Clinical Decision Analysis

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Sadeesh K. Srinathan and Feng Xie

Abstract

Clinical decisions are often difficult as we try to balance the benefits or harms of one decision pathway compared to another possible pathway. Further, this has to be done in the face of incomplete information. In this chapter we describe a useful tool termed Clinical Decision Analysis to allow for a transparent and explicit description of the decision making process to guide us in identifying areas of uncertainty around the existing evidence.

Keywords

EBM · Evidence based medicine · GRADE · Bias · Study design · Systematic reviews · Trials

Introduction

This book is about difficult decisions; implicit in the title is that a clinician and the patient have to take action, even it that action is to wait for further information. The source of the difficulties lies in the uncertainties in the information upon which the decision is made. Heuristic methods of decision making do not explicitly and

S. K. Srinathan (✉)
Winnipeg Health Sciences Centre, Department of Surgery, University of Manitoba, Winnipeg, MB, Canada
e-mail: ssrinathan@exchange.hsc.mb.ca

F. Xie
Department of Health Research Methods, Evidence and Impact, Faculty of Health Sciences, McMaster University, St. Joseph's Hospital, Hamilton, ON, Canada
e-mail: fengxie@mcmaster.ca

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systematically identify the nature or extent of these uncertainties. These heuristic means of decision which often misinterprets statistical information, can lead to errors [1]. In this chapter we will present a useful tool, Clinical Decision Analysis (CDA), which allows a more transparent and explicit description of the decision-making process, a means of explicitly identifying available evidence and the uncertainty around existing evidence.

What Is Decision Analysis?

Decision analysis is a formal system that details all the possible outcomes and the clinical pathway leading to each outcome for a decision and its alternate and provides means of choosing the best course among the alternatives under uncertainty. Or to quote Weinstein "Decision analysis is a systematic approach to decision making under conditions of uncertainty" [2]. It is (1) explicit, (2) quantitative and (3) prescriptive.

The potential benefits of CDA are that (a) it is an explicit process where the logic and assumptions made in the analysis are made clear, (b) it highlights points of uncertainty and deficits of information by explicitly incorporating into the analysis, (c) it allows an exploration of the impact of the uncertainties on the final decision.

It must be kept in mind that although CDA models a problem, it does so only to aid in the decision-making process. By necessity, these models simplify the problem, and a number of simplifying assumptions are made, but the model assumptions are made explicit. A decision analysis is also not an explanatory model of a clinical scenario, and it does not explain the pathophysiology of a clinical situation.

A CDA is not an algorithm. Although they may appear similar, the branching structure of a decision tree are to allow for the calculation of the best possible decision at a specific point. In contrast, an algorithm provides a path to follow given certain information with multiple decision-making points.

A challenge with CDA is that it demands specification of the probabilities of outcomes and the values of the outcome. However, this is not limited to decision analysis and is inherent in all decision making. In fact, a major strength of the value of CDA is that this aspect of decision making is made explicit and a value is assigned to this uncertainty.

Many of these issues are common for any type of decision making, and the formality of the process ought not to lead to unreasonable expectations of the process.

Why Know About This?

As discussed in the previous chapter, EBM is about actually *using the best available* evidence in delivering patient care. Systematic reviews and guidelines go some way in guiding decisions, but they do not in themselves allow you to come to a specific decision in a given scenario. For example, a systematic review can state that a particular intervention may yield a 15% improvement in survival over a 5-year period but at the cost of a 5% increase in the risk of a major stroke. This information does not in itself tell you if the intervention should be carried out since the decision

hinges on the positive value the patient places on the outcome of survival and on the negative value on the outcome of a stroke.

Clinical guidelines go further in providing recommendations, but they are predicated on "average" patients with "average risks" and assume that patients will make consistent value judgments. In the major grading systems such as GRADE, there is acknowledgment that different decisions can be made depending on the individual patient values and preferences and the strength of recommendation reflect this, but recommendations do not give a measure of the sensitivity of a clinical decision to these changes. Certainly, at a policy level and even in routine patient level care, it is valuable to have an understanding of the robustness of a decision to variations in factors considered important and relevant for the decision.

It may be challenging in carry out a formal analysis in making individual clinical decisions. However, we believe that familiarity with this process will at least make it easier to consider existing evidence and identify areas of uncertainty so that further effort can be made to reduce this uncertainty or to at least to raise a warning as to the degree of confidence that one can place on the decision one makes. Awareness of this process may also make it easier to "hang" medical evidence in a framework so that it can be integrated into clinical practice. Furthermore, this is a basic technique used by decision makers in health care and as such impact on every practicing surgeon.

