Paper to be presented to the 1995 System Dynamics Conference, Tokyo.

Decision Analysis using Dynamic Simulation

Eric F. Wolstenholme
Professor of 21st Century Business Learning,
Leeds Metropolitan University Business School/Cognitus Ltd.

Abstract

This paper describes work to contrast the use of decision analysis and system dynamics simulation in the field of pharmacoeconomics.

The importance of economic outcomes to support the clinical evaluation of pharmaceutical drugs is growing in importance as public health service resources are constrained and clinical trial data support by decision analysis has become the established mode of evaluation.

This paper describes research carried out with a major drugs company to investigate alternative pharmacoeconomics drug evaluation procedures, in particular the use of dynamic simulation methods. An evaluation methodology based on these principles is presented here and applied to a disease management case study to contrast the analysis with decision analysis.

The conclusion of the work to date is that decision analysis can be considered a special case of dynamic simulation and that the latter technique using 'ithink' has a large potential for providing transparent, economic analysis of the potential benefits of new drugs at their research and development stage.

Introduction

Traditional approaches to evaluating new pharmaceutical products have centred on balancing the cost of the product against the clinical benefits to individual patients, where the latter has been assessed in clinical trials. The development of pharmacoeconomics as a subject has been based on the need to expand the evaluation of outcomes of new products to include their economic as well as clinical merits. There is a growing need in the current climate of most public health services to demonstrate the costs and benefits of new products in terms of their economic and resource impact within the end-user domain.

One of the problems in this trend toward economic assessment has been the lack of suitable tools. The predominant methodology for current economic assessment is that of decision analysis. This involves the creation of decision trees which are used to combine data on the success (probabilities and outcomes) of individual products collected from clinical trials, using an expected value criterion.

This report describes initial work to develop and apply an entirely original framework for new product evaluation which is equally applicable to any drug or indeed any new piece of technology. The approach involves the creation with end users of a set of maps and dynamic simulation models of the anticipated domain of application of the product which can be used as

a test bed to evaluate its systemic impact. The work builds on earlier research concerning the application of this type of methodology to the evaluation of management information systems (Wolstenholme et al, 1993).

The methodology used is that of systems thinking and system dynamics which are gaining increasing importance in business as high level mapping and modelling tools for testing the operational effects of business re-engineering, new strategies and organisational change in general.

The work described in this paper is a subset of the research into the development of the approach. It concerns the the application of the method to a disease management situation and a comparison within this case study of dynamic simulation and decision analysis.

An overview of the dynamic simulation methodology will be given prior to presenting the case study and its conclusions.

Dynamic Modelling in Pharmacoeconomics - A Three Stage Methodology for Drug Evaluation.

The first stage of application of the evaluation method is to create, calibrate and validate a base model of the intended domain of application of the product. This domain model will vary dependent on the product.

For example, in the case of a disease control product the base model may be a model of the disease progression. In the case of a clinical product the model may be a specific or typical representation of some of the many settings and procedures in which the product will be used, since these might vary considerably, say between and within types of institutions or countries.

This base model must assume the use of existing products and should define appropriate scenarios and global performance measure by which to assess performance, although the actual process of modelling may itself help with the definition of appropriate performance measures.

The medium for the creation of the base model is the high-level and very friendly mapping and modelling software 'ithink' (Richmond et al, 1994) and an important part of the method is that the process of model building facilitates knowledge capture. A major objective of the approach in pharmacoeconomics is to help potential customers understand the economic viability of a product within their own environment. It is vital, therefore, that the base model is constructed with a variety of people from the domain in which the product will be used and that the model forms an acceptable and credible representation of the domain to them.

The second stage of the method is to use the model as a test bed on which to evaluate the new product. This stage involves superimposing on the model the anticipated effects of the new treatment throughout the domain described by the model. The model then assumes the role of a test flight simulator for the product and forms a dynamic experiential learning environment, where both clients and product developers can explore the interaction of assumptions and parameter values they have defined and learn holistically about the potential impact of the new product.

The third stage of the method is perhaps the most significant and builds on the fact that to make

the best use of any new product it is necessary to change procedures and policies to accommodate it. The modelling process described facilitates experimentation to redesign the domain of application to achieve this. It could involve modifying any aspect of the domain. For example:

* re-engineering processes,
* changing information paths and policies,
* changing responsibilities for particular activities,
* eliminating delays or reducing capacities,
* identifying high-leverage intervention points where changes might produce the greatest outcome for the smallest input.

In summary the method provides a risk-free way for managers to explore the complex and systemic impact of a new product.

