Connect :
Prognostic awareness and structured serious illness conversations in stage IV cancer patients

Submitted in fulfilment of the requirements in respect of the Master’s Degree MMed in the Department of Oncology in the Faculty of Health Sciences at the University of the Free State.

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I, Dr George Murray, declare this coursework Master’s Degree mini-dissertation that I herewith submit in a publishable manuscript format for the Master’s Degree qualification MMed (Radiation Oncology) at the University of the Free State is my original independent work, and that I have not previously submitted it for a qualification at another institution of higher education.

Table of Contents

Abstract

Prognostic awareness has been shown to be a key aspect regarding a patient's understanding of their diagnosis, the available treatment options and the likely treatment and disease outcomes. It is recognised as essential to informed decision making in the setting where there is no curative therapy available, such as in advanced cancer. Palliative care aims to deliver holistic care to both the patient and their carers by enhancing the quality of life of a patient while also considering the role and burdens of the carers and family. A patient's prognostic awareness is critical in advance care planning and studies have shown that patients and their families wish to discuss prognosis so as to help with decision making regarding a patient's wishes at the end of life. Advanced care planning has been shown to result in reduced ICU admission and intensive interventions at end of life, while end of life discussions resulted in earlier hospice enrolment for patients and better quality of life and reduced depression in bereaved caregivers. This study represents the first South African study to evaluate prognostic awareness in stage IV cancer patients.

An interventional study was used to evaluate the baseline prognostic awareness of 40 patients with incurable cancer being treated with palliative intent and attending our oncology outpatient clinic. Patients were randomised to standard of care with the addition of a measurement of prognostic awareness vs. the same plus a structured communication intervention designed to explore patients' understanding of their diagnosis and expected illness trajectory, concerns and wishes for end-of-life care.

The baseline subjective prognostic awareness of all patients was measured using face to face interviews utilising three questions based on different timeframes to adjudge the risk of death from cancer as described by Helft *et al* during two consecutive outpatient visits. Objective prognosis was determined using survival curves relevant to the specific cancer type and stage and discussed with the oncologist, while subjective prognosis was evaluated at both visits using the three questions which evaluated the patient's perceived level of risk of dying from their disease over one year, five years and beyond five years.

Thus, the unstructured approach used with half the patients consisted of the standard of care with the addition of three questions to determine prognostic awareness followed by an open ended, patient directed prognostic discussion of questions and views the patient may have had following the prognostic questions, these patients comprised the control group. In contrast with the interventional group, the same standard of clinical care and three questions to determine prognostic awareness was followed by a physician directed guided serious illness conversation administered in the standardised format as described by Bernacki *et al.*

By comparing the objective prognosis with the patient's subjective prognosis, patients were grouped as having high, low or poor prognostic awareness in each of the three timeframes. Data was analysed to evaluate the change from baseline values.

There was a high level of willingness to participate in the study and discuss prognosis with a >95% participation rate. Results indicated that at baseline most patients had low to poor prognostic awareness with the majority significantly overestimating their prognosis. More patients in the interventional group had high PA both at baseline and at the second visit while

there was a greater increase in high PA within the control group with the unstructured approach to discussing prognosis. The difference in baseline PA may be a confounding factor to parallel comparison of the groups.

In evaluating for change in prognostic awareness within the control and intervention groups, both groups showed a trend towards increased prognostic awareness, however statistical analysis of the interventional and standard of care groups for the 1 year ($p = 0.52$ and $p = 0.6$), five year ($p = 0.84$ and $p = 0.26$) and open timeframe ($p = 0.84$ and $p = 0.38$) did not reach statistical significance. Thus, the addition of a structured guided prognostic discussion compared to an unstructured approach was not shown to be superior in this study.

At baseline the percentage of patients in the population as a whole with high prognostic awareness was 20%, 25% and 35% for the three timeframes. In contrast after a single application of the interventions used in our study, a trend for improved prognostic awareness from baseline in the population was evident with high prognostic awareness measured in 22.5%, 37.5% and 52.5% of patients for the three timeframes. It may be that the inclusion of a formal evaluation of prognostic awareness in itself results in a trend towards improved prognostic awareness, this study did not provide evidence that following such an evaluation the administration of a structured prognostic discussion yielded superior results to an unstructured discussion on prognosis.

Further study in South African patients may advance the role and utility of high prognostic awareness in patients, families and caregivers faced with incurable illness.

Keywords:

Prognostic awareness, Palliative care, awareness of prognosis, stage IV cancer, advanced cancer, advanced care planning, serious illness conversation guide, illness trajectory, cancer bereavement.

List of abbreviations

FIGO	The International Federation of Gynaecology and Obstetrics
HPCSA	Health professions council of South Africa
NHLS	National Health Laboratory Service
NHS	National Health Service
PA	prognostic awareness
SEER	Surveillance, Epidemiology, and End Results Database
SICG	Serious illness conversation guide
UK	United Kingdom
US	United States
WHO	World Health Organisation

List of Appendices

A	Letter of approval from Research Ethics Committee
B	Participant information form and Consent form (if applicable
C	Permission from DOH/NHLS (if applicable)
D	Permission from HOD's etc.
E	Copy of the research protocol approved by the HSREC
F	Forms for collecting data - e.g., questionnaire/data capture instrument(s). +
G	Any other relevant material e.g., laboratory techniques, statistical formulae,
H	If desired selected supplementary tables or figures, with brief explanatory text,
I	Instructions to authors of the named peer reviewed journal (which you have chosen)
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Chapter 1

Literature review

A patient's awareness and level of understanding of their prognosis and expected illness course (the likely illness trajectory) in the context of the available knowledge, expertise and experience is termed prognostic awareness (PA) or awareness of prognosis (1). It incorporates dimensions of understanding physiological reserves and capacity, disease curability, purpose of treatment and life span estimates. (2)

Palliative care encompasses an approach focused on improving the quality of life of patients and their families in the face of life-threatening illness by treatment and prevention of symptoms that cause distress. The focus is not on curative treatment but rather on managing pain and other physical symptoms resulting from the underlying illness, as well as focusing on emotional, psychosocial and spiritual distress so as to optimise and enhance the quality of life (3). Palliative care in oncology especially applies when a patient has an incurable cancer. Palliative medicine is a growing speciality practised not only by specialists in palliative medicine but is intended to be used by multi-disciplinary teams to address the diverse physical, emotional, psychological, spiritual and nursing needs of a seriously ill patient and to communicate the care options between health care professionals, patients and their carers (4).

Palliative care which provides a parallel process to life prolonging care and was introduced early after diagnosis with an incurable illness provided the best results allowing advanced care planning, adequately assessing caregiver needs, streamlining communication between role players, psychosocial support and allowing early introduction to hospice services (5).

A large proportion of cancer patients in our centre cannot be cured of their cancer and are treated with palliative intent (non-curative treatment) as a result of late presentation with advanced disease in line with the findings of resource constrained African state healthcare facilities. (6) In palliative medicine high quality care goes beyond management of physical disease and symptoms and provides emphasis on the wishes of the patient and aligning the treatments and interventions with the priorities, values, goals and preferences of the patient. (7).

Bereaved family members have been studied in an attempt to improve end of life care, and they emphasised inadequate communication regarding end of life care, with Hanson *et al* noting that: "discussions that focus on specific treatment decisions may not satisfy the real needs of dying patients and their families" (8).

Prognostic awareness was found to be central to decision making by patients in the palliative setting (9) and it has been demonstrated that good prognostic awareness enabled patients in terms of mental health status and accurately estimating benefits of chosen treatment options, while being associated with reduced hopefulness. Good prognostic awareness addresses four out of the five dimensions of quality care identified by Singer *et al*, namely: relief of burdens on family especially regarding care decisions, achieving a sense of control regarding care decisions, Strengthening relationships with loved ones when they are included in communication that addresses prognosis and avoidance of inappropriate prolongation of life (10).

In modern medicine increasing recognition of evidence showing patient preference to know their diagnosis and prognosis(11), full disclosure has become the norm, with a shift away from the perceived beneficence of physicians deciding on behalf of patients, in favour of greater recognition of individual patient autonomy. This has been adopted in western countries as well as many others in the East, Americas and Africa, as described in published literature originating from Japan (12), Taiwan (13), Argentina(14), Zimbabwe (15), and in South Africa. Locally this was contained in the ethical rules regarding the rights of patients to information pertaining to their diagnosis and prognosis(16). The point of departure of the statutory body for health in South Africa, the health professions council of South Africa, was that a patient must be provided detailed information so as to enable a patient to “make proper choices as partners in the health care process”.

Denial was found to often precede the acceptance of a prognosis, and may present on multiple levels: encompassing denial of the diagnosis itself, the implications of the illness and its physical manifestations and denial of feelings associated with the illness. This becomes further complicated by the observation that “hope for a cure is inexhaustible in terminal illness” (17), meaning that despite cognitive acknowledgement of the prognosis (and seemingly good prognostic awareness) there is not always emotional recognition that hope and dreams for cure are futile (18). Poor prognostic awareness was related to both deficiencies in communication from the side of the health care provider, as well as attempts by patients and families to manage the threat of death and maintain hope(19).

Hope in cancer patients has been described as “the inner energy that drives one to keep on living well, until the end of life” (20). Hopefulness is both a coping factor and a component of quality of life for patients with advanced cancer, Mok *et al* explored the meaning of hope as defined by care providers and described four themes that define hopefulness in a patient with incurable cancer: Initially expected hopelessness followed by hope fostering strategies and a dynamic process of hopefulness, lastly peace as the ultimate hope (21). This study described the initial expected hopelessness as a normal response to the realisation of advanced disease and thus can be expected initially when a patient develops increased prognostic awareness of a terminal cancer.

Alexander *et al* reported that “the experience of having a life-threatening illness like cancer is normally expected to produce significant psychological distress” (22). Hope fostering strategies were implemented by the palliative care services and included: “affirmation of worth, relational connectedness, partnership, religious support, and resolution of unfulfilled family responsibilities.” This allowed positive change in some patients who initially had a sense of hopelessness, illustrating the dynamic process of hopefulness. In 1990 Herth was one of the first to research how patients receiving palliative care define hope and showed that the focus of hope of patients with advanced disease gradually shifts from having or doing to being (23). It is at the end of this shift that the care providers in Mok *et al* felt that being at peace in the face of death was the ultimate hope.

Poor and inaccurate prognostic awareness was common (24)(25) and associated with triple the rate of depression, unrealistic patient and family expectations, in addition to overestimating the value of futile life sustaining interventions such as ICU admission, intubation and ventilation (26). In contrast, accurate prognostic awareness has been shown to be of benefit to patients with regards to being more open to end of life care discussions and enabled informed and value-based care decision making, and were significantly less likely to prefer life sustaining treatments (27). A 2019 secondary analysis by Chen et al noted that implementation of an interactive intervention for advance care planning and prognostic information resulted in increased prognostic awareness five to six months prior to death, and lower rates of cardiopulmonary resuscitation (28).

It has been observed that patients chose between care options based on their values, their understanding of their illness (prognostic awareness) and their understanding of the risks and benefits associated with the different available treatment options. The provision of prognostic information that is understood by patients was found to change care preferences in an American study where patients with metastatic cancer who believed they had a >90% chance of living another six months chose life extending therapy in 51% of cases, compared to patients that believed they had 25% chance of living another six months who only chose life extending therapy in 31% of cases. The same study noted that (especially in the context where life expectancy can be minimally enhanced) when patients do not understand their prognosis accurately, then their decisions about the inevitable trade-offs between treatment choices aimed at increasing duration of remaining life expectancy versus quality-of-life may not reflect their true values (29).

The structured illness conversation guide (SICG) is an evidence based tool developed in Boston Massachusetts that has been integrated into practice in both the US (currently used officially in eight Texas hospitals, five hospitals in Massachusetts and three hospitals in Pennsylvania), and the UK (being tested by the NHS in their serious illness care pilot program) and is used in the palliative care curriculum in South Africa as an example of structured serious illness conversations, to teach care providers how to communicate with patients diagnosed with incurable illness (Kirkbride, P et al., 2017; McGlinchey et al., 2017).

Structured interventions designed to facilitate the identification and discussion of serious illness care goals were found to be time intensive as illustrated by the patient priorities identification process reported by Naik *et al* that took between 35 and 45 minutes to complete by trained facilitators (30), while it took trained physicians 22 to 26 minutes to complete the serious illness conversation guide (31). Earlier research aimed at completion of a written advanced directive indicated that on average a median time of only 5.6 minutes was needed for an advanced directive conversation (32), however these conversations have been criticised for being delivered by non-expert medical doctors with the doctor talking most of the time, not exploring a patient's values and being directed primarily at the possible procedures that may be needed and available at the end of life. In contrast Roter *et al* found that experts spent significantly more time – 14.7 minutes on average, and were less verbally dominant, allowing patients more time to talk as well as being more focussed on patient goals as opposed to procedures and aiming for a partnership in treatment decisions (33).

Care provider factors included adequacy of training, uncertainty about prognostic accuracy and the comfort level in discussing end of life issues. Importantly Keating *et al* found that physician factors were more common than patient factors as barriers to end of life communication (34), a systematic review in 2005 found that there was a lack of guidance for clinicians to communicate prognosis(35). While prognostic awareness has been found to increase a patient's understanding of their likely illness trajectory, decreasing depression and anxiety in addition to reducing futile end of life interventions, there has also been studies that found negative associations between increased PA, mental health and quality of life (36). A systematic review found that PA was a complex phenomenon that was affected by the age, personality and stage of disease among others, it was concluded that individual preferences and patient values must be considered when discussing prognosis and that adverse outcomes may potentially result (37).

Physicians reported feeling uncomfortable with the emotions that were stirred up by end of life discussions (38) and not necessarily equipped to manage the patients' reactions (39). However this fear contrasted with findings that patients and family wish to discuss prognosis (40), and that these discussions helped with decision making, bereavement adjustment and were not associated with more worry or depression. In addition it was found that hope is not reduced with serious illness care discussions. Cancer patients who died in ICU or hospital has been associated with worse quality of life and a four times increased risk for development of prolonged grief disorder in bereaved caregivers when compared to those who died at home with hospice (41). In an earlier paper the same author studied the bereaved caregivers of 332 patients and reported end of life discussions with patients were associated with lower rates of aggressive medical care near death and earlier hospice referral, no increase in rates of major depression and no increase in worry. In turn adjusted analyses indicated that patient quality of life was significantly worse with more aggressive medical care at end of life and this translated to higher risk of depression in bereaved caregivers. The patients that reported having end of life discussions had better quality of life with earlier hospice enrolment and this was associated with significantly better caregiver quality of life (42). Mack *et al* studied the way a patients oncologist communicated with patients and caregivers and the effect on hopefulness, they found no evidence that prognostic disclosure made caregivers feel less hopeful and instead found that increased prognostic disclosure and high quality communication supported hope even when prognosis was poor (43).

Areas requiring further research

Areas identified include prognostic disclosure, the measurement of Quality of Life related to prognostic awareness and mood disorders in South African patients with advanced cancer as areas that require further study so as to inform palliative care in the South African context.

Research question and aim

Following questions to establish prognostic awareness, does a physician directed structured serious illness conversation guide improve prognostic awareness to a greater extent than patient directed unstructured prognostic discussions in incurable stage IV cancer patients?

