LOW OSMOLAR (NON-IONIC) CONTRAST MEDIA VERSUS HIGH OSMOLAR (IONIC) CONTRAST MEDIA IN INTRAVENOUS UROGRAPHY AND ENHANCED COMPUTERIZED TOMOGRAPHY : A COST-EFFECTIVENESS ANALYSIS

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Abstract. The cost-effectiveness of three alternative policies for the use of intravenous contrast media for urography and enhanced computerized tomography (CT) are analyzed. Alternative #1 is to use high osmolar contrast media (HOCM) in all patients, the historical policy. Alternative #2 is to replace it with low osmolar contrast media (LOCM) in all patients. Alternative #3 is to use LOCM only in the high risk patients. Data on the 6,242 patients who underwent intravenous urography and enhanced CT at the Department of Radiology, Chulalongkorn Hospital in 1989 were used. Both societal and hospital viewpoints were analyzed. The incremental cosst-effectiveness (ICE) between #2 and #1 was 26,739 Baht (US$1,070) per healthy day saved (HDS), while the ICE between #3 and #1 was 12,057 Baht (US$482) per HDS. For fatal cases only, ICE between #2 and #1 was 35,111 Baht (US$1,404) per HDS, while the ICE between #3 and #1 was 18,266 Baht (US$731) per HDS. The incremental cost (IC) per patient was 2,341 Baht (US$94) and 681 Baht (US$27) respectively. For the hospital viewpoint the ICE between #2 and #1 was 13,744 (US$550) and between #3 and #1 was 6,127 Baht (US$245) per HDS. The IC per patient was 1,203 Baht (US$48) and 346 Baht (US$14), respectively. From the sensitivity analysis, #3 should be used if the LOCM price is reduced more than 75% (equal to 626 Baht or less) and more than 80% of the patients are able to pay for the contrast media.

INTRODUCTION

High osmolar ionic contrast media (HOCM) have been in intravenous use for a long time with well documented risks including death (Table 1) (Pendergrass et al, 1958; Wolfromm et al, 1966; Ansell, 1970; Witten et al, 1973; Shehadi, 1975; Shehadi and Toniolo, 1980; Ansell et al, 1980; and Hartman et al, 1982). Low osmolar (non-ionic) contrast media (LOCM) are now in widespread use due to their ideal characteristics. In fact they are replacing HOCM despite their higher costs. Kinnison et al (1989) recently reviewed 43 Randomized Control Trials judged to be of the highest quality, and suggested that the efficacy of LOCM in imaging is equal or superior to that of HOCM for all routes of administration. Overall incidence of non fatal adverse reactions to HOCM varies between 3.8% (Palmer, 1988) and 12.66% (Katayama et al, 1990). Katayama et al (1990), in their preliminary report of large prospective study (337,647 cases), showed the superiority of LOCM relative to HOCM, an approximate four fold reduction in the overall

incidence of adverse reactions (Table 2). The Palmer study (1988), which included the use of both LOCM and HOCM in high risk and low risk patients, also supports these conclusions (Table 3).

Intravenous use of contrast media (CM) for urography and enhanced computerized tomography is a major expenditure of the Department of Radiology at Chulalongkorn University Hospital, Bangkok, Thailand, a tertiary charity hospital under the egis of the Thai Red Cross Society. Thus, clinical assessment and economic evaluation of LOCM should be performed to help determine the indications for the use of appropriate intravenous contrast media.

Three alternative policies for the use of intravenous contrast media are examined in this study. Alternative 1 (#1) is to use HOCM in all patients. This is the conventional historical policy. Alternative 2 (#2) is to replace HOCM with LOCM in all patients. Alternative 3 (#3) is to use LOCM only in the high risk patients (patients who have history of adverse drug reaction (ADR) at exposure to contrast media, underlying cardiac or renal

Table 1

Mortality rates in intravenous use of high osmolar ionic contrast media.

Series	Year	Deaths (no.)	Examinations (no.)	Mortality rate
Pendergrass et al	1958	99	11,546,000	1:117,000
Wolfromm et al	1966	15	912,300	1:61,000
Ansell	1970	8	318,000	1:40,000
Witten et al	1973	1	33,000	1:33,000
Shihadi	1975	6	81,278	1:14,000
Shihadi et al	1980	11	214,033	1:20,000
Ansell et al	1980	4	158,500	1:40,000
Hartman et al	1982	4	300,000	1:75,000

Mortality rates in intravenous use of low osmolar non-ionic contrast media.

