

## Cost effectiveness analysis of intravenous ketorolac and morphine for treating pain after limb injury: double blind randomised controlled trial

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### Abstract

**Objectives** To investigate the cost effectiveness of intravenous ketorolac compared with intravenous morphine in relieving pain after blunt limb injury in an accident and emergency department.

**Design** Double blind, randomised, controlled study and cost consequences analysis.

**Setting** Emergency department of a university hospital in the New Territories of Hong Kong.

**Participants** 148 adult patients with painful isolated limb injuries (limb injuries without other injuries).

**Main outcome measures** Primary outcome measure was a cost consequences analysis comparing the use of ketorolac with morphine; secondary outcome measures were pain relief at rest and with limb movement, adverse events, patients' satisfaction, and time spent in the emergency department.

**Results** No difference was found in the median time taken to achieve pain relief at rest between the group receiving ketorolac and the group receiving morphine, but with movement the median reduction in pain score in the ketorolac group was 1.09 per hour (95% confidence interval 1.05 to 2.02) compared with 0.87 (0.84 to 1.06) in the morphine group ( $P=0.003$ ). The odds of experiencing adverse events was 144.2 (41.5 to 501.6) times more likely with morphine than with ketorolac. The median time from the initial delivery of analgesia to the participant leaving the department was 20 (4.0 to 39.0) minutes shorter in the ketorolac group than in the morphine group ( $P=0.02$ ). The mean cost per person was \$HK44 (£4; \$5.6) in the ketorolac group and \$HK229 in the morphine group ( $P<0.0001$ ). The median score for patients' satisfaction was 6.0 for ketorolac and 5.0 for morphine ( $P<0.0001$ ).

**Conclusion** Intravenous ketorolac is a more cost effective analgesic than intravenous morphine in the management of isolated limb injury in an emergency department in Hong Kong, and its use may be considered as the dominant strategy.

### Introduction

Patients commonly present to accident and emergency departments with severe pain after limb injury and

need early treatment with effective analgesia. The use of analgesia in emergency departments and intensive care units may be suboptimal.<sup>1-4</sup> Some analgesics, such as morphine (the opiate morphine sulphate), have a perceived risk of dependency and therefore, although relatively cheap, are regarded as "dangerous."<sup>5 6</sup> In single doses they are associated with serious adverse effects that need monitoring and further treatment by both nursing and medical staff. Therefore these drugs, although inexpensive to buy, may have a substantial financial impact on health resources. The impact on emergency departments has never been investigated quantitatively. Non-steroidal anti-inflammatory drugs are also effective at relieving moderate to severe pain and are believed to have fewer adverse effects than opiates.<sup>7-10</sup> In North America, the United Kingdom, other parts of Europe, and in Hong Kong ketorolac (ketorolac tromethamine) is the only non-steroidal anti-inflammatory drug currently licensed for managing pain by rapid intravenous administration.<sup>5 10</sup>

Although intravenous morphine titrated according to the patient's needs is a current recommended gold standard against which all strong analgesics may be evaluated and compared for efficacy and safety,<sup>1</sup> little is known about the economic aspects of its use. The few controlled trials comparing doses of intravenous ketorolac and intravenous morphine were all either perioperative studies or associated with cancer.<sup>8 9 11-18</sup>

We performed a cost effectiveness analysis comparing intravenous ketorolac with intravenous morphine in the management of pain after blunt limb injury (non-penetrating injury to a limb) in an accident and emergency department setting. We hypothesised that, although ketorolac is about three times as expensive as morphine in Hong Kong, ketorolac would be the more cost effective option if all additional related costs were taken into account.

### Methods

We conducted the study in the accident and emergency department of the Prince of Wales Hospital, Shatin, a 1400 bed university teaching hospital in the New Territories of Hong Kong.

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We obtained ethical approval from the local institutional research ethics committee and informed written consent from each patient.