In this interventional study we used quantitative data gathered by means of standardised checklists and questionnaires to analyse the prognostic awareness in incurable stage IV cancer patients attending our oncology clinic.

The aim of this study was to evaluate the effect on the PA of incurable stage IV cancer patients when prognostic questions were added to the standard of care. Secondly the study evaluated if there was a statistical difference between following the prognostic questions with structured physician directed versus unstructured patient directed prognostic discussions when utilising a specific serious illness guided conversation intervention.

Objectives

1. To establish what the baseline prognostic awareness is by comparing subjective and objective risk of death at different future timepoints.
2. To establish the prognostic awareness by the same method as mentioned in objective 1, after the control group received evaluation of prognostic awareness followed by an unstructured discussion compared to the change in PA for the intervention group who were evaluated for prognostic awareness followed by a structured conversation.
3. The third objective was to compare the change in prognostic awareness for the population as a whole and between the two groups.

Hypothesis

Determination of the subjective view of the patient regarding their prognosis and illness trajectory would result in increased levels of prognostic awareness when followed by discussion of the patient’s views. It is anticipated that physician directed structured discussions would be superior to patient directed unstructured discussions.

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Chapter 2

Connect :Prognostic awareness and structured serious illness conversations in stage IV cancer patients

Abstract

Background: Prognostic awareness has been shown to be a key aspect regarding a patient's understanding of their diagnosis, the available treatment options and the likely treatment and disease outcomes. It is recognised as essential to informed decision making in the setting where there is no curative therapy available, such as in advanced cancer. Palliative care aims to deliver holistic care to both the patient and their carers by enhancing the quality of life of the a patient while also considering the role and burdens of the carers and family. A patient's' prognostic awareness is critical in advanced care planning and studies have shown that patients and their families wish to discuss prognosis so as to help with decision making regarding a patient's wishes at the end of life. Advanced care planning has been shown to with resultant in reduced ICU admission and intensive interventions at end of life, while end of life discussions resulted in earlier hospice enrolment for patients and better quality of life and reduced depression in bereaved caregivers. This study represents the first South African study to evaluate prognostic awareness in stage IV cancer patients.

Aim: The aim of this study was to evaluate the effect on the PA of incurable stage IV cancer patients when prognostic questions were added to the standard of care. Secondly the study evaluated if there was a statistical difference between following the prognostic questions with structured physician directed versus unstructured patient directed prognostic discussions when utilising a specific serious illness guided conversation intervention.

Method: All patients received standard clinical care in addition to being asked three specific questions used to measure their subjective prognostic awareness for three timeframes: one year, five years and for an undefined long term open timeframe. The evaluation was followed by an opportunity for discussion of prognosis. Half the patients were randomised to a physician directed structured serious illness guided conversation on prognosis following the measurement of PA, while the other half of patients were given the opportunity for patient directed unstructured discussions on prognosis, this second group served as the control group. Answers to the three questions were recorded as the subjective prognosis. The Objective prognosis was determined using applicable survival curves and by consultation with a registered radiation oncologist. By comparing objective prognosis with the patient's subjective prognosis, patients were grouped as having high, low or poor prognostic awareness for three timeframes.

At the second visit all patients received standard clinical care and were again evaluated for their subjective prognosis using the same three questions used at the first visit. Data was analysed to determine: 1. The baseline prognostic awareness; 2. The change in prognostic awareness within the intervention and control groups respectively; 3. The impact of using a physician directed structured SICG intervention in comparison to using unstructured patient directed prognostic discussions.

Results: At baseline most patients had low to poor prognostic awareness with the majority significantly overestimating their prognosis. There was no significant difference in PA shown within either the interventional or control groups from the first to the second visit. There was also no significant difference between the change seen in the interventional group when compared to the change in the control group. In this study there was thus no advantage shown for using physician directed structured discussions on prognosis.

However, despite the lack of statistically significant improvement in the subgroups, for the population as a whole at baseline the percentage of patients with high prognostic awareness was 20%, 25% and 35% for the three timeframes. In contrast after a single application of the simple interventions described in our study, a trend for improved prognostic awareness from baseline in both groups was evident with high prognostic awareness measured in 22.5%, 37.5% and 52.5% of patients for the three timeframes. Statistical significance was not reached,

Conclusion: Initial prognostic awareness of patients attending the Universitas Oncology Out-patient clinic sampled in this study was poor to low with the majority of patients significantly overestimating their prognosis. The trend towards increased prognostic awareness seen when incorporating and recording the subjective prognostic awareness of a patient and following that with prognostic discussions is in line with published literature and we encourage investigation in larger groups of patients and over a longer timeframe.

Consultations focussed on direct discussions of short-, medium- and long-term prognosis using both structured and unstructured approaches showed a statistically non-significant trend towards increased levels of prognostic awareness for both patient sub-groups and across all three timelines and may warrant further study.

Introduction

A patient's awareness and level of understanding of their prognosis and expected illness course (the likely illness trajectory) in the context of the available knowledge, expertise and experience is termed prognostic awareness (PA) or awareness of prognosis (1). It incorporates dimensions of understanding physiological reserves and capacity, disease curability, purpose of treatment and life span estimates. (2)

A large proportion of cancer patients in our centre are treated with palliative intent as a result of late presentation and advanced disease in line with the findings of other African state healthcare facilities. (6) In palliative medicine high quality care goes beyond management of physical disease and symptoms and provides emphasis on the wishes of the patient and aligning the treatments and interventions with the priorities, values, goals and preferences of the patient. (7).

Singer *et al* focused on the patient's perspective of dimensions that define quality end of life care. The five most important and common aspects that patients with incurable diagnoses desired was: "receiving adequate pain and symptoms management; avoiding inappropriate prolongation of dying; achieving a sense of control; relieving the burden their death would place on loved ones; and strengthening relationships with loved ones."(10).

Prognostic awareness was found to be central to decision making by patients in the palliative setting (9) and good prognostic awareness enabled patients in accurately estimating benefits of chosen treatment options, while being associated with reduced hopefulness. Good prognostic awareness addresses four dimensions of quality care identified by Singer *et al,* namely: relief of burdens on family especially regarding care decisions, achieving a sense of control regarding care decisions, Strengthening relationships with loved ones when they are included in communication that addresses prognosis, and avoidance of inappropriate prolongation of life (10).

Sharing of prognosis was a complex task in patients with advanced cancer as highlighted by the findings of a systematic review of prognostic awareness by Diamond *et al*. Patients with malignant glioma, which carries a poor prognosis and typically advances with relentless functional and mental decline, desired prognostic information communicated in a manner that preserved hope (9). Hope in cancer patients has been described as "the inner energy that drives one to keep on living well, until the end of life" (20). Hopefulness was both a coping factor and a component of quality of life for patients with advanced cancer, Mok *et al* explored the meaning of hope as defined by care providers and described four themes that define hopefulness in a patient with incurable cancer: Initially expected hopelessness followed by hope fostering strategies and a dynamic process of hopefulness, lastly peace as the ultimate hope (21). This study described the initial expected hopelessness as a normal response to the realisation of advanced disease and thus can be expected initially when a patient develops increased prognostic awareness of a terminal cancer.

Accurate prognostic awareness has been shown to be of benefit to patients with regards to being more open to end-of-life care discussions and enabled informed and value-based care decision making, and were significantly less likely to prefer life sustaining treatments (27). A 2019 secondary analysis by Chen et al noted that implementation of an interactive intervention for advance care planning and prognostic information resulted in increased prognostic awareness five to six months prior to death, and lower rates of cardiopulmonary resuscitation (28).

In modern medicine increasing recognition of evidence showing patient preference to know their diagnosis and prognosis (11), full disclosure has become the norm, with a shift away from the perceived beneficence of physicians deciding on behalf of patients, in favour of greater recognition of individual patient autonomy. Locally this was contained in the ethical rules regarding the rights of patients to information pertaining to their diagnosis and prognosis(16). The point of departure of the statutory body for health in South Africa, the health professions council of South Africa, was that a patient must be provided detailed information so as to enable a patient to "make proper choices as partners in the health care process".

It has been observed that patients chose between care options based on their values, their understanding of their illness (prognostic awareness) and their understanding of the risks and benefits associated with the different available treatment options. When patients do not understand their prognosis accurately, then their decisions about the inevitable trade-offs between treatment choices aimed at increasing duration of remaining life expectancy versus quality-of-life may not reflect their true values (29).

The structured serious illness conversation guide (SICG) was an evidence based tool developed in Boston Massachusetts that was integrated into practice in both the US (used officially in eight Texas hospitals, five hospitals in Massachusetts and three hospitals in Pennsylvania), in the UK as a pilot program and was used in select palliative care curricula in South Africa (Kirkbride, P et al., 2017; McGlinchey et al., 2017).

Care provider factors included adequacy of training, uncertainty about prognostic accuracy and the comfort level in discussing end of life issues. Importantly Keating et al found that physician factors were more common than patient factors as barriers to end of life communication (34), a systematic review in 2005 found that there was a lack of guidance for clinicians to communicate prognosis (35). While prognostic awareness has been found to increase a patient's understanding of their likely illness trajectory, decreasing depression and anxiety in addition to reducing futile end of life interventions, there has also been studies that found negative associations between increased PA, mental health and quality of life (36). A systematic review found that PA was a complex phenomenon that was affected by the age, personality and stage of disease among others, it was concluded that individual preferences and patient values must be considered when discussing prognosis and that adverse outcomes may potentially result (37).

Cancer patients who died in ICU or hospital have been associated with worse quality of life and a four times increased risk for development of prolonged grief disorder in bereaved caregivers when compared to those who died at home with hospice (41). Adjusted analyses indicated that patient quality of life was significantly worse with more aggressive medical care at end of life and this translated to higher risk of depression in bereaved caregivers.

The patients that reported having end of life discussions had better quality of life with earlier hospice enrolment and this was associated with significantly better caregiver quality of life (42). Mack *et al* studied the way a patients oncologist communicated with patients and caregivers and the effect on hopefulness, they found no evidence that prognostic disclosure made caregivers feel less hopeful and instead found that increased prognostic disclosure and high quality communication supported hope even when prognosis was poor (43).

Given the benefit seen with prognostic discussions, and the absence of a structured approach currently, we were motivated to study the effect of including such aspects into our standard clinical care of appropriately selected patients.

The aim of this study was to evaluate the effect on the PA of incurable stage IV cancer patients when prognostic questions were added to the standard of care. Secondly the study evaluated if there was a statistical difference between following the prognostic questions with structured physician directed versus unstructured patient directed prognostic discussions when utilising a specific serious illness guided conversation intervention.

Methodology

Study design

This was a prospective interventional study, evaluating the baseline prognostic awareness, as well as to compare whether a structured physician directed conversation effected a greater increase in PA than an unstructured patient directed discussion of prognosis.

The first ten patient's data comprised a pilot study, this data was evaluated by a biostatistician to ensure that the format, recording and completeness was adequate for comprehensive analysis of the final data.

Setting:

The Department of Radiation Oncology outpatient clinic, Universitas Hospital Annex, Bloemfontein, South Africa

Study participants

42 ambulant adult patients attending the Oncology outpatient clinic and diagnosed with an incurable stage IV cancer being treated with palliative intent and attending our outpatients at least once every three months between August 2019 and January 2020 met screening criteria and were offered the information document to consider participation in the study. After having had the opportunity to read the document, pose questions and consider answers 40 patients gave written informed consent and completed both sessions of evaluation over two visits.

Inclusion criteria included being diagnosed with a high incidence incurable stage IV cancer for which robust survival data is available so as to inform the objective prognosis. According to the most recent report available from the South African National Cancer Registry the highest incidence cancers for women was in the breast, cervix and skin, while for men it was prostate, colorectal and skin (NHLS/NCR, 2014).

Exclusion criteria extended to patients that were bed bound, in the terminal phase of their illness (life expectancy of days – weeks), not scheduled to attend the clinic in the next three months, or diagnosed with a cancer that was not of high incidence or potentially curable stage IV cancer e.g., lymphoma. Patients that were stage IV but potentially curable with surgery e.g., oligometastatic colorectal carcinoma were also excluded, this resulted in the long term open timeframe prognosis being universally one of death likely due to cancer.

Consecutive patients were screened and invited to participate during allocated research time in the clinic. All patients were reassured that participation was entirely voluntary, was not aimed at any alteration of their current treatment and that even if they decided to withdraw from the study or decline to answer questions at any point there would be no negative consequences. All screened patients were further reassured that the principal investigator, the oncology social worker were able to assist regardless of the decision to participate or not, and that referral to psychology and psychiatry services was available to manage any distress that the patient may experience.

Randomisation into the interventional (group 1) and control (group 2) divisions was by means of a computer-generated random number list provided by the biostatistician.

Prior to commencing the study, approval was obtained from the Universitas Department of Oncology, the Health Sciences Research Ethics Committee and the Free State Department of Health. An information document with details of the study in the language of their choice and written informed consent was obtained prior to participation. Half of the patients were randomised to the interventional arm of the study and each participant was evaluated twice.

Measurement

Our primary aim was to establish a baseline objective level of prognostic awareness in patients being seen with incurable stage IV cancer and who were attending our clinic as out patients at least three monthly.

The measured data comprised the documented questionnaire results of the awareness scores,. analysis of which allowed determination of the prognostic awareness. Patients in the control group were assessed using the three questions while the interventional arm patients started out with the three questions and then also completed the structured intervention. At the second visit, all patients again answered the same set of three important questions. We used the same measurement instrument as Helft and colleagues to determine the prognostic awareness by asking three simple, structured questions read from the survey form during face-to-face interviews that were incorporated into clinical consultation (44). The three questions were:

1. I am going to read four statements about the possibility of cancer causing your death. I would like you to tell me which of the four statements best describes your feelings as to the chances of your death occurring from your cancer: it is not possible, it is improbable, it is probable, or it is certain.
2. Now I would like you to tell me which of the four statements best describes your feelings as to the chances of your death occurring from your cancer within the next 5 years. It is not possible, it is improbable, it is probable, or it is certain.
3. Lastly please tell me which of the four statements best describes your feelings as to the chances of your death occurring from your cancer within the next year. It is not possible, it is improbable, it is probable, or it is certain.

The structured intervention consisted of an evidence based serious illness conversation guide (SICG) developed by Ariadne Labs (45) (a joint centre between Brigham and Women's Hospital and the Harvard University School of Public Health) (46) verified for use in the United States of America (47) and in the United Kingdom by the NHS for use in their serious illness care pilot program (48)(7).

The SICG comprises five sections, completion of each point within each section was recorded on the answer sheet by checking the appropriate tick box.

Firstly, the conversation was initiated by asking the patient if they were open to discussing the state of their health by asking "I'm hoping we can talk about where things are with your illness and where they might be going — is this okay".

If the patient agreed the second section was started. Secondly the patient was asked for their understanding by means of first an open question, and then by asking the three structured questions described above. Following this the patient was asked how much information they would like from the physician about the likely future illness path.

Thirdly prognosis was shared according to the doctor's understanding of prognostic uncertainty, temporality and level of function. Depending on the amount of information requested by the patient the expected objective prognosis data was also shared for that specific cancer type.

Fourthly key topics were discussed and lastly the session was concluded by summarising what the patient had communicated as being really important to them, what the best plan for their care would currently be, what their thoughts were at that point in time and they were reassured that they were not alone and the medical team was there to help them in this difficult time.The SICG was administered by the primary investigator in each case, and both interviews were conducted within a three-month timeframe. We subsequently evaluated the effect of the interventions on prognostic awareness.

