Chemotherapy Waste Reduction Through Shelf-Life Extension

Scott E. Walker, John Iazzetta, Carlo De Angelis and Amiram Gafni

ABSTRACT

Minimization of total drug expenditures within the health care system, without affecting patient outcome has become a rational goal in today's economic, environment. The objective of this study was to observe the effect of extending the shelf-life for three chemotherapy medications, [doxorubicin, epirubicin and mitoxantrone] on wastage of these medications. Prior to and following the introduction of new, longer, shelf-lives for these three medications, prospective, non-randomized, unblinded four-month chemotherapy wastage audits for all chemotherapy medications were completed at 18 institutional sites within Ontario (six Ontario Cancer Treatment and Research Foundation clinics, ten Ontario hospitals and two preparation sites in a large cancer treatment centre).

Data were provided by 18 sites in 1989 but from only 12 sites in 1990. Ten of the 12 sites extended their shelf-lives for each of doxorubicin, epirubicin and mitoxantrone, and on average, waste at these sites was reduced to less than 1% of the 1989 total for epirubicin, less than 15% for doxorubicin and 35% for mitoxantrone. Many sites eliminated waste entirely for these drugs. For sites which did not extend their shelf-lives, the waste remained unchanged.

We conclude that appropriate extension of the shelf-life for chemotherapy medications can reduce waste, and is a relatively simple method of reducing expenditures without affecting health outcomes or adding additional complications to IV chemotherapy.

Key Words: *chemotherapy, stability, waste*

RÉSUMÉ

Face à la situation économique que nous connaissons aujourd'hui, réduire les dépenses totales de médicaments au minimum sans pour autant nuire aux patients est devenu un objectif rationnel pour le système des soins de santé. L'étude avait pour but d'examiner l'effet d'une prolongation de la date de péremption de trois médicaments utilisés en chimiothérapie (doxorubicine, épirubicine et mitoxantrone) sur le gaspillage. On a vérifié la quantité de trois médicaments gaspillée grâce à une étude prospective de quatre mois, non randomisée et sans inconnue sur les produits en question, dans 18 établissements de l'Ontario, avant et après l'introduction de nouvelles dates de péremption plus longues (six cliniques de l'Ontario Cancer Treatment and Research Foundation, dix hôpitaux et deux services de préparation d'un grand centre de traitement du cancer.

Les dix-huit établissements ont fourni des données en 1989, mais seulement 12 l'ont fait en 1990. Dix des 12 établissements avaient prolongé la date de péremption pour la doxorubicine, l'épirubicine et la mitoxantrone et, en moyenne, avaient réduit le gaspillage à moins de 1p. 100 du volume enregistré en 1989 pour l'épirubicine, à moins de 15 p. 100 pour la doxorubicine et à 35 p. 100 pour le mitoxantrone. À de nombreux endroits, on a totalement mis fin au gaspillage. Là où on n'a pas prolongé la date de péremption, le gaspillage demeurait le même. On en conclut que prolonger de la façon appropriée la date de péremption des médicaments utilisés en chimiothérapie peut réduire le gaspillage. Cette méthode relativement simple permet de diminuer les dépenses sans compromettre l'issue du traitement ni compliquer la chimiothérapie par perfusion.

Mots clés: *chiothérapie, gaspillage, stabilité*

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INTRODUCTION

Although drug expenditures within a health care institution often represent less than 5% of the institutions total annual budget, within a 500-bed institution these expenditures often exceed one million dollars annually. In the acute care setting more than 50% of the money spent on medication can be due to intravenous drugs, primarily antibiotics and chemotherapeutic agents. On a provincial scale, expenditures on antineoplastic drugs can reach into the millions. In Alberta, a province where approximately 7.5% of new cases of cancer in Canada were diagnosed in 1991[1], 8.2 million dollars was spent on antineoplastic drugs in 1991[2]. Direct extrapolation of these figures indicates that in excess of 100 million dollars is spent annually on antineoplastic drugs in Canada, with about 40% of this total being spent in Ontario[1].