Series	Year	Deaths (no.)	Examinations (no.)	Mortality rate
Katayama et al	1988	1	168,363	1:170,000

diseases or history of allergy).

MATERIAL AND METHODS

Statistical data from the Department of Radiology at Chulalongkorn Hospital in 1989 were reviewed. There were 2,438 cases enrolled in intravenous pyelography (IVP) and 3,804 enhanced CT scan studies. Thus, the total intravenous use of CM involves 6,242 cases.

MD 76 (Mallinckrodt, Inc), a HOCM, was used in both IVP and enhanced CT scans. Omnipaque (Winthrop Products) is a LOCM which is planned to replace HOCM. The properties and prices of these CM are shown (Fischer, 1986) in Table 4.

The alternative policies for the use of intravenous contrast media are listed in Fig 1. High risk patients comprised of 28.3% of total patients (Katayama et al, 1990) (we use an estimate of 30% in this study).

In order to compare HOCM and LOCM, it is necessary to obtain estimates of the rates of incidence of fatal and non-fatal reactions for both kinds of media. The incidence of fatal reactions for low risk patients who receive HOCM was calculated under the assumption that 30% of a mixed group of patients are high risk, 70% are low risk, and the overall rate of fatal incidence is 1:40,000 (see Ansell et al, 1980, in Table 1). The detailed calculations are shown in Appendix 1.

In an economic analysis of a health-care manoeuvre, it is essential that benefits and costs of the competing alternatives be considered (Torrance, 1986). Cost (input) and consequences (ADRs) will be analyzed by comparing #2 and #3 with the conventional #1 to obtain incremental cost-effectiveness. Cost of treatment of the adverse effects and cost from production losses due to treatment of complications in each alternative will be included. Healthy days saved from complications will be used as an outcome measure although the quality of life of a healthy day lost in each complication is not equal. (The complication is, however, temporary and of short duration; see Appendix 2. Thus, the results are unlikely to be sensitive to the substitution of patient utilities for healthy days saved). Analyses

Table 2

Incidence of non fatal adverse drug reactions in high osmolar ionic contrast media (HOCM) and low osmolar non-ionic contrast media (LOCM).

Series	Incidence of ADR to CM.			
	HOCM		LOCM	
		AVR		AVR
Overall incidence:				
Ansell G	8.5%			
Witten DM et al	7.0%			
Shehadi WH et al	5.5%			
Palmer FJ	3.8%		1.2%	
Katayama H et al	12.66%		3.13%	
		7.49%		2.17%
Severe reaction:				
Ansell G	0.13%			
Palmer FJ +	0.09%		0.02%	
Katayama H et al #	0.22%		0.04%	
		0.15%		0.03%
Moderate reaction:				
Ansell G	1.47%			
		1.47%		*0.40%
Mild or minor reaction:				
Total minus severe and moderate		6.02%		*1.74%

AVR = Average incidence of adverse drug reaction.
+ Urgent therapy required and considered at risk, hospital admission required.
# One or any combination of the symptoms (dyspnea, sudden drop of blood pressure, cardiac arrest, loss of consciousness) which required some form of treatment or intervention of an anesthesiologist or hospitalization.
* Mild and moderate reaction incidence of LOCM obtained from total incidence minus severe reaction incidence (2.17% - 0.03% = 2.14%) and assume that mild reaction is about four times the moderate reaction as in HOCM.

will be done from the societal and hospital viewpoints.

Cost effectiveness analysis requires a comparison of the resources consumed (costs) to the health improvements (benefits created by the program). Costs are direct (C1), indirect (C2), and intangible cost (C3).

Alternative 1

Cost (C1) direct cost.

