What Are Cancer Patients Willing to Pay for Prophylactic Epoetin Alfa?

A Cost-Benefit Analysis

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BACKGROUND. Anemia, one of the most common complications of cancer chemotherapy, has been managed with red blood cell (RBC) transfusions. As an alternative, the agent epoetin alfa has the potential to reduce the transfusion requirements of patients receiving cancer chemotherapy. To estimate the value that cancer patients place on the drug, an economic analysis using the concept of willingness to pay (WTP) was conducted.

METHODS. The method of WTP was used within the framework of a classical cost-benefit analysis to estimate the net cost or benefit of administering prophylactic epoetin alfa to cancer patients. This estimate included the direct cost of epoetin alfa administration and savings secondary to reduced RBC transfusions. A cohort of 100 cancer patients who received or were scheduled to receive cisplatin or noncisplatin chemotherapy (50 per group) were then interviewed to measure the maximum WTP (net benefit) that they experienced with epoetin alfa.

RESULTS. Regarding the benefits they would experience after 3 months of epoetin alfa administration, patients receiving cisplatin and noncisplatin therapy stated that they would be willing to pay an average of 587 U.S. dollars (U.S.$587) (95%CI: $300–$875) and U.S.$613 (95%CI: $324–$902), respectively. These benefits were then subtracted from the total cost of the drug when administered to patients receiving cisplatin (U.S.$3530) and noncisplatin (U.S.$3653) therapy. This produced a net incremental treatment cost of U.S.$2943 (95%CI: $2655–$3230) and U.S.$3039 (95%CI: $2750–$3328) for the respective treatment groups.

CONCLUSIONS. The results of the current study suggest that the routine administration of epoetin alfa to cancer patients receiving myelosuppressive chemotherapy is a highly resource-intensive treatment policy with modest benefit to patients. Additional research is required to identify high risk patient subgroups who would benefit most from the drug. [See editorial on pages 2427–9, this issue.] ***Cancer* 1998; 83:2588–96.** © *1998 American Cancer Society.*

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Anemia is one of the most common hematologic complications in patients undergoing treatment for cancer. Although the severity may vary among individuals, the majority of cancer patients become anemic at some point during the course of their illness.[1] A patient is considered anemic if his or her blood hemoglobin level drops below the normal physiologic requirement that is necessary for adequate tissue oxygenation, generally below 12 g/dL.[2] The onset of anemia is often characterized by shortness of breath, fatigue, vertigo, loss of appetite, and impairment of a patient's physical capacity.[3]

One of the most prominent risk factors for the onset of anemia in oncology patients is the administration of intensive chemotherapy.

These compounds induce anemia by suppressing red blood cell production, inhibiting erythroid cell maturation, and suppressing the synthesis of erythropoietin by the kidneys.[4] Among the many antineoplastic agents, cisplatin has been implicated to cause moderate to severe anemia. In several studies, it was reported that clinically significant anemia developed in 10–40% of patients receiving cisplatin.[5,6] The severity was a consequence of both the total drug dose and the pretreatment hemoglobin concentration.

Anemia in cancer patients has been traditionally managed with the administration of blood transfusions because they offer a rapid correction of hemoglobin levels, particularly in urgent situations. In the absence of active bleeding, 1 unit of packed red cells can increase an adult's peripheral hematocrit level by 3% and hemoglobin by 1 g/dL.[7] However, the use of blood transfusions may carry risks such as disease transmission, administration errors, or transfusion reactions.[8] In addition, a critical blood shortage was recently reported by some large Canadian medical centers.[9,10]

