# SIMULATION MODELLING: PROBLEM UNDERSTANDING IN HEALTHCARE MANAGEMENT

A thesis submitted for the degree of Doctor of Philosophy

By

Tillal Eldabi

Department of Information Systems and Computing, Brunel University

May 2000

# Abstract

One of the main problems that face decision makers in healthcare systems is complexity and the lack of a well-defined problem. This causes a lack of understanding about the system. Another problem associated with healthcare systems is that usually there are several stakeholders involved in decision making. In such cases different stakeholders may have different views about the problem. In addition to the lack of understanding and intercommunication, there is the tendency in healthcare management to use quantitative methods for analysing the system. These methods are highly data dependant and usually based on historical data, which may not reflect the system's performance under the present circumstances, given the changing pace of healthcare services and structure. Also data may not be available in the first place.

This research looks at how modelling techniques may help healthcare stakeholders to understand their system and increase their level of intercommunication (in the case of multiple stakeholders) with minimum dependency on data. Two main aspects are considered in this research: first appraising the existing modelling techniques with regard to problem understanding and intercommunication, and second, looking for an effective modelling approach for achieving such objectives. Discrete Event Simulation (DES) offers good facilities for modelling for understanding. However, DES could be used more effectively to enable viable understanding and means of communication. It is assumed that in order to enhance stakeholders' understanding and intercommunication, that it is better to involve them in the process of modelling from the beginning, using an iterative modelling process, and without being restricted to logical steps.

To achieve this a case study strategy is followed in order to devise a modelling framework that helps in enhancing stakeholders' understanding and intercommunication. In this particular research Single Case approach is employed using two case studies. The first case study is used as an attempt to evaluate the hypotheses and tackle research questions which are raised based on an analysis of findings from the literature. The experimentation and analysis part are used to refine the initial hypotheses. These hypotheses are then examined using the second case study to establish a picture about how to achieve the research objectives. In both case studies simulation modelling is examined with regard to the research questions.

The thesis concludes by identifying a modelling approach that has high versatility and flexibility to enhance stakeholders understanding and intercommunication. The approach is called MAPIU2, which stands for a Modelling Approach that is Iterative Participative for Understanding. From its name it can be deducted that the main factors of this approach are based on involving the stakeholders in the modelling process from the beginning in an iterative behaviour. One of the main lessons learned is that to achieve better results from the simulation modelling it is important that stakeholders should be involved with modelling process rather than just getting the final results, which helps implanting any decisions or recommendations arising from the model.

# Acknowledgement

I would like very much to thank my supervisor Professor Ray J. Paul for his constant support throughout my work in this thesis and for what I had learned from him about life.

I would to thank both my external examiner and my internal examiner for taking the trouble of reading this dissertation and their valuable and constructive criticism.

I would like to thank my colleagues at the Health Economics Research Group, as my work with them constituted some vital elements in this thesis.

I would like also to thank Dr Andrew Burroughs for his cooperation for conducting parts of this research at the Royal Free Hospital.

I am very much indebted to the people at the department of Information Systems and Computing for their support and understanding during my writing of this dissertation.

I am very much grateful to my family and friends for their understanding and patience throughout my years as a PhD student.

# Table of Contents

ABSTRACT ..... I

ACKNOWLEDGEMENT ..... II

TABLE OF CONTENTS ..... I

LIST OF TABLES ..... VII

LIST OF FIGURES ..... VIII

PUBLICATIONS ARISING FROM THE DISSERTATION ..... IX

1 CHAPTER ONE: INTRODUCTION ..... 1

1.1 INTRODUCTION ..... 1
1.2 HEALTHCARE SYSTEMS AND MODELLING (BACKGROUND) ..... 3
*1.2.1 Uses of Modelling and Healthcare Systems ..... 3*
*1.2.2 Healthcare Complexities ..... 4*
*1.2.3 Multiple Stakeholders ..... 5*
*1.2.4 Multifaceted Systems ..... 5*
1.3 PROBLEMS WITH MODELLING APPROACHES ..... 6
*1.3.1 Limitations of Modelling Approaches ..... 6*
*1.3.2 What May Help ..... 8*
1.4 RESEARCH OBJECTIVES ..... 9
1.5 RESEARCH METHODOLOGY ..... 11
1.6 OUTLINE OF THE DISSERTATION ..... 13
1.7 SUMMARY ..... 15

2 CHAPTER TWO: THEORETICAL REVIEWS ..... 17

2.1 INTRODUCTION ..... 17
*2.1.1 Chapter Objectives ..... 18*
*2.1.2 Chapter Outline ..... 18*
2.2 PROBLEMS AND PROBLEM UNDERSTANDING ..... 19
*2.2.1 "Problems" ..... 20*
*2.2.2 Frameworks for Problem Solving ..... 22*
*2.2.3 Problem Understanding ..... 24*
*2.2.4 Communicating Understanding ..... 28*
2.3 MODELLING APPROACHES IN HEALTHCARE ..... 30
*2.3.1 Decision Tree ..... 30*
*2.3.2 Markov Chains (MC) Modelling ..... 33*
*2.3.3 Simulation Modelling ..... 35*

2.4 SIMULATION FRAMEWORKS AND PROBLEM SOLVING ....37
*2.4.1 Overview of the Simulation Process* ....37
*2.4.2 Healthcare Overview of the Simulation Process* ....40
2.5 RESEARCH QUESTIONS ....41
2.6 SUMMARY ....43

**3 CHAPTER THREE: AN ALTERNATIVE MODELLING APPROACH ....46**

3.1 INTRODUCTION ....46
*3.1.1 Objective of the Chapter* ....47
*3.1.2 Outline of the Chapter* ....47
3.2 REQUIREMENTS FOR MODELLING AND PROBLEM UNDERSTANDING ....48
*3.2.1 The Simulation Process (Revisited)* ....49
3.3 ISSUES IN DEVELOPING A MODELLING FRAMEWORK ....51
*3.3.1 Theoretical vs. Practical Modelling* ....52
*3.3.2 Sequential vs. Iterative Approach* ....54
3.4 THE PROPOSED FRAMEWORK: BASIC STRUCTURE AND COMPONENTS ....58
*3.4.1 Structure* ....58
*3.4.2 Components* ....59
3.5 THE PROPOSED FRAMEWORK: BASIC MODELLING PRINCIPLES ....60
*3.5.1 The Modelling Process (Overview)* ....60
*3.5.2 Modelling Factors* ....63
3.6 COROLLARY ....67
3.7 SUMMARY ....68

**4 CHAPTER FOUR: ABCSIM CASE STUDY ....70**

4.1 INTRODUCTION ....70
*4.1.1 Objective of the Chapter* ....71
*4.1.2 Outline of the Chapter* ....71
4.2 ADJUVANT BREAST CANCER (ABC) ....71
*4.2.1 Background of the Adjuvant Therapies* ....72
*4.2.2 The ABC Trial Structure* ....73
4.3 THE ECONOMIC EVALUATION ALONGSIDE THE ABC TRIAL ....76
*4.3.1 The Need for Modelling* ....78
4.4 THE ABCSIM MODEL ....78
*4.4.1 Key Issues in Building the Simulation Model* ....79
*4.4.2 The Conceptual Model (ACD)* ....80
*4.4.3 The Computer Model* ....82
4.5 THE MODEL'S DETAILS ....84
*4.5.1 Inputs to the Model* ....84
*4.5.2 The Model's Outputs* ....88

4.5.3 *Verification of the Model* ....89
4.5.4 *Validation of the Model* ....90
4.6 USE OF THE MODEL ....93
4.6.1 *An Example of Use* ....94
4.7 SUMMARY ....97

**5 CHAPTER FIVE: APPROACH ANALYSIS ....99**

5.1 INTRODUCTION ....99
5.1.1 *Objective of the Chapter* ....100
5.1.2 *Outline of the Chapter* ....100
5.2 METHOD OF ANALYSIS AND EVALUATION ....100
5.2.1 *Factors Specifically Related to Modelling* ....102
5.3 ABCSIM REVISITED ....103
5.3.1 *General Factors for Understanding* ....103
5.3.2 *Modelling Factors for Understanding* ....107
5.4 WEAKNESSES IN THE ABCSIM EXPERIENCE ....109
5.4.1 *Stakeholders' Aspect* ....110
5.4.2 *Modelling Aspects* ....113
5.5 REQUIREMENTS ....114
5.5.1 *Requirements Based on Stakeholders* ....115
5.5.2 *Requirements Based on Modelling* ....116
5.6 MAPIU REVISITED ....118
5.6.1 *Stakeholders Based Modifications* ....118
5.6.2 *Modelling Based Modifications* ....121
5.7 MAPIU REVISED ....124
5.7.1 *Initialisation* ....125
5.7.2 *Processing* ....127
5.8 SUMMARY ....131

**6 CHAPTER SIX: THE LIVERSIM EXPERIENCE ....134**

6.1 INTRODUCTION ....134
6.1.1 *Objectives of the Chapter* ....135
6.1.2 *Outline of the Chapter* ....135
6.2 LIVER TRANSPLANTATION ....135
6.2.1 *The Current Situation and Problems* ....136
6.2.2 *The Case for modelling* ....138
6.2.3 *Background of the System* ....139
6.3 THE LIVERSIM MODEL USING MAPIU2 ....140
6.3.1 *Initialisation* ....141
6.3.2 *Processing* ....143

6.4 MODELLING ISSUES ........ 144
*6.4.1 The Conceptual Model* ........ *144*
*6.4.2 The Time-Based Model* ........ *149*
*6.4.3 Inputs to the Model* ........ *152*
*6.4.4 Survival Prognosis* ........ *154*
*6.4.5 Outputs from Model* ........ *156*
*6.4.6 Experimentation Issues* ........ *157*
*6.4.7 An Example of Use* ........ *162*
6.5 COMMUNICATION ISSUES ........ 164
*6.5.1 Intercommunication in LiverSim* ........ *165*
*6.5.2 Communication in LiverSim* ........ *165*
6.6 INFORMATION ........ 166
6.7 SUMMARY ........ 168

**7 CHAPTER SEVEN: SUMMARY AND CONCLUSIONS ........ 171**

7.1 SUMMARY ........ 171
*7.1.1 Detailed Chapters' Summaries* ........ *172*
7.2 CONCLUSIONS ........ 177
*7.2.1 MAPIU2 and Problem Understanding* ........ *178*
*7.2.2 MAPIU2 and Intercommunication* ........ *180*
*7.2.3 Corollary* ........ *181*
7.3 FUTURE RESEARCH ........ 182

**REFERENCES ........ 185**

**APPENDIX A: ABCSIM SAMPLE ACD'S ........ 194**

**APPENDIX B: EVOLVED STAKEHOLDERS' UNDERSTANDING USING ACD ........ 196**

**APPENDIX C: LIVERSIM INPUTS (BASE CASE) ........ 194**

**APPENDIX D: VALIDATION GRAPHS (LIVERSIM) ........ 207**

**APPENDIX E: RESULTS OF SENSITIVITY ANALYSIS (LIVERSIM) ........ 208**

# List of Tables

TABLE 3.1: AN EXAMPLE OF INPUT PROBABILITY DISTRIBUTION ....65
TABLE 4.1: THE RANDOMISATION OPTIONS FOR THE ABC TRIAL....74
TABLE 4.2: COMPARISON FOR THE CLINICAL END-POINTS....75
TABLE 4.3: INPUT VARIABLES ASSOCIATED WITH ABCSIM....85
TABLE 4.4: RESULTS CATEGORIES DERIVED FROM THE MODEL....89
TABLE 4.5: ELEMENTS OF THE INTERACTIONS FORMULATED IN THE MODEL....92
TABLE 4.6: AN EXAMPLE OF ALTERING VALUES OF MODEL'S VARIABLES....94
TABLE 4.7: COST-EFFECTIVENESS RESULTS OF ALTERING OS COSTS....95
TABLE 5.1: STAKEHOLDERS' DETAILS IN MAPIU2....126
TABLE 5.2: DETAILS OF THE MAPIU2 PROCESS....129
TABLE 6.1: CLASSIFIED STAKEHOLDERS AND CORRESPONDING FEATURES....142
TABLE 6.2: COMPONENTS OF MAPIU2 PROCESS....142
TABLE 6.3: DETAILS OF SIMUL8 REPRESENTATION OF THE LIVERSIM MODEL....152
TABLE 6.4: INPUT VARIABLES ASSOCIATED WITH THE LIVER TRANSPLANTATION MODEL....155
TABLE 6.5: INPUT VARIABLES ASSOCIATED WITH THE LIVER DISEASE MODEL....155
TABLE 6.6: SELECTION CRITERIA FOR TRANSPLANTATION....159
TABLE 6.7: BASE CASE RESULTS: (1000 PATIENTS)....164
TABLE C.1: KEY DATA ELEMENTS INCLUDED IN THE MODEL FOR LIVER TRANSPLANT PATIENTS....203
TABLE C.2: KEY DATA ELEMENTS INCLUDED IN THE MODEL FOR LIVER DISEASE PATIENTS....205
TABLE B.3: RATE OF CHANGE OF CLINICAL VARIABLES OVER TIME....205
TABLE C.4: POST-TRANSPLANT SURVIVAL PROBABILITIES....206
TABLE C.5: MATCHING CRITERIA BETWEEN DONOR AND RECIPIENT....206
TABLE E.1: SENSITIVITY ANALYSIS....208
TABLE E.2: SUMMARY RESULTS: MEAN OF 25 SIMULATIONS (150 PATIENTS)....208

# List of Figures

FIGURE 2.1: AN EXAMPLE OF A DECISION TREE MODEL ........ 31
FIGURE 2.2: A STANDARD MARKOV PROCESS MODEL ........ 33
FIGURE 2.3: STEPS IN A SIMULATION STUDY (LAW AND KELTON, 1991) ........ 38
FIGURE 3.1: A MODELLING APPROACH THAT IS PARTICPATORY (MAPIU) ........ 61
FIGURE 3.2: MAPIU: DETAILED MODELLING EFFORTS ........ 63
FIGURE 4.1: ACD OF THE ABC TRIAL – TREATMENT PHASE ........ 81
FIGURE 4.2: ACD OF THE ABC TRIAL – POST-TREATMENT PHASE ........ 81
FIGURE 4.3: A SIMUL8 VISUAL REPRESENTATION OF THE TREATMENT PHASE ........ 83
FIGURE 4.4: A SIMUL8 VISUAL REPRESENTATION OF THE RECURRENCE PHASE OF THE MODEL ........ 83
FIGURE 4.5: ABCSIM MAIN CONSOLE ........ 84
FIGURE 4.6: COST-EFFECTIVENESS RESULTS: PERCENTAGES OF CHANGES BASED ON MODEL 1 AND 2 ........ 96
FIGURE 5.1: MODIFICATIONS BASED ON STAKEHOLDERS ........ 119
FIGURE 5.2: MODIFICATIONS BASED ON MODELLING ........ 123
FIGURE 5.3: MAPIU2 OVERALL STRUCTURE ........ 126
FIGURE 6.1: LIVERSIM OVERALL MODELLING PROCESS ........ 144
FIGURE 6.2: ACD FOR THE LIVER TRANSPLANTATION MODEL ........ 146
FIGURE 6.3: ACD FOR THE LIVER DISEASE MODEL ........ 147
FIGURE 6.4: THE NEW ACD FOR THE LIVER TRANSPLANTATION MODEL ........ 149
FIGURE 6.5: SIMUL8 REPRESENTATION OF THE LIVER TRANSPLANTATION MODEL ........ 150
FIGURE 6.6: SIMUL8 REPRESENTATION OF THE LIVER DISEASE MODEL ........ 151
FIGURE 6.7: LIVERSIM MAIN CONSOLE ........ 153
FIGURE 6.8: AN EXAMPLE OF AN INPUT WINDOW IN THE LIVERSIM MODEL ........ 153
FIGURE 6.9: LIVERSIM OUTPUT PRESENTATION ........ 157
FIGURE 6.10: LIVERSIM WINDOWS FOR BLOOD AND BODY WEIGHT MATCHING ........ 158
FIGURE 6.11: SELECTION STRATEGY WINDOW IN LIVERSIM ........ 160
FIGURE A.1: INITIAL ACD FOR ABCSIM ........ 194
FIGURE A.2: A MIDDLE VERSION FOR THE ABC TRIAL ........ 195
FIGURE B.1: VERSION ONE OF ACD OF LIVERSIM ........ 196
FIGURE B.2: VERSION TWO OF ACD OF LIVERSIM ........ 197
FIGURE B.3: VERSION THREE OF ACD OF LIVERSIM ........ 198
FIGURE B.4: VERSION FOUR OF ACD OF LIVERSIM ........ 199
FIGURE B.5: VERSION FIVE OF ACD OF LIVERSIM ........ 200
FIGURE B.6: VERSION SIX OF ACD OF LIVERSIM ........ 201
FIGURE B.7: VERSION SEVEN OF ACD OF LIVERSIM ........ 202
FIGURE D.1: SURVIVAL FOR ALD PATIENTS ........ 207
FIGURE D.2: SURVIVAL FOR PBC PATIENTS ........ 207

## Publications arising from the Dissertation

### *Journals:*

1. Ratcliffe, J., Eldabi, T., Young, T., Buxton, M., Burroughs, A., Paul, R. J., Papatheodoridis, and Rolles, K., A simulation Modelling Approach to evaluating Alternative Policies for the Management of the Waiting List for Liver Transplantation, *Health Care Management Science*, submitted.

2. Baldwin, L. P., Eldabi, T., and Paul, R. J., Simulation as A Medium of Communication and Problem Understanding in Healthcare Systems, *International Journal of Computers & Industrial Engineering*, submitted.

3. Eldabi, T., Macredie, R., and Paul, R. J., Simulation Modelling as a Decision Making Aid in Randomised Clinical Trials: a Case Study, *ACM TOMACS*, under revision 2.

4. Eldabi, T., Paul, R. J., and Taylor, S. J. (2000) Simulating Economic Factors in Adjuvant Breast Cancer Treatment, *Journal of the Operational Research Society*, vol. 51 (4), pp. 465 – 475.

5. Brown, J., Karnon, J., Eldabi, T., and Paul, R. J. (1999) Using Modelling in a Phased Approach to the Economic Evaluation of Adjuvant Therapy for Early Breast Cancer, *Critical Reviews in Oncology/Haematology*, vol. 32(2), pp. 95 – 103.

6. Taylor S. J. E., Eldabi T., and Paul R. J. (1998) Clinical Trials, Economic Evaluation and Simulation, *OR Insight*, vol. 11(4), pp. 22 – 28.

### *Conferences:*

1. Baldwin, L. P., Eldabi, T., and Paul, R. J. (2000) Simulation Modelling as an Informative Tool in Healthcare Management Decision Making, *In Proceedings of 5^th^ UKAIS Conference*, Cardiff, Eds: Beynon-Davies, P., Williams, M., and Beeson, I., Maidenhead, McGraw-Hill, pp. 473 – 480.

2. Baldwin, L. P., Eldabi, T., and Paul, R. J. (1999) Simulation as A Medium of Communication and Problem Understanding in Healthcare Systems, *In Proceedings of the*

*26th Conference on Computers & Industrial Engineering*, Melbourne, Eds: Shayan, E., IRIS, Melbourne, pp 49 – 54.

3. Baldwin, L. P., Eldabi, T., and Paul, R. J. (1999) Simulation Modeling as an Aid to Decision-Making in Healthcare Management: the Adjuvant Breast Cancer (ABC) Trial, *In Proceedings of the 1999 Winter Simulation Conference*, Phoenix, Eds: Farrington, P. A., Nembhard, H. B., Sturrock, D. T., and Evans, G. W., New York, Association of Computing Machinery, pp. 1523 – 1531.

4. Eldabi T. and Paul R. J. (1999) Simulating Healthcare Systems For Problem Understanding: The ABC Trial Example, *In Proceedings of the 4th UK Simulation Society Conference*, Cambridge, Eds: Al-Dabass, D. and Cheng, R., United Kingdom Simulation Society, pp 81 – 87.

5. Eldabi T. and Paul R. J. (1997) Flexible Modelling of Manufacturing Systems with Variable Levels of Details, *In Proceedings of the 1997 Winter Simulation Conference.* Atlanta, Eds: Andradóttir, S., Healy, K. J., Withers, D. H., and Nelson, B., New York, Association of Computing Machinery, pp. 801 – 808.

6. Eldabi, T., Paul, R. J., and Taylor, S. J. (1998) Computer Simulation in Healthcare Decision Making, *Computers & Industrial Engineering*, London, Eds: Dessouky, M. I., Hindi, K. S., and Sadek Eid, M., Oxford, Elsevier Science Ltd, pp 235 – 238.

7. Taylor S. J. E., Eldabi T., Macredie R. D., Paul R. J., Brown J. and Karnon J. (1998) Economic Evaluation of Adjuvant Breast Cancer Treatment Using Simulation Modelling, *In Proceedings of the 1998 Medical Sciences Simulation Conference*, Eds: Anderson, J. G. and Katzper, M., The Society for Computer Simulation International, San Diego, California, pp. 42 – 47.

***Abstracts:***

1. Eldabi, T., Paul, R. J., and Ratcliffe, J. (1999) Discrete Event Simulation as a Tool for Understanding Healthcare Management, *Operational Research Society Annual Conference (OR41)*, pp 107 – 108.

2. Ratcliffe, J., Young, T. and Eldabi, T. (1999) Using Simulation Modelling Techniques to Facilitate the Management of the Waiting List for Liver Transplantation, *The Journal of the International Society for Pharmacoeconomics and Outcome Research*, vol. 2(3), pp 141.

3. Brown, J., Karnon, J., Eldabi, T., and Paul, R. J. (1997) Economic Evaluation of Adjuvant Treatment for Early Breast Cancer, *The European Journal of Cancer*, 33, Supplement 9: S18.

***Discussion Papers:***

1. Ratcliffe, J., Young, T., and Eldabi T. (1999) Using Simulation Modelling Techniques to Facilitate the Management of the Waiting List For Liver Transplantation – A Pilot Study, *Health Economists' Study Group Conference*, University of Birmingham, Birmingham.

# Chapter One

# 1 Chapter One: Introduction

## 1.1 Introduction

Three major issues associated with healthcare systems are their *complexity, multifaceted structure*, and *multiple ownership.* This research attempts to provide ways of applying a modelling tool to help these issues and ease the process of healthcare management and decision making. The research assumes that there are two main aspects to be considered in order to achieve its aim and those are problem understanding and communication.

It is widely accepted that problem understanding is of paramount importance for decision making. It is better to understand the exact nature of the problem then select a suitable method for solution than to start solving the problem without understanding it, only to discover the proposed solution was not really relevant. This may cost more money and waste more time, especially if the method used is expensive. Despite the importance of problem understanding, most research has concentrated on finding methods for problem solution, with less emphasis on methodologies to support problem understanding. In other words, most of the existing methodologies implicitly assume that the real world problem is well defined in terms of its components and related assumptions. They usually concentrate on providing answers to what is thought to be the problem, based on some initial or later modified assumptions. This approach, however, is in danger of making the findings of a modelling exercise subject to the initial ideas regardless of them being true or false. In this case problem owners will only be restricted to their basic assumptions without having the chance to rethink these assumptions.

The importance of communication stems from the fact that healthcare problems are usually owned by more than one group of health professionals. For example, hospital managers and clinicians may be involved in specifying what type of care certain patients may have. Thus, it is important to have a modelling technique that enables or helps different stakeholders to communicate and share their ideas. The role of modelling here will be of quantifying the different interests, and putting them on a common footing for communication.

In this research, we propose *Dynamic Stochastic Discrete Event Simulation Modelling* as a modelling technique that may enable healthcare decision makers to cope with problem understanding and communication between stakeholders. The use of simulation in healthcare is not a new idea or even new practice. Simulation and other modelling techniques have been used for quite a while in the health area (Lagergren, 1998).

The following section explores the different uses of modelling in healthcare decision making. Whilst, Chapter Two explores the different modelling techniques used in healthcare, including simulation, concerning the advantages and disadvantages of those techniques for problem solving. The section also explores the problems and complexities associated with healthcare systems with regard to modelling. Section 1.3 outlines the problems and limitations associated with the current modelling techniques with regard to healthcare systems understanding. Section 1.4 presents the objectives of this research. The last sections present the research methodology, outline of the dissertation, and chapter summary, respectively.

## 1.2 Healthcare Systems and Modelling (Background)

As stated in the previous section, modelling is not a new concept with regard to healthcare management. However, there are a number of problems associated with applying different modelling techniques to healthcare systems. In this research, we concentrate on three main problems. Those are the complexities of healthcare systems, multiple stakeholders, and the multifaceted nature of all or part of the components of healthcare systems. This section briefly discusses these problems. Before that, the following subsection provides a discussion about modelling and healthcare systems in general attempting to briefly identify the uses of modelling in this area.

### 1.2.1 Uses of Modelling and Healthcare Systems

One way to explore the different consequences of alternative decisions is modelling. Modelling in general is one of the most widely used tools to support decision making. The main purpose of modelling is to present an abstract picture of the real system and examine the system's responses to different levels of inputs without risking the real system including people and resources (Pidd, 1996). There are many types of modelling techniques that are already used in healthcare problems. Lagergren (1998) presents some of the areas within the healthcare domain where modelling has been effectively used. He states that modelling is used in the *Epidemiology* area for modelling and predicting future incidence, prevalence and mortality for broad sets of chronic diseases or for different specific diseases. Modelling is used in *health care systems design*, where the main concern is designing healthcare systems and estimating future resource needs. It is also used for *healthcare systems operation*, where the main objective of modelling is to improve the performance by offering techniques for analysing how existing resources could be used more efficiently. One last example of the use of modelling in healthcare is in *medical decision making*, where it is developed as a support for analysis and decision making in medical practice.

There are many modelling techniques used in healthcare modelling, such as, decision trees, Markov modelling, simulation modelling, Monte Carlo simulation, and other statistical methods. However, the most commonly used method is Markov modelling (Sonnenberg and Beck, 1993). Section 1.3 presents a brief discussion of the limitations of such techniques to offer facilities for problem understanding. We propose simulation not as an alternative technique, since it is included among the above mentioned techniques based on the uses of simulation in healthcare, but in the way in which simulation is used. The following three subsections explore the main problems faced during modelling healthcare systems.

### 1.2.2 Healthcare Complexities

One of the main problems that face decision makers and modellers in healthcare systems is the complexity and lack of a well defined shape for the problem (Delesie, 1998). Many health problems have the characteristic of being complex with many interdependent entities competing for limited resources. Modellers in general resort to assumptions in order to define the basic features of the problem, particularly when using mathematical models. However, these assumptions may not help in representing the system in the best way possible. For example, if we assume that there is a type of care that might consist of two types of treatment. The patient may suffer from side effects from the first treatment while receiving the second one. These effects may have a time duration, which means that the health state of the patient who is receiving the treatment depends on the durations of the side effect in addition to the duration of the particular treatment. This type of interdependency is a common feature in healthcare systems, which may not be easily tackled using mathematical models.

### 1.2.3 Multiple Stakeholders

The second problem is that, usually, healthcare systems are related to more than one type of health professional, for example, clinicians and health managers (Delesie, 1998). In this case both types have different views about the problem, expecting different outcomes, and tend to make different decisions based on the same model. Sometimes the problem may arise as a result of misunderstanding amongst the problem owners with no real problem with the system itself. The issue of multiple stakeholders usually leaves the modeller with a major problem, and that is how to combine the different thoughts involved in the problem in terms of modelling and communicating their ideas.

### 1.2.4 Multifaceted Systems

Another problem with healthcare systems is that many of their components are multifaceted. This aspect could be classified as a subset of the aspect of complexity. However, in healthcare systems it is considered as quite important and hence seen as a separate issue. An example of a multifaceted system can be demonstrated in decisions about what treatment to give a patient. The clinician has to look at different personal attributes of the patient in addition to the costs of treatments and the availability of resources to conduct such treatments. One of the common features in healthcare systems is the existence of some entities that are engaged in more than one activity simultaneously. For example, a patient may be having long run treatment while having another treatment during the course of the first one. This feature raises a problem in modelling because of the asynchrony of computer software, as it deals with one activity at a time. This is assuming that all modelling techniques use computers nowadays. It will not be a problem if one activity interrupts the other one. That is, stopping one activity until the second one is finished then continue with the first one. A proposed solution is to clone the entity into a number of entities based on the number of activities involved. This may add some reality to the model, yet more complexity.

## 1.3 Problems with Modelling Approaches

This section discusses problems and limitations associated with the different modelling approaches applied in healthcare systems. These limitations are related to the inability of these approaches to cope with healthcare systems problems shown in the previous section and their lack of flexibility to provide practical decision making assistance for healthcare managers. The subsequent subsection discusses some of the favoured modelling features, assumed by this research, for solving the above problems.

### 1.3.1 Limitations of Modelling Approaches

There are two aspects regarding the limitations of the different modelling approaches applied in healthcare systems modelling. Those are, the nature of such techniques and the approach to modelling. One of the main problems behind the use of statistical modelling techniques, like Markov modelling, is that they only represent aggregate levels of the system without much of a view about individual cases or rare events. For example, Markov modelling is restricted to fixed time intervals, that means entities can only change their state at the end of each period of time. This approach is not flexible enough to cope with models containing activities with short and long durations at the same time. Another limitation is that transition probabilities are time independent and are not influenced by previous states experienced by the entities. This restricts the model from evaluating the effect of previous experiences on current and future situations. It is possible to overcome that in Markov modelling yet at the expense of simplicity. In addition, these models are usually not accessible to non-experts and they do not offer enough transparency given the diverse perspectives of the problem owners.

Statistical models are mostly data dependent, in fact they usually require a large amount of data to enable them to present a more precise picture of the situation. Most models are built based on an initial understanding without attempting to revise this understanding, especially when there is more than one stakeholder. Although simulation has been used in many healthcare problems, most of these studies have concentrated on deriving specific answers for pre-defined problems (Davies and Roderick, 1998; Halpern et al, 1994). The modelling stage usually came after identifying the variables of the model. In addition, most of them were inclined to predict future behaviour based on specific data collected from previous situations (Delesie, 1998). This is not a problem in itself. However, there is no guarantee that previous situations can be repeated. On the other hand, using simulation is expensive, and it has no advantage over the other methods if it is used for only predicting aggregated behaviour. This is possible to achieve using, for example, Markov modelling or may be even spreadsheet modelling. Chapter Two provides more details about why features, discussed in this section, may hinder the process of problem understanding in healthcare systems.

### 1.3.2 What May Help

This subsection discusses why an alternative way of modelling may overcome the above mentioned limitations. For example, allowing entities to experience events at any point of time after the previous event without being restricted to fixed time intervals. In addition, a modelling technique is required to record and retain the entity's history throughout the course of the model, and then this history can be used to influence the entity's future levels and pathways throughout the model. Other information about entities may be needed individually, such as, costs and quality of life effects associated with the events undergone.

Simulation is one technique which offers such facilities. However, it could be used more efficiently to give more help in the decision making process. The model is usually built based on data collected from previous records, then this data is analysed to establish an understanding of the system. Nevertheless, there is a high possibility that this data could be misleading. The reason being that data is a sample of reality. Even if this sample is a good representation of reality, there is no guarantee that reality will be the same in the future. That is, the system in future may not retain the same behaviour given the changing nature of healthcare systems. In addition, data collection is expensive and it takes time as well. Another aspect about data collection is that sometimes the process of data collection is not reliable.

Simulation is used to derive answers to already established questions. But it could be used better by improving the understanding of the system and capture the relevant elements to the problem in hand, without going into unnecessary details. An alternative way of modelling may be needed to enable the stakeholders to understand the system under study and reconsider this understanding while communicating with each other by using the model. That is, the model may be considered as a systematic debating vehicle rather than as a calculator. This discussion is expanded in Chapter Two with more details on the currently practised simulation process.

## 1.4 Research Objectives

This research is looking for means or a tool to enable health practitioners to understand the problems they face and critically evaluate the situation by identifying and studying the implications of their decisions. As a means for that this research attempts to devise a modelling approach for coping with problem understanding and intercommunication. This is looking at ways for building flexible models that may accommodate as many changes as possible in a way that is accessible to the stakeholders. The aim of this research is based on two main issues. First, understanding the system in order to identify the real problem and minimise the activities of data collection and pre-modelling analysis. Secondly, the structure of the model, that is, a model should be built in a way that enables the stakeholders to interact with the model and amongst each other, as they are the owners of the problem.

By understanding the system we mean identifying the key elements that are relevant to the problem or an issue about which a decision is supposed to be made. On the other hand, knowing the relevant factors will contain the data collection process within these factors. With a simulation model it is always tempting to go into unlimited details that may blur the required picture. To achieve this aim it is suggested that some objectives towards that have to be set as stepping stones. These objectives are summarised as follows:

**Objective 1: Review of the Literature**

The first objective in this research is to know the state of practice and how the exiting tools may help in achieving our aim. For this reason the literature is going to be reviewed and critically analysed to examine the existing tools. At least – if no suitable tool is found – it is possible to elicit the most relevant tool and learn from its weaknesses. Existing tools would be appraised with regard to their capability to aid in understanding the problem.

**Objective 2: Development of Research Question and Hypothesis**

After identifying and analysing the existing tools or modelling techniques, to be precise, this paves the way for establishing the research questions and hypotheses. Research questions are mainly related to whether our hypotheses are true or false. In this particular research the main hypothesis would be: it is possible to devise a modelling approach that enables stakeholders to gain acceptable problem understanding and facilitates the way they intercommunicate.

**Objective 3: Establishing the Basic Principles of the Framework**

The research hypothesis represents the gap between the existing framework and the research aim. The third objective is about identifying the means to close this gap. Mainly identifying the principles of developing a modelling approach that achieve our research aims. At this level the basic constructs of the framework should be identified.

**Objective 4: Testing the Basic Framework**

After establishing the initial theory of the modelling framework it is important to test it and identify the main weaknesses that may hinder the framework from achieving the aim of this research and that is enhancing stakeholders understanding and intercommunication.

**Objective 5: Identifying Areas for Improvement**

After identifying the strengths and weaknesses, the next objective is to realise areas for improving the modelling framework. Areas for improvement are based on strengthening the positive features of the framework and eliminating or minimising the weaknesses associated with it.

**Objective 6: Extrapolating Conclusions**

After the framework is refined, then it may need to be appraised again for its operability and suitability to achieve the main aim of this research. The objective at this stage is to extrapolate final conclusions about the framework and how it would be reusable for other problems in the healthcare systems – which represents the main application area of this research – and how it would be helpful in the process of problem understanding and intercommunication amongst stakeholders.

It is hoped by achieving these objective to reach the aim of this research. The aim of this research is not just about developing a framework to enable healthcare mangers to understand their problems it is also about drawing the attention to such a problem and why it is important to research into it even beyond the boundaries of this thesis.

## 1.5 Research Methodology

Irani et al (1999) emphasises on the importance of having relevant research methodology based on the research problem in hand, either related on natural sciences or social sciences both with their corresponding features. A well-developed methodology provides an understanding, in the broadest possible terms, not of the products of the scientific enquiry but the process itself. A research methodology also serves as a set of rules for reasoning, whereby the evaluation of the facts can be used to draw inferences. However, a research methodology, must not, regardless of all other conditions, dominate the research procedure. The research methodologies must be regarded as mere intellectual frameworks and should not be overused (Quinn, 1988).

The aim of this research is related to finding a modelling approach that could be practised within the arena of healthcare systems. A suitable research strategy for that is case study based. A case study strategy is one that uses the case study method as a systemised way of observing (Weik, 1984). This strategy is characterised by the following two features, which, we think, are valid features for conducting this research: firstly, its ability not to explicitly control or manipulate variables, secondly, the ability to study a phenomena in its natural context. These two features are quite suitable for research into identifying a modelling framework where the aim is to study within realistic settings.

Case study as strategy could be employed for three main scenarios: for discovery and theory building, for theory testing, and for discovery, building and theory testing. For this particular research both case studies are used as an attempt to evaluate the hypotheses and tackle research questions. Hence, the aim is to observe the process rather than the results uncovered using the case studies. This means this particular case study strategy will be employed for theory testing rather than building or discovery.

Case study strategy is divided between single case approach and multiple-case approach (Yin, 1994). It was felt important to clarify this point as there are two case studies applied in this research. Although there are two case studies in this research, they are not employed simultaneously or for testing the same inputs. The research strategy followed here could be called sequential single case approach. The first case study is used as an attempt to evaluate the hypotheses and tackle research questions which are raised based on an analysis of findings from the literature. The experimentation and analysis part will be used to refine the initial hypotheses. These hypotheses are then examined using the second case study to establish a picture about how to achieve the research objectives. In both case studies simulation modelling would be examined with regard to the research questions which elicited in Chapter Two.

## 1.6 Outline of the Dissertation

This section presents an outline of the dissertation giving a brief summary of the contents of each one of the seven chapters in this research. The structure of this dissertation is as follows:

Chapter One gives an introduction to the problem area of this thesis, which is the use of simulation modelling in healthcare decision making and its related problems. Some of the problems associated with the different modelling approaches in healthcare systems are briefly discussed in the third section. The fourth section provides the objectives of the research. The research methods and outline of the dissertation are given in sections 1.5 and 1.6 respectively.

Chapter Two expands the concepts addressed in Chapter One starting by reviewing the concepts of problems, problems solving, and problems understanding for decision making. The chapter then reviews the different modelling approaches and methodologies used in healthcare management in terms of model structures, complexities and users' likely requirements. Some technical aspects related to the different types of modelling, including simulation, used in healthcare management are presented. It also discusses the different advantages and disadvantages of using simulation over the other modelling techniques, which are commonly used at the present time. The chapter ends by putting the case for the research question. That is, can simulation be used more efficiently to enhance the process of problem understanding?

Chapter Three presents an alternative modelling framework, which is developed as an attempt to provide the modelling process with facilitates for enhancing problem understanding and intercommunication of stakeholders using simulation. Before presenting the framework, the chapter briefly discusses the requirements for modelling for the sake of problem understanding and what are the main aspects to consider for developing a framework.

Chapter Four presents a case study related to a healthcare application area and shows how a simulation model is designed, built, and run based on the proposed framework. The objective of this case study is to identify the main features and problems that may characterise the modelling of healthcare systems. This paves the way for refining our research question.

Chapter Five analyses the findings from Chapter Four and re-establishes the modelling framework based on these findings with close consideration to the research questions mentioned in Chapter Two. The chapter aims at deriving some guidelines and hypotheses for the modelling process targeting healthcare management.

Chapter Six presents a second case study also related to a healthcare application area. This case study is designed and built in order to examine the guidelines and suggestions given in Chapter Five. Chapter Six illustrates an analysis for this framework and presents results of the analysis conducted in this research. The purpose is an attempt to generalise these results into the different areas of heathcare systems modelling.

Chapter Seven includes detailed summaries of the chapters in this dissertation. The chapter also presents final conclusions for this research and lessons learned. Chapter Seven ends by identifying some areas as continuation of this research in future.

## 1.7 Summary

This chapter starts with a brief introduction to healthcare systems presenting some basic concepts related to the subject, stressing the aspects of *problem understanding* and *communication* amongst the problem owners. Section 1.2 presents a discussion about the problem domain of this dissertation, which is the use of modelling in healthcare. The section manifests the current uses of modelling in healthcare systems and describes the different problems associated with healthcare management and decision making. Three main problems are presented in this section that characterise healthcare systems.

Section 1.3 presents the main aspects related to modelling healthcare problems in general. The section briefly discusses the limitations associated with the different approaches including simulation. There are two main features regarding those limitations. Those are, model structure and the approach to solve the problem. The section argues that there are not many techniques that offer flexibility for solving healthcare problems. Simulation is one technique that can offer such flexibility. However, previous studies suggest that simulation is often used to derive some answers and predict future behaviour rather than problem understanding. Usually the model is required to provide precise estimates based on sampled data, which does not guarantee that the system will retain the same behaviour in future.

Section 1.4 presents the objectives of this research, which can be summarised as follows: firstly, reversing the existing process, which is based on data collection, analysis, then modelling. The proposed approach aims at understanding the problem by identifying the important variables and components of the system given their respective interrelationships using the model (then, pursue the data collection for the relevant variables). This objective aims at reducing the effort spent on data collection at the beginning of each modelling process. The second objective aims at enabling the users to experiment with the model by altering the different input variables and output responses, as users are the problem owners and they are the ones with the most need to understand the model. Section 1.5 manifests the research method followed in this research which is based on hypotheses and research question, a case study, re-hypotheses, a second case study, analysis of lessons learnt and limitations of the proposed approach. Section 1.6 presents an outline of the dissertation, briefly describing the contents of the seven chapters that are contained in this dissertation.

# Chapter Two

# 2 CHAPTER TWO: Theoretical Reviews

## 2.1 Introduction

This chapter reviews the existing literature about the different modelling methodologies and strategies with respect to healthcare decision making. It examines them with regard to their abilities to enable problem understanding and communication amongst stakeholders. This chapter also examines the advantages and disadvantages of data orientated modelling in relation to decision making about future situations. The main modelling techniques used in healthcare management (decision trees, Markov modelling, and simulation modelling) are discussed. The chapter goes into depth about the limitations of these techniques, mentioned in Chapter One, with regard to the objectives of the thesis, which are based on enabling healthcare managers to understand the problem to hand by identifying its key components and directly experimenting with it in an easy fashion.

Simulation is taken into more detail in this chapter with regard to methodologies, approaches to modelling and uses. After that some analysis of these methodologies are presented. These methodologies are evaluated with respect to problem understanding and communication. The importance of these two factors is presented in Chapter One. Finally some assumptions are given about what can be done to use simulation in an alternative way that may help in problem understanding and communication. These assumptions are therefore put as the research questions to be tackled throughout the rest of the dissertation.

### 2.1.1 Chapter Objectives

The first objective of this chapter is to identify the existing modelling approaches in healthcare decision making and their corresponding limitations regarding the issues of problem understanding and communication amongst different decision makers. This is undertaken by reviewing and evaluating the different modelling methods with respect to the above issue. The chapter also aims to establish why simulation could be a different candidate if it is used in a better way for the problem to be solved. This will be established as the research questions to be put as bases for an alternative framework given in Chapter Three, which is appraised in Chapter Four using a case study. The framework is then refined in Chapter Five to be tackled again in Chapter Six using a second case study.

### 2.1.2 Chapter Outline

This subsection presents a brief outline of Chapter Two, which starts with section 2.1 giving a brief introduction to the chapter. The next section presents a brief background on problems and problem understanding, and how problem understanding is an important factor for problem solving. Section 2.3 examines the three most commonly used modelling techniques in healthcare systems management and decision making. These techniques are evaluated with respect to their abilities to offer facilities for problem understanding. The techniques are; *Decision Trees*, *Markov Chains*, and *Simulation*

*Modelling.* Section 2.4 then goes into more detail about the currently practised frameworks for simulation modelling. The section gives a general overview of the simulation process and an overview that is mostly related to the use of simulation in healthcare systems. This framework is then evaluated and analysed based on that. Section 2.5 presents the main research questions and hypotheses in order to tackle the limitation of the practices of simulation process for the purpose of enabling simulation to enhance problem understanding. Section 2.6 then presents a summary of the chapter.

## 2.2 Problems and Problem Understanding

As mentioned in chapter one there are three main problems that face healthcare decision makers, which also influence the modelling process. Those are, *complexity*, *multifaceted components*, and *multiple ownership.* All these factors together make it difficult to understand the exact nature of healthcare systems in order to reach the best decision. It was also mentioned that some modelling techniques are used to solve such problems. However, most approaches, discussed in section 2.3 are based on the supposition that the problem is already well defined. In this research we think that, it is important to establish an understanding of the problem before applying a suitable solution strategy. That is because of the cost and time involved with healthcare studies. Having a better understanding about the problem reduces the probability of fatal mistakes later, hence, saving money and time. In addition, decisions in healthcare systems often involve human life.