### Inclusion and exclusion criteria

All patients aged  $\geq 16$  years presenting to the emergency department between 9 am and 5 pm, Monday to Friday, with an isolated painful limb injury (limb injury without other injury) were considered for the study. Patients were excluded if they had a history of substance misuse, dementia, indigestion, peptic ulceration or gastrointestinal haemorrhage, recent anticoagulation, pregnancy, adverse reaction to morphine or ketorolac, renal or cardiac failure, hepatic problems, rectal bleeding, recent ( $< 24$  hours) use of non-steroidal anti-inflammatory drugs, asthma, chronic obstructive airways disease, chronic pain syndromes, or previous treatment with analgesia for the same injury.

### Interventions and randomisation

Patients were randomly allocated to one of the two treatment groups by using a random number table.<sup>19</sup> Ketorolac was prepared as a 2 mg/ml solution and morphine as a 1 mg/ml solution. One group would receive intravenous ketorolac as a 10 mg (5 ml) loading dose over 60 seconds followed by 5.0 mg (2.5 ml) every 5 minutes up to 20 minutes (maximum 30 mg) as required. The other group would receive intravenous morphine as a 5 mg (5 ml) loading dose over 60 seconds followed by 2.5 mg (2.5 ml) every 5 minutes up to 20 minutes (maximum 15 mg) as required.

A nurse with clinical responsibilities opened a pre-coded envelope with details of the drug and randomisation number. Either morphine or ketorolac was prepared in the emergency department according to normal practice except that the syringe was labelled with a coded number rather than the drug name. This nurse was not involved in the administration of analgesia, the assessment of the participant, or the treatment of adverse effects. Both the research nurse, with non-clinical duties, and the participant were blinded to the treatment. The aim was to achieve total pain relief

at rest—that is, a pain score of 0—provided that the maximum dose was not exceeded and there were no adverse effects.

### Clinical measurements and data collection

A 10 inch (254 mm), numbered (0-10), horizontal, visual analogue pain score was used for baseline measurements and at subsequent time intervals after the first injection.<sup>20</sup> A large scale (inches rather than centimetres) was used because disability from poor vision is particularly high in Hong Kong. Routine observations, pain scores, and adverse effects were recorded every five minutes for the first 30 minutes after drug administration, at 30 minute intervals for the subsequent one and a half hours, and once more at six hours. Participants were aware of their previous scores at all stages of recording. The type, number, duration, and severity of adverse effects were documented.<sup>21</sup> Data were analysed with SAS Statview for Windows, version 5.0 (Abacus Concepts, SAS Institute, Cary, NC, USA).

### Clinical and perception outcomes

The primary clinical outcomes were pain relief measured as changes in the pain score, and adverse effects. Pain relief is presented as odds ratios of reaching 50%, 75%, and 100% reduction in pain score (both at rest and with activity) and as median changes in the pain score estimated with the Kaplan-Meier product limit method. "Activity," for the purpose of this study, involved the research nurse gently moving the injured limb to assess pain. The perception outcome measures were participants' satisfaction with pain relief and their satisfaction with the care given by staff in the emergency department at the time of discharge from the department.

The end point was six hours after the administration of analgesia if the patient was discharged from the emergency department.

### Cost measurements and data collection

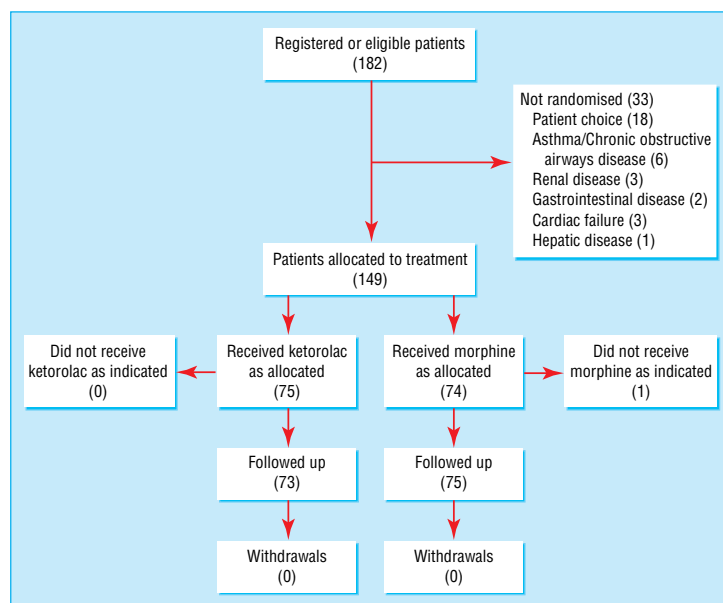
Costs were calculated according to activities, which included the preparation and administration of analgesics and other drugs, care relating to adverse events, and admission to hospital. We obtained estimates for the time required to use each resource in each activity and the unit costs for each of these resources. Drugs were costed separately according to dose, and cost estimates were made for the actual treatment time for adverse events.