Direct cost includes use of x-ray rooms, use of x-ray equipments (x-ray machine, CT scan), films, developing process (processing chemicals), administrative supplies and services, laundry, needles and syringes for contrast medium injection, salary of technicians (per month @ 4,240 Baht), salary of radiologists (per month @ 13,091 Baht), salary of nurses (per month @ 4,900 Baht), salary of residents (per month 4,700 Baht), and contrast media HOCM (total 6,242 cases) = 761,524 Baht (US$30,461).
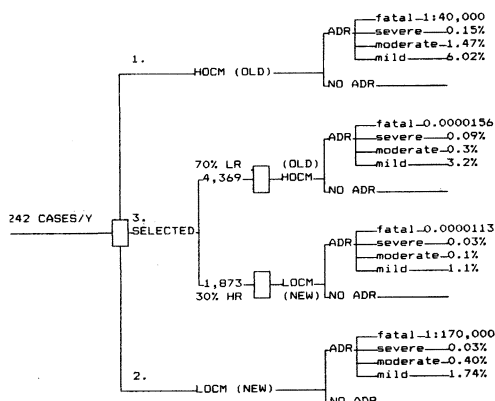
Fig 1—Decision tree for three alternatives of intravenous contrast medium use.

Table 3

Reactions (%) in the high risk and low risk patients receiving both HOCM and LOCM (Palmer, 1988).

	Mild	Moderate	Severe
HOCM			
High risk	7.2	2.7	0.36
Low risk	3.2	0.3	0.09
LOCM			
High risk	1.1	0.1	0.03
Low risk	0.9	0.09	0

Cost (C2) indirect cost.

Cost of lost production due to the time required to receive the examination which is average two hours (including transportation time)

Cost (C3) intangible cost.

Value of pain and suffering of patients due to participation in the examination is an intangible cost. In the case of fatal reaction or sequelae from non-fatal reactions, there are additional intangible costs.

The direct costs for radiographic studies of the three alternatives are identical except for the cost of the contrast media. Indirect costs relate to costs of production losses due to the time required to receive the examination, which is on the average two hours. This cost as well as the intangible cost should also be approximately the same for all alternatives. Hence, the difference in the cost of the contrast media will be the only cost considered in this study.

Alternative 2

Contrast media LOCM (total 6,242 cases) = 15,636,210 Baht (US$625,448).

Alternative 3

Contrast media HOCM 70%, LOCM 30% = 5,224,883 Baht (US$208,995). [patients 4,369 cases use HOCM = 533,018 Baht (US$21,321) patients 1,873 cases use LOCM = 4,691,865 Baht (US$187,675)

Table 4

Properties and price of the proposed HOCM and LOCM.

Generic name	Trade name	Iodine (mg/ml)	Osmolar (mOsm/Kg)	Size	Price/US$ Baht (25B = US$1)
Diatrizoate sodium 10% meglumine 66%	MD 76	370	2,140	50 ml/V	B122.00 (US$4.88)
Iohexol	Omnipaque	300	709	50 ml/V	B2,505.00 (US$100.20)

The output created by a health-care program is health improvement which may be measured by health effects (E = healthy days saved), economic benefits (B = money saved from treatment of adverse drug reactions), and value of health improvement *per se* (which will not be considered in this study).

The economic benefits may be direct, indirect or intangible. Direct benefits (B1) are the treatment costs averted due to reduction in the rate of adverse drug reactions (ADR) with the LOCM. Indirect benefits (B2) relate to production gains to society because more people are well or alive and able to return to work.

B1 = treatment costs averted due to reduction in the rate of ADRs with LOCM. This will be the difference in the treatment cost of ADRs between #1 and #2 and the difference in the treatment cost of ADRs between #1 and #3.

Treatment costs depend on severity of the ADRs, classified as (see Appendix 2):

1. Mild or minor reaction :
Cost per case in treatment of mild ADR
    = 30.63 Baht (US$1.23)

2. Intermediate or moderate reaction :
Total cost per case in treatment of moderate ADR
    = 1,165.50 Baht (US$46.62).

3. Severe reaction :
Total cost per case in treatment of severe ADR
    = 8,911.00 Baht (US$356.44)

For patients with acute renal failure, approximately 1.7% need renal dialysis (Gomes *et al*, 1985). We assume that 1.7% of the severe ADR group need renal dialysis, approximately two times in the course of the acute renal failure.
    Cost of peritoneal dialysis @ 1,000 Baht
    = 2,000 Baht (US$80).

B2 = Production gains to society because more people are well or alive and able to return to work. This will be the difference in the cost of production lost from time off work due to the treatment of the ADRs between #1 and #2, and between #1 and #3.
Average income of patients per day per case
    = 243.45 Baht (US$9.74) (see Appendix 3).
Value production of mild ADR/case = 243.45/8
    = 30.43 Baht (US$1.22).