The following two subsections discuss aspects about problems and problem solving. The discussion acts as a threshold for the analysis of existing modelling techniques and methodologies in terms of enhancing problem understanding. This discussion offers guidelines or criteria for analysing different modelling approaches with regard to problem understanding. The following subsection discusses what is meant by problems within the context of this research. The subsection after that discusses some frameworks for problems solving.

### 2.2.1 "Problems"

In this research we hope to find basic elements that may help different stakeholders to reach a common understanding, rather than measuring their understanding of the problem. In this case we need to define what is meant by a problem and what are our postulates regarding problem understanding. We start by establishing the definition of a problem in the following discussion.

There are many definitions of a "problem". However, one definition that seems suitable to our research is given by Bransford and Stein (1993): "A problem exists when there is a discrepancy between an initial state and a goal state, and there is no ready-made solution for the problem solver". An example for that could be a situation where problem owners in health authorities are interested in finding the cost-effectiveness of introducing a new drug. In this example the initial, or current, state is the lack of knowledge of the effect of adding the new drug. The goal state, on the other hand, could be establishing knowledge of the impact and cost-effectiveness of such a drug. Simple as it may seem the story is actually different in reality. Bransford and Stein (1993) look at problems as opportunities to achieve goals and invent new tools or a better quality of life. In fact the existence of problems is based upon motives to accomplish a certain objective in life (Jackson, 1975).

Bransford and Stein's definition implies that when there is a ready-made solution then the situation is not considered as a problem. It could be added here that even if there is no solution, yet the problem is well understood, then applying a specific solution method is a straightforward activity. However, a problem is a problem when the current situation or the impact of actions to be taken is not well understood. Regarding the above example, the main sources of complication could be: identifying the different types of patients involved, their different responses to the treatment, their different treatment paths, and the different patterns of care that could be assigned to them. In addition to side effects on other parts of the hospital.

Unlike, for example, business systems, healthcare decision making must give quality of life for patients a great deal of consideration. The picture is not just about value for money. Rather it is about quality for money. In this case, central tendencies, for example, may not be the best way for measuring the impact of decision making. In a pure business sense, to measure survival rates, having a drug combination of 75% success on one type of patient and 25% on the other type (50% for both) is as good as having 60% and 40% successes (50% for both). Choice will then be about which drug combination will cost more. For healthcare decision makers, the situation is more complicated than that. Decisions here might include considerations of side effects, quality of life, or even psychological effects for those patients even if it costs more.

It can be seen from the above discussion that the heart of problem solving is through understanding. It is said that understanding a problem is half the solution. This means the rest is applying the method for solving it. However, if we look at the technology advancement, this proportion is different. There are many solution methodologies with highly advanced computational power. It does not take more than a day to apply a good deal of them. The main problem is knowing which one to use. This leaves us with the fact that understanding a problem is actually much more significant than just the half of solving it.

### 2.2.2 Frameworks for Problem Solving

This section presents some aspects that define problem solving from a general perception. There are a number of established theoretical problem solving methodologies in the literature (Bransford and Stein, 1993; Jackson, 1975; Francis, 1990; Lyles, 1982). Most of these frameworks propose similar views in tackling problems. In this section we will briefly discuss each of the common steps incorporated in problem solving.

*Step 1: Problem Identification*:

Most of the established frameworks start the process of problem solving by defining the problem and the obstacles that may exist in the way of achieving the desired objectives. From subsection 2.2.1, a problem is defined as a discrepancy between the current state and the goal. It could be implied that the initial step is to identify the discrepancy between the current state and the desired state. For example, a goal could be raising profit in a firm. In healthcare related problems, a goal could be finding the best way to allocate hospital beds amongst different departments. Lyles (1982) suggests that defining the problem is actually understanding the situation and what is wrong with it or, so to speak, what could go wrong with it.

*Step 2*: *Objectives Setting*:

After defining the problem, objectives which are to be achieved are set. According to Francis (1990), setting the objectives is the clarification of the desired outcomes from the activities to be taken and the type of strategy to follow to overcome the existing problem. There are two types of objectives; overall objectives, which are the general objectives related to the strategic policy of the organisation and problem related objectives which are objectives set to solve a particularly existing problem.

*Step 3*: *Generating Alternative Strategies*:

This step is concerned with finding different ways to achieve the desired objectives (Bransford and Stein, 1993; Lyles, 1982). Sometimes there may be more than one path to reach the desired objective(s). It is worthwhile to note that a path is actually a strategy decision makers have to follow rather than a specific solution methodology. Examples for that are redesigning the whole or part of a health service delivery system, or may be changing the existing policy for scheduling patients in an outpatient clinic. Generally, a strategy is the change that has to happen to achieve the desired state. A solution methodology would be the means to implement changes towards suggested strategy. Hence, it is of paramount importance to understand what is considered as the best strategy to achieve the desired state based on the understanding of the problem and the objectives. In this case it is worthwhile to understand the different obstacles and constraints that may restrict decision makers from reaching the already identified goals in any of the possible paths.

*Step 4*: *Actions and Action Plans*:

This step is about comparing and analysing the various courses of actions that will be conducted in order to implement the solution strategy generated from the previous step. At this stage decision makers are concerned with selecting the right means for closing the gap between the current situation and the desired state given the existing constraints after selecting the best strategy for solving the problem. This step relates to making the decision about what action to take and taking the action itself.

*Step 5: Review and Improve*:

To evaluate the success of decisions made and their implementation it is important to sit back and review the actions taken (Francis, 1990). This step is meant to enable decision makers to identify the drawbacks of their decisions. On the other hand, decision makers use this step to identify new problems/opportunities that may arise from their previous decisions and the courses of actions followed in order to implement such decisions and achieve the desired objectives.

It is not intended from the above discussion to standardise the process of problem solving. The above discussion presents a brief summary of what is theoretically known to be a framework for problem solving (Bransford and Stein, 1993; Lyles, 1982; Francis, 1990). In practice this framework may not be applied in the same way nor follow the same sequential structure presented above. The following sections will discuss the existing modelling techniques and methodologies as tools for enhancing the above framework. However, before that the next subsection discusses the process of problem understanding within the process of problem solving.

### 2.2.3 Problem Understanding

The first step in problem solving *defining the problem* is the most important part of problem solving. Lyles (1982) argues that if a problem is not clearly understood, then the likelihood of a chosen solution being successful is much less than if the problem is clearly understood. Going back to the above framework it can be seen that it is not possible to proceed to the next steps if the problem is not defined. Yet, more dangerously, if the problem is misunderstood, then there is a high possibility for misfortune to happen sooner or later. Consider the case of setting a whole strategy for the wrong objectives which are initiated based on a misunderstanding of the problem or the current situation. The implications of such cases are even worse in strategic situations. For example, in healthcare systems when there is a need to create policies for disease management or similar long term situations. In such situations it could be too late to review and improve an ongoing process of the above framework and could be very costly indeed.

Lyles (1982) presents a set of factors to consider when defining different types of problems, which are summarised below. These factors are not necessarily standardised for all situations, yet they are worth considering for defining a problem:

*Nature of the available information*: the type of problem usually dictates what type of information is expected to be found when tackling the problem. For example, in problems related to operations engineering information may easily be quantified and analysed. On the other hand, in healthcare systems problems, information is normally vague and not necessarily quantifiable. The main reason for such a discrepancy between the two types is the degree of involvement of humans as either part of the system or as decision makers. This is not to be taken that humans are problematic. However, people have different perceptions of the existing situations. For the different types of problems there might be specific solution methodologies. Yet it is quite important to understand the type of problem to know what information to ask for.

In the case where the information required is quantifiable it is important to understand that this is actually the information required for defining and solving the problem. A more difficult situation is when information is not readily available or it can never be quantified for quantitative methods. The difficulty comes when decision makers insist on quantifying such information or pursuing quantitative analysis. The following discussion explains the importance of understanding the information required. That is in terms of identifying the structure of the system, assumptions made, what questions to ask during problem definition, and what are the likely objectives to be drawn from the solution.

*The nature of the cause-and-effect relationship*: this aspect is quite important for understanding the problem. It is accepted that for every effect or set of effects there is/are cause(s). A major step in understanding the problem is identifying the cause-and-effect relationships. In complex problems this may prove to be very difficult.

The importance of this aspect stems from the fact that whatever is seen to be going wrong is usually a symptom of a hidden genuine problem. Solving a symptom as a problem is like using pain killers: the problem is bound to come again in worse circumstances. Hence, it is important to understand the causes of the symptoms by understanding the different cause-effect relationships in the system under study.

*Assumptions accepted as facts*: this is actually a warning rather than a step to follow. Lyles (1982) states that one of the main problems that face decision makers is establishing assumptions and then pertaining them as facts. This is a major cause of misunderstanding of the problem which might have unwanted consequences later.

Assumptions can be used either constructively or destructively. They can be used positively to prevent overcomplicating the problem that may lead to lack of understanding. On the other hand, they could be used negatively to oversimplify the problem when they are used excessively. Assumptions can be considered as a vital aspect for problem understanding. Hence they should be revisited and revised during the process of problem solving and more specifically and cautiously during the phase of defining the problem.

*Interrelationship of data*: data is irrelevant unless a specific relationship to a problem can be delineated. Lyles (1982) argues that data which is reported under one set of circumstances, or in groupings with other data might imply one interpretation. Reported with another set of data they might imply no problem at all or a completely different interpretation. It is also important to be alert to any interrelationship that may exist amongst data.

This discussion unveils the problem of data interpretation. Although having data is usually related to quantitative analysis implying a concrete solution, there is always the controversy of the subjectivity of how such data are grouped or presented. It is then possible to say that data could be a source for problem misunderstanding rather than the common belief that the existence of data helps to solve the problem. As mentioned earlier, the process of problem understanding is about what questions to ask rather than what answer to expect. To put it in context, it is about understanding what data to collect rather than having a set of data readily available.

In the case of healthcare, data is a problem in itself. It takes too long, for example, to understand the survival rate of a certain therapy over a span of ten years. Also circumstances are changing continuously. At the end of a period of data collection the whole medical technology may change, which makes the collected data useless. Data is not always reliable. This can be due to errors in recording or it may be collected under unrepeatable conditions. If collected data is sampled then it is not safe from sampling fluctuations and also there is no guarantee that the collection of circumstances under which the data is collected will be the same in normal situations.

These steps are related to problem understanding, yet problem understanding is not just related to the stage of problem definition. Actually the above factors for problem understanding can be considered throughout the process of problem solving. Understanding a problem can be considered as a continuous process along the framework for problem solving. For example in the second step of the problem solving framework, *objectives setting*, it is important to understand the objectives and their suitability to the strategic vision of the organisation. Also stakeholders have to understand the different strategies they consider to follow and the implication of each one on the system. It is noteworthy that during the process of understanding those different stages it is wise to consider the above mentioned factors.

The above discussion presents, in general, the main aspects to consider when trying to understand a certain problem. The main factors are suggested by Lyles (1982). Each of those aspects is briefly discussed and critiqued. The following section reflects upon one of the problems mentioned in Chapter One, that is a typical healthcare system usually has multiple stakeholders. This makes it necessary for stakeholders to communicate their understandings about the particular problem in order to make a joint decision.

### 2.2.4 Communicating Understanding

The previous subsection discusses the process of problem understanding from a single owner perspective. This subsection stresses the importance of communicating such understanding amongst the different stakeholders involved with the problem. In healthcare systems there is more than one party involved in the process of decision making. They may not be opposed all the time. However, ideas may be misunderstood between the different decision makers. The main reason for this is that they usually have different dimensions for looking at the problem. It is possible that all decision makers have a sound understanding of the problem yet they may not conform with each other based on their different understandings. What is required is a tool that establishes the commonality of the different understandings alongside the different steps in the framework. Such a tool may enhance effective two-way communications of the different stockholders amongst each others. Having a great idea is not regarded as such unless it is accepted by all the stakeholders.

The importance of having good communication facilities between the different stakeholders is to clear up all points that may create misunderstanding between them. Usually having such misunderstanding causes the existence of unnecessary problems either throughout the process of decision making or from actions taken based on those decisions. These types of problems might disappear if such misunderstanding is cleared up. It is important to have a good understanding about the problem and good tools to enhance this understanding and communication amongst stakeholders.

To sum up the discussion about problem solving it can be said problem understanding is the most important aspect of problem solving. Problem understanding is in itself divided into two levels; the first level is understanding the problem itself and the consequences of any action taken to solve such a problem. The other level is having a common understanding between stockholders who are involved with the problem to be solved.

The following section presents a discussion about the different modelling techniques used for problem solving and decision making in healthcare systems. The section discusses the abilities of such modelling techniques and methodologies in facilitating problem understanding and communicating this understanding amongst the different stakeholders. It is worth noting that the modelling techniques provided in the following discussion are the ones most used and are by no means all the tools used for decision making in healthcare systems.

## 2.3 Modelling Approaches in Healthcare

The concept of modelling in healthcare systems has been briefly discussed in Chapter One. The main theme of the discussion is about the uses of modelling in healthcare systems and what are the main problems related to this area specifically that may increase the difficulty of the modelling process. On the other hand, Chapter One discusses the general problems of modelling techniques used in healthcare systems and what is required from such techniques to cope with healthcare problems. This chapter reviews those issues in relation to problem understanding and the problem solving framework mentioned in the previous section. The objective of this is to explore ways of using modelling techniques for problem understanding and communication amongst stakeholders.

This section discusses *Markov Modelling*, *Decision Trees*, and *Simulation Modelling*. The discussion concentrates on the relationship between these techniques and the framework discussed in the previous section, rather than the technicalities of such techniques. Discussion about the Markov Modelling and Decision Trees techniques concentrates on their abilities to offer flexible facilities for problem understanding. However, discussion of simulation takes more depth and digs into the different methodologies followed. The following subsections present the existing three main techniques used for healthcare systems modelling.

### 2.3.1 Decision Tree

Decision tree is the simplest of the most commonly used decision modelling techniques (Karnon and Brown, 1998; Roberts, 1992; Dittus and Klein, 1992). The Decision tree technique is mostly used for modelling relatively simple problems. This technique provides a means for structuring problems, and an effective method for combining data from various sources. The Decision tree technique is usually used for modelling entities' flows taking the shape given in Figure 2.1.

A decision tree model is composed of nodes containing estimates of outcome measures connected by probabilistic branches. Creating a standard decision tree involves formulating a decision problem, assigning probabilities and measuring outcomes (Dittus and Klein, 1992). The standard solution to these problems is calculated by "averaging out and folding back", which produces an expected value of a particular decision; the branch with the highest expected value of the outcome variable is the "optimal" choice (Roberts, 1992).

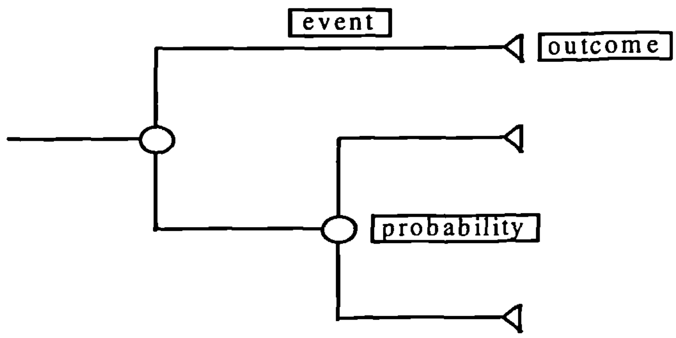



*Figure 2.1: An Example of a Decision Tree Model*

Decision trees are most appropriate for modelling programmes in which the relevant events occur over a short period of time, or evaluations which use an intermediate outcome measure. Antenatal and neonatal screening programmes, for example, are particularly suited to appraisal using decision trees (Karnon and Brown, 1998).

Although this technique is simple and easy to implement, it has a number of problems when applied in heathcare systems modelling. Mainly, this technique cannot explicitly account for the passage of time within the model (Karnon and Brown, 1998). One serious limitation of this technique is modelling complex situations as it becomes quite cumbersome (Roberts, 1992). A major shortcoming of the decision trees technique is the inability to model the variability inherent in a real life system (Dittus and Klein, 1992).

Mapping this technique to the framework of problem solving and factors for problem understanding presented in section 2.2 we find that decision tree helps in quickly identifying the sequences of events in a healthcare system. It provides simplicity in drawing the basic structure of the system and it is understandable to novice observers. On the other hand, we find that this technique is completely inflexible in terms of modelling and experimentation as it only gives a static picture of the aggregated behaviour with no consideration for variation amongst the different entities involved and through time. It is quite useful in identifying relationships of the different pathways, yet it does not provide any information about interrelationships of individual properties that may affect the movement of, for example, patients through the different pathways. We can also see that a decision tree model does not validate any assumptions initiated for building the model, it is actually based on assumptions. Independence of assumptions helps stakeholders to elicit more realistic picture out of the model.

Based on the discussion in section 2.2 data is preferably collected after defining the relevant factors to the problem, however, a typical decision tree model is built based on data collected from previous studies. Apart from the different pathways of the model its behaviour may involve some interdependencies that cannot be explored without data. Being data hungry, this technique does not give stakeholders the chance to explore and understand the problem before conducting data collection. The next subsection discusses the Markov modelling technique which was introduced to overcome the disadvantages of decision trees presented above (Roberts, 1992).

### 2.3.2 Markov Chains (MC) Modelling

Within a Markov chain model, events are modelled as transitions from one health state to another. The time horizon covered by the model is split into cycles of equal length, at the end of each cycle an entity may move to a consequent health state, or remain in the same state (see Figure 2.2). This process of moving between states continues until an entity, for example a patient, enters an absorbing state, such as death (Karnon and Brown, 1998). The length of a cycle is chosen by the analyst so as to represent a clinically meaningful time interval. The occurrences of events are determined by conditional probabilities. As in decision trees the probabilities are conditional upon the last health state visited, although transitional probabilities may be allowed to vary over time (Karnon and Brown, 1998).

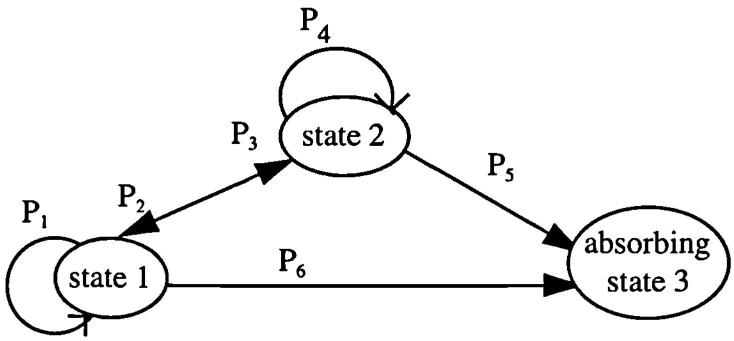



*Figure 2.2: A Standard Markov Process Model*

Considering healthcare systems, Markov chains models are particularly suitable for modelling programmes in which events occur over a long period of time (Karnon and Brown, 1998). Evaluation using this technique is typically carried out by cohort analysis, where the portion of patients in each state is multiplied by the value (probability P) of being in that state. These values are summed over all time periods and states, and produce an expected outcome (utility, survival, etc.) for the cohort who started the model (Roberts, 1992).

Markov modelling techniques appears to provide certain benefits. Unlike the decision trees technique, in Markov modelling patient pathways can be defined in some detail by the specification of health states and the routes between them. The cost-effectiveness of the intervention can easily be tested for different patients cohorts (Hillner and Smith, 1991). Another advantage of this technique is its ability to incorporate time in the model.

This approach, however, is hindered by its strict Markovian assumption that transition probabilities are "path independent". Markov probabilities may vary only by state, and cannot use information about how and when a particular member of the cohort arrived in the state (Roberts, 1992). To overcome this problem a Markov chain can be extended to cohort based analysis or a quasi-Markov process (Astin et al, 1997). This may be more accurate, yet it requires a large number of calculations and in complex situations it becomes quite cumbersome to follow.

Markov chains suffer from the same problems as decision tree when it comes to flexibility and facilitation for problem understanding. For example, a fundamental limitation of Markov processes is that a fixed time period must be chosen for state transition. Patients can only change health states at the end of each time period. The choice of such period is based on assumptions and the balancing between long and short health states. If a relatively short time period had been chosen, then the total number of time periods needed to analyse each cohort of patients would increase, requiring a longer model running time. On the other hand, if a long period is chosen then the model will not be able to detect changes of health states with small durations.

Both the decision trees technique and the Markov modelling technique lack the flexibility that will allow stakeholders to explore different aspects of the problem. Reflecting back to section 2.2 it can be seen that both techniques do not enable analysts to explore different strategies to follow in order to reach the desired objectives. Also it will be quite difficult to examine the impact of different decisions to be made using such models, as they do not offer a realistic picture of the problem. Considering the aspects of understanding, we find that both techniques may be able to identify states relationships but fail to identify any extra factors that may affect entities pathways, especially with their inherent feature of lack of memory. We also find that both techniques rely heavily on simplifying assumptions which may reduce the model validity and on data which may prove to be problematic later.

To support the process of decision making in healthcare systems more effectively, an alternative modelling approach, which does not encompass those characteristics, would be helpful. Such an approach should offer the flexibility to ease problem understanding and the process of problem solving. It should deal with systems at individual as well as aggregate levels, allow patients to experience events at any point of time after the previous event, support the recording and retention of the patient's history throughout the course of the different pathways so that it can be used to influence the pathways through the model, and allow the recording of other information about a patient, such as cost and quality of life effects associated with the events undergone. In summary, a modelling technique is required to follow patients individually as well as in aggregate through the model and decide their next states based on their history and current state. The following subsection will present simulation modelling as an alternative technique to overcome some of the disadvantages faced so far. This technique will also be examined with regard to principles of problem understanding and problem solving.

### 2.3.3 Simulation Modelling

The use of Simulation techniques is now rapidly increasing in healthcare systems modelling (Barnes and Quiason, 1997; Jun et al, 1999). There are a number of types of simulation. In this research, concentration is on Discrete Event Simulation. One of the main reasons that simulation is becoming a popular technique in healthcare problem solving is because it deals with some of the problems faced using *decision trees* and *Markov modelling* techniques. If we put together the main problems of those techniques; inflexibility, lack of versatility, non-economic use of time and resources, we can see that simulation is well suited to cope with these problems.

Technically speaking, we think simulation is able to retain entities' individual properties so that they could be used as decision factors for transferring such entities from one state to another (Law and Kelton, 1991). Events in simulation are not restricted to period boundaries, as events occurrence have autonomous scheduling and they occur as time goes by. This makes it possible to overcome the problem of variable events as opposed to uniform beginnings and endings of events. A very important factor that could be added here is that simulation may be used for dynamic analysis of the situation rather than static analysis. This presents stakeholders with a more realistic picture of the situation (Banks et al, 1996). In terms of flexibility we find both decision trees and Markov chains have assumptions embedded in the model itself. In simulation, assumptions are independent of the model and can be switched on or off at any time or re-scaled in a probabilistic fashion. This is a great advantage that helps users to examine their assumptions rather than be driven by them in building the model and solving the problem.

Simulation offers better features to cope with problem understanding and solving. However, looking back to section 2.2, we find that in practice it is not exploited in the best way to yield greater understanding of the problem. The following section presents in detail the existing approaches to modelling frameworks using the simulation technique with particular reference to tackling healthcare systems problems. These frameworks are evaluated with respect to the different aspects presented in section 2.2 with regard to problem solving.

## 2.4 Simulation Frameworks and Problem Solving

This section goes more into detail about the practised simulation frameworks and their abilities to offer valid means for problem understanding. As mentioned earlier solving an emergency may prove to be only a pain killer for known symptoms of a hidden problem. Understanding the problem enables decision makers to take radical actions for the current problem with a strategic vision. The following subsection presents an overview of the process of simulation modelling based on the theoretical frameworks available in the literature. The subsection after that discusses the practicality of these frameworks with regard to healthcare problem understanding.

### 2.4.1 Overview of the Simulation Process

This research conveys the simulation process as presented by the main authors in this area. Due to the fact that most authors agree on the process flow, it is more convenient that discussion of the process is represented by one framework presenting the different views available in the subject. A typical simulation process can be shown in Figure 2.3 below.

Figure 2.3 is produced from Law and Kelton (1991). Other literature produces similar graphical representations of the simulation process. All steps mentioned in the following discussion are based on Figure 2.3. Law and Kelton (1991) define step 1 *problem formulation* as setting the objectives of the study and the specific issues to be considered. Resources available for such a study should also be considered (Law and Kelton, 1991). Pedgen et al (1990) agree with that and expands on the importance of clarifying the issues to be considered, such as, hardware design issues and operational issues. In addition to that, measure of performances have to be defined before starting the study.

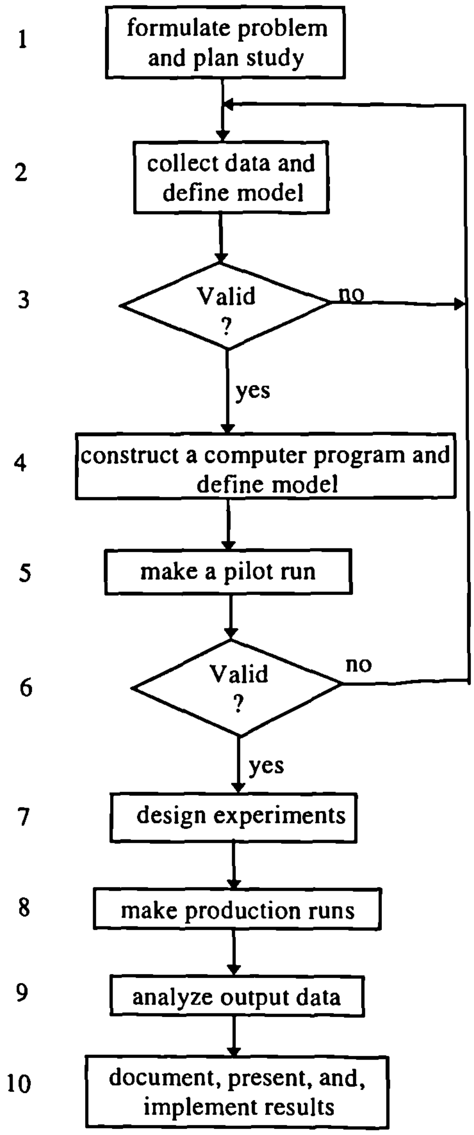



*Figure 2.3: Steps in a Simulation Study (Law and Kelton, 1991)*

Pidd (1998) defines this phase as the *problem structuring* phase. He suggests that this phase is the attempt to take a 'mess' and to extract from it some agreement about the particular problems which might be amenable to analysts. Pidd (1998) adds that this process should not remove all meaning from the 'mess' itself. Other authors, such as

Robinson (1994), Paul and Balmer (1993), Nance (1994), Balci (1994) and Banks et al (1996), divide this step into two or more stages. For example, Paul and Balmer (1993) and Banks et al (1996) tend to distinguish between *problem formulation* and *setting the objectives*.

Whilst Nance (1994) and Balci (1994) divide this step into establishing the *communicated problem*, *formulated problem*, *proposed solution technique*, and *systems and objectives definition*. On the other hand, we find that Robinson (1994) divides this step into five stages; *identify the problem and set the objectives*, *define experimental factors and reports*, *determine the scope and the level of the model*, *collect and analyse the data*, and *provide a project specification*.

The second step in Figure 2.3 is *data collection*. Data is collected if it exists based on the objectives of the study (Law and Kelton, 1991). Most authors, mentioned in the above paragraph, agree with the importance of data collection and stress the validation of such data which is step 3 in Figure 2.3. Robinson (1994) puts the process of data collection at the first phase of his definition of the project phases. On the other hand, Law and Kelton (1991) and Banks et al (1996) suggest that data collection should coincide with developing the conceptual model. Paul and Balmer (1993), however, put *data collection* as a separate step after the *conceptual model*.

After data is validated then step 4 is *constructing a computer model* that is based on the conceptual model. After that a *pilot run* is done in step 5 (Law and Kelton, 1991; Paul and Balmer, 1993). Banks et al (1996), however, suggest translating the *conceptual model* into a *computerised model* before starting step 6 and that is conducting the *verification* and the *validation* steps. It must be noted that most authors agree on the fact that *validation* and *verification* process should be throughout the study. A more thorough discussion about this process of *validation* and *verification* is given by Balci (1997).

Steps 7 through 10 in Figure 2.3 are *design of experiments* for defining the different alternatives for experimentation, *production runs* for providing performance data on systems designs of interest, *output analysis* which consists of statistical techniques for analysing output from production runs, and *implementation* of model's findings (Law and Kelton, 1991). Those finalising steps are also typical of those given by Banks et al (1996), Paul and Balmer (1993), Robinson (1994), and Pidd (1998). It must be noted that all of the above authors agree on two facts. Those are; all frameworks are not necessarily sequential and the first stage, problem formulation, is an art as much as it is science. Basically it depends on available resources, the problem, the problem owners, and involved analysts.

### 2.4.2 Healthcare Overview of the Simulation Process

Reflecting on the above discussion, it can be seen that a simulation modelling process is more or less similar to the framework for problem solving presented in section 2.2. It can be concluded that simulation is a powerful technique for problem solving. However, considering healthcare and problem understanding, this may not be the case. Most of the existing methodologies do not give much attention to the stage of problem formulation/structuring, which is the most important stage for problem understanding. As mentioned above, this stage is implicitly suggested to be outside the boundaries of simulation model development. Even so, it is part of a simulation project. Some agree on the fact that problem structuring is more of an art than science. Looking at healthcare problems and their complexities, the situation is even worse as the model is only used for modelling well defined problems, while problem definition is the main concern in healthcare problems. Despite the fact that simulation is more capable of tackling healthcare problems than *Markov modelling* and *decision trees*, considering the cost and time spent on a simulation project the return value of using simulation as a problem solver is definitely low.

Coming down to the second step in Figure 2.3 and that is *data collection*, we find that the problem mentioned in section 2.2 is even worse when considering healthcare. That is conducting the process of data collection at this early stage on factors which are defined based on art as much as science is a clear danger. On the other hand, and in healthcare systems particularly, data is not reliable enough to be qualified as the driving force of the model. There are two main reasons for healthcare data to be unreliable. Firstly, in the case of predicting long term effects data has to be collected from records that go well back in history. This type of data will not be reliable because of the changes that may occur in medical technology, policies, and socio-economic values. On the other hand, having data collectors in the premises sometimes may spark some anxiety from the professionals to the extent that they may provide less than 100% truthful data.

## 2.5 Research Questions

The main hypothesis of this research which can be elicited from the discussion so far: *simulation could be used more usefully in terms of problem understanding if it is employed in the actual process of problem structuring.* Based on this hypothesis the underlying question for this research is that: could simulation (as a modelling technique) be used differently to enhance problem understanding during the process of decision making in healthcare systems? In other words, the process of modelling could even be started at step 1 in Figure 2.3. The main benefit of simulation is 'understanding' and rethinking our assumptions about the situation. This does not happen after the problem is structured and data is collected to build the model, this 'understanding' is achieved as the problem is being defined. The purpose should be establishing the validity of perceptions of the problem for the stakeholders, as perceptions are rarely what they are thought to be.

Discussion from this point on is going to be built around the question given in the previous paragraph. This question is actually the underlying question of this research, however, it could be quite convenient to put it into perspective by deriving more direct questions that could be tackled from the studies within this research:

- What is the simulation framework (which is the overall activities and tasks towards producing a simulation model such as in Figure 2.3) that should be followed to enhance problem understanding stakeholders' communications?

    This question is related to the possibility of developing a modelling framework that concentrates on providing facilities for stakeholders that enable them to understand the problem and to communicate their understandings amongst each other. May be it is impossible to develop that magic framework which guarantee such requirements, however, this research will tackle this issue by exploring some guidelines that may bring decisions makers closer to the essence of their problems. Some may say that the problem will still be there after we understand it. Yet it is definitely easier to solve a well understood problem than otherwise.

- Who is supposed to understand the problem and how much should be their degree of involvement in the modelling process?

    There is no use if the problem is understood by somebody who is not going to take any decisions to tackle it. It is vital to identify who is the problem owner and whose decision is vital for changing the situation. This research stresses this issue and puts a great deal of consideration on the relationship between identification of problem ownership and problem understanding. This research will look into ways of identifying such relationship via the use of simulation.

- Is simulation better suited for solving complicated problems than other statistical techniques or does it depend on the type of the problem?

  Although this research does not directly tackle comparative issues between simulation and other modelling techniques with regard to problem understanding, the situation in the healthcare decision making process calls for such comparison. The reason is that there are more than one technique applied. However, this question may be resolved in the previous discussion (section 2.3) as it shows that simulation may offer better facilities for achieving such goals.

The first and second questions are initially tackled in Chapter Three. This is undertaken by the attempt to develop a modelling framework that may help in answering these questions. Chapter Four presents the first of two case studies for handling these questions. Chapter Five gives us a chance to look back at these questions and rethink the initial hypothesis used to derive them. It must be noted that this research is attempting to find some answers with regard to the above mentioned questions. However, the expected value of such research is not by finding straightforward answers, rather, the value lies in attempting to explore different ways in employing simulation to the best for problem solving and problem understanding.

## 2.6 Summary

Chapter Two starts with section 2.1, which gives a brief introduction to the settings of the problem. Section 2.1 also presents the chapter objective and that is establishing the case for the research question. That is, whether simulation could be used more efficiently for the process of problem understanding and communication amongst problem owners, when tackling problems related to healthcare systems. Section 2.1 concludes by giving an outline for the whole chapter.

Section 2.2 presents a detailed discussion about problems and problems understanding. The section starts by introducing the concept of "problems" within the context of this research. The section defines "problems" based on the existing literature. Discussion then goes on to the process of problem solving. A general framework for problem solving is given. After that the process of problem understanding is presented. The section examines the importance of problem understanding as an integral part of problem solving. Factors to consider for the purpose of understanding problems are also briefly discussed.

Section 2.3 presents the three most widely used modelling techniques in healthcare systems. Those are: *Decision Trees*, *Markov Chains*, and *Simulation Modelling*. Each one of these techniques is then analysed with regard to their abilities to offer facilities for enabling decision makers in healthcare systems to understand the problem to hand. Simulation modelling is shown to be able to offer more flexibility and versatility in problem solving.

Based on discussions conducted in section 2.3 simulation modelling is analysed in more detail in section 2.4. A general overview of the process of simulation, based on the literature, is presented in this section, see Figure 2.3. The discussion is then focused on an overview of the simulation process in healthcare systems. Attention here is drawn to the fact that heathcare systems may be a little problematic for the use of the framework mentioned in subsection 2.4.1. Section 2.5 lays down the main research questions of this thesis. These questions are derived based on the discussion generated in the previous sections.

# Chapter Three

# 3 Chapter Three: An Alternative Modelling Approach

## 3.1 Introduction

Chapter Two presented a number of problems which are related to the currently applied simulation methodology. The chapter ended by putting a number of research questions in order to explore the use of simulation to enhance problem understanding for stakeholders. This chapter starts by discussing some suggested requirements for modelling to enhance problem understanding in the process of healthcare decision making. The discussion is based on modelling techniques with more emphasis on the simulation process, discussed in the previous chapter. Another aspect discussed is the ability of the existing simulation framework to offer viable facilities to enhance problem understanding. The underlying question is that if the current practice of simulation does not support problem understanding, is it possible to make it able to help in that aspect?

This chapter presents some issues with regard to the use of simulation. Mainly, issues related to the relationship between the theoretical and the practical application of the simulation methodology. The methodology presented in the previous chapter only represents a theoretical structure of the simulation process. There is no indication of the practicality of this methodology. On the other hand, this chapter looks at the use of sequential or iterative/spiral methodology from a Software Engineering point of view. These issues are then used as a basis for proposing an alternative approach to modelling. This approach is mainly concerned with an understanding based on the process of simulation. This approach will regard simulation as a dynamic process rather than a methodology that produces static output. The approach is trying to tackle some of the weaknesses existing with in the traditional method. It does not completely differ from the traditional methods as some of the aspects may be overlapping. The difference is mainly related to the approach to modelling rather than techniques of modelling. It can even be regarded as a complementary approach rather than an alternative one.

### 3.1.1 Objective of the Chapter

The main objective of this chapter is the proposition of a modelling framework that deals with problem understanding and communications amongst stakeholders. The chapter tackles some of the issues related to modelling requirements for problem understanding and the practicality of simulation methodology as a stepping stone towards the proposition of a modelling approach that enhances understanding and also takes into account the practical nature of simulation processes. By the end of this chapter it is hoped to provide a workable version of a modelling approach that can be explored in the following chapter.

### 3.1.2 Outline of the Chapter

This chapter starts with a brief introduction of what it is intending to address in addition to the chapter's objective. The following section presents some requirements for modelling for understanding and revisiting the traditional approach to modelling. Section 3.3 talks about issues related to developing a framework. The section basically discusses the structure and behaviour of the framework. Section 3.4 introduces the basic structure of the proposed framework based on findings from discussion in the previous two sections. Section 3.5 presents an alternative modelling framework to that presented in Chapter Two. The assumption is that this framework is not a substitute for the traditional one, yet it adds more concentration on new aspects related to problem understanding. Section 3.6 gives a corollary to the discussion in the preceding section, whilst section 3.7 gives a summary for the chapter.

## 3.2 Requirements for Modelling and Problem Understanding

Modelling can be thought of as a tool for thinking during the process of decision making (Pidd, 1996). It is known to be one of the most important tools for problem solving either using hard or soft methodologies. In this section we identify the usefulness of employing modelling for the purpose of problem understanding based on the factors mentioned in Chapter Two.

It is important to have a modelling tool that enables stakeholders to identify the nature of the problem to hand. This actually becomes more important when tackling strategic problems or problems where humans and human decisions are considered as integral parts of the overall process. Certainly, at this stage modelling techniques are used to identify the basic structure of the problem (Pidd, 1996). However, the use of modelling may also be employed at the stage of defining the causes and effects integrated in the model. Modelling techniques may identify the flow of information and paths of temporary entities along nodes of permanent entities and other resources. It is very important to establish the dynamics of the system and what are the relevant parts of the problem before indulging in the detailed and precise behaviour of the system and data collection. A form of modelling may be used to identify what are the symptoms and what are the problems. Such a technique could also be used to identify the different interrelationships that may exist in the system. Not just the existence of such interrelationships but also the dynamics related to them and the impact that they may have on the rest of the system as a whole. Instead of having the problem based on assumptions, the use of modelling may also be helpful in testing the validity of the different assumptions made at the beginning and throughout the process. For the purpose of understanding it is very important to identify what data to be collected by using the model, rather than building the model based on data. Data may be the last thing to add to the model, the process of data collection is bitter and time wasting. If the wrong data is collected before identifying the structure of the model then repeating the same process may not be feasible and even catastrophic, especially of that is discovered at later stages of the model. Discussion in Chapter Two argues why data could be a problem in itself.

One important use of modelling here is as a means for communicating understandings amongst different stakeholders. As mentioned in section 2.2 problem understanding can never be considered as valid unless it is accepted by all other parties involved. We think there is an important role for modelling to act as a debating vehicle amongst stakeholders. It enables them to mutually experiment and measure the impact of the different scenarios that are suggested by the different stakeholders.

### 3.2.1 The Simulation Process (Revisited)

Looking back at the discussion about the simulation process in Chapter Two we find that simulation is mainly used for problem solving, even with the outstanding claim that simulation helps to understand the problem. Unfortunately simulation is used to understand the problem in a way that is similar to other statistical techniques which raises the question of the use of simulation. We find that the exact modelling process starts after defining the problem (see Figure 2.3 on page 38). This shows that the model is actually developed after the problem is well defined and understood, which implies that simulation is not actually used for understanding the problem, rather it is used for solving well-defined problems. This means the model is always based on stakeholders' initial understanding with less possibility of examining such understanding. We find that the second step in Figure 2.3 is *data collection* and this is agreed, to some extent, by the main authors in this field. However, the discussion at the beginning of this section and in subsection 2.2.3 suggests that data may not be collected until all the relative factors are known for reasons presented in both discussions. Also as mentioned previously we realised that models should not be built based on data. Data is not reliable and it is changing. In fact the modelling should drive the data not vice versa (Pidd, 1996). This means that if data is an absolute necessity then collection of data should not start until it is known to be so.

One other use of data is to produce plausible output. In most simulation studies output data are usually not analysed (Law and Kelton, 1991), at least not the extent it suggested to be, even though it is widely believed to be important. Yet the reason for that is when people reach a certain level of understanding they actually abandon the model and rely on other less intricate techniques if they find a symptom that needs solving i.e. have understanding. When models are built based on data then they can only produce plausible output given the input data. There is no guarantee that sampled input data will be regenerated in the future, even less so in healthcare systems where change is the ever stable feature for such systems and, as mentioned earlier, humans are part of the process itself.

Understanding the problem in this context is not just about establishing the physical and the logical relationships in the system under study. Understanding the problem is about establishing the right assumptions and perceptions of the system and having these assumptions flexible with the changes of the system. The model should be used as a tool to examine these assumptions and perceptions and rethinking them. The model should also be used as a means for debate to establish a common understanding of the understandings of the other parties involved in the problem to hand.

The above discussion expresses the problems or difficulties associated with the currently practised simulation process for problem understanding. The discussion evolves around the fact that simulation is particularly useful for problem solving, however, the existing frameworks suggests that its ability to enhance problem understanding is less than perfect. The next section addresses some general issues related to developing simulation frameworks. The section also looks at sequential and iterative methodologies from a Software Engineering point of view.

## 3.3 Issues in Developing a Modelling Framework

The previous section addressed the different requirements of a simulation model in order to enhance stakeholders' understanding and intercommunication of their understandings about the given system. These requirements are suggested based on analysis of the traditional approach and issues of problem solving and problem understanding, which are discussed in the previous chapter. Before jumping into developing a framework that may enable the modelling process to cope with such requirements, this section discusses two important aspects, which might be acting as a threshold for developing such a framework. The first aspect deals with the motivating foundation for such a framework with regards to its objectives and its practicality to achieve these objectives. This is related to the main principle behind it, be it the current practice or an ideal, theoretically viable, situation. The second aspect relates to the functional approach of the framework. In this aspect the discussion evolves around sequential and iterative approaches to modelling. It is believed that these two approaches are most used in any sort of analytical or developmental methodologies. In order to develop a viable framework for modelling, it is important to identify the different approaches to do so, in this case sequential or iterative. The following section will identify the basic components and strategies for the proposed framework. These are based on the modelling requirements and the following discussion.

### 3.3.1 Theoretical vs. Practical Modelling

Given the fact that we are intending to establish a framework for modelling, it is important to establish what actually drives such a framework. There are two main issues that should guide this process and those are the objectives of such a framework and the practicality of it. It is obvious that some objectives have to be set for any thing to go ahead. In this particular case the main objective of the intended framework is endowing the process of modelling to enhance the understanding of the stakeholders and their mutual communications.

The intended framework is supposed to promote the understanding of the stakeholders. There is no specific methodology that can guarantee an acceptable level of understanding for the stakeholders. Yet if common sense is applied here, for stakeholders to gain more understanding about the system using the model, they should have confidence and authority over the model. This can only be achieved by two important factors. The first factor is understanding the structure of the model and how to use it, whilst the second factor is being able to use the model to relate to the real system. In this research concentration is upon healthcare decision makers. There is a considerable possibility that they are not familiar with principles of modelling and how to use modelling tools for experimentation. In this case the framework, in building the model, should facilitate the development of tools that are understandable to the users and also relate to the particular problem to hand. One way to achieve that is keeping the stakeholders involved throughout the process of model building. Keeping stakeholders involved also contributes to their perception of the system using the model. Because they are the expert of the real system, so having them continuously contributing to the process of model building will give them more confidence in the validity of the model as a means for better understanding the model.