Objective estimates of expected survival were based on published overall survival curves for the included diagnoses based on available data for stage IV cancer, of note stage specific cancer mortality data for South Africa was not available. In order to calculate the objective prognosis for patients in this study the date on which they fulfilled the criteria for stage IV disease was recorded and they were then plotted on the survival curves for the relevant cancer with which they were diagnosed so as to calculate the objective prognosis for each patient. The values were reviewed and discussed with the specialist radiation oncologist to ensure relevance and accuracy.

Prostate adenocarcinoma has a one year overall survival for ±75% and five year overall survival of ±35% with little variation between developed nations (49) and developing nations such as Brazil (50). For patients with stage IV breast cancer the one year overall survival was ±60 %. However by five years the expected survival was only ±19% based on data from SEER (51). For stage IV Cervical cancer the one year objective overall survival was determined to be ±30% and at five years ±18% based on consideration of survival data from the SEER database (52) as well as less developed nations so as to more accurately reflect the South African population that utilises state health care services and included data from Brazil (53) (54) and Russia (55)

SEER data (56) as well as South Korean studies (57) was reviewed for colorectal cancer patients and the one year expected overall survival was ±30% while five year survival was only ±10%. While overall survival of patients diagnosed with stage IV non-small cell lung cancer was based on data from the SEER database (58) as well as Brazilian Data with a one year expected overall survival of ±29%, while that for five years was very low for both developed and developing nations at only ±5% (59). For Metastatic melanoma stage IV disease is associated with an estimated 50% one-year survival. The overall five year survival of ±10% based on data from the United Kingdom where the five year survival was 10% (60) and in Brazil where patients with access to chemotherapy only have a five year overall survival of <10% (61).

For this study, death was considered certain within a selected timeframe if data indicated expected overall survival < 10% (coded 1), likely if < 50% (coded 2) and death due to cancer was considered unlikely if survival was > 50% (Coded 3) within the specified timeframe.

Death in a stage IV patient diagnosed with incurable cancer was never objectively considered impossible (Coded 4 if the patient answered they believed death from their cancer was impossible).

Data from Objective and subjective survival was coded as 1; 2; 3 or 4. 1 represented that death from cancer was certain within the specified timeframe, 2 that it was likely, 3 that it was unlikely and 4 that it was impossible to succumb to cancer within the specified timeframe.

In this study when the expected survival for the timeframe in question was <50%, patients that acknowledged that their risk of dying of cancer within that timeframe was likely or certain were adjudged to show a "high prognostic awareness". For the same level of risk patients that reported that they believed their risk of dying of cancer was unlikely were adjudged to have "low prognostic awareness" and if they considered it impossible to die as a result of their stage IV cancer they were assigned to the "poor prognostic awareness" category. Conversely when the expected survival of patients for the timeframe being investigated was >=50%, patients who indicated they believed their risk of dying from their cancer within that time period was unlikely had "high prognostic awareness", those who believed it likely had "low prognostic awareness". Patients that believed it either impossible or certain had "poor prognostic awareness".

Analysis of the data

Continuous variables including awareness scores were summarised by means, standard deviations or medians and percentiles. Categorical variables were summarised by frequencies and percentages. Within group changes were evaluated using appropriate tests and confidence intervals for paired data. Differences between groups were evaluated using appropriate statistical tests including Chi-Square, Likelihood Ratio Chi-Square, Mantel-Haenszel Chi-Square, Phi Coefficient, Contingency Coefficient, Cramer's V, Fisher's Exact Test and confidence intervals for unpaired data.

Results

40 patients were evaluated at the first and second visits and awareness of prognosis measured for three distinct temporal periods: one year, five years and long term - more than five years. 20 patients were randomised to group 1 and completed the structured intervention. In comparing the intervention (Group 1) with the control (Group 2) populations, in each group there were eight patients with breast cancer while for prostate cancer there were seven patients in Group 1 and eight patients in Group 2. In Group 1 there were three patients with cervical cancer and two patients with the same diagnosis in Group 2. The patient with metastatic melanoma was in Group 2 while the patient with lung cancer was in Group 1.

Expected objective survival was determined for each patient and scored either 1, 2 or 3 while subjective survival was noted according to patient’s answers and scored 1; 2; 3 or 4. The results showing prognostic awareness as a function of objective vs. subjective expected temporal prognosis were presented in Table 1.

Objectively at one year the expected survival was > 5% in all cases, with 17 patients having likely survival < 50% and 23 patients could expect survival rates > 50%.

Objectively at five years two patients had expected survival < 10%, while the remaining 38 had expected survival < 50%. No patients had expected survival > 50%.

Objectively all patients had <5% chance of survival in the open timeframe and all were expected to succumb to their inoperable and incurable stage IV cancer in the future.

In evaluating for any difference between the intervention and control groups for their objective prognosis there was no significant difference at the first visit for 1yr, 5yr or open timeframes with respective p values of $p = 0.19$; $p = 0.52$ and $p = 0.17$.

There were more patients in the control group that had poor prognostic awareness at the first visit and less that had high prognostic awareness for all three timeframes when compared to the interventional group as illustrated in Table 1 - Prognostic Awareness by group, timeframe and visit. At the second visit there was again no significant difference between the subjective prognosis between the intervention and control groups at 1yr, 5yr or open timeframes: p = 0.395, p = 0.130 and p = 0.235 respectively.

The below table reports the number of patients in each group, time category and visit that were judged to have high, low or poor prognostic awareness respectively.

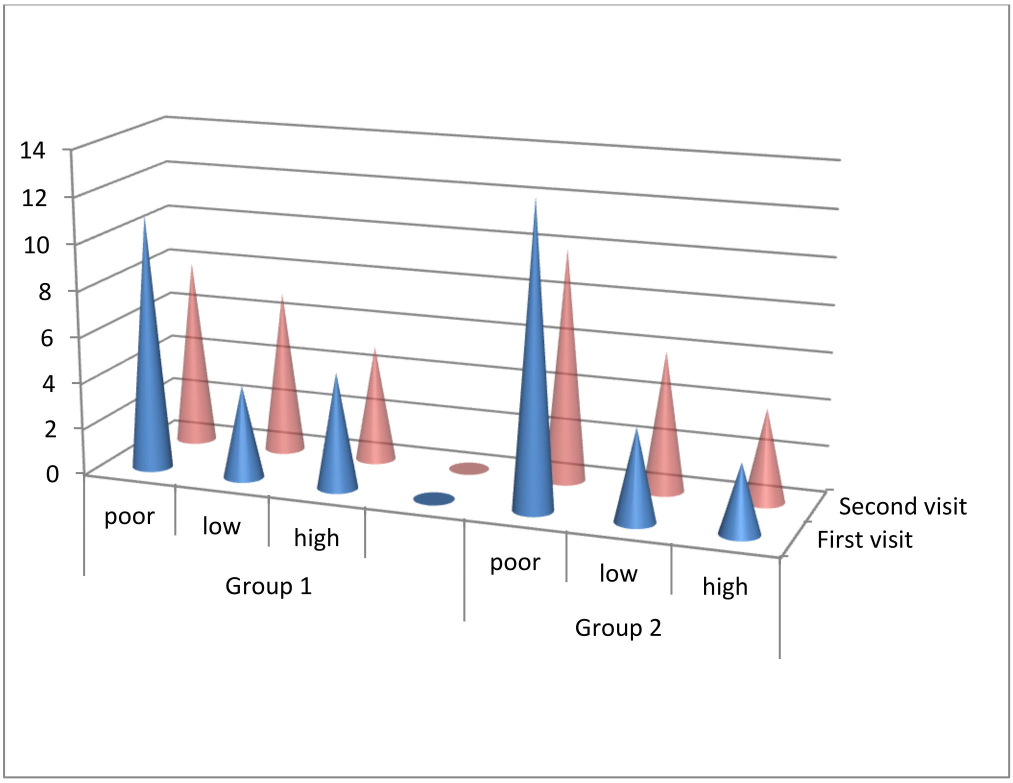
Table 1 - Prognostic Awareness by group, timeframe and visit

All Patients	**Prognostic awareness**	**1yr visit 1**	**1yr visit 2**	**5yr visit 1**	**5yr visit 2**	**open visit 1**	**open visit 2**
	poor	24	18	11	12	14	10
	low	8	13	19	13	12	9
	high	8	9	10	15	14	21
Group 1 Interventional							
	poor	11	8	4	3	4	3
	low	4	7	9	8	8	7
	high	5	5	7	9	8	10
Group 2 Control							
	poor	13	10	7	9	10	7
	low	4	6	10	5	4	2
	high	3	4	3	6	6	11

For the one-year timeframe, when comparing the answers given by the participants to the objective prognosis it was found that at the first visit eight patients had high prognostic awareness (20%), eight had low prognostic awareness (20%) and twenty-four (60%) showed poor prognostic awareness. At the first visit for the patients that had low prognostic awareness seven overestimated their prognosis, while one patient underestimated the prognosis compared to the objective prognosis. For the poor prognostic awareness group, 22 patients overestimated their prognosis while two underestimated it.

For the second visit analysis of the answers given showed that nine patients (22.5%) had high prognostic awareness, 13 had low prognostic awareness (32.5%) with 10/13 patients overestimating their prognosis and three underestimating their prognosis. The patients with poor prognostic awareness all overestimated their prognosis and were 18 in total (45%).

Figure 1- One-year prognostic awareness

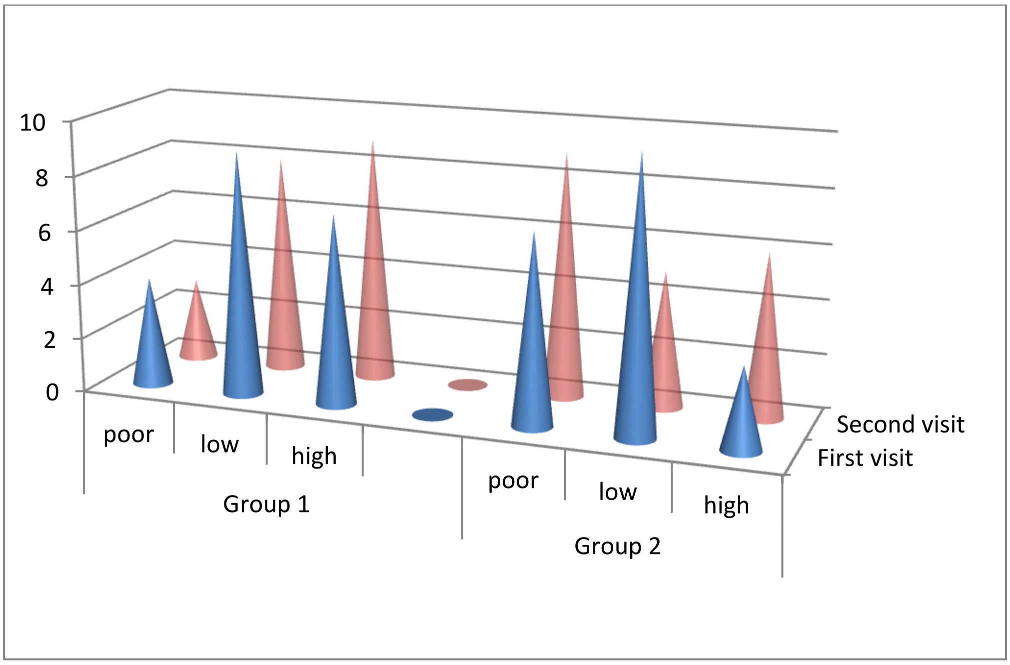


Considering the level of prognostic awareness measured for the three timeframes, for the one-year prognosis it was found that for the intervention population (Group 1) there was a trend to improved prognostic awareness by the patients that had poor prognostic awareness to start off with as three less patients were found to have poor prognostic awareness at the second visit. There was an improvement in the accuracy of prognostic awareness shown with two less patients in the poor prognostic awareness group underestimating their prognostic awareness. There were more patients with low as opposed to poor prognosis compared to the first visit. However, there was no migration from low to high prognostic awareness in Group 1 which still only had 25% (5/20) patients with good one-year prognostic awareness at the second visit.

A similar trend was seen for the one year timeframe in the control population (Group 2) with migration of three patients from the poor to low prognostic awareness group, and one additional patient in the high prognostic awareness category for the one-year timeframe as illustrated in Figure 1. The total number of patients with high prognostic awareness remained very low at 20% (4/20), while 14/16 patients with low or poor prognostic awareness overestimated their prognosis.

For the five-year timeframe 10 (25%) of patients had high prognostic awareness at the first visit, 19 (47.5%) showed low prognostic awareness and 11 (27.5%) had poor prognostic awareness in comparison to 15 (37.5%), 13 (32.5%) and 12 (30%) with high, low and poor prognostic awareness respectively at the second visit. For the patients with low and poor prognostic awareness at both the first and second visit, they uniformly overestimated their prognosis to be greater than the objective prognostic awareness.

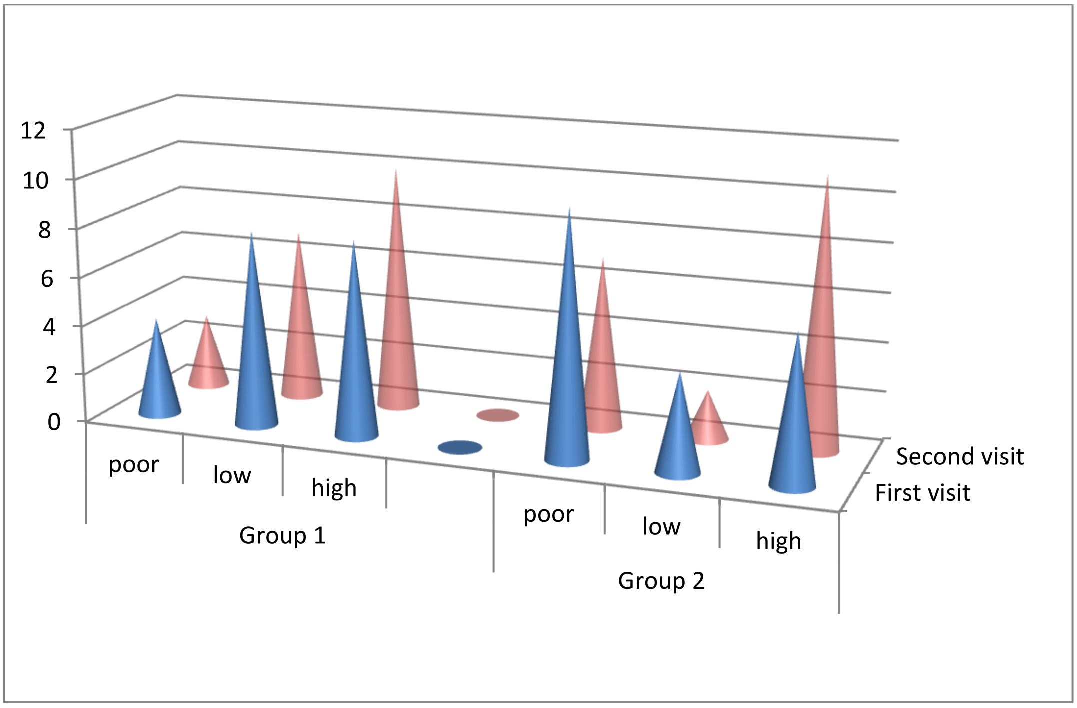
Figure 2- Five-year prognostic awareness



The measured prognostic awareness for the five-year timeframe in Group 1 indicated that from the first to the second visit the number of patients with high prognostic awareness increased from seven (35%) to nine (45%), those with low prognostic awareness decreased from nine (45%) to eight (40%), while those with poor prognostic awareness as a result of overestimating their prognosis decreased from four (20%) to three (15%). A similar trend was seen with twice the number of patients in Group 2 having high prognostic awareness at the second visit (6/20) compared to the first visit (3/20), thus an increase from 15% to 30%, while the number of patients with low prognostic awareness decreased from 10 (50%) to 5 (25%). However, in contrast to Group 1 where no groups showed a decrease in prognostic awareness the number of patients with poor prognostic awareness in Group 2 increased from seven (35%) to nine (45%). The patients with low and poor prognostic awareness all overestimated their prognosis.