Anatomy of Clinical Decision Analysis

The best decision is one that maximizes the preferred outcome. For instance, in business decision making, the best decision is one that maximizes profit. In general terms, a clinical decision maximizes health for a patient or population. The clinical decision is contingent on the probability of preferred outcomes occurring and the desirability assigned to the outcomes that may occur.

A Clinical Decision Analysis is composed of three main steps: (1) construct the decision analytic framework (Figs. 2.1 and 2.2), (2) carry out the calculations to

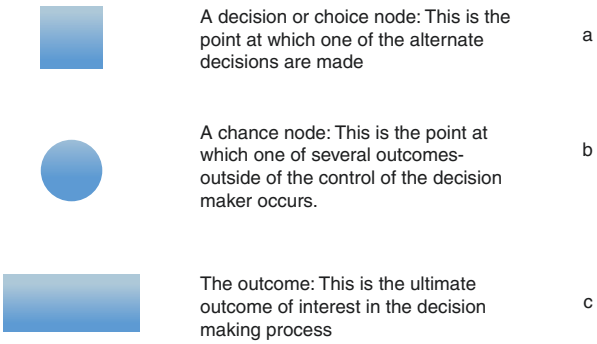


Fig. 2.1 Explanation of symbols used in clinical decision analysis. (**a**) A decision or choice node: This is the point at which one of the alternate decisions are made. (**b**) A chance node: This is the point at which one of several outcomes—outside of the control of the decision maker occurs. (**c**) The outcome: This is the ultimate outcome of interest in the decision making process

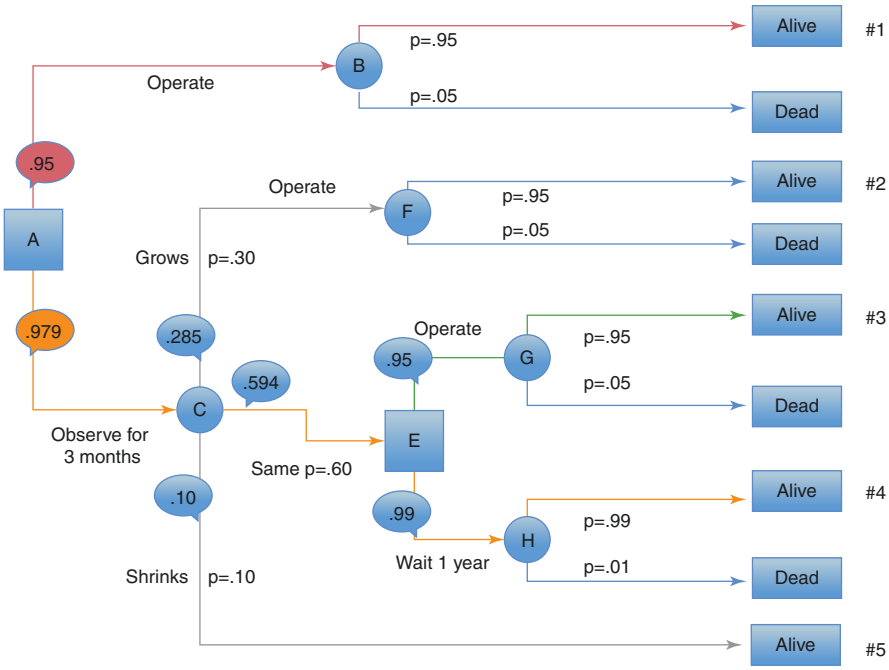


Fig. 2.2 Hypothetical CDA—should we operate on a tumour identified incidentally on imaging?

choose the best pathway or decision and (3) carry out a sensitivity analysis to determine the robustness of the decision, i.e. to what extent does the decision change across plausible values of probabilities of the outcome and the values assigned to the outcome.

Constructing the Decision Analytical Framework

The first step is to construct the decision analytical framework. This starts with framing the question of interest in terms of alternate possible decisions which are available to us at the outset, i.e. when the outcomes are unknowable. Nearly all scenarios in clinical practice present alternative scenarios and if these can be explicitly stated, then CDA can be applied. This initial point is the first decision node (Fig. 2.1a) and a key feature of the decision node is that it sets out what the alternative decisions are, and these alternatives at the decision node are mutually exclusive. The decision node is usually noted by a square box on a diagram.