As for the practicality aspect, it is important to make sure that the framework is useful and applicable in practical and more specifically in complex situations. If we look back to Figure 2.3 we realise that the traditional framework for the simulation process is quite rational and idealistic. A top-down process with all the steps are defined in a logical order. Yet there is no evidence to support the fact that people actually follow these steps. In other words, there is no guarantee that these steps are followed in practical situations. However, there are some reports suggesting that the specified steps of a simulation modelling exercise may not be followed completely or some other steps may be added (Maria, 1997; Lowery, 1998). Bear in mind that the existing methodology is derived from theoretical accounts of problem solving frameworks and not from how simulation is usually conducted. The researcher assumes that for this framework, or any other framework in that matter, to be useful and practical it has to derive its very essence from the existing practice of simulation modelling or whatever fields in which a framework is developed. The opposite extreme of such a stance is to develop the framework based on theoretical ideas known to be effective if they are followed to the letter without paying much attention whether practitioners may follow it or not. This discussion can be concluded by saying that a more useful modelling methodology can be derived based on how actually the modelling process should be conducted based on practical aspects, rather than how it should be conducted based on a logical or theoretical account.

### 3.3.2 Sequential vs. Iterative Approach

The discussion in this subsection evolves around the technicality of the intended framework. The purpose of this discussion is to establish a perception of what type of structure a modelling framework should follow to enhance the process of modelling for understanding. As mentioned earlier, it is assumed for the sake of argument that there are two approaches for developing modelling framework; sequential structure and iterative structure. A sequential approach takes either a top-down or a bottom-up structure. It is based on a sequence of steps arranged in a specific order. An iterative approach is based on specified categories or classes where the process goes in iteration – taking a loop shape – between these categories until certain objectives are realised. For the sequential structure the first step always marks the beginning of the process and the last step marks the end of the process. For the iterative structure the beginning step may or may not be defined, whilst the end of the process is controlled by achieving certain objectives. A sequential process is usually precise and restricting, whilst an iterative process structure is usually open-ended.

From the discussion about the currently applied simulation methodology in Chapter Two, it can be seen that the existing process is a sequential one, see Figure 2.3. This process actually indicates the theoretical structure. There are no studies suggesting that other methodologies are used. However, many studies indicate that in practice the existing methodology may have local iterations between some of the steps specified in Figure 2.3 (Lowery, 1998; Maria, 1997; Banks et al, 1996). Nance (1994) presents a conical methodology which can be described as partly sequential and partly iterative. The conical methodology can be seen as the closest formal simulation modelling methodology to an iterative approach. For more information about the methodology please refer to Nance (1994) and Balci (1994).

Unfortunately there is no direct comparative analysis or research about the suitability of either approaches in the process of simulation. It could be because only the sequential structure is applied in this field. In this subsection, however, some of the literature of Software Engineering methodologies is consulted as it contains some direct comparisons between the two approaches to frameworks. The reason for that is because both approaches are actually used in Software Engineering development cycles (Yeates and Cadle, 1997). This discussion does not cover the specific types of software development methodologies nor tries to identify which is the better of the two for that matter. The main purpose is to try from the Software Engineering comparison to draw an understanding of the appropriateness of each type of approach to modelling, given the issues of problem understanding. The discussion is made of some summary points derived from Pressman (1997), unless otherwise stated, who provides the comparison in terms of the problems associated with each:

*Sequential Methods*

1. Even though it is the oldest most widely adopted paradigm, it is rarely followed in real life. Although the sequential model can accommodate some iteration, it

does so indirectly or unintentionally. As a result, changes can cause confusion as the project proceeds.

2. It is often difficult for the customer to state all their requirements explicitly. This structure depends on explicit requirements and has difficulty accommodating the natural uncertainty that exists at the beginning of many projects.

3. A customer must have patience. A working version of the program(s) will not be available until late in the project time-span. A major blunder, if undetected until the working program is reviewed, can be disastrous.

4. Projects are often delayed unnecessarily. Sometimes team members may be blocked if their corresponding activities are dependent on other which are yet to finish.

*Iterative Methods*

1. The most important software development methodology, which follows iterative mode, is referred to as prototyping model.

2. During the earlier stages, the customer may be deceived by the external structure of the software thinking that it is working without considering the overall software quality.

3. Developers often make implementations compromises in order to get a prototype working quickly. Inappropriate tools may be used to run the prototype only to become integral parts of the product later.

4. A newer version of "prototyping" model called "spiral" model reflects a more realistic revolutionary structure, yet it is usually difficult to convince customers that this revolutionary structure is controllable.

The above summary points, extracted from Pressman (1997), present the problems associated with both methodological structures. This discussion will analyse these points for the purpose of realising the suitability of either approach for modelling for understanding. Starting with the sequential model it can be seen that it does not lend itself to users so easily. It is actually very rarely applied to the letter. This may be based on the fact that things in real life are not as straightforward. Maybe people are able to accommodate changes. However, the methodology always presents a source of confusion if any of these changes is to occur. The sequential methodology implies a specific order of stages. Usually the requirement specification step is the first one. This implies that users have to have a fair idea of what they want beforehand. This means they should have a good understanding of their requirements, which is not always the case. It can be seen that an iterative approach is more appropriate for situations where users do not know their exact requirements (Boehm, 1997). Sequential structure means that the product – any version – can only be delivered at the end of the process. Because of that customers will not see it until it is operational. If it turns out with some flaws, then changing these problems will have disastrous results on both suppliers and customers. The iterative approach may treat this in a better way by providing initial versions – prototypes that are not working versions yet they present how it will work when it is ready – to the customers while development is ongoing. This, however, may have a negative effect, as it is possible that these interim versions may affect the customers' original requirements. It is worth adding that the main problem of the iterative approach is related to handling customers' requirements rather than the process itself, which implies that user handling is what is important rather than technical enhancement of the process.

It can be realised from the above points by Pressman (1997) that the iterative approach is more suitable in situations where the requirements are not well understood. Mapping that to the process of simulation, it could be put as a hypothesis that an iterative way of the modelling process is more appropriate to enhance the understanding of users. However, simulation is not software engineering, and modelling is not solely about model development it also includes model use and experimentations. Yet still there is a close relationship between the two fields when we talk about giving users absolute ownership of the model.

Two issues have been discussed in this section; the reasoning behind establishing a framework in a particular way and the structure of such a framework. From the first issue we realised that a framework should derive its essence from the practicality of the field that it is applied to. On the second issue we realise that an iterative approach can be more appropriate when the modelling objective is to enhance stakeholders' understanding about the problem rather that an answer finder through input–output operations. with all the previous discussion in mind, the following section presents the basic principles for the proposed framework and its components.

## 3.4 The Proposed Framework: Basic Structure and Components

### 3.4.1 Structure

As mentioned earlier that this framework is supposed to enhance stakeholders' understanding. Based on the previous discussion it can be seen that an iterative approach is more reliable in establishing understanding than a sequential one. This is evident in cases where the problem is not well understood and simulation is used as a contributing. A sequential structure for a simulation framework could prove to be useful when the problem is well understood and defined, so the simulation is used as a problem solving tool. As can be seen in Figure 2.3 on page 38 where the problem is defined then the model is based on the sets of data collected based on the initial understanding. In cases where the problem is not understood then the situation may not be as straightforward. A common feature for such is not knowing the basic factors on which concentration should be for data collection. A sequential structure makes it very difficult to model or at least the model is usually not a valid representation of the system. This discussion suggests that the structure followed in this framework is iterative in its behaviour between the stakeholders and the model.

### 3.4.2 Components

Given the considerable focus on enabling stakeholders to gain more understanding about their problem, it is important to cater for that in the framework. The existing modelling framework represents a modelling life cycle and does not indicate any involvement of the stakeholders. If stakeholders are to be involved then there should be, at least, some form of indication of how that can be done. Therefore stakeholders would represent a major wing of the components of the proposed framework.

An iterative approach is usually related to two wings and an iteration process between them. In such a case if one wing is represented by stakeholders, then naturally the other wing is represented by the modelling process. The basic idea can then be seen as an iterative process between stakeholders and the modelling process. The following section describes in detail the basic modelling principles of the proposed framework. The section will be the final stage of composing the framework based on the discussion in the preceding sections

## 3.5 The Proposed Framework: Basic Modelling Principles

The main objective of this approach is to explore ways of using simulation to aid the understanding of problem owners about their systems. As mentioned in the previous chapter, the existing simulation frameworks do not provide the stakeholders with viable facilities that will enable them to understand the system under study. In this exercise we are attempting to use a different framework to tackle the problems mentioned in the previous two chapters. The proposed approach followed in this research reverses or shuffles some of the steps mentioned in the currently practised simulation process (depicted in Figure 2.3). In this approach the overall modelling process represents an active element in the process of problem identification. The basic concept of the underlying approach is that the process is iterative – yet progressive in terms of understanding the problem – between stakeholders and the model. This decision is based on the discussion in the previous sections. We believe that an iterative approach between modellers and stakeholders gives both sides a better and more in-depth vision of the situation. The following section presents details of the concepts behind the proposed framework.

### 3.5.1 The Modelling Process (Overview)

Figure 3.1 demonstrates the basic concept behind the framework. The box identified as "MODELLING" represents the modelling efforts, such as, model building, input facilitation, and output representation. The other box, which is named "STAKEHOLDERS", represents the problem owners or users of the model and the system to be modelled. The arrows from the modelling box to stakeholders represent the information received from the model, that includes insights and understanding of the situation. The reader is reminded that this is meant to be a continuous process. The underlying principle of the proposed modelling approach is based on participatory modelling where stakeholders are involved in the modelling process from the beginning in an iterative manner. For simplicity this approach will be referred to as a Modelling Approach that is Participatory Iterative for Understanding (MAPIU). The main difference between MAPIU and Prototyping for software development is that Prototyping aims to produce a final tangible product, while MAPIU is a process that aim to enhance stakeholders' understanding about their system which is intangible.

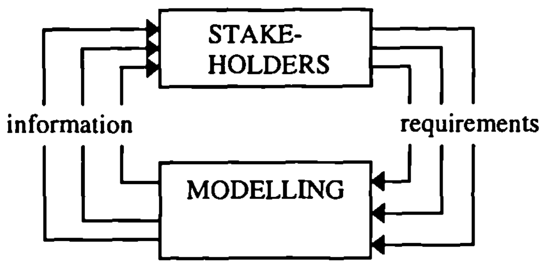



*Figure 3.1: A Modelling Approach that is Particpatory (MAPIU)*

Arrows from the stakeholders to the modelling box represent the validation of the model and refined requirements of stakeholders. These arrows represent feedback to the model. It is possible then to decide whether to build on the current structure or redirect the course of modelling to another structure or objectives. As can be seen from Figure 3.1 the theory is to have mutual feedback between the model and stakeholders.

Considering Figure 3.1 we will now discuss the "MODELLING" box, which may be subdivided into two more boxes, the *conceptual model* and the *computerised model* see Figure 3.2. The conceptual modelling level may be used for identifying the path flows of patients or other temporary entities. This level could also be used for identifying entities' interrelationships. The technique proposed for building the conceptual model is the Activity Cycle Diagram (ACD) (Paul and Balmer, 1993). One of the main reasons for using the ACD technique is its ability to depict the different activities and entities involved in them. This is useful in determining the different cause-and-effect relationships. At this stage the conceptual level is normally used for organising the thoughts of the collaborators, modellers and stakeholders, acting as a threshold for building the computer model. This level used to be more important for giving people involved a visual sense of the logical and physical relationships in the systems. However, with the advance of computer software this type of use is diminishing. Now simulation packages can build and rebuild models easier than the pen-and-paper method. However, it is still advisable to stick to the pen-and-paper method until computer technology starts to become easy for non-computer experts.

After the conceptual model has reached a desired level the next step is the *computerised model*, see Figure 3.2. It is important to remember that the problem is still under construction at this level. The computer model is similar to that mentioned in Figure 2.3. The most important issue to have in mind while building the computer model is to allow the decision makers or the model user(s) to be able to manage the model themselves.

It is assumed that for the model to help users to gain more understanding it is necessary for them to be able to "play" with it. Building the model in this way evolves around three basic factors. Those are the *physical and logical interrelationships*, *input levels*, and *output processing* in addition to *information* exchange between the model and user(s) (see Figure 3.2). This is not a completely new way of thinking in terms of model building, however, the difference between this approach and the framework discussed in Chapter Two is that in the latter these factors are considered part of the problem structuring. The actual model is usually built after they are defined. They may be revisited during model building, yet it is not usually the initial intention to do this. The intention in MAPIU is to use the model to define these aspects as it is being built.

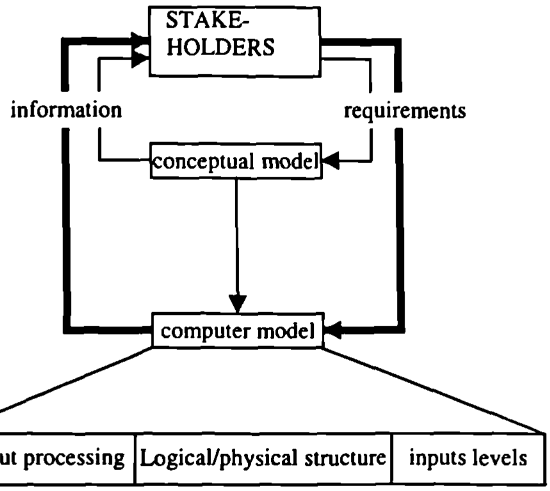



*Figure 3.2: MAPIU: Detailed Modelling Efforts*

### 3.5.2 Modelling Factors

*Physical* and *logical interrelationships* may be determined partly using the ACD. ACD's are generally useful in identifying inter-entities relationships. Yet an ACD model is not quite helpful when it comes to activities conditioned on entities' individual properties, where, for example, the path or the state of the entity is determined by its individual properties, such as history, age, sex etc. It is important to establish a simpler version of the model first before indulging in unnecessary details. The loop shape in Figure 3.2 implies continuous negotiations between the stakeholders and the modellers. Hopefully this decreases the possibility of overcomplicating the model. Feedback from and to the computerised model were purposefully portrayed as thicker than that of the conceptual model in Figure 3.2 to imply the intensity of iterations.

*Input levels*, in this framework, are defined by "what" types of input are required for this particular model. This is done throughout the iterative process of model building. Part of the understanding of the situation is knowing what factors could be experimented with to examine the behaviour of the system. This is supposed to be determined depending on the problem to hand, tools used for modelling, and most importantly, the budget for the simulation project. In the traditional simulation process input variables are usually determined before building the model and that includes their corresponding behaviours, being deterministic or stochastic. One problem with that is it restricts the model building to the selected way of behaviour for those variables. Before that analysts have to go through a data collection process in order to establish the best suitable way of behaviour, which is a thoroughly painful process in its own right. MAPIU assumes that these input levels are defined with non-standardised (empirical) probability distributions. This is helpful in letting the stakeholders experiment with the model given any type of behaviour that might be followed by the input variables. Experimentation here could be based on historical data or any hypothetical situation in order to examine its impact. As long as the internal structure is well modelled then input's behaviour does not influence the validity of the model that much. This supports the argument that data may not be needed at the early stages of model building. It is believed that this way of model building may enable stakeholders to gain more understanding with more flexible experimentation facilities. On the other hand, it reduces the effort spent on data collection and input modelling for deciding which distribution to allocate for each variable, which is usually carried out during model building in the traditional frameworks. What may be required at this stage is to assign the number of all possible classes to represent each variable based on expert opinions. Each class is then given a box for assigning the corresponding probability value.

The probabilities may be based on the basic probability axioms (Hines and Montgomery, 1990). That is, each probability value lies between zero and one, with the sum of all values being "1". For example, each patient has a probability of falling within one of the four age groups – rather than giving a mean and a standard deviation or certain parameters based on a named distribution for age – where these probabilities can be categorised as in Table 3.1.

*Table 3.1: An Example of Input Probability Distribution*

| Probability | value |
|---|---|
| Pr(Age < 40) | $A_1$ |
| Pr(40 <= Age < 50) | $A_2$ |
| Pr(50 <= Age < 60) | $A_3$ |
| Pr(Age >= 60) | $A_4$. |

where $A_1 + A_2 + A_3 + A_4 = 1.00$.

Even though this may seem a simplistic structure for modelling probabilistic behaviour, it is quite flexible and it is not restricted to standard probability distributions. This method is appropriate for cases where there is no known input data or behaviour. It allows users to model input data in any form or shape. The reader is reminded that in asking "what if" questions, stakeholders will be able to examine the system's behaviours not just by changing the values of the defining parameters, but also by changing the entire distribution of the input variable and in an easy yet powerful way.

Establishing the way *output* values are *organised* is more straightforward than that of the input levels. Again, through the iterative approach stakeholders will be able to establish what they need to get out of the model. During the process of modelling users will be able to establish what sort of output they need from the model, at what level of aggregation, and how it should be organised and represented in a way that will add to their understanding about the real system. It must, however, be remembered that the iteration process should be used for identifying the main factors to be encapsulated in the model and the main measures of performances to be extracted from the model. Another important point is that the iterative process is not just restricted to model building as it may also be extended to the model's use as well. There is no defined boundary between the end of model building and model use. The change between the two phases is a gradual process that starts on day one and ends on the last day of the particular simulation project.

*Information* coming out of the modelling box in Figure 3.2 represents the general structure and behaviour of the model on one side, and on the other side it represents feedbacks to stakeholders about their own understanding of the problem. This is actually an ongoing process and starts during model building. Stakeholders, by contributing to the model building are continually examining their perceptions and views about the modelled system. During the running of the model, and by switching on and off or probably re-scaling their assumptions, they will be able to see the system's reaction to different possible situations.

The increased understanding of the stakeholders is translated back to the model in terms of new *requirements* and refined assumptions. Stakeholders also send validation feedback to the model when they sense that the model is not built or behaving within the context of the problem. The validation at this stage is still dependent upon expert opinions. Mainly, validation is concerned with the structure of the model. For example, the set of treatments a patient is more likely to go through represents whether the patient is following the right pattern of care, especially if there are a number of types of patients requiring different types of patterns of care. In this sense validation is to make sure the structure is acceptable by the stakeholders. Up to this level the only data that is incorporated in the model is information about the different levels or possibilities of an occurrence of events.

## 3.6 Corollary

The above discussion presented the theoretical structure of a newly proposed framework for applying simulation to aid the understanding of stakeholders. Looking at Figure 3.2 on page 63 and Figure 2.3 in the previous chapter, one can see that the most important change in the alternative framework is that the "MODELLING" step has been brought forward to be step 1 with respect to the traditional framework. It can also be seen from Figure 3.2 that *data collection* has been removed. One of the disadvantages of the traditional framework is that the model is usually data hungry and data collection is time consuming, given the collected data is the right data (Shannon, 1998). Using the traditional approach, simulation can not compensate for inadequate data (Shannon, 1998). The proposed approach, however, ignores the step of data collection for a while to save the time spent on that, and it can be useful with systems where data can not be collected. We also see that the validation step is infused alongside the model building as it usually happens in practice. It was not wise to regard the validation process as a separate step because it can never be identified with boundaries, that is there no boundary between model building and validation or they classified as separate steps.

The overall conceptual difference between the newly proposed framework to modelling and the traditional one is that the new framework tends to use the model to help stakeholders rethink their perceptions of the system, whilst in the traditional one the model is based on stakeholders' initial perceptions of the system. To explore the proposed approach more realistically and practically a case study is presented in the following chapter. The study describes a typical healthcare system and the problems associated with it. It then goes into more detail about how the model is built based on the framework discussed above.

## 3.7 Summary

This chapter starts by giving a brief introduction of the contents. The main objective of this chapter is to present an alternative modelling framework (MAPIU) to tackle the problems faced in Chapter Two with regard to the traditional modelling approach and problem understanding. Section 3.2 presents some requirements to enable a framework for modelling for the sake of problem understanding. The section revisits the traditional framework and analyses it with the requirements for modelling for understanding. Section 3.3 takes the discussion a step towards establishing a new framework. The section discusses two factors that should be considered before developing the framework. These factors are the deriving principles of the framework and its structure. The driving principles are usually based on either theoretical or practical domains. The discussion concluded that practical approaches might be more suitable as a basis for building the framework. The structure is usually based on either a sequential or an iterative structure. The discussion concluded that an iterative approach is more suitable for such frameworks. Section 3.4 proposes the basic factors that should be encapsulated in the proposed framework, which are based on the findings from the discussion in the previous two sections. That is in terms of behaviour (i.e. iterative in this case) and the components (stakeholders and modelling in this case). Section 3.5 presents in detail the proposed modelling framework. The section discusses the underlying concept of using the framework, which is based on defining the relationship between the modelling effort and the stakeholders. The main aspect of this framework is that it works as a continuous loop between both sides. The section then goes into the technicalities of the modelling side. Steps of the traditional approach are redefined to conform to the underlying process of MAPIU. Section 3.5 ends the discussion about the proposed framework by providing a corollary about the framework.

# Chapter Four

# 4 Chapter Four: ABCSim Case Study

## 4.1 Introduction

To assess the proposed framework, and as this research is concentrating on healthcare decision making, a typical healthcare system is used as a case study. The case study presented in this chapter is about economic evaluation alongside a Randomised Clinical Trial of Adjuvant Breast Cancer treatment. This chapter discusses the aspects which are related to the use of modelling in this case study using the proposed approach to modelling. All of the modelling steps included in this approach to modelling will be mapped to the process of modelling. Findings from this exercise are then going to be analysed in the next chapter for redefining MAPIU where appropriate.

### 4.1.1 Objective of the Chapter

The chapter also examines the proposed framework with the aim of identifying its effectiveness and whether there is a need for modification to enhance the process of problem understanding. By building a model based on MAPIU findings we will then be ready to assess the research questions mentioned in Chapter Two.

### 4.1.2 Outline of the Chapter

This chapter starts by an introduction in section 4.1 describing the main objective of the chapter and its relation to the rest of the chapters. Section 4.2 presents the case study to which the alternative framework is applied. The case presented here is about a Randomised Clinical Trial (RCT) related to Adjuvant Breast Cancer. Section 4.3 presents a brief description of the application of economic evaluation techniques alongside the RCTs. The section also goes into the need for modelling for the purpose of economic evaluation. Section 4.4 presents the process by which the model is built based on the proposed framework presented in the previous chapter. Section 4.5 presents the details of the model in terms of inputs, outputs, verification, and validation. Section 4.6 concentrates on the use of the model in order to see how this model is used to achieve the stated objectives. An example of use is also given in this section. The last section also gives a summary of the chapter.

## 4.2 Adjuvant Breast Cancer (ABC)

This case study talks about a Randomised Clinical Trial (RCT) where the particular concern is the economic evaluation of the Adjuvant Breast Cancer (ABC) treatment. The problem owners (or stakeholders of the problem) are health economists, who are interested in the economic assessment of the treatments, and clinicians, who are experts in the way that the treatments are followed and the different possible side effects and relapses that may occur. The trial structure may be thought of as a representative of a typical healthcare system in terms of its complexity and the large number of variables that are included. This also includes the problems associated with healthcare systems mentioned in Chapter One. The remainder of this section gives a detailed description of the Adjuvant Breast Cancer therapy, the trial itself, and the economic evaluation alongside the trial. The discussion also includes reasoning for the use of a modelling technique to support decision making for economic evaluation during the RCT.

### 4.2.1 Background of the Adjuvant Therapies

Following local treatment for early breast cancer by surgery and/or radiotherapy to the breast and/or axilla, there still exists a risk of micrometastatic disease present in distant areas which can cause systemic relapse. The purpose of the adjuvant therapy is to destroy this micrometastatic disease. Two types of adjuvant therapy may be used with early breast cancer: adjuvant chemotherapy, which involves a cocktail of cytotoxic 'anticancer' drugs, for example, cyclophosphamide, methrotrexate, and fluorouracil (CMF). The second type is adjuvant endocrine therapy, which deprives cancer cells of oestrogen, which in turn inhibits the growth of cancer cells. Endocrine therapy may be in the form an antioestrogen drug, such as tamoxifen which competes with endogenous oestrogens by binding onto oestrogen receptors, or ovarian suppression, where ovarian production of oestrogen is inhibited. The latter may be done either by surgical removal of the ovaries, radiation of the ovaries or the use of luteinising hormone-releasing hormone (LHRH) agonists. LHRH agonists are often the choice in women of reproductive age since the effect is reversible.

### 4.2.2 The ABC Trial Structure

The UK Co-ordinating Committee on Cancer Research (UKCCCR) Adjuvant Breast Cancer (ABC) Trial was launched in 1993 following the publication of the Early Breast Cancer Trialists' Collaborative Group overview (ABC Trial Protocol, 1993). The overview showed that adjuvant chemotherapy and ovarian suppression prolonged survival in pre/perimenopausal women (Early Breast Cancer Trialists' Collaborative Group, 1992). Tamoxifen was also shown to significantly improve disease free survival, with a significant trend of greater benefit with longer tamoxifen treatment. The overview suggested tamoxifen alone may well be as effective, for pre/perimenopausal women, as chemotherapy or ovarian suppression. Given that tamoxifen is less toxic than either chemotherapy or ovarian suppression, all pre/perimenopausal women in the ABC trial are being given prolonged tamoxifen. What is still unclear is whether the benefits of chemotherapy and/or ovarian suppression are additive. In post menopausal women the benefits of adjuvant tamoxifen are well established. The overview showed that the addition of chemotherapy to tamoxifen leads to a highly significant relapse-free survival gain. What is unclear, is the size of any survival benefit and whether it is large enough to outweigh the disadvantages of chemotherapy in terms of toxicity and quality of life. Hence the ABC Trial was set up to determine:

i) the value of adding cytotoxic chemotherapy and/or ovarian suppression to prolonged adjuvant tamoxifen in order to treat pre/perimenopausal women with early breast cancer and

ii) the value of adding cytotoxic chemotherapy to prolonged adjuvant tamoxifen in order to treat postmenopausal women with early breast cancer.

The trial provides various randomisation options for pre/perimenopausal women. A woman whose treatment plan is tamoxifen and ovarian suppression may be randomised as to whether she is to receive chemotherapy. A woman whose treatment plan is tamoxifen and chemotherapy may be randomised as to whether she is to have ovarian suppression. A woman whose treatment plan is tamoxifen may be randomised as to whether she is to receive chemotherapy and/or randomised as to whether she is to have ovarian suppression. The randomisation set of options most appropriate for the individual is chosen. Postmenopausal women treated with tamoxifen may be randomised as to whether they are to receive chemotherapy. The randomisation options are summarised in Table 4.1.

*Table 4.1: The Randomisation Options for the ABC Trial*

| | Treatment plan | Randomisation |
|---|---|---|
| Pre/perimenopausal women: | Tamoxifen+OS | CT |
| | Tamoxifen+CT | OS |
| | Tamoxifen | CT and OS |
| Postmenopausal women: | Tamoxifen | CT |

Key: OS = ovarian suppression; CT = chemotherapy

For the ABC trial, the recommended chemotherapy schedule is six cycles of CMF at 28 day intervals. Ovarian suppression may be by radiation, surgical oophorectomy (removal of one or both ovaries) or LHRH agonists.

A total of 2000 pre/perimenopausal women are being randomised as to whether they receive chemotherapy and 2000 as to whether they have ovarian suppression. In addition 2000 post menopausal women are to be randomised as to whether they receive chemotherapy. The clinical end-points of the trial are overall and relapse-free survival, initially at 5 years, but the intention is to seek further funding for a longer follow-up. Economic evaluation and quality of life studies are being conducted alongside the clinical trial. Comparisons are to be made in terms of the clinical end-points for the groups shown in Table 4.2. In Table 4.2 where it says *given* means the particular type of treatment is taken by this arm either prescribed by clinician or as a result of randomisation. Whilst *not given* means the treat was not prescribed or not randomised for the particular arm

*Table 4.2: Comparison for the Clinical End-Points*

| | | |
|---|---|---|
| Pre/perimenopausal women: | | |
| 1 | Randomised to +OS, regardless of whether they have CT | Randomised to -OS, regardless of whether they have CT |
| 2 | Randomised to +CT, regardless of whether they have OS | Randomised to -CT, regardless of whether they have OS |
| 3 | Tamoxifen+CT(given)<br>+OS(randomised) | Tamoxifen+CT(given)<br>-OS(randomised) |
| 4 | Tamoxifen -CT(not given)<br>+OS(randomised) | Tamoxifen-CT(not given)<br>-OS(randomised) |
| 5 | Tamoxifen+OS(given)<br>+CT(randomised) | Tamoxifen+OS (given)<br>-CT(randomised) |
| 6 | Tamoxifen-OS(not given)<br>+CT(randomised) | Tamoxifen-OS (not given)<br>-CT(randomised) |
| Postmenopausal women: | | |
| 7 | Tamoxifen+CT(randomised) | Tamoxifen-CT(randomised) |

The main comparisons for pre/perimenopausal women will be all those women randomised to ovarian suppression with those women randomised not to have ovarian suppression, regardless of whether they have had chemotherapy or not. Also, to compare all those women randomised to chemotherapy with those women randomised not to receive chemotherapy, regardless of whether they have had ovarian suppression or not. For postmenopausal women, the comparison will be between those randomised to receive chemotherapy and those randomised not to receive chemotherapy.

## 4.3 The Economic Evaluation alongside the ABC Trial

Economic evaluation is concerned with the systematic comparison of alternative treatment options in terms of their resource consequences (costs) and non-resource use consequences (effectiveness) ratios (Drummond et al, 1997; Russel et al, 1996; Weinstein et al, 1996). It is the difference in costs and effects between the options which are of interest. On the basis of differential costs and effects, an option can be said to be cost-effective if:

i) it costs less and is at least as effective on all dimensions of effectiveness,

ii) it costs the same but is more effective on at least one dimension of effectiveness and no worse on any other,

iii) it costs more than its comparators but delivers overall greater effectiveness, and this is worth the extra cost.

The addition of chemotherapy or ovarian suppression to tamoxifen will increase the overall cost of treatment for early breast cancer. Additional resources are not only incurred in administering the adjuvant therapies, but in the management of possible side-effects resulting from these therapies. The adverse effects of ovarian suppression are menopausal symptoms (ABC Trial Protocol, 1993; Daly et al, 1993). Similarly, early menopausal symptoms can also be an adverse side effect of chemotherapy for pre-menopausal women (Early Breast Cancer Trialists' Collaborative Group, 1992; Bines et al, 1996). Other possible adverse effects of chemotherapy include nausea, vomiting, deep vein thrombosis, thrombolitic events, and neutropenic sepsis (Love et al, 1989). The additional costs incurred, as a result of administering the adjuvant therapies, may be offset by the resource savings associated with a reduction in the number of relapses.

Since survival is the main end-point of the ABC trial, it makes sense that the effectiveness measure for the economic evaluation is life years gained. The adverse effects of the adjuvant therapies obviously have an effect on a patient's quality of life, however, and need to be weighed against any survival advantages associated with the additional adjuvant therapies. Some of the disease specific quality of life measures are being used in the trial and are useful for detailed information on the quality of life dimensions. They are not so helpful, however, when determining whether one treatment is overall more effective than the alternative treatment. For example, in cases where individuals feel better on one dimension of the quality of life measure, such as feeling tired, but worse on another, such as pain. Nor are these types of measures able to make trade-offs between quality and quantity of life. This requires a single uni-dimensional measure of effectiveness which combines and values the various dimensions. The economic evaluation for the ABC trial is thus also intending to measure effectiveness in terms of quality adjusted life years gained (QALYs).

QALYs incorporate both the programme's impact on survival as well as health related quality of life. The quality of life associated with a health state is measured on a scale of zero to one, where death is assigned a value of zero and full health assigned a value of one. A number of techniques exist to elicit such utility values for specific health states. These techniques include the visual analogue scale, time trade-off and standard gamble (Drummond et al, 1997). The duration of each health state is then weighted or multiplied by its utility value. Where a series of health states is experienced, the weighted durations are summed to give the quality adjusted life years.

The results of the economic evaluation for the ABC trial are to be expressed in terms of the difference in costs, the difference in life years, and difference in QALYs for the comparison groups shown in Table 4.2. Where appropriate the additional cost per additional life year gained (cost-effectiveness ratio) and the additional cost per QALY gained (cost-utility ratio) will be estimated.

### 4.3.1 The Need for Modelling

Given the pragmatic nature of the ABC trial, it was felt that data collection for the economic evaluation should be kept to a minimum, in order to overcome the practical difficulties experienced by others in trying to assess at the outset of a trial those data which might be important. The example of others was followed in the phasing of the economic evaluation (Drummond and Stoddart, 1983; Sculpher et al, 1997). The first phase of the evaluation was to conduct a modelling exercise using existing data and 'expert opinion', prior to any primary data collection, in order to determine the key parameters influencing the cost-effectiveness of adjuvant therapies for early breast cancer. Further data collection could then be concentrated on those key parameters, thus ensuring data collection during the trial was kept to a minimum.

## 4.4 The ABCSim Model

The basic objective behind the modelling exercise was to produce a simulation model that enables the health economists to understand the ABC RCT and establish the major variables that might affect the behaviour of the cost-effectiveness of the adjuvant therapy. In this case and based on discussion in section 3.2, the model aims to provide facilities for flexible input alteration which enables stakeholders to 'play' with the model in order to establish the patterns of the different outputs. Another use of the model is as a medium of communication between health economists and clinicians. This means that the model had to be built in a way that is easy to understand by both parties.

Given the complicated nature of the trial with so many randomisation options, treatment options, side-effects, and relapses, this approach provides a mechanism for participants to run a range of 'what if' scenarios. This allows the effect of many different assumptions – such as ways in which treatment is delivered, the age of the patients, and the effect of varying the values assigned to the costs and utilities – to be tested. These features would have been difficult to implement in other modelling techniques such as *Decision Trees* for their lack of fallibility in accommodating such features (see Chapter Two). This section presents in detail ABCSim which is the model built to simulate the ABC trial behaviour and achieve its objectives.

### 4.4.1 Key Issues in Building the Simulation Model

According to MAPIU to meet the factor mentioned in section 3.2 the model building process is divided into two phases. The first phase was building the *conceptual model* (ACD) for the ABCSim trial. The second phase was building the *computer model.* For the second phase, and to conform to the objectives of facilitation understanding amongst users, the model is split into two distinct parts: the simulation engine and the user interface. The role of the simulation engine is to represent the model's structure and behaviour in terms of treatment durations, patient routing, and clock setting. The interface is used as the input/output facility for the health economists. There are many aspects to the interface. Firstly, the look and feel of the interface to the model are based on the stakeholders' requirements – this helps ensure that they are able to 'play' with the model. That is, the interface ensures that the model is accessible to them, overcoming the problems that non-experts often find in using and making sense of simulation packages. In this case, the user interface was seen as a medium through which they could communicate with the model.

The interface also had to be built to accommodate all the input factors and output responses that may be important in the ABC RCT. The interface had to offer the users enough flexibility to modify the values associated with variables in the model. Since an aim of the model was to identify the important variables prior to data collection, there were no specific values or standard probability distributions for the model's variables at the start of the modelling exercise. We can think of the model's parameters as being divided into two main classes: parameters with discrete values such as treatment costs; or those with probabilities such as different types of menopausal symptoms. Dealing with the first class of variables was straightforward; all that had to be done was to identify the parameters and provide variables in the model to hold their corresponding values. The stochastic parameters were modelled using the MAPIU non-standardised input probability distribution discussed in section 3.5.2 in Chapter Three.

### 4.4.2 The Conceptual Model (ACD)

The conceptual modelling technique used to capture the system behaviour was an ACD, although there is no restriction on what type of technique to use for the conceptual model (Taylor et al, 1998). The process of building the ACD in this case was performed by regular meetings between simulationists and the health economists. The process was iterative as proposed in Figure 3.1 on page 61. The final version reached was number 9 in a period of three months.

The basic structure of the economic factors was captured in terms of treatment pathways and health states. The model was divided into two phases; the treatment phase and the recurrence phase (post-treatment phase). Figure 4.1 represents the ACD of the treatment phase, whilst Figure 4.2 represents the ACD of the post-treatment phase. Generally, boxes in an ACD denote activities with pre-specified durations, whilst circles denote queues or idle states (Paul and Balmer, 1993).

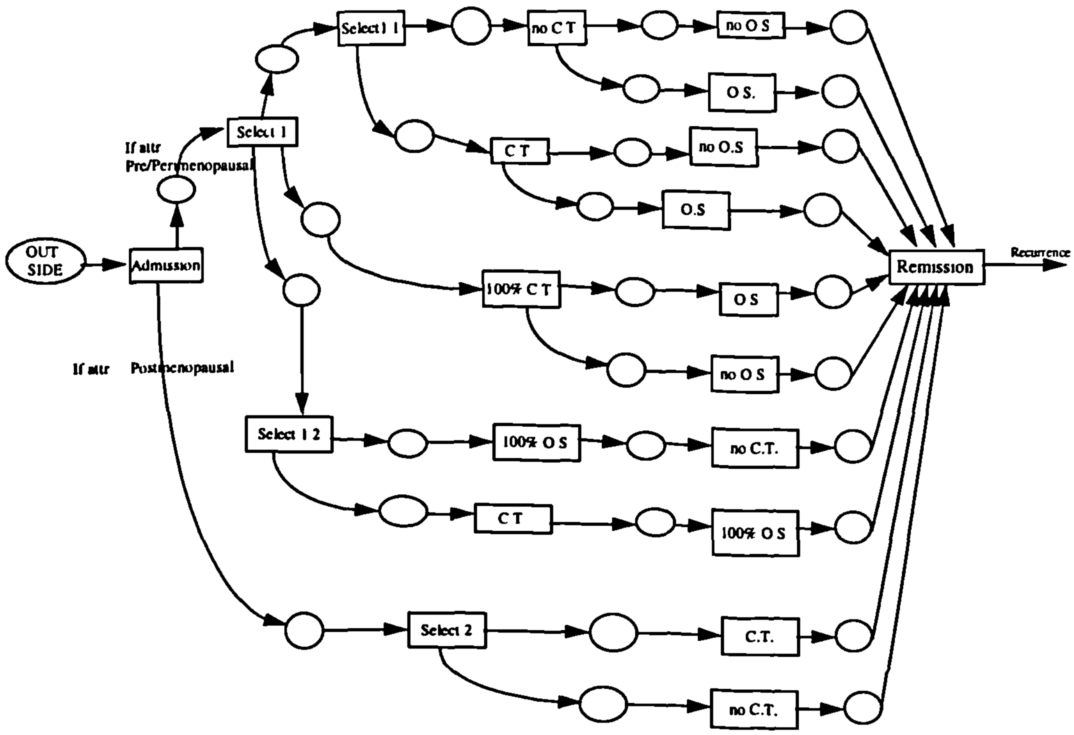



*Figure 4.1: ACD of the ABC Trial – Treatment Phase*

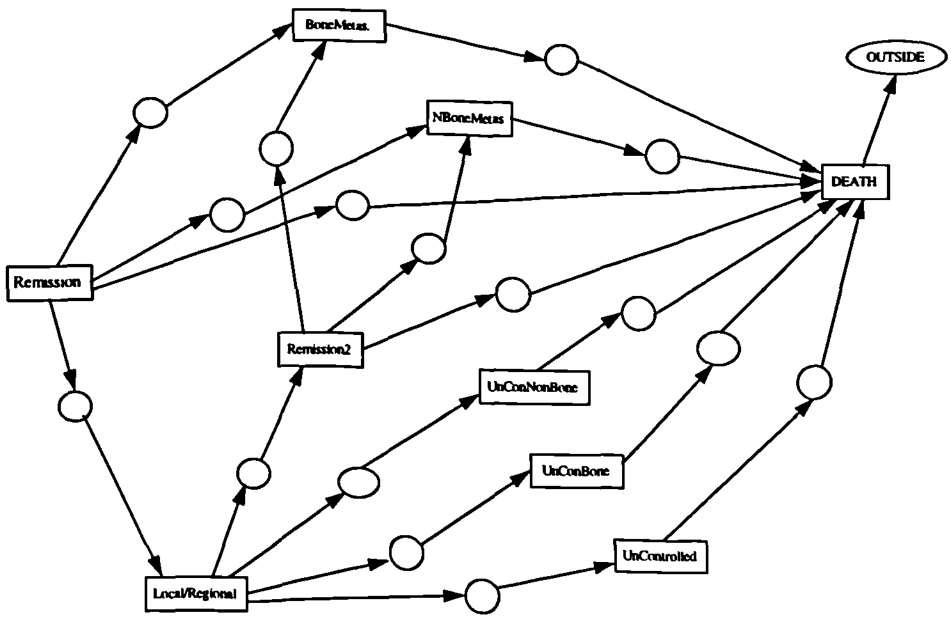



*Figure 4.2: ACD of the ABC Trial – Post-Treatment Phase*

The events modelled using the ACD were the administration of the adjuvant therapies (chemotherapy and ovarian suppression) in addition to tamoxifen which is common in all treatments. After the administration of the adjuvant therapy the patient could remain in remission until death or relapse. Relapse was modelled as local/regional recurrence, non-bone metastases and bone metastases. Non-bone and bone metastases are followed by death. The division between non-bone and bone metastases was based on prognosis and intensity of resource use. Local regional recurrence may be operable and followed by a second remission, or may become an uncontrolled local/regional recurrence, uncontrolled non-bone or uncontrolled bone metastases which are followed by death. After entering a second remission, after operable local/regional recurrence, the patient could stay at this state until death or develop non-bone or bone metastases. The event pathways were drawn up using specialist help from clinical oncologists involved in the ABC RCT.

### 4.4.3 The Computer Model

After reaching an acceptable ACD model, this model was then translated into a computerised one. The computerised model was built in Simul8, a commercially available simulation package, in close collaboration with the health economists. Figure 4.3 represents the Simul8 layout of the treatment phase, whilst Figure 4.4 represents the Simul8 layout of the post-treatment phase.

The programming tool Visual Basic was used to build an interface (ABCSim) between Simul8 and the users (health economists). ABCSim provided the facilities for inputting data and to display the model's outputs, to export the output to spreadsheets for further analysis, and to save the different model configurations for comparison and analysis. Figure 4.5 shows the main page for the ABCSim model.