Value production of moderate ADR/case
    = 243.45 Baht (US$9.74).
Value production of severe ADR/case (7 day hospitalization)
    = 1,704.20 Baht (US$68.17)

For fatal cases, the average age of patients undergoing examination is 43 years (Statistics of Department of Radiology, Chulalongkorn Hospital, 1989). Life expectancy at 43 years of age is 76 years (Thai Public Health Statistics, 1987). The value of production per case, using a discount rate of 10% over 33 years (a reasonable discount rate for a developing country).
    = 243.45 × 247 × 9.5573 = 574,701 Baht (US$22,988)

In order to compare alternatives, it is necessary to compute the treatment costs due to ADRs for each alternative. These costs are comprised of the costs of treating severe ADR, including acute renal failure in the 1.7% of the severe reactions, the costs of treating cases of moderate ADR and the costs of treating cases of mild ADR. The total cost of treating ADRs for a cohort of 6,242 patients will be labeled as T1.

Alternative 1

T1 = 202,205 Baht (US$8,088)
T2 represents the production loss to society due to ADRs to contrast media. It is comprised of time off work for the one hour associated with observation following a mild ADR, time off work for a day observation associated with moderate ADR, and seven days off work for hospitalization associated with treatment for severe ADR. For fatal reactions, the present value of future earnings are included.
T2 = 139,411 Baht (US$5,577)
T Total #1 = 341,616 Baht (US$13,665)

Alternative 2

T1 = 49,177 Baht (US$1,967)
T2 = 33,676 Baht (US$1,347)
T Total #2 = 82,854 Baht (US$3,314)

Alternative 3

T1 = 62,571 Baht (US$2,503)
T2 = 67,520 Baht (US$2,701)
T Total #3 = 130,091 Baht (US$5,204)

The outcome or health effect will be considered in terms of both fatal and non-fatal complications of the ADR. The outcome will be measured in the same unit as patient healthy days lost (HDL) for each alternative.

Alternative 1

There are 6,242/40,000 = 0.15605 fatality per year. This will be equal to (0.15605 × 9.5573) = 1.49142 life years lost or 544.37 HDL (discount rate 10%).
Healthy days lost for ADR = 172.96 HDL.
Total healthy days lost = 544.37 + 172.96 = 717.

Alternative 2

There are 6,242/170,000 = 0.03672 fatality per year. This will be equal to (0.03672 × 9.5573) = 0.35094 life years lost or 128.09 HDL.
Healthy days lost for ADR = 42.61 HDL.
Total healthy days lost = 128.09 + 42 = 171.

Alternative 3

There are (0.0000156 × 4,369 + 0.0000113 × 1,873) = 0.08932 fatality per year. This will be equal to (0.08932 × 9.5573) = 0.8537 life year lost or 311.60 HDL.
Healthy days lost for ADR = 53.09 HDL.
Total healthy days lost = 311.60 + 53.09 = 365.

RESULTS

Incremental cost-effectiveness between #2 and #1 (Table 5).

= incremental cost (C) minus (incremental treatment cost due to ADR and cost of production lost, T Total) divided by incremental healthy days lost (healthy days saved).
= 26,738 Baht (US$1,070) per healthy day saved (HDS).

Incremental cost-effectiveness between #3 and #1

= 12,057 Baht (US$482) / HDS.
For fatal cases only, the incremental cost-effectiveness between the #2 and the #1 is 35,111 Baht (US$1,404) / HDS. The incremental cost-effectiveness between the #3 and the #1 is 18,265

Baht (US$731) / HDS.

The incremental cost (cost of contrast media plus cost of treatment due to ADR plus cost of lost production from work due to ADR) between #1 and #2 is 14,615,924 Baht (US$584,637) and between #1 and #3 is 4,251,834 Baht (US$170,073).

The cost per patient in the alternative 1, 2, and 3 is 177 Baht (US$7), 2,518 Baht (US$101), and 858 Baht (US$34) respectively.

From the hospital point of view, 20% of the patients cannot pay for the drug using the conventional procedure (Statistics of Department of Radiology, Chulalongkorn Hospital in 1989).

If we adopt LOCM, assume that 50% of the patients will not be able to pay for the drug.