Fortunately, epoetin alfa has been identified as an agent with the potential to decrease the utilization of red blood cell transfusions within the first 3 months of cancer chemotherapy. In one study, Abels et al.[11] conducted a randomized, double blind placebo controlled trial to measure the ability of epoetin alfa to reduce the incidence of transfusion requirements for patients receiving cisplatin and noncisplatin chemotherapy. Following a 1-month induction period, the investigators reported that by the third month of cisplatin-based chemotherapy, 31 of 55 patients (56.4%) in the placebo group required at least 1 blood transfusion compared with only 15 of 56 (26.8%) in the epoetin alfa group (absolute risk reduction = 29%, $P < 0.005$). In the noncisplatin trial, the corresponding rates of transfusion utilization in placebo and epoetin alfa patients was 36.8% and 28.6%, respectively (absolute risk reduction = 8%). However, the difference was not statistically significant ($P = 0.3$). Abels et al. concluded that prophylactic epoetin alfa is an important adjuvant treatment for patients receiving cancer chemotherapy.[11]

From a health policy point of view, a major obstacle against the widespread use of epoetin alfa in the treatment of cancer patients is that it is an expensive agent, with a monthly cost of approximately 1200 U.S. dollars (U.S.$1200). To measure the value of epoetin alfa as an adjunct treatment in oncology, a cost-benefit analysis (CBA) using the subjective method of consumer willingness to pay (WTP) was conducted.[12–14] Within the framework of a CBA, the maximum that a patient would pay for the drug represents the net benefit of the intervention.[12,14] Therefore, the primary objective of the current study was to determine whether the reduced need for blood transfusions during chemotherapy is worth the additional cost of the product, as perceived by cancer patients and members of the general public.

METHODS

Estimation of Costs

A CBA using the WTP approach was conducted from the societal perspective. The analytic time period was the first 3 months of cisplatin and noncisplatin chemotherapy, as reported in the epoetin alfa randomized study.[11] The cost portion of the CBA consisted of medical resources required for 12 weeks of epoetin alfa treatment, assuming a dose of 150 IU/kg 3 times per week for a 70 kg patient. The estimate also included costs for patient education and laboratory monitoring. The final estimate was then adjusted for potential savings secondary to the absolute risk reductions (ARRs) in red blood cell (RBC) transfusions for cisplatin and noncisplatin chemotherapy reported in the Abels et al. study.[11]

Cost savings secondary to RBC transfusion avoidance were estimated by multiplying the ARRs for cisplatin (ARR = 29%) and noncisplatin (ARR = 8%) patients during the second and third months of chemotherapy by the average transfusion cost per patient over that period of time.

The transfusion cost per patient was estimated by combining published Canadian RBC unit cost data for general medicine patients,[15] with resource utilization specific to cancer patients. The latter information was obtained from a retrospective chart review of 100 randomly selected Princess Margaret Hospital (PMH) patients. Half of the sample received a cisplatin-containing regimen, and the latter half was treated with a noncisplatin protocol. To be consistent with the epoetin alfa randomized trial,[11] hospital resource data were collected for the second and third months of cancer chemotherapy. This estimate and the ARR for cisplatin and noncisplatin patients was then used to adjust the total cost of 12 weeks of epoetin alfa therapy. The final figure represented the "cost" portion of the cost-benefit analysis and is reported in U.S. dollars.

Estimation of Benefits

The "benefits" portion of the study was measured using the WTP method to evaluate 100 cancer patients and 50 subjects selected from the general population. Of the 100 cancer patients, half of the sample consisted of respondents with solid tumors that would

typically be treated with a cisplatin-containing regimen (lung, gynecologic, and genitourinary cancers). The other half of the sample consisted of patients whose neoplasms would not routinely be treated with cisplatin (lymphoma, breast carcinoma, and multiple myeloma). To be consistent with the incidence of these malignancies in the Canadian population,[16] the following numbers of patients were included from each disease site: 36 patients with breast carcinoma, 11 with lymphoma, and 3 with myeloma for the noncisplatin group. The cisplatin group contained 31 patients with lung carcinoma and 19 with gynecologic or genitourinary tumors. With a sample of 50 patients in each group, the maximum WTP was measured with a precision of ± $70, 95 times out of 100.