Minimization of total drug expenditures without affecting patient outcome has become a rational and desirable goal in today's economic environment. Recent reviews[3,4] describe many strategies designed to optimize drug utilization and control drug costs. Examples of these initiatives include: drug formulary management[5,6]; prescribing restrictions[7,8]; automatic substitution[9] or therapeutic interchange[10] of one drug for another; antimicrobial surveillance[11] or target drug monitoring[12]; the use of structured antibiotic order forms[13]; physician education through "academic detailing"[14]; provision of drug cost data[15]; and conversion from intravenous to oral drug therapy.[16,17] These programs have met with varying success and, in some cases, have inadvertently contributed to an increase in overall health care costs while reducing drug expenditures. This can occur when a less expensive agent requires increased utilization of resources for drug administration, drug therapy monitoring, or management of complications which would not have been necessary had the higher cost drug been used.[18,19]

Conspicuous in its absence from the list of strategies for drug cost reduction is that of drug wastage reduction, even though it can contribute considerably to drug expenditures[20] and disposal costs. In 1986, a prospective study designed to establish a relationship between the shelf-life and medication waste, observed reductions in intravenous additive wastage for two antibiotics when the shelf-life for each antibiotic was extended.[20] When extrapolated to other antibiotics and intravenous medication[21-25], an annual savings of $80,000 was projected in 1987 for that one institution alone. Following completion of additional stability studies[26-34] and increases in drug cost, this estimate now exceeds $120,000 annually. Waste reduction has additional theoretical advantages over other methods of controlling drug expenditures[3-19] in that it is not subject to spin-off increases in total health care costs and the effects are maintained with drug use, whereas the success of clinical programs is often transient. However, the amount and cost of drug waste is often unknown or not readily available[35].

Although many chemotherapy medications are manufactured in sizes equivalent to common patient dosages, almost all patients receive doses which are individualized to body surface area. Therefore, many patients may receive only a portion of the contents of a vial. The medication in these unused part vials is discarded if it cannot be used in a second patient prior to expiration. The amount of medication which is discarded is, therefore, variable, since it is dependant on the amount remaining on any day, the shelf-life of the medication and the length of the interval between patients requiring the same drug. Other factors, including individual patient dosages, the number of patients appearing on any given clinic day, and the manufacturer's vial size all affect either the amount remaining on any day or the interval between patients. In theory, as the shelf-life is extended, the amount of waste should decrease, but overall use may have little affect on waste if the interval between patients remains unchanged, as it would in institutions that have tumour specific clinics on predetermined days. Individuals involved in product preparation do not have complete control over many of the factors which determine waste (i.e., the number of patients, the required dose, etc.). Furthermore, although some factors such as the interval between patients could be changed, these changes would require behaviour or pattern modification of clinics, physicians and patients, and this may be unrealistic.

This leaves the shelf-life. This factor is often under the control of the pharmacist, especially if the medication is inherently stable and the current shelf-life, recommended by the manufacturer, is based solely on sterility. Most pharmacies prepare chemotherapeutic agents for patients using a Class II laminar air flow biological safety cabinet and aseptic technique. While the use of this equipment is expected to reduce the rate of microbial contamination, most hospital pharmacy departments will have difficulty properly demonstrating that their contamination rate is at or near the

industry standard of 0.1%[36]. At Sunnybrook Health Science Centre, in December of 1987, a prospective evaluation of 556 syringes [1112 transfers, each syringe requiring two transfers], observed two syringes to be contaminated. The observed contamination rate was 0.36% with an upper 90% confidence interval of 0.87% based on syringes or 0.18% with an upper 90% confidence interval of 0.43% based on transfers. However, this test does not meet the regulated industry guideline of 3000 units filled within one hour[36]. Nevertheless, when the risk of microbial contamination is low, patients have negligible risk of suffering morbidity as a result of extending the expiry date to the limit of known stability. Extending the shelf-life for a product prepared under these conditions is possible and reasonable since the manufacturers' recommendation is often based primarily on the concern for sterility of the product once opened, and manufacturers are understandably reluctant to recommend a shelf-life longer than that indicated within their product monograph[37]. However, if the shelf-life is determined in the same way that the manufacturer completes a stability study, according to the degree of chemical degradation using validated analytical methods[38-40] then, if the data support a longer shelf-life and if the product is prepared using aseptic technique, then extension of the shelf-life is reasonable and will not place patients at increased risk. However, inappropriately extension of a shelf-life, based on data generated using non-specific analytical methods such as UV spectroscopy or microbiologic assays could potentially recommend a shelf-life which is inappropriately long and could result in a patient receiving degraded drug products. Outdated tetracycline products have been reported to cause Fanconi's syndrome[41] and outdated penicillin G products have been observed to increase anti-penicillin antibody titres after one week of therapy.[42] Therefore, extension of a shelf-life should not be taken lightly, nor done without consideration of patient care in anticipation of financial saving.

