Support Care Cancer (2012) 20:2755–2764
DOI 10.1007/s00520-012-1397-8

ORIGINAL ARTICLE

Health-related quality of life anticipated with different management strategies for febrile neutropenia in adult cancer patients

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Received: 3 August 2011 / Accepted: 25 January 2012 / Published online: 17 February 2012

Abstract
Purpose To describe anticipated health-related quality of life (HRQL) for different hypothetical strategies of febrile neutropenia (FN) management in adult cancer patients.
Methods Seventy-eight adult cancer patients were enrolled. Our study considered four different hypothetical treatment strategies for FN: (1) entire inpatient management with intravenous (IV) antibiotics; (2) oral treatment at home after an initial observation in hospital with IV antibiotics; (3) entire outpatient management with IV antibiotics; and (4) entire outpatient management with oral antibiotics. Initially, patients were asked to rank the different treatment strategies for FN based on their personal preference. Subsequently, HRQL was rated using visual analog scale (VAS), time trade-off (TTO), and willingness-to-pay (WTP).
Results Seventy-five percent of all respondents preferred an outpatient strategy for FN (36% oral, 21% intravenous, 18% early discharge). Further, outpatient strategies were associated with higher mean VAS scores (possible range 0–10) (oral: 6.1 (standard deviation (SD) 3.1); intravenous: 6.2 (SD 2.2); early discharge: 5.7 (SD 2.1)) as compared to inpatient care (5.3 (SD 2.9)). On the aggregate level, patients were willing to give up between 9 and 10 weeks of their life (TTO; corresponding to <1% of remaining life expectancy) and to pay between $255 and $327 Canadian dollars (WTP) to avoid treatment in hospital.
Conclusions Our study indicates that the majority of adult cancer patients would prefer an outpatient strategy for FN. However, patients' preferences vary substantially at the individual level. Implementation of outpatient strategies into routine clinical practice should consider this variability.

Keywords Fever · Neutropenia · Quality of life · Patient preference · Outpatients

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Introduction

Febrile neutropenia (FN) remains a frequent complication of chemotherapy for patients with cancer despite recent advances in infection prevention [1]. For many decades, the standard treatment of FN had been inpatient management with broad-spectrum intravenous (IV) antibiotics for all patients [2]. It is now well-recognized, however, that patients with FN are a heterogeneous population, with only a small proportion developing a serious medical complication [3]. Consequently, current national and international guidelines

have endorsed less aggressive empiric antibiotic strategies, including outpatient and/or oral (PO) antibiotic regimens, for adult cancer patients with low-risk FN [2, 4, 5].

Outpatient strategies may be broadly divided into those in which patients are admitted for a short period of hospitalization followed by early discharge, or those in which patients are discharged home the same day following a brief baseline assessment without hospitalization. Outpatient treatment of FN, either early discharge or entirely outpatient management, is attractive for a number of reasons including reduced risk of healthcare-related infection and considerable cost savings, as the major financial burden of conventional FN management is the cost of inpatient care [6, 7].

A recent survey among American physicians revealed that 82% of respondents use outpatient antibiotics for selected low-risk FN patients, indicating a substantial change in clinical practice over the last few years [8]. These data suggest that outpatient management is a popular approach for physicians. However, reports in the literature are sparse about the patient's perspective, and no study, thus far, has systematically assessed patients' preferences in regard to different outpatient strategies for FN [9–11]. We believe that this information is important, since different treatment strategies for FN may be associated with different profiles of short-term and long-term expected health-related quality of life (HRQL). Optimal decision-making requires an understanding of expected health during these different treatment strategies in addition to knowledge of probabilities of treatment success and valuation of different outcomes from the patient and healthcare provider perspectives [12]. Both validated scaling techniques (i.e., time trade-off (TTO), willingness-to-pay (WTP)) and rating scales (i.e., visual analog scale (VAS)) can be used to describe expected HRQL (or preferences) for health states [13, 14].

The primary objective of this study was to describe anticipated HRQL for different strategies of FN management in adult cancer patients. Our hypothetical strategies included entire inpatient management, treatment at home after an initial observation in hospital, entire outpatient management with IV antibiotics, and entire outpatient management with PO antibiotics. The secondary objective was to describe characteristics of patients who preferred inpatient management of FN.