Once informed consent was received, each patient was interviewed face-to-face by the principal investigator. The first part of the interview attempted to standardize the knowledge base of all patients by presenting to them a detailed description of anemia in cancer, treatment with blood transfusions, and its associated risks.

To introduce the WTP scenario to each patient, the probability of requiring a blood transfusion during the second and third month of chemotherapy, with or without epoetin alfa (referred to as the hypothetical new drug), was presented both numerically and graphically. This was similar to the approach used by O'Brien et al. and others.[14,17] Information on the dosage, the method of administration, and the toxicity profile of the new drug (e.g., hypertension) was also provided to each participant.

Once all of the information was presented, patients were asked to indicate, on a 10-point ordinal scale, how important they considered the benefit of the new drug (1 = not at all important, 10 = very important). Responders were then asked, "Now imagine that you are about to receive chemotherapy for the next 3 months and that the new drug is not provided by the Canadian health care system. Thinking realistically about how much you can afford to pay, what is the maximum amount you would be willing to pay per month, for 3 months, to receive the new drug?" To minimize the effect of the starting-point bias, the payment-card method was used as described by Mitchell and Carson.[18]

In the second part of the study, 50 members of the general population living in metropolitan Toronto were selected by random telephone digit dialing. Once subjects were contacted, they were asked to participate in the study. If informed consent was received, a copy of the WTP questionnaire was mailed to each respondent. After 7 working days, they were once again contacted by telephone to complete the survey.

During the telephone interview, participants from the general population were initially given the Canadian incidence rate for cancer[16] as well as background information on chemotherapy, anemia, and treatment with blood transfusions, including associated risks. The transfusion requirements with and without the hypothetical new drug in both cisplatin and noncisplatin patients were then provided as separate scenarios to each subject. To avoid an order effect, the two treatment scenarios were presented in a random fashion.

Once all the information was presented, participants were asked how important it would be to make this drug available to them in case they needed it in the future (on a 10-point ordinal scale). To make the scenario realistic relative to Canada's publicly funded health care system, the WTP was presented in the form of a hypothetical taxation question. Specifically, respondents were asked, "Now imagine that the drug is not provided by the Canadian health care system. Thinking realistically about how much you can afford to pay, what is the maximum income tax increase per year you would be willing to pay to make the drug available to you for possible use in the future? Remember that you cannot stop payments once they get started." As with patient respondents, the pay card method was used to avoid starting point bias.[18] Had this study been conducted in the U.S., the WTP question would have been posed as a hypothetical insurance premium for the new drug.[13]

Demographic data were also collected from all participants. This consisted of respondent age, gender, marital status, education, employment status, household income, number of children, and personal experience with blood transfusions. Subjects were also asked the main reason behind their decision to pay (or not pay) for the drug.

Comparison of Costs and Benefits

A classical cost-benefit analysis was then performed, in which a patient's maximum WTP was subtracted from the total cost of 3 months of epoetin alfa (adjusted for the potential savings in blood transfusions). Due to differences in anemia risks between cisplatin and noncisplatin chemotherapy, an individual cost-benefit analysis was performed for each subgroup.

In subjects from the population at large, the maximum WTP was multiplied by their life expectancy, because WTP tax contributions would only cease at the end of a subject's lifetime. Life expectancies for men and women were obtained from Statistics Canada.[19] Because payments would continue into the future, the maximum WTP for epoetin alfa was also

discounted at a rate of 5%. The final age-adjusted WTP estimate represented the societal value for epoetin alfa therapy and was used in the cost-benefit analysis.

Statistical Analysis

Demographic data, rating scale responses, and WTP estimates were presented with descriptive statistics as either means, medians, or proportions. In calculating the average WTP, the denominator was all surveyed persons, with zero imputed for those subjects who would not pay for the drug. Differences in maximum WTP between the two patient groups (cisplatin vs. noncisplatin) were assessed by the nonparametric Mann–Whitney *U* test. Intrasubject differences within the public volunteers were assessed by the Wilcoxon signed rank test.