Hospital costs are then as follows :

Alternative 1

= 20% C1 + T1 (treatment cost)
= 354,510 Baht (US$14,180)

Alternative 2

= 50% C1 + T1 (treatment cost)
= 7,867,282 Baht (US$314,691)

Alternative 3

= 20% C (HOCM) + 50% C (LOCM) + T1 (treatment cost)
= 2,515,108 Baht (US$100,604)

The incremental cost-effectiveness between the #2 and #1, and between the #3 and #1 will be 13,744 Baht (US$550) and 6,127 Baht (US$245) / HDS.

The incremental cost (cost of contrast media plus cost of treatment due to ADRs) between #1 and #2 is 7,512,733 Baht (US$300,511) and between #1 and #3 is 2,160,598 Baht (US$86,424).

The cost per patient in the alternative 1, 2, and 3 is 57 Baht (US$2), 1,260 Baht (US$50), and 403 Baht (US$16) respectively.

Sensitivity analysis

Reduction in the price of LOCM due to competition in the market or bulk purchases with competitive bidding will be taken into account in the sensitivity analysis. The range of price

Table 5

Cost-effectiveness analysis in three alternatives: in societal and hospital viewpoints in Baht (25 Baht = US$1). A cohort of 6,242 patients.

Viewpoint		Alternative 1	Alternative 2	Alternative 3
Society	Cost (a)	1,103,140 (US$44,126)	15,719,064 (US$628,763)	5,354,974 (US$214,199)
	IC		14,615,924 (US$584,637)	4,215,834 (US$170,073)
	Effect HDL	717	171	365
	Cost per Patient	177 (US$7)	2,518 (US$101)	850 (US$34)
	CE		26,739 (US$1,070)	12,058 (US$482)
Hospital	Cost (b)	354,510 (US$14,180)	7,867,282 (US$314,691)	2,515,108 (US$100,604)
	IC		7,512,773 (US$300,511)	2,160,598 (US$86,424)
	Effect HDL	717	171	365
	Cost per patient	57 (US$2)	1,260 (US$50)	403 (US$16)
	CE		13,744 (US$550)	6,127 (US$245)

Note: Cost (a) = C1 + T1 + T2
         Cost (b) = (20% of HOCM drug cost in alternative 1, 50% of LOCM drug cost in alternative 2, and 20% of HOCM plus 50% of LOCM drug cost in alternative 3) + T1
         IC   = Incremental cost.   CE = Cost-effectiveness.
         HDL = Healthy days lost.

reductions considered will be 25%, 50%, and 75% (Table 6). For the hospital viewpoint estimates 20%, 30% and 50% of the patients who cannot pay the reduced drug price, will also be considered (Table 7).

DISCUSSION

Incremental cost per patient healthy day saved will be about twofold less if we switch contrast media use from #1 to #3 compared with switching from #1 to #2 in both the societal and hospital viewpoints (Table 5). However, compared to #1 society has to pay 12,058 Baht (US$482) more per patient healthy day saved in #3 and pay 26,739 Baht (US$1,070) more in #2. The incremental cost per HDS is higher than estimates for North America (CJ Zylak, personal communication), because the cost of LOCM is much higher while the treatment cost of ADR is lower in Thailand. Results of the sensitivity analysis lead to the same

Table 6

Sensitivity analysis in societal viewpoint depending on percentages of reduction in LOCM drug price (25 Baht = US$ 1).

Alternative in Baht	Cost, 25%	Cost 50%	Cost 75%
1	1,103,140	1,103,140	1,103,140
2	11,810,011	7,900,959	3,991,906
3	4,182,008	3,009,042	1,836,075

Price reduction %		Alternative 2 compared to 1	Alternative 3 compared to 1
25	IC	10,706,871 (US$428,275)	3,078,868 (US$123,155)
	CE	19,588 (US$784)	8,731 (US$349)
50	IC	6,797,819 (US$271,913)	1,906,011 (US$76,240)
	CE	12,436 (US$498)	5,405 (US$216)
75	IC	2,888,766 (US$115,551)	732,935 (US$29,317)
	CE	5,285 (US$211)	2,079 (US$83)

conclusion (2 - 2.5 times less in #3, shown in Table 6). Society would pay the least amount at the 75% reduced LOCM drug price if #3 is used (2,079 Baht = US$83/HDS). The hospital would pay the least amount at the 75% reduced LOCM drug price when the percentage of patients unable to pay for the drug is the same as using HOCM (20%). This incremental cost will be 140 Baht (US$6)/HDS (Table 7). Nevertheless, using the conventional contrast media (HOCM) which is #1, the hospital will subsidize the least cost per patient (57 Baht), which is approximately sevenfold less than in #3 and twentyfold less than in #2. Thus, #3 should be considered if the LOCM price is reduced more than 75% (= 626 Baht (US$25) or less), and more than 80% of the patients are able to pay.