Methods

Participants

Preferences were elicited from adult patients receiving active treatment for cancer at a large tertiary care adult cancer center (Princess Margaret Hospital (PMH), Toronto, Canada). We recruited eligible participants in a consecutive fashion from the outpatient clinics and inpatient units (enrollment period July 1–August 31, 2009). There was no limitation by age, and a current episode of FN was not mandatory. Patients who could not read English and patients receiving hematopoietic stem cell transplantation were excluded. The Research Ethics Boards at PMH approved the study and all respondents provided written informed consent.

Initially, we collected demographic data of each patient and assessed HRQL at the time of the interview using a VAS. For the VAS, respondents were asked to mark their current HRQL on a horizontal 10-cm line anchored at the left end by the worst possible health or death (score of 0) and at the right end by perfect health (score of 10). In addition, we used the Health Utilities Index (HUI) to describe the respondent's current HRQL (HUI2/3, 40-item questionnaire, interview-administered; Health Utilities Inc., Dundas, Canada) [15]. The HUI is a family of multi-attribute health status classification systems which currently consists of two complementary systems, HUI2 and HUI3 [16]. HUI2 is composed of seven attributes: sensation, mobility, emotion, cognition, self-care, pain, and fertility. HUI3 is composed of eight attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain. Health states defined by a comprehensive set of HUI levels can be used to determine individual-attribute and overall utility scores.

Hypothetical scenarios

Our primary objective was to describe anticipated HRQL/preferences from adult cancer patients with respect to four hypothetical FN management strategies. We considered options for FN management that we believed to be most likely to be adopted in clinical practice in adult oncology. These options were (1) entire inpatient management with IV antibiotic administration (HospIV); (2) early discharge (within 24–48 h) with initial inpatient IV antibiotic administration followed by PO outpatient antibiotic administration (EarlyDC); (3) entire outpatient management with IV antibiotics (HomeIV); and (4) entire outpatient management with PO antibiotic administration (HomePO). The attributes related to the four scenarios were presented to the respondents and are illustrated in Table 1. The attributes in the scenarios were obtained from a literature review considering both randomized controlled trials and observational studies [17–27]. Hypothetical scenarios were presented to the respondents because the current clinical practice at PMH does not include all four FN treatment strategies.

Experimental maneuver

Trained research assistants conducted face-to-face interviews with the respondent using standardized scripts and props that had been extensively pilot-tested prior to implementation

Table 1 Hypothetical scenarios for management of febrile neutropenia

Strategy 1–Entire inpatient management
Admission in hospital with intravenous antibiotics; CBC blood testing 3× per week; if initial blood cultures are negative, patient is discharged after fever resolves and blood counts recover; probability of complications leading to intensive care unit (ICU) admission is 2 in 100 patients; probability of mortality is 1 in 100 patients
Strategy 2–Early discharge strategy
Admission in hospital with intravenous antibiotics; early discharge within 24–48 h with oral antibiotics (two antibiotics given 2–3× per day) if blood culture is negative and patient is feeling well; clinic visits for follow up and CBC blood testing 3× per week; once discharged, if patient is feeling unwell, they must return to the emergency department; probability of re-admission is 5 in 100 patients; probability of complications leading to intensive care unit (ICU) admission is 2 in 100 patients; probability of mortality is 1 in 100 patients
Strategy 3–Outpatient management with parenteral antibiotics
No initial hospitalization, but blood culture and CBC will be drawn; discharge home with intravenous antibiotics; home care nurse will come to patient's home and administer two antibiotics once daily; clinic follow up and CBC blood testing 3× per week; if the blood culture comes back positive OR if fever persists OR if the patient becomes unwell, the patient must return and be admitted to hospital; probability of admission is 5 in 100 patients; probability of complications leading to intensive care unit (ICU) admission is 2 in 100 patients; probability of mortality is 1 in 100 patients
Strategy 4–Outpatient management with oral antibiotics
No initial hospitalization, but blood culture and CBC will be drawn; discharge home with two oral antibiotics to be taken 2–3× per day; clinic follow up and CBC blood testing 3× per week; if the blood culture comes back positive OR if fever persists OR if the patient becomes unwell OR the patient cannot tolerate oral antibiotics, the patient must return and be admitted to hospital; probability of admission is 10 in 100 patients; probability of complications leading to intensive care unit (ICU) admission is 2 in 100 patients; probability of mortality is 1 in 100 patients