The Decision Analysis Approach

Decision analysis as a pharmacoeconomic tool largely centres on the use of decision trees. A decision tree is a diagram which illustrates alternative courses of action in response to a specific problem.

In order to illustrate the approach, a decision tree used in the Swedish disease management analysis of reflux esophagitis, is displayed in Figure 1. The tree consists of three treatment periods, decision nodes and outcome nodes. The first decision at the start of treatment period 1 is to choose one of two strategies. These are to treat the condition with omeprazole (ome) or to treat the condition predominantly with ranitidine (rani). In each treatment period, which comprise the application of different doses of the product, there is a chance node, represented by a circle, where a chance event takes place. In this example the patient has a particular probability of being healed and a particular probability of being unhealed in each treatment period. The probabilities are taken from clinical trials of the products.

The ovals represent end states in the decision tree. They are reached either when a patient is healed or when the end of the time period is reached, which in this example occurs after 12 weeks. Each end state is assigned a cost and a benefit. In Figure 1 only benefits are considered, but the analysis could easily have also included costs. The benefit is the number of healthy weeks achieved at each end point of the tree. It is assumed that healing on the average takes place at the middle of each treatment period.

In order to calculate the overall, average or expected benefit for each treatment strategy it is necessary to fold back the tree. This means simply that the benefit of each end state is multiplied by the product of all probabilities preceding it. The benefits of each end state folded back in this way are thereafter summed in order to get the expected benefit for the treatment strategy to which they belong.

Using the data given here it is found that the omeprazole strategy is more effective in providing healthy days than the ranitidine strategy. During the time period studied, i.e.12 weeks, the omeprazole strategy provides 6.8 healthy weeks compared to 2.94 for the ranitidine strategy.

The Dynamic Simulation Approach.

Stage 1 - Modelling the Disease Progression Process.

Figure 2 shows the same problem formulated as a dynamic simulation model to demonstrate that simulation can produce exactly the same results as decision analysis for this example.

Figure 2 effectively shows the system dynamics model under-pinning the stage 1 representation of the disease management problem and identifies a very important difference in interpretation from that contained in Figure 1. The difference is that Figure 2 shows the potential of dynamic simulation to model the general **disease progression** process, whereas decision analysis models the **treatment** of the disease. Another way of saying this is that dynamic simulation relates to the **problem** of the disease and identifies the current treatment regime as one possible intervention, whereas decision analysis models and contrasts possible **solutions**.

However, in order to relate dynamic simulation to decision analysis in this case study the stage 1 model is constructed in terms of treatments. It will be seen from Figure 2 that patients progress though three distinct stages of treatment, each represented by two sub-states.

The stages are depicted in simulation as a set of delayed processes (conveyors with leakage in the ithink language - the hatched boxes in Figure 2) through which patients pass.Again, in order to match the assumptions of the decision analysis approach, each treatment period is split into two treatment processes of equal duration so that success of the treatment is achieved half way through the treatment application.

In Figure 2, 100 patients are committed to the disease progression process and 'treat 1' represents the administration of the first half of treatment 1 as defined in Figure 1. 'Treat 1' lasts for two weeks after which time a percentage of patients move into the state 'success of treat 1'.This percentage corresponds to the probability of success in the first stage of treatment in Figure 1. If the treatment is unsuccessful patients spend another two weeks in treatment (treat 11) before moving on to a second stage treatment (treat 2).

'Treat 2' is the first half of treatment 2 defined in Figure 1 after which a percentage of patients move into a success state (success treat 2). This percentage corresponds to the probability of success of the second stage of treatment in Figure 1.If the second stage of treatment is unsuccessful then again patients spend another two weeks (treat 21) before moving onto the third stage of treatment and the same procedure continues.

At the end of a 12 week simulation time there will be a number of patients in each of the end states of the process. If, as in Figure 1, each of these numbers is multiplied by an outcome measure, say the number of healthy weeks achieved and each of the products summed, the figure achieved will match the expected value derived from decision analysis for the equivalent strategy.

Stage 2 - Superimposition of the treatment on the Model.

Figure 2 can be thought of as a set of generic process structures on which the data for each treatment will be superimposed for stage 2 of the method. Each treatment is represented in the model as a separate drug treatment strategy in terms of the time of each stage of treatment and

the percentage of recipients of each treatment being successful. The model is then run separately for each strategy in turn.

In the case of a strategy based on using ome:
'treat 1' and 'treat 11' correspond to using 20 mg ome,
'treat 2' and 'treat 21' correspond to using a further 20 mg of ome,
'treat 3' and treat 31' correspond to using 40 mg of ome,
and the treatment times and success percentages are corresponding to ome are used in the simulation run.