Because the intangible cost which involves pain and psychic costs from fear of ADRs is omitted, the advantages of LOCM are underestimated in this analysis. From the hospital viewpoint, if the patients are willing to pay for LOCM to avoid pain and psychic costs, the hospital will have the advantage of ADR treatment cost saved.

The possibility of using premedication such as corticosteroid to counteract the ADR of HOCM (Lasser, 1988) should also be considered in further cost-effectiveness evaluations.

In sum, the substitution of LOCM for HOCM at Chulalongkorn Hospital would represent and expensive way to obtain additional healthy days and avoid additional treatment costs associated with ADRs. The use of LOCM for high risk patients (Alternative 3) is more attractive than its use for all patients (Alternative 2). Nonetheless, under current conditions, it is likely that a number of other health-care programs in Thailand would represent less costly means to obtain additional

Table 7

Sensitivity analysis in hospital viewpoint depending on percentages of reduction in LOCM drug price and the percentages of the patients who cannot afford the corresponding drug price.

Price reduction	Hospital cost at diff rate		Alternative 2 compared to 1	Alternative 3 compared to 1
25%	20%	IC	2,040,099 (US$81,604)	518,445 (US$20,738)
		CE	3,730 (US$149)	1,469 (US$59)
	30%	IC	3,212,814 (US$128,513)	923,636 (US$36,945)
		CE	5,874 (US$235)	2,617 (US$105)
	50%	IC	5,558,246 (US$222,330)	1,734,020 (US$69,361)
		CE	10,161 (US$407)	4,912 (US$197)
50%	20%	IC	1,258,288 (US$50,332)	283,852 (US$11,354)
		CE	2,300 (US$92)	804 (US$32)
	30%	IC	2,040,099 (US$81,604)	571,747 (US$22,870)
		CE	3,730 (US$149)	1,620 (US$65)
	50%	IC	3,603,720 (US$144,149)	1,147,537 (US$45,902)
		CE	6,588 (US$264)	3,251 (US$130)
	20%	IC	476,478 (US$19,059)	49,258 (US$1,970)
		CE	871 (US$35)	140 (US$6)
		IC	867,383 (US$34,695)	219,857 (US$8,794)

Table 7 (cont.)

Price reduction	Hospital cost at diff. rate		Alternatives 2 and 1	Alternatives 3 and 1
75%	30%			
		CE	1,586 (US$64)	623 (US$25)
		IC	1,649,194 (US$65,968)	561,053 (US$22,442)
	50%			
		CE	3,015 (US$121)	1,589 (US$64)

IC = Incremental cost. CE = Cost-effectiveness.

healthy days than the substitution of LOCM for HOCM.

REFERENCES

Ansell G. Adverse reactions to contrast agents: scope of problem. *Invest Radiol* 1970; 5 : 374-84.

Ansell G, Tweedie MCK, West CR, Evans P, Couch L. The current status of reactions to intravenous contrast media. *Invest Radiol* 1980; 15 : (suppl) S32-S9.

Fischer HW. Catalog of intravascular contrast media. *Radiology* 1986; 159 : 561-3.

Gomes AS, Baker JD, Paredero VM, *et al.* Acute renal dysfunction after major arteriography. *Am J Radiol* 1985; 145 : 1249-53.

Hartman GW, Hatterly RR, Witten DM, Williamson B. Mortality during excretory urography: Mayo Clinic experience. *Am J Radiol* 1982; 139 : 919-22.

Katayama H, Yamaguchi K, Kozuka T, Takashima T, Seez P, Matsuura K. Adverse reactions to ionic and nonionic contrast media: A report from the Japanese committee on the safety on contrast media. *Radiology* 1990; 175 : 621-8.

Kinnison ML, Powe NR, Steiberg EP. Results of randomized controlled trials of low-versus high-osmolarity contrast media. *Radiology* 1989; 170 : 381-9.