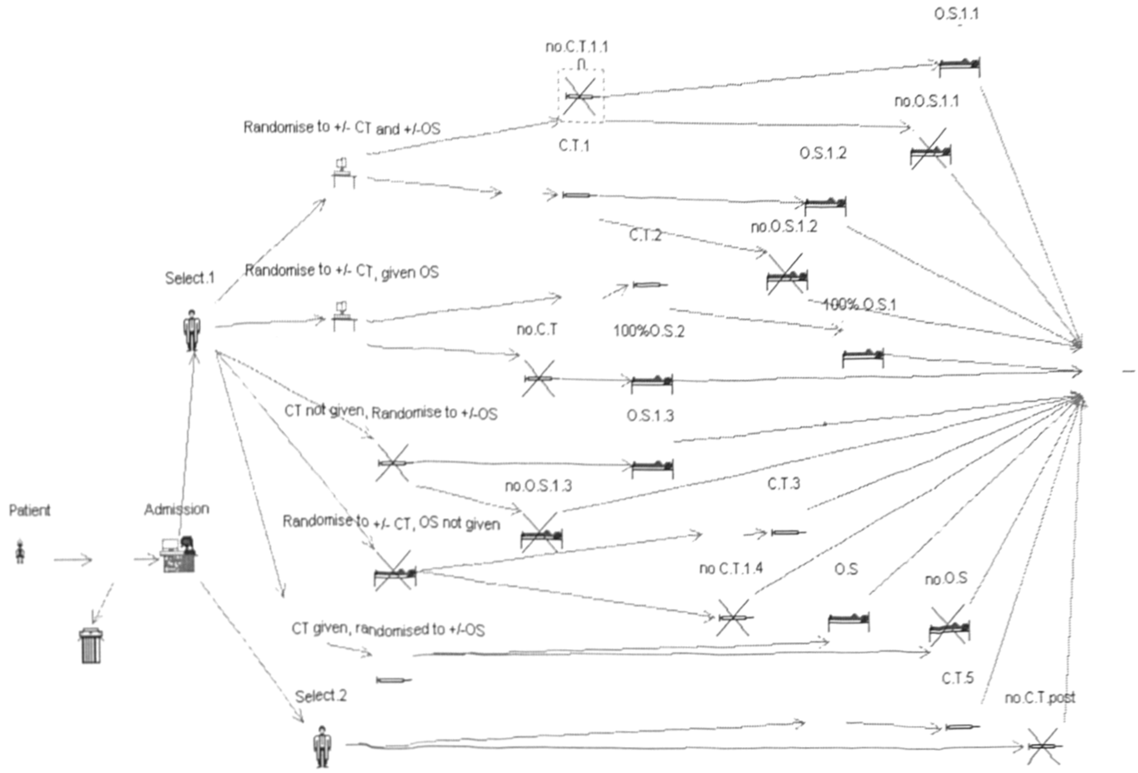



*Figure 4.3: A Simul8 Visual Representation of the Treatment Phase*

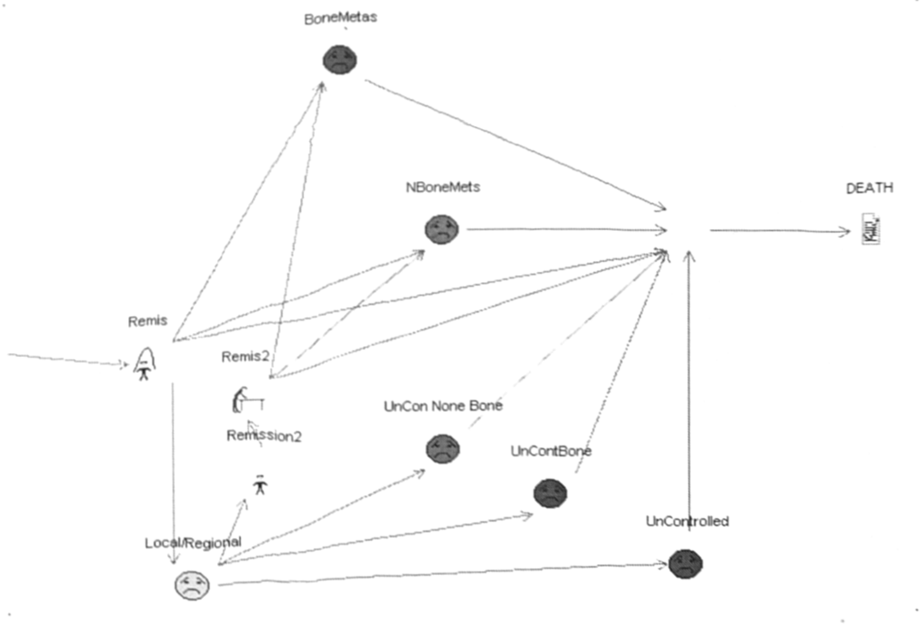



*Figure 4.4: A Simul8 Visual Representation of the Recurrence Phase of the Model*

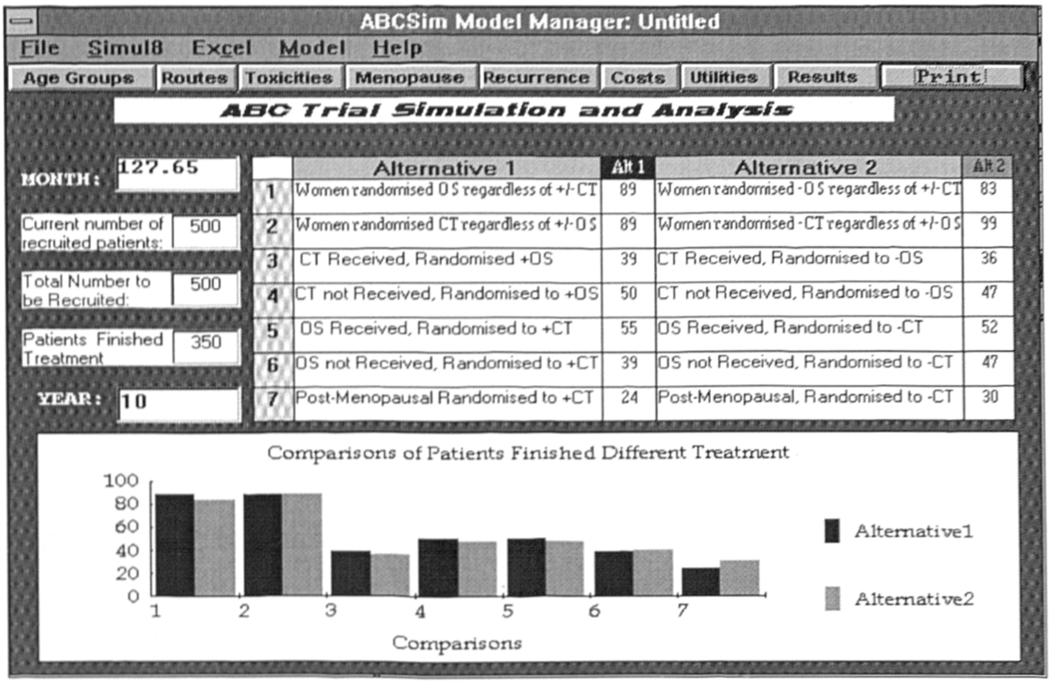



*Figure 4.5: ABCSim Main Console*

## 4.5 The Model's Details

The previous section presented the main aspects and steps for building the ABCSim model. This section, provides all the details that went into building the model. Details of the model are divided into four categories; inputs to the model, output presentation, and the processes of verification and validation.

### 4.5.1 Inputs to the Model

As discussed in the previous chapter, the basic idea behind the inputs of ABCSim is to define unspecified distributions for the input variables. The purpose behind that is to give users of the model more flexibility to experiment with the model. That is not just by changing the values of the variables but also changing the entire mode of behaviour of such variables by altering their corresponding probability distributions. Most of these inputs are assigned for each individual patient as attributes. This is one of the advantages of using simulation as patients are allowed to have attributes and carry them as they move through the model's pathways. It is possible then, using these attributes, to decide a patient's destination based on their prior health states and the treatment they had received before reaching this point. On the other hand, this information could be presented individually or aggregated at the end of the model to produce the desired output.

Table 4.3 shows all the input variables associated with the ABCSim model, the discussion after that gives more details about these variables. Variables such as "Age" are presented as probability distribution of age groups. Some other probabilistic variables such as "Second Remission" were presented as one probability value. In the latter case it means either the patient has second remission or not and the one value gives the probability of having it. In Table 4.3 if a range of variables are given then this is a probability distribution, if one variable is given, then only one probability value is given.

The age at which a patient is diagnosed as having breast cancer is important as it influences the adjuvant therapy that she will receive, the probability of therapy induced menopausal symptoms, and the maximum number of future years of life. Age levels in this model are given as; 20 to 39, 40 to 49, 50 to 59, and 60 and over. The maximum age is 75 yet the model has facilities to increase or decrease this value

The menopausal side effects were modelled as none, mild, moderate, or severe. The modelling of menopausal symptoms as a side effect of adjuvant therapy was complicated by the fact that use of tamoxifen alone can also induce early menopause (Canney and Hatton, 1994). Menopausal effects associated with tamoxifen alone were thus modelled so that the net effects due to the adjuvant ovarian suppression and/or chemotherapy could be estimated.

*Table 4.3: Input Variables Associated with ABCSim*

**Age**

4 groups: (20 – 39, 40 – 49, 50 – 59, 60 or over)

**Cost Variables**

Administering the adjuvant therapy (ovarian suppression, chemotherapy)
Treating the toxicity side effects (mild, moderate, non-fatal major)
Treating the menopausal symptoms (mild, moderate, severe)
Treating the relapses (local/regional recurrence, non-bone metastasis, bone metastasis, uncontrolled local/regional recurrence, uncontrolled non-bone metastasis, uncontrolled bone metastasis)

**Durations Variables**

Toxicity
Menopausal symptoms
Relapses
First and second remissions

**Effectiveness Variables**

Probability distribution of:

Permanent and temporary induced menopause
Menopausal effects (mild, moderate, severe)
Toxicity effects (mild, moderate, non-fatal)

Relapses

Second remission
Duration of remissions
Effect of toxicity on the number of chemotherapy cycles

Utility values associated with:

Menopausal effects occurring during:
*Administering the adjuvant therapy*
*First remission*
*Relapses*
*Second remission*

Toxicity effects occurring during
*Administering the adjuvant therapy*
*First remission*
*Relapses*
*Second remission*

Menopausal and toxicity effects occurring during
*Administering the adjuvant therapy*
*First remission*
*Relapses*
*Second remission*

Administering the adjuvant therapy and no menopausal nor toxicity effects
First remission and no menopausal nor toxicity effects
Relapses and no menopausal nor toxicity effects
Second remission and no menopausal nor toxicity effects

**Discount rate:**

value showing the discount rate per one year

The model assumed that all women naturally have a permanent cessation of menses once they reached the age of 50. However, before the age of 50 induced menopause resulting from the use of LHRH agonists is temporary. A proportion of women following the use of chemotherapy or tamoxifen may also experience temporary menopausal effects. The toxicity side effects were modelled as none, mild, moderate, or non-fatal major, each assignment depending on the corresponding complications. Chemotherapy itself is based on sets of six month treatments, each comprised of six monthly treatment cycles. The model allowed for the number of chemotherapy cycles completed to be affected by the toxicity side effects. Probability distributions are also required for the permanent and temporary induced menopause, menopausal and toxicity effects, the relapses and second remission. Probability distributions are required for the duration of remissions as well information on the duration of menopausal and toxicity symptoms, and relapses.

Cost attributes were assigned to administering the ovarian suppression and each cycle of chemotherapy. A monthly cost was assigned to the mild, moderate and non-fatal major toxicity effects and to the mild, moderate and severe menopausal symptoms. A fixed cost was assigned to local/regional recurrence, regardless of its duration, and monthly costs to the treatment of the non-bone metastases, bone metastases and uncontrolled local/regional recurrence, uncontrolled non-bone and uncontrolled bone metastases.

The model assigned separate utility values to the mild, moderate and non-fatal major toxicities plus the mild, moderate and severe menopausal effects and combinations of toxicity and menopausal effects, all of which could be experienced whilst administering the adjuvant therapy and subsequently during the events of remission and relapse. A separate utility value was also assigned to the events of administering the treatment, and each of the remissions and relapses without any toxicity nor menopausal effects.

Information is also required on the discount rate. Individuals and societies as a whole exhibit a degree of 'positive time preference'. That is, they are not indifferent as to when costs or benefits arise. Individuals and societies prefer to postpone costs. Incurring costs now forgoes the opportunity to invest those resources in other benefit producing activities. This is allowed for in economic evaluation by discounting future cost to estimate their present value. The rate of discount will vary between societies and over time. In 1997 for example, the UK Treasury recommended a rate of 6% per annum for discounting the cost of public sector projects (HM Treasury, 1997). What is less clear is the degree of time preference that relates to benefits measured, for example, in terms of life years or QALYs gained.

### 4.5.2 The Model's Outputs

The model estimates, for each of the options, the average cost, average life years and average QALYs. Then for each comparison shown in Table 4.2 it estimates the difference in cost, life years and QALYs, undiscounted and discounted. Where appropriate the additional cost per life year gained and additional cost per QALY gained, undiscounted and discounted, is presented. Table 4.4 gives summary of the model's output categories to be derived from the model.

In Table 4.4 the first three categories represent average results from all of the 14 arms included in Table 4.2 on page 75. The average differences are actually derived for each comparison pair in Table 4.2. For example, the average cost difference for 'pair 1' indicates the average cost/patient for arm 1 minus the average cost/patient for arm 2, and so on. That means the average differences are dealing with seven pairs. The cost-utility ratio and cost effectiveness are also calculated for the comparison arms. Cost-utility ratio is equal to the net cost for one arm divided by the net QALY's for the same arm. The same principles apply for the cost-effectiveness ratio, it is the net life years gained rather than the net QALY's. It must be noted that these values could be positive or negative.

*Table 4.4: Results Categories derived from the Model*

| |
|---|
| Average cost/patient |
| Average QALY/patient |
| Average life years gained/patient |
| Average cost difference |
| Average QALY difference |
| Average life years gained difference |
| Cost-utility ratio |
| Cost-effectiveness ration |
| Discounted results |
| 10 years cut-off results |

'Discounted results' is an option to give the results mentioned above discounted from the beginning of the trial until the death of the last patient. '10 years cut-off results' is another option that allows results to be collected for a period of 10 years after the beginning of the trial. The reason for that is for assessment purposes, because most of the available data in the literatures is taken from studies over a span of 10 years. These two options can be activated separately or simultaneously.

### 4.5.3 Verification of the Model

The purpose of verification is to make sure that the model is running as it is supposed to be or as is expected (Paul and Balmer, 1993). In this study, the model was verified collectively and individually in terms of the variables, and throughout the process of modelling. Collective verification was performed by running the model with values for which there are logical expected results which can easily be estimated without the computerised model. The results produced by the model are then compared to those that are expected. For the individual verification, the technique followed was to set a deterministic value to the variable of interest while resetting other unrelated variables to zero. For example, to verify the average cost for certain patients they were given constant cost values. If the average value is equal to the particular cost value then that cost variable is verified otherwise the model was revised before repeating the verification.

### 4.5.4 Validation of the Model

The purpose of validation is to make sure that the developed model is the right model bearing in mind the objectives of modelling (Paul and Balmer, 1993; Balci, 1997). Given the purpose of this particular modelling exercise and the fact that the modelled system is a non-existent sampling process, the validation process concentrated on the structure and behaviour of the model rather than on producing estimated values. For example, it was not feasible to estimate the exact probabilities for which type of recurrence would occur after remission. The validation of the structure is based on making sure that the pathways are the correct representation of the trial. Acceptance of the validity of the model is mainly involved with the stakeholders. Owing to the wide-ranging discussions and consultations that took place with the stakeholders during the formative stages of the project, the structural validity was considered high. As discussed earlier the model is built and validated based on the opinions of expert who are involved in the trial, either health economists or clinicians. Information was supplemented by expert opinion to identify crude estimates of the overall expected effectiveness and costs of the different treatment options. This was used to validate the model's behaviour. The validation process in itself was a continuous one throughout the model building phase conforming to the suggestions of the proposed framework to modelling.

Given the large number of interactions in the model based on the different factors that may affect any individual patient at a particular health state, it was necessary to validate these interactions. For example, a patient may experience some side effects from a previous treatment while undergoing a new treatment with similar side effects, such as menopausal symptoms. It was important in cases like this to identify the effect of such interactions and their corresponding entities. It must be noted that interactions in this model are not interactions between different classes of entities competing for different resources. Rather, they are interactions between different attributes of the same entity in general simulation terms. More specifically, these interactions are between patients' health states and effects from previous or current treatments. The results of such interactions affect patients' quality of life. Treatment effects do not have a direct influence on the quantity of life, however, life expectancy is affected by the treatment combination.

Table 4.5 gives detailed accounts of the different elements in the interactions integrated in the model based on the validation process. The first section of the table gives the different possible treatment effects experienced by the patients. Effects may occur individually or combined, and there are 16 possible occurrences (derived from the possible combinations of the levels of toxicity and menopausal symptoms). Health states can be seen in Figure 4.3 and 4.6. The 'treatment phase' in Figure 4.3 is considered as a single health state; each of the seven nodes in Figure 4.4 are considered as separate health states. This gives eight health states in total. Having 16 possible effects and eight possible health states gives 128 possible interactions. The second section of Table 4.5 gives the expected results arising from such interactions in terms of QALYs. QALYs are calculated by multiplying the utility value of a health state Figure 4.3 and 4.6) by the duration of that health state (in years). These are summed up to give overall QALYs for each patient. The quantity of life

– duration of the post-treatment phase – that is the probabilities of remission durations and types of recurrences (shown in Figure 4.4), is directly affected by the treatment paths shown in Figure 4.3.

*Table 4.5: Elements of the Interactions Formulated in the Model*

| effects | |
|---|---|
| Toxicity | Reflects side effects of CT and may affect the course of the treatment. Four levels of toxicity are possible (none, mild, moderate, non-fatal). User defined distribution specifies which level of toxicity a patient will have as a result of chemotherapy treatment. Treatment duration is then determined on basis of severity of toxicity. Post treatment phase is also affected if effect is existing. |
| Menopausal Symptoms | Reflects Menopausal side effects of CT, OS, and Tamoxifen. Three levels of symptoms are possible (mild, moderate, severe). User defined distribution specifies which level of severity a patient will have as a result of each treatment. Post treatment phase is also affected if effect is existing. Note for CT and Tamoxifen there is a possibility of not having menopausal symptoms. |
| results | |
| Utilities | Quality of life utility range is between 0 and 1. Assigned to a patient based on the health state and the effects of toxicity and menopausal symptoms. |
| Recurrences | Recurrences of cancer possibly occur after adjuvant treatment. Different recurrences exist. The model provides input facilities for each recurrence in terms of duration and recurrence probabilities based on the current health state of the patient. |

Once the structural and behavioural validation had been established, it was possible to measure the effects and trends of the different variables in order to identify the major factors. For example, it is possible to vary the durations of disease-free periods based on chemotherapy to see the subsequent trend of survival. Validation of some of the estimates in the model had to be deferred, so that the users could alter the estimates as necessary after more data had been collected from the on-going ABC RCT. This type of validation will depend on the early streams of data generated from the trial. The purpose of such validation is to predict the effects of the different variables on the model's results more accurately.

## 4.6 Use of the Model

As stated earlier, the central purpose of the model was to identify the main variables of the ABC RCT and to act as a communication vehicle between the stakeholders. Accordingly, the model has mainly been used for pilot experimentation without real data, developing an understanding of the interdependencies in the model. Health economists have full control of the model. That is, they are able to change all of the variables in the model based on their experimentation plan to establish the significant variables. Health economists are also able to explain the results of their economic evaluation to clinicians using the simulation model.

Health economists follow two steps for identifying the important variables defined in terms of sensitivity to model's outputs. The first step is to examine whether such variable(s) is/are important or whether the results are highly sensitive to them. Input sensitivity is measured by the percentage of change in the Cost-Effectiveness Ratio (CER), arising from the use of different sets of input variables, from initial results arising from initial input values. Initial input values are suggested by expert opinions involved in the trial. If the change of the CER for a comparison pair (see Table 4.2 on page 75) is agreed to be significant, this means the variable is significantly important with regard to that particular pair. So far there is no specific methodology which defines a percentage which should be considered as significant enough to suggest that the model is sensitive to such parameter(s). Usually health economists and clinicians agree on a certain percentage as being significant based on the situation to hand. In our case the model acts as a communication medium between health economists and clinicians in deciding what would be regarded as a significant change in percentage. This reflects one of the main objectives of this exercise: to facilitate this type of communication between stakeholders.

The second step is to examine the impact of changing the initial value on the order of the different comparison pairs based on their corresponding CER. This is done by ranking the effects of these variables on the different comparison pairs. The previous step measures the significance of the model's sensitivity to the specific variable(s) within the same pair, whilst the second step measures the significance of the model's sensitivity to the specific variable(s) between the different pairs of comparison. The following section gives an example to demonstrate how this process is conducted

### 4.6.1 An Example of Use

The following discussion presents an example of how the model can be used for identifying important variables and the impact of changing input variables on overall results. This example shows the results of altering the values of the cost of Ovarian Suppression (OS). As mentioned earlier such changes are often conducted in an arbitrary manner and there is no standard methodology for such changes. Changing of cost of OS are detailed in Table 4.6 below.

*Table 4.6: An Example of Altering Values of Model's Variables*

| | Base value | Change 1 | Change 2 |
|---|---|---|---|
| OS Cost | £1968 | £2952 [50% more] | £3936 [100% more] |

The initial values, like most values in the model so far, are suggested by expert opinion. "Change 1" represents the first change carried out on the variable. "Change 1" represented an increase on initial costs for OS of 50%, whilst "Change 2" represented a 100% increase.

For the purpose of this example the model was populated with 2000 patients arriving in span of around 13 months, based on expert opinions of health economists and clinicians involved in the trial. Table 4.7 shows the results for the above example. "Model 1" shows results of runs with the initial values, "model 2" shows results for "Change 1" (see Table 4.6) and "model 3" shows results for "Change 2" (see Table 4.6). Results are given in terms of CER's. CER's are calculated as follows:

$$\frac{Cost_A - Cost_C}{Effect_A - Effect_C}$$

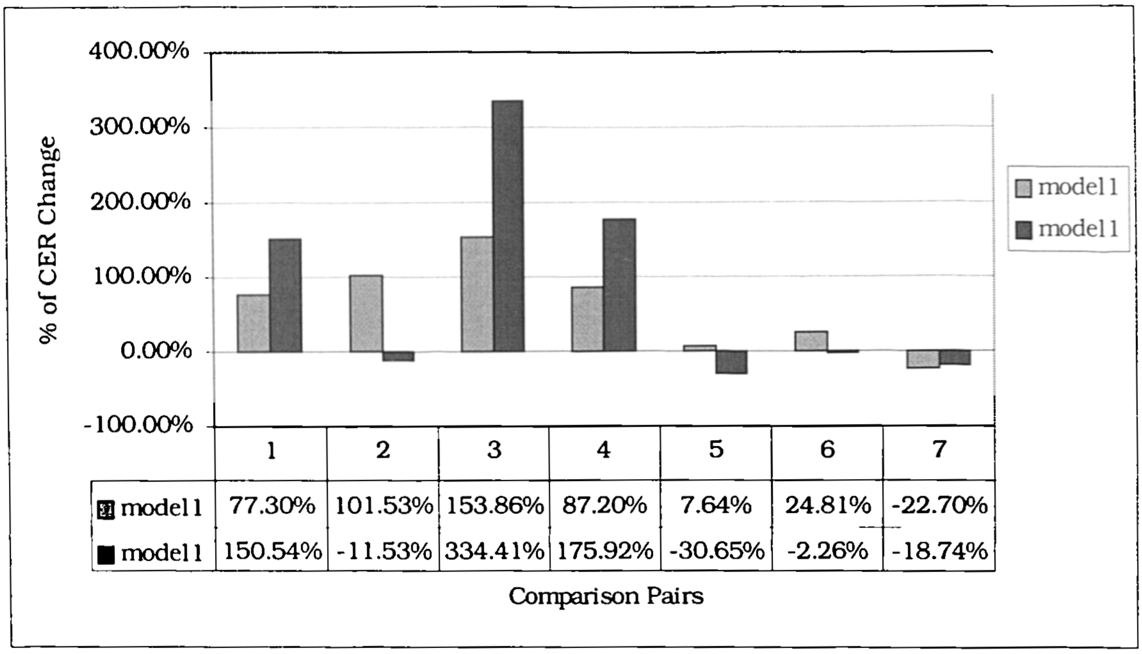
where $Cost_A$ is the average cost of the Adjuvant treatment, $Cost_C$ is the average cost for the control treatment, and $Effect_A$ and $Effect_C$ are average life years gained for Adjuvant and control treatments respectively.

*Table 4.7: Cost-Effectiveness Results of Altering OS Costs*

| | Model1 | Model2 | Model3 |
|---|---|---|---|
| Pair 1* | 1907.11 | 3381.34 | 4778.11 |
| Pair 2 | 1362.02 | 2744.88 | 1205.02 |
| Pair 3 | 2100.26 | 5331.62 | 9123.81 |
| Pair 4 | 1287.75 | 2410.69 | 3553.13 |
| Pair 5 | 1993.48 | 2145.78 | 1382.45 |
| Pair 6 | 1034.26 | 1290.88 | 1010.85 |
| Pair 7 | 1596.68 | 1234.19 | 1297.41 |

* See Table 4.2 for identifying comparison pairs

It can be seen from Table 4.7 that the effects of changing the variables are actually more noticeable on some comparison pairs than others. Naturally, in arms where, for example, OS is not prescribed or randomised then the change in CER is irrelevant. A change in such arms is mostly based on sampling fluctuations. Table 4.7 shows that as an effect of increasing OS cost percentages of changes from original results, "pair 1" is less sensitive to the 50% change than to the 100% increase in OS cost. Yet "pair 3" is moderately sensitive for 50% and strongly sensitive for 100% increments. We also find in Table 4.7 that "pair 2" is positively sensitive for a 50% increase with a minute negative sensitivity to 100%. This is due to the fact that both comparators may or may not have women who had OS and whether the cost will increase or decrease will depend on the number of women who had OS in that particular run. As for pair 4, results are similar to those of "pair 1" with "pair 4" being more sensitive to the 100 % increase. For "pair 5" we find that there was no change in results as both groups include women who had OS. The same principle applies for "pair 6 and "pair 7", as there were no OS patients.




| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| model1 | 77.30% | 101.53% | 153.86% | 87.20% | 7.64% | 24.81% | -22.70% |
| model1 | 150.54% | -11.53% | 334.41% | 175.92% | -30.65% | -2.26% | -18.74% |

*Figure 4.6: Cost-Effectiveness Results: Percentages of Changes based on Model 1 and 2*

The process of selection, as mentioned earlier, is based on the percentage of increase or decrease of a factor and its corresponding percentage of change in the CER. This analysis is actually conducted by the health economists. Based on the above example, health economists may decide, in the case where the cost of OS is 100% more, that OS data is only important for "pair 3". Yet the decision making process may take other factors into consideration. The purpose of the model is mainly to help the heath economists to take better decisions, rather than taking the decision for them. This example shows the flexibility of the ABCSim model to accommodate all types of possible change for experimentation, by being able to alter input values (aggregately or individually) and examine their impacts on the output. Facilities for such changes are advantageous in this exercise because they are tailor-made with regard to user requirements. As mentioned earlier, in addition to so many input variables, there are also output variables other than the CER, such as Cost/Utility Ratios. Exploring the effects of variable changes on outputs enables the users to examine other angles of the problem.

The discussion so far concentrated on presenting the case study and the model that is built in a specific way to explore the use of simulation in enhancing problem understanding for stakeholders with regard to the alternative modelling framework presented in Chapter Three. The following chapter presents some analysis for ABCSim with regard to the alternative approach. This analysis will be used to explore the strength and weaknesses of this framework. Then, if appropriate some modifications will be made to the framework to enhance the strong points and reduce its weak points.

## 4.7 Summary

This chapter starts with a brief introduction to its contents. The first section also includes the chapter's objectives and outline of the chapter. Section 4.2 presents the case study used for applying the alternative framework. The case study is about an economic evaluation alongside a Randomised Clinical Trial of Adjuvant Breast Cancer treatment. The section gives a background to the adjuvant therapies and their proved efficiency. After that the economic evaluation of the adjuvant therapies is explained is section 4.3. Section 4.3 also includes the importance and the need for the use of modelling to fulfil the process of economic evaluation. The main objective of modelling is to identify the key factors of the trial in order to concentrate on them for data collection and analysis.

Section 4.4 provides the main strategy followed for modelling the trial. The section describes the key issues for building the model. These issues are related to the use of the model to help understand the problem. Section 4.5 gives more details about the model. The section starts by presenting the different inputs to the model and each one is incorporated in the model. The expected outputs are also given. All input and output variables are specified and re-specified throughout the process of model building as part of the continuous relationship between the model and the stakeholders. The section then briefly discusses issues related to the verification and validation of the model. Section 4.6 gives an account of how the model may be used. The section also gives an example demonstrating the use of the model for identifying the importance of one of the variables in the model with regard to the Cost-Effectiveness ratio.

# Chapter Five

# 5 Chapter Five: Approach Analysis

## 5.1 Introduction

Chapter Three defined an alternative framework (MAPIU) - from the traditional framework illustrated in Figure 2.3 - for the process of simulation modelling. This framework was depicted in the form of a structure that is iterative in its behaviour concentrating on the "stakeholders" and the "modelling" parts. Chapter Four the results of applying this framework. Apparently this chapter intends to draw some reflections on the proposed framework. The chapter will analyse the framework based on the factors of understanding, mentioned in Chapter Two and factors arising from using the ABCSim model. The chapter is then supposed to identify the missing ingredients in the proposed framework in order to be tested again in the next chapter. The chapter will first establish an analysis methodology for identifying the missing ingredients and then it goes into ways of how to incorporate the missing issues in the framework.

### 5.1.1 Objective of the Chapter

This chapter aims to clarify the advantages and disadvantages of using the proposed approach to modelling framework. It is obvious that it may not be possible to identify all of the positive factors and the negative factors form a single case study. However, this chapter is trying to identify what are the obviously missing ingredients are in order to modify the framework and test it using a second case study. In summary the main objective of this chapter is to conduct some initial assessments for MAPIU based on the objectives of this research.

### 5.1.2 Outline of the Chapter

This chapter evolves around the evaluation of MAPIU based on the ABCSim example. The next section addresses the main methods used for evaluating the framework. Section 5.3 presents the evaluation and analysis, which are undertaken based on the analysis method established in Section 5.2. Section 5.4 draws the missing ingredients in the proposed framework based on findings from the analysis in the previous section. Section 5.5 then presents the main requirements for modification of the proposed framework in order to enable the framework to cope with modelling for problem understanding. Section 5.6 provides the main modifications applied to the framework based on the previous sections. Section 5.7 presents a revised version of MAPIU called MAPIU2.

## 5.2 Method of Analysis and Evaluation

The initial analysis of the proposed framework is based on its very objective, and that is facilitating understanding to stakeholders. The basic idea is to examine the ability of this approach in achieving that by reflecting on the ABCSim experience. Evaluative criteria are based on two main sets of factors. The first set encompasses factors which are already identified from the discussion about problem understanding in Chapter Two. Those factors are: *the nature of the available information* where the aim in this case is to identify the ability of this approach of modelling to enable stakeholders and people involved to understand the general type of problem to hand. This is mainly accomplished by establishing the key players in the system and the key components. It is important to know whether this information can be measured quantitatively or not. The second factor to look at is enabling users to understand *the nature of the cause-and-effect relationship.* Probably one of the main uses of modelling (should be) is to understand the different interrelationships inside the system, as mentioned in Chapter Two. Identifying such interrelationships is a vital link in the process of problem understanding. The third factor is being flexible in manipulating the different assumptions for establishing a viable representation of the system's behaviour. The analysis of this situation will look at how this modelling approach may enable users to manipulate their assumptions about the real life system. The fourth factor in this set is identifying the *interrelationships of data.* This factor is used to examine the ability of this approach to detect the relevant pieces of data to be collected for the exercise. The last factor is to see how this approach may enable stakeholders to *communicate their understanding* amongst each other. As mentioned earlier these factors are already agreed upon as important to achieve an acceptable understanding of the problem. Also as mentioned earlier, the purpose of this chapter is to evaluate MAPIU about its capability to handle these factors. The following subsection, however, presents the second set of evaluative criteria which are based on factors specifically related to modelling for problem understanding.

### 5.2.1 Factors Specifically Related to Modelling

The second set of factors for the analysis is based on factors that arose from the discussion in section 3.2. As mentioned earlier, factors for problem understanding address this issue from a general point of view. However, it is assumed that there are some other factors which need to be considered for the process of problem understanding when using a modelling tool. These are considered as factors for making a modelling tool effective for problem understanding. Stemming from the discussion in section 3.2 it is preferable that the model is not built based on assumptions, or at least it should not be required to do so, as more assumptions reduce the model transparency in reflecting the real life's systems behaviour. One important way for gaining understanding is to examine *the initial assumptions* about the problem to hand, also to evaluate the consequences of taking any decisions.. Based on that, one evaluative factor could be the capability of the model to test the different assumptions given by users or any one who is involved with the problem. The second important factor to consider is *flexibility*. This factor is quite important for enabling stakeholders to change what they want as they model or communicate amongst each other. Also the model should be adaptable to any types of changes that may be suggested by the stakeholders.

All of the factors mentioned in this section represent evaluative criteria for the assessment of the modelling framework, which is discussed in Chapter Two. The following section addresses the ABCSim experience, presented in the previous chapter, to be analysed based on the above mentioned factors. This will hopefully bring about some of the missing features for using MAPIU framework.

## 5.3 ABCSim Revisited

### 5.3.1 General Factors for Understanding

The general process of building the ABCSim model was based on the modelling approach discussed in Chapter Three. The initial phase of the model was to identify the basic aspects of the problem. Those are; objectives of the modelling process, the domain of the problem – in this case the ABC trial – in general terms, and the basic entity flows. This particular problem was more restrictive in terms of objectives and domain, as the whole study is about identifying the key variables for data collection in the ABC trial for the sake of economic evaluation. Restricting the model means it is not needed to explore different types of dimensions for the problem. That made the process of identifying the objectives of the problem understudy easier. The domain of the problem was also straightforward, (where in this case the domain is supposed to be the ABC trial) and that is in terms of patients' flows and the patterns of care they receive in addition to the economic measurements used for the evaluation. The basic plans for the different treatments were identified using the ACD modelling approach. The previous chapter gives an overview of the ACD of the ABCSim model. The ACD model is also used for establishing *the physical interrelationships* of the model. An example of such interrelationships could be the different nodes to be visited by a particular cohort of patients. These nodes are sequenced depending on the type of patient, whilst the different types of patients are classified based on disease and treatments randomised or prescribed to them. In some other cases, in general simulation terms, if an entity requires another entity, from a different class type, to perform an activity, then this can be classified as a relationship between these two entities. This type of relationship can also be depicted in the ACD and physically explained. Building the ACD model was based on MAPIU through the iterative process.

Understanding the physical structure via the ACD was reached through a process of a number of refinements. It was evident that the latest ACD model was completely different from the original view of the system (see Appendix A). Figure A.1 shows the initial ACD of the ABC Trial model and Figure A.2 shows the state of the model al later stages. The two figures show how the stakeholders' understanding is evolved, especially regarding the paths of the trial. One important example to illustrate the evolution of stakeholders' understanding is the addition of the "100%" route for some of the patients. This route means there would be no randomisation in this particular path, either a clinician suggests a patients should take a particular treatment or should not take it and the patient should not be randomised. This was not understood or grasped by heath economists at the early stages of modelling and could only be understood by discussing the earlier versions of the model with clinicians involved. It must be noted that this approach tries to avoid a sequential model building process, however, it was preferable to reach an accepted understanding of the physical layout of the trial before starting the computer model. The reason for that is because it would be easier to modify the model during the ACD phase than during the computer model phase. This reason will still be valid until new simulation software is available that is easier to use for building models than the traditional ACD technique.

After reaching a point where the *logical interrelationships* are needed to be identified – while they can not be identified using the ACD – then the modelling effort is directed towards the computer level. The reason for that, as mentioned in the previous chapter, is because the logical interrelationships may not be explained or at least clearly drawn in the ACD. The same method of communication is conducted between the users and the model as it was for the ACD. The basic principles of communication is that users put their requirements and assumptions about the system into the model, the model then produces feedback to them for validation and possibly re-establishing their own assumptions about the real system. The evolution procedure is conducted in an iterative manner until reaching an acceptable understanding of the system by establishing the relevant factors in the model. Since the main objective of modelling is *to identify the key variables for data collection*, this made it easier for the stakeholders to familiarise themselves with this type of modelling. The computer model for the trial structure and the ABCSim interface for input entering and output presentation were all built over a period of 12 months without the need for real data. The only need for information, which was mainly sought from an involved clinician, was based on the different patterns of care. That is based on the possible routes to be taken, or not to be taken, by patients. The likely side effects from each combinations of treatment also sometimes needed to be determined. The reason is to establish this a reliable distribution of all possible occurrences is included. It is then possible to eliminate any of them by giving the variables values of "0" probability, which it is certainly not going to occur at any time during the running of the model.

All experimentations with the model are conducted to establish the logical interrelationships without being interfered with by the existence of data. It was believed that if the model is populated with historical data then all findings and understandings about the trial's behaviour would be restricted to this particular data. By establishing the logical and physical interrelationships of the components of the ABC trial it was possible to identify the *interrelationships of data* – either collected or generated from the model. It must be noted that this model has benefited from the original structure of the ABC trial by avoiding one of the main data problems involved with simulation modelling and analysis. That is having statistically autocorrelated data. Because there are no interactions between the different entities in the trial, where there is a need for more than one entities, of different types, to start an activity (see the ACD in Chapter Three). That means there will be no interrelationships from data inputted or arising from the model. Usually analysts – when there is a case of interrelated variables – spend a great deal of time trying to sort these relationships in order to manage the interrelationship built-in within the collected data.

It may seem as if this case does not provide a good test for the proposed framework in finding the interrelationships of data. However, in the case of the ABC trial there exist different type of relationships. These interrelationships of data are actually based on interrelationships of the entities driving such data. If the model is able to identify the interrelationships of the different entities involved, such as those illustrated in Table 4.5, then it will be easy to anticipate interrelationships of data arising from such interactions. If the model is flexible enough then users will be able to change the model's factors to gain an understanding of data and any interrelationships accompanying such data without the need to collect such data.

It can be seen from the previous chapter and the above discussion that ABCSim provided the stakeholders with facilities that encapsulated most of the trial's components in terms of direct inputs or probability distributions. This gave the stakeholders the ability to *examine their assumptions* with regard to the values of those components. The main concept behind that is to enable the stakeholders to apply different "what if" questions about the trial and the economic variables. This is mainly conducted after model building. During the model building some of the initial assumptions or visions of the stakeholders about the trial were changed dramatically as the structure of the model started to converge into its final shape. These assumptions were particularly related to the treatment flows of the different types of patients. Before that the types of patients were also changed continuously throughout the model building process. Types of patients are represented by the 14 comparison arms in Table 4.2 on page 81, whilst treatments flows were specified by the 14 paths in Figure 4.3 on page 83. It must be noted that having 14 arms and 14 paths was completely coincidental, as there is no relationship between the number of arms and the number of paths.

Other main changes in the original assumptions were the different side effects for having chemotherapy and ovarian suppression. These changes were based on the different levels of each side effect and their corresponding extensions to subsequent health states. Changes for the treatment arms were mainly carried out during the building of the conceptual model (ACD) and that is due to the fact that they are physically manipulated, whilst changes in effects were changed during the computer model building as they are logically manipulated. The reader in this case is referred to the previous discussion about the physical and logical relationships in the model.

### 5.3.2 Modelling Factors for Understanding

The above discussion briefly presented an evaluation of how ABCSim was built and ready to be used to facilitate understanding based on the factors mentioned in Chapter Two. The discussion now takes another dimension and looks at ABCSim with regard to factors for problem understanding specifically related to modelling. These factors (*independence of assumptions* and *flexibility*) bear some relationship to the previously mentioned factors. However, it is believed that to achieve an acceptable level of coping with the previous factors the model must be built with the latter factors under consideration.

To enable users to examine and rethink their own assumptions fewer assumptions should be incorporated in the model. From discussion in Chapter Two, it is seen that simulation as a technique in general enables analysts to build models with less assumptions than those of Markov models and decision trees. Yet it is found from the ABCSim experience that building the model in an iterative way is more useful than the sequential approach in terms of assumptions. For the iterative approach we find that assumptions may be laid in the model yet they could be changed throughout the model building process as the main effort is spent in building the model and understanding at the same time. As for the sequential approach we find that it is difficult to change any initial assumptions incorporated at the beginning. That is for two reasons. Firstly, analysts and stakeholders would be busy in conducting other steps, such as data collection. Secondly, building a model in a sequential way, while questioned in one step of validation does not give a chance for the stakeholders to reflect upon those assumptions. Even if these assumptions are to be changed, that usually proves costly for many components of the model are to be changed subsequently. It can be concluded that even though traditionally simulation is useful for incorporating fewer assumptions, an iterative approach to simulation offers more effective ways for refining and redefining these assumptions than the sequential way. Bear in mind that assumptions are actually driven by stakeholders' understanding of the system. When assumptions are changed this indicates the change in the basic understanding. So stakeholders and modellers should always pay attention to the changes of assumptions as they reflect redefining their understanding.

As discussed earlier, the model provided users with viable *flexibility* in terms of experimenting with the model by changing the different values of the desired component. It was advantageous to build the ABCSim interface from scratch in order to answer the requirements of the stakeholders so they can have a simulation interface designed to their own prerequisites. This also includes the way output values are presented. Building the interface from scratch added more strain on the modelling effort, yet it helped stakeholders to understand the model and the ABCSim package and that reduced the training time after the model building. This draws attention to a very important point and that is the inclusion of stakeholders throughout the model building process gave them a sense of ownership and raised their confidence in the model.

It can be seen that the model played a key role in stimulating and facilitating the development of understanding of the problems associated with adjuvant treatments of breast cancer. The model has offered a configurable and accessible way for the different stakeholders to develop and negotiate their problem understandings. However, they were a number of missing ingredients with regard to MAPIU which were noticed during the ABCSim experience. The following section discusses in details the different drawbacks that arose from the ABCSim modelling exercise. The section after that gives some new requirements for the framework which is redefined in section 5.6 based on that.

## 5.4 Weaknesses in the ABCSim Experience

The previous section gave a brief description of ABCSim with regard to problem understanding issues. Although most of these issues were addressed when modelling the ABC trial, some problems still persist with MAPIU. This section tries to expose the missing ingredients with this approach. The aim is to modify the approach based on these problems and re-enhance it. The following chapter will then assess it using another case study.

The problems of the proposed framework evolve around two main aspects; the stakeholders' side and model building side. It is felt that the framework did not address these two aspects with enough detail, particularly the stakeholders' side. The following two sections will explain why these two aspects create some problems for the proposed approach.

### 5.4.1 Stakeholders' Aspect

Looking back to the discussion in Chapter Three, two main components are involved in the modelling process. Those are the model and stakeholders. It can be seen from the discussion that the modelling part may have been well explained. But there is no explanation of the "stakeholders" side of the equation. Based on the underlying principle of the proposed framework it is important to identify who wants to understand the problem and how they are involved in the problem. Users, stakeholders, and problem owners are usually used interchangeably in the simulation arena. However, all these categories are common players in the modelling exercise. There is no standard categorisation of types of stakeholders with regard to simulation. Most of the existing simulation methodologies do not represent actual users of the model or stakeholders of the problem or who is going to actually make the decisions based on the results arising from the model.

The researcher assumes that it is important to understand the relationship between the "stakeholders" side and the modelling side before carrying out the modelling process. For every simulation model there is a set of input data, so it is important to know who provides that, who validates it, and on top of it all, who decides its relevance to the problem needed to be tackled. There is also output coming out of the model, so people need to know who uses that and who decides this is the required output or measure of performance. If an output is going to be generated for people who would not appreciate it or would not be able to use it then what is the use of modelling? It should also be remembered here that inputs and outputs might not be decided without a sound and an acceptable understanding of the problem.

