The feasibility of adapting an over the counter multi-criteria decision analysis (MCDA) model to assess the benefit/risk profile of postoperative analgesics to inform prescribers’ optimal choice of medication

R. Pawinski,¹ L. Phillips,² R. Xia,³ M. Noyes Essex³

¹Pfizer Ltd, Walton Oaks, Tadworth, UK; ²London School of Economics and Political Science, London, UK; ³Pfizer Inc, New York, NY, USA

INTRODUCTION

- Quantifying the benefit/risk profile of medicines can be challenging.^{1–3}
- This may be exacerbated by limited published adverse event data, or because clinical studies and meta-analyses use different measures of efficacy, safety, and tolerability.³
- Clinicians require simple and easy to understand tools to assist in balancing the benefit and the risk of individual medicines.
- This is a problem of particular importance for clinicians choosing a suitable postoperative analgesic, because multiple options are available that have different mechanisms of action, and different efficacy and safety profiles.^{4,5}
- Computer-based models that analyse multiple criteria, such as multi-criteria decision analysis (MCDA), provide a useful framework for assessing benefit/risk profiles.^{6–8}
- These models enable enhanced quality and consistency of decision-making based on the interpretation of best evidence by experts in the field.
- This analysis tested the ability of an adapted MCDA model⁸ to incorporate published or freely available efficacy and safety data of varying quality for postoperative analgesics, and used clinical judgement to assess the benefit/risk profile of each analgesic.

METHODS

- A MCDA model that was developed for over the counter medicines⁸ was adapted for postoperative analgesics.
- Efficacy and safety data from 5 injectable analgesics (drugs A–E) commonly used for postoperative pain management were examined.
 - Data were obtained from published meta-analyses or systematic reviews and the freely available European Public Assessment Reports and Summary of Product Characteristics of individual analgesics from the European Medicines Agency.
- Data for each analgesic were evaluated against 3 favourable criteria and 3 unfavourable criteria considered to be the most important to clinicians (**Figure 1**).

Figure 1. Favourable and unfavourable criteria that were assessed for each postoperative analgesic

- Based on the available clinical evidence or clinical assessment, each criterion was scored from 0 to 100, with a score of 100 for the drug that performs best and 0 for the drug that scores worst, with the remaining drugs scored according to their standing compared with each other (**Figure 2A**).
- Data were weighted by (i) relative weighting of the criteria for the favourable criteria, (ii) relative weighting comparing swings for the unfavourable criteria, and (iii) relative weighting of the highest-weighted favourable criterion against the highest-weighted unfavourable criterion (**Figure 2B**).
- Sensitivity analyses were performed by varying the weighting of the criteria to see how this affected the overall results.
- The data presented are quantitative only; no statistical comparisons were made between or among analgesics.

Figure 2. Scoring (A) and weighting (B) of the favourable and unfavourable criteria

RESULTS

Comparison of benefit/risk profiles among analgesics

- The MCDA model provides an overall picture of the benefit/risk profile of each of the 5 analgesics (**Figure 3**).
- In this example, drug B had the best overall benefit/risk profile, driven by higher scores on the favourable criteria.

Figure 3. Overall benefit/risk profiles for each of the 5 analgesics assessed

- The MCDA model also permits a breakdown of the benefit/risk profile for each drug by the individual favourable and unfavourable criteria (**Figure 4**).
- The greater benefit of drug B over the other analgesics was driven by a combination of higher scores for pain relief and duration of action.

Figure 4. Benefit/risk profiles for each of the 5 analgesics assessed by individual favourable and unfavourable criteria

The favourable and unfavourable criteria can be ranked by which provided the greatest benefit

- Ranking of the favourable and unfavourable criteria by greatest benefit for drug B is shown in **Figure 5**. Duration of Action was the greatest strength and Renal Effects the largest potential weakness.

Figure 5. Main strengths of drug B

	Model Order	Cumulative Weight	Difference	Weighted Difference	Sum
Favourable Criteria	Duration	26.6	100	26.6	26.6
Favourable Criteria	Pain Relief	29.6	85	25.1	51.8
Favourable Criteria	Opioid Sparing	14.8	100	14.8	66.6
Unfavourable Criteria	Resp. Depression	11.2	100	11.2	77.8
Unfavourable Criteria	Cardiac Effects	11.8	40	4.7	82.5
Unfavourable Criteria	Renal Effects	5.9	70	4.1	86.7
		100.0		86.7	

Longer green bars are strengths, shorter green bars are potential weaknesses.

The advantages and disadvantages of the different analgesics can be compared

- In this example (**Figure 6**), drug B had better Pain Relief and Duration of Action than drug A, but drug A was associated with fewer Cardiac Effects than drug B.

Figure 6. Comparison of the advantages and disadvantages of drug B with drug A

	Model Order	Cumulative Weight	Difference	Weighted Difference	Sum
Favourable Criteria	Pain Relief	29.6	85	25.1	25.1
Favourable Criteria	Duration	26.6	80	21.3	46.4
Favourable Criteria	Opioid Sparing	14.8	0	0.0	46.4
Unfavourable Criteria	Resp. Depression	11.2	0	0.0	46.4
Unfavourable Criteria	Renal Effects	5.9	0	0.0	46.4
Unfavourable Criteria	Cardiac Effects	11.8	-60	-7.1	39.3
		100.0		39.3	

Green bars represent advantages of drug B over drug A. Red bar indicates advantages of drug A over drug B. There were no differences between drugs for Opioid Sparing, Respiratory Depression, or Renal Effects.

Sensitivity analyses permit substitution of criterion values to assess impact on model outputs

- Sensitivity analyses showed that the model was robust and that results remained relatively unchanged even with significant changes to the weights of the favourable and the unfavourable criteria.
- For instance, the weight on the unfavourable criteria would have to increase by ≥ 2.5 times before the preferred drug would be drug A (**Figure 7**).

Figure 7. Sensitivity analysis on the unfavourable effects

CONCLUSIONS

- The MCDA model can be successfully applied to assess the benefit/risk profiles of different postoperative analgesics.
- The overall benefit/risk profile for each drug can be determined and compared across drugs.
- The model permits the breakdown of the overall benefit/risk by individual favourable and unfavourable criteria for each drug.
- The criteria that provide the greatest and least benefit for each drug can be identified.
- The advantages and disadvantages of different drugs can be compared.
- Sensitivity analyses allow the weighting of individual criteria to be altered to assess the impact of changes on model outputs.
- Validation of the data inputs, scoring, and weighting by independent clinical experts would provide an additional tool to assist clinicians in making informed choices based on the benefit/risk profile of the treatment options available.

REFERENCES

1. Mussen F, et al. *Pharmacoeconom Drug Saf*. 2007;16 Suppl 1:S2–S15. 2. Curtin F and Schulz P. *Dialogues Clin Neurosci*. 2011;13:183–90. 3. Hughes D, et al. *Pharmacoeconom Drug Saf*. 2016;25:251–62. 4. Pogatzki-Zahn EM, et al. *Pain Rep*. 2017;2:e588. 5. Chou R, et al. *J Pain*. 2016;17:131–57. 6. Nutt DJ, et al. *Lancet*. 2010;376:1558–65. 7. van Amsterdam J, et al. *J Psychopharmacol*. 2015;29:655–60. 8. Moore A, et al. *J Pharm Pharmacol*. 2017;69:1364–73.

DISCLOSURES

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