To make a decision is to choose a specific path in the framework emanating from the decision node. The goal of CDA is to determine which of the paths taken at the first decision node is most likely to be the best one, i.e. will maximize the outcome, although there may be other decisions to be made subsequently throughout the framework.

Any decision results in, often multiple possible, consequences. This is reflected by the paths emanated from the nodes diagrammed as a circle (called "chance node) following each decision (Fig. 2.1b). A probability is attached to each of these consequences to show how likely one consequence occurs following a decision. The sum of the probabilities at each chance node is always 1. The framework ultimately terminates at the outcomes of interest, (Fig. 2.1c) which occurs as some defined point. This is usually diagrammed as a rectangle or triangle. The outcomes can be measured using relevant clinical measures or utility value to indicates its relative desirability. For instance, an ideal outcome such as being alive and well will have a value of 1, and death has a value of 0. An intermediate outcome such as alive but having suffered a major disability may have a value of 0.7, a value somewhere between well and dead.

Figure 2.2 provides a very simple, hypothetical CDA where the initial question is whether or not to operate on a tumour identified by an imaging test and where the outcome is to be determined over a 15-month time horizon. At the first decision node (A), the options are either to operate immediately (B) or alternatively, to reassess the tumour after 3 months (C). The possible outcomes associated with immediate surgery include alive after the operation with a utility value of 1, and postoperative death with utility value of 0. The probability of being alive is 0.95 and 0.05 for dying. If the decision is made to follow the tumour for 3 months at the outset, then possible outcomes include that the tumor either shrinks in which case nothing is done and the patient is always alive (outcome #5), remains unchanged in which case a further decision to be made (E), or the tumour grows, in which case an operation is always performed with the attendant risk of death. Each of these outcomes occurs with a probability of 0.30 for tumour growth, 0.60 for tumour size unchanged, and 0.10 for the tumour shrinkage. If the tumour size remains unchanged after the 3-month observation, then at the second decision node (E) the decision could be either to proceed to operation or to watch for a further 12 months. Again, the outcome of operation is either alive or dead with the same probabilities already stated. If the decision is to continue the observation, then the outcome is either stability which result in being alive with a probability of 0.99, or the tumor spreads leading to death with a probability of 0.01.

Determining Probabilities and Utility Values

From studying Fig. 2.2, the obvious question is where the values of the probabilities and utility come from? Probabilities and outcome measures are the critical inputs to the CDA and determining the probabilities of these outcomes occurring can be difficult. Ideally the information can be derived from clinical studies that report on outcomes after an intervention, such as from clinical trials that report the cure rate of an operation and also the risk of complication and mortality. Else but less ideal, the probability may have to be derived from a consensus among experts. The probability in a CDA, is ultimately a statement of belief about an outcome, and if there is objective means of establishing (e.g. clinical trials), then that is ideal. However,

in the absence of this objective evidence, a statement of belief of the likelihood of an outcome occurring in itself can be used (e.g. expert opinions). Clearly, the confidence in the validity of the estimate of this probability will vary according to the source of this estimate of probability.

The patient and clinician are aware of the outcomes that are of interest, e.g. being alive, well and cured of a disease, or being cured of a disease but having suffered a complication, dying from the disease or dying from the treatment. The probability of the outcome may be discussed with patients, e.g. a 95% chance of being cured but a 4% chance of major complication and a 1% mortality, but the value that is placed on each of these outcomes by the patient are usually not discussed. Much like the probability of an outcome, the utility values used to measure the relative desirability of an outcome can be gleaned from the literature where patients were asked to rate their desirability of the outcome. Alternatively, one may ask the patient directly what their values are. This is not quite straightforward but is possible.

Calculating the Utility of Each Decision

The second step of CDA is coming to a decision by calculating the overall utilities associated with each of the decision. This overall utility of a decision is the sum of the product of the probabilities and the utility values assigned to the corresponding outcomes for all paths under each decision. Calculating the overall utility for each decision starts from the rightmost and then moves to the leftmost part of the framework (called "foldback"). We need to determine the probability and the utility value of the outcome at the end of each path. The utility is then multiplied by the probability of that outcome occurring. The probability of being alive after immediate surgery is 0.95. So in our framework, we have assigned utility values of 1 for alive and 0 for dead. So starting at outcome #1, at the chance node, the utility value is $0.95 \times 1 + 0.05 \times 0 = 0.95$. Since these leads directly to the first decision node, the utility expected from immediate operation is 0.95.