(among involved researchers, naïve research colleagues, and by-proxy among parents of children with cancer (see Appendix: Interview Script)). Respondents were asked to imagine that they had FN that could be treated in one of the four ways described in the previous paragraph. The scenarios were explained in detail to the respondents. In addition to verbal description of the scenarios (Table 1), the research assistants used visual aid boards to facilitate understanding of the scenarios. It was emphasized that these scenarios were hypothetical and that some management options might not be appropriate for them.

In the first step, the respondents were asked to simply rank the four scenarios from 1 to 4 based on their personal preference. In the second step, the respondents quantified their HRQL/preferences for the different FN management strategies in more detail using VAS, TTO and WTP approaches. The order of presentation of VAS, TTO, and WTP was fixed.

VAS Participants were asked to estimate their anticipated HRQL/preference for each strategy by drawing a vertical line across a horizontal 10-cm VAS anchored at the left end by the worst possible HRQL (score of 0) and at the right end by perfect HRQL (score of 10) [28, 29].

TTO We used the TTO technique to determine how much of their remaining life a patient would be willing to give up to avoid inpatient treatment for FN [10, 30–32]. Scenario A (HospIV; see Table 1), in which they would live x years (actual age subtracted from normal life expectancies, e_x, which was determined using Statistics Canada "Life Tables", Canada, 1995–1997), was presented to the respondents. In Scenario B (one of the three outpatient strategies; see Table 1), they would live that same number of years. Since we assumed that respondents would prefer a non-inpatient strategy, Scenario B (encompassing one FN episode) was then sequentially altered with different proportions of time followed by death using a ping-pong and then a titration approach, while Scenario A remained at x years until the point of indifference was reached. The point of indifference reflected the amount of time respondents would be willing to give up in order to receive an alternative FN management strategy. This maneuver was then repeated for the two other non-inpatient strategies, again relative to Scenario A.

WTP Another measure of a respondent's preference for a management strategy is how much they would be willing to pay to receive that strategy [33, 34]. Similar to the TTO approach, we assumed that HospIV was the standard approach. Then, using a WTP visual aid board, we asked participants to state how much they would be willing to pay to receive one of the three alternative management strategies for FN. In detail, participants were asked if they would choose to have the alternative treatment if it were free. If they responded yes, they were asked if they would pay $1,000 CAD. If they responded no, we asked if they would pay $100 CAD. If they would not pay $100 CAD, we titrated up from zero by $20 CAD increments. If they would pay $100 CAD, we titrated up by increments of $100 CAD, and then $20 CAD. If participants were willing to pay $1,000 CAD, we titrated up by $1,000 CAD, then $100 CAD, then $20 CAD.

Predictors of preferences

Our secondary objective was to determine predictors of preference for inpatient management. The following variables were examined as potential predictors: age, gender, marital status, educational status, employment status, health benefit plan, income, travel time to hospital, history of FN, diagnosis, and current HRQL estimate.

Statistical analyses

The primary objective was descriptive. In order to compare the four different management strategies for VAS, WTP and TTO within each respondent type, we conducted repeated measures of linear regression. Univariate logistic regression was used to determine predictors of preference for inpatient management (secondary objective). This was accomplished by dichotomizing responses to whether inpatient management was ranked first versus any other management strategy. All statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA). All significance tests were two-sided, and statistical significance was defined as $P < 0.05$.

Results

A total of 107 adult cancer patients were identified for participation in the study. Of the identified patients, six were excluded because they did not meet the inclusion criteria. Of the 101 patients approached, 23 declined to participate. Demographic and disease characteristics of the 78 participants, together with HRQL scores at the time of the interview, are given in Table 2.