### Cost effectiveness analysis

The primary efficiency measure was a cost consequences analysis<sup>22</sup>—that is, a comparison of costs with several different outcomes. Qualitative, rather than quantitative, descriptions were made in comparing outcomes and efficiency measures.<sup>23</sup> The sensitivity analysis of cost measures was conducted with regard to observational periods.

### Statistical analysis

Data were analysed on an intention to treat basis, and we used two tailed tests in all statistical analyses. Baseline characteristics of the two treatments were compared using the  $\chi^2$  test or the Mann-Whitney U test. Time to event variables were evaluated by using the Kaplan-Meier product limit method, and the log rank test was used to compare the treatment groups. A regression line indicating the change in pain score over



Flow chart describing progress of patients through randomised trial

time was found, and its slope was therefore a summary measure for each patient.<sup>24</sup> The likelihood of achieving pain reduction was presented as hazard ratios.

## Results

During the defined study period 182 patients attended the emergency department with acute, painful limb injuries, 149 of whom were allocated to receive blinded analgesia (figure).

### Baseline characteristics and clinical outcomes

Baseline characteristics of the 148 participants in the two groups were similar (table 1).

According to the doses and methods used in this study, the odds of achieving 50%, 75%, and 100% pain relief at rest favoured morphine, but the results were not statistically significant (table 2). With activity, the odds of achieving 50% and 75% pain reduction favoured ketorolac, although only the result for 75% pain reduction was statistically significant (table 2). The median rate of a decrease in pain score at rest was 11.40 (95% confidence interval 9.40 to 12.80) with ketorolac and 10.80 (10.20 to 13.54) with morphine ( $P=0.54$ ); with activity the median decrease in pain score was higher in the ketorolac group (1.09 (1.05 to 2.02) *v* 0.87 (0.84 to 1.06)).

Participants were 16 times more likely to develop adverse effects with morphine than with ketorolac (table 3), with an odds ratio of 144.2 (95% confidence interval 41.5 to 501.6;  $P<0.0001$ ). The commonest adverse effects are shown in table 3.

No difference was found between the two drugs for time between injury and arrival at the emergency department (table 1) or for time between arrival at the emergency department and prescription of analgesia, preparation of analgesia, or time taken for radiography (table 4). Participants waited longer (between prescription and administration of initial bolus) to receive morphine than ketorolac ( $P=0.0002$ ) and therefore spent longer in the emergency department, although total time spent in the emergency department was not statistically significant ( $P=0.11$ ). The total time that nurses and doctors spent managing adverse effects was also longer for the morphine group than for the ketorolac group.

### Cost analysis

Marginal costs were used to measure the difference in costs between the two interventions. The mean cost per person, excluding admissions for orthopaedic reasons, was \$HK43.60 (£4; \$5.6) for those in the ketorolac group and \$HK228.80 for those in the morphine group ( $P<0.0001$ ). Overall mean cost per person, including admissions unrelated to analgesia, was \$HK11 361.20 for those in the ketorolac group and \$HK7279.62 for those in the morphine group ( $P=0.45$ ). If admission costs are excluded, much of the difference between the costs for the two groups was the result of the management of adverse effects.