To evaluate the association between maximum WTP and respondent characteristics (e.g. age, income, etc.), a multivariate analysis was also performed. The dependent variable in the model was a respondent's maximum WTP for epoetin alfa. The independent variables were chemotherapy regimen (noncisplatin vs. cisplatin), respondent group (public vs. patient), gender, marital status, postsecondary education, children, history of blood transfusions, family income, and respondent's age. The cutoff for significance for all the statistical procedures was $P = 0.05$.

TABLE 1
Epoetin Alfa and Blood Transfusion–Related Costs

	Cost (U.S.$)	Cost/patient (U.S.$)
Epoetin alfa treatment costs[a]		
Drug acquisition cost	$94/10,000 IU	$3564[b]
Laboratory tests		
Transferrin saturation	7.15/test	7.15
Serum ferritin	23.84/test	23.84
Serum Vit B12	23.84/test	23.84
Serum folate	58.42/test	58.42
Nursing time for patient education	23.00/hour	23.00
Total		$3700
Transfusion costs during the second and third months of chemotherapy[c]		
Cost of RBC (15)	274.00/2 units	410
Ambulatory unit admission[d]	78.00/visit	36.20
Laboratory tests		9.30
Complete blood count with differential	7.70/test	
ABO-Rh blood group	3.00/test	
Adverse effects management		53.35
Hospitalization	450/day	
Physician visit	12.00/visit	
Nurse time	23.00/hour	
Outpatient costs	15.00/RBC unit	30.80
Patient time	8.40/hour	44.00
Total cost (95% CI)		$583 (377–788)

U.S.$: U.S. dollars; RBC: red blood cells; CI: confidence interval.
[a] Epoetin alfa treatment costs were estimated for a typical 70 kg cancer patient.
[b] Assuming 150 IU/kg 3 times per week for 12 weeks.
[c] Estimated via a retrospective chart review of 100 cancer patients.
[d] Included only if the reason for admission was to receive a blood transfusion.

RESULTS

Estimation of Costs

The cost for 3 months of epoetin alfa therapy for cancer patients was U.S.$3700 (Table 1). This was based on a dose of 150 IU/kg 3 times per week and included incremental treatment-related costs, such as laboratory tests for drug monitoring and patient education. This value was then adjusted for the potential savings secondary to RBC transfusion avoidance for patients receiving cisplatin-containing and non-cisplatin-containing chemotherapy.

The cost of RBC transfusions per patient during the second and third months of treatment was estimated at U.S.$583 (Table 1). Savings related to reducing blood transfusions secondary to epoetin therapy were then calculated by multiplying the transfusion cost per patient with the ARRs for patients who required an RBC transfusion.[11] Therefore, the final incremental health care system cost of prophylactic epoetin alfa per patient receiving cisplatin and noncisplatin chemotherapy would be approximately U.S.$3530 (95%CI: $3470–$3590) and U.S.$3653 (95%CI: $3636–$3669), respectively.

Estimation of Benefits

The benefits portion of the analysis was determined by asking patients how much they would be willing to pay for the value offered by epoetin alfa. The plan was to administer the survey to 50 cisplatin and 50 noncisplatin patients (total, 100). One hundred six patients were approached and only 6 refused to participate, for an overall response rate of 94%.

To measure societal WTP, a random digit telephone dialing strategy was then adopted. For those subjects who consented to be interviewed, the necessary information was mailed to them and a follow-up telephone call was made. However, unlike the participation rate for patient respondents, the participation rate for the general public was disappointingly low. Among the 161 people contacted, 90 subjects refused to participate and 21 were unable to complete the survey because they stated that the mailed information was not received. Thus, a final sample of 50 subjects was obtained, for an overall response rate of 31%.