Ranking lists for treatment preferences are shown in Fig. 1. Seventy-five percent of all respondents preferred some kind of outpatient management; thus, only one in four patients would choose traditional inpatient care for FN. Although HomePO was most commonly ranked first, a substantial fraction of respondents preferred one of the other two outpatient strategies (see Fig. 1).

As outlined in Table 3, all three outpatient strategies were associated with higher mean VAS scores as compared to entire inpatient care. While these data reflect the aggregate level, they also reveal a wide dispersion of scores (maximum range for all strategies between 9 and 10) indicating substantial variation at the individual level. We further used a TTO approach to determine how much remaining life patients would be willing to give up to avoid inpatient care. There was no substantial difference between the three outpatient strategies with TTO values between 9 and 10 weeks (approximates 0.18 years) (see Table 3). Based on the average age of 54 years in our cohort with a life expectancy of an additional 29 (females) and 25 years (males) (Statistics Canada "Life Tables", Canada, 1995–1997), this means that patients would, on average, give up less than one percent of their remaining lifetime to avoid inpatient care for FN. Similar findings were observed using a WTP approach as shown in Table 3. WTP thresholds for all three alternative outpatient strategies did not differ substantially (mean threshold values between $255 CAD and $327 CAD). However, whereas some patients would not be willing to pay anything to avoid inpatient care, the maximum WTP score to receive IV treatment at home instead of IV treatment in hospital was $4,500.

Table 2 Baseline characteristics

	Patients (n =78)
Respondent variables	
Mean age in years (range) [a]	54.3 (20–88)
Male (%)	32 (41.0)
Married (%)	53 (67.9)
Education (%)	
Professional/graduate	11 (14.1)
College/university	39 (50.0)
High school	24 (30.8)
Primary/middle school	1 (1.3)
Full time employment (%)[b]	34 (47.2)
Health benefit plan[a]	54 (70.1)
Annual income ≥$60,000 (%) [c]	35 (66.0)
Median travel time to hospital, minutes (range)	48 (290)
Febrile neutropenia experience and cancer variables	
History of FN (%)[d]	14 (18.4)
Cancer type (%)	
Genital cancer	21 (26.9)
Gastrointestinal cancer	17 (21.8)
Leukemia	14 (17.9)
Lymphoma	7 (9.0)
Breast cancer	7 (9.0)
Multiple myeloma	3 (3.8)
Lung cancer	3 (3.8)
Other malignancy	6 (7.7)
Relapsed disease (%)	26 (33.3)
Current quality of life estimates	
Mean VAS score (range)	6.3 (1.8–10)
Mean HUI2 score (range)[e]	0.79 (0.18–1)
Mean HUI3 score (range)[e]	0.73 (0.04–1)

SD standard deviation, *FN* febrile neutropenia, *VAS* visual analog scale, *HUI* health utilities index

[a] missing for one patients

[b] missing for six patients

[c] missing for five patients, 20 patients did not disclose

[d] missing for two patients

[e] missing for eight patients

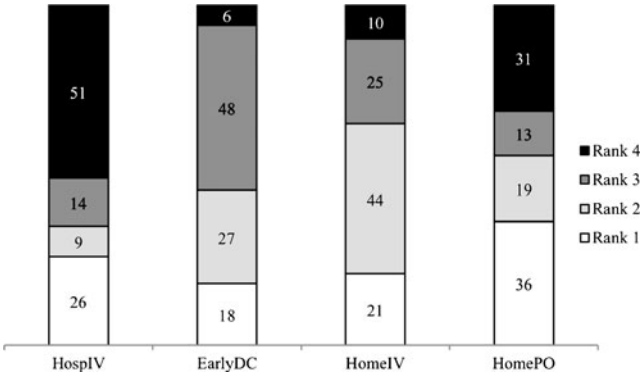

Fig. 1 This stacked column chart shows how each treatment option was ranked by the respondents. A rank of 1 reflected the most preferred option while a rank of 4 reflected the least preferred option. The proportions (percentages) of each rank on the aggregate level are displayed within the columns. *HospIV* indicates entire inpatient management with intravenous antibiotics; *EarlyDC*, oral treatment at home after an initial observation in hospital; *HomeIV*, outpatient management with intravenous antibiotics; *HomePO*, outpatient management with oral antibiotics

Finally, several demographic factors and disease specific variables were tested whether they predicted treatment preference (logistic regression). However, none of the tested variables was a statistically significant predictor of preference for inpatient management. Odds ratios and corresponding *P* values for all variables are shown in Table 4.