For the long-term timeframe beyond five years at the first visit 14 (35%), 12 (30%) and 14 (35%) of patients had high, low and poor prognostic awareness respectively. At the second visit 21 (52.5%) had high prognostic awareness, nine (22.5%) had low prognostic awareness and 10 (25%) had poor prognostic awareness. All patients that had demonstrated low or poor prognostic awareness overestimated their prognostic awareness.

<u>Figure 3- Long term prognostic awareness</u>



As can be seen in Figure 3 for the long term evaluation of prognostic awareness subgroup analysis showed that there was a trend for increased prognostic awareness from the first to the second visit in both groups, with the number of patients in Group 1 with poor prognostic awareness decreasing from four (20%) to three (15%), those with low prognostic awareness decreasing from eight (40%) to seven (35%) and lastly the number of patients with high prognostic awareness increasing from eight (40%) to ten (50%).

In Group 2 a more pronounced migration from poor and low prognostic awareness to high prognostic awareness was seen with more than half the subgroup determined to have high prognostic awareness at the second visit (11/20 = 55%), a large increase from six (30%) patients with high prognostic awareness at the first visit. The number of patients with poor prognostic awareness at the first visit (10/20 = 50%) decreased to seven (35%) at the second visit and similarly the number with low prognostic awareness decreased from four (20%) to two (10%) from the first to the second visit.

Discussion

To our knowledge, this study represents the first South African study to evaluate prognostic awareness in stage IV cancer patients. There was a high level of willingness on the part of patients to take part in the study and discuss their prognosis with a >95% participation rate by patients invited to be included, this is higher than that seen in a recent study by Chen *et al.* where 20 – 26% of patients did not want to know their prognosis (28).

In comparing the intervention and control groups, at baseline there was found to be a very limited number of patients with high prognostic awareness in both groups: However, it was noted that there were differences at baseline between the intervention and control groups in that the control group had fewer patient with high prognostic awareness for all three timeframes when compared to the interventional group. The proportions of patients with high PA at first visit for the control vs. intervention group was 15% vs. 25% for the one year timeframe, 15% vs. 35% for the five year timeframe and 30% vs. 40% for the open timeframe. This is a potential confounding factor since the groups differed at baseline and thus the degree of change in PA for the two groups may be more difficult to interpret

There was not a statistically significant increase in PA for the interventional group vs. the control group as evidenced by the lack of change within the 1 year ($p = 0.52$ and $p = 0.6$), five year ($p = 0.84$ and $p = 0.26$) and open timeframe ($p = 0.84$ and $p = 0.38$). It is considered that there may be multiple factors contributing to the lack of difference between the groups including small sample size, the fact that this measurement was not repeated over multiple interventions in the discussion of a complex and multi-faceted emotive subject, as well as the possibility that after a single discussion there is no clear benefit of a structured conversation over an unstructured conversation.

At baseline for the three timeframes only eight (20%), 10 (25%) and 14 (35%) of patients showed high prognostic awareness for one year, five years and long term respectively. There was a trend towards increased prognostic awareness at the second visit with nine (22.5%), 15 (37.5%) and 21 (52.5%) patients showing high prognostic awareness for the one year, five years and long-term timeframes respectively. There were more patients with high prognostic awareness for the long-term timeframe than for the five year and one-year timeframes. At the first visit 35% of patients had high prognostic awareness for the long term while only 25% and 20% showed high prognostic awareness for the five- and one-year timeframes respectively. At the second visit, though there was an overall increase, the pattern remained the same with 52.5%, 37.5% and 22.5% of patients having high prognostic awareness for the long term, five year and one-year timeframes respectively.

In the control arm there was open ended unstructured prognostic discussions utilising the three prognostic awareness questions and then giving the opportunity for further questions and discussion. These discussions may have had a significant impact when compared to consultations that do not broach the topic of prognosis and death at all as evidenced by the improvement in prognostic awareness from between the first and second visits in group 2 towards better prognostic awareness. It is recognised that there may be factors in addition to discussions with the doctor that affect the prognostic awareness of patients.

Limitations of the study

The study was limited by sample size, lack of previous data on South African patients, limited follow up and a single administration of the respective interventions. In terms of addressing the limitations of this study, a larger cohort of patients that is followed for a longer period and has repeated structured vs. unstructured prognostic discussions may further define the level of prognostic awareness, key elements that inform increasing prognostic awareness and the role for structured vs. unstructured approaches.

Conclusion

The findings of this study are that the baseline prognostic awareness of patients attending the Universitas Oncology Out-patient clinic sampled in this study was poor to low with the majority of patients significantly overestimating their prognosis.

It may be that the inclusion of a formal evaluation of prognostic awareness into the clinical consultation in itself results in a trend towards improved prognostic awareness, and that following such an evaluation with structured prognostic discussion does not yield superior results to unstructured discussions on prognosis.

Consultations focussed on direct discussions of short-, medium- and long-term prognosis using both structured and unstructured approaches showed a statistically non-significant trend towards increased levels of prognostic awareness for both patient sub-groups and across all three timelines and may warrant further study.

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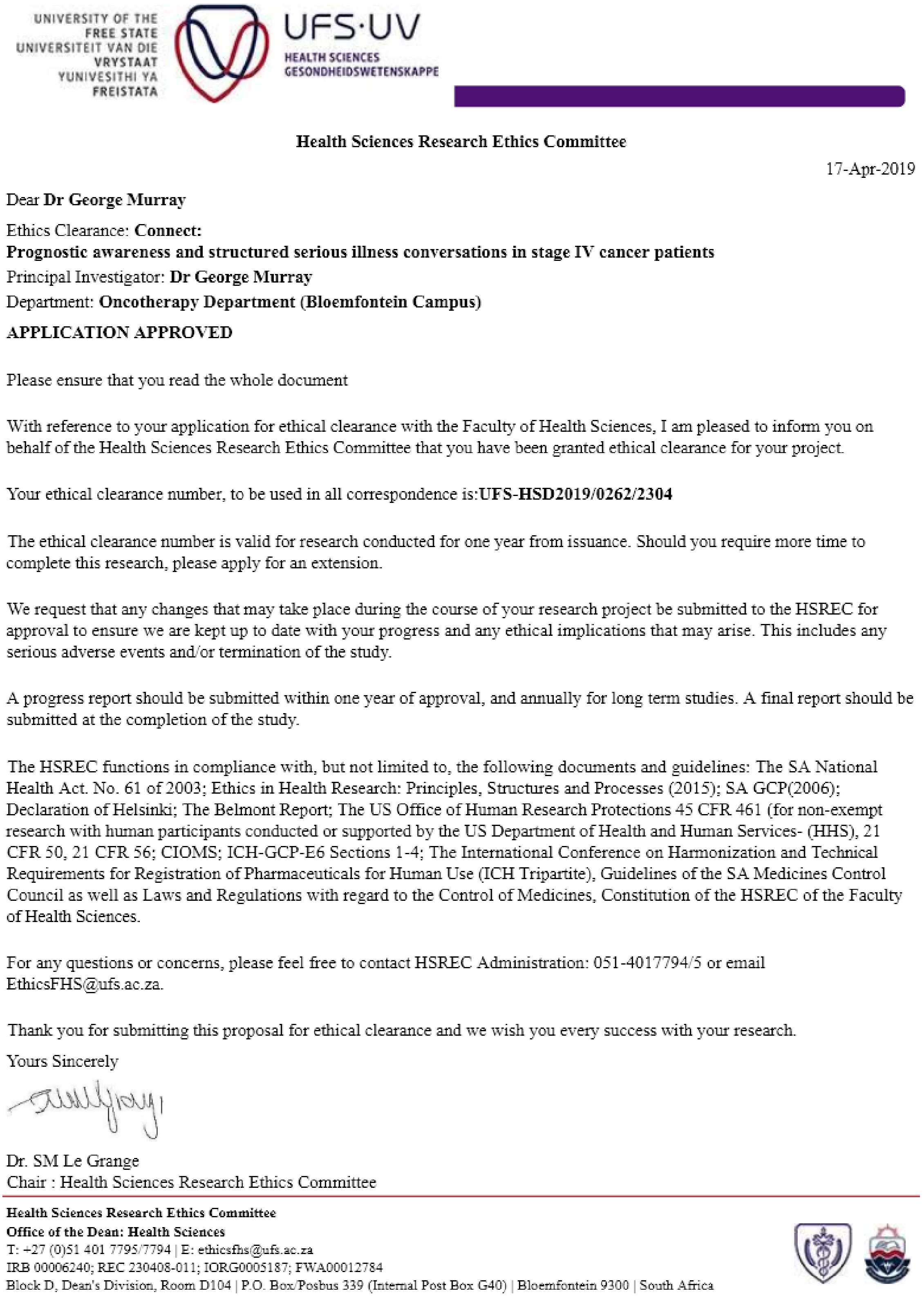
Appendix A : Letter of approval from Research ethics committee



UNIVERSITY OF THE
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HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

Health Sciences Research Ethics Committee

17-Apr-2019

Dear **Dr George Murray**

Ethics Clearance: **Connect:**
Prognostic awareness and structured serious illness conversations in stage IV cancer patients
Principal Investigator: **Dr George Murray**
Department: **Oncotherapy Department (Bloemfontein Campus)**

APPLICATION APPROVED

Please ensure that you read the whole document

With reference to your application for ethical clearance with the Faculty of Health Sciences, I am pleased to inform you on behalf of the Health Sciences Research Ethics Committee that you have been granted ethical clearance for your project.

Your ethical clearance number, to be used in all correspondence is:**UFS-HSD2019/0262/2304**

The ethical clearance number is valid for research conducted for one year from issuance. Should you require more time to complete this research, please apply for an extension.

We request that any changes that may take place during the course of your research project be submitted to the HSREC for approval to ensure we are kept up to date with your progress and any ethical implications that may arise. This includes any serious adverse events and/or termination of the study.

A progress report should be submitted within one year of approval, and annually for long term studies. A final report should be submitted at the completion of the study.

The HSREC functions in compliance with, but not limited to, the following documents and guidelines: The SA National Health Act. No. 61 of 2003; Ethics in Health Research: Principles, Structures and Processes (2015); SA GCP(2006); Declaration of Helsinki; The Belmont Report; The US Office of Human Research Protections 45 CFR 461 (for non-exempt research with human participants conducted or supported by the US Department of Health and Human Services- (HHS), 21 CFR 50, 21 CFR 56; CIOMS; ICH-GCP-E6 Sections 1-4; The International Conference on Harmonization and Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH Tripartite), Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines, Constitution of the HSREC of the Faculty of Health Sciences.

For any questions or concerns, please feel free to contact HSREC Administration: 051-4017794/5 or email EthicsFHS@ufs.ac.za.

Thank you for submitting this proposal for ethical clearance and we wish you every success with your research.

Yours Sincerely

Dr. SM Le Grange
Chair : Health Sciences Research Ethics Committee

Health Sciences Research Ethics Committee
Office of the Dean: Health Sciences
T: +27 (0)51 401 7795/7794 | E: ethicsfhs@ufs.ac.za
IRB 00006240; REC 230408-011; IORG0005187; FWA00012784
Block D, Dean's Division, Room D104 | P.O. Box/Posbus 339 (Internal Post Box G40) | Bloemfontein 9300 | South Africa

Appendix B : Patient information regarding participation in a research study to assess awareness of prognosis in cancer patients

Dear Healthcare User, within our Department of Oncology we are currently conducting a research study to better understand the views and beliefs of our patients regarding their cancer. Your understanding of the disease is critically important on the choices you make and views you hold regarding your health and treatment.

Bearing this in mind, we are conducting a study based on discussions with our patients and the posing of simple but important questions to you as part of your consultation with the doctor. Your answers give us valuable insight into our patients’ views and your participation is sincerely appreciated.

There is no penalty should you prefer not to participate in the study. In addition, there will be no negative consequences should you initially participate and then at any point decide to stop participating in the study. You are entitled to withdraw from the study or decline to answer at any point should you so wish.

All data analysed in the study will remain confidential and no identifying information will be captured in the final dataset, to ensure your answers and information are kept confidential.

Once the study has been concluded, you are welcome to enquire after the results of the study as a whole; however, since data are anonymous, it may be difficult to provide you with specific answers relating to your personal results.

While we hope to be able to publish the results of this study in medical literature, there is no financial reward for the doctors or patients involved in the study and we hold no conflict of interest in this matter.

Please discuss any questions you may have regarding the above information with your doctor at the Oncology clinic, they will be able to clarify points that may not be clear to you.

Please keep this document, and you are welcome to refer to it in future should you have any questions later.

If you agree to participate in this research, please sign the informed consent document supplied.

Sincerely

Dr G. M. Murray – Universitas Department of Oncology – 051 405 3911 x7536

Appendix C : Informed consent for participation in medical research – Prognostic awareness and structured serious illness conversations in stage IV cancer patients

I …………………………. (Name of patient) hereby confirm that I have been fully informed as to the nature and details of the above study. I have been given the opportunity to ask for an explanation and further details after reading the information document and this has been provided to my satisfaction.

I understand that participation is voluntary and I do so free of any obligation. It has been emphasised that there will be no penalty or loss of benefits should I refuse to participate or decide to terminate my participation at any stage. I have been informed that I may withdraw from the study or decline to answer any questions at any time without any adverse consequences.

I understand that all personal details will be confidential and not made available in the final dataset.

This study based on discussions and the posing of simple but important questions to you as part of your consultation with the doctor. Participants will be randomly split into two groups using a predefined number list, both groups will be asked four important questions regarding cancer and death caused by cancer. One group will receive the standard care without any specific structure being followed for the care discussions, while the other group will receive the standard care with the addition of a structured conversation which includes the four important questions. Your answers to the questions are documented. While the structured conversation is only performed once, the four important questions are asked twice, firstly at the initial visit and once with the follow up visit. Dr. Murray will conduct the first visit, while either Dr. Murray or one of the senior doctors that work at the oncology clinic will conduct the follow up visit.

The important questions address serious concerns regarding cancer and death caused by cancer and it is understandable that this can be a distressing discussion to have, even just reading this study’s information page and informed consent document may cause you to feel emotional or distressed. Dr Murray and the oncology social worker are available to assist you regardless of whether you agree to participate in the study or not, and if need be further referral to psychology or psychiatry services is also available. Please discuss this with us so we can support you.