Respondent demographic data are presented in

TABLE 2
Respondent Demographic Data

	Patients		
	Noncisplatin (n = 50)	Cisplatin (n = 50)	Public volunteers (n = 50)
Age (yrs) (mean [SD])	51 (10)	61 (11)	49 (15)
Marital status (%)			
Married/common law	74	64	54
Widowed	2	12	8
Single	12	10	32
Divorced	12	14	4
Missing	—	—	2
Children (%)			
Any age	70	80	54
Under 16 years of age	16	8	16
Employment (%)			
Full time	38	20	54
Part time	10	4	10
Unemployed	52	76	36
Education (%)			
Less than high school	8	28	6
High school graduate	24	36	32
Postsecondary/university	68	36	62
Household income (%)			
$0–$20,000	20	52	28
$21,000–$49,000	38	32	44
+$50,000	24	12	22
Missing	18	4	6
Received a blood transfusion (%)	26	29	16

SD: standard deviation.

TABLE 3
Rating Scale Estimates

	Median rating scale (range)[b]	
Absolute risk reduction[a]	Patients[c]	Public volunteers[d]
Cisplatin	9	8
29%	(3–10)	(0–10)
Noncisplatin	7	6
8%	(1–10)	(0–10)

[a] Absolute risk reduction (ARR) in the no. of patients receiving at least one blood transfusion during the second and third month of cancer chemotherapy.[11]

[b] The benefit of epoetin alfa was measured on an ordinal scale from 1 to 10. Importance rating score differences between cisplatin and noncisplatin patients were evaluated by the nonparametric Mann–Whitney *U* test. The Wilcoxon signed rank test was used to compare intrasubject variability from the general population. The results showed that the transfusion risk reduction in cisplatin-containing protocols was considered significantly more important compared with noncisplatin regimens by both patients ($P = 0.02$) and volunteers ($P < 0.01$).

[c] Respondents consisted of 50 patients who received or were scheduled to receive cisplatin-containing and non-cisplatin-containing chemotherapy (total = 100).

[d] Respondents consisted of 50 randomly selected volunteers from the general public. Each participant answered both a cisplatin and a noncisplatin questionnaire.

TABLE 4
Maximum WTP Estimates

	Mean (95% CI)	
Absolute risk reduction[a]	Patients WTP[b]	Public volunteers WTP[c]
Cisplatin[d]	$587	$800
29%	($300–$875)	($321–$1278)
Noncisplatin[d]	$613	$680
8%	($324–$902)	($226–$1134)

[a] Absolute risk reduction (ARR) in the no. of patients receiving at least one blood transfusion during the second and third month of cancer chemotherapy.[11]

[b] Respondents consisted of 50 patients who received or were scheduled to receive cisplatin or non-cisplatin-containing chemotherapy (total = 100).

[c] Respondents consisted in 50 randomly selected volunteers from the general public. Each participant answered both the cisplatin and noncisplatin treatment scenario. Respondent's maximum annual WTP was then multiplied by their life expectancy and discounted at a rate of 5%. Life expectancy for each public volunteer was obtained from Statistics Canada.[19]

[d] WTP differences between cisplatin and noncisplatin were evaluated by the nonparametric Mann–Whitney *U* test. Wilcoxon's signed rank test was used to determine intrasubject differences among public volunteers. The results showed that public volunteers were willing to pay more for the transfusion risk reduction in cisplatin-containing protocols compared with non-cisplatin-containing regimens ($P < 0.01$). However, differences in WTP between patient groups were not statistically significant ($P = 0.72$).

Table 2. Socioeconomic differences between cisplatin patients and the other groups were evident. A higher proportion (76%) of cisplatin patients were unemployed, and only 36% had received postsecondary/university education. Patients receiving noncisplatin chemotherapy and public volunteers also appeared to have higher incomes compared with the cisplatin group (Table 2). The final parameter of interest was the proportion of respondents who had previously received a blood transfusion. Between 25% and 30% of patients in either chemotherapy group had previously experienced an allogenic blood transfusion. Surprisingly, 16% of subjects from the general public also stated that they had received a transfusion in the past.