It is therefore, important to know who is doing what with regard to the *problem*, the *model use*, and the *correspondence validation* between the model and the problem. It is important to know the audience who is interested to understand the problem so the model when it is being built should cater for the specific interests of such stakeholders. From the above discussion and looking at the previous uses of simulation, there appear to be three categories for classification of stakeholders. Those are problem owners, actual users, and experts. These categories can are explained as follows:

*Problem owners*:

Problem owners are usually the ones who are involved with the decision making process which is supposed to be based on the proposed simulation model. Examples regarding healthcare systems are health managers, and clinicians. It is important to take an account of such stakeholders, as they are the ones who are meant to understand the problem in hand and get the most benefit from using a simulation model to take a particular problem by taking particular decisions. Problem owners may also be the ones who commission the simulation study in the first place, so regarding the model they are the ones who will decide the credibility of the model. In many cases they might not be using the model, yet they are involved in the problem and the final decision making. Problem owners may benefit from the model by examining their understanding of the system to make more informed decisions.

*Actual users*:

The term "actual users" is used here so not to be confused with the umbrella term "users" which is used sometimes to indicate stakeholders. The term *users* is applied to any one who is directly contributing to, or benefiting from, the model. *Actual users* is applied to any one who is involved in manipulating and experimenting with the model to gain certain responses. They may or may not be the direct decision makers based on results arising from the model. They must understand the model, yet not necessarily the real system, at least not the parts which are not directly related to the problem. Actual users can be defined as the ones who are supposed to use the model to help problem owners understand the system. They could still be represented in the category of problem owners or decision makers if the decisions are made by them are based on the model.

*Experts*:

This category represents those who are experts about the behaviour of the system and they are involved with the design and structure of the system. They may or may not be decision makers or users, yet experts are important in validating the model. Experts are also used to provide more ideas and visions about the technical structure of the real system. For example, clinicians could be experts in specifying the possible treatment paths for particular patients. Experts usually make sure that the model which is used to enhance the understanding of decision makers are not highly deviate from and that is in terms if whether to apply these decisions or not. The importance of having experts is that the decision makers might not be familiar with the considerable technicalities of the system. This means they may not have a realistic picture of the system and also they may not know whether the model used to enhance their understanding about the system is a valid tool for that or not.

The above categorisation of the model's users is not a standardised one, yet it is the experience of the researcher that these categories represent all types of simulation users. It is assumed that it is important to make such identification for the purpose of model building in order to establish the best way to intercommunicate amongst stakeholders and between stakeholders and the model. This is evident from the ABCSim experience where the *problem owners* and *actual users* are health economists with clinicians as *experts.* Even though the main problem owners in ABCSim were health economists, it was important to consult clinicians about the validity of the model in terms of structure and behaviour. The issue of identifying the different roles of stakeholders was not strongly discussed in Chapter Three and it could be seen as one of the missing ingredients with regard to the proposed methodology.

### 5.4.2 Modelling Aspects

For modelling, the proposed framework does not address issues of experimentation and the use of the model, which includes subsequent steps after building the model and delivering it to the user. It seems as if the purpose is to build the model and the effort stops there. On the other hand, there is no indication for analysts or stakeholders about the termination of the study or when it is appropriate to stop the modelling process. The underlying principle for this approach is to enhance stakeholders' understanding of their own problem – either individually or collectively – and that is through the process of model building and using it later. The concentration was mainly on the model building process, yet there is no indication of how to manipulate the model to extract an acceptable understanding of the problem. Generally, the process of experimentation and model building may be similar to the traditional method (see Chapter Two), or it may be different altogether. Yet this issue needs to be addressed to add to the effectiveness of MAPIU to see how the issue of experimentation can be incorporated in the overall approach to enhance the understandings of the stakeholders.

One of the steps that have not been addressed is *data collection.* It is true that the new framework does not support a fully comprehensive data collection mechanism at the earlier stages of the model. The approach does not express where there is a possibility that data may be required at later stages for building the model. Again, while using this approach data may or may not be required at all stages, this issue has to be addressed.

These two issues are brought to focus because of the objective of the research. It is important to use the model to gain more understanding about the problem. On the other hand, MAPIU tries to avoid restricting itself to sequential steps that may or may not, in the end, provide the desired objectives. The approach calls for including all possible steps to the modelling process that may add to the understanding of the stakeholders. That includes *data collection* and *experimental design.* The main objective is to gain understanding so that – quite naturally – the termination of the modelling exercise should mainly be related to the fact that stakeholders agreed to have gained an acceptable level of understanding about the problem. That level may even be reached before collecting any data or conducting any sort of experimentation (Paul and Thomas, 1996).

## 5.5 Requirements

This section discusses the different requirements for modifying MAPIU. These requirements are established based on the discussion in the previous section. Hence, they are based on the stakeholders and model building factors. Requirements for handling stakeholders are based on finding ways to identify the different categories of stakeholders, their respective interrelationships, and their relations with the model. For model building, requirements will concentrate on defining possibilities for adding extra steps MAPIU when they are needed, that is with regard to understanding the real system under study. The following subsection will discuss requirements with regard to the stakeholders' aspect, whilst the subsection after will discuss requirements with regard to the model building and facilitation aspects.

### 5.5.1 Requirements Based on Stakeholders

As mentioned in Chapter One, healthcare systems processes – particularly the process of decision making – are usually carried out by a group of people rather than one person. It was indicated that one of the problems is maintaining valid means of communications amongst decision makers to reach an acceptable decision. On the other hand, in conducting a simulation study different people may also be involved either directly with the model or indirectly with the decision making process. This subsection will define requirements for the proposed modelling approach to incorporate these issues.

For the problem of communications, especially between the model and the stakeholders, and based on the experience from ABCSim, it was important to involve stakeholders in the process of model building from the very beginning and throughout the process. Another positive factor was creating an interface between the simulation engine and the stakeholders. This interface was made in the interests of the problem owners. Having this interface, and stakeholders being part of the development process, made it easy for them to manipulate the model and understand it more quickly, bearing in mind that they are not experts in the simulation modelling process.

An important issue that should be addressed in the model is establishing ways of communications between stakeholders and the model. There was only one group of stakeholders that was directly connected with the model and they are the *problem owners* themselves. Yet in other situations things might not be the same. It is possible to have more than one group of stakeholders, so some helping guidelines for communication are preferably applied. One of the drawbacks of the ABCSim experience was the lack of communication between clinicians and analysts. According to the above classification, clinicians represent the *experts* part of the stakeholders, whilst analysts are part of the modelling side. Clinicians did not have the chance to be involved or to directly contribute to the model building process. They did contribute, yet with the *problem owners* – health economists – as a medium of communication. The main effect is that the model could have been built faster had clinicians been engaged more often in the process. Having clinicians involved with the model was also important for the validation of the model. It is therefore a central requirement to define how these different groups of stakeholders can communicate with each other and with the model.

### 5.5.2 Requirements Based on Modelling

One of the main advantages of using simulation is for it to be used as an experimental tool for the real system. It is an important requirement to incorporate an experimental facility for the proposed modelling framework. The ABCSim example represents a pragmatic approach to identify the experimental factors and build an input/output interface based on that through an iterative learning process. Even though the experimentation issue was not included in the proposed framework, yet the ABCSim experience proved that this issue could be, and should be, added to the other components of the process.

The traditional experimentation process is divided into three main steps; defining the experimental factors, designing the experiments, and conducting of the experiments (Law and Kelton, 1991; Kleijnen, 1987; Kleijnen and Groenendaal, 1992). The first step was more or less applied in the ABCSim example. The model was built in a way that would help stakeholders to identify the most important, or relevant, factors of the model. The process was also based on the iterative principle followed for building the model. The second step was conducted in the ABCSim example in terms of sensitivity analysis rather than systematic experimental design. Conducting the experimentation is a straightforward issue – with regard to both traditional experimentation and the sensitivity analysis followed in the ABCSim, it is all about conducting the experimentation based on how it is planned to do so.

Looking back at MAPIU in Chapter Three and the above discussion, the issue of defining the experimental factors may be added to the modelling box. Experimental factors can be defined as part of the model's inputs as variables to be targeted for experimentation. And the output variables can be designed based on these inputs and how they are supposed to be measured. This whole process actually falls within the overall iterative model building and validation process. The experimentation process may also need to be classified with regard to the existence of data.

Data collection may need to be added throughout the modelling process. However, a great deal of care should be taken here. As mentioned in the previous chapters, data collection is a waste of time if the problem is not fully understood. Yet it is possible after the problem is understood, some of the components need to be more accurately modelled based on observations from the real system. This is true if the objective is to measure specific responses to changes in the real data. A warning should be put here that these measurements are only true *ceteris paribus* – all other things being equal – while there is a very minute chance of that happening in real life, especially when considering healthcare systems. In summary, a 'data collection' step can be added with a strong emphasis on the fact that it should be added after the stakeholders have reached an acceptable level of understanding, while having this sort of data is vital for gaining more understanding or helps in the process of decision making.

This section provided the likely requirements for enhancing the proposed modelling approach based on the missing ingredients discussed in the previous section. The following section revisits the proposed framework and presents ways of adding the above-mentioned requirements. The new version is then going to be assessed using a case study in the next chapter.

## 5.6 MAPIU Revisited

The structure of this section follows the previous two sections in that it classifies the aspects of requirements with regard to the proposed framework. The first subsection addresses some modifications for the 'stakeholders' component, whilst the second subsection addresses some modifications related to the 'modelling' component. After establishing the modifications for both components they are then integrated into a modified framework for modelling.

### 5.6.1 Stakeholders Based Modifications

With respect to the "stakeholders" side of the process a significant modification is undertaken here by adding categories for the different stakeholders involved in the process. Whether they are problem owners, experts, or actual users. Ways of intercommunications amongst each other and communicating with the model are established. The purpose of classifying the stakeholders into the above mentioned three categories is to ease the process of establishing ways of communications (see Figure 5.1). *Actual users* of the model are required to be involved with the model building and development throughout the process. They are the ones who are supposed to use the model and communicate the results to other stakeholders. *Experts* are needed to make sure the model depicts the system in a way that makes it understandable to other stakeholders. There may not be a typical representation of the system, yet experts are there to eliminate any aspects of the model that may be entirely wrong and do not necessarily help other stakeholders to understand the system. Generally, they are responsible for the validation aspects of the model. *Problem owners* – including decision makers – are needed to be addressed because they are supposed to derive their understandings from the model. They also need to communicate with other stakeholders to convey their requirements. It is believed that these categories exist for every modelling exercise (albeit not identified) and they should communicate with each other. However, they could be overlapping in this structure. It is possible, and it is quite normal, that one stakeholder may be represented by more than one category. For example, a problem owner could be an expert in the system and also the main actual user of the model. The reader is reminded that one category may also contain more than one person.

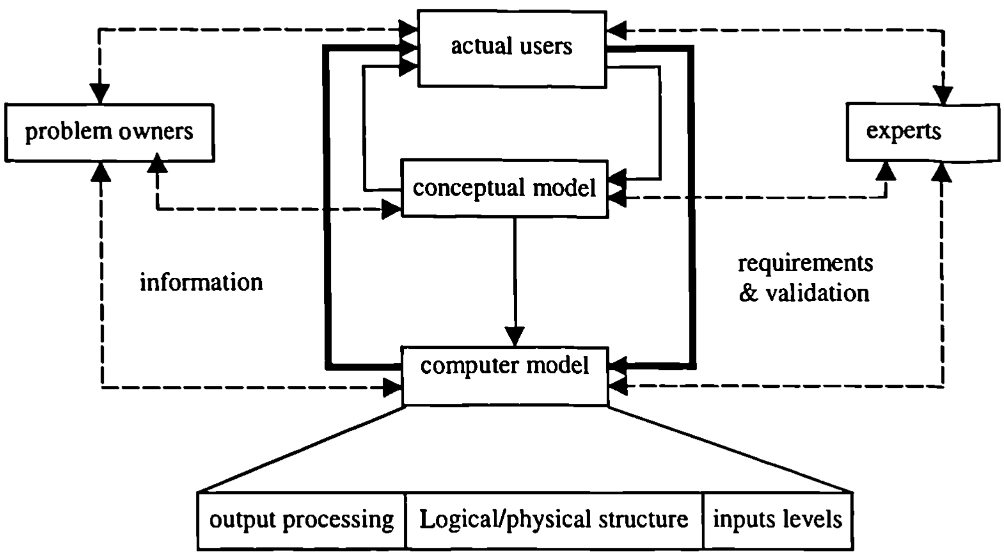



*Figure 5.1: Modifications Based on Stakeholders*

Figure 5.1 shows a modified version of Figure 3.2 on page 63. The main modification at this stage is located on the 'stakeholders' part. In Figure 5.1 the three categories of stakeholders are now explicitly portrayed. The process of classifying these categories is based on the iterative process. It is felt that part of understanding the problem is understanding the responsibilities. Even though the people who take the decision to apply a simulation modelling exercise may be taken automatically as the problem owners, this does not necessarily means that they will turn out to be the decision makers who will use the model's output as sources for their decisions. And the same applies for the other categories. Based on that, the process of stakeholders' categorisation is left to them as they intercommunicate amongst themselves and with the model. Also – and as part of the modelling strategy of leaving all decisions in the model to the stakeholders – modelling analysts are not supposed to establish this categorisation. On the other hand, the three categories are actually specific roles with regard to the particular model rather than specific people in the particular organisation. Which means any of these specific roles will always be the same; however, it could be played by different stakeholders depending on the problem under study. Knowing who will play what role is part of understanding the problem which is another output of the modelling exercise.

The rest of the diagram is similar to that of Figure 3.2 on page 63. It represents how the different types of stakeholders are interacting amongst themselves and the model. There is an extra modification, however, and that the *experts* are located in the requirements and validation part of the process, whilst the *problem owners* are located in the information part of the process. *Problem owners* are generally more concerned with setting out the needs and *experts* are concerned with adapting these needs to be represented by the model in valid way. *Experts* and *problem owners* are assumed similar in terms of level of interactions with the model. Communications from and to these two categories are denoted by dashed lines meaning that their levels of interactions with the model are less than that of the actual users, whose interactions are depicted by straight lines.

### 5.6.2 Modelling Based Modifications

Modelling based modifications can be divided between the two factors discussed in the previous two sections; *data collection* and *experimentation.* Based on the proposed framework data may be needed for two purposes, either for model building, or it can be employed for model use for the sake of experimentation and 'what if' questions. For model building the need is for well-understood data i.e. information. This information is sometimes needed for describing certain behaviour of one of the model's components. This is actually mentioned in the ABCSim example. It may be considered as qualitative data rather than quantitative data. An example of this is expert opinion, which may be needed for identify all possible health states for certain types of patients after the treatment phase. At later stages data may be needed to examine the system's behaviour under known situations or situations that actually happened in the past and see how the model will react given some changes. From this the process of data collection, for key relevant variables, can be incorporated throughout the process of modelling, which includes model building and model use and only triggered by the modelling requirements.

As for the experimentation aspect, things may be a bit different from the traditional approach. As mentioned in Chapter Two, the problem is formulated and data is collected before the modelling and the experimental design phases. This means all experimental factors are identified and understood. In the case of the proposed approach, the modelling process starts at an earlier stage to help understand the problem, in order to identify the relevant factors. For this reason it may not be feasible to establish and design an experiment where these factors are not known. On the other hand, it is not wise to go about the modelling process without having a plan of how to conduct the experiment. Another way that may cater for a planned experimentation phase is having systematic what-if questions and sensitivity analysis throughout the process. This will not require the availability or identification of the important factors at the beginning of the modelling process. At the same time, experimentation may be based on a systematic process rather than muddling through. Even so, this plan should not be so strict so that it may restrict the stakeholders from trying different routes throughout the experimentation process. This whole process of having systematic what-if questions is highly dependent on the initial objectives of the modelling exercise. These objectives are the driving force for the model.

Another modification that was thought important is a terminological one. In MAPIU the modelling process starts with the *conceptual model* then progresses on to the *computer model.* This would be confusing. Currently most conceptual modelling methods are more or less applied using computers. Even if they are 'used' on paper, the computer plays an important role in producing these models. This means the computer model could also be a conceptual model on certain cases. Whilst it may be quickly understood which term means what, there is room for confusion. On the other hand, given the main objective of MAPIU, the change from the conceptual modelling level to a more detailed modelling should be related to the modelling quotient with regard to the level of information and requirements interchanged with stakeholders rather than which is the modelling tool in use. For this reason the second stage of modelling in MAPIU is called the "time-based model".

Time-based means that time is incorporated (whether running or being developed). This term is used because the change of the model from a static to a dynamic behaviour represents a significant change with respect to the amount of information that can be generated from the model, based on a wider range of scenarios which are fed into it. There are certain issues of understanding that are acquired from the static level (conceptual model) and other issues yet more complicated are acquired from time-based models. Advances in technology in visualisation simulation packages could be used for the conceptual modelling and the computer model. We believe that the difference between the two levels of modelling is the incorporation of time and the logical features that come with it.

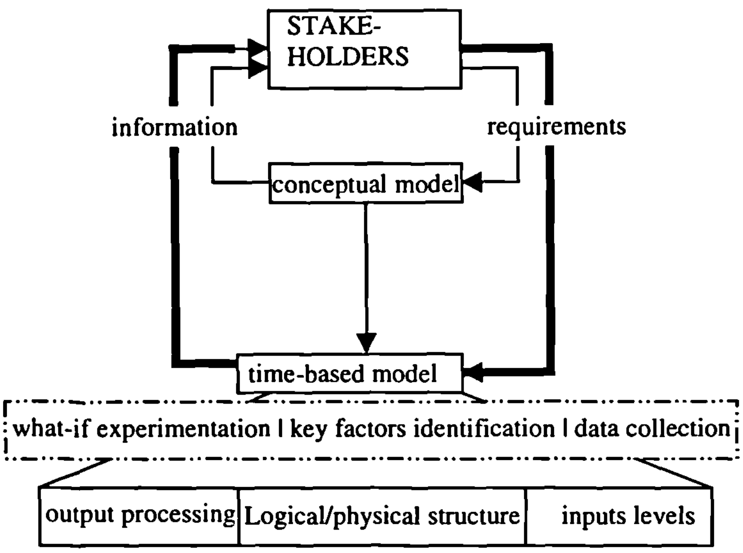



*Figure 5.2: Modifications Based on Modelling*

Based on the above discussion the suggested pattern of modelling can be thought of as what-if experimentation, identifying of key relevant factors, and, if necessary, data collection for these variables. Most systems contain more than a few factors, some important, some not. The relevance and importance of factors depends on the problem and how it is addressed. This pattern is actually conducted in the same order in an iterative process. Figure 5.2 shows the modifications from the modelling side only. The dashed-dotted box contains three elements; what-if experimentation, key factors identification, and data collection. The box is dashed-dotted to denote the fact that it actually falls within the iterative dynamic process of the modelling side.

'What-if' experimentation is a constant element of the modelling process whether systematic or non-systematic. This type of experimentation is mainly used by decision makers to either examine the impact of certain decisions or identify key factors in the system to enhance their understanding about the system. Identifying key factors is usually helpful in the process of conducting a study about a system, and when there is a phase of data collection. Identification of key variables in this case will ease the process of data collection by reducing the effort of collecting data for unnecessary variables. The data collection element in Figure 5.2 may not be a constant element like the what-if experimentation. Data collection may only take place if there is a need for it and the variables related to this data are well understood. However, if there is a need for data collection, then this step should follow the experimentation and identifying of key variables. It should be noted that the elements of the dashed-dotted box are sequentially ordered steps during the process of modelling, while the elements which are in the normal boxes are either contributions or products of these steps.

## 5.7 MAPIU Revised

In the light of the above discussion with respect to the original version of MAPIU, the main principles for the modelling process are discussed in this section. Figure 5.3 shows the overall structure illustrating the proposed framework (now named MAPIU2) with its new additions. The structure and process of MAPIU2, which are explained below, represent the main guidelines for testing in Chapter Six. The modelling process for MAPIU2 is based on two main issues; *initialisation* and *processing*. Initialisation is about identifying the components of MAPIU2 whilst processing is about how these components work together given the objective of modelling. It is worth stressing that MAPIU2 is an approach to modelling that is not restricted by formal and logical rules, aiming to be adaptive to changing requirements. These guidelines provide overall principles while leaving detailed technicalities flexible based on the particular case for modelling.

As can be seen on the left side of Figure 5.3 problem owners will be concerned with information coming out of the model and they examine the model by defining certain what-if questions. On the right side experts are concerned with the validity of the representation of the model to the real system given the needs of the problem. They may also be concerned with providing any data needed for the model. Note that all participants are mutually linked.

### 5.7.1 Initialisation

The classification of stakeholders remains an important issue in fitting the players to the roles in MAPIU2 at the initialisation stage. This is assuming that the model and the stakeholders are the main players in the process with their mutual feedbacks. It is preferable to assume that the identification of stakeholders may not be straightforward. If stakeholders do not understand the problem it is more likely that they cannot fit themselves into their corresponding roles, particularly if they are not familiar with the modelling process. To break the first barrier a first draft of the *conceptual model* could be developed in order to help in the process of stakeholders' classification. This represents the first step in the modelling process. In some cases classification could be done without an initial conceptual model. Table 5.1 shows how the different types of stakeholders can be identified using the defining features available in the right hand side of the table. Note that these features are based on the experience of the researcher as there is no specific literature or research findings regarding this issue.

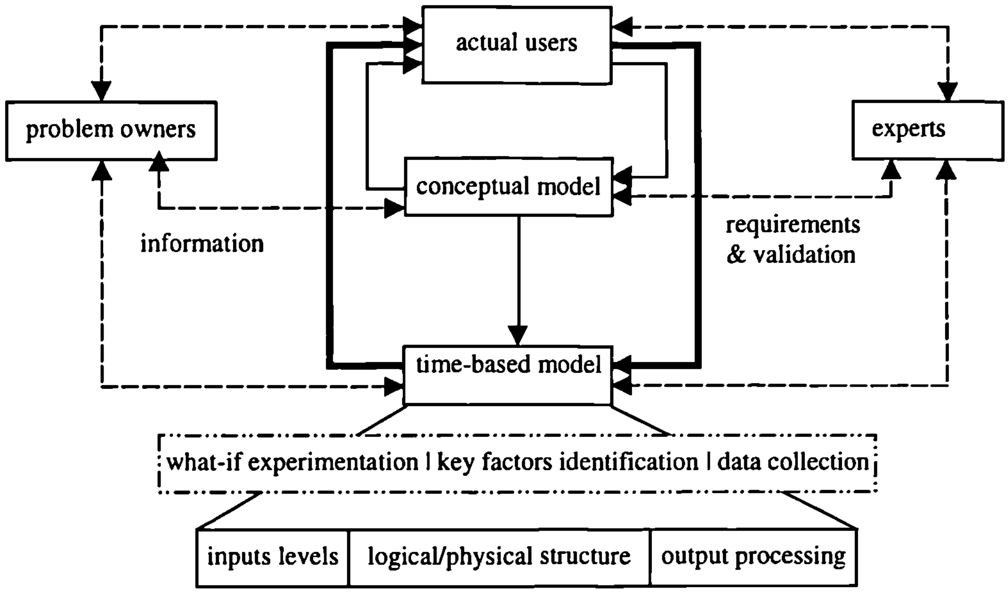



*Figure 5.3: MAPIU2 Overall Structure*

In MAPIU2 all decisions taken regarding the model's structure are not final and can change at any time to any structure that fits the stakeholders' needs at the time including stakeholders categories.

*Table 5.1: Stakeholders' Details in MAPIU2*

| Stakeholders | features |
|---|---|
| Problem owners | • Decision makers (corporate or overall picture)<br>• Pay for the study or the process under study<br>• High interest in solving the problem<br>• High interest in the success of the system<br>• Make use of model's output (one way or another) |
| Experts | • Detailed knowledge of the system<br>• Detailed decision makers (day-to-day) |
| Actual users | • Will directly work with the model<br>• Process and interpret the model's results |

The classification that takes place at the *initialisation* stage is only a starting point and by no means fixed. The main purpose of this classification is to ease the process of collecting the right information based on the needs of the problem owners for a given problem. It is possible to have different requirements for the same problem depending on the problem owners at any given time.

### 5.7.2 Processing

The process of modelling according to MAPIU2 starts by feeding the initial thoughts and needs for developing the model. Obviously these *needs* are then incorporated in the model. The model then presents the stakeholders with information. For *problem owners* this information is used for enhancing their understanding about the problem, hence, their understanding about the relevant issues in the system regarding the problem, their needs from the model, and the expected outputs from the model. For *experts*, information represents a measure of the validity of the model with regard to the new requirements from the *problem owner*. They use the new information and new needs in specifying which inputs they should use for the model. One may think that the *actual users* are only interested in the later stages of model building. However, their engagement in the development process from the beginning gives them the opportunity to better understand the model and why it is built the way it was built.

In MAPIU2 the modelling process is made up of two main factors; modelling and communication. If we consider stakeholders and the model as the two components in the MAPIU2 process, then modelling here means any thing to do with the model, such as specifications of the model, incorporation of such specifications, and experimentation. Communication is related to the mutual relationships between the different players: *problem owners*, *experts*, *actual users*, and the *model* itself.

Table 5.2 explains the different components mentioned here and how they work. Table 5.2 is divided into three main parts. First, the *modelling* part which deals with the model itself. Secondly, *communication* which deals with the interaction between the participants in the process. Lastly, *information* which explains what is meant by information in the context of MAPIU2. The discussion after that explains the components of the table in more detail.

<u>Modelling</u>

The modelling component is concerned with all the activities dealing with the model, such as development, data handling, and output processing. The modelling process entails both the conceptual model and the time-based model (see Figure 5.3). The following categories are the main steps taken with regard to the model. These steps are usually taken sequentially in a single modelling cycle, but not necessarily all of them:

- Specifications: the first cycle of modelling specifications represent the initial needs and ideas of the problem owners about the problem. From the next cycle on, specifications represent refined requirements from the problem owners and validation notes from the experts. As mentioned earlier refined requirements arise as a combination of information from the model and discussion with stakeholders. It should be stressed that requirements are not fixed and they change all the time based on a refined understanding of the problem.

- Incorporation: is for developing the model or modifying it based on the new needs and thoughts from the problem owners. Incorporation also includes validation notes for the experts. Incorporation is concerned with all the activities that add new features or alter existing ones for either the conceptual model or the time-based model (for example, structure, inputs, and outputs).

*Table 5.2: Details of the MAPIU2 Process*

| Modelling | | Features |
|---|---|---|
| | Specifications | Requirements + validation notes (based on problem owners and experts) |
| | Incorporation | Building or modifying the model according to requirements and validation notes |
| | Experimentation | Changing model's structure and parameters (sensitivity analysis and data requirements) |
| Communication | | |
| | Stakeholder <-> stakeholder | Communication amongst stakeholders (intercommunication) |
| | Stakeholder <-> model | Communication between any of stakeholder(s) and the model |
| Information | | |
| | Tangible | Quantifiable results or indicators arising from the model (usually after running the time-based model) |
| | Intangible | Non-quantifiable information from the model (during development or use) |

- Experimentation: is concerned with altering the model's structure and parameters and reflects on stakeholders' understanding. Experimentation is mainly conducted by the stakeholders or under their direct authorisation. Experimentation lies at the heart of the iterative process, as it represents a change in the model that has to be seen by the stakeholders. Experimentation is usually about what-if scenarios, identification of relevant variables, and conducting data collection when it is necessary (based on the previous two elements). As noticed in Figure 5.3 the three elements are tackled sequentially to avoid unnecessary complications.

*Communication*

Communication is an important issue in the iterative process as it represents the link between the participants of the process. As can be seen from Figure 5.3 there are no specific rules of communication, which means problem owners, for example, can feed their needs and ideas directly to the model or via the other two types of stakeholders, and this goes for the rest. It will be more beneficial for the stakeholders to communicate with the model in a route that is suitable to them. That is, the communication process can be carried out regardless of geographical restrictions and making use of any technological enablers of communication. Communication is divided into two categories; stakeholders-to-stakeholders communication and stakeholders-to-model communication. The two categories are defined below:

- stakeholders-to-model: is communication between the stakeholders and the model where the model is either a destination where requirements and needs are fed into the model (such as in the case of incorporation), or it could be a source where information is retrieved form the model as in experimentation results.
- stakeholders-to-stakeholders: is communication that is between the stakeholders and not directed to the model. The model could be used as a means of communication but not a source nor a destination. Note that this communication is mutual. For clarity and to be able to differentiate between the two terms from now on, stakeholders-to-stakeholders communication will be named *intercommunication* and stakeholders-to-model communication will just be named as *communication*.

*Information*

It is felt important to define what is meant by information in the context of this research (see Figure 5.3). Information in MAPIU2 is any feedback that is retrieved by any of the stakeholders from the model. Information here is divided into two categories; *tangible* information and *intangible* information. Tangible information is quantifiable such as output figures from the model or even animated behaviour in the model. The main principle for this type is the fact that it is gathered after the model is run (i.e. incorporation of the time factor in the model) and this information is purposefully retrieved from the model. Tangible information is mainly used for evaluative study and direct experimentation and what-if questions. Intangible is not so easily detectable information or it could be non-quantifiable. This type is not restricted to any modelling stage and usually it is not necessarily retrieved intentionally from the model. An example of intangible information can be seen in the ABCSim experience (Chapter Four) where health economists gained more ideas about the courses of the different treatment combinations in the trial during the model building process. Intangible information is about understanding the structure and the behaviour of the system under study.

## 5.8 Summary

This chapter starts by presenting a brief introduction relating to the use of MAPIU in the ABCSim example, discussed in Chapter Four. The main objectives of this chapter were to identify the weaknesses in MAPIU, establish some requirements for the modifications, and incorporate any required modifications in the framework.

Section 5.2 provides the main factors for analysing MAPIU. Analysis is based on two sets of factors; factors related to understanding in general and factors which are related to modelling for understanding specifically. Section 5.3 provides an analysis of MAPIU based on the ABCSim approach. The main theme of the analysis is drawing any correspondence between the framework and the steps taken in the ABCSim experience. Section 5.4 discusses the main missing ingredients in MAPIU. This section represents a critical evaluation stage for MAPIU, it concentrates on the problem of the framework with regard to problem understanding. The missing ingredients identification is based on the two main components of the framework, which are the 'stakeholders' component and the 'modelling' component. The section also goes into defining the two components in more detail. Stakeholders are divided into three types. Those types are *problem owners*, *experts*, and *actual users*. The modelling component is divided between the *model building* process and the *modelling/model use* process.

Section 5.5, presents a set of requirements for modifying the approach to achieve the objectives of enhancing stakeholders' understanding and intercommunication. Requirements are also divided in the same way between stakeholders and modelling. Stakeholder based requirements concentrate on defining the different interrelationships between the different players and the model. Requirements for the modelling component are based on defining the different steps throughout the modelling process and how they are fitted to cope within the overall iterative process. Another modification added to the modelling component is changing the term "computer model" to "time-based" model to cope with the essence of MAPIU.

Section 5.6 translates the requirements from the previous section and incorporates them in MAPIU. The same pattern is followed in this section of highlighting the stakeholders' component and the modelling component. At the beginning, modifications with regard to the stakeholders' block were added, followed by modifications for the modelling block.

In section 5.7 both sets of modifications in the previous section are joined in Figure 5.3 on page 126 to show the overall modifications to MAPIU, renamed MAPIU2. Section 5.7 presents the overall picture of MAPIU2 in terms of structure and process. MAPIU2 represents an iterative process between stakeholders and the model. MAPIU2 is divided into two main steps; initialisation and processing. Initialisation is based on defining the different stakeholders and their interrelationships amongst themselves and with the model.

Process is how these participants interact with the modelling through the different communication links exchanging information. This structure is tested in the next chapter.

# Chapter Six

# 6 Chapter Six: The LiverSim Experience

## 6.1 Introduction

Chapter Five represented MAPIU2 as an iterative modelling process. This chapter presents how MAPIU2 works in action. The chapter presents a testing platform for the proposed approach and draws a final analysis from it. The main orientation of this chapter is similar to that of Chapter Four, which is based on providing a typical healthcare system to examine how MAPIU2 would tackle it. The analysis will be based on the components of MAPIU2 presented in Chapter Five. The model looks at the stakeholders' side by identifying the main players in the problem (initialisation phase). As with regards to the modelling side, concentration is on ways to handle 'what-if' experimentation and data collection issues (processing phase). The case study used in this chapter is related to the management of liver transplantation. The main issues tackled in this problem are related to the economic evaluation of liver transplantation and examining different policies for prioritisation of the patients' waiting list for transplantation.

### 6.1.1 Objectives of the Chapter

The main objective of this chapter is to examine the features added to the proposed framework in Chapter Five. The results should calibrate the final assessment of the framework by defining its strengths and weaknesses. This framework will not represent the "Holy Grail" for healthcare decision makers but may help them reach an acceptable understanding of the problem they are facing. This chapter provides assessment results of how the proposed framework helps to achieve better understanding and means of communication.

### 6.1.2 Outline of the Chapter

The following section presents a brief introduction to the process and technology of Liver Transplantation and the problems associated with it. In addition, the section explains why modelling is needed for tackling such problems. Section 6.3 gives a general overview of the model built for this case study (LiverSim). Section 6.4 provides the model's details, specifically about the computer model with regard to input/output manipulation and what-if experimentation. Section 6.5 presents the communication issues in MAPIU2 and how it was applied in LiverSim. Section 6.6 presents the information dimension in MAPIU2 and how tangible and intangible information helped in enhancing stakeholders' understanding. Section 6.7 gives an overall summary for the chapter.

## 6.2 Liver Transplantation

There has never been a formal study to examine the efficiency of liver transplantation. However, there is a growing body of evidence to suggest that for certain types of liver diseases transplantation offers improved survival and quality of life for the individual recipient (Bryan et al, 1998; McMaster and Dousset, 1992). On the other hand, liver transplantation represents a highly complex medical technology which is intensive in resource consumption (Bryan et al, 1998; Bonsel et al, 1990). No evaluative study has yet attempted to consider the potential influence of a centre's liver transplantation selection policy upon the long term survival on patients with end stage liver disease, and the impact of such changes in survival in influencing the overall cost effectiveness of this technology. This study has applied a simulation modelling approach to address these issues at the liver transplant unit at the Royal Free Hospital in the inner London region.

### 6.2.1 The Current Situation and Problems

The technology of liver transplantation has developed rapidly within the last two decades. In 1980, fewer than 50 liver transplants were performed throughout Europe (Neuberger and Lucey, 1994). However in 1997 over 600 liver transplants were performed in England and Wales alone (HERG, 1998). The liver transplant waiting list has increased considerably during this period. However, in recent years the supply of donor organs has remained relatively constant. This is in spite of the increased use of split liver transplantation, which allows one donor organ to be used for two smaller recipients, and livers from donors classified as marginal, for example non-heart beating donors and those over 60 years of age. Unfortunately, as a result of the shortage of donor organs, a substantial minority of patients on the transplant waiting list die before a donor liver becomes available (Neuberger, 1997). Given this situation, some decision criteria have necessarily to be employed to determine which patients should be given priority in receiving a donor organ.

The United States has a formal points system which of allocates donor liver grafts based upon the medical status of the patient (with sicker patients receiving a higher priority), the blood type compatibility with the donor organ and the length of time already spent waiting

(Pritsker et al, 1998). Patients are re-ranked on the list at every graft arrival. Unlike the United States, the UK has no formal criteria for the allocation of donor liver grafts. There is a broad agreement amongst transplant centres that any NHS eligible patients within the UK on the liver transplant waiting list who are unlikely to survive for more than three days without a new liver should be given urgent priority to receive donor liver grafts (Neuberger, 1997). Such patients form the super urgent waiting list. Patients are ranked on the super urgent waiting list according to the amount of time spent waiting and the blood group of the patient. Patients with the same blood group (A, B, or O) as the donor take priority over patients with a compatible (but not identical) blood group. If there are no patients on the super urgent list for whom a liver graft is available, then NHS eligible patients on the routine waiting list will be considered. The same criteria are used for routine patients as for super-urgent patients; that is, length of time on the waiting list and blood group compatibility.

In a review of the criteria for prioritisation of patients on the waiting list for transplantation of all solid organs, Jonasson (1989) argues that "Length of time on the waiting list is the least fair, most easily manipulated and most mindless of all methods of organ allocation".

The reasoning behind this argument stems from the observation that as the period on the waiting list is extended, the health of the patient tends to deteriorate. Traditionally, such patients are given the highest priority based on the fact that they have waited for the longest period of time and they may not otherwise survive. However, from the point of view of cost effectiveness, this policy may not be optimal since such patients tend to have a lower rate of success than that of less severely ill patients who have been waiting for a shorter time period. In a study undertaken in the USA of patients undergoing liver transplantation (Williams, 1987), it was found that patients receiving intensive care prior to the time of transplantation had only half the survival rate at 12 months of a group of patients who were well enough to be waiting at home (41% versus 83% 12 month survival respectively). In addition, the total costs of transplantation for the less severely ill patient group were only 43% of the total costs for the critically ill group. A very recent study, also in the USA, found that patients who were in intensive care immediately prior to the time of transplantation had 42% greater mean resource utilisation than that of patients who were not in intensive care (Showstack et al, 1999).

### 6.2.2 The Case for modelling

From the above discussion it could be considered desirable to find some ways for prioritisation of the patients in a way that is considered fair by all parties involved in the process. To achieve such an objective of finding such a golden rule is almost impossible. Firstly, it is very difficult to measure it quantitatively. There is no absolute definition of what could be fair for every body. For example, is it fair to give priority to the sickest patients with relatively smaller survival prognosis or give it to less sick patients but with higher survival prognosis? There is no answer to this question and it is unfair to provide a generalised answer for it. The answer to this question depends on the particular situation and the circumstances faced by the decision makers and the contributing factors. What is needed is a tool to examine different policies for manipulating the waiting list and their likely impact on the system and the involved stakeholders.

From the discussion in the first two chapters it may be easy to deduce that modelling is a suitable way to undertake such a process. However, the technology of liver transplantation for the treatment of end stage liver disease represents a complex clinical situation which changes over time. Analytical approaches such as decision trees and Markov modelling fell short of giving a reliable picture in order to examine the real situation with all its robust features. Discrete Event Simulation represented a stronger candidate, and that is for the reasons mentioned in Chapter Two.

### 6.2.3 Background of the System

This section gives a brief description of the mechanism of the system to be modelled. It represents the initial understanding of the stakeholders regarding the Liver Transplantation process. All patients enter the system with end stage liver disease (ALD or PBC). Each patient is then assessed in order to determine his or her suitability for transplantation. If the patient is selected for transplantation then he/she joins the waiting list for transplantation. Patients are classified as either routine or super urgent listing. As indicated previously super urgent patients have priority for a donor liver over routine patients. During the candidacy phase (the period whilst the patient is waiting to receive a new organ) complication(s) may occur. These complications may be fatal or they may change the value of the clinical variables that predict estimated survival following transplantation. For routine patients waiting at home, the advent of complications may mean that hospital in-patient admission(s) are required. If a suitable donor organ becomes available, the patient is transplanted. If the patient survives the peri-operative period, he/she may survive without developing complications. The patient may develop complications post-transplant that require either one or a series of post transplant admissions to hospital. The patient may require re-transplantation (and hence loop back through the system to the assessment stage) or die at any time as a result of graft failure.

If the patient is rejected for transplantation, then the control is the pattern of care for patients receiving treatment for their on-going liver disease. This structure is far less complex than that for patients going forward for transplantation. Patients with liver disease require constant monitoring through regular out-patient visits and may develop complications which require in-patient admission(s). As in the transplantation system, patients enter the system with end stage liver disease with ALD or PBC.

The simulation model was applied to patients waiting for transplantation with two main types of liver disease; alcoholic liver disease (ALD) and primary biliary cirrhosis (PBC). There are two reasons for choosing these two diseases. Firstly, patients with these diseases represent the majority of liver transplants currently undertaken in the Royal Free Hospital transplant centre and more generally in the UK (O'Grady and Williams, 1993). It is worth noting that the UK is divided into seven transplant centres, where each is managed by a central hospital such as the Royal Free Hospital. Secondly, several published and validated prognostic indices are available for these diseases which can be used to predict survival in the absence of transplantation given the values of the clinical variables specified (Anand et al, 1997; Hughes et al, 1992; Dickson et al, 1989).

## 6.3 The LiverSim Model using MAPIU2

LiverSim represents the first test-drive for MAPIU2 after it has been refined in Chapter Five. This section shows how MAPIU2 is used for modelling the above problem presenting how the model was processed from an overall perspective, concentrating on the initialisation and processing aspects. The following sections discuss the technical detail and the components of the process as mentioned in Table 5.2 on page 129. The main objective of this particular modelling exercise is to enable stakeholders to understand the situation and experiment with the different policies with regard to prioritising patients on the waiting list for the purpose of economic evaluation.

### 6.3.1 Initialisation

According to MAPIU2 the first step is to classify the stakeholders involved. In messy situations an initial conceptual model could be used to assist at this stage, (see Chapter Five). In this particular case the LiverSim project is funded by a research council who is not particularly involved with the problem, whilst the idea is originated from health economists with the help of clinicians who specialise in the field of liver disease. This leaves us with two types of stakeholders (health economists and clinicians) to classify. Given the above-mentioned objective of the project, it was relatively straightforward to realise that health economists are the *problem owners*, which means the model should help them in taking decisions (see Table 5.1 on page 126). Their decision in itself represents a recommendation to other healthcare professionals on how to economise their resources. Yet, because in this case they are taking decisions primarily based on the simulation results, then in this case they represent the problem owners. It must be noted that as much as it is important to identify the different stakeholders this classification or identification is open to change at any time during the modelling process whenever it is necessary. Based on the definitions in Table 5.1 clinicians represented the *expert* type of stakeholders because of their detailed knowledge of the system and because they are managing the day-to-day operations. On the other hand, clinicians do not use outputs from LiverSim directly in their day-to-day practice, which excludes them from being part of the problem owners. They may, however, be concerned with the economy of the transplant process overall as the decision arising from it may indirectly affect the resources available for them to carry out the transplantation procedure. Given the fact that health economists are going to use the model for further analysis then this makes them also *actual users*.

Table 6.1 shows the stakeholders' classification for LiverSim and their corresponding features with reference to Table 5.1 on page 126. As mentioned earlier extra care should be taken when different types of stakeholders possess close classifying features. It is possible, for example, to have different types of stakeholders needing to take decisions based on information retrieved from the model.

*Table 6.1: Classified Stakeholders and Corresponding Features*

| Class | Stakeholders | Features |
|---|---|---|
| Problem owners | Health economists | • High interest in solving the problem<br>• Use model's results for further decisions |
| Experts | Clinicians | • Detailed knowledge of the system<br>• Detailed decision makers (day-to-day) |
| Actual users | Health economists | • Will work directly with model<br>• Process and interpret model's results |

In cases like this concentration should be directed towards other aspects such as who pays for the model, who benefits more, or who will suffer more from the failure of the system. It is, on the other hand, possible to have more than one type of stakeholder as problem owners if they share the same needs from the model. This is why it is best to use the model for classifying the stakeholders as it enhances the understanding of each stakeholder and helps to put the point across to others to realise who is more involved. The same principle may apply to experts and actual users, even though the latter could be difficult because, according to MAPIU2 the model's facilities should be built around the requirements of the actual users and different types may have different requirements of the model's interface.