This study was designed to evaluate the cost savings resulting from waste reduction following proper extension of a medication's shelf-life. However, additional monetary considerations related to waste management were not considered in this evaluation. Medication waste will contribute to additional medication packaging waste and disposal costs, which have risen dramatically in recent years in Ontario[45]. There are also environmental concerns associated with the disposal of chemotherapy medications due to their biohazardous nature.

METHODS

Study Setting: Eighteen centres in Ontario were identified based on their willingness to provide waste and use data on all intravenous chemotherapy drugs prepared within their site and the knowledge that there was a reasonable number of chemotherapy injections prepared at each site. These centres were spread throughout Ontario and include cancer clinics, teaching hospitals and community hospitals in Ottawa, London, Hamilton, Toronto, Kingston and Sudbury.

All sites were known to prepare chemotherapy under "ideal conditions" (chemotherapy prepared under a class II laminar air flow biological safety cabinet by experienced personnel using aseptic technique).

Shelf-lives Used: During the 1989 audit period each centre used their own shelf-lives for all chemotherapy medication. Following the completion of stability studies for epirubicin, doxorubicin and mitoxantrone, each of the 18 sites was supplied with information documenting the stability of each medication and indicating that the shelf-life for each of these medications could be extended to 30 days.[32-34] Each site was encouraged to consider extending their shelf-life for these medications; however, the principle investigators did not insist that a particular shelf-life be used at any site be changed. The data coordinating centre documented the shelf-lives used at each site for all chemotherapeutic medications.

Waste and Use Monitoring: Each centre involved in the study completed chemotherapy drug usage logs. Some centres used their own log, but in all cases each log recorded, minimally; the date, the drug, and the dose given to each patient on each day. Each centre involved in the study completed chemotherapy drug wastage logs. Some centres used their own wastage log, but in all cases each log recorded, minimally; the date, the drug, vial strength, and volume or milligrams discarded, and the form of discard vial, syringe, or minibag. All drug discarded was recorded, regardless of the reason for discard. The reasons for discard were not recorded and it is an assumption inherent in this study design that the reasons did not change dramatically from year to year.

Analysis: Each centre submitted copies of their use and waste logs to the data coordinating centre. Use and waste data for each medication were analyzed indepen-

dently of other medications. Amounts used (mg) and wasted (mg) for all intravenous chemotherapy medications during each audit period were totalled by site, and by drug, to allow calculation of total use and waste at each site, and total use and waste for each drug across all sites. Based on 1989 procurement costs at each site for each chemotherapy drug, the total waste, in dollars, was summed for all centres and for each drug in each year. Annual wastage at each site was estimated based on the number of days monitored and extrapolated to the number of days of operation in a year. A two-way analysis of variance (blocking for sites and drugs by year) was used to detect significant differences in waste between the two audit periods. Fisher's Least Significant Multiple Range Test was used to find significant differences. Chi-square with Yates correction was used to test the differences in proportions. The *a priori* level of significance was chosen as 5% for all tests.

A post-hoc power calculation was completed, using a published formula[43], to estimate the power of the study.

Table I: Use and Waste in Dollars for Each Site in 1989 and 1990.