Discussion

In some centers, outpatient management for cancer patients with low-risk FN has been implemented into routine clinical practice [4, 5]. However, a systematic assessment of patients' preferences in regard to outpatient strategies has not previously been conducted. Our study is important because it is the first study, to our knowledge, to quantitatively describe anticipated HRQL estimates for different outpatient strategies for FN in adult cancer patients. Our data suggest that outpatient strategies appear acceptable to the majority of patients. However, our findings also reveal that patients' preferences vary substantially at the individual level, with one in four patients still preferring traditional inpatient care.

We assessed preferences in the following two ways: (1) by asking respondents to rank their preferred strategy and (2) by asking them to describe their anticipated HRQL with each strategy. Seventy-five percent of all respondents preferred an outpatient strategy for FN. This is consistent with

Table 3 Anticipated health-related quality of life estimates for different treatment strategies for febrile neutropenia

	Mean score (SD)	Range	Respondents	Statistics
Visual analog scale				
HospIV	5.3 (2.9)	0.4–10	76	N.S.
EarlyDC	5.7 (2.1)	1.0–10	76	
HomeIV	6.2 (2.2)	0.3–10	76	
HomePO	6.1 (3.1)	0.0–10	76	
Time trade-off (weeks)				
HospIV	Reference	–	–	
EarlyDC	9.1 (34.4)	0–260	70	N.S.
HomeIV	9.6 (34.7)	0–260	69	
HomePO	9.3 (34.6)	0–260	69	
Willingness-to-pay (CAD)				
HospIV	Reference	–	–	
EarlyDC	282 (391)	0–2,000	75	N.S.
HomeIV	327 (608)	0–4,500	74	
HomePO	255 (371)	0–1,500	72	

SD standard deviation, *CAD* Canadian dollars, *HospIV* indicates entire inpatient management with intravenous antibiotics, *EarlyDC* oral treatment at home after an initial observation in hospital, *HomeIV* outpatient management with intravenous antibiotics, *HomePO* outpatient management with oral antibiotics,

Reference indicates that HospIV is the baseline comparator for the other treatment strategies, *N.S.* indicates "not significant" (*F*-statistic; repeated measures analysis)

Table 4 Univariate logistic regression: Predictors of preference for inpatient treatment

	OR (95% CI)	*P* value
Respondent variables		
Age >55 years	0.78 (0.28–2.17)	0.64
Male	0.71 (0.25–2.04)	0.53
Married	1.14 (0.38–3.42)	0.82
University or higher degree	0.81 (0.27–2.41)	0.71
Full time employment	1.98 (0.54–7.31)	0.31
Health benefit plan	2.00 (0.59–6.82)	0.27
Annual income ≥$60,000	1.40 (0.37–5.30)	0.62
Travel time to hospital ≥50 min	1.61 (0.58–4.49)	0.36
Febrile neutropenia experience and cancer variables		
History of FN in the past	0.78 (0.19–3.17)	0.73
Diagnosis of leukemia, lymphoma, or myeloma	2.35 (0.81–6.76)	0.11
Relapsed disease	0.81 (0.27–2.44)	0.71
Current quality of life estimates		
Visual analog scale score	1.00 (0.79–1.27)	0.99
Health Utilities Index 2	0.84 (0.03–21.91)	0.92
Health Utilities Index 2	0.71 (0.08–5.95)	0.75