*Table 6.2: Components of MAPIU2 Process*

| Modelling | | Features |
|---|---|---|
| | Specifications | ▪ Initial *specifications* from Health Economists (HE): building a Liver Transplantation (LT) model and Liver Disease (LD) model for comparison and economic evaluation (see description in system's background)<br>▪ Prioritisation criteria for the waiting list (for comparison and economic evaluation)<br>▪ Validation is related to changes of the structure of the model based on HE's changed requirements and views of clinicians with to the model and its relevance to the system |
| | Incorporation | ▪ Iterative ACD's for LT and LD as conceptual models<br>▪ Time-based model for LT and LD based on the ACD<br>A Simul8 model for the structure (patient flow)<br>Input variables: durations, costs, prognosis for the interface (using Visual Basic)<br>Output responses (net survival, net cost, and discount) |
| | Experimentation | ▪ Prioritisation criteria (what-if, Sensitivity analysis)<br>▪ Variables identification (relevant)<br>▪ Data collection (based RFH data) |
| Communication | | |
| | Stakeholders <-> stakeholders | ▪ Communication between HE and clinicians mainly for identifying relevant variables and model's structure |
| | Stakeholders <-> model | ▪ Communication between HE, clinicians and LiverSim for debating and experimentation |
| Information | | |
| | Tangible | ▪ Results from the each run |
| | Intangible | ▪ Understanding the behaviour of LD and LT<br>▪ qualitative issues such as fairness of allocation of livers |

### 6.3.2 Processing

According to MAPIU2 processing is related to how the stakeholders interact with the model and with each other in an iterative manner throughout the modelling process. It represents the process of modelling during both the conceptual modelling phase and the time-based modelling phase. In this particular case processing is based on interactions between health economists, clinicians, and LiverSim through specified routes of communications. The different components involved in the processing of LiverSim – guided by Table 5.2 on page 129 – are shown in Table 6.2. The components in Table 6.2 are introduced and refined throughout the process and not necessarily in the same iteration or cycle of modelling. Figure 6.1 represents a static structure of the overall modelling process for LiverSim with the specified interrelationships – with reference to MAPIU2.

As can be seen, 'health economists' and 'clinicians' are allocated their roles as part of the stakeholders. More detailed discussion about these components are given in the following sections.

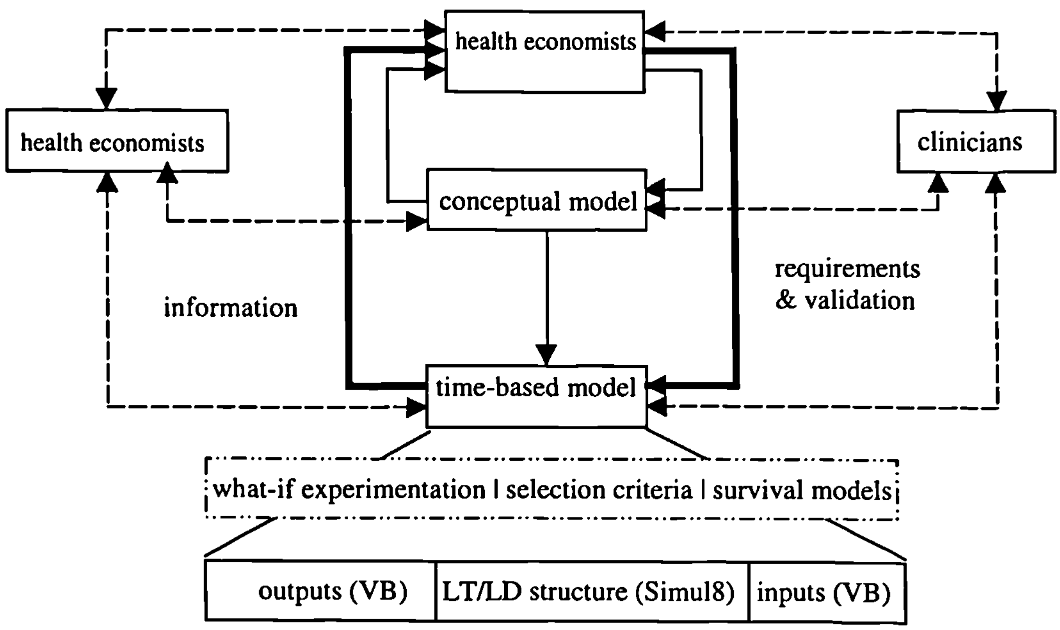



*Figure 6.1: LiverSim Overall Modelling Process*

## 6.4 Modelling Issues

This section describes in detail the development of the conceptual model and the time-based model using MAPIU2. Concentration here is on how these models are developed by incorporating the specifications of the stakeholders in the iterative process. Details of the communication process and the type of information and understanding retrieved from the model are given in the following sections.

### 6.4.1 The Conceptual Model

According to MAPIU2 the modelling process starts by building a conceptual model, then the model is expanded to the time-based model. As in the ABCSim model, an Activity

Cycle Diagram was used as the conceptual modelling method for the LiverSim project. Figure 6.2 shows the ACD for the Liver Transplantation model. The model given here represents the semi-final version of the conceptual model. The iterative process took eight versions to finalise this model (Appendix B). Figure B.1 shows the initial ACD of LiverSim which was drawn as a starting point for debate between the health economists and the clinicians. On the other hand, this ACD represents the first point of information retrieved from the model for enhancing the stakeholders' understanding. As can be seen in Figure B.2 through to Figure B.7 that the state of the model was continuously changing reflecting the evolution of the understanding stakeholders. This does not necessarily means the ACD is getting more complex as the model development is progressing. For example, there is a noticeable decrease in complexity from Figure B.5 to Figure B.6 where the rejected patients are allocated to the liver disease model in Figure 6.3. It must be noted that information retrieved from the model at this point are mainly intangible and related the understanding of the structure of the system rather than evaluating specific policies.

The final version of the ACD model (see Figure 6.4) was derived mainly as the health economists evolved their understanding with a help of the clinicians for validation. An explanation of the different activities in the model will be given with the time-based model; however, a general description of the ACD may help to give an overall understanding of what is going on. Firstly, it is important to know that 'gate1' and gate2' are imaginary entities for organising the arrivals of patients and livers to the model. The straight lines represent the movement for patients throughout the model, while the dashed line shows the stream of donated livers where both lines meet at transplantation.

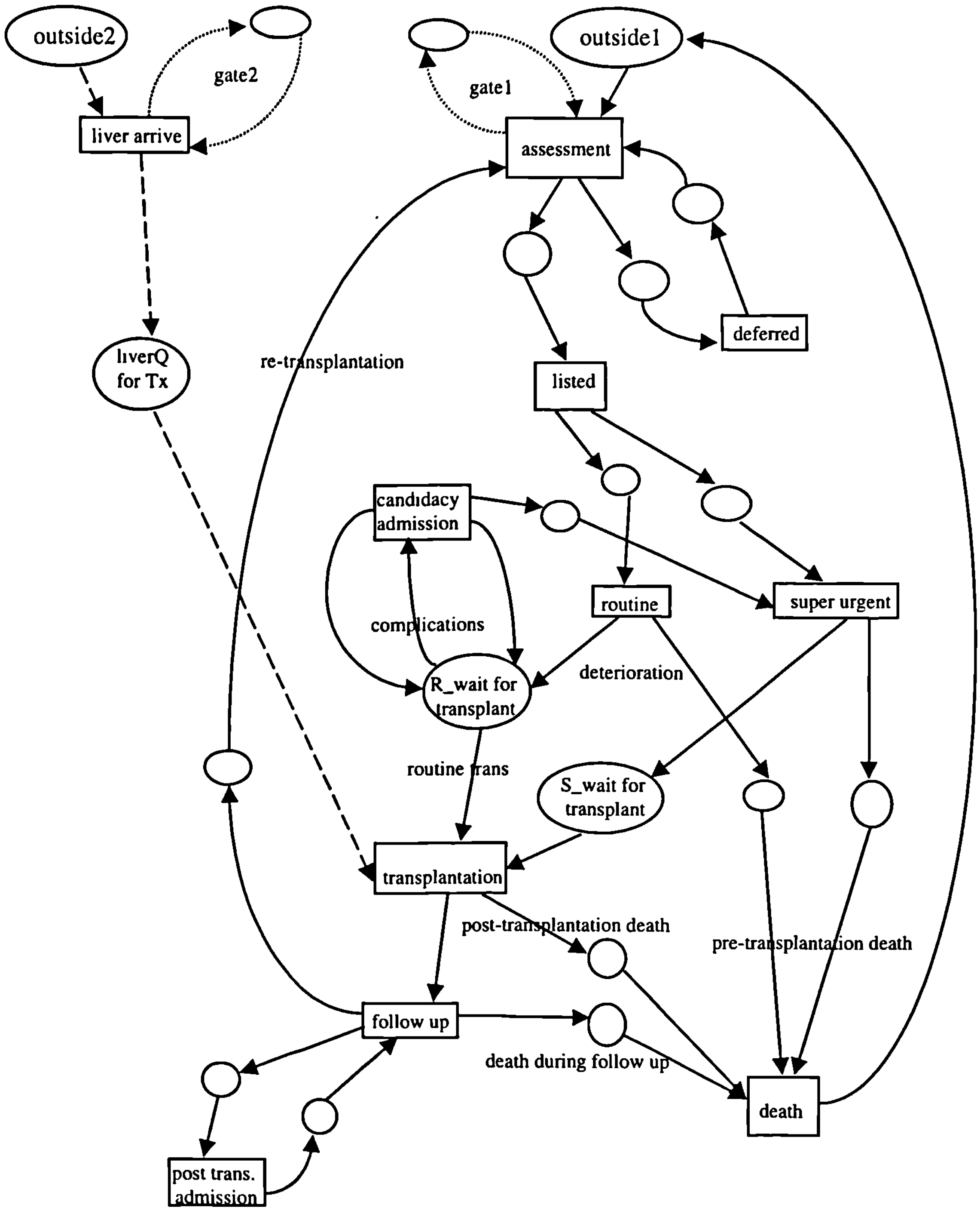



*Figure 6.2: ACD for the Liver Transplantation Model*

All states for patients before the transplantation phase are either parts of the assessment phase – where patients are assessed for the suitability of transplantation – or the candidacy phase – where selected patients wait for transplantation. On the other hand, states after transplantation belong to the post-transplantation phase – follow-up period of two years and normal survival after that. It is also worth noting that 'death' is the last event in the system and all entities are supposed to end there. It is possible that some patients may die before they are transplanted, so the model makes room for the assumption that some patients may die while they are waiting for transplantation for various reasons.

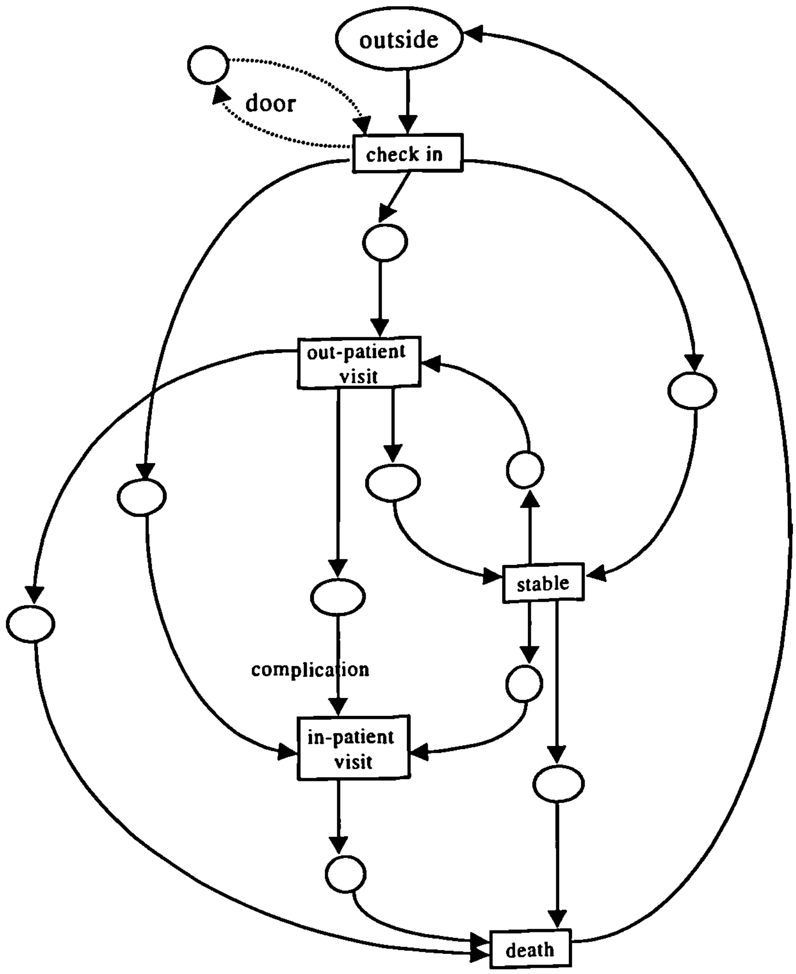



*Figure 6.3: ACD for the Liver Disease Model*

Figure 6.3 shows the ACD for the Liver Disease Model. This model represents patients with liver disease who are not suitable for transplantation. The entity 'door' is another imaginary entity that regulates the arrival of patients. As can be seen, this model is less complex than the previous one, because it does not contain complicating factors such as resource competition factors. The main purpose of the second model is to provide some insights into resource use by patients who are not transplanted, so that they can be compared with resources used by transplanted patients.

The development of the Liver Transplantation model and the Liver Disease model followed the iterative behaviour of MAPIU2. At some stage both models were combined in one ACD model. However, for clarity the two models were separated as stakeholders' understanding about the system started to mature.

One of the main changes in the model – which demonstrates an enhanced understanding by the stakeholders – that was made during the conceptual modelling is deleting the 'super urgent' patients in Figure 6.2. This decision was taken for two reasons. Firstly, due to the severity of their condition, super urgent patients are relatively inflexible in the timing of transplantation. Typically, such patients will die within three or four days if a donor liver is not made available. Secondly, super urgent patients generally receive very different patterns of care from routine patients, both in terms of the quantity and type of resources used and in terms of the timing of treatments administered.

This understanding was reached after a number of dialogues that have taken place between health economists and clinicians using the model (ACD). This example demonstrates how MAPIU2 can be quite informative even at the early stages. The main concept is not about including all the system's entities in the model to ensure its validity. It is rather about using the model to validate stakeholders' understanding about the system. Figure 6.4 shows the final ACD for the transplant model after deleting the super urgent patients from the model. More detail for the process of understanding are given in sections 6.5 and 6.6

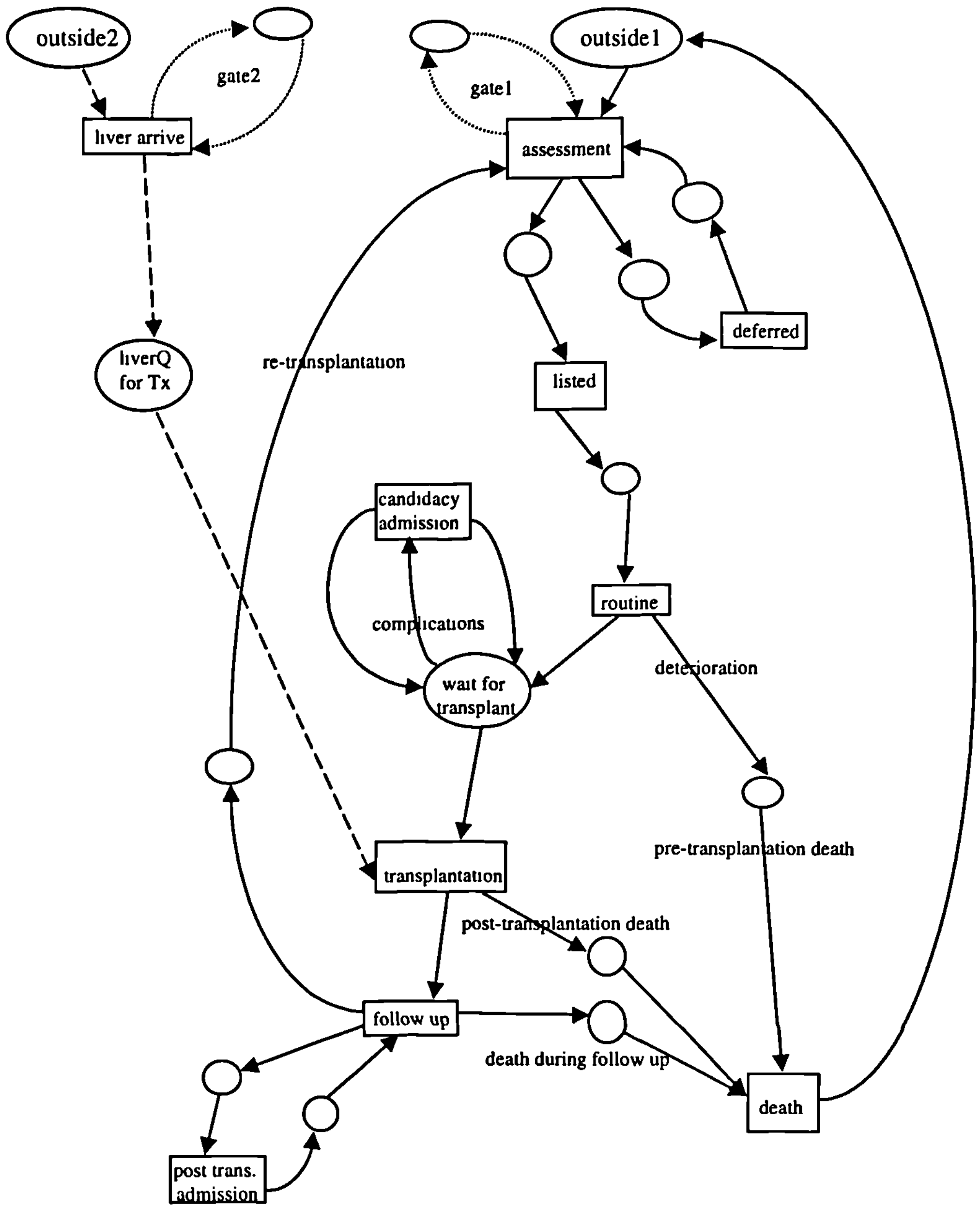



*Figure 6.4: The New ACD for the Liver Transplantation Model*

### 6.4.2 The Time-Based Model

According to Figure 6.1 on page 144 after reaching an agreed conceptual model in MAPIU2 the next stage is to transfer to the time-based model. LiverSim followed the same methods in developing the time-based model as in the ABCSim model, which means the time-based model for LiverSim is developed using Simul8 and Visual Basic. The Simul8 model provides the structural details and the physical layout of the system. In other words, it portrays the pattern of care received by patients from the moment they enter the system until they die. It is also responsible for the simulation engine making sure it depicts the structure agreed by the stakeholders. Visual Basic was used to develop the interface for input/output manipulation and what-if experimentation to enable stakeholders to feed the model with their requirements and retrieve information in a manner that is understandable to the stakeholders.

Even though the two models are still separated in the time-based model, both models are actually run simultaneously in Simul8. This helped in getting the results quicker, rather than running each model at a time. Also results are displayed simultaneously in LiverSim. Figure 6.5 shows the liver transplantation model while Figure 6.6 shows the liver disease model. Both models are represented on the same screen in Simul8.

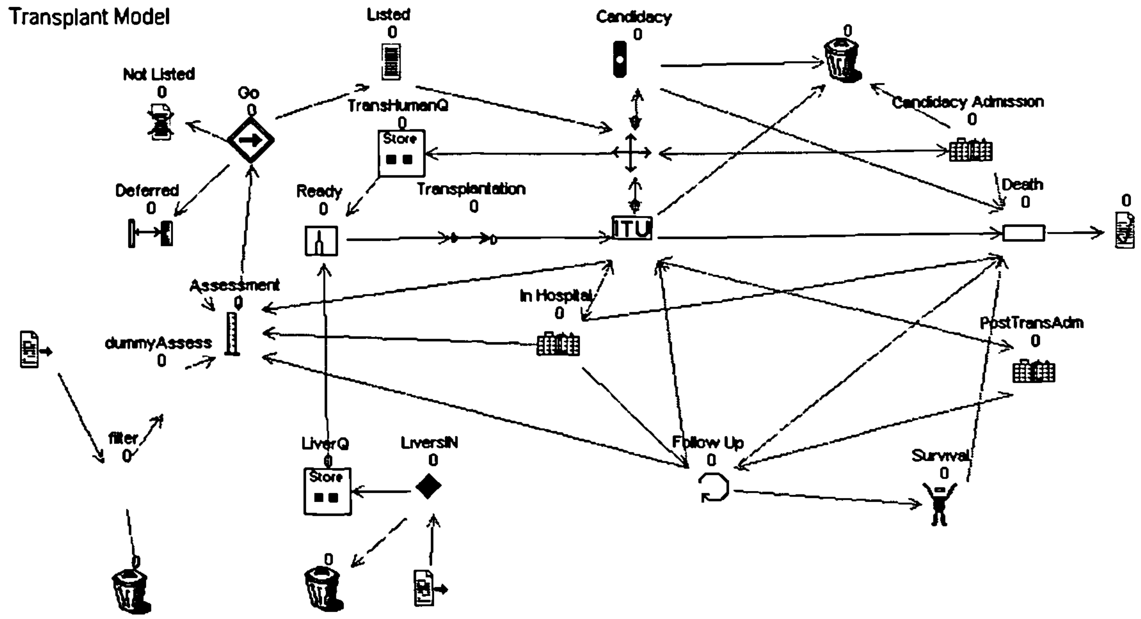



*Figure 6.5: Simul8 Representation of the Liver Transplantation Model*

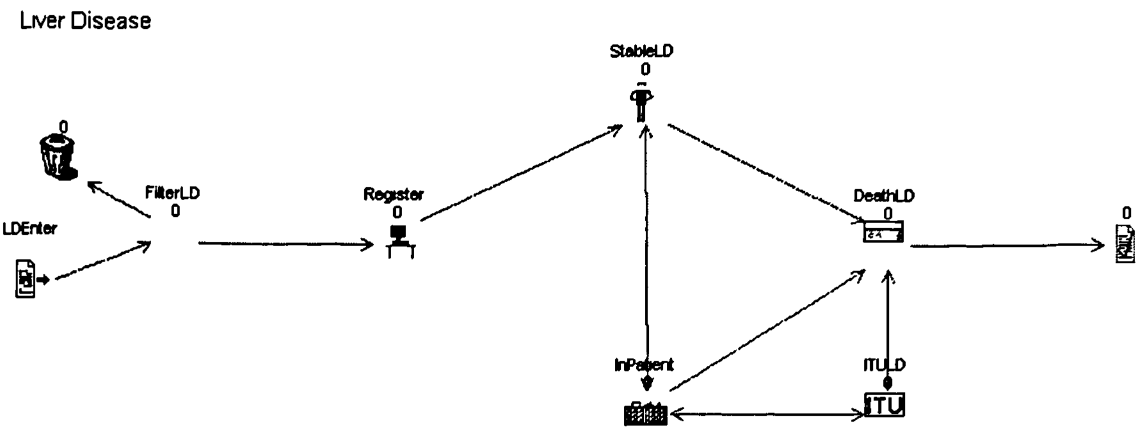



*Figure 6.6: Simul8 Representation of the Liver Disease Model*

There are some differences between the Simul8 models and the ACD models, and that is for technical reasons. For example, it was not possible to put one idle state for all people waiting for transplantation. That is because there are some patients who would be waiting at home (Candidacy), some other patients may be admitted to the hospital for any sort of complications (Candidacy Admission), and there is another type of patient who would be admitted to the intensive care unit (ITU) if their health state is severe. Bear in mind these situations change continuously. Although these may be regarded as waiting states, they have active features with predefined durations, which makes them activities in a technical sense.

There are also some logical "bins" located in some parts of the screen and those represent termination of entities from the model. For example, the first bin from the left in Figure 6.5 and the one in Figure 6.6 receive the patients who would arrive to the model after the maximum number of recruited patients is reached. In Figure 6.5 the second bin from the left is for livers that are rejected. This is used to model livers when there are no matches for them. The structure of the model requires patients to be prioritised and selected instantly for transplantation. However, that was not technically possible in Simul8. To cope with this, selected patients had to be cloned, the original clone is sent to the third bin (top right in Figure 6.5), while the new clone is sent to the transplantation procedure. Table 6.3 shows explanations of the different nodes in Figure 6.5 and Figure 6.6.

*Table 6.3: Details of Simul8 Representation of the LiverSim Model*

| | |
|---|---|
| Entry | The point where all patients enter the model |
| DummyAssess | A logical point for establishing patients' individual properties |
| Assessment | Assess patients' suitability for transplant |
| Go | To distribute patients based on assessment results |
| Deferred | Deferring transplant decision |
| Listed | Listing for transplant |
| Candidacy Admission | Hospital admission during candidacy phase |
| Candidacy | A patient being at candidacy phase in a stable state |
| Transplantation | The transplantation procedure |
| Not Listed | Rejected from transplantation |
| PostTransAdm | Hospital admission after transplantation |
| Follow Up | Two years medical follow up after transplantation |
| Survival | Being alive after the follow up period |
| LiverQ | Logic state for searching for the best match |
| In Hospital | Being in the hospital after the transplantation procedure |
| ITU | Intensive care unit |
| LiversIN | The point where livers enter the system |
| TransHumanQ | Where the best matched is transferred from the waiting list |
| Ready | A patient being ready for transplantation |
| LDEnter | The point where liver disease patients enter the model |
| Register | Registered as being liver disease patient |
| StableLD | A liver disease patient at a stable state |
| InPatient | In-patient hospital admission |
| ITULD | Intensive care for liver disease patients |
| Filter | Stopping extra patients from entering the system |

### 6.4.3 Inputs to the Model

The previous discussion concentrated on the model's structure in Simul8. The discussion in this subsection and the following is directed to the interface, which was built using Visual Basic. Figure 6.7 represents the main window for LiverSim. The 'Transplanted" button leads to the inputting of values for the liver transplantation model, 'Liver Disease' is for the liver disease patients model, 'Selection Strategies' is for defining different policies for patients prioritisation, 'Pooled Results' for combined liver transplantation and livers disease results, 'Exit' for exiting the model.

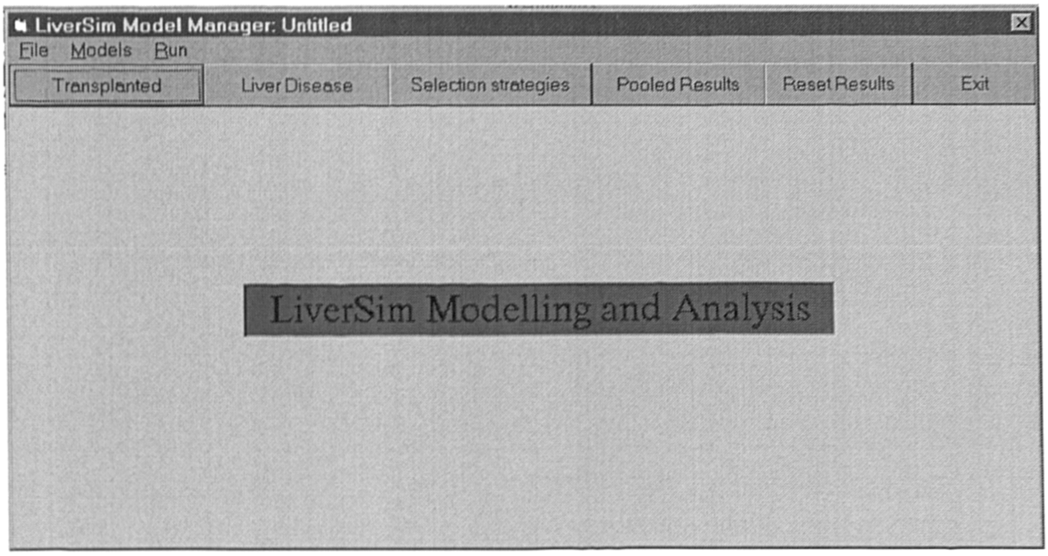



*Figure 6.7: LiverSim Main Console*

Input variables for LiverSim varied from identifying the patient's types, length of stays, resources and costs, probabilities of tests and treatments. Figure 6.8 provides an example of how data is entered in the LiverSim model during the assessment phase. As can be seen the window is quite similar to the interface in ABCSim.

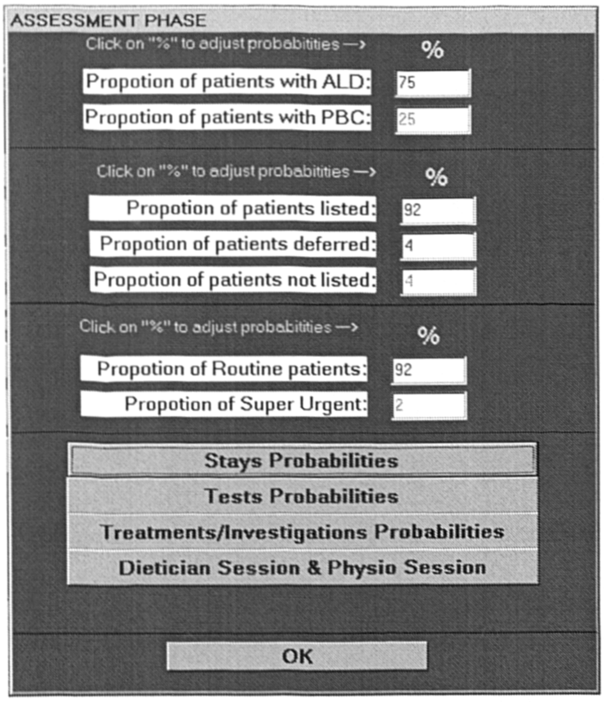



*Figure 6.8: An Example of an Input Window in the LiverSim Model*

Table 6.4 and Table 6.5 present the input variables associated with both the liver transplantation and the liver disease model. Some variables have the sign [£] associated with them which means that there is cost involved with these particular variables, for example 'length of stay' in a hospital. It should be noted that these costs are assigned as per unit, for example the 'length of stay' costs are per day, whilst drugs costs are per unit of drugs or per session in the case of, for example, physiotherapy sessions. Some other variables have a lump sum cost, such as having a specific test.

In Table 6.4 severity group means that all patients are divided into four groups where 'group A' represents patients with the least severe liver disease, whilst 'group D' represents patients with the severest liver disease. The reason for having some of the input variables categories depending on the group is because each group may have different sets of requirements, at least in terms of quantity.

### 6.4.4 Survival Prognosis

One of the main sections for input variables is the survival probabilities for the post transplantation phase and survival in the absence of transplantation. Usually these probabilities are developed for each patient based on their clinical status at defined time intervals following their inclusion on the transplant waiting list. There are several well-validated prognostic models available for estimating survival in the absence of transplantation (Hughes et al, 1992; Dickson et al, 1989; Anand et al, 1997). These models predict survival on the basis of the values of several clinical variables immediately prior to transplantation. The Royal Free model for PBC patients (Hughes et al, 1992) and the Anand model for ALD patients (Anand et al, 1997) have been incorporated into the simulation to provide estimates of survival in the absence of transplantation. This was based on stakeholders' requirements for modelling survival predicators.

*Table 6.4: Input Variables Associated with the Liver Transplantation Model*

**Assessment phase**
- Assessed with (PBC or ALD)
- Listed patients (listed, deferred, rejected)
- Severity groups (A, B, C, D)
- Length of stay based on groups [£]
- Assessment out-patient visits: no. of visits (0,1,2,3) [£]
- Investigations and tests in: probabilities based on groups [£]
- Physiotherapy sessions in assessment phase (1, 2 or more sessions): probabilities based on groups [£]
- Dietician sessions in assessment phase (1,2,3: sessions) [£]
- Length of time between end of assessment and listing: probabilities based on groups

**Candidacy Phase**
- Probability of candidacy admission (PBC, ALD)
- Inter-candidacy admissions
- Candidacy admission length of stay [£]

**Transplant phase**
- Length of stay in transplant phase [£]
- Length of transplant operation [£]
- Investigations and tests in transplant phase: probabilities based on groups [£]
- Drugs in transplant phase: probabilities based on groups [£]
- Physiotherapy sessions in transplant phase [£]
- Dietician sessions in transplant phase [£]

**Post-Transplant phase**
- Probability of one or more post-transplant admission [£]
- Frequency of post-transplant admissions
- Post-transplant admission length of stay [£]
- Drugs during post-transplant admission: probabilities based on groups [£]
- Investigations and tests during post-transplant admission: probabilities based on groups [£]
- Proportion of patients re-transplanted (PBC, ALD)
- Out-patient visits in follow up phase [£]
- Investigations and tests at follow-up phase: probabilities based on groups [£]
- Drugs in follow up phase: probabilities based on groups [£]

*Table 6.5: Input Variables Associated with the Liver Disease Model*

***Liver Disease Data***
- Probability of patients with PBC or ALD
- Length of time between admissions
- Length of stay for admission reasons (diagnosis and treatment): [£]
  - Ascites
  - Malnutrition
  - Hepatocellular carcinoma
  - Sepsis including SPB
  - GI bleeding varices
  - GI bleeding non varices
  - Hepatic encephalopathy
  - Electroylte abnormalities
  - Alcohol withdrawal
  - Liver failure
- Frequency of out-patient visits annually [£]

It was agreed by the health economists and the clinicians that in order to estimate the probabilities of survival, serial data is required for the values of those clinical variables which are important in determining survival in the absence of transplantation. These variables include serum bilirubin levels, serum albumin levels, blood urea, prothombin time, the patient's age and the presence of ascites or spontaneous bacterial peritonitis. Similarly, where transplantation was assumed to occur at some fictitious point of time beyond the actual time of transplantation for an individual patient, the changing values of key clinical variables up until that fictitious time point are estimated using the same linear regression techniques and incorporated into the model.

### 6.4.5 Outputs from Model

The final output measures are divided into two classes. Firstly, identifying the cost-effectiveness of liver transplantation against no transplantation. Secondly, identifying the cost-effectiveness of the different policies for prioritisation of patients on the waiting list. Hence, the structural development of a simulation model should reflect the patterns of care received by patients referred for liver transplantation, and a subsidiary model should reflect the patterns of care received by patients receiving treatment (other than transplantation) for liver disease.

For each model there are the average life years and the average cost incurred by the patient. The average life for the liver transplantation model is calculated after the point of transplantation, whilst the average life for patients in the liver disease model is calculated from the point of registration. Average costs for both models are calculated from the point where the patient enters the model. Figure 6.9 shows how results are presented in LiverSim. This window provides combined results for both models as per a single run. Stakeholders can then take these results for analysis in spreadsheets for comparisons with other runs or configurations of the model.

### 6.4.6 Experimentation Issues

The previous two subsections discussed inputs and outputs of LiverSim and how they are incorporated in the interface. This subsection continues on the interface issues with respect to the facilitation of experimentation, which represents an important component in the MAPIU2 process. Experimentation in LiverSim included setting up a number of prioritisation criteria in the waiting list as what-if questions, how these questions were conducted in terms of sensitivity analysis, and what are the data requirements (see Figure 6.1 on page 144 and Table 5.2 on page 129).

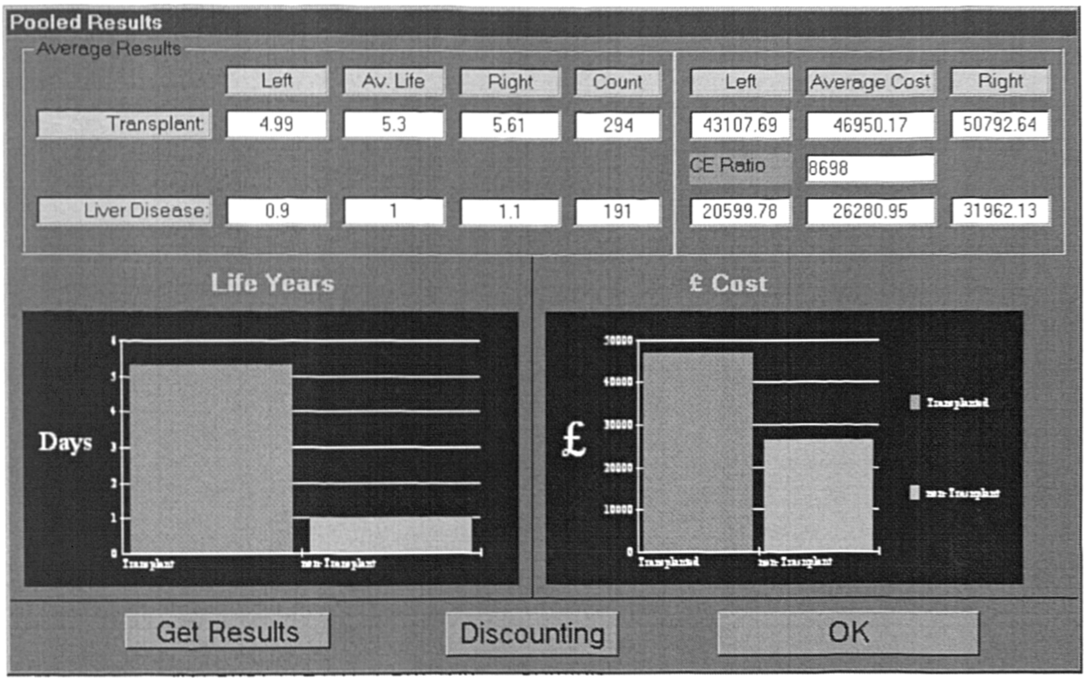



*Figure 6.9: LiverSim Output Presentation*

***Prioritisation Criteria***

As mentioned above, one of the main purposes of this model is to facilitate the economic evaluation of the different prioritisation criteria for patients on the waiting list. Based on Figure 6.1 on page 144 this point represents an important issue in MAPIU2 as it represents a dialogue between the involved stakeholders for identifying the most suitable prioritisation criteria and how it affects the system in one way or another. This section discusses the different proposed criteria and how they are incorporated in LiverSim.

Before discussing the prioritisation criteria, which are applied to suitable patients only, a background to the matching criteria ought to be given. Matching criteria are used to assess whether a patient is suitable for the available liver or not. Once all suitable patients are identified then the next step is prioritising them according to the criterion in use. The two main matching criteria currently used throughout UK liver transplantation centres are blood group compatibility and the body weight of the donor and recipient, the body weight acting as an indicator of the size of the donated liver. Any selection strategy employed in the model is constrained by the frequency of supply of donor liver grafts and the need to ensure that all donor liver grafts allocated are matched accordingly.

The variables incorporated into the model to reflect the matching criteria of recipients was based upon the characteristics of the ALD and PBC patients. Figure 6.10 shows how probability distributions for both matching criteria for donors and both types of recipients (ALD and PBC) are arranged in LiverSim. These criteria are assigned as attributes for both donors and recipients.

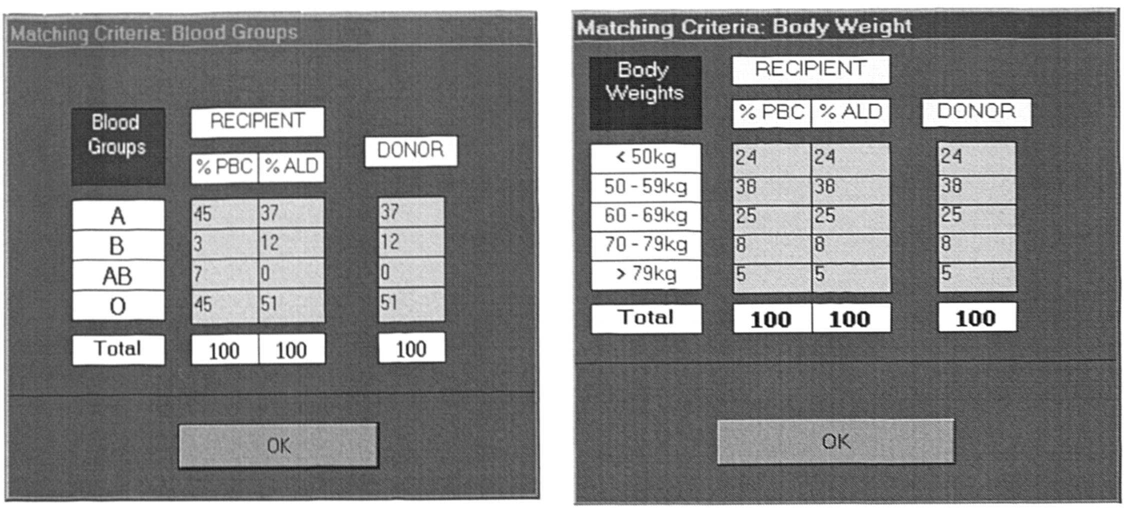



*Figure 6.10: LiverSim Windows for Blood and Body Weight Matching*

Once patients are matched and classified to be suitable, selection criteria are used to rank these patients for priority of transplant. A number of alternative selection criteria for liver transplantation are then evaluated in terms of their incremental cost effectiveness ratio. Incremental costs were defined in terms of the total costs with transplantation minus total costs without transplantation, and incremental effectiveness was defined in terms of life years gained with transplantation minus life years gained without transplantation (see Chapter Four). The selection criteria in Table 6.6 were chosen for evaluation by the health economists in collaboration with clinicians.

*Table 6.6: Selection Criteria for Transplantation*

| | |
|---|---|
| High wait | Patients on the waiting list in order of highest time spent waiting |
| Low wait | Patients on the waiting list in order of lowest time spent waiting |
| High age | Patients on the waiting list in order of highest age at time of listing |
| Low age | Patients on the waiting list in order of lowest age at time of listing |
| High PI | Patients on the waiting list in order of highest clinical severity |
| Low PI | Patients on the waiting list in order of lowest clinical severity |
| Groups | Patients on the waiting list by clinical severity groupings |

The 'High wait' selection policy represents the reference policy for comparative purposes since this policy represents the system that presently operates throughout the UK for routine patients. The 'Low wait' policy represents the reverse of the current one. For the 'High PI' and 'Low PI' selection policies, clinical severity was defined in terms of prognostic indices without transplant at the time of listing, with patients with a poorer prognosis defined as more clinically severe than patients with a better prognosis. For the final selection policy (Groups) patients were first ranked in order of clinical severity as previously defined and then placed in one of four groups (A, B, C or D) where 'group D' represented the most clinically severe group. Patients in 'group D' were then given a lower priority for a donor organ than patients in 'groups A, B or C'.

*Sensitivity Analysis*

After identifying the relevant experimental factors, the selection criteria in this case, then the next stage in MAPIU2 is to conduct some sensitivity analysis. As the prioritisation criteria are changed, the order and/or timing of transplantation for the cohort of patients changes. These changes are then investigated by their impact upon the estimated net life expectancy, average net costs and overall cost effectiveness of the transplantation programme. Figure 6.11 shows how the different prioritisation criteria were incorporated in LiverSim.

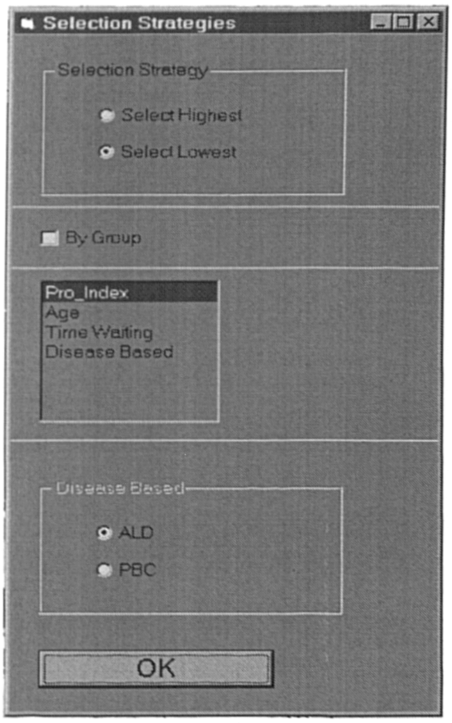



*Figure 6.11: Selection Strategy Window in LiverSim*

In MAPIU2 there is no specific methodology for conducting sensitivity analysis. The main principle is to develop the model flexibly according to stakeholders requirements with regard to how they plan to conduct their analysis. In this case stakeholders agreed to undertake sensitivity analysis based on two main alternatives; firstly, by incorporating the lower and upper bounds of the confidence intervals of the base case results; secondly, by incorporating different discounts rates. For the interested reader, Table E.1 (see Appendix C) shows the effect of incorporating the lower and upper bounds of the confidence intervals for the post-transplant survival estimates. Table E.1 also illustrates how the incorporation of alternative discount rates for future costs and survival affects the results.