Site[a]	1989			1990		
	Reporting Days	Annual Usage ($)	Annual Waste ($)	Reporting Days	Annual Usage ($)	Annual Waste ($)
1.CH	54	104,442	6,582	54	95,886	1,323
2.Combined	123	284,109	10,041	184	DNR[c]	6,779
3.TH	112	202,278	8,732	123	208,751	1,237
4.CC	108	667,746	16,455	109	434,000	6,642
5.TH	153	227,128	17,232	153	222,173	9,381
6.CC	86	323,455	8,220	109	456,401	6,777
7.CC	99	469,205	8,142	247	436,829	2,001
8.TH	92	2,168,929	5,503	92	2,308,380	10,139
9.TH	88	178,399	6,647	122	133,478	10,522
13.CH	69	579,893	39,967	153	523,052	43,668
17.CH	153	304,095	25,190	123	154,522	6,474
18.CH	138	146,873	36,864	122	113,313	4,938
Total [n=12]	1275	5,656,552	189,575	1591	5,086,785	109,881
Mean [n = 12]		471,379	15,798		423,899	9,157
Sites which did not provide complete data in 1990						
10.TH	60	175,030	7,520	91	DNR[c]	[d]4,135
11.CC	89	181,932	[b]2,252	DNR[c]	DNR[c]	DNR[c]
12.TH	123	594,349	[b]2,158	DNR[c]	DNR[c]	DNR[c]
14.TH	71	614,874	15,571	DNR[c]	DNR[c]	DNR[c]
15.CC	45	662,532	21,483	DNR[c]	DNR[c]	DNR[c]
16.CC	64	285,980	25,549	DNR[c]	DNR[c]	DNR[c]
Total [n=6]	452	2,514,697	74,533			
Mean [n=6]		419,116	12,422			
Grand Total	1727	8,171,249	264,108			

a CH indicates Community Hospital; TH indicates Teaching Hospital; CC indicates Cancer Clinic; and Combined indicates a Cancer Clinic and Teaching Hospital with common Chemotherapy Preparation Site.
b Data Reported for only four medications (Doxorubicin, Epirubicin, Mitoxantrone and Carboplatin)
c Indicates that Data was Not Reported in 1990.
d Data reported not broken down by drug.

RESULTS

Use and waste audits were completed at each of the 18 institutional sites in Ontario where intravenous chemotherapy was prepared during May - September of 1989. Two sites reported data only for four drugs; carboplatin, doxorubicin, epirubicin, and mitoxantrone. In 1990, 13 sites submitted data for their use and waste audit but site 10 submitted data which were not broken down by drug. This left 12 sites which provided complete data for chemotherapy waste in 1989 and 1990.

Table I compares projected annual waste and use of all chemotherapy medications for 1989 and 1990 (in 1989 Canadian dollars). Data for the six sites which did not report complete information in 1990 are also provided. The sites which dropped-out were roughly similar in average waste and use to those that reported data for both 1989 and 1990, but are differentiated primarily by a change in contact pharmacist. Five of six sites which reported data in 1989 only had a change in contact pharmacist in 1990, while only three of the 12 sites that reported in both years had a change in pharmacist contact ($p<0.02$, Chi-square).

Table II provides the total dollar value of waste (in 1989 dollars) for each drug in both 1989 and 1990. The average 1989 price per mg of each drug is provided in Table II. This price did range by more than 15% between the lowest and highest reported costs for individual drugs. In 1989, approximately one third (36%; $95,184) of the dollar value of this waste was due to three medications: mitoxantrone, doxorubicin, and epirubicin (Table II). However, in 1990 only 17% of the dollar value of this waste was due to these medications. Of the 12 sites reporting waste in both years, 10 sites changed their shelf-lives for doxorubicin, epirubicin and mitoxantrone in 1990. The shelf-life used at each site in 1989 and

Table II: Total Amount of Each Drug Wasted in Dollars

DRUG	Price /mg ($)	1989			1990	
		WASTE (in $) [18 sites]	WASTE (in $) [12 sites]	% of Total Waste [12 sites]	WASTE (in $) [12 sites]	% of Total Waste [12 sites]
Mitoxantrone	15.62	37,958	17,288	9.63	5730	6.35
Carboplatin	1.19	32,211	21,855	12.15	16,523	15.06
Doxorubicin	4.19	32,018	30,681	17.06	9,035	8.23
Epirubicin	4.18	25,208	20,129	11.19	3,036	2.77
Bleomycin	9.96	22,484	16,577	9.22	13,342	12.16
Etoposide	0.59	15,020	12,529	6.97	3,389	3.09
Mitomycin	14.09	13,639	8,529	4.74	3,382	3.08
Leucovorin	0.73	9,499	5,546	3.08	2,118	1.93
Teniposide	0.58	9,343	2,871	1.60	0	0.00
Cisplatin	0.59	8,990	7,396	4.11	3,277	2.99
Ifosfamide	0.06	8,597	6,950	3.86	8,499	7.35
Melphalan	4.01	6,576	2,497	1.39	2,520	2.30
Vincristine	28.67	6,496	6,496	3.61	6,436	5.87
Vinblastine	4.81	6,217	5,688	3.16	4,690	4.27
Cytarabine	0.08	6,052	4,103	2.28	3,941	3.59
Methotrexate	0.32	5,969	4,952	2.75	4,495	4.10
Amsacrine	0.72	4,722	4,714	2.62	8,589	7.83
Dacarbazine	0.08	4,402	2,747	1.53	1,905	1.74
Carmustine	0.39	3,174	3,152	1.75	1,334	1.22
Cyclophosph.	0.01	2,003	1,826	1.02	1,563	1.04
Methchloreth.	0.62	1,107	832	0.46	712	0.65
Vindesine	49.39	1,101	1,101	0.61	102	0.09
5-Flurouracil	0.003	976	771	0.43	195	0.18
Actinomycin	14.30	306	306	0.17	380	0.35
TOTALS		264,108	189,575		109,881	