If we start at path #2 (i.e. the top branch following the chance node C). The probability of being alive after a surgery due to the tumour growth after the 3-month observation 0.285 (i.e. 0.95×0.3) and the probability of death 0.015 (i.e. 0.05×0.3). The expected utility for this path is then $0.285 \times 1 + 0.015 \times 0 = 0.285$.

It is important to note that there is another decision node (E) embedded in the framework, when we calculate the expected utility value for the middle path from chance node C. Following the above-mentioned method, the expected utility of choosing surgery (path #3) is 0.95 and 0.99 for continuing the observation for another 12 months at the decision note E (path #4). Since one path results in a higher expected utility value 0.99 than the other 0.95, we can ignore path #3 from further consideration and carry back only the utility value of 0.99 further towards the left. When the utility of the orange path is multiplied by the probability of ending up on this path, 0.60, then back at the chance node, the overall utility of this path is 0.594. The expected utility value for path #5 is 0.10. At the decision node, the

overall value is now the sum of the total utility of each path emanating from the chance node C, 0.979 (i.e. 0.285 + 0.594 + 0.10).

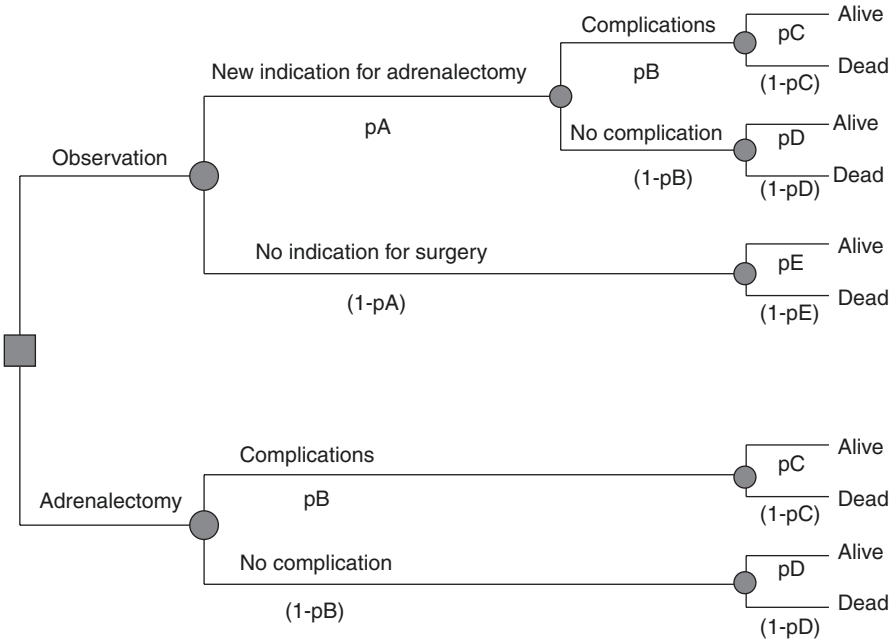
When this is folded back towards the first decision node, we see that going straight to surgery, we obtain an expected utility value of 0.95, whereas if we waited for 3 months, then the expected utility of this path is 0.979. Since the waiting, gives a higher utility value, we determine that the best decision in this scenario is to wait for 3 months.

Our conclusions in this example are dependent on the values we selected for the probabilities of an event e.g. rate of post-operative deaths and also the desirability of the outcomes e.g. value of 1 for alive and 0 for dead. It is quite apparent that if post-operative mortality was lower than 0.05, then the decision to observe is likely to change. A formal exploration of how the decision will change according to the values of the inputs (the probability of the outcome and utility values associated with the outcome), is call sensitivity analysis and is a fundamental part of CDA. There are a number of ways in which this can be carried out, and an example from the literature demonstrates this.

Management of an Incidentaloma

Brunaud et al., carried out a clinical decision analysis which illustrates the features of a CDA [3]. The questions posed in their study is "What is the optimal management approach to a patient with a non-functioning adrenal "incidentaloma" with no suspicious image characteristics for a malignant adrenal neoplasm, and a tumor size between 4 and 6 cm?" They made clear that this question is one in which there is genuine uncertainty. In cases of tumours greater than 6 cm or those with suspicious features on imaging, there is little difference of opinion, so that the value of investing the effort on a CDA to those scenarios is limited. They provide two alternate decisions (Fig. 2.3), to observe the tumour or proceed to a unilateral laparoscopic adrenalectomy. A fundamental feature of CDA is that the decision to be made is explicitly stated and just as important, the alternative is explicitly stated. A not uncommon scenario in a guideline statement is that some course of action ought to be followed, but without explicitly stating what the alternatives are [4]. There is also an explicit statement of when the decision is to be made; in this case at the time the tumour is initially found. This allows the two alternative of proceeding to resection or waiting.