It can be seen in Table E.1 in Appendix C that although the absolute values of the Incremental Cost-Effectiveness Ratios (ICER's) for each selection criteria are changed by the sensitivity analysis, the overall rankings of alternative policies do not change as a result of variation in the parameter values highlighted. The lowest ICER is associated with 'Groups' where the higher confidence interval for post-transplant survival is incorporated into the model (£8491), and the highest ICER is associated with the 'High age' selection policy where future survival is discounted at 10% (£14,773). These findings are based on analysis conducted by the stakeholders after they had received the model as a continuation of the MAPIU2 process. More detailed analyses are illustrated in section 6.4.7.

***Data Collection***

In MAPIU2 data collection is not recommended unless it is absolutely necessary. This could be useful in, for example, attempting to draw some conclusions from historical situations or it may be because it is one the requirements of the stakeholders. MAPIU2 is to help stakeholders gain more understanding from the model rather than predetermining certain methodologies. For this particular model, a forecasted performance – survival of patients after transplantation – was one of the requirements of the stakeholders. This made it necessary to populate the model with realistic data, which forms the basis for forecasting regression models. This was helpful in the sensitivity analysis for evaluating the different prioritisation criteria based on the estimated average net life.

Data on actual post transplant survival in the ALD and PBC transplanted patient populations at the Royal Free hospital are incorporated into the model. The two discrete cohorts (ALD or PBC) were accepted for the transplantation programme and had received a liver transplant during a nine year period commencing January 1989 and were classified as routine listing were identified (n=160). Routine patients make up the majority of patients transplanted at the hospital centre (85-90% of transplants annually). A random sample of patients with ALD or PBC who were rejected for transplantation and who received treatment at the hospital centre for their on-going liver disease over a similar time period were also identified (n=100). The samples' information were gathered and analysed to feed the model. See Appendix C for more detailed information about the collected data.

Another estimate is also required which is for life expectancy while the patient is on the waiting list. Ideally, these data are required at frequent time intervals from the date of entry on the waiting list until the point of transplantation for every patient in the study. However, such data are only routinely recorded at the transplant centre and at two distinct time points: at the point of listing and immediately prior to transplantation. For the purpose of this modelling exercise, linear regression techniques were used to forecast the rate of change of key clinical variables during the intervening period.

### 6.4.7 An Example of Use

According to MAPIU2 the process of modelling is continuous from model development through to model use. This subsection presents an example of how stakeholders work with the model to conduct their analysis. The reader is reminded that health economists are the problem owners and the actual users as well. This section particularly presents examples of results from the base case scenario and of the sensitivity analysis conducted. The analysis examined the different section criteria, which are explained in Table 6.6. Results for both the transplanted model and the non-transplanted model are presented for comparison. All results and analysis presented are based on stakeholders' conclusions.

Table 6.7 presents the summary simulation results for the base case analysis – data is collected from the Royal Free Hospital – which assumes a cohort of 1000 patients entering the model. The base case is the original scenario of the model based on the data collected from the Royal Free Hospital. In Table 6.7 'costtx' and 'costld' are expected costs for transplanted and non-transplanted patients respectively, whilst 'survtx' and 'survld' denote expected survival for transplanted and non-transplanted patients respectively. The reference selection criteria, 'High wait', gives an expected total cost per patient transplanted over the ten years of £59,086 (CI: £52,361 – £66,545), where future costs are discounted at 6%, with an expected post-transplant survival time of 4.12 years (CI: 3.03 – 4.99 years). The expected total discounted cost per patient not transplanted over the same time period is £24,185 (CI: £19,029 – £29,834), with an expected survival time of 1.1 years (CI: 0.94 – 1.21 years).

The ICER for the reference selection policy is £11,557 (1999 prices). This estimate can be compared with the ICER generated using alternative selection policies. The results in Table 6.7 shows that the ICER's associated with 'Low wait' 'High age' 'HighPI' and 'Low PI' policies are all higher than the reference selection policy. The ICER associated with 'Low age' is £10424 and the ICER associated with 'Groups' is £9077, both of which are lower than the reference policy. Therefore, these results indicate that the overall cost effectiveness associated with policies where younger patients are given priority, and selection on the basis of clinical severity groupings (where the most severely ill patients are given lower priority) would result in improved cost effectiveness relative to the reference prioritisation criteria.

*Table 6.7: Base Case Results: (1000 patients)*

| Policy | Costtx (£) | Costld (£) | Survtx (years) | Survld (years) | ICER (£) |
|---|---|---|---|---|---|
| High wait | 59086 | 24185 | 4.12 | 1.1 | 11557 |
| Low wait | 57667 | 22686 | 3.97 | 1.01 | 11818 |
| High age | 54725 | 16907 | 4.07 | 0.96 | 12160 |
| Low age | 57382 | 25694 | 4.18 | 1.14 | 10424 |
| High PI | 57613 | 18952 | 4.26 | 1.03 | 11969 |
| Low PI | 59520 | 24078 | 4.09 | 1.14 | 12014 |
| Groups | 59100 | 32777 | 4.02 | 1.12 | 09077 |

The alternative prioritisation criteria were evaluated for 25 simulations of cohorts of 150 patients (reflecting the current annual activity levels at the Royal Free hospital) in order to illustrate the distribution of costs and life years. These results emphasise the variability in costs and outcomes that can occur. However, overall, the results (Table C.2 in Appendix C) are not strikingly different from the base case analysis results presented in Table 6.7, with the optimal selection policy remaining 'Groups' from the cost effectiveness view-point.

## 6.5 Communication Issues

In MAPIU2 communication is divided into two types, *intercommunication* which is amongst stakeholders and *communication* which is between stakeholders and the model (see Table 5.2 on page 129). This section shows how this aspect of MAPIU2 is applied in

LiverSim. The discussion concentrates on the importance of the two types of communication in enhancing the effectiveness of the modelling process by gaining more understanding about the real system and improving the validity of the model.

### 6.5.1 Intercommunication in LiverSim

LiverSim gives a good demonstration of intercommunication between the stakeholders. The LiverSim experience showed that by using the model health economists and clinicians managed to get higher level of information than they previously would without using the model. Higher level of information leads to focussed discussion towards achieving certain objectives. This is actually a classical example of how the model could be used as a debating vehicle for intercommunication. For example, in this case health economists consider the alternative criteria for prioritising the liver transplants waiting list as alternative variables or policies, and the most cost-effective policy would be the most favoured. However, clinicians will look at such policies as a means for providing the service for the most needy regardless of the price. The model here acts as bridge to balance both sides in order to reach a commonly accepted policy. The model does not just provide mutual information about both sides, it also provides the reasoning behind each side. Some changes may arise in the structure of the model itself. For example, one of the main changes in the model that was made during conceptual modelling was deleting the 'super urgent' patients. This decision was based on intercommunication whilst having the model as a means to demonstrate each of the stakeholders' argument.

### 6.5.2 Communication in LiverSim

Communication with the model relates mainly to the requirements and validation of the model and to information received from the model. Information will be discussed in the following section. This section concentrates more on the validation process. The validation process was performed alongside the model building process. The main aspect of this process is keeping in touch with the experts. Unlike the ABCSim experience, where health economists acted as a medium between the modelling analysts and the experts, the LiverSim model was built based on direct meetings between the three participants; problem owners, experts, and modelling analysts. This helped in speeding up the process of model building and validation. This is for two reasons. The first reason is that the model was fed by the original information directly. Secondly, involving the modelling analysts in the process helped them to quickly absorb the system's aspects. This demonstrated that it was important to make this modification in MAPIU2 with regard to the stakeholders' side.

In a more traditional sense the behaviour of the model was also validated by checking the model's outputs against existing data sources. Information from the internal data source at the Royal Free Hospital, supplemented by information from the literature and expert opinion were used to identify estimates of the overall expected effectiveness and costs of the reference case policy and the magnitude of the direction of the effect upon the ICER of the introduction of alternative selection policies. It was found that the results generated from the model corresponded well with the estimates obtained from existing data sources (see Appendix D).

## 6.6 Information

As mentioned in Table 5.2 on page 129 according to MAPIU2 information retrieved from the model is either *tangible* or *intangible*. This section discusses how both types of information retrieved from the model helped the stakeholders to gain more understanding about the system. Tangible information is mentioned in the previous section it is usually concerned with results such as in Table 6.7. in this particular example *tangible* information is using the model to evaluate the cost-effectiveness of the technology of liver transplantation. This type of information could also be used for predicting the behaviour of the larger system. By applying certain sampling techniques the convergence of the average performance may aid in predicting the behaviour of the overall population.

Obviously intangible information is not straightforward to identify. This mainly for understanding the system and any unknown behaviour. in the LiverSim case an understanding was gained from such information when it was suggested to use disease types (ALD and PBC) as the bases of comparison for prioritising patients. This proved to be insignificant, as it is possible that there may not be a matching patient amongst the assigned type of disease, so the liver goes to the other type. In this case the final result averages out the same for both types. Because of that this selection criteria was ignored as a basis of evaluation, yet it is available in case stakeholders become interested in pursuing experimentation with this factor.

In a more general view stakeholders realised that the pursuit of efficiency in the provision of liver transplantation also needs to be reconciled with the important issues of equity and fairness in donor liver allocation. The findings of this modelling study suggest that the overall cost effectiveness of the liver transplantation programme could be improved if the current selection criteria were modified to take account of the age of the patient and the reduced chances of success of the most severely ill patients.

Stakeholders also indicated that although the focus was initially upon patients with ALD and PBC, it is possible that the model could be extended to take account of patients who receive liver transplants but have other types of liver diseases. The structure of the model could also be developed at a national level by including data on the national supply of donor organs over time and the characteristics of patients at other transplant centres. The approach may also be applicable in evaluating alternative selection policies for other solid organ transplant procedures.

Stakeholders concluded that discrete event simulation (DES) does enable the modelling of complex and dynamic systems which are less easily modelled using other techniques. As the number of liver transplants performed in the UK continues to increase, the calls for explicit guidelines for prioritising patients on the waiting list are likely to escalate in the future. DES may prove to be a powerful tool in assessing the impact of alternative selection strategies for transplantation. It may also prove to be useful in facilitating the timing of other surgical interventions and in health care decision-making more generally (LiverSim, 1999).

## 6.7 Summary

The chapter undertakes a final assessment for the proposed modelling framework using a second case study. The case study is about the economic evaluation of the process of Liver Transplantation and the evaluation of the ranking criteria for prioritising patients awaiting transplant.

Section 6.2 presents a brief background about the process and the technology of liver transplantation and problems associated with it. The process of liver transplantation is portrayed as a very complex issue with high resource use. One of the main problems stated in the section is that the number of donated livers is in decline in relation to the number of patents. To find cost-effective policies for tackling waiting list prioritisation, simulation seemed to be a good candidate. The section then presents the background to the particular transplant centre to be modelled and how the pattern of care is followed there.

Section 6.3 discusses how MAPIU2 was applied to develop a model for the above-mentioned problem. This particular section explains the main aspects of the MAPIU2 process in building the LiverSim model. Initialisation is discussed showing how the different stakeholders are classified. Then follows an overview of the processing part. This included modelling, communication, and information parts of the process.

Section 6.4 discusses the first part of the process and that is modelling. The section starts by discussing the conceptual phase of the process and how even at this stage the MAPIU2 structure helped stakeholders to gain a better understanding about their system. The discussion then moves on to the time-based model. This includes the different patterns of care received by patients throughout their stay in the system. Details are given about the different input variables for the model and the different output responses to be gained from the model. Survival predictors as input variables were discussed in more detail. Attention is drawn to the experimentation issues which included how a number of experimental factors were identified using the MAPIU2 process for what-if questions, then how these factors are experimented on using sensitivity analysis. It is not suggested by MAPIU2 to follow a systematic analysis, yet it calls for building facilities that enable the particular stakeholders to carry out the analysis the way they prefer. In this case stakeholders varied the model within the confidence interval of the base case, which is given as an example of use in this section. Some issues relating to why data was needed in certain parts of the model were also discussed in this section.

Section 6.5 discusses the communication issues in LiverSim. It concentrates on the use of communication throughout the modelling process whether in terms of intercommunication or in terms of communication with the model. The section discusses how intercommunication helped stakeholders to understand each other. Section 6.5 also discusses how simulation helped in validating the model and retrieving more refined information from the model. The main finding of the underlying principle of MAPIU2 is not about building a better validated model, it is about validating stakeholders' understanding about the system and other stakeholders using the model as a medium of communication.

Section 6.6 presents an overview of the role of information in LiverSim for the purpose of enhancing stakeholders' understanding. The section provides an example of tangible information, which is based on a model's output and its impact on the modelling process. A more difficult task was realising how intangible information helped in enhancing stakeholders' understanding about the system. The section then gives some interpretation for the stakeholders of the initial results arising from the model. One of the main important points mentioned in this section is about the need to reconcile the efficiency of prioritisation with other qualitative issues such as equity and fairness in donor liver allocation.

# Chapter Seven

# 7 Chapter Seven: Summary and Conclusions

## 7.1 Summary

This dissertation is made up of seven chapters. The first chapter presents an overall introduction to the story of this research by stating the main problem. Chapter Two gives a theoretical background of the existing practices for tackling the research problem and the research questions. Chapter Three presents an alternative framework for tackling the problem and attempting to answer the research questions. Chapter Four provides a case study in order to examine the viability of the proposed framework. Chapter Five analyses the findings from the case study and proposes some modifications and improvements for the framework. Chapter Six presents a second case study to re-evaluate the proposed framework.

This section presents a brief summary of this dissertation describing the road taken for the purpose of tackling these issues. The section summarises the contents of Chapters One through to Chapter Six. The section after that presents what could be learned from this thesis with regard to the objectives in the form of conclusions. The last section discusses what could be improved to gain more effectiveness from this line of research in the future.

### 7.1.1 Detailed Chapters' Summaries

Chapter One starts by manifesting the main problems associated with healthcare systems and what the causes for uninformed decisions are. It was stated that there are some major issues associated with healthcare systems; those are *complexity*, *multifaceted structure*, and *multiple ownership*. The main objective of this research is to provide ways of applying a modelling tool to help in these issues and thus ease the process of healthcare management and decision making. To achieve such an objective it was suggested that there are two main aspects to be considered; those are problem understanding and stakeholders' communication.

It is suggested that there are limitations associated with the different approaches for tackling healthcare modelling problems. That is with regard to the models' structures and the approaches to solving the problem. It is argued that the model is required to provide precise estimates based on sampled data, which does not guarantee that the system will retain the same behaviour in the future. Hence, the objectives of the study were to attempt to develop a modelling framework that enables stakeholders to better understand their problems.

Chapter One could be summarised as the need for modelling to deal with the complicated structure of healthcare systems by focussing on problem understanding and communication. Chapter Two expands Chapter One and mainly concentrates on the research context and literature survey and evaluation. The chapter starts by giving a detailed discussion of *problems* and *problem understanding*. The concept of "problems" is introduced within the context of this research. Then the discussion continues with the topic of the process of problem solving. Theoretical problem solving techniques are presented and also issues for problem understanding and intercommunication. This is done in terms of what factors to consider for the process of problem understanding. This part mainly discusses the usefulness of problem understanding for effective problem solving, particularly in complicated situations.

Chapter Two then discusses the three most widely used modelling techniques in healthcare management and decision making. Those are: *Decision Trees*, *Markov Chains*, and *Simulation Modelling*. The three techniques are evaluated with regard to problem understanding in supporting decision making, where simulation modelling appeared to offer more flexibility and versatility in problem understanding.

The simulation modelling approach is analysed in more detail in the following sections. A general framework for the process of simulation, based on the literature, is presented and analysed with regard to healthcare systems. This framework represents the current practice and theory of simulation. It was realised that heathcare systems may be a little more problematic with regard to problem understanding as presented in this chapter. This paved the way for the main research questions of this thesis, which are:

- What is the simulation framework that should be followed to enhance problem understanding and stakeholders' communications?
- Who is supposed to understand the problem and how much should be their degree of involvement in the modelling process?

- Is simulation better suited for solving complicated problems than other statistical techniques or does it depend on the type of the problem?

For the third question, it was found that simulation does represent a viable approach for tackling healthcare problems as it offers a higher level of agility, and this was tackled in Chapter Two. The first and the second questions are mainly tackled in the following chapters.

By establishing the fact that problem understanding is an important issue in healthcare systems and simulation modelling with its current practice might be better exploited to offer comprehensive facilities to facilitate rich understanding, Chapter Three is mainly focussed on presenting an alternative simulation modelling framework for healthcare systems. The main objective of this framework is to enable stakeholders to better understand their problem and intercommunicate with each other. The chapter first starts by initiating the important factors for developing a modelling framework. Two factors were considered for developing the framework. Those are the driving principles of the framework and its structure. The driving principles represent the general background from which the particular framework is developed whether it is based on theoretical principles or practical principles. Analysis in Chapter Three suggests that in this case a practical approach might be followed in developing such a framework. The structure for the framework is usually based on either a sequential or an iterative structure. The discussion concluded that an iterative approach is more suitable for such frameworks. The proposed framework is called Modelling Approach that is Participative Iterative for Understanding, MAPIU for short. The basic elements that may be included in MAPIU are addressed. An iterative structure was chosen for this framework between the two main elements and those are *stakeholders* and the *modelling* process. The chapter discusses the underlying concept of using the framework, which is based on defining the relationship between the modelling effort and the stakeholders and how they should interact.

After developing the initial concepts behind MAPIU, it was necessary to provide a case study to examine the strengths and weaknesses of it. Chapter Four presents the case study used for applying MAPIU. The case study is about economic evaluation alongside a Randomised Clinical Trial of Adjuvant Breast Cancer treatment. The background to the adjuvant therapies and their proven efficiency are given. The economic evaluation of the adjuvant therapies is explained, in addition to the importance and the need for the use of modelling to aid the process of economic evaluation. The main objective of modelling is to identify the key factors of the trial in order to concentrate on them for data collection and analysis.

Chapter Four gives the different inputs and the expected outputs to the ABCSim model, and how each one is incorporated in the model. All input and output variables are defined and re-defined throughout the process of model building as part of the continuous relationship between the model and the stakeholders. Issues related to the verification and validation of the model are also discussed. The chapter concludes by giving an example of how the model would be used, demonstrating ways for identifying the importance of one of the variables in the model with regard to the Cost-Effectiveness ratio.

It was then thought necessary to analyse MAPIU in more detail after the case study was conducted. Chapter Five focuses on identifying the main weaknesses in MAPIU based on the modelling exercise in Chapter Four. The main objective of this chapter is to establish a set of requirements for modifying the framework and incorporating any required modifications. The chapter provides the main factors for analysing MAPIU. Analysis factors are divided into two sets; factors related to the process of problem understanding in general and factors which are related to modelling for problem understanding specifically. Another set of factors arose from the first modelling exercise. The main theme of the analysis was to draw some correspondence between the framework and the steps taken in the ABCSim experience. The chapter also goes into defining the two components into more detail. Stakeholders have been divided into three types. Those are *problem owners*, *experts*, and *actual users*. The modelling component is divided between the *conceptual model* process and *time-based modelling*. The modification of "computer model" to "time-based model" is because the new term relates more suitably to the essence of MAPIU. After establishing the above modification the proposed framework is renamed MAPIU2. The overall process is then described by introducing the main steps for using MAPIU2. Those are *initialisation* and *processing*. Initialisation is related to classifying the different stakeholders and their relationships with the model. Processing includes the modelling process, communication and information.

Chapter Six undertakes an assessment of MAPIU2 using a second case study. The case study is about the economic evaluation of the process of Liver Transplantation and an evaluation of the ranking criteria for prioritising patients awaiting transplant. A brief background about the process and technology of liver transplantation and problems associated with it are given. One of the main problems is that the number of donated livers is in decline in relation to the number of patients. To find cost-effective policies for tackling waiting list prioritisation, simulation seemed to be a suitable candidate.

The chapter then presents how the model (LiverSim) was built. The process based on MAPIU2 started with the initialisation steps. According to MAPIU2 the health economists were classified as problem owners and actual users, while clinicians were classified as experts of the system. The processing step is given from an overall point of view. This step is explained in more detail in the following sections, which include the conceptual model for both the transplant model and the liver disease model. The time-based model (which is developed using Simul8 in conjunction with Visual Basic) is also presented. Input variables and output responses are identified. The last issue in the modelling component was given with respect to experimentation. An example was shown to illustrate how health economists use the model in order to conduct their analysis. The chapter then goes into explaining the communication issues in LiverSim including stakeholders-to-model type (communication) and stakeholders-to-stakeholders type (intercommunication). Finally the chapter discusses how both tangible and intangible information were used to enhance the stakeholders' understanding and restructuring of the model based on the communication process mentioned in the preceding section.

## 7.2 Conclusions

The previous section provides an overall picture of the story of this research starting by stating the problem and the research questions and ending by assessing the proposed solution or answer. This section examines the proposed solution and takes it back to the research questions. Before doing that it must be noted that this what has been achieved represents a mere attempt to draw attention to the issues mentioned in Chapter One with regard to problem understanding in healthcare systems. This section is about how "MAPIU2 might be useful for the research problem". The main issues tackled were problem understanding and communication. Hence, the following discussion is divided between these two issues.

### 7.2.1 MAPIU2 and Problem Understanding

As seen from Chapters Four and Six, stakeholders were satisfied with their level of understanding with regard to the model and the real system. This can be attributed to a set of factors. Firstly, involvement of stakeholders in building the model. This had a considerable impact on gaining more understanding. The benefit was actually mutual, stakeholders' understanding about the system was continually enhanced as more features were added to the model. On the other hand, as stakeholders' understanding about the system was improved, their contribution to the model was more effective. This is a progressive iterative process and can be thought of as spiral behaviour; the more the model is answering stakeholders' requirements the more their understanding is increased, which means they contribute more to the model's value and usefulness. In comparison to the sequential approach in Chapter Two, MAPIU2 shows itself to be potentially more valuable.

Another lesson learned concerns the identification of stakeholders. The identification of stakeholders has helped a great deal to enhance this process. It is important to identify, amongst stakeholders, who would provide the model with technical validity and who would provide it with purpose validity. Technical validity is building the model to depict the real life system as it really works, which is the classical definition of validation (Robinson, 1999), whilst purpose validity is building the model to provide sound understanding for the stakeholders. In other words, building a technically valid model may not necessarily mean it provides stakeholders with viable understanding, especially in complicated models. It is vital to balance between the two types. However, generally speaking, purpose validity is given more priority than technical validity. Yet purpose validity is subjected to the understanding of the problem owners at specific points of time, which may change at any time, which means changing the model towards the new understanding. The importance of the technical validity comes as a guide or a bottom line for the variable purpose validity. In this case rather than just making sure that the model is sound enough, experts should also be concerned with the validity of the understanding of the problem owners through their perception about the model. For the importance of both types of validity we realise that it is important to identify the problem owners and the experts who are concerned with each validity type. To ensure the smoothness of operation between the two types of stakeholders it is important to ease the communication process between them.

Having the stakeholders engaged in the process of model building produces the third lesson, and that is the enhanced confidence of the model by the stakeholders. Confidence in the model is very important for decision making. In fact this is the only factor that makes decision makers start using the model. This tends not to happen in the traditional framework so much. One of the problems associated with the traditional framework is the lack of implementation, and that is due to the fact that stakeholders may not get what they want at the end of the project or due to the lack of confidence in the model.

It can be seen that an iterative approach is quite valuable for achieving some of the objectives by enhancing the stakeholders' understanding. Yet all of this will not be fully workable without enabling stakeholders to communicate what they have achieved to other stakeholders and to the model. The following section discusses the communication part of the modelling process and how it is catered for using MAPIU2. It must be noted that this particular feature was not part of any of the processes in the traditional frameworks. Usually it is represented as additional skills of the modellers for conducting successful modelling exercises (Sadowski and Grabau, 1999).

### 7.2.2 MAPIU2 and Intercommunication

Using MAPIU2 we realised that the stakeholders are continuously communicating with the model. This process is described in Chapter Three and Chapter Five, where stakeholders are providing modelling requirements to the model and receiving some information from it. In section 7.2.1 we see the importance of this process for enhancing stakeholders' understanding. One important issue, however, is the facilitation of the model to ease the process of communication. This actually, as seen in the previous chapter, relates to the type of stakeholders and their problem. To make sure the process is flowing, the model must be developed in a way that suites the stakeholders. MAPIU2 is more suitable for that, as developers get to know more about the stakeholders as they interact, which is unlike the sequential approach where stakeholders start communicating with the model after it had been developed.

Intercommunication is a different dimension. This is where the purpose validity and the technical validity surface again. Problem owners usually have a problem to be solved and they are looking for specific goals from the model regardless of whether it mimics reality or not. On the other hand, experts will be more inclined to make sure that the model mimics reality, even if unintentionally. The model can be put between the different types of stakeholders and act as a means of communication. From the discussion in Chapter Six it can be seen how MAPIU2 was effective in enhancing the stakeholders intercommunication and the impact of that on the structure of the model. The problem owners will use the model to express their requirements while the experts will use it to portray the system's constraints. Between this pulling and pushing process and through the iterative behaviour both types might reach more conclusive decisions rather than using a number-crunching tool such as spreadsheet modelling.

It can also be seen from Chapter Six that involving the problem owners, the actual users, and the experts in developing the model eases the process of intercommunication during model use. This is evident in the fact that by the end of the development phase all sides would gain enough knowledge about the content and structure of the model and the model would be built on common ground between the stakeholders which makes for an effective tool for intercommunication amongst stakeholders (see section 6.4 in Chapter Six). Having the different stakeholders restricted to a sequential, or strictly semi-sequential, framework (i.e. a formal process of model development) may not offer the same useful effectiveness.

### 7.2.3 Corollary

From the above discussion it can be concluded that MAPIU2 provides many comprehensive facilities for enhancing stakeholders' understanding and enables them to communicate such understanding amongst themselves in a way that is relatively more effective than traditional frameworks. MAPIU2 can, therefore, realise and to a great extent some answers to the questions presented in Chapter Two. This conclusion is based on the assessments conducted in this research using the two case studies mentioned above. The basic principles MAPIU2 proved to be very valuable for enhancing understanding and communication.

It was quite valuable to base the development of MAPIU2 on a practical approach rather than theoretical or logical methods. The theoretical approach is driven by how things should happen, whilst the practical approach is driven by how people actually do things. A framework or guidelines to be followed must be relevant to real practice. One of the problems faced by traditional frameworks is that they are based on logical methods and there no proof that this may be useful for modelling healthcare systems.

We believe that the elements in Tables 5.1 and 5.2 (see Chapter Five) could act as starting points for successfully applying MAPIU2 in other problems. Table 5.1 on page 126 is more concerned with the initialisation step and Table 5.2 on page 129 is more concerned with the main components to consider during the processing stages. It must be noted that these guidelines are for assistance only and may not necessarily be followed depending on the problem to hand. Generally, problem-owners/decision-makers may need to understand the system more than the other two stakeholders, yet it is usually the case that they do not have the time to get involved in the whole process of model development. This means the actual users have to be more involved. For example, when the model is built to clarify a situation then decision makers are to be more involved, whilst if the model is for mimicking the situation then to a large extent experts should be more involved.

## 7.3 Future Research

Most simulation studies are usually based on pre-specified term projects to achieve certain objectives. Whilst MAPIU2 is based on an iterative process until a satisfactory level of understanding is achieved, the concept of a pre-specified project may represent an obstacle of some sort to the process. That is, the duration of a project is determined by a particular deadline, yet in MAPIU2 the duration is not necessarily pre-fixed as it is determined by when the problem is understood. Future research could concentrate on finding ways for balancing project durations and achieving acceptable levels of understanding. Maybe a simulation project should not be considered as a product based project, especially if the objective is to achieve an understanding rather than produce tangible products. In the case where stakeholders do not have sound knowledge about their problem then a simulation project would be a journey that has no pre-specified destinations, which means that pre-specified deadlines are not necessarily relevant. Yet, on the other hand, when dealing with public services like healthcare, or even in the private sector, it is not usually viable to leave any type of projects open-ended, especially if there are budget constraints.

There is also more room for research into the facilitation of stronger communication means between the stakeholders and the modellers. Even though the alternative framework defines the relationship between the model and stakeholders, a more specific relationship with the modellers themselves is required. In the end modellers are responsible for translating stakeholders' requirements efficiently in the model. To avoid time wasting in the first stages of a simulation exercise where stakeholders and modellers get familiarised with each other, some expert guidance for speeding up the process may be of value. However, it must be noted that, as mentioned earlier, this part is more or less dependent on the people involved and how they work together.

An important issue that may be of concern is software. For building tailored models more flexible tools are required. Most of the simulation packages are based on certain features which may not suit all types of requirements. As mentioned in Chapters Four and Six, ABCSim and LiverSim are both built using Simul8 as the simulation engine and Visual Basic as the interface builder. A great deal of time was spent trying to make both packages talk to each other. The danger in using such tools, especially if they are produced by different vendors, is that these packages may interact well in certain versions, yet things could be more difficult if later versions are not compatible. For example, both packages used in this research were quite compatible in earlier versions while they started to become incompatible when higher versions were introduced. There is room for research into flexible environments such as Component Based Packages, where a simulation model could be developed using a set of components assembled together. The important feature of such concept is the possibility to easily assemble, disassemble, and reassemble the model according to stakeholders' understanding. This may have a great impact on MAPIU2 as the process would mainly concentrate on modelling for understanding while the model development is a minor activity regarding the overall process.

One last issue that might be considered for future research is extending MAPIU2 into other modelling techniques. Although MAPIU2 is a modelling framework for discrete event simulation, which is known to be classified as a hard technique, the main concept of MAPIU2 could be related to the soft techniques. The main concept behind MAPIU2 is avoiding restrictions of logical and formal steps. One room for research is to see how MAPIU2 would compare with soft methodologies and system dynamics and, on the other hand, considering the co-application of MAPIU2 as a simulation technique and other soft techniques for the same problem.

# References

# References


- ABC Trial Protocol (1993), UKCCCR Randomised Trial of Adjuvant Endocrine Therapy and Chemotherapy in Women with Early Breast Cancer, *The Adjuvant Breast Cancer (ABC) Trial*, Sutton, ABC Clinical Trials Office.

- Anand, A. C, Ferraz-Neto, B. H., Nightingale, P., Mirza, D. F., White, A. C., McMaster, P., and Neuberger, J. (1997), Liver Transplantation For Alcoholic Liver Disease: Evaluation Of A Selection Protocol, *Hepatology*; **vol.** 25(6) pp 1478 – 1484.

- Astin, J., Stewart A. and McIntosh, E. (1997), Economic Evaluation of Chronic Conditions: Framework for a Quasi-Markov Process, *Journal of the Operational Research Society*, **vol.** 48(6) pp 623 – 628.

- Balci, O. (1994), Validation, Verification, and Testing Techniques Throughout the Life Cycle of a Simulation Study, *Annals of Operations Research*, **vol.** 53 pp 121 – 173.

- Balci, O. (1997), Principles of Simulation Model Validation, Verification, and Testing, *Transactions of the Society of Computer Simulation International*, **vol.** 14(1) pp 13 – 23.

- Banks, J., Carson, J. S., and Nelson, B. L. (1996), *Discrete-Event System Simulation*, Second Edition, New Jersey, Prentice-Hall, Inc.

- Barnes, C. D. and Quiason, J. L. (1997), Success Stories in Simulation in Health Care, *In Proceedings of the 1997 Winter Simulation Conference*, Atlanta, Editors: Andradóttir, S., Healy, K. J., Whithers, D. H., and Nelson, B. L., New York, Association for Computing Machinery, pp 1280 – 1285.

- Bines, J., Oleske, D. M., and Cobleigh, M. A. (1996), Ovarian Function in Premenopausal Women Treated with Adjuvant Chemotherapy for Breast Cancer, *Journal of Clinical Oncology*, **vol.** 14(5) pp1718 – 1729.

- Boehm, B. W. (1997), A Spiral Model of Software Development and Enhancement, *In Software Project Management: Readings and Cases*, Edited: Kemerer, C. F., Chicago, Irwin, pp 254 – 270.

- Bonsel, G. J., Klompmaker, I. J., Essink-Bot, M. L., Sloof, M. J. (1990), Cost-Effectiveness Analysis of the Dutch Liver Transplantation Programme, *Transplantation Proceedings*, **vol.** 22(4) pp 1481-1484.

- Bransford, J. D., and Stein, B. S. (1993), *The Ideal Problem Solver*, Second Edition, New York, W. H. Freeman and Company.

- Bryan, S., Ratcliffe, J., Neuberger, J. M., Burroughs, A. K., Gunson, B. K., and Buxton, M. J. (1998), Health-Related Quality of Life Following Liver Transplantation, *Quality of Life Research*, **vol.** 7(2) pp 115 – 120.

- Buxton M. J., Drummond M. F., van Hout B. A., Prince R. L., Sheldon T. A., Szucs T., and Vray, M. (1997), Modelling in Economic Evaluation: an Unavoidable Fact of Life, *Health Economics*, **vol.** 6(3) pp 217 – 227.

- Canney, P. A. and Hatton, M. Q. F. (1994), The Prevalence of Menopausal Symptoms in Patients Treated for Breast Cancer, *Clinical Oncology*, **vol.** 6(5) pp 297 – 299.

- Daly, E., Gray, A., Barlow, D., McPherson, K., Roche, M., and Vessey, M. (1993), Measuring the Impact of Menopausal Symptoms on Quality of Life, *British Medical Journal*, **vol.** 307(6908) pp 836 – 840.

- Davies, R. and Roderick, P. (1998), Planning Resources for Renal Services throughout UK using Simulation, *European Journal of Operational Research*, **vol.** 105(2) pp 285 – 295.

- Delesie, L. (1998), Bridging the Gap between Clinicians and Health Managers, *European Journal of Operational Research*, **vol.** 105(2) pp 248 – 256.

- Dickson, E. R., Grambsch, P. M., Fleming, T. R., Fisher, L. D., and Langworthy, A. (1989), Prognosis in Primary Biliary Cirrhosis: Model for Decision Making, *Hepatology*, **vol.** 10(1) pp 1 – 7.

- Dittus, R. S. and Klein, R. W. (1992), Simulating Medical Decision Trees with Random Variable Parameters, *In Proceedings of the 1992 Winter Simulation Conference*, Virginia, Editors: Swain, J., Goldsman, D., Crain, R. C., and Wilson, J. R., New York, Association for Computing Machinery, pp 1050 – 1056.

- Drummond M. F. and Davies, L. (1991), Economic Analysis alongside Clinical Trials–Revisiting the Methodological Issues, *International Journal of Technology Assessment in Health Care*, **vol.** 7(1) pp 561 – 573.

- Drummond, M. F., O'Brien, B., Stoddart, G. L., and Torrance, G. W. (1997), *Methods for the Economic Evaluation of Health Care Programmes*, Oxford, Oxford University Press.

- Drummond, M. and Stoddart, G. L. (1984), Economic Analysis and Clinical Trials, *Controlled Clinical Trials*, **vol.** 5(2) pp 115 – 128.

- Early Breast Cancer Trialists' Collaborative Group (1992), Systemic Treatment of Early Breast Cancer by Hormonal, Cytotoxic, or Immune Therapy, *The Lancet*, **vol.** 339(1–15) pp 71 – 85.

- Francis, D. (1990), *Effective Problem Solving*, London, Routledge.

- Halpern, M. T., Brown, R. E., Revicki, D. A., and Togias, A. G. (1994), An Example of using Computer Simulation to Predict Pharmaceutical Costs and Outcomes, *In Proceedings of the 1994 Winter Simulation Conference*, Orlando, Editors: Tew, J. S., Manivannan, S., Sadowski, D. A., and Siela, A. F., New York, Association of Computing Machinery, pp 850 – 855.

- HERG (1998), *Interim Data 'Economic Evaluation of the Liver Transplantation Programme in England and Wales'*, Unpublished Project Report, Health Economics Research Group, Brunel University, Uxbridge.

- Hillner B. E., and Smith T. J. (1991), Efficacy and Cost Effectiveness of Adjuvant Chemotherapy in Women with Node-Negative Breast Cancer–a Decision-Analysis Model, *New England Journal of Medicine*, **vol.** 324(3) pp 160 – 168.

- Hines, W. W. and Montgomery, D. C. (1990), *Probability and Statistics in Engineering and Management Science*, Third Edition, Singapore, John Wiley & Sons, Inc.

- HM Treasury (1997), *Appraisal and Evaluation in Central Government*, Treasury Guidance, London, The Stationary Office.

- Hughes, M. D., Raskino, C. L., Pocock, S. J., Biagini, M. R., and Burroughs, A. K. (1992), Prediction of Short Term Survival with an Application in Primary Biliary Cirrhosis, *Statistics in Medicine*, **vol.** 11(13) pp 1731 – 1745.

- Irani, Z., Ezingeard, J. -N., Grieve, R. J., and Race, P. (1999), A Case Study Strategy as part of an Information Systems Research Methodology: A Critique, *International Journal of Computer in Technology*, **vol.** 12(2/3/4/5) pp 190 – 198.

- Jackson, K. F. (1975), *The Art of Solving Problems*, London, William Heinmann.

- Jonasson O. (1989), Waiting in Line: Should Selected Patients Ever be Moved Up? *Transplantation Proceedings*, **vol.** 21(3) pp 3390 – 3394.

- Jun, J. B., Jacobson, S. H., and Swisher, J. R. (1999), Application of Discrete-Event Simulation in Health Care and Clinics: A Survey, *Journal of the Operational Research Society*, **vol.** 50(2) pp 109 – 123.

- Karnon, J. and Brown, J. (1998), Selecting a Decision Model for Economic Evaluation: a Case Study and Review, *Health Care Management Science*, **vol.** 1(2) pp 133 – 140.

- Kelton, W. D. (1994), Analysis of Output Data, *In Proceedings of the 1994 Winter Simulation Conference*, Orlando, Editors: Tew, J. S., Manivannan, S., Sadowski, D. A., and Siela, A. F., New York, Association for Computing Machinery, pp 62 – 68.

- Kleijnen, J. P. C. (1987), *Statistical Tools for Simulation Practitioners*, New York, Marcel Dekker, Inc.

- Kleijnen, J. P. C. and van Groenendaal, W. (1992), *Simulation a Statistical Perspective*, Chichester, John Wiley and Sons Ltd.

- Lagergren, M. (1998), What is the Role and Contribution of Models to Management and Research in the Health Services? A View from Europe, *European Journal of Operational Research*, **vol.** 105(2) pp 257 – 266.

- Law, A. M. and Kelton, W. D. (1991), *Simulation Modelling and Analysis*, Second Edition, Singapore, McGraw-Hill.

- Lewis, P. A. W. and Orav, E. J. (1989), *Simulation Methodology for Statisticians, Operations Analysts, and Engineers*, Volume One, Pacific Grove, Calif., Wadsworth & Brooks/Cole Advanced Books & Software, a division of Wadsworth inc.

- LiverSim (1999), *End of Project Report*, ESRC Grant Number: R 000222620, Unpublished Report, Health Economic Research Group, Brunel University, Uxbridge.

- Love, R. R., Laventhal, H., Easterling, D. V., and Nerenz, D. R. (1989), Side Effects and Emotional Distress During Cancer Chemotherapy, *Cancer*, **vol.** 63(3) pp 604 – 612.

- Lowery, J. C. (1998), Getting Started in Simulation in Healthcare, *In Proceedings of the 1998 Winter Simulation Conference*, Washington, Editors: Medeiros, D. J., Watson,

E. F., Carson, J. S., and Manivannan, M. S., New York, Association for Computing Machinery, pp 31 – 35.

- Lyles, R. (1982), *Practical Management Problem Solving and Decision Making*, New York, Van Nostrand Reinhold Company Inc.

- Maria, A. (1997), Introduction to Modelling and Simulation, *In Proceedings of the 1997 Winter Simulation Conference*, Atlanta, Editors: Andradóttir, S., Healy, K. J., Whithers, D. H., and Nelson, B. L., New York, Association for Computing Machinery, pp 7 – 13.

- McMaster, P. and Dousset, B. (1992), The Improved Results of Liver Transplantation, *Transplant International*, vol. 5(3) pp 125 – 128.

- Nance, R. E. (1994), The Conical Methodology and the Evolution of Simulation Model Development, *Annals of Operations Research*, vol. 53 pp 1 – 45.

- Neuberger J. (1997), Allocating Donor Livers, *British Medical Journal*, vol. 314(7088) pp 1140 – 1141.

- Neuberger J. and Lucey, M. R. (1994) *Liver Transplantation: Practice and Management*, British Medical Journal Publishing Group, London.

- O'Grady, J. and Williams, R. (1993), Selection for Transplantation. *Journal of Hepatology*, vol. 19(3) pp 485 – 486.

- Paul, R. J. and Balmer, D. W. (1993), *Simulation Modelling*, Lund, Chartwell-Bratt.

- Paul, R. J. and Thomas, P. (1996), Computer-Based Simulation Models for Problem-Solving: Communicating Problem Understandings, *In Computers, Communication and Mental Models*, Edited: Day, D. L. and Kovacs D. K., Bristol, Taylor & Francis Ltd, pp 67 – 73.

- Pedgen, C. D., Shannon, R. E., and Sadowski, R. P. (1990), *Introduction to Simulation using Siman,* New Jersey, System Modeling Corporation and McGraw Hill, Inc.

- Pidd, M. (1998), *Computer Simulation in Management Science,* Fourth Edition, Chichester, John Wiley & Sons.

- Pidd, M. (1996), *Tools for Thinking: Modelling in Management Science,* Chichester, John Wiley & Sons.

- Pressman, R. S. (1997), *Software Engineering: a Practitioner's Approach,* Fourth Edition, European Adaptation, New York, McGraw-Hill.

- Pritsker A. (1998), Life and Death Decisions, *OR/MS Today* vol. 25(4) pp 23 – 28.

- Quinn, J. B. (1988), *The Strategic Process, Concepts, Context and Cases,* Edited: Quinn, J. B.. Mitzberg, I. Y., and James, R. M., New Jersey, Prentice Hall.

- Roberts, M. S. (1992), Markov Process-Based Monte Carlo simulation: A Tool for Modeling Complex Disease and its Application to the Timing of Liver Transplantation, *In Proceedings of the 1992 Winter Simulation Conference,* Virginia, Editors: Swain, J., Goldsman, D., Crain, R. C., and Wilson, J. R., New York, Association for Computing Machinery, pp 1034 – 1040.

- Robinson, S. (1994), *Successful Simulation: A Practical Approach to Simulation Projects,* Maidenhead, McGraw-Hill Book Company Europe.

- Robinson, S. (1999), Simulation Verification, Validation and Confidence, *Transactions of the Society of Computer Simulation International,* vol. 16(2) pp 63 – 69.

- Russell, L. B., Gold, M. R., Siegel, J. E., Daniels, N., and Weinstein, M.C. (1996), The Role of Cost-Effectiveness Analysis in Health and Medicine, *JAMA,* vol. 276(14) pp 1172 – 1177.

- Sadowski, D. A. and Grabau, M. R. (1999), Tips for Successful Practice of Simulation, *In Proceedings of the 1999 Winter Simulation Conference*, Phoenix, Editors: Farrington, P. A., Nembhard, H. B., Sturrock, D. T. and Evans, G. W., New York, Association for Computing Machinery, pp 60 – 66.