* Arranged in descending order of projected dollar value wasted in 1989.

1990 is shown in parenthesis in Table III. Two sites did not change their shelf-life for doxorubicin, epirubicin, or mitoxantrone. Site 6 was already using a seven-day expiration period for each of these three medications and site 13 has a policy of only using the manufacturer's recommended shelf-life. At the 10 sites in which the expiration period was extended, waste was dramatically reduced for these three medications (Table III, Figure 1).

For doxorubicin, nine of the ten sites reported some doxorubicin waste in 1989. Following the introduction of new shelf-lives in 1990, doxorubicin waste was reduced to less than 15% of the 1989 level through reductions in waste at each of the nine sites ($p<0.05$). Three sites completely eliminated waste. For epirubicin, five of the ten sites reported some waste in 1989. Following the introduction of new extended shelf-lives in 1990, epirubicin

Table III: Projected Annual Wastage for Study Drugs. Shelf-Lives for Room Temperature storage (in days) in parenthesis[a].

Site	Doxorubicin		Epirubicin		Mitoxantrone	
	1989	1990	1989	1990	1989	1990
Sites which extended expiry dates						
1. CH	532.60 (*)	0.00 (14)	422.64 (*)	0.00 (14)	1,218.36 (7)	0.00 (14)
2. Combined	223.19 (1)	0.00 (30)	1,434.93 (1)	85.30 (30)	231.13 (IND)[c]	929.56 (30)
3. TH	1,018.17 (*)	198.94 (30)	[b]0.00 (*)	62.02 (30)	468.60 (2)	0.00 (30)
4. CC	3,137.07 (*)	999.58 (90)	1,259.88 (*)	0.00 (90)	1,616.96 (14)	0.00 (30)
5. TH	2,232.91 (*)	239.90 (90)	1,650.80 (*)	0.00 (90)	2,757.37 (14)	2,049.49 (30)
7. CC	1,254.46 (*)	419.00 (30)	0.00 (*)	0.00 (30)	2,092.13 (2)	0.00 (30)
8. TH	[a]0.00 (*)	597.09 (60)	0.00 (*)	0.00 (60)	[b]0.00 (*)	[b]0.00 (30)
9. TH	4,810.81 (1)	0.00 (30)	0.00 (1)	0.00 (30)	1,938.30 (*)	654.25 (30)
17. CH	9,483.47 (1)	1,308.65 (7)	[b]0.00 (*)	[b]0.00 (7)	4,270.39 (1)	0.00 (7)
18. CH	3,945.28 (1)	199.48 (30)	15,107.75 (1)	33.17 (30)	1,702.13 (1)	1,984.65 (30)
TOTALS	26,637.96	3,962.64	19,876.00	180.49	16,295.37	5,617.95
Sites which did not change expiry dates						
13. CH	6,852.17 (1)	4,108.04 (1)	[b]0.00 (1)	2,612.64 (1)	[b]0.00 (1)	111.79 (1)
6. CC	152.09 (7)	964.15 (7)	252.74 (7)	243.30 (7)	991.69 (7)	0.00 (7)
TOTALS	7,004.26	5072.19	252.74	2,855.94	991.69	111.79

a. Shelf-lives are given for glass vials stored at room temperature at each site. A '*' indicates that the site did not permit room temperature storage of this drug. Drug stored at room temperature would be discarded.
b. Indicates that no use was documented for this drug during this period.
c. IND indicates that this site used an "indefinite" expiry date or "until used" storage policy.
d. See Table I for definitions of CM, TM, CC and Combined.