In the case of a strategy based on using ran:
'treat 1' and 'treat 11' correspond to using 300 mg ran,
'treat 2' and 'treat 21' correspond to no treatment,
'treat 3' and treat 31' correspond to reverting to using 40 mg of ome,
and the treatment times and success percentages are corresponding to ran are used in the simulation run.

The data of each strategy can be switched in or out via the 'sw' parameter in Figure 2.

Figures 3 (a, b and c) shows the output achieved from the stage 2 model. Stage 3 of the method is not considered in this case study, but could, for example, have included different policies for administering the treatments.

A Comparison of the Two Approaches

The foregoing example demonstrates that a dynamic simulation model, although different in concept from a decision analysis, can produce exactly the same results of comparing the merits of 2 strategies for the treatment of a condition using expected value as a performance criterion.

In general, the two methods are very compatible, particularly when they represent multi-stage strategy or decision processes which are sequential over time. This type of structure is the usual case in pharmacy based applications. In such cases decision analysis can be considered as a simple method of open-loop simulation focussed on one performance measure. Very importantly both approaches focus attention on the 'process' of analysis

The main differences between the methods centre on the generality of their purpose and their ability to cope with complex situations efficiently.

The first of these issues centres on the point made earlier that dynamic simulation models the underlying processes of the problem domain and does not simply analyse a particular strategy or policy. This gives it the potential to open thinking to many alternative ways of intervening in a problem.

The second issue relates to what happens in more complex and multiple-time period situations than those covered in the case study here. The advantage of dynamic simulation in these circumstances is that it is much more flexible in its formulation and can represent feedback situations much more readily. The advantages can be classified into three categories as follows.

Firstly, the only way to represent feedback (say, of patients to previously defined states) in

decision trees is to replicate previous states on the tree at the current time period. This makes trees very large, complicated and difficult to communicate to others. Therefore, trees are not very useful for evaluations of maintenance treatment or for long-term analysis of intermittent treatment, particularly where relapses are included. On the other hand dynamic simulation can directly and concisely represent recycling.

Secondly, because of the rigid means of formulation in discrete time periods, decision trees are poor at representing the way in which a strategy may slow down or speed up the attainment of a particular state, say to hold back the onset of a disease.

Thirdly, decision trees are predominantly formulated by incorporating independent inputs or outcomes into each decision stage. It is difficult to incorporate links which relate the strategy/decision or probabilities at one stage to the results or states achieved in previous stages. Such dependence between time periods may be important in the analysis.

Conclusions

In general decision analysis and dynamic simulation are conceptually similar in that they address sequential decision processes. They can produce similar results in simple situations where decisions are sequential over time and where the main effect of a decision is a re-routing. Decision analysis can be considered as a subset of simulation which focusses on solutions rather than problem definition and understanding. It can also be very restricted in complex situations. This is particularly true in those involving multiple time periods, dependent state and stages, feedback and feed-forward effects and situations where the main effects are to change the timing of activities. This latter effect was of great importance in the case study contained in the main body of this report.