I understand that this study is in no way aimed at altering any treatment, nor designed to change the treatment options available to me, but rather to gain insight into my views regarding the cancer for which I am being treated.

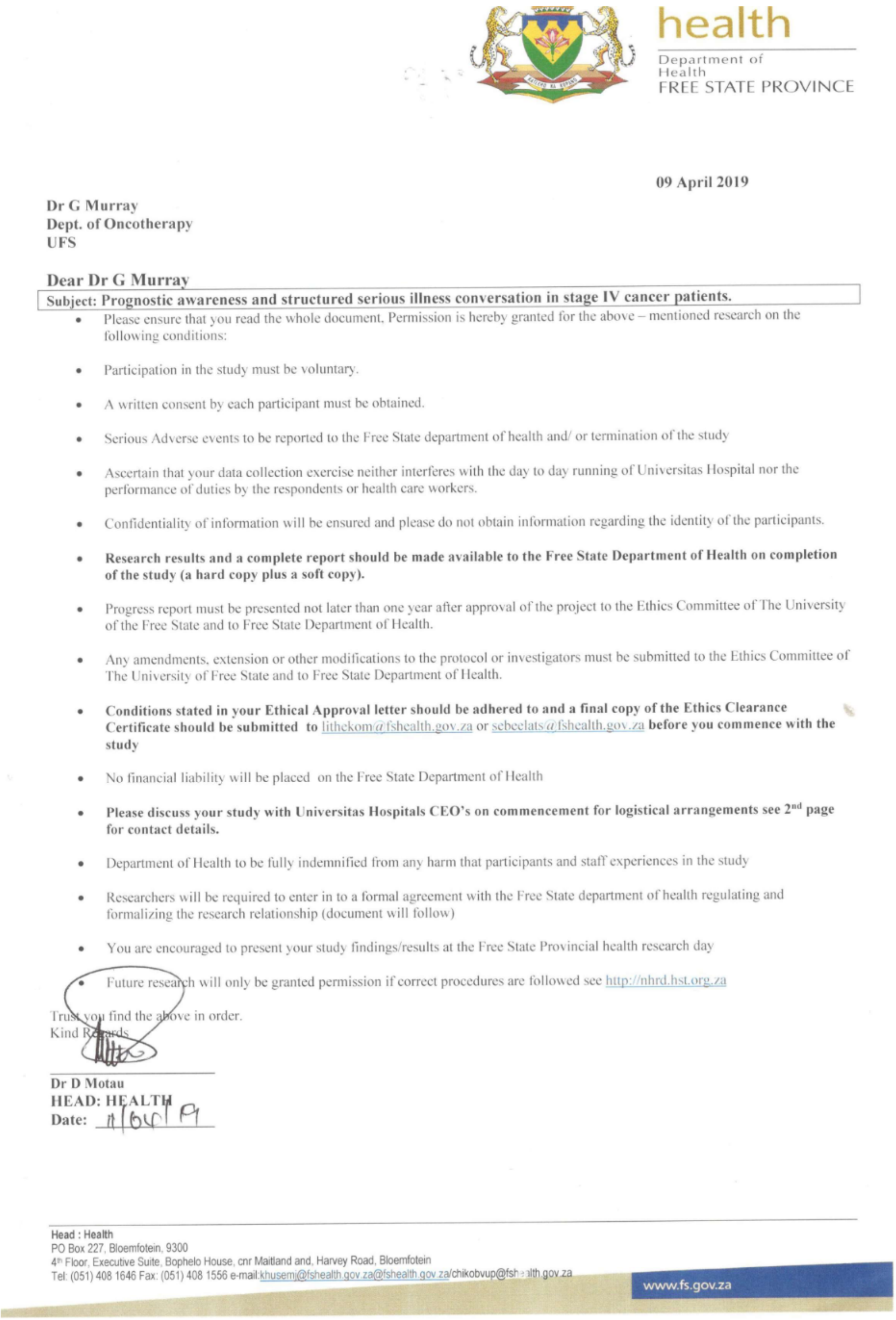
I consent to being included in the study and understand that this may involve a structured verbal intervention and subsequent questionnaires that will form part of my routine clinic consultation with the doctor.

Signed at: ………………………. Date: ……………/……………/…………………..

Name: ………………………… Signature: ……………………………………………

Witness name …………….. Signature: ……………………………………………

Appendix D : permission from FS DOH



health
Department of
Health
FREE STATE PROVINCE

09 April 2019

Dr G Murray
Dept. of Oncotherapy
UFS

Dear Dr G Murray

Subject: Prognostic awareness and structured serious illness conversation in stage IV cancer patients.

- Please ensure that you read the whole document, Permission is hereby granted for the above – mentioned research on the following conditions:
- Participation in the study must be voluntary.
- A written consent by each participant must be obtained.
- Serious Adverse events to be reported to the Free State department of health and/ or termination of the study
- Ascertain that your data collection exercise neither interferes with the day to day running of Universitas Hospital nor the performance of duties by the respondents or health care workers.
- Confidentiality of information will be ensured and please do not obtain information regarding the identity of the participants.
- **Research results and a complete report should be made available to the Free State Department of Health on completion of the study (a hard copy plus a soft copy).**
- Progress report must be presented not later than one year after approval of the project to the Ethics Committee of The University of the Free State and to Free State Department of Health.
- Any amendments, extension or other modifications to the protocol or investigators must be submitted to the Ethics Committee of The University of Free State and to Free State Department of Health.
- **Conditions stated in your Ethical Approval letter should be adhered to and a final copy of the Ethics Clearance Certificate should be submitted to** lithekom@fshealth.gov.za **or** sebeelats@fshealth.gov.za **before you commence with the study**
- No financial liability will be placed on the Free State Department of Health
- **Please discuss your study with Universitas Hospitals CEO's on commencement for logistical arrangements see 2nd page for contact details.**
- Department of Health to be fully indemnified from any harm that participants and staff experiences in the study
- Researchers will be required to enter in to a formal agreement with the Free State department of health regulating and formalizing the research relationship (document will follow)
- You are encouraged to present your study findings/results at the Free State Provincial health research day
- Future research will only be granted permission if correct procedures are followed see http://nhrd.hst.org.za

Trust you find the above in order.
Kind Regards

Dr D Motau
HEAD: HEALTH
Date: 11/04/19

Head : Health
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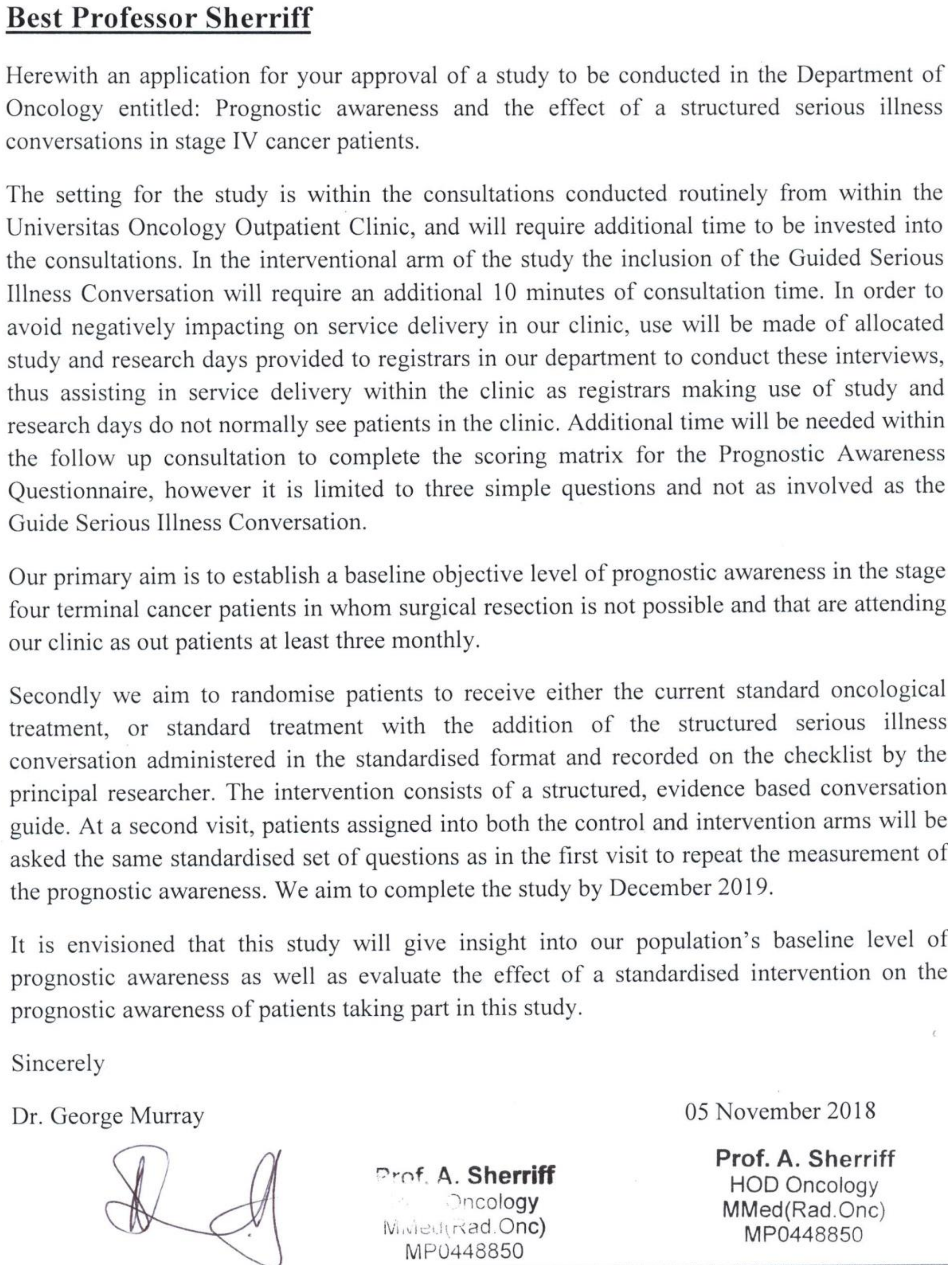
Appendix E : letter to Department of Oncology to conduct research and approval by HOD



Best Professor Sherriff

Herewith an application for your approval of a study to be conducted in the Department of Oncology entitled: Prognostic awareness and the effect of a structured serious illness conversations in stage IV cancer patients.

The setting for the study is within the consultations conducted routinely from within the Universitas Oncology Outpatient Clinic, and will require additional time to be invested into the consultations. In the interventional arm of the study the inclusion of the Guided Serious Illness Conversation will require an additional 10 minutes of consultation time. In order to avoid negatively impacting on service delivery in our clinic, use will be made of allocated study and research days provided to registrars in our department to conduct these interviews, thus assisting in service delivery within the clinic as registrars making use of study and research days do not normally see patients in the clinic. Additional time will be needed within the follow up consultation to complete the scoring matrix for the Prognostic Awareness Questionnaire, however it is limited to three simple questions and not as involved as the Guide Serious Illness Conversation.

Our primary aim is to establish a baseline objective level of prognostic awareness in the stage four terminal cancer patients in whom surgical resection is not possible and that are attending our clinic as out patients at least three monthly.

Secondly we aim to randomise patients to receive either the current standard oncological treatment, or standard treatment with the addition of the structured serious illness conversation administered in the standardised format and recorded on the checklist by the principal researcher. The intervention consists of a structured, evidence based conversation guide. At a second visit, patients assigned into both the control and intervention arms will be asked the same standardised set of questions as in the first visit to repeat the measurement of the prognostic awareness. We aim to complete the study by December 2019.

It is envisioned that this study will give insight into our population's baseline level of prognostic awareness as well as evaluate the effect of a standardised intervention on the prognostic awareness of patients taking part in this study.

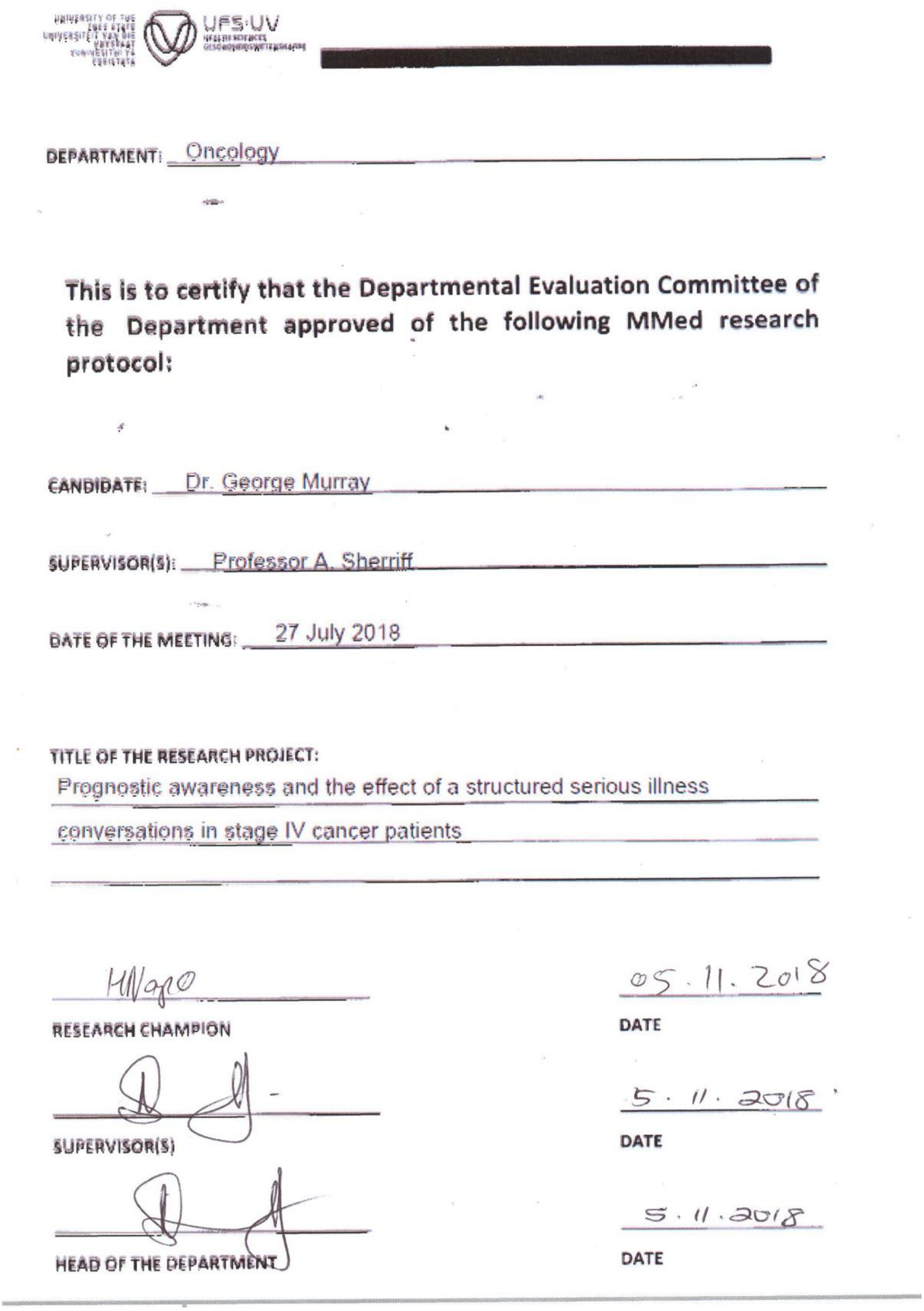
Sincerely

Dr. George Murray

05 November 2018

Prof. A. Sherriff
Oncology
MMed(Rad.Onc)
MP0448850

Prof. A. Sherriff
HOD Oncology
MMed(Rad.Onc)
MP0448850



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GESONDHEIDSWETENSKAPPE

[redacted]

DEPARTMENT: Oncology

This is to certify that the Departmental Evaluation Committee of the Department approved of the following MMed research protocol:

CANDIDATE: Dr. George Murray

SUPERVISOR(S): Professor A. Sherriff

DATE OF THE MEETING: 27 July 2018

TITLE OF THE RESEARCH PROJECT:
Prognostic awareness and the effect of a structured serious illness conversations in stage IV cancer patients

HNapo
RESEARCH CHAMPION

05.11.2018
DATE

SUPERVISOR(S)

5.11.2018
DATE

HEAD OF THE DEPARTMENT

5.11.2018
DATE

Appendix F : Copy of research protocol approved by HSREC

Connect

Prognostic awareness and structured serious illness conversations in stage IV cancer patients

August 2020

Table of Contents

Researchers

Dr G. M. Murray	Registrar in the department of Oncology at Universitas Hospital Annex
Supervisor:	Professor A. Sherriff Head of department of Clinical Oncology at Universitas Hospital Annex
Research assistants	Dr S. Mhlongo; Dr T. Buthelezi; Dr M. Rothman; Dr J. Mthombeni.