Next the authors describe how they calculate the expected utilities for each path. They then provide a table (Table 2.1) that lists the probabilities associated with each of the chance nodes which are derived from published studies and their own institutional experience. They include both a baseline value upon which they base the primary analysis and the range of values to be used for sensitivity analysis. They also state the utility values for the three possible outcomes, (1) a new indication for resection during the period of observation, (2) complications after adrenalectomy and (3) being alive during the observation without surgery, which assumed some degree of psychological morbidity associated with the uncertainty of the nature of



pA: P of developing new indication for adrenalectomy during observation

pB: P of complications from unilateral laparoscopic adrenalectomy

pC: P of being alive after a complicated adrenalectomy

pD: P of being alive after uncomplicated laparoscopic adrenalectomy

pE: P of being alive during observation without surgery

Fig. 2.3 Decision analysis framework for management of non-functional adrenal tumor. From Brunaud et al. [3] with permission

the mass. Since there were no published utility values for the outcomes, they undertook a survey of surgeons to estimate this. From this analysis they came to the conclusion that with the baseline values of the probabilities and utilities, the observation strategy had the highest expected utility. Although it may be reasonable to stop and come to a conclusion, at this point, it is quite clear that their conclusions will be expected to change if the values of the probabilities of the outcomes or the utility values ascribed to the outcomes change. In fact they found that if the complication rate for laparoscopic adrenalectomy was lower, as observed at their own institution, then the resection strategy was the preferred decision. To what extent does the decision change, and is there some value of one of the variables or of a number of variables at which the decision switches from one to another? To answer this question, a threshold analysis may be carried out which is a type of sensitivity analysis. Essentially, one calculates utility values for each value of the probability or utility both individually and as a combination and determines at what value or combination of values the decision changes.

Table 2.1 Values used for calculating probabilities and assigning utilities in the CDA for the management of a non-functioning adrenal tumor

Variables	Baseline (%)	Reported range (%)	Median (year)	Authors
Laparoscopic adrenalectomy				
Morbidity (pB)[a]	7.84	0–11	–	[5,20–27]
Mortality	0.36	0–2	–	
1 − mortality (pC)	99.64	98–100	–	[5,20–24]
Observation				
Indication for adrenalectomy during observation (pA)				
Malignancy	2.95	0–13	4.3	[4,28–34]
Size increase	6.91	0–25	3.6	[2,4,28–30,32,33,35–37]
Hypersecretion	1.19	0–20	2.8	[2,4,28,30,32,33,36–41]
Overall (pA)	3.13	0–25	3.6	
Surgeons questionnaire	68.00	30–90	–	

From Brunaud et al. [3] with permission

[a]Bleeding, wound (early and late), pulmonary, organ injury, gastrointestinal, urinary, thromboembolic, cardiac

An interesting and important finding from this analysis is the sensitivity of the conclusion to the utility value associated with observing the tumour. It was in fact the patient's perspective that had the most impact on which decision was best, but this was the one piece of the analysis which had large uncertainty (i.e. based on subjective, expert opinions). This illustrates very clearly the nature of the statement made in guidelines about the patient's perspectives and illustrates graphically the importance of this in clinical decision making.

Cost Effectiveness

In both individual patient care and in making policy, the role of the costs of different strategies is very important. Cost effectiveness analysis is helpful in addressing this issue. The analytical framework used in cost effectiveness analyses share a lot of similarities as in CDA but where resource utilization and costs are important extra information incorporated in the model. Cost effectiveness is a key piece of evidence to support health policymaking and its importance in clinical decision-making is being recognized. A description of cost effectiveness analysis through modeling is beyond the scope of this chapter.

Conclusion

This chapter was a brief overview of Clinical Decision Analysis. Much like a surgical procedure, the concepts of the procedure may be straightforward, but it is often in the carrying out of the procedures and the details that pose the challenge. However, it is still important to understand the main concepts, as this type of analysis is of great value in practicing evidence-based medicine and in doing the best for our patients.

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