After the background information was presented, respondents were asked to rate the importance of the benefits offered by the new drug on a scale from 1 (not at all important) to 10 (very important). Patient and public volunteers both gave significantly higher rankings for the risk reductions of epoetin alfa when used in conjunction with cisplatin-containing chemotherapy (Table 3). In addition, it was noted that patients gave significantly higher importance rating scores than public volunteers ($P < 0.05$), regardless of chemotherapy treatment (cisplatin vs. noncisplatin).

All respondents were then asked about the maximum amount they would pay for the benefit of the drug. For 3 months of epoetin alfa treatment, cisplatin

TABLE 5
Motivation Associated with Willingness to Pay for the Drug

	Patients (%)		
Motivation	**Noncisplatin**	**Cisplatin**	**Volunteers**
1. Reduce the risk of getting infected blood	28	40	40
2. Increase energy level	30	40	16
3. Both (combination of 1 and 2)	30	14	24
4. Other[a]	8	6	16
5. Missing	4	—	4

[a] Could not afford or were unwilling to pay for the drug.

and noncisplatin patients were willing to pay a mean of U.S.$587 and U.S.$613, respectively (Table 4). However, contrary to the rating scale scores, these differences were not statistically significant ($P = 0.72$). The results imply that the increased clinical benefit of epoetin alfa to patients receiving cisplatin did not translate into an increased expenditure. This outcome may be related to socioeconomic differences among patients (vide infra).

In contrast, public volunteers were willing to pay more for the use of the drug during cisplatin chemotherapy. As an annual tax increase, they were willing to pay an average of U.S.$45 (95%CI: $20–$69) for the benefits of epoetin alfa in cisplatin and U.S.$38 (95%CI: $15–$62) for the drug in noncisplatin protocols. For each participant, this estimate was then multiplied by their life expectancy and discounted at a 5% rate to obtain the age-adjusted maximum WTP for the drug (Table 4). Overall, members of the general public were willing to pay U.S.$800 and U.S.$680 to be able to use epoetin alfa in cisplatin-containing and non-cisplatin-containing protocols, respectively ($P < 0.01$).

At the conclusion of the interview, both patients and public volunteers were asked about the main reason driving their WTP responses. At least one-quarter of all respondents (cisplatin patients, noncisplatin patients, and public volunteers) stated that reducing the risk of receiving infected blood was the main motivating factor behind their WTP responses (Table 5). However, a higher proportion of patients than volunteers were willing to pay for the drug in order to have an increase in their energy level (Table 5).

Multivariate Analysis

The maximum WTP estimate from respondents in each of the three groups was then used as the dependent variable in a multivariate analysis. The results of the procedure revealed that subjects with household incomes above U.S.$50,000 were willing to pay an average of U.S.$715 more than those with incomes below this threshold ($P = 0.013$). Age was also identified as a statistically significant factor in that younger patients were willing to pay more for the drug than older people. Respondents were willing to pay approximately U.S.$19 less for each year of advancing age ($P = 0.046$). The results of the model also supported the earlier conclusions of the bivariate analysis, in that the chemotherapy protocol (cisplatin vs. noncisplatin) and the type of respondent (patient vs. public volunteer) were not statistically significant factors contributing to maximum WTP.

Comparison of Costs and Benefits

The maximum WTP (Table 4) was then subtracted from the overall cost of adjuvant epoetin alfa therapy (U.S.$3530 for cisplatin and U.S.$3653 for noncisplatin patients). This resulted in a net cost of approximately U.S.$2943 (95%CI: $2655–3230) and U.S.$3039 (95%CI: $2750–$3328) for epoetin alfa use in the treatment of cisplatin and noncisplatin patients. These results suggest that the use of epoetin alfa for the prevention of anemia produces a situation that is very resource-intensive for a modest clinical benefit, as perceived by the cancer patients at the point of consumption. In fact, only 4% of patients were willing to pay the actual amount required to cover the cost of the epoetin alfa treatment.

