hereby grant permission for Dr Janet Stanford to conduct a survey into the availability of essential drugs for palliative care by administering a questionnaire for completion by the person in charge of stock control (pharmacist or professional nurse). This will be for the purpose of fulfilling the requirements for the degree of M Phil (Palliative Care) and the results of the survey will be reported back to the participating health services.

Signature:.... Signed by candidate

Date:.....28/10/2003.

APPENDIX FIVE c
PERMISSION TO CONDUCT RESEARCH FROM THE KNYSNA MUNICIPALITY

Ethics committee
Medical school
University of Cape Town

Re: PERMISSION TO CONDUCT RESEARCH

I LAUREL SPIES (NAME)

In my capacity as PHARMACIST (POSITION)

In KNYSNA MUNICIPALITY (INSTITUTION)

Hereby grant permission for Dr Janet Stanford to conduct a survey into the availability of essential drugs for palliative care by administering a questionnaire for completion by the person in charge of stock control (pharmacist or professional nurse). This will be for the purpose of fulfilling the requirements for the degree of M Phil (Palliative Care) and the results of the survey will be reported back to the participating health services.

Signature: Signed by candidate

Date: 3/6/2004

APPENDIX FIVE d
PERMISSION TO CONDUCT RESEARCH FROM THE RESEARCH ETHICS COMMITTEE OF THE UNIVERSITY OF CAPE TOWN

UNIVERSITY OF CAPE TOWN

Research Ethics Committee
Faculty of Health Sciences
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02 August 2004

REC REF: 261/2004

Dr. E. Gwyther
Public Health & Family

Dear. Dr. Gwyther

A SURVEY OF THE AVAILABILITY OF PALLIATIVE CARE DRUGS TO PATIENTS SERVED BY THE PUBLIC SECTOR IN THE KNYSNA HEALTH SUBDISTRICT

Thank you for submitting your study to the Research Ethics Committee for review.

Date considered: 23 July 2004

Decision: Approved

Attached please find the list of committee members who attended the meeting.
Please quote the above REF REC in all your correspondence

Yours sincerely

Prof. T. Zabow
Chairperson

APPENDIX SIX
WORKPLAN:

1. Obtain permission from the Western Cape Health Department , the George and Knysna Provincial Hospitals and the Knysna Municipality to conduct the research.
2. Compile and submit the research proposal to the supervisors, department of family medicine, ethics committee and scientific research committee. (Make recommended changes and resubmit until proposal is approved)
3. Make appointments with the 3 relevant pharmacists and complete the questionnaire with each.
4. Analyse and write up results, discussion and recommendations.

(Format of document: Title page, declaration of original work, acknowledgements, definition of terminology, table of contents, list of tables, list of figures, introduction, literature review, methods and research design, results, discussion of results, recommendations, conclusions, summary, bibliography, appendices)

5. Submit to supervisors for comment and revise as recommended.
6. Submit for examination.
7. Revise as recommended by examiners if required.
8. Disseminate findings. A copy of the summary of the research will be sent to each of the respondents and a follow-up appointment made to discuss the findings with them. A verbal feedback session will be held with the district hospital pharmacists and doctors and with the pharmacist and nursing staff of the municipal clinics in order to discuss ways in which the findings may improve palliative care delivery to patients in the district. A copy of the research will be sent to the UCT department of pharmacology in order for any recommendations concerning the compilation of the EDL should be brought to the attention of the relevant parties.