Introduction

Palliative care encompasses an approach focused on improving the quality of life of patients with life-threatening illness by treatment and prevention of symptoms that cause distress. The focus is not on curative treatment but rather on managing pain and other physical symptoms resulting from the underlying illness, as well as focusing on emotional, psychosocial and spiritual distress so as to optimise and enhance the quality of life. (WHO, 2018) In oncology palliative care is relevant in the setting where a patient has incurable disease and palliative medicine is a growing speciality practised not only by specialists in palliative medicine but ideally makes use of a multi-disciplinary team approach so as to address the diverse physical, emotional, psychological, spiritual and nursing needs of a seriously ill patient. Palliative care in addition to focusing on providing relief from symptoms, affirms life while at the same time regarding dying as a normal process which is neither hastened nor postponed and is relevant early during incurable illness in parallel with therapies and investigations aimed at identifying and treating aspects of the disease so as to prolong life. (HPCA, 2018). Indeed it is now recognised that early, integrated palliative care delivered to patients attending out-patient clinics from home in parallel with disease modifying treatment is associated with improved quality of life, lower rates of depression and even prolonged survival. (Bakitas et al., 2009) (Temel et al., 2010). This contrasts with the dated approach of only referring patients to palliative care when treatment options for life prolonging care are exhausted and the patient is in the phase of decompensation and dying, with worse outcomes compared to early palliative care. Palliative care which provides a parallel process to life prolonging care and was introduced early after diagnosis with an incurable illness provided the best results allowing advanced care planning, adequately assessing caregiver needs, streamlining communication between role players, psychosocial support and allowing early introduction to hospice services. (Wang, 2017)

A large proportion of cancer patients in our centre cannot be cured of their cancer and are treated with palliative intent (non-curative treatment) as a result of late presentation with advanced disease in line with the findings of resource constrained African state healthcare facilities. (Parkin et al., 2008) In palliative medicine high quality care goes beyond management of physical disease and symptoms and by taking cognisance of the wishes of the patient and aligning the treatments and interventions with the priorities, values, goals and preferences of the patient. (Kirkbride, P et al., 2017). This was elegantly demonstrated by Singer et al in a publication which focused on the patient’s perspective of the dimensions that define quality end of life care, previously the focus had been on measurable end of life care dimensions as identified by medical experts and clinicians. The five most important and common aspects that patients with incurable diagnoses desired was: “receiving adequate pain and symptoms management; avoiding inappropriate prolongation of dying; achieving a sense of control; relieving the burden their death would place on loved ones; and strengthening relationships with loved ones.” (Singer, Martin and Kelner, 1999). Bereaved family members have been studied in an attempt to improve end of life care, and they emphasised inadequate communication regarding end-of-life care, with Hanson et al noting that: “discussions that focus on specific treatment decisions may not satisfy the real needs of dying patients and their families” (Hanson, Danis and Garrett, 1997).

A patient’s awareness and level of understanding of their prognosis and expected illness course (the likely illness trajectory) in the context of the available knowledge, expertise and experience is termed prognostic awareness (PA) or awareness of prognosis. (Jackson et al., 2013) It incorporates dimensions of understanding capacity, disease curability, purpose of treatment and life span estimates. (Andruccioli et al., 2007)

Prognostic awareness was found to be central to decision making by patients in the palliative setting (Diamond et al., 2014) and it has been demonstrated that good prognostic awareness enabled patients in terms of mental health status and accurately estimating benefits of chosen treatment options, while being associated with reduced hopefulness. Good prognostic awareness addresses four out of the five dimensions of quality care identified by Singer et al, namely: relief of burdens on family especially regarding care decisions, achieving a sense of control regarding care decisions, strengthening relationships with loved ones when they are included in communication that addresses prognosis and avoidance of inappropriate prolongation of life. (Singer, Martin and Kelner, 1999)

Sharing of prognosis was a complex task in patients with advanced cancer or with a poor prognosis as highlighted by the findings of a systematic review of prognostic awareness by Diamond et al. It was found that patients with malignant glioma, which carries a poor prognosis and typically advances with relentless functional and mental decline, desire prognostic information communicated in a manner that preserves hope(Diamond et al., 2014), yet prior studies had already established that willingness to answer questions related to prognostic awareness was negatively correlated with hopefulness while noting that hopefulness and coping were positively correlated (Helft et al., 2003).

Historically, this complexity has been avoided by either not disclosing the diagnosis of cancer or by disclosing to someone other than the patient. To elaborate: prior to the advent of platinum chemotherapy in the early 1970’s it was common practice for physicians not to disclose the diagnosis to their patients in Western society as found in an American study in the 1960’s (Oken, 1961) while in Eastern Society disclosure of the diagnosis and prognosis to the family of the patient rather the patient themselves as was still common practice in Japanese medical circles in the 1980’s (Yosuke and Shigeto, 2006).

In modern medicine increasing recognition of evidence showing patient preference to know their diagnosis and prognosis, full disclosure has become the norm, with a shift away from the perceived beneficence of physicians deciding on behalf of patients, in favour of greater recognition of individual patient autonomy. This has been adopted in western countries as well as many others in the East, Americas and Africa, as described in published literature originating from Japan (Yosuke and Shigeto, 2006), Taiwan (Wang et al., 2004), Argentina (De Gonzalez Victorica, Bertolino and PavlovskyS., 2006), Zimbabwe (Levy, 2006), and in South Africa. Locally this was contained in the ethical rules regarding the rights of patients to information pertaining to their diagnosis and prognosis (HPCSA, 2008). The point of departure of the statutory body for health in South Africa, the health professions council of South Africa, was that a patient must be provided detailed information so as to enable a patient to “make proper choices as partners in the health care process”.

Symptoms associated with poor prognostic awareness included depression, most likely to arise in patients who were struggling psychologically and emotionally. An Indian study in 1993 found that adjustment and affective disorder rates were increased in patients admitting a diagnosis of incurable cancer in comparison to patients who considered their treatment to be curative (Alexander, Dinesh and Vidyasagar, 1993). However, a more recent Canadian study had contrasting findings and demonstrated that depression was nearly three times more common in patients who did not acknowledge their prognosis, compared to those who demonstrated partial / complete awareness of their prognosis (Chochinov et al., 2000).

Key differences between these studies was that in the Indian study of Alexander et al the patients were not universally palliative but comprised 60 unselected consecutive patients attending the oncology unit of Kasturba Medical college, Munipal, India. There was no selection for diagnostic classification or duration of illness. In addition to social and cultural differences between India and Canada, within the study time (and noted by the authors in this same article) there was still a culture of not informing patients of their cancer diagnosis but instead informing the relatives: 82% of the patients expected to be cured and 33% of the study participants were unaware of having cancer. This possibly led to a false low rate of depression in advanced cancer patients with poor prognostic awareness compared to those that were fully informed and showed good prognostic awareness.

In contrast Chochinov et al studied 200 patients, all of whom had advanced stage cancer and were in the final weeks of their life, only 9.5% of patients denied being aware of both their terminal prognosis as well as their short life expectancy while 73.5% showed complete awareness of both their terminal prognosis and had a realistic time expectation. Chochinov et al noted that studies where a reduced incidence of psychiatric morbidity was reported in patients who did not acknowledge their prognosis were “largely conducted outside of a Western cultural context in settings where diagnostic information was often withheld” and that in current Western clinical practice the reverse trend was seen with “physicians almost always fully disclosing diagnostic and prognostic information to patients”.

Furthermore, the prevalence of major depression in the study by alexander et al was 13% across the study and was not reported separately for the group that showed awareness of having cancer, having identified a range of pshyciatric diagnoses in the 40% of their sample, they reported that “psychiatric morbidity was significantly lower in those who were unaware of the diagnosis of cancer”. Chochinov et al focused their interview only on affective disorders (major and minor depression) and found that 32% of patients who did not acknowledge their prognosis had clinical depression compared to 9% who demonstrated partial awareness and 11% of patients that had complete awareness of prognosis.

Denial was found to often precede the acceptance of a prognosis, and may present on multiple levels: encompassing denial of the diagnosis itself, the implications of the illness and its physical manifestations and denial of feelings associated with the illness. This becomes further complicated by the observation that “hope for a cure is inexhaustible in terminal illness” (Benzein, E, Norberg, A and Saveman, B.I, 2001), meaning that despite cognitive acknowledgement of the prognosis (and seemingly good prognostic awareness) there is not always emotional recognition that hope and dreams for a future may be curtailed (Buckley and Herth, 2004)

Hope in cancer patients has been described as “the inner energy that drives one to keep on living well, until the end of life” (Benzein and Saveman, 1998). Hopefulness is both a coping factor and a component of quality of life for patients with advanced cancer, Mok et al explored the meaning of hope as defined by care providers and described four themes that define hopefulness in a patient with incurable cancer: Initially expected hopelessness followed by hope fostering strategies and a dynamic process of hopefulness, lastly peace as the ultimate hope (Mok et al., 2010). In this study described the initial expected hopelessness was a normal response to the realisation of advanced disease and thus can be expected initially when a patient develops increased prognostic awareness of a terminal cancer, Alexander et al reported that “the experience of having a life-threatening illness like cancer is normally expected to produce significant psychological distress” (Alexander, Dinesh and Vidyasagar, 1993). Hope fostering strategies were implemented by the palliative care services and included: “affirmation of worth, relational connectedness, partnership, religious support, and resolution of unfulfilled family responsibilities.” This allowed positive change in some patients who initially had a sense of hopelessness, illustrating the dynamic process of hopefulness. In 1990 Herth was one of the first to research how patients receiving palliative care define hope and showed that the focus of hope of patients with advanced disease gradually shifts from having or doing to being (Herth, 1990). It is at the end of this shift that the care providers in Mok et al felt that being at peace in the face of death was the ultimate hope.

Poor and inaccurate prognostic awareness was associated with triple the rate of depression, unrealistic patient and family expectations, in addition to overestimating the value of futile life sustaining interventions such as ICU admission, intubation and ventilation. (Tang et al., 2017). Further, accurate prognostic awareness has been shown to be of benefit to patients with regards to being more open to end-of-life care discussions and enabled informed and value-based care decision making.

It has been observed that patients chose between care options based on their values, their understanding of their illness (prognostic awareness) and their understanding of the risks and benefits associated with the different available treatment options. The provision of prognostic information that is understood by patients was found to change care preferences in an American study where patients with metastatic cancer who believed they had a >90% chance of living another six months chose life extending therapy in 51% of cases, compared to patients that believed they had 25% chance of living another six months who only chose life extending therapy in 31% of cases. (Weeks et al., 1998) The same study noted that: ”When patients do not understand their prognosis accurately, then their decisions about trade-offs between treatment choices quality and quantity of life favouring may not reflect their true values”.(Weeks et al., 1998)

Internationally work on serious illness care programs has stemmed from the emergence of palliative care as a mainstream speciality and the realisation that early palliative care improves the quality of life of patients including mood, coping, reduction of treatment side effects, better pain and symptom control and even enhanced overall survival, while simultaneously having health system benefits in the form of fewer futile procedures and better resource utilisation (Temel et al., 2010)

There was found to be no gold standard for conducting serious illness care planning with different approaches being utilised to assess and discuss serious illness care goals, most commonly unstructured, unscripted conversations that form part of clinical contact sessions (Ramsaroop, Reid and Adelman, 2007), in terms of structured interventions guiding advance care planning conversations Fahner et al identified 34 unique interventions in a recent systemic review of advanced care planning conversation guides (Fahner et al., 2018).

The structured illness conversation guide is an evidence based tool developed in Boston Massachusetts that has been integrated into practice in both the US (currently used officially in eight Texas hospitals, five hospitals in Massachusetts and three hospitals in Pennsylvania), and the UK (being tested by the NHS in their serious illness care pilot program) and is used in the palliative care curriculum in South Africa as an example of structured serious illness conversations, to teach care providers how to communicate with patients diagnosed with incurable illness (Kirkbride, P et al., 2017; McGlinchey et al., 2017).

Structured interventions designed to facilitate the identification and discussion of serious illness care goals were found to be time intensive, the patient priorities identification process reported by Naik et al took between 35 and 45 minutes to complete by trained facilitators (Naik et al., 2018), while it took trained physicians 22 to 26 minutes to complete the serious illness conversation guide (Lakin et al., 2017). Earlier research aimed at completion of a written advanced directive indicated that on average a median time of only 5.6 minutes was needed for an advanced directive conversation (Dow et al., 2010), however these conversations have been criticised for being delivered by non-expert medical doctors with the doctor talking most of the time, not exploring a patient’s values and being directed primarily at the possible procedures that may be needed and available at the end of life. In contrast Roter et al found that experts spent significantly more time – 14.7 minutes on average, and were less verbally dominant, allowing patients more time to talk as well as being more focussed on patient goals as opposed to procedures and aiming for a partnership in treatment decisions (Roter et al., 2000).

Time constraints were not the only barriers to effective serious illness care communication. Patient, care provider and health system factors have all been found to contribute significantly to deficiencies in discussion of serious illness care goals (Bernacki and Block, 2014). Patient factors included anxiety and denial, with the observation that "all patients with a serious illness experience some anxiety", while denial of having a terminal illness was common (Miovic and Block, 2007).

Care provider factors included adequacy of training, uncertainty about prognostic accuracy and the comfort level in discussing end of life issues. Importantly Keating et al found that physician factors were more common than patient factors as barriers to end of life communication (Keating et al., 2010).