### Cost effectiveness

When we included admission costs we observed no significant differences in costs between the two groups. We found a significant reduction in pain with activity in the ketorolac group and significantly fewer common adverse events. Additionally, the participants in the

**Table 1** Participants' characteristics (n=148). Values are numbers (percentages\*) of participants unless stated otherwise

Variable	Ketorolac group (n=75)	Morphine group (n=73)	P value
Mean (SD) age (years)	53.9 (21.7)	53.2 (21.8)	0.85‡
No (%) of men	38 (51)	33 (45)	0.51§
Mean (SD) body mass index (kg/m <sup>2</sup> )	22.8 (3.2)	23.0 (3.7)	0.77‡
Mean (interquartile range) time between injury and arrival at hospital (minutes)	95 (30-630)	82 (33-921)	0.75
Cause of injury:			
Motor vehicle crash	6 (8)	4 (5)	0.58¶
Falls	46 (61)	51 (70)	
Crush	20 (27)	14 (19)	
Other	3 (4)	4 (5)	
Fractures:	50 (67)	48 (66)	0.91§
Clavicle, humerus, elbow	5 (7)	8 (11)	
Radius, ulnar	8 (11)	11 (15)	
Hand	15 (20)	13 (18)	
Femur, patella	14 (19)	12 (16)	
Tibia, fibula	5 (7)	3 (4)	
Foot	2 (3)	1 (1)	
Non-fractures:			
Dislocation, upper limb	2 (3)	1 (1)	
Soft tissue injury, upper limb	10 (13)	10 (14)	
Soft tissue injury, lower limb	14 (19)	14 (19)	
Initial mean (SD) pain score:			
At rest	3.8 (1.1)	3.9 (1.1)	0.65‡
With activity	8.1 (1.2)	8.1 (1.2)	0.85‡
Referred for orthopaedic assessment	41 (55)	36 (49)	0.52§
Admitted to hospital†	38 (51)	29 (40)	0.18§
Admitted with adverse effects	0	3 (4)	

\*Percentages may not sum to 100 because of rounding.

†Patients admitted to hospital (to orthopaedic or emergency observation ward).

‡‡ test for unpaired means comparison.

§ $\chi^2$  test.

¶Fisher's exact test.

**Table 2** Likelihood of achieving pain reduction

Activity level	Hazard ratio*	P value†
At rest:		
50% reduction in pain	0.83 (0.60 to 1.15)	0.271
75% reduction in pain	0.84 (0.60 to 1.16)	0.279
Complete pain relief	0.93 (0.66 to 1.30)	0.654
With activity:		
50% reduction in pain	1.18 (0.85 to 1.63)	0.330
75% reduction in pain	1.49 (1.05 to 2.12)	0.027

\* $>1$  means that ketorolac performed better than morphine for pain relief.

†Wald test.

**Table 3** Numbers (percentages) of participants with adverse events\*

Variable	Ketorolac group (n=75)	Morphine group (n=73)	P value†
Total‡	4 (5)	65 (89)	<0.0001
Drowsiness	1 (1)	43 (59)	<0.0001
Sleeping	0	8 (11)	0.0054
Dizziness	2 (2)	55 (75)	<0.0001
Nausea	0	27 (37)	<0.0001
Vomiting	0	12 (16)	<0.001
Phlebitis	0	20 (27)	<0.0001

\*Some participants reported more than one adverse effect.

†Fisher's exact test.

‡Includes participants with uncommon adverse effects that are noted in the text but not in the table.

ketorolac group showed a greater degree of satisfaction with analgesia (6.0; 5.0 to 6.0) than the participants in the morphine group showed with their drug (5.0; 4.0 to 6.0) ( $P<0.0001$ ). The satisfaction with emergency department management was similar for both groups (6.0 (5.0 to 7.0) *v* 6.0 (5.0 to 6.0);  $P=0.3$ ). Ketorolac administration therefore is the "dominant" strategy,