A similar procedure was conducted with the age-adjusted WTP responses from members of the general public. Subtracting the maximum WTP for cisplatin and noncisplatin (U.S.$800 and U.S.$680) chemotherapy from the total cost of the drug generated a net societal cost of U.S.$2731 (95%CI: $2252–$3209) and U.S.$2973 (95%CI: $2799–$3426), respectively. Similarly, only 6% of the volunteers were willing to pay the actual cost of epoetin alfa, implying that the drug may not provide sound economic value for our limited health care resources.

Sensitivity Analysis

A comprehensive sensitivity analysis was then conducted to test the robustness of the primary results. Data were initially reanalyzed using variations in blood transfusion costs. The results were insensitive to extremes in the cost of a transfusion. As an illustration in cisplatin patients, using the upper 95% CI limit for transfusion costs decreased the net epoetin alfa cost from U.S.$2943 at the baseline to U.S.$2883. Using the lower confidence limit, the net cost of epoetin alfa increased to U.S.$3002.

To estimate the maximum WTP from healthy volunteers, their annual income tax payment for epoetin alfa was multiplied by the respondent's life expectancy[19] and discounted at a rate of 5%. In the sensitivity analysis, the data were reanalyzed with the discount rate lowered to 3%. Consequently, the net cost of epoetin alfa decreased to U.S.$2555 (95%: $2122–$3088). However, these estimates were still well above the zero break-even point, as indicated by the lower limit of the 95%CI.

DISCUSSION

Several randomized trials have demonstrated that epoetin alfa prevents anemia during chemotherapy and reduces transfusion requirements for some patients.[11,20] However, the drug is available at a cost of approximately U.S.$3500 for 3 months of therapy. The results of the current study revealed that cisplatin and noncisplatin patients were willing to pay only U.S.$587 and U.S.$613 for 3 months of epoetin alfa administration (Table 4). As a matter of fact, only 4% of patients interviewed were willing to pay the total cost of the drug. Despite what cancer patients said about the importance of avoiding transfusions, it appears that they do not have a great deal of aversion to actually receiving blood products for the symptomatic management of anemia. This observation may be related to the fact that cancer patients have multiple symptomatic complications (emesis, neutropenia, mucositis, etc.) in which anemia is only part of the problem.

The analysis was then extended to members of the general Canadian public. The WTP question was structured in the form of a hypothetical lifetime income tax payment to make the drug available to the respondent in case they require chemotherapy in the future. The results of the survey were similar to the responses reported by patients. Members of the general public were willing to pay only U.S.$800 in order to use the drug during cisplatin chemotherapy and U.S.$680 in the case of noncisplatin protocols. However, unlike the results from patients, the maximum WTP in the cisplatin scenario was significantly higher than the noncisplatin situation ($P < 0.01$). This observation may be due to the fact that, unlike patients, public volunteers received the absolute risk reductions of epoetin alfa for both cisplatin and noncisplatin chemotherapy. As a result, this would allow for an easy comparison of the incremental benefit of epoetin alfa when used in cisplatin chemotherapy.

A socioeconomic comparison between groups suggested that patients receiving cisplatin tended to be older and less educated and have lower family incomes than the other groups. It is possible that these socioeconomic differences could have compromised the effectiveness of the WTP interviews. However, the multivariate regression analysis was able to adjust for differences in age and income between subjects. Furthermore, it failed to identify education level as a statistically significant factor in respondent WTP. Therefore, the regression model supported the findings of the bivariate statistical analysis because there were no significant differences between groups (cisplatin vs. noncisplatin), even after adjustment for age, income level, and education.