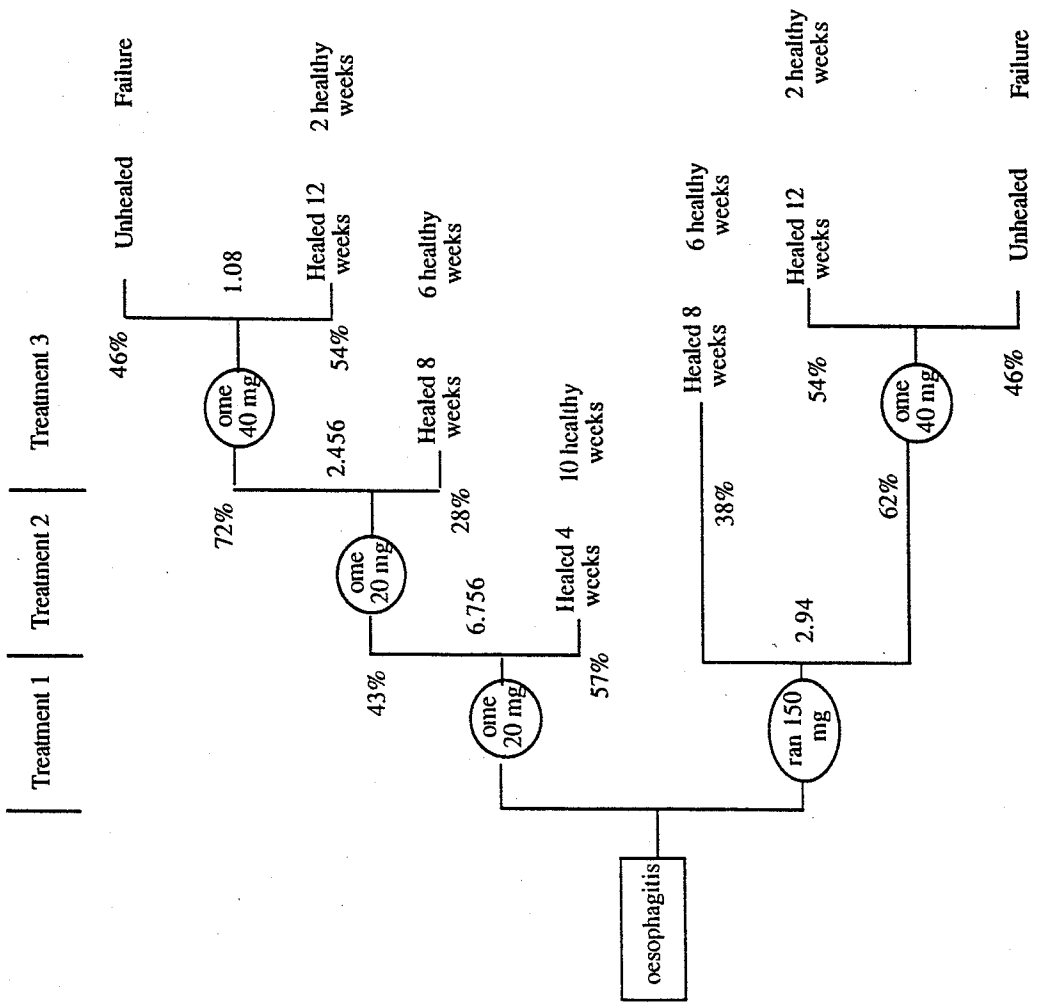
References

Richmond, B. M., Vescuso, P. and Peterson, S. (1994) 'Ithink' User Manual, High Performance Systems Publications, Lyme, NH, U.S.A..

Wolstenholme, E.F. (1990) 'System Enquiry - A System Dynamics Approach', Wiley.

Wolstenholme, E. F., and Stevenson R.W., 'Systems Thinking and Systems Modelling - New Perspectives on Business Strategy and Process Design', Management Services, September 1994.

Figure 1



Decision Tree describing the choice between omeprazole and ranitidine in the treatment of reflux esophagitis. In the strategy the upper branch treatment starts with ome 20 mg.. Patients unhealed after four weeks treatment are given the same dose for a further four weeks. Patients not responding to a total treatment of eight weeks are given ome 40 mg. for another four weeks. In the rani strategy in the lower branch treatment starts with rani 150 mg. for eight weeks. Patients not responding to this treatment are given ome 40 mg. for four weeks.