**Table 4** Median number (interquartile range) of minutes relating to participants' treatment

Variable	Ketorolac group (n=75)	Morphine group (n=73)	Median difference (95% confidence interval)	P value*
Interval between arrival in emergency department and doctor prescribing analgesia	38.0 (30.0 to 54.0)	39.0 (29.0 to 53.0)	1.0 (-5.0 to 7.0)	0.72
Preparation for analgesia	5.0 (5.0 to 10.0)	10.0 (5.5 to 12.5)	2.0 (0 to 5.0)	0.0002
Undergoing radiography	5.0 (5.0 to 10.0)	5.0 (4.0 to 10.0)	0 (-1.0 to 0)	0.75
Total time spent in emergency department	155.0 (112.0 to 198.0)	171.0 (126.0 to 208.5)	15.0 (-4.0 to 33.0)	0.11
Interval between receiving analgesia and leaving emergency department	115.0 (75.0 to 149.0)	130.0 (95.0 to 170.0)	20.0 (4.0 to 39.0)	0.02

\*Mann-Whitney U test.

with significantly better outcomes, lower costs when costs for the emergency department and pharmacy are combined, but not significantly higher overall costs.

## Discussion

This study shows that, although intravenous morphine costs less than intravenous ketorolac in Hong Kong, ketorolac is a cheaper option than morphine once all additional costs incurred by the accident and emergency department and the pharmacy are taken into account. When admission costs are included, however, the difference in cost is not significant. When both drugs are administered intravenously in titrated doses according to individual patients' needs, ketorolac is at least as efficacious as morphine and may afford a small advantage when the injured limb is moved. Ketorolac had fewer adverse effects than morphine, made fewer demands on doctors' and nurses' management time, resulted in earlier discharge or admission to a ward, and was associated with greater satisfaction among patients. Morphine may afford a small clinical advantage, however, with better odds of relieving pain at rest than with ketorolac.

### Strengths and shortcomings

The strengths of the study lie in its randomised controlled design, delivery of analgesia according to individual needs, and its attempt to reflect the real world as far as reasonably possible. The economic evaluation follows recent guidelines published in the *BMJ*.<sup>25-27</sup> Although every effort was made to blind both the research nurses and the participants to treatment, certain clinical clues—such as pinpoint pupils—might reveal the identity to discerning medical and paramedical staff. This is a shortcoming that is probably unavoidable and applies to all double blind studies comparing opiates with other drugs. In an ideal double blind regimen, treatment should not be prepared anywhere near the scene of research, so that contamination is completely impossible. In this study, nurses prepared the drugs within the department and used normal stock. This was important if we were to monitor the “real” time taken to prepare drugs for delivery and the different grades of nurses taking part in the process. The delay in starting to administer morphine compared with ketorolac was due to the extra checking procedures necessary for administering opiates.

Although more participants were admitted to hospital in the ketorolac group, the overall greater costs were not significant. No participant was admitted to an orthopaedic ward because of adverse drug effects (admission was principally for management of the

injured limb). Only three of the six participants observed in an emergency observation ward were admitted specifically for adverse effects, and all were in the morphine group. Admission costs are much greater and more variable than for analgesia and associated drugs, which may explain why, when all additional costs are included, no difference was found between the two treatments. Others have noted that non-urgent visits to emergency departments cost relatively little when compared with the cost of admission.<sup>28</sup>

Baseline pain scores at rest were not high, and it may be argued that many of the participants did not need strong analgesia. With only minor degrees of movement, however, the average pain score rose to over 8 (out of a possible 10), showing that these participants did experience severe pain and that the administration of strong analgesia was appropriate. We could not study a placebo effect as it would have been both unethical and unjustified to deny some participants appropriate analgesia when they were in moderate to severe pain. Limb injuries are clearly painful, however, and most participants in this study had fractures confirmed by radiography. The reductions in pain score exceeded the minimum required for clinical significance.<sup>29 30</sup>

Participants were studied between 9 am and 5 pm and only on weekdays. It is therefore unclear whether out of hours ratios of staff to patients, case mix, and demand would affect the results. Emergency departments function on a priority system, whereby the efficiency of processing an individual patient depends on the number of patients with higher priority in the department at a given time and the available resources. This study did not address the difficult and complex relations between the individual patient and the total demand on the rest of the department at the time that patient attended. If it is assumed that staff are always doing something useful while at work, then minutes of freedom from managing one patient means that other duties may be attended to, and this has an impact on cost effectiveness.