The combined results for patients and members of the general public imply that the routine use of epoetin alfa during cancer chemotherapy is a resource-intensive treatment with only a modest patient benefit, as perceived by respondents. Therefore, the symptomatic management of anemia with blood transfusions should remain the treatment of choice for the majority of patients. Epoetin alfa may have a role in patient specific subgroups at high risk for prolonged anemia and multiple transfusions. This would include patients who have chronic anemia and are scheduled to receive high dose cisplatin chemotherapy.[21]

Given the differences in health care systems between the U.S. and Canada (private insurance vs. publicly funded), the issue of study generalizability to the U.S. oncology setting must be addressed. In Canada, all cancer patients have access to publicly funded health care that provides coverage for hospitalization and outpatient chemotherapy administration. In addition, seniors older than 65 years have access to provincial formulary drug insurance. The Ontario formulary includes epoetin alfa, provided that the prescription meets the provincial treatment guidelines and is accompanied by a letter of intent from the prescribing oncologist.

For those patients who do not qualify for the provincial drug program (e.g., younger than 65 years, epoetin alfa prescription for a nonapproved indication), reimbursement must be sought through private insurance (if the patient has insurance) or out of pocket.

Because the majority of cancer patients and public respondents interviewed were younger than 65 years (Table 2), most of them would not qualify for provincial drug benefits. Consequently, they would have to seek some alternative form of coverage (e.g., private insurance, out of pocket, etc.). As a result, Canadian cancer patients would have to face the same questions about epoetin alfa reimbursement as their U.S. counterparts. Therefore, it can be argued that the study results are generalizable to the U.S. health care

system because the epoetin alfa reimbursement scenarios are similar between countries.

There are a number of limitations in the current study that have to be addressed. The first is related to the small sample size in each group (n = 50). As a result, a comparison of maximum WTP estimates between groups may not have had the power to detect statistically significant differences. Another drawback of the cost-benefit analysis is related to the absolute risk reduction in noncisplatin patients reported by Abels et al.[11] By the second and third month of epoetin alfa therapy, the investigators in that trial were unable to detect significant differences in the proportion of epoetin alfa and control patients requiring blood transfusions. Consequently, the WTP as stated by the noncisplatin group may be for a nonexistent benefit.

Another limitation of the current study is related to the economic parameters evaluated in the cost-benefit analysis. These included direct hospital and drug-related expenditures, and indirect patient transfusion costs (e.g., travel time) for the first 3 months of chemotherapy. However, the indirect costs for time off work and long term transfusion-related infectious complications (e.g., HIV) were not included in the analysis. The addition of these societal costs would improve the economic profile of epoetin alfa.

An important issue that was not considered in this investigation is the current blood shortage that is faced by many Canadian hospitals.[9,10] As a consequence of this shortage, the cost of procuring and processing a unit of blood is expected to rise. As a result, the increased cost of a unit of blood should improve the epoetin alfa cost-benefit ratio. Whether this factor alone would make prophylactic epoetin alfa economically attractive to cancer patients remains unknown.

Considering the low response rate (31%), the cohort of volunteers from the general public may have come under the influence of selection bias. This was evident from the high proportion of subjects (16%) in that group who had personally received an allogenic blood transfusion. This estimate is much higher than the 1% prevalence of RBC transfusions in the Canadian population (personal communication: C. Izaguire, Canadian Red Cross 1993–1994 statistics). This difference in transfusion prevalence suggests that subjects who consented to be interviewed were those people who were most interested in issues related to blood transfusions. As a result, one would expect this respondent subset to report higher WTP estimates than the general population. Had the random selection strategy been able to procure a representative sample, it is likely that the WTP estimates would have been lower. Notwithstanding, it is recommended that future WTP studies should use a face-to-face interview strategy to improve response rates.

In conclusion, the results of this cost-benefit analysis revealed that neither cancer patients nor members of the general public were willing to pay a sufficient amount to cover the cost of epoetin alfa for reducing blood transfusion requirements. Therefore, the prophylactic administration of epoetin alfa to cancer patients receiving myelosuppresive chemotherapy would require a large health care expenditure for a modest patient benefit. Epoetin alfa should only be considered for those high risk patients who would be expected to require multiple transfusions during cancer chemotherapy. Future studies should focus on identifying the patient subgroups who would benefit most from the drug.

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