Lasser EG. Pretreatment with corticosteroids to prevent reactions to IV contrast material: overview and implications. *Am J Radiol* 1988; 150 : 257-9.

Palmer FG. The RACR survey of intravenous contrast media reactions final report. *Australasian Radiol* 1988; 32 : 426-8.

Pendergrass HP, Tondreau L, Pendergrass ET, Ritchie DJ, Hildreth EA, Ascovitz SI. Reactions associated with intravenous urography: historical and statistical review. *Radiology* 1958; 71 : 1-12.

Shehadi WH. Adverse reactions to intravascularly administered contrast media: a comprehensive study based on a prospective survey. *Am J Radiol* 1975; 124 : 145-52.

Shehadi WH, Toniolo G. Adverse reactions to contrast media. *Radiology* 1980; 137 : 299-302.

Thai Public Health Statistics, Division of Health Statistics, Office of the Permanent Secretary,

Ministry of Public Health 1987, p 18.

Torrance GW. Measurement of health state utilities for economic appraisal. *J Health Econ* 1986; 5 : 1-30.

Witten DM, Hirsch FD, Hartman GW. Acute reaction to urographic contrast media; incidence, clinical characteristics and relationship to history of hypersensitivity states. *Am J Radiol* 1973; 119 : 832-40.

Wolfromm R, Dehouve A, Degand F, Wattez E, Lange R, Crehalet A. Les accidentes graves par injection intraveineuse de substances iodees pour urographie. *J Radiol Electrol* 1966; 47 : 346-57.

APPENDIX 1. Details in calculation for the incidence of fatal reactions in low risk patients who receive HOCM were computed under the assumption that 30% of a mixed group of patients are high risk, 70% are low risk, and the overall rate of fatal incidence is 1:40,000 (see Ansell *et al,* 1980 in Table 1).

$$0.7 X_1 + 0.3 X_2 = 1/40,000$$

We further assume $X_2 = 3 X_1$. According to Palmer, 1988 (Table 3), rate of complications for high risks (HR) is about 3 times the rate of complications for low risks (LR) in every level of complications.

$$0.7 X_1 + 0.9 X_1 = 1/40,000$$
$$1.6 X_1 = 1/40,000$$
$$X_1 = 0.0000156 \text{ (LR with HOCM)}$$
$$X_2 = 0.000469 \text{ (HR with HOCM)}$$

Hence, incidence of mortality in low risk patients who received HOCM = 0.0000156

We can compute the mortality incidence of high risk patients who received LOCM using the same assumptions.

$$0.7 X_1' + 0.3 X_2' = 1/170,000$$
$$0.7 X_1' + 0.9 X_1' = 1/170,000$$
$$1.6 X_1' = 1/170,000$$
$$X_1' = 0.00000368 \text{ (LR with HOCM)}$$
$$X_2' = 0.0000113 \text{ (HR with HOCM)}$$

Hence, incidence of mortality in high risk patients who received LOCM = 0.0000113

APPENDIX 2. Treatment costs depend on severity of the adverse drug reaction, classified as :

1. Mild or minor reaction means heat, pain, nausea, limited urticaria. There is no treatment required for this condition. However, the patient should be observed for one hour.
Nursing time (1 hour for each patient)   =   30.63 Baht   (US$1.23)
Cost per case in treatment of mild ADR   =   30.63 Baht   (US$1.23)

2. Intermediate or moderate reaction (usually completely reversible within 24 hours) involves faintness, severe vomiting, extensive urticaria, dyspnea, chest pain, seizure, bronchospasm, or transient hypotension.

Costs of treatment include :

Prolonged length of procedure about 60 minutes.
2.1   Radiology technician time 1 hour   =   4,240/160   =   26.5 B
2.2   Radiologist time 1 hour   =   13,091/160   =   81.8 B
2.3   Resident time 1 hour   =   4,700/160   =   29.4 B
2.4   Physician who takes care of patient   =   81.8 B