CI confidence interval, *OR* indicates odds ratio and refers to probability of preferring inpatient rather than outpatient treatment (outpatient = early discharge, intravenous treatment at home, or oral treatment at home), *Binary dummy variables* were created for predictor variables (e.g., male versus female; age >55 years versus age ≤55 years, diagnosis of leukemia, lymphoma, or myeloma versus other cancer types, etc)

our findings that outpatient strategies were also associated with higher mean VAS scores as compared to inpatient care. However, it is important to note that these observations were made on the aggregate level; thus, conclusions for individualized patient care have to be drawn very carefully. It is possible that some patients may prefer one strategy but would rate anticipated HRQL higher for another strategy since other considerations such as feeling safe, convenience and costs could also be contributing to the choice of the most preferred strategy. Further, we attempted to determine which factors predicted patients' preferences for FN management. However, none of the tested variables could predict whether patients preferred inpatient or outpatient care. It is possible that this is related to the fact that we investigated a very heterogeneous cohort in terms of underlying disease and demographic variables. Given the complexity of decision-making, we cannot exclude that the study was underpowered to address our secondary objective.

None of the three outpatient strategies clearly dominated among respondents. Perhaps this finding is not surprising, since preferences for drug administration and/or an initial observation period in hospital may vary among patients. Two different scaling techniques, namely TTO and WTP, were used to further gain information about anticipated HRQL comparing the three different outpatient strategies. However, on the aggregate level, there were no substantial differences between the three strategies when we asked the respondents (1) how much time of their remaining life expectancy they would give up, and (2) how much they would be willing to pay to avoid one episode of FN treated as inpatients and to be treated in one of the alternative outpatient strategies. There are several possible explanations for these results. First, differences for preferences may indeed be very small; second, aggregate data might obscure differences on the individual level; and third, scaling techniques such as TTO and WTP may not be sensitive enough to detect differences. Our data revealed that respondents were not willing to give up more than one percent of their remaining lifetime to avoid inpatient care, indicating that TTO with a death baseline might not be an appropriate technique to elicit preferences for transient, non-fatal health states [35]. TTO techniques with a non-death baseline or conjoint analysis to estimate healthy-time equivalents for acute conditions might be alternative approaches to be considered for future research [36]. Beyond our findings, WTP techniques may also help to measure anticipated HRQL for acute conditions. However, WTP data have to be interpreted carefully, taking different individual economic resources and economic environments into account [37].

It would have been desirable to obtain utilities for all four treatment strategies. Thus, we initially attempted to measure absolute values for TTO and WTP for all options. However, given the short-term nature of FN, pilot testing illustrated that respondents were unable to conceptualize absolute TTO/WTP values for the four different strategies. Thus, we modified the scaling techniques to obtain relative preference scores for the three outpatient strategies. As such, these values cannot be considered utilities which could be used, for example, in economic evaluations such as cost–utility analyses [38].

There are several important limitations in our study. First, our center had not implemented different outpatient strategies into routine clinical practice when this study was conducted. Even though our scenarios were meant to be hypothetical, it is possible that experience with alternate strategies could change patients' perspectives. Second, attributes related to the hypothetical strategies as described in Table 1 may differ from center to center in real clinical practice, and our estimates may not accurately reflect differences between strategies. We performed a systematic literature review to include data from randomized controlled trials [27]. In addition, information from observational studies was included to use the best available evidence to generate the hypothetical scenarios. However, published literature directly comparing various FN strategies is somewhat sparse. Third, only English-speaking participants were included into our study, and perspectives of non-English-speaking patients could be very different. Fourth, all patient types were included in our study. We did not restrict our sample to diagnoses compatible with low-risk FN. However, in our study, diagnosis type did not appear to impact on the preferred strategy, and scenarios were meant to be hypothetical rather than reflect the patient's own situation. Fifth, sample size was modest, and results may be limited in detecting small differences between certain groups (e.g. prior history of FN). Sixth, study design did not consider preferences on avoidance of FN episodes altogether. To our knowledge, so far, no studies have been published reporting the value of avoidance of FN episodes. Such data would definitely help to better conceptualize our findings (i.e., we could learn what the value of avoiding FN is versus the incremental value of different treatment strategies). In the absence of directly measuring respondents' preferences on avoiding FN altogether, our study design may have inflated the differences between FN management strategies. We think that future research is warranted to explore this important issue. Finally, respondents may answer in different ways at different treatment centers or geographic regions. Thus, our study requires confirmation in other settings prior to assuming external validity.