It is difficult to know how far these results may be applied to settings outside Hong Kong. If one assumes, however, that the difference in costs between ketorolac and morphine is 7.5-fold rather than 2.5-fold, that doctors and nurses salaries are a third of those in Hong Kong, and that all other variables are the same, then ketorolac and morphine are equally cost effective (data not shown).

### Implementing results

The management of pain remains one of the great challenges for emergency departments worldwide, and

### What is already known on this topic

Intravenous morphine sulphate is generally as effective as intravenous ketorolac tromethamine for surgical and cancer related pain

Morphine may cause more adverse events than ketorolac

No cost effectiveness analyses have compared the use of intravenous ketorolac and morphine titrated according to patient needs and none has evaluated such use in emergency departments

### What this study adds

For limb injury in an emergency department ketorolac is as effective as morphine for pain at rest; for pain with movement, however, ketorolac may be marginally better than morphine

Ketorolac produced fewer, less severe, and shorter adverse events than morphine

Participants receiving ketorolac left the emergency department sooner than those receiving morphine

Ketorolac is a more cost effective analgesic than morphine in this setting and is associated with greater patient satisfaction

so policies on rapid, cost effective, and safe analgesia are essential for good patient care and patient satisfaction. High demand and prolonged waiting times also provide a drain on emergency departments' resources, and so any intervention that reduces the time that patients spend in the department is also important. This study showed that intravenous ketorolac is more cost effective than intravenous morphine in the management of acute pain after blunt limb injury in an emergency department. Doctors may be more confident about using an effective analgesic with no risk of dependence, fewer adverse effects, reduced arrival to discharge times in their departments, and reduced costs. These results are relevant to emergency departments in Hong Kong and are likely to be applicable to other systems that are organised along similar lines. Differences in staff salaries and other costs, however, may limit the application of our findings to some environments.

**Contributors:** THR had the idea for the study, obtained approval, and has overseen the entire planning, execution, and analysis of the study, and the preparation of the manuscript. He is guarantor of the paper. PJ and YCN participated in planning a detailed economic analysis. NKC, MT, and RAC participated in the planning, execution, and analysis. PKWL and THR prepared the statistical analysis. RW was involved in planning and costing analysis. THR wrote the first draft of the paper, and all authors have contributed to the final version.

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**Competing interests:** None declared.

- 1 Yealy DM. Ketorolac in the treatment of acute pain: The pendulum swings. *Ann Emerg Med* 1992;21:985-6.
- 2 Goodacre SW, Roden RK. A protocol to improve analgesia use in the accident and emergency department. *J Accid Emerg Med* 1997;13:177-9.