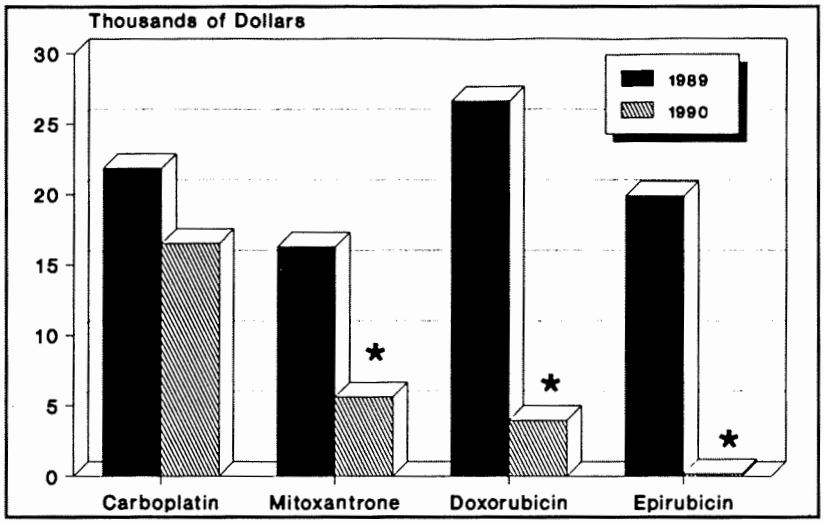

Figure 1: Waste (in dollars) of carboplatin, mitoxantrone, doxorubicin and epirubicin in 1989 and 1990 from the 12 sites reporting complete data in 1990. Carboplatin waste is calculated from all 12 sites with no change in shelf-life; mitoxantrone, doxorubicin and epirubicin waste is calculated from sites which changed shelf-lives and documented use of the drug in 1990 - nine sites for mitoxantrone and epirubicin, ten sites for doxorubicin. The (*) indicates a significant difference between waste in 1989 and 1990 for that drug.

Table IV: Power Table Estimating Detectable Percentage Change

Drug [sites reporting use]	Detectable Percentage Change in Waste				
	Beta = 0.20	Beta = 0.15	Beta = 0.10	Beta = 0.05	Beta = 0.01
Doxorubicin [n=10]	20.5	21.6	22.8	24.8	28.7
Epirubicin [n=9]	21.6	22.8	24.0	26.1	30.2
Mitoxantrone [n=9]	21.6	22.8	24.0	26.1	30.2

waste was reduced to less than 1% of the 1989 level through reductions in waste at four of the five sites ($p<0.05$), with three of the five sites completely eliminating waste. For mitoxantrone, nine of the ten sites reported some waste in 1989. Following the introduction of new extended shelf-lives in 1990, mitoxantrone waste was reduced to less 35% of the 1989 level through reductions in waste at seven of the nine sites, five of which completely eliminated waste ($p<0.05$).

Carboplatin served as a control drug during the study. As a control, the shelf-life for carboplatin remained the same at each of the 12 sites during both monitoring periods. In 1989, along with doxorubicin, epirubicin and mitoxantrone, carboplatin wastage, in terms of dollars, was one of the top four most wasted drugs. In 1990, five of the 12 sites increased carboplatin waste compared to 1989, although, the total waste from all sites for this drug was reduced to 75% of the 1989 level ($p>0.05$). Wastage data for these four drugs are illustrated in Figure 1. Although not intended prospectively as control sites, since sites 6 and 13 did not change the shelf-life for any of their three index drugs (or any others), these sites can also serve as control for the study. Total waste at these two sites in 1990 was within 18% of 1989 value of waste ($p>0.05$).

Post-Hoc Power Calculation: Complete data from one or several sites over a period of years are unavailable. However, analysis of monthly wastage data from 1989 indicate that variability [coefficient of variation as a percent] is about 20% with a 60 day reporting period and is reduced further as the collection period is extended. However, all sites do not use or waste all drugs. Only ten of the twelve sites reporting complete data in 1990 had changed their shelf-lives, and at least one site did not report any use of one of the three drugs (Table III). The ability to detect changes in waste at a range of different levels of confidence is calculated in Table IV, using an accepted formula[43], assuming an intra-site coefficient of variation of 20%, and a normal level of Type I error [5%].