Our findings indicate that outpatient management for FN would be an acceptable alternative to traditional inpatient care for the majority of patients. However, aggregate data might obscure the observation that individual preferences may substantially differ from the average estimation. Thus, we advocate that healthcare providers in centers that implement outpatient care for FN should carefully assess individual preferences to guarantee an optimal decision-making process,

which may improve patient satisfaction and treatment adherence [39]. Finally, more research is necessary to measure HRQL in patients who actually experience FN episodes in different treatment settings. We suggest that large observational studies from a variety of health settings would substantially add information to this area. Additional insights around FN treatment preferences may be gained from qualitative approaches involving cancer patients.

Funding Source A bursary from the Swiss Cancer League supports OT; LS is supported by a New Investigator Award from the Canadian Institutes of Health Research (Grant No. 87719)

Conflicts of interest SMHA is a Research Scientist of the Canadian Cancer Society. There is no financial disclosure from any author

Appendix: Interview Script

Introduction

Good morning/afternoon. My name is _____ and I am a research student that is working on a research study with Dr. Sung, one of the Oncologists at The Hospital for Sick Children, and with Dr. Alibhai, one of the physicians at the Princess Margaret Hospital. I was hoping to take a few minutes of your time to tell you about this study to see if you would be interested in participating.

The research study is about febrile neutropenia in both pediatric and adult cancer patients. Our aim is to assess the health-related quality of life in patients who are or may be treated for febrile neutropenia. Febrile neutropenia means that a person has a fever (likely due to some kind of infection) and they have a low neutrophil count. Neutrophils are a type of white blood cell that fights infection. You may or may not have experienced this before. Febrile neutropenia is taken seriously because the low neutrophil count could compromise the person's own ability to fight off infection. Thus, patients are usually admitted to hospital for intravenous antibiotics and close monitoring.

The study involves a 30-minute interview and filling in some questionnaires; it does not involve any blood tests, needles, or treatment. The purpose of our study is to try to understand how febrile neutropenia affects or may affect your quality of life. Your thoughts and experiences are valuable to us because we hope they will help us to develop better management options for the treatment and management of febrile neutropenia in the future for both children and adults. Do you think this is something you would like to participate in? **[YES/NO]**

If **NO:** That's alright. Thank you for your time!

If **YES: [Give them consent form]*****

This will describe in more detail the goals of our research study. I will leave this with you and give you a few minutes to read through and sign the consent form. There are no harms in participating in this study, and all the information you provide to us will be kept confidential. Whether you choose to participate or not, it will not affect the care you receive at this hospital. So please take your time, and I will come back in a few minutes (or later on during the day) and answer any questions you might have. When is the best time to carry out our interview? **[Make an appointment]**

Optional Review:*Our study will focus on how the management of febrile neutropenia may affect your quality of life. Febrile neutropenia is taken seriously because the low neutrophil count could compromise your own ability to fight off an infection. The current management of this condition usually requires hospital admission with intravenous. We are studying if there may be different management possibilities that would be equally as safe and efficacious, and are aiming to assess how it may affect your quality of life.*

Part I: Demographics

The first portion of this involves the completion of a demographics form. If there is any information you prefer not to disclose, please leave it blank. Remember, any information you will provide is confidential. [**Hand out Demographics Form]**

Part II: VAS Scale

This first exercise we are going to do is called a Visual Analogue Scale. **[Show VAS scale]** Now think about how your day-to-day life has been over the last 7 days. I am going to ask you to place straight line across this scale to show me how healthy you think you are. When I say health, I mean physical health, mental health and your ability to do your normal day to day tasks. The left side of the scale means that your current health is the worst possible health you could imagine, and the right side of the scale means that your current health state is considered the best possible health state you could imagine, or perfect health. Please draw a straight line across this scale to indicate what you think your current health state is.