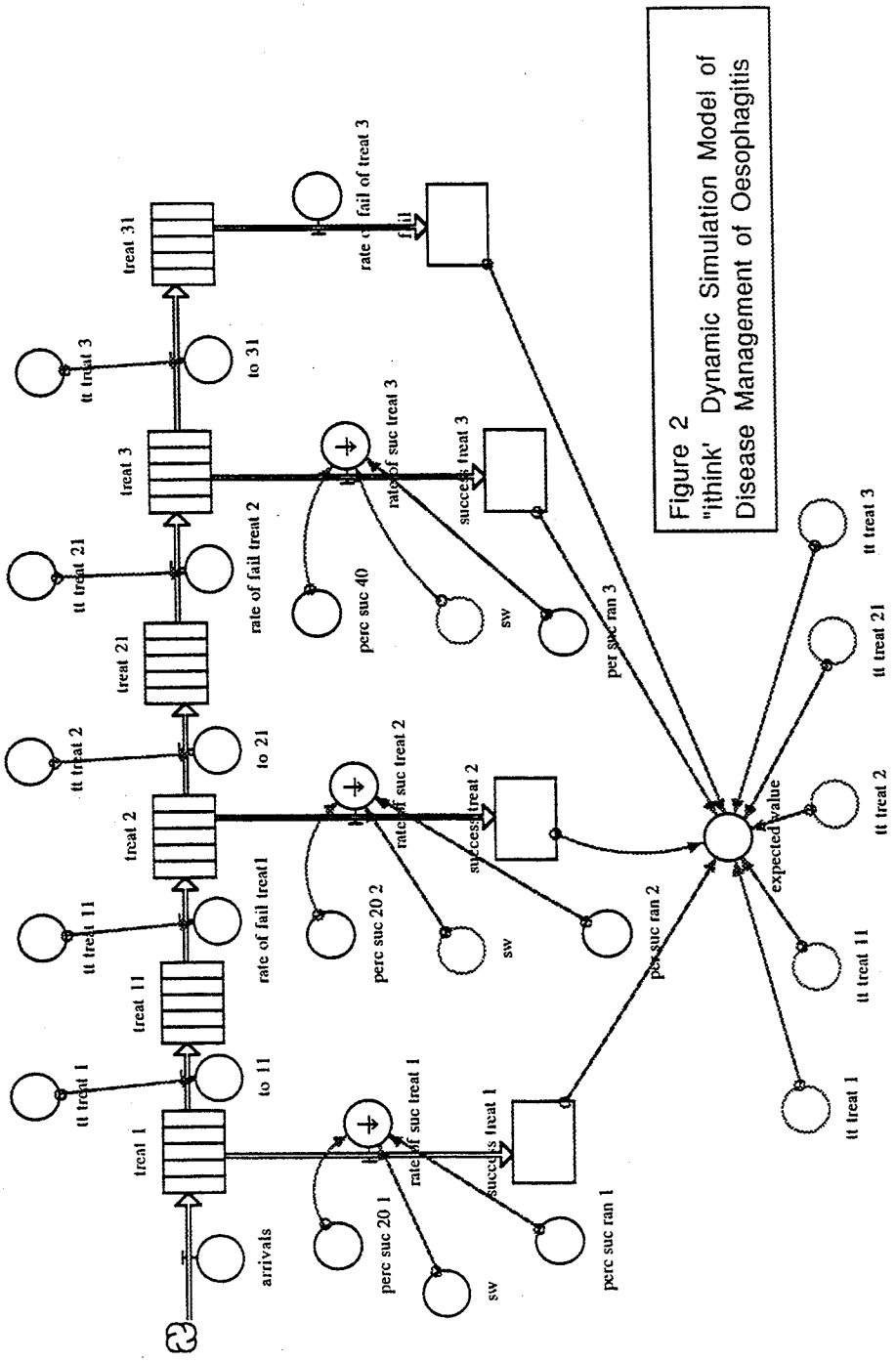


Figure 2
"ithink' Dynamic Simulation Model of
Disease Management of Oesophagitis

Weeks	fail	success treat 1	success treat 2	success treat 3	expected value
Initial	0.00	0.00	0.00	0.00	0.00
0	0.00	0.00	0.00	0.00	0.00
1	0.00	0.00	0.00	0.00	0.00
2	0.00	57.00	0.00	0.00	570.00
3	0.00	57.00	0.00	0.00	570.00
4	0.00	57.00	0.00	0.00	570.00
5	0.00	57.00	0.00	0.00	570.00
6	0.00	57.00	12.04	0.00	642.24
7	0.00	57.00	12.04	0.00	642.24
8	0.00	57.00	12.04	0.00	642.24
9	0.00	57.00	12.04	0.00	642.24
10	0.00	57.00	12.04	16.72	675.68
11	0.00	57.00	12.04	16.72	675.68
12	14.24	57.00	12.04	16.72	675.68

Figure 3 (a) Expected values from Ome treatment: (1)

Weeks	fail	success treat 1	success treat 2	success treat 3	expected value
Initial	0.00	0.00	0.00	0.00	0.00
0	0.00	0.00	0.00	0.00	0.00
1	0.00	0.00	0.00	0.00	0.00
2	0.00	0.00	0.00	0.00	0.00
3	0.00	0.00	0.00	0.00	0.00
4	0.00	0.00	0.00	0.00	0.00
5	0.00	0.00	0.00	0.00	0.00
6	0.00	0.00	38.00	0.00	228.00
7	0.00	0.00	38.00	0.00	228.00
8	0.00	0.00	38.00	0.00	228.00
9	0.00	0.00	38.00	0.00	228.00
10	0.00	0.00	38.00	33.48	294.96
11	0.00	0.00	38.00	33.48	294.96
12	28.52	0.00	38.00	33.48	294.96

Figure 3 (b) Expected values from Rani treatment: (1)

Weeks	1: expected value	2: expected value
Initial	0.00	0.00
0	0.00	0.00
1	0.00	0.00
2	570.00	0.00
3	570.00	0.00
4	570.00	0.00
5	570.00	0.00
6	642.24	228.00
7	642.24	228.00
8	642.24	228.00
9	642.24	228.00
10	675.68	294.96
11	675.68	294.96
12	675.68	294.96

Figure 3(c) Comparison of Expected values from Ome and Rani: (1)