Physicians reported feeling uncomfortable with the emotions that were stirred up by end-of-life discussions (Jones et al., 2011) and not necessarily equipped to manage the patients' reactions (Wenrich et al., 2003). However, this fear contrasted with findings that patients and family wish to discuss prognosis (Gwilliam et al., 2015), and that these discussions helped with decision making, bereavement adjustment and were not associated with more worry or depression. In addition, it was found that hope is not reduced with serious illness care discussions. Cancer patients who died in ICU or hospital has been associated with worse quality of life and a four times increased risk for development of prolonged grief disorder in bereaved caregivers when compared to those who died at home with hospice (Wright et al., 2010). In an earlier paper the same author studied the bereaved caregivers of 332 patients and reported end of life discussions with patients were associated with lower rates of aggressive medical care near death and earlier hospice referral, no increase in rates of major depression and no increase in worry. In turn adjusted analyses indicated that patient quality of life was significantly worse with more aggressive medical care at end of life and this translated to higher risk of depression in bereaved caregivers. The patients that reported having end of life discussions had better quality of life with earlier hospice enrolment and this was associated with significantly better caregiver quality of life (Wright et al., 2008). Mack et al studied the way a patient's oncologist communicated with patients and caregivers and the effect on hopefulness, they found no evidence that prognostic disclosure made caregivers feel less hopeful and instead found that increased prognostic disclosure and high-quality communication supported hope even when prognosis was poor (Mack et al., 2007).

Research question, aim and objectives

In this interventional study we aim to use quantitative data to be gathered by means of standardised checklists and questionnaires designed to analyse the prognostic awareness in stage IV cancer patients with unresectable disease in our oncology clinic.

Patients taking part in the study will be randomised into control and intervention arms, with the intervention consisting of a guided serious illness conversation administered to patients in the interventional group.

The study objectives are to establish a baseline for the level of prognostic awareness of the included patients attending our clinic, record the prognostic awareness as well as evaluate the effect of a standardised intervention on the prognostic awareness of patients taking part in this study by comparing the prognostic awareness scores of the control and intervention arms of the study.

Methodology

Study design

We plan an interventional study, evaluating the baseline of a measurable variable, as well as the effect of a clinical tool on that variable, in this case, prognostic awareness

Study participants

Patients that will qualify to be included in this study will have to be ambulant adult patients attending the oncology clinic as out patients with a diagnosis of high incidence and unresectable stage IV cancer being treated with palliative intent and attending our outpatients at least once every three months. According to the most recent report available from the South African National Cancer Registry the highest incidence cancers for women was in the breast, cervix and skin, while for men it was prostate, colorectal and skin (NHLS/NCR, 2014). Prior to inclusion informed consent will be obtained to participate in the study. We aim to study one hundred patients in total, half of whom are to receive the intervention.

Measurement

Our primary aim is to establish a baseline objective level of prognostic awareness in stage four terminal cancer patients in whom surgical resection is not possible and who will be attending our clinic as out patients at least three monthly.

The results of the awareness scores constitutes the data that will be analysed allowing determination of the prognostic awareness of patients attending our institution while taking into cognisance the most likely prognosis based on the stage and type of cancer in oncological literature on two subsequent visits.

We will use the same measurement instrument as Helft and colleagues to determine the prognostic awareness by asking three simple, structured questions read from the survey form during face-to-face interviews that will be incorporated into clinical consultation. Responses are adjudged into four possible options, with further discussion should the response either indicate that the patient does not fully understand the question, or if the answer cannot be placed within one of the four categories.

The responses will be hand written onto the survey form by recording the answer in a tick box which will assign the response a pre-determined score (Helft et al., 2003). A higher mark will be assigned to responses indicating greater awareness of poor prognosis and will be compared to the expected prognosis as predicted by the patient’s consultant and available literature. Each case will be discussed with a consultant oncologist so as to provide an objective prognosis for the five year and one-year timeframes. Since this study is limited to investigating prognostic awareness of stage IV terminal cancer patients with unresectable disease, the prognosis will unfortunately be universally palliative, and this will simplify the determination of the patient’s objective prognosis and prognostic awareness.

At the first visit the principal researcher will conduct the interviews regardless of whether the patient is assigned to the control or intervention arm.

In the interventional component patients will be randomised to receive either the current standard oncological treatment with no specific structure used for conversations regarding care and prognosis, or standard treatment with the addition of the structured serious illness conversation administered in the standardised format and recorded on the checklist by the principal researcher. Randomisation will be by means of a computer-generated random number list, with patients assigned a number that will be based on the number of patients on the study and compared to the random number list to determine if they will be part of the control or intervention arm. The intervention consists of a structured, evidence based conversation guide developed by Ariadne Labs (Bernacki, Hutchings, et al., 2015) (a joint centre between Brigham and Women's Hospital and the Harvard University School of Public Health) (Ariadnelabs, no date) verified for use in the United States of America (Bernacki, Paladino, et al., 2015) and in the United Kingdom by the NHS for use in their serious illness care pilot program (McGlinchey et al., 2017)(Kirkbride, P et al., 2017).

Within the Department of Oncology at Universitas hospital Annex a number of registrars (including the principal researcher) are trained in palliative care by means of a module included in their specialisation syllabus. These include Dr M. Rothman, Dr S. Mhlongo, Dr T. Buthelezi, Dr J. Mthombeni and Dr G. Murray. They will be research assistants. Part of this training encompassed the delivery of the Serious Illness Conversation guide developed by Ariadne Labs.

In order to optimise standardisation, only the principal researcher will deliver the intervention with patients randomised to the interventional arm, while registrars that completed the course and obtained the palliative care certificate will be deemed qualified to participate in this study and will repeat the measurement of prognostic awareness at the second visit.

At the second visit, patients assigned into both the control and intervention arms will be asked the same standardised set of three important questions as in the first visit to repeat the measurement of the prognostic awareness. This data will be recorded in the same format as will be used in the first visit. In comparing the control and intervention arms we will evaluate the effect of the structured illness conversation on prognostic awareness.

Informed consent will be obtained from the participants prior to including them in the study; the study data set will be confidential so as to exclude identifiable characteristics such as name, unit number and ID number.

Methodological and measurement errors

Error may be introduced by the administration of the questionnaires and the serious illness conversation. In order to minimise this, the questionnaires are standardised and the phrasing is to be identical between study participants. In addition, only one investigator will administer the serious illness conversation, again with pre-determined phrases and the responses will be recorded on pre-defined checklists. Phrases and language have been carefully selected to be clear and simple, and this has been verified internationally in multiple centres. (Kirkbride, P et al., 2017; McGlinchey et al., 2017)

Due to the fact that multiple registrars will be participating in the completion of the follow-up questionnaire there is the risk of variation in the delivery of the questionnaires between investigators. By only using registrars qualified in palliative care that are trained in serious illness conversations and by using simple phrasing combined with a pre-defined checklist on which responses are recorded, we hope to mitigate this risk.

Pilot study

We plan a pilot study in which the first ten patients' data will be analysed to provide an opportunity for the methodology to be refined. The pilot study results are to be included in that of the larger study.

Analysis of the data

Continuous variables will be summarised by means, standard deviations or medians and percentiles. Categorical variables will be summarised by frequencies and percentages. Within group changes will be evaluated using appropriate tests and confidence intervals for paired data. Differences between groups will be evaluated using appropriate statistical tests and confidence intervals for unpaired data.

Implementation of findings

It is hoped that this analysis can serve to assist our department in tailoring our treatment and training to optimally address simultaneously the clinical and holistic care of our patients and to ensure that our care goals and those of our patients are aligned.

This study may play a part in the holistic patient centred care at our clinic in addition to affirming existing successful practices in the complex task of communicating and assisting our patients in the dimension of prognostic awareness.

Time schedule

The study will commence as soon as permission has been obtained from the Ethics Committee and Department of Health. We aim to complete the study by December 2019.

Budget

Printing of Serious illness conversation guide	1 page x 75	1.17 x 75 =	R87.75
Follow up prognostic awareness questionnaire	1 page x 150	1.17 x 150 =	R175.50
Printing of informed consent document	1 page x 150	1.17 x 150 =	R175.50
Printing of patient information handout	1 page x 150	1.17 x 150 =	R175.50
Translation services	4 pages	=	R660.00
		Total =	R1126.50

Ethical aspects

Ethics Committee

Ethics approval will be sought prior to the commencement of both the pilot and main study from the Health Sciences Research Ethics Committee of the University of the Free State as well as the Free State department of Health.

Ethical conduct

The study aims to enhance the quality of palliative care offered to patients participating in this study by honest discussion centred on serious illness and the implications thereof in the lives and treatment of our patients.

Views held by the patient will be treated respectfully and the process of discussion aims to open the door to questions from the patient’s side regarding their illness and treatment. It is not an aim of the study to enter into conflict with a patient but rather to offer a clinical opinion and listen to the view of the patient and be open to their perceptions and beliefs, in this way respecting their unique view of their cancer.

As is our standard practice, assistance with translation will be made available in the clinic so as to answer patient’s questions in their language of choice.

All data analysed in the study will remain confidential and no identifying information will be captured in the final dataset, to ensure your answers and information are kept confidential.

Once the study has been concluded, participants are welcome to enquire after the results of the study as a whole; however, since data is confidential, it will be difficult to provide specific answers relating to individual results.

Informed Consent

All potential participants will be provided with the patient information page, so as to clearly explain the details of the study to the potential participants. Informed consent will be obtained from the participants prior to including them in the study; the study data set will be confidential so as to exclude identifiable characteristics such as name, unit number and ID number. Participants will be informed that there is no cost or remuneration for study participation.

Participants will be informed that they are free to choose whether to participate in the study or not, with no penalty should they decide not to participate. Additionally, should they choose to participate they will have the choice of withdrawing from the study at any time should they so wish.

Opportunity will be provided for questions and further explanation of any aspect's patients would like to better understand prior to signing the informed consent document.

Permission from appropriate authorities

Prior to commencing the study, permission will be obtained from the Universitas Department of Oncology, the Health Sciences Research Ethics Committee and the Free State Department of Health.

Appendix G - Prognostic awareness assessment

Study number:

Date …/……/…..…..

First visit☐ OR Second visit ☐

I am now going to ask you some pretty difficult questions about the possibility of death from your cancer.

If you wish, you do not have to answer the questions

1. I am going to read four statements about the possibility of cancer causing your death. I would like you to tell me which of the four statements best describes your feelings as to the chances of your death occurring from your cancer. *[Read the statements and then code on the table below]*
2. Now I would like you to tell me which of the four statements best describes your feelings as to the chances of your death occurring from your cancer within the next 5 years. *[Read the statements and then code on the table below]*
3. Lastly please tell me which of the four statements best describes your feelings as to the chances of your death occurring from your cancer within the next year. *[Read the statements and then code on the table below]*

Probability	**Open**	**5 years**	**1 year**
It is not possible	4 ☐	4 ☐	4 ☐
It is improbable	3 ☐	3 ☐	3 ☐
It is probable	2 ☐	2 ☐	2 ☐
It is certain	1 ☐	1 ☐	1 ☐
Declined to answer	☐	☐	☐

NB: If a patient declines to answer the question(s) note the reason below – it will **EXCLUDE** them from the study. Please inform the patient that their contributions cannot be included in the study if they don’t answer all three questions; however also remind them that as undertaken in the information page as well as the informed consent document they have the right to choose not to answer a question if they wish not to.

…………………………………………………………………………………………

Diagnosis:……………………. Stage………………………… ECOG PS……..

Consultant and literature guided prognosis and relevant timeframe

5yr: certain ☐ / probable ☐ / improbable ☐

1yr: certain ☐ / probable ☐ / improbable ☐

Appendix H - Serious illness conversation guide

Set up the conversation - ASK

- ☐ I'm hoping we can talk about where things are with your illness and where they might be going — **is this okay**

Assess understanding and preferences - ASK

- ☐ What is **your understanding** now of where you are with your illness?
  assess using prognostic awareness assessment - (Appendix 1)
- ☐ How much **information** about what is likely to be ahead with your illness would you like from me?

Share prognosis - TELL

- ☐ I want to share with you **my understanding** of where things are with your illness...
- ☐ UNCERTAIN PROGNOSIS
  It can be difficult to predict what will happen with your illness. I hope you will continue to live well for a long time but I'm worried that you could get sick quickly, and I think it is important to prepare for that possibility.
- ☐ TEMPORAL PROGNOSIS
  "I wish we were not in this situation, but I am worried that time may be as short as _____ (*express as a range, e.g. days to weeks, weeks to months, months to a year*)
- ☐ FUNCTIONAL PROGNOSIS
  I hope that this is not the case, but I'm worried that this may be the best health you're likely to be in, and that things are likely to get more difficult.

Explore key topics - ASK

- ☐ What would be most important for you to achieve if your health situation worsens?
- ☐ What are your biggest fears and worries about the future with your health?
- ☐ What gives you strength as you think about the future with your illness?
- ☐ What abilities are so important to your life that you can't imagine living without them?
- ☐ If you become sicker, how much are you willing to go through for the possibility of gaining more time?
- ☐ How much does your family know about your priorities and wishes?

Wrap up

- ☐ I've heard you say that ___ is really important to you. Keeping that in mind, and what we've been talking about, at this stage, the best plan for your care is …………………
- ☐ What are your thoughts on that?
- ☐ I will do everything I can to help you through this

Appendix I : instructions to authors : South African Journal of Oncology

Overview

The author guidelines include information about the types of articles received for publication and preparing a manuscript for submission. Other relevant information about the journal's policies and the reviewing process can be found under the about section. The **compulsory cover letter** forms part of a submission and must be submitted together with all the required **forms.** All forms need to be completed in English.

Original Research Article

An original article provides an overview of innovative research in a particular field within or related to the focus and scope of the journal, presented according to a clear and well-structured format. Systematic reviews should follow the same basic structure as other original research articles. The aim and objectives should focus on a clinical question that will be addressed in the review. The methods section should describe in detail the search strategy, criteria used to select or reject articles, attempts made to obtain all important and relevant studies and deal with publication bias (including grey and unpublished literature), how the quality of included studies was appraised, the methodology used to extract and/or analyse data. Results should describe the homogeneity of the different findings, clearly present the overall results and any meta-analysis.

Word limit	3500-4000 words (excluding the structured abstract and references)
Structured abstract	250 words to include a Background, Aim, Setting, Methods, Results and Conclusion
References	60 or less
Tables/Figures	no more than 7 Tables/Figure
Ethical statement	should be included in the manuscript
Compulsory supplementary file	ethical clearance letter/certificate

Cover Letter

The format of the compulsory cover letter forms part of your submission. Kindly download and complete, in English, the provided **cover letter**.

Anyone that has made a significant contribution to the research and the paper must be listed as an author in your cover letter. Contributions that fall short of meeting the criteria as stipulated in our policy should rather be mentioned in the 'Acknowledgements' section of the manuscript. Read our **authorship** guidelines and **author contribution** statement policies.

Original Research Article full structure

Title:

- Full title: Specific, descriptive, concise, and comprehensible to readers outside the field. Max 95 characters (including spaces).
- Tweet for the journal Twitter profile: This sentence/statement will be used on the journal Twitter profile to promote your published article. Max 101 characters (including spaces). If you have a Twitter profile, please provide us your Twitter @ name. We will tag you to the Tweet.

Abstract: The Abstract should provide the context or background for the study and should state the study's purpose, basic procedures (selection of study participants, settings, measurements, analytical methods), main findings (giving specific effect sizes and their statistical and clinical significance, if possible), and principal conclusions. The Abstract should not exceed 250 words. Please minimize the use of abbreviations and do not cite references in the abstract. Refer to the relevant article type's guideline you are submitting for the abstract sections.