2.5	Nursing time (observe 24 hours)	= 4,900 × 24/160	=	735.0 B
2.6	Use of observation room (100 B/day at Chulalungkorn Hospital)		=	100.0 B
2.7	Drugs administered			
	2.7.1 Epinephrine 1:1000 1 mg/Amp		=	4.0 B
	2.7.2 Aminophylline 250 mg/Amp		=	5.0 B
	2.7.3 Pyriton 10 mg/ml/Amp		=	6.0 B
	2.7.4 Hydrocortisone 100 mg/Amp		=	40.0 B
	2.7.5 Normal saline 0.9% 1,000 ml		=	35.0 B
2.8	IV set and needle		=	21.0 B

Total cost per case in treatment of moderate ADR = 1,165.50 Baht (US$46.62)

3. Severe reaction (patients need 7 day hospitalization on average) means shock, anaphylactoid effects, pulmonary edema, cardiac arrest, myocardial infarction, laryngeal edema, or acute renal failure.

Costs of treatment include :

Prolonged length of procedure about 60 minutes.

3.1	Radiology technician time 1 hour	= 4,240/160	=	26.5 B
3.2	Radiologist time 1 hour	= 13,091/160	=	81.8 B
3.3	Resident time 1 hour	= 4,700/160	=	29.4 B
3.4	Physician who takes care of patient		=	81.8 B
	Daily visiting and treatment in ICU for 7 days (30 minutes each day)		=	286.4 B
3.5	Anesthetist 1 hour		=	81.8 B
3.6	Nursing time (2 nurses, 1 hour each)	= 2 × 4,900/160	=	61.3 B
3.7	Drugs administered			
	3.7.1 Epinephrine 1:1000 1 mg/Amp		=	4.0 B
	3.7.2 Aminophylline 250 mg/Amp		=	5.0 B
	3.7.3 Hydrocortisone 100 mg/Amp		=	40.0 B
	3.7.4 Atropine gr 1/100/Amp		=	3.0 B
	3.7.5 Dopamine 50 mg/Amp		=	58.0 B
	3.7.6 Sodium bicarbonate 7.5% in 50 ml @ 22 B X 3		=	66.0 B
	3.7.7 Normal saline 0.9% 1000 ml		=	35.0 B
3.8	IV set and needle		=	21.0 B
3.9	Use of endotracheal tube and anesthetic machine		=	200.0 B
3.10	Oxygen 5,000 liters/tank @ 7,500 B 2 liters/minute for 60 minutes		=	180.0 B
3.11	Hospitalization			
	3.11.1 Seven days in ICU (per diem cost for ICU = 1,000 B/day)		=	7,000 B
	3.11.2 Blood gas study @ 100 Baht (at least 3 studies)		=	300.0 B
	3.11.3 Portable chest X-ray @ 150 Baht (at least 2 studies)		=	350.0 B

Total cost per case in treatment of severe ADR = 8,911.00 Baht (US$356.44)

For patients with acute renal failure, approximately 1.7% need renal dialysis. We assume that 1.7% of the severe ADR group need renal dialysis, approximately two times in the course of the acute renal failure.

Cost of peritoneal dialysis @ 1,000 Baht = 2,000 B

APPENDIX 3. Computing average income of the patients.

Per capita income at current market prices in Bangkok (BKK) and vicinity in the year 1987 was 71,586 Baht (Source: Gross Regional and Provincial Product 1981-1987 reported by National Economic and Social Development Board of Thailand, in 1989).

Assume per capita income in BKK is equal to per capita income of the patients. However, the per capita income includes payments for labor, and capital/land as factors of production.

In 1987, compensation of employees $=$ $352,014 \times 10^6$ Baht..1

Income from farms, professions and other unincorporated enterprises received by households and private non-profit institutions (partly labor, partly capital/land)

$$= 449,527 \times 10^6 \text{ Baht..2}$$

National income $=$ $958,421 \times 10^6$ Baht..3
(Source: National Income of Thailand 1988 Edition : p 15)

Hence, upper bound estimate labor as a percent of national income $= (1 + 2)/3 = 83.63\%$

Lower bound estimate labor as a percent of national income $= 1/3 = 36.7\%$

For BKK, capital is relatively more important than in the rest of the country. Therefore using upper bound which is 84% of per capita in BKK as average labor income in BKK will be appropriate. This will be equal to $0.84 \times 71,586 = 60,132$ Baht per year.

There are 247 working days in a year. Thus, the average income of the patients in BKK $= 60,132/247 = 243.45$ Baht (US$10) per day. This figure will be used to estimate the values of production loss per day for patients who suffer adverse drug reactions.