- 3 Whipple JK, Lewis KS, Quebbeman EJ, Wolff M, Gottlieb MS, Medicus-Bringa M, et al. Analysis of pain management in critically ill patients. *Pharmacotherapy* 1995;15:592-9.
- 4 Jantos TJ, Paris PM, Menegazzi JJ, Yealy DM. Analgesic practice for acute orthopaedic trauma pain in Costa Rican emergency departments. *Ann Emerg Med* 1996;28:145-50.
- 5 British Medical Association, Royal Pharmaceutical Society of Great Britain. *British national formulary*. London: BMA, RPS, 1997. (No 32.)
- 6 Benedetti C, Butler SH. Systemic analgesics. In: Bonica JJ, ed. *The management of pain*. 2nd ed. Philadelphia: Lee and Febiger, 1990;1640-75.
- 7 Gillis JC, Brogden RN. Ketorolac. An appraisal of its pharmacodynamic and pharmacokinetic properties and therapeutic use in pain management. *Drugs* 1997;53:139-88.
- 8 Brown CR, Moodie JE, Wild VM, Bynum LJ. Comparison of intravenous ketorolac tromethamine and morphine sulphate in the treatment of postoperative pain. *Pharmacotherapy* 1990;10:116-21S.
- 9 Purday JP, Reichert CC, Merrick PM. Comparative effects of three doses of intravenous ketorolac or morphine on emesis and analgesia for restorative dental surgery in children. *Can J Anaesth* 1996;43:221-5.
- 10 Cordell WH, Wright SW, Wolfson AB, Timerding BL, Maneatis TJ, Lewis RH, Bynum L, Nelson DR. Comparison of intravenous ketorolac, meperidine, and both (balanced analgesia) for renal colic. *Ann Emerg Med* 1996;28:151-8.
- 11 Watcha MF, Jones MB, Laguere RG, Schweiger C, White PF. Comparison of ketorolac and morphine as adjuvants during pediatric surgery. *Anaesthesiology* 1992;76:368-72.
- 12 Maunukela EL, Kokki H, Bullingham RE. Comparison of intravenous ketorolac with morphine for post-operative pain in children. *Clin Pharmacol Ther* 1992;52:436-43.
- 13 Etches RC, Warriner CB, Badner N, Buckley DN, Beattie WS, Chan VW, et al. Continuous intravenous administration of ketorolac reduces pain and morphine consumption after total hip or knee arthroplasty. *Anesth Analg* 1995;81:1175-80.
- 14 Bosek V, Miguel R. Comparison of morphine and ketorolac for intravenous patient-controlled analgesia in postoperative cancer patients. *Clin J Pain* 1994;10:314-8.
- 15 Peirce RJ, Fragen RJ, Pemberton DM. Intravenous ketorolac tromethamine versus morphine sulfate in the treatment of immediate postoperative pain. *Pharmacotherapy* 1990;10:111-5S.
- 16 Gunter JB, Varughese AM, Harrington, Wittkugel EP, Patankar SS, Matar MM, et al. Recovery and complications after tonsillectomy in children: a comparison of ketorolac and morphine. *Anesth Analg* 1995;81:1136-41.
- 17 Cepeda MS, Vargas L, Ortegon G, Sanchez MA, Carr DB. Comparative analgesic efficacy of patient-controlled analgesia with ketorolac versus morphine after elective intraabdominal operations. *Anesth Analg* 1995;80:1150-3.
- 18 Munro HM, Riegger LQ, Reynolds PI, Wilton NC, Lewis IH. Comparison of the analgesic and emetic properties of ketorolac and morphine for paediatric outpatient strabismus surgery. *Br J Anaesth* 1994;72:624-8.
- 19 Kirkwood BR. *Essentials of medical statistics*. Oxford: Blackwell Science, 1988:167-72.
- 20 Huskisson EC. Measurement of pain. *Lancet* 1974;2:1127-31.
- 21 Morrow GR, Lindke J, Black P. Measurement of quality of life in patients: psychometric analyses of the functional living index—cancer (FLIC). *Qual Life Res* 1992;5:287-96.
- 22 Drummond MF, O'Brien B, Stoddart GL, Torrance GW. *Methods for the economic evaluation health care programmes*. Oxford: Oxford Medical, 1997.
- 23 Bakker C, Hidding A, Linden S. Cost-Effectiveness of group physical therapy compared to individualized therapy for ankylosing spondylitis: a randomized controlled trial. *J Rheum* 1994;21:264-8.
- 24 Matthews JNS, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. *BMJ* 1990;300:230-5.
- 25 Byford S, Raftery J. Perspectives in economic evaluation. *BMJ* 1998;316:1529.
- 26 Palmer S, Byford S, Raftery J. Types of economic evaluation. *BMJ* 1999;318:1349.
- 27 Torgerson D, Raftery J. Main outcomes in economic evaluation. *BMJ* 1999;318:1413.
- 28 Williams RM. The costs of visits to emergency departments. *N Engl J Med* 1996;334:642-6.
- 29 Todd KH, Funk JP. The minimum clinically important difference in physician-assigned visual analog pain score. *Acad Emerg Med* 1996;3:142-6.
- 30 Todd KH, Funk KG, Funk JP, Bonacci R. Clinical significance of reported changes in pain severity. *Ann Emerg Med* 1996;27:485-9.

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### Endpiece Fads in medicine

One is instantly reminded of the malign influence of fashion on medicine, more than any other science. Even nowadays it is subject to fads, although no science is actually more profitable.

Pliny the Elder, AD 23-79

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