Therefore, due to unspecified changes in the factors which could theoretically affect waste (the length of the interval between patients, dosage, the number of patients, overall usage), fluctuations in wastage are to be expected. The post-hoc power calculation indicates that these estimates are accurate within 20-25% for drugs with reasonable usage. Control data in this study show this variability. Overall, carboplatin waste at all 12 sites was reduced by approximately 25% in 1990 without any intentional intervention. This would imply that other factors, such as the interval between patients, may have changed and as a result waste was reduced by 25%. Similarly sites 6 and 13 show changes in waste of -18% and +9%, respectively, without any change in shelf-life. Again, these changes represent variation within the expected

range of experimental error. Drugs with lower usage [and, therefore, greater variability in use and waste] will require greater changes in waste before the difference would be identified as significant. We believe that reductions in waste greater than 25% for drugs that are frequently used represent important changes and that differences exceeding this are practically, economically, and statistically significant.

DISCUSSION

Reducing the level of service is often viewed as the most convenient method of reducing expenditures within the established health care system. However, improving efficiencies and eliminating waste represents an alternative method to reduce costs which does not adversely affect patient care. Extending shelf-lives and reducing waste in an intravenous additive program within a hospital represents one of the ways such cost reductions can be achieved. Appropriate extension of the shelf-life is a relatively simple method of reducing expenditures. The dollar value of waste reduction was observed to vary between sites and was dependant on the medications which contribute to waste. However, one site was observed to reduce waste for epirubicin by $15,000 in one year and, overall, we have demonstrated that extending the shelf-life of a chemotherapy medication can reduce wastage for that drug in most centres and completely eliminate waste at some sites. Nevertheless, several other factors, including use and the interval between patients, can affect waste and for these reasons it is likely that a reduction in carboplatin waste was observed in this study. The point at which an extension of the shelf-life begins to reduce waste is dependant on the interval between patients and would vary between sites. When the shelf-life is extended so that it is longer than the interval between patients, waste would, theoretically, begin to decrease. Therefore, in this study when site 1 increased the shelf-life from 7 to 14 days, waste was eliminated; however, the increase from 14 to 30 days for site 5 only reduced waste by 25%. Therefore, the shelf-life extension that would reduce waste at any site would be dependant on the frequency of use of that drug (interval between patients) at that site. Bressler et al[44] reached a similar conclusion, recommending that a multi-dose vial for doxorubicin be used in sites which use more than 150 mg of doxorubicin per month.

Appropriate extension of the shelf-life should not expose the patient to a degradation product in a concentration or amount greater than that allowed by the pharmaceutical manufacturer under government regulation. Any increase in the risk of infection to a patient as a consequence of receiving contaminated product is extremely low, when appropriate equipment and proper aseptic technique are used to prepare the product.

Additional monetary considerations related to waste management were not considered in this evaluation. Medication waste will contribute to additional medication packaging waste and disposal costs, which have risen dramatically in Ontario in recent years. There are also environmental concerns with the disposal of chemotherapy medications due to their biohazardous nature.

The results of this study may be useful in estimating chemotherapy waste or in suggesting ways to avoid waste. Extrapolation of this data to estimate total intravenous chemotherapy waste in Ontario is also possible assuming that these sites are representative of the entire population of chemotherapy preparation sites. In Ontario, there are approximately 70 active chemotherapy usage sites. Using the average figure of $16,146 dollars of annual waste (1989 data), total waste at 70 sites would be estimated to exceed $1,000,000 dollars annually, whereas based on 1990 data, waste would be estimated at $613,000 annually. These statistics, or those utilizing specific drugs as examples, might assist in justifying an intravenous additive program. Savings in drug expenditures obtained through reductions in waste could be used to offset personnel or capital equipment costs. If such a system was being proposed for an institution similar to site 13, which has recorded approximately $40,000 of chemotherapy waste in each of the last two years, a savings of about $34,000 per year in chemotherapy expenditures alone might reasonably be expected. Further savings through extension of the shelf-lives for antibiotics[18] could push the total savings within one institution well beyond $100,000 per year. However, it must be remembered that extension of a shelf-life should only be done after proper consideration of product stability and sterility.

We conclude that if an expiry date for an intravenous chemotherapy medication can be extended without placing patients at risk (from outdated or contaminated medication), then extension of an expiry date is likely to reduce expenditures for that medication and would appear to be a reasonable step towards cost containment.

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