Introduction: The Introduction should put the focus of the manuscript into a broader context and explain its social and scientific value. Address this to readers who are not experts in this field and include a brief review of the key literature. If there are relevant controversies or disagreements in the field, they should be mentioned. Conclude with a brief statement of the overall aim of the experiments and a comment about whether that aim was achieved. Cite only directly pertinent references, and do not include data or conclusions from the work being reported.

Methods: The Methods section should provide clarity about how and why a study was done in a particular way. It should provide enough detail for reproduction of the findings. Protocols for new methods should be included, but well-established methodological procedures may simply be referenced. A full description of the methods should be included in the manuscript itself rather than in a supplemental file. Only information that was available at the time the plan or protocol for the study was being written must be included; all information obtained during the study belongs in the Results section. If an organization was paid or otherwise contracted to help conduct the research (examples include data collection and management), then this should be detailed in the methods.
The methods section should include:

- The selection and description of participants or description of materials.
- The aim, design and setting of the study.
- The description of the processes, interventions and comparisons. Generic drug names should generally be used. When proprietary brands are used in research, include the brand names in parentheses.
- The type of statistical analysis used, including a power calculation if appropriate.
  The Methods section should include a statement indicating that the research was approved or exempted from the need for review by the responsible review committee (institutional or national). If no formal ethics committee is available, a statement indicating that the research was conducted according to the principles of the Declaration of Helsinki should be included.

  Results: Present your results in logical sequence in the text, tables, and figures, giving the main or most important findings first. Do not repeat all the data in the tables or figures in the text; emphasize or summarize only the most important observations. Provide data on all primary and secondary outcomes identified in the Methods Section. Give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical significance attached to them, if any. Restrict tables and figures to those needed to explain the argument of the paper and to assess supporting data. Use graphs as an alternative to tables with many entries; do not duplicate data in graphs and tables. Avoid nontechnical uses of technical terms in statistics, such as "random" (which implies a randomizing device), "normal," "significant," "correlations," and "sample." Separate reporting of data by demographic variables, such as age and sex, facilitate pooling of data for subgroups across studies and should be routine, unless there are compelling reasons not to stratify reporting, which should be explained.

  Conclusion: It is useful to begin the discussion by briefly summarizing the main findings, and explore possible mechanisms or explanations for these findings. Emphasize the new and important aspects of your study and put your findings in the context of the totality of the relevant evidence. State the limitations of your study, and explore the implications of your findings for future research and for clinical practice or policy. Discuss the influence or association of variables, such as sex and/or gender, on your findings, where appropriate, and the limitations of the data. Do not repeat in detail data or other information given in other parts of the manuscript, such as in the Introduction or the Results section.Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, distinguish between clinical and statistical significance, and avoid making statements on economic benefits and costs unless the manuscript includes the appropriate economic data and analyses. Avoid claiming priority or alluding to work that has not been completed. State new hypotheses, when warranted and label them clearly.

  Acknowledgements: Those who contributed to the work but do not meet our authorship criteria should be listed in the Acknowledgments with a description of the contribution. Authors are responsible for ensuring that anyone named in the Acknowledgments agrees to be named. Refer to the acknowledgement structure guide on our *Formatting Requirements* page.

  Also provide the following, each under their own heading:

- Competing interests: This section should list specific competing interests associated with any of the authors. If authors declare that no competing interests exist, the article will include a statement to this effect: *The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article.* Read our **policy on competing interests**.
- Author contributions: All authors must meet the criteria for authorship as outlined in the **authorship** policy and **author contribution** statement policies.
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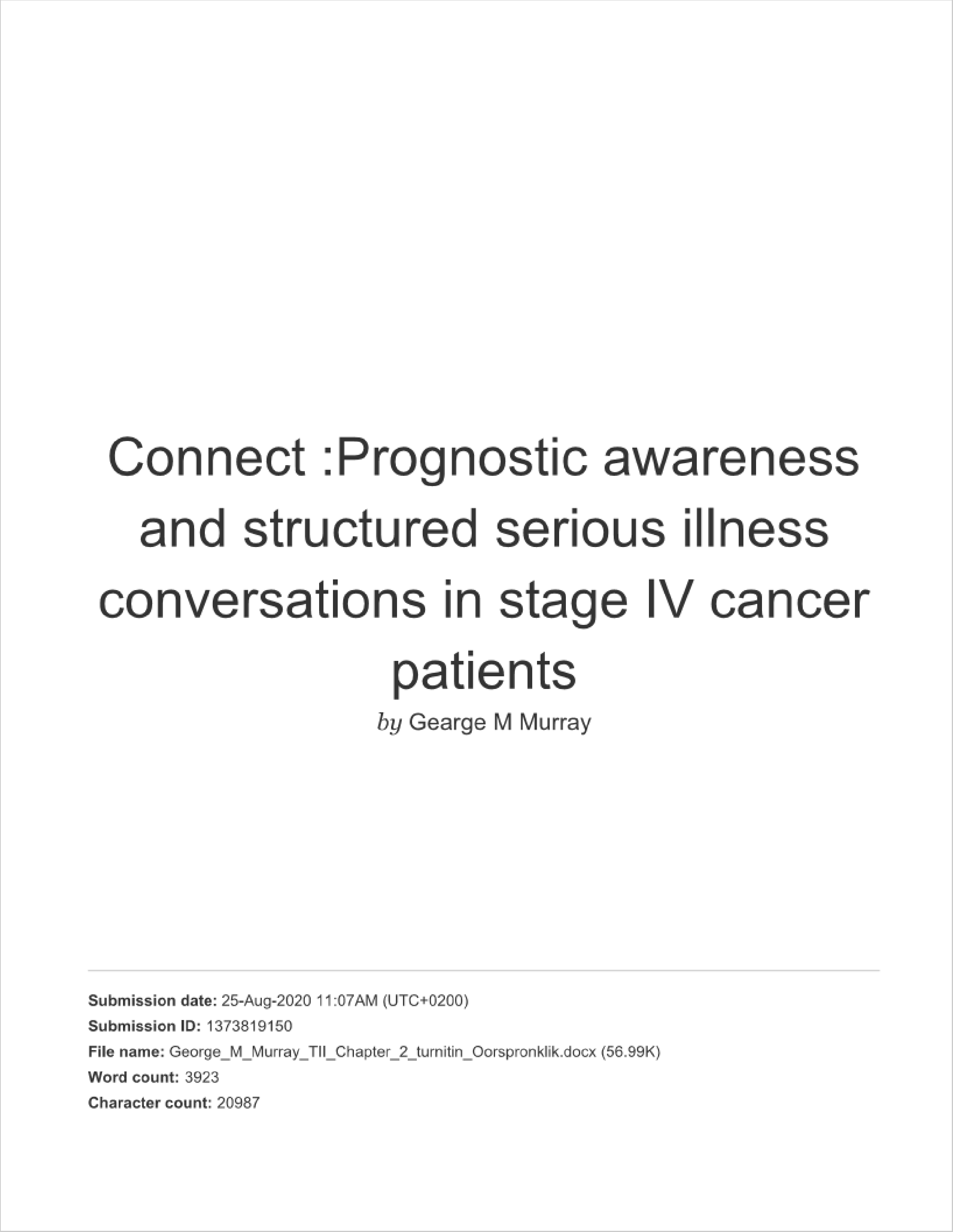
- Data availability: All research articles are encouraged to have a data availability statement.
- Disclaimer: A statement that the views expressed in the submitted article are his or her own and not an official position of the institution or funder.
  References: Authors should provide direct references to original research sources whenever possible. References should not be used by authors, editors, or peer reviewers to promote self-interests. Refer to the journal referencing style downloadable on our *Formatting Requirements* page.

Appendix J : Turnitin report



Connect :Prognostic awareness and structured serious illness conversations in stage IV cancer patients

by Gearge M Murray

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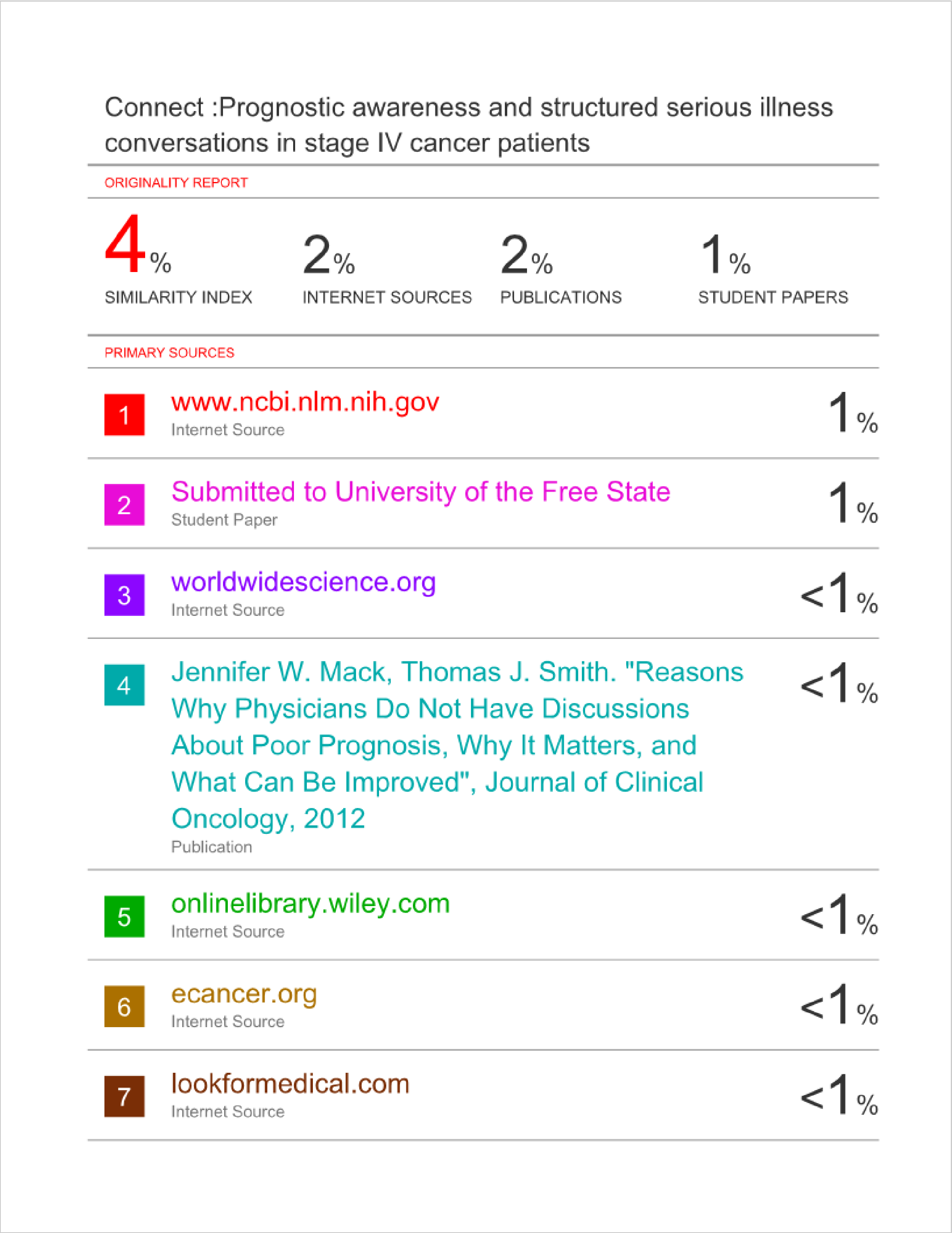

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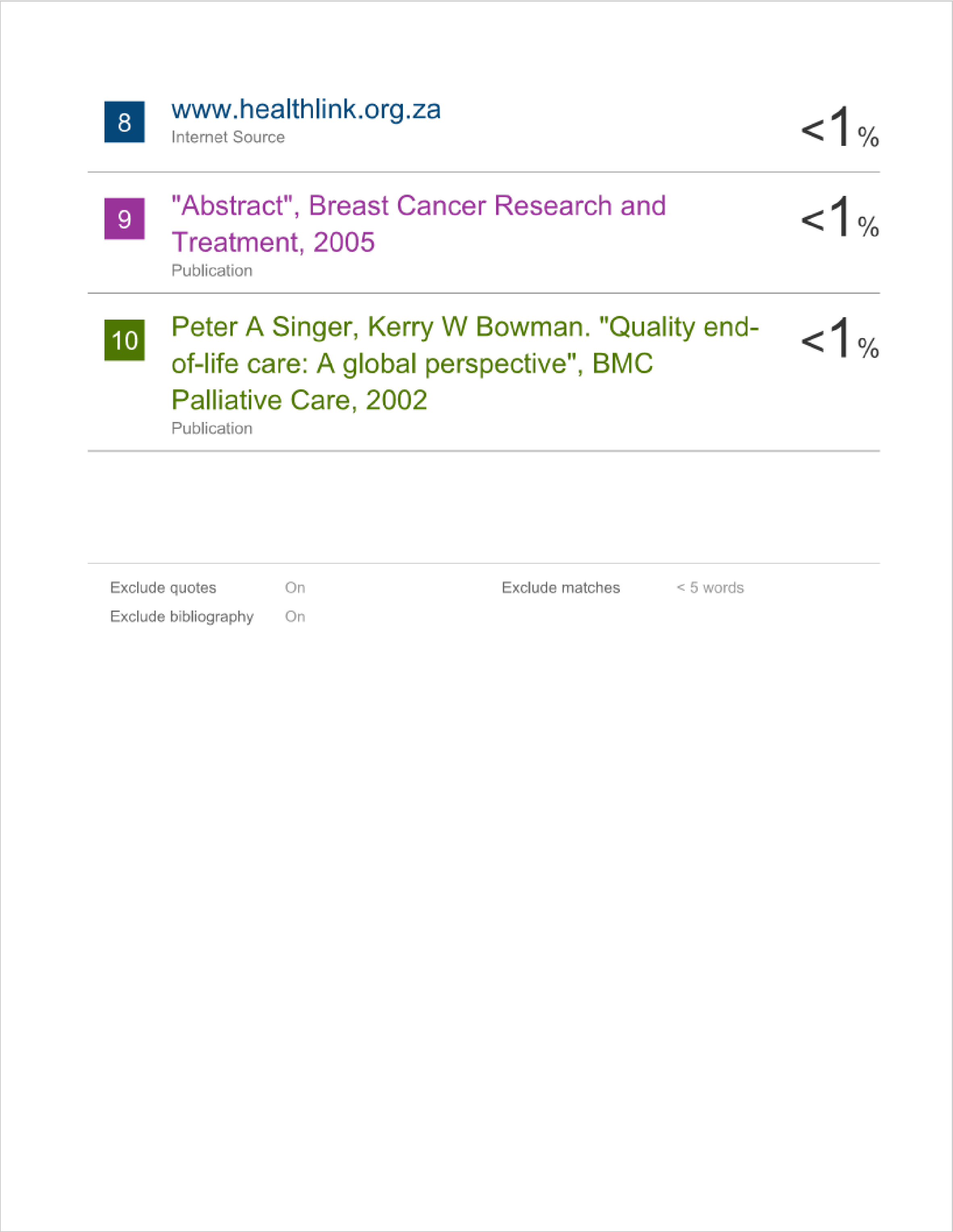

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