Part III: Health Utilities Index (HUI)

Now you will be answering some questions from the Health Utilities Index. **[HUI]**

Part IV: Scenarios

All right. Now remember how I was talking about how I am studying fever neutropenia? I am going to talk about four different possible ways that fever neutropenia can be treated; some of them involve treatment in the hospital and some involve treatment at home **[show titles and pictures as go through].** The treatment option currently used involves staying in hospital to receive antibiotics through IV. I will call this treatment option Hospital IV. The second treatment option would consist of a short 1-2 day stay in hospital with IV antibiotics, followed by going home to receive antibiotics by mouth. I will call this treatment option Early Discharge. In the third situation you will be treated

entirely at home taking antibiotics by IV. I will call this treatment option Home IV. The last treatment option is also at home and involves taking antibiotics by mouth. I will call this treatment option Home Mouth. All of these treatment options last for the same amount of time. I will now give you a little more information on each treatment option **[present extra info]**. Possible reasons for re-admission are persistent or increasing fever, positive blood tests, and not being able to take the medications by mouth. There are also other differences between the four treatment options. For each treatment we will now look at the number of clinic visits required **[give clinic example]**, the chance of re-admission, the chance of ICU admission, which is intensive care unit and the chance of death. Do you have any questions?? **[present board information, say 1 green person out of 100]** (see Fig. 2)

*******[Reiterate all the information presented on the board/remind that Hospital IV is the only option that is currently used]********

[Make sure you emphasize the similarities and differences between each scenario]

i) *RANK ORDER*

Now that I have shown you these 4 scenarios, I would like you to take a moment to go over these scenarios again. Once you have familiarized yourself with these scenarios, I would like you to rank them according to your preference, 1 being most preferable to 4 being least preferable.

ii) *VAS*

Now we are going to use the Visual Analogue Scale again, and we are going to ask you about what you think your health state would be in these 4 different situations. Like the activity we did earlier, consider physical and mental health as part of your health state. The left side of the scale means that your current health is the worst possible health you could imagine, and the right side of the scale

Fig. 2 Board representing the different scenarios and associated event probabilities

means that your current health state is considered the best possible health state you can imagine, or perfect health. Please place a straight line through the scale to indicate what you think your current health state is in each situation #1 through 4.

Part V: Willingness to Pay

Now we are going to use the same treatment options we have been talking about to do an exercise called willingness to pay. We want to get an idea of your preference for the three potential future options **[point to Early Discharge, Home IV and Home Mouth]** compared to the currently used treatment option **[point to Hospital IV]**. In each situation you will imagine you have fever neutropenia and will be treated in hospital with IV antibiotics unless you are willing to pay money for a treatment option you prefer more.

Let's begin.

Pretend you are going to get fever neutropenia after your next cycle of chemotherapy and will get the Hospital IV treatment option. The doctor is offering you the Early Discharge treatment option. However this option is not covered by OHIP or your insurance. You will have to pay out of pocket. We want to know the most you would be willing to pay, if anything, for the early discharge treatment option instead of the Hospital IV treatment option. Would you choose Early Discharge if it were of no cost to you? What about if it cost $1000? **[titrate up $100 at a time, then $20]**

Just to make sure I understand, you would be willing to pay $**X** for the Early Discharge treatment option instead of the Hospital IV treatment option?

[repeat for other treatment options]

Part VI: Time Trade Off

The next exercise is called Time Trade Off. It is much like the last exercise we just did, where you are going to have a chance to switch from the Hospital IV treatment option to one of the other treatment options. The difference this time is that instead of costing money to switch it will take some time off your life.

Again, pretend you are going to get fever neutropenia after your next cycle of chemotherapy and will get the Hospital IV treatment option. The doctor is offering you the Early Discharge treatment option, but switching to it would take some time off your life. Would you switch to the Early Discharge situation if it was going to take all 60 years off your life, meaning you would die tomorrow? Would you switch to the Early Discharge situation if it was going to take 1 day off your life? **[titrate up to 1 week, 1 month, 1 year, 2 years…]**

Just to make sure I understand, you would be willing to give up X time of your life to take the Early Discharge treatment option instead of the Hospital IV treatment option? **[repeat for other treatment options]**

Part VII: Conjoint Analysis

(not part of this manuscript)

All right, we are all done! Thank you very much for your help! It will be very helpful for lots of people in the future. Do you have any questions?

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