- Schulman K. A., Lynn L. A., Glick, H. A., and Eisenberg, J. M. (1991), Cost Effectiveness of Low-Dose Zidovudine Therapy for Asymptomatic Patients with Human Immunodeficiency Virus (HIV) Infection, *Annals of Internal Medicine*, **vol.** 114(9) pp 798 – 802.

- Sculpher, M., Drummond, M., and Buxton, M. J. (1997), The Iterative Use of Economic Evaluation as Part of the Process of Health Technology Assessment, *Journal of Health Services Research*, **vol.** 2(1) pp 26 – 30.

- Shannon, R. E. (1998), Introduction to the Art and Science of Simulation, *In Proceedings of the 1998 Winter Simulation Conference*, Washington, Editors: Medeiros, D. J., Watson, E. F., Carson, J. S., and Manivannan, M. S., New York, Association for Computing Machinery, pp 7 – 14.

- Showstack, J., Katz, P. P., Lake, J. R., Brown Jr, S. R., Dudley, R. A., Belle, S., Wiesner, R. H., Zetterman, R. K., and Everhart, J. (1999) Resource Utilization in Liver Transplantation: effect of Patient Characteristics and Clinical Practice, *Journal of the American Medical Association*, **vol.** 281(15) pp 1381 – 1386.

- Sonnenberg, F. A. and Beck J. R. (1993), Markov Models in Medical Decision Making, *Medical Decision Making*, **vol.** 13(4) pp 322 – 338.

- Taylor, S. J. E., Eldabi, T., Macredie, R. D., Paul, R. J., Brown, J., and Karnon, J. (1998), Economic Evaluation of Adjuvant Breast Cancer Treatment Using Simulation Modelling, *In Proceedings of the 1998 Medical Sciences Simulation Conference*, San Diego, Editors: Anderson, J. G. and Katzper, M., San Diego, The Society for Computer Simulation International, pp 42 – 47.

- Weik, K. E. (1984), *Theoretical Assumption and Research Methodology Selection,* The Information Systems Research Challenge, Edited: McFarlan, F. W., USA, Harvard Business School.

- Weinstein, M. C., Siegel, J. E., Gold, M. R., Kamlet, M. S., and Russell, L. B. (1996), Recommendations of the Panel on Cost-Effectiveness in Health and Medicine, *JAMA*, **vol.** 276(15) pp 1253 – 1258.

- Williams, J. W., Vera, S., and Evans, L. S. (1987), Socioeconomic Aspects of Hepatic Transplantation, *American Journal of Gastroenterology*, **vol.** 82(11) pp 1115 – 1119.

- Yeates, D. and Cadle, J. (1997), *Project Management for Information Systems*, Second Edition, London, Pitman Publishing.

- Yin, R. K. (1994), *Case Study Research: Design and Methods,* Applied Social Research Methods Series, USA, Sage Publications Vol. 5.

# Appendices

# Appendix A: ABCSim Sample ACD's

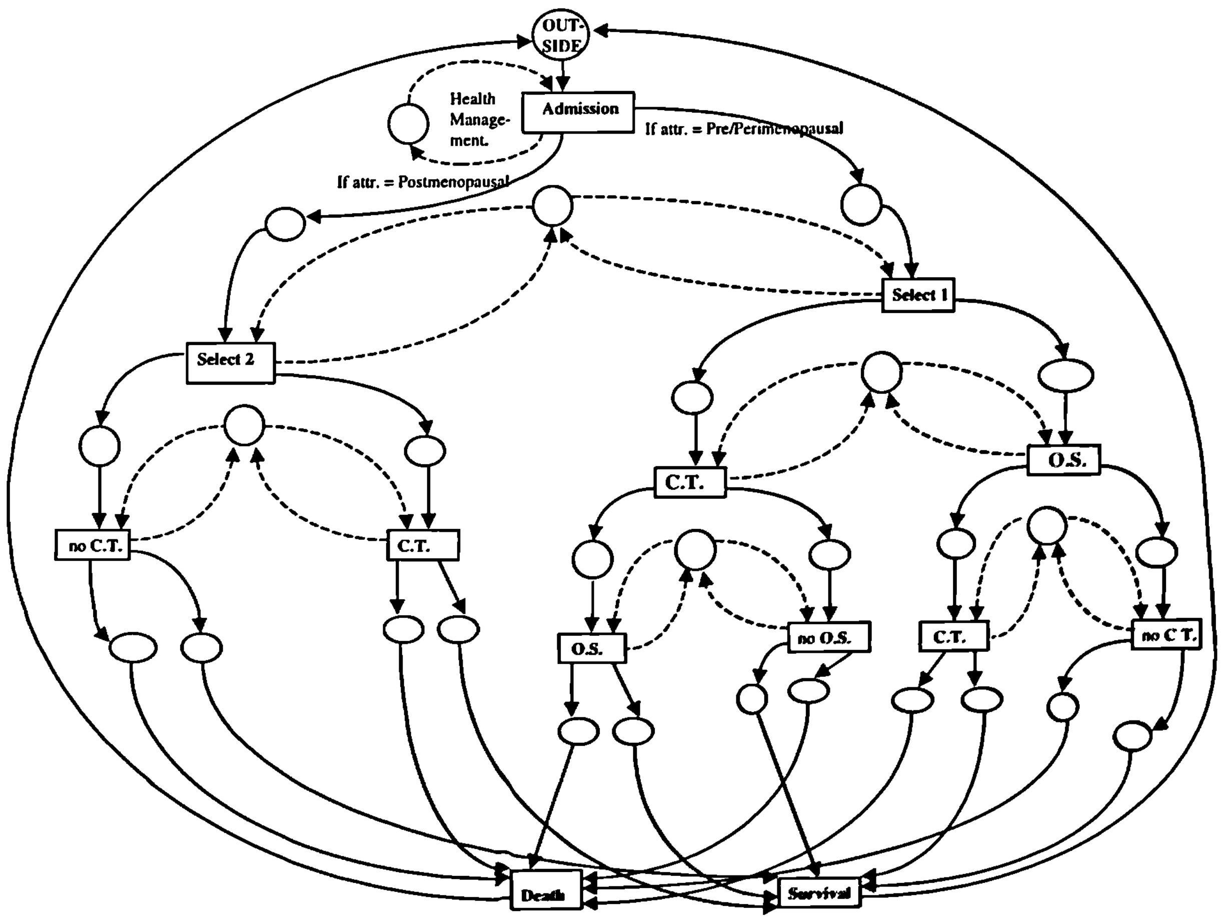



*Figure A.1: Initial ACD for ABCSim*

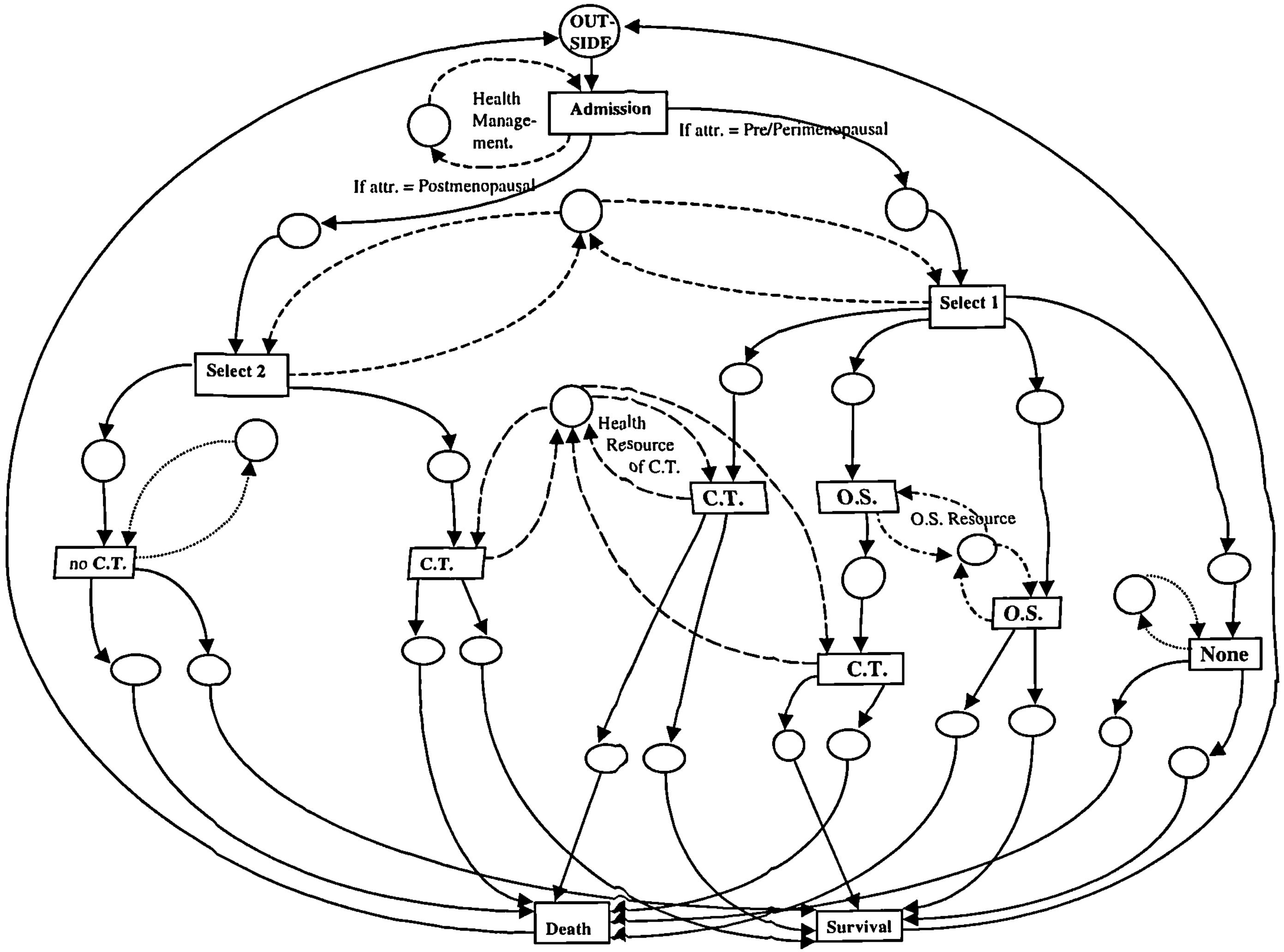



*Figure A.2: A middle Version for the ABC Trial*

# Appendix B: Evolved Stakeholders' Understanding using ACD

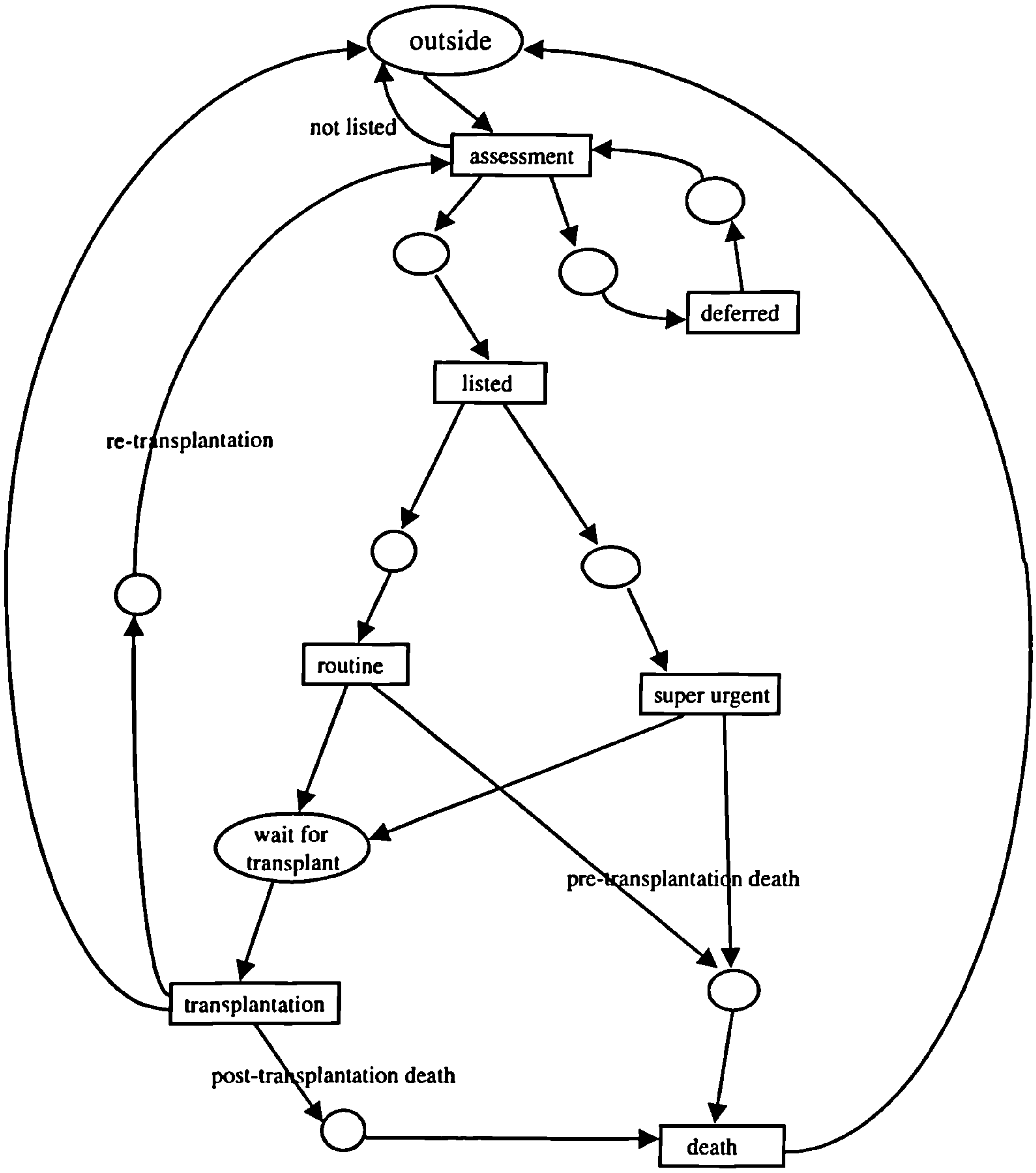



*Figure B.1: Version One of ACD of LiverSim*

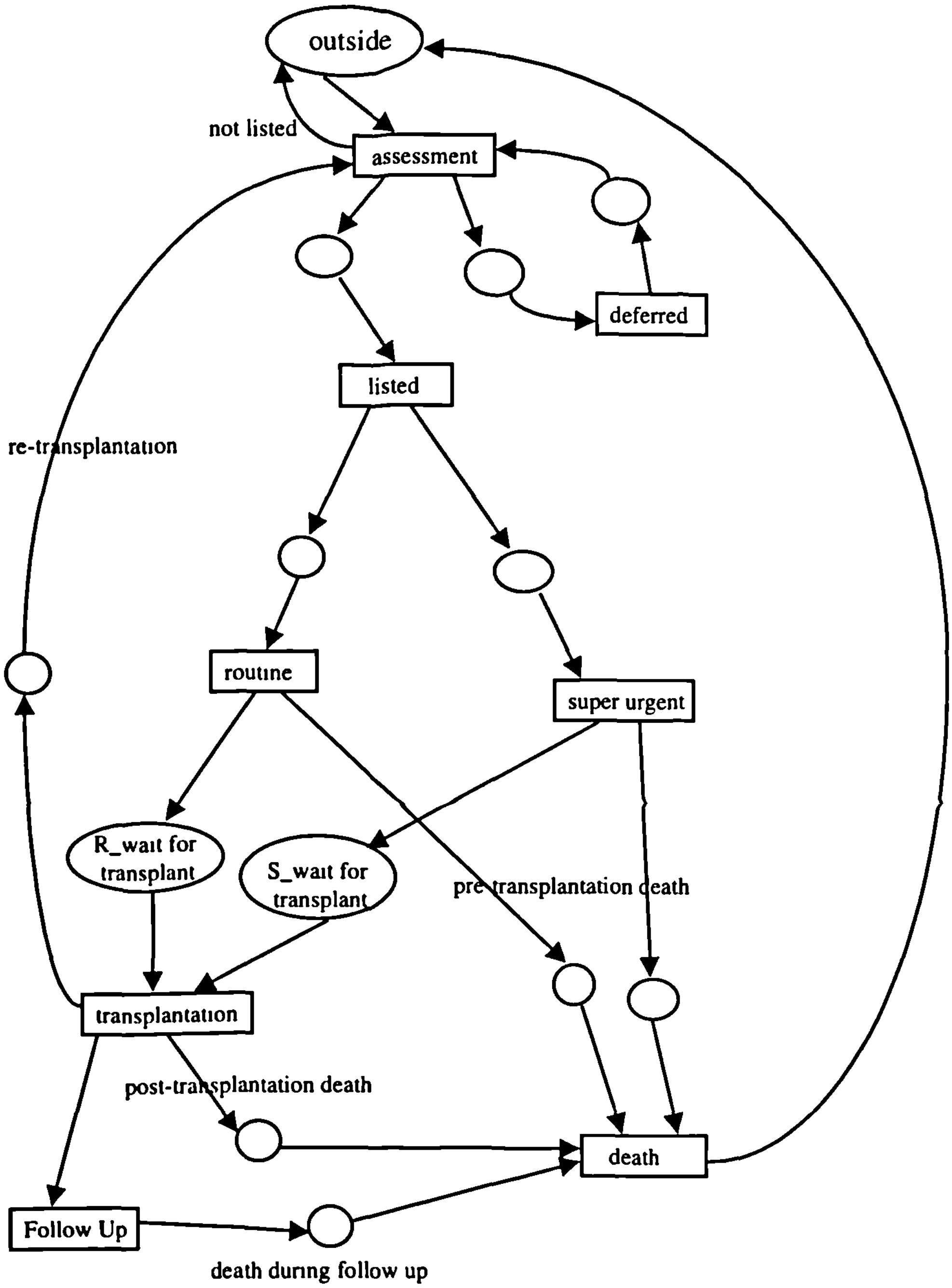



*Figure B.2: Version Two of ACD of LiverSim*

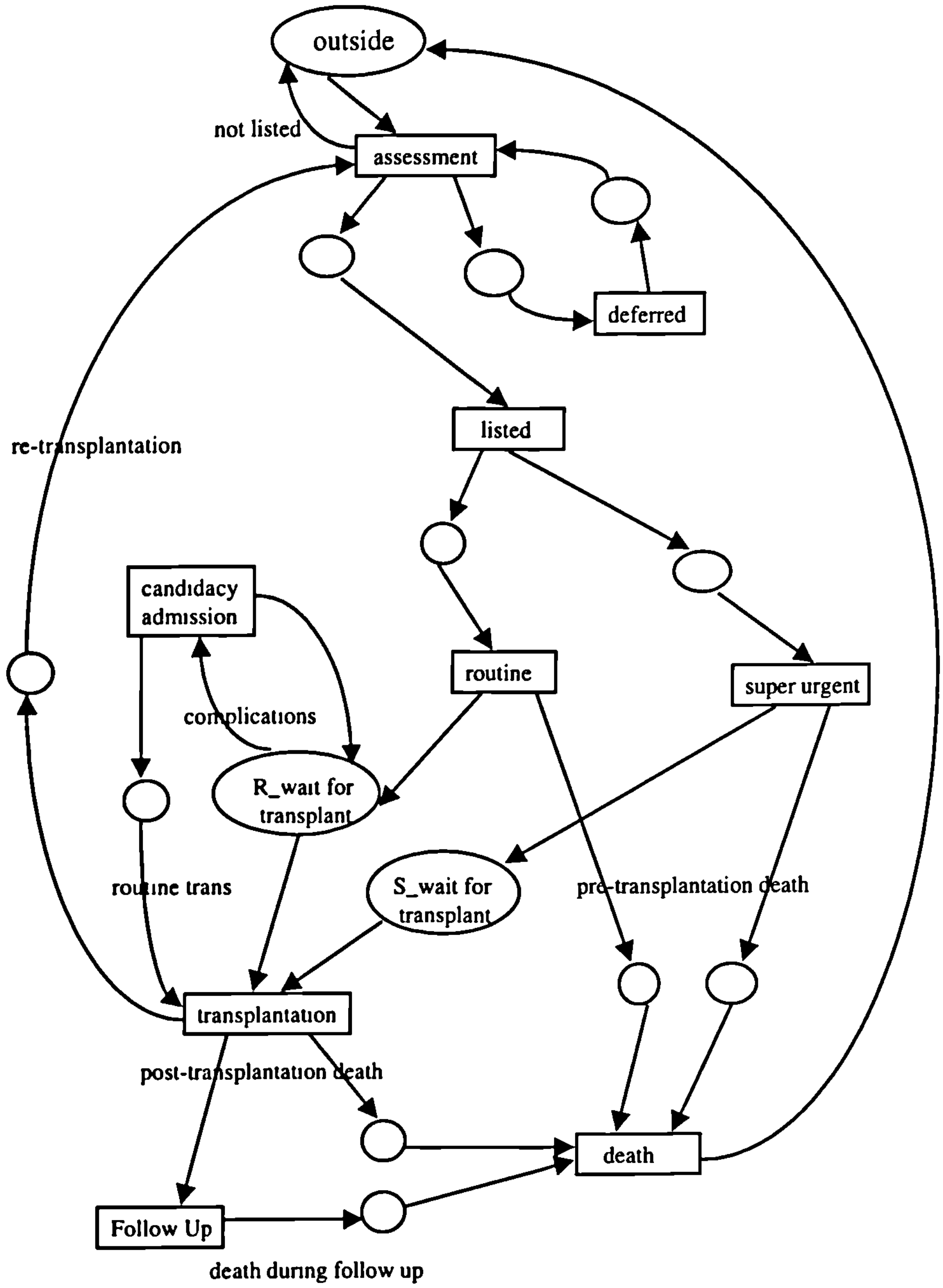



*Figure B.3: Version Three of ACD of LiverSim*

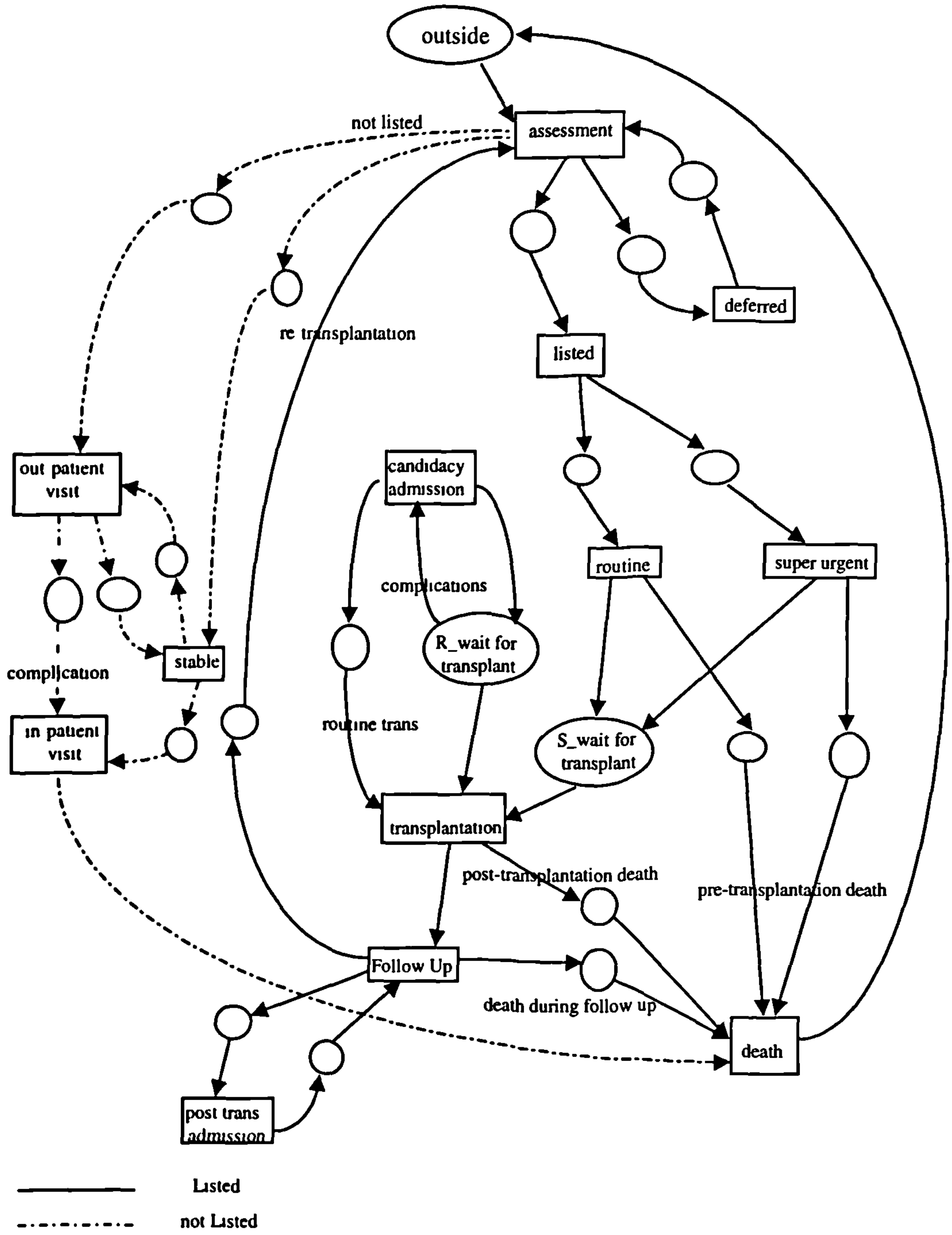



*Figure B.4: Version Four of ACD of LiverSim*

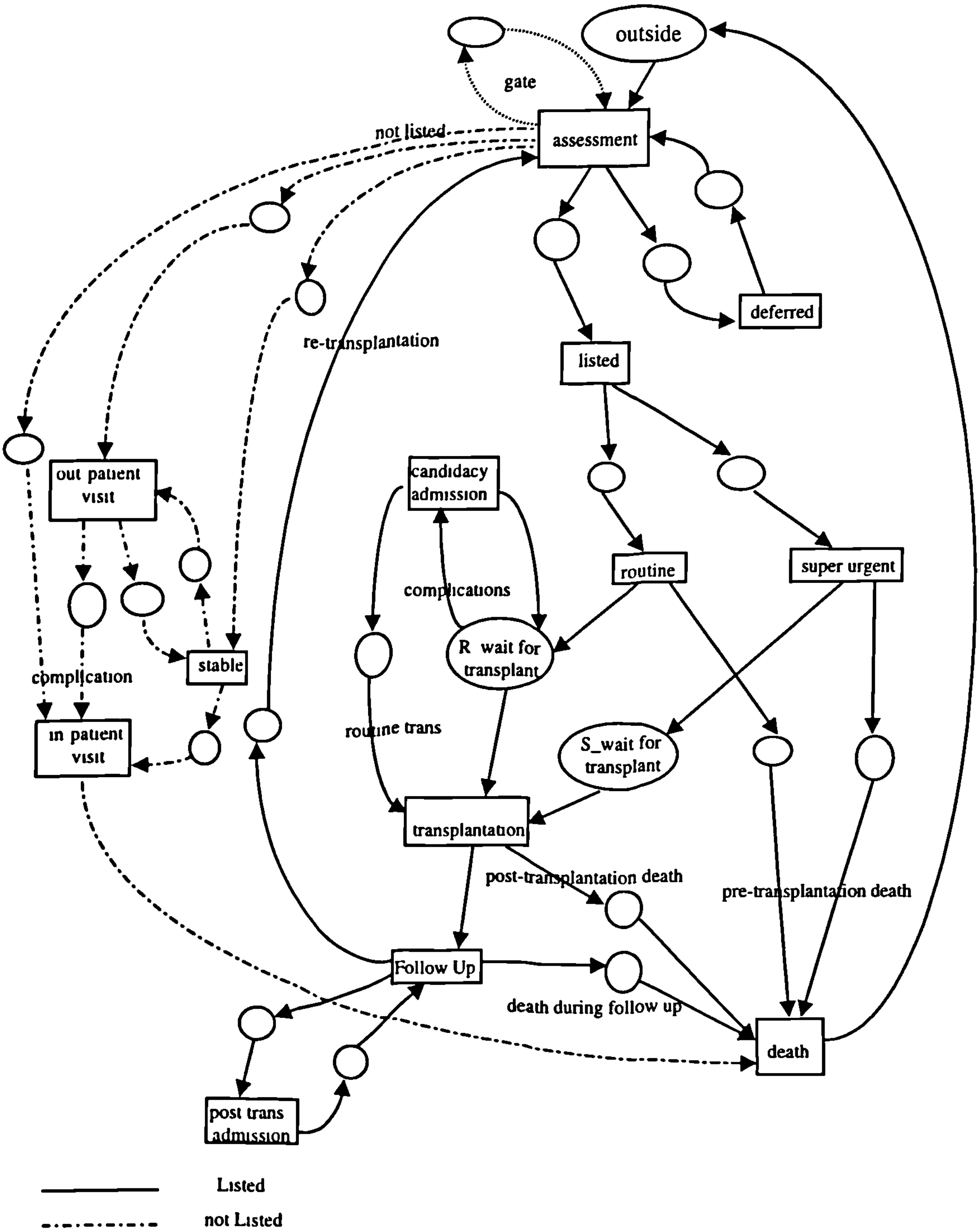



*Figure B.5: Version Five of ACD of LiverSim*

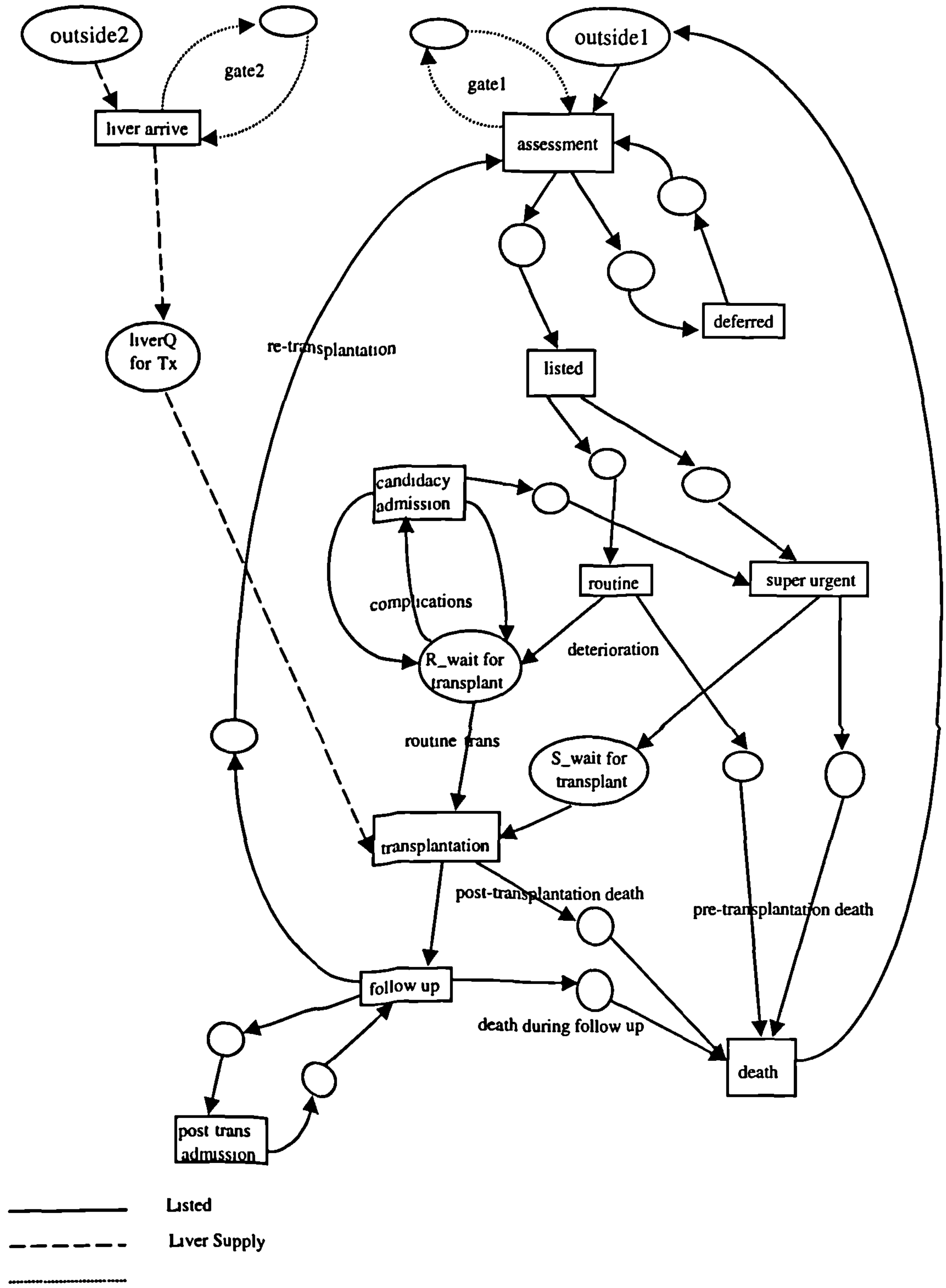



*Figure B.6: Version Six of ACD of LiverSim*

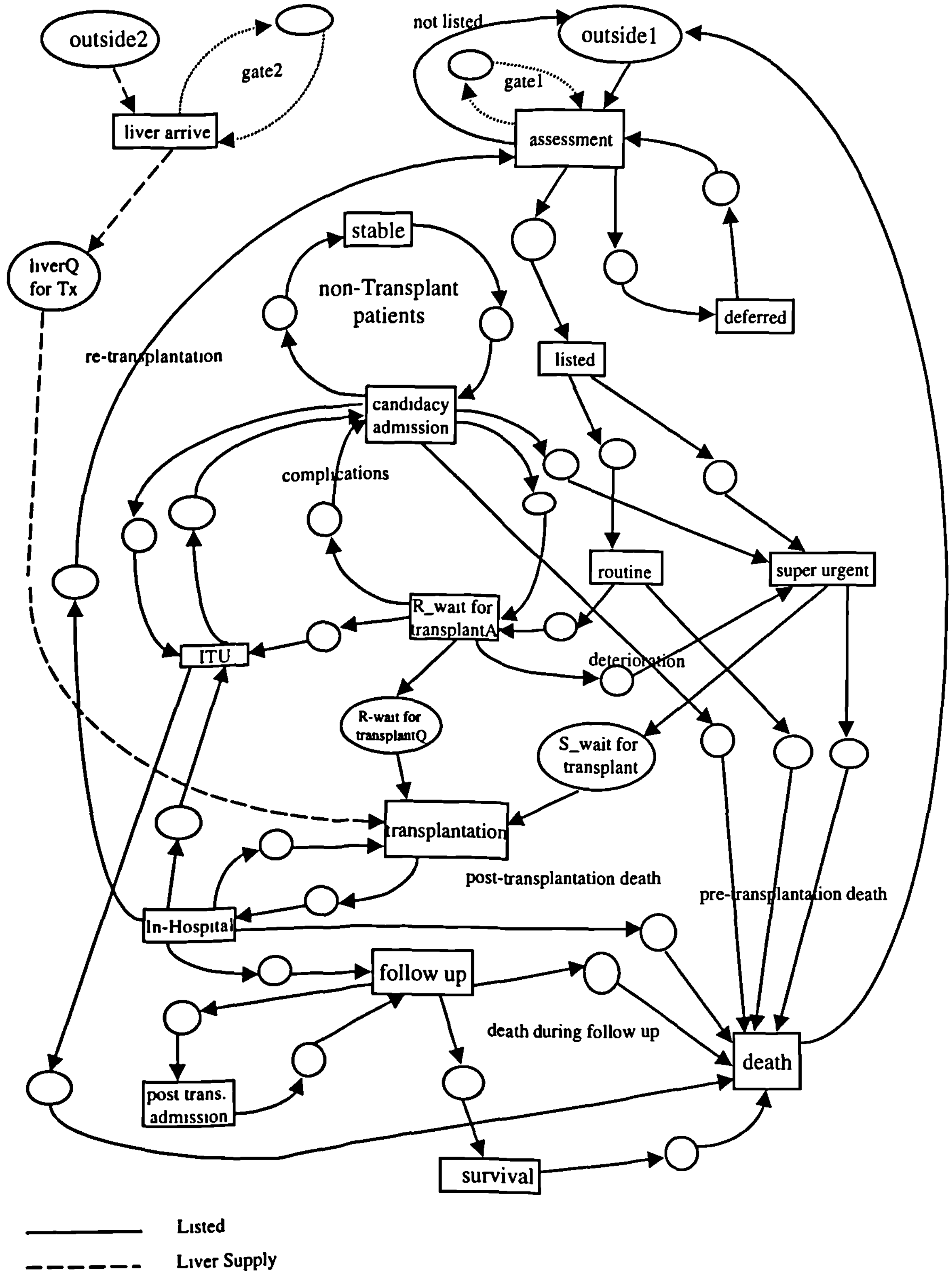



*Figure B.7: Version Seven of ACD of LiverSim*

# APPENDIX C: LiverSim Inputs (Base Case)

*Table C.1: Key Data Elements Included in the Model for Liver Transplant Patients*

| ***Data element*** | **Form of representation** | **Value** |
|---|---|---|
| Proportion of patients assessed with PBC | Probability | 46% |
| Proportion of patients assessed with ALD | Probability | 54% |
| Proportion of patients listed | Probability | 100% |
| Length of stay in assessment phase | Median (range) days by clinical severity groupings | Group A = 3 (1-5)<br>Group B = 8 (6-10)<br>Group C = 13 (10-15)<br>Group D = 20 (15-25) |
| Assessment out-patient visits | Probability of number of visits | 0 visits=0.73<br>1 visit=0.16<br>2 visits=0.08<br>3 visits=0.003 |
| Investigations and tests in assessment | Probability by clinical severity groupings | Group A =45%<br>Group B = 60%<br>Group C = 79%<br>Group D = 100% |
| Physiotherapy sessions in assessment phase | Probability of session frequency by clinical severity groupings | 1 session:<br>Group A=85%<br>Group B=60%<br>Group C=56%<br>Group D=53%<br>2 or more sessions:<br>Group A=15%<br>Group B=36%<br>Group C=35%<br>Group D=37% |
| Dietician sessions in assessment phase | Probability of session frequency by clinical severity groupings | 1 session:<br>Group A=55%<br>Group B=45%<br>Group C=30%<br>Group D=18%<br>2 sessions:<br>Group A=35%<br>Group B=35%<br>Group C=29%<br>Group D=16%<br>3 sessions:<br>Group A=10%<br>Group B=17%<br>Group C=21%<br>Group D=14% |
| Length of time between end of assessment and listing | Median (range) of days by clinical severity groupings | Group A= 5 (1-8)<br>Group B= 10 (7-12)<br>Group C= 16 (12-18)<br>Group D= 22 (17-28) |
| Proportion of patients assessed who received at least one candidacy admission | Probability | PBC=54%<br>ALD=45% |
| Frequency of time interval between candidacy admissions | Median (range) of days | 60 (30-90) |
| Length of stay per candidacy admission | Median (range) of days by reason | Routine treatment: 7 (2-9)<br>Deterioration in condition: 7 (2-16)<br>Transplant cancellation: 1 (1-3)<br>Other reason: 2 (1-3) |

| | | |
|---|---|---|
| Length of stay in transplant phase | Median (range) of days | 34 (23-57) |
| Length of transplant operation | Median (range) of hours in theatre | 6.5 (4-9) |
| Investigations and tests in transplant phase | Probability | Group A=62%<br>Group B=65%<br>Group C=74%<br>Group D=100% |
| Drugs in transplant phase | Probability | Group A=56%<br>Group B=70%<br>Group C=74%<br>Group D=100% |
| Physiotherapy sessions in transplant phase | Probability of session frequency | 0 sessions=23%<br>1-3 sessions=21%<br>4-6 sessions=29%<br>7-12 sessions=27% |
| Dietician sessions in transplant phase | Probability of session frequency | 0 sessions=23%<br>1-3 sessions=25%<br>4-6 sessions=25%<br>7-12 sessions=28% |
| Proportion of patients transplanted who received at least one post-transplant admission | Probability | PBC=52%<br>ALD=48% |
| Frequency of post-transplant admissions | Median number (range) of admissions by reason | Routine follow up: 2 (1-4)<br>Deteriorating liver function: 2(1-3)<br>Problem relating to graft: 2 (1-3)<br>Planned medical/surgical procedure 2 (2-4) |
| Length of stay per post-transplant admission | Median number (range) of days by reason | Routine follow up: 3 (1-5)<br>Deteriorating liver function: 5 (1-15)<br>Problem relating to graft: 7 (2-12)<br>Planned medical/surgical procedure 3 (1-9) |
| Drugs during post-transplant admission | Probability | Group A=82%<br>Group B=85%<br>Group C=93%<br>Group D=100% |
| Investigations and tests during post-transplant admission | Probability | Group A=61%<br>Group B=64%<br>Group C=72%<br>Group D=100% |
| Proportion of patients re-transplanted (PBC) | Probability | 0.08 |
| Proportion of patients re-transplanted (ALD) | Probability | 0.06 |
| Out-patient visits in follow up phase | Median number (range) | 30 (15-45) |
| Investigations and tests during follow up phase | | Group A=100%<br>Group B=100%<br>Group C=100%<br>Group D=100% |
| Drugs in follow up phase | | Group A=100%<br>Group B=100%<br>Group C=100%<br>Group D=100% |

*Table C.2: Key Data Elements included in the Model for Liver Disease Patients*

| ***Data element*** | **Form of representation** | **Value** |
|---|---|---|
| Proportion of patients with PBC | Probability | 46% |
| Proportion of patients with ALD | Probability | 54% |
| Length of time between admissions | Median (IQ range) days | 65 (35-120) |
| Length of stay for admission | Median (IQ range) days by reason | Ascites: 6 (2-10)<br>Malnutrition: 6 (4-12)<br>Hepatocellular carcinoma: 12 (8-18)<br>Sepsis including SPB: 11 (4-15)<br>GI bleeding varices: 11 (6-16)<br>GI bleeding non varices: 12 (5-15)<br>Hepatic encephalopathy: 6 (3-8)<br>Electroylte abnormalities: 12 (3-16)<br>Alcohol withdrawal 7 (5-12)<br>Liver failure: 12 (6-20) |
| Frequency of out-patient visits annually | Probability of number of visits | 1-3 visits=0.43<br>4-6 visit=0.42<br>7-12 visits=0.15 |

*Table B.3: Rate of Change of Clinical Variables Over Time*

| Clinical variable | Daily rate of change PBC | Daily rate of change ALD |
|---|---|---|
| Serum bilirubin | 0.3034 | 0.4046 |
| Serum albumin | 0.0228 | 0.0304 |
| Blood urea | 0.00226 | 0.00302 |
| Prothombin time | 0.0433 | 0.0482 |
| Presence of ascites | Constant (0/1) | Constant (0/1) |
| Spontaneous bacterial peritonitis | Constant (0/1) | Constant (0/1) |

*Table C.4: Post-Transplant Survival Probabilities*

| Year | PBC (CI) | ALD (CI) |
|---|---|---|
| 1 | 0.84 (0.74-0.94) | 0.86 (0.76-0.96) |
| 2 | 0.81 (0.71-0.91) | 0.79 (0.69-0.89) |
| 3 | 0.81 (0.71-0.91) | 0.76 (0.64-0.88) |
| 4 | 0.78 (0.66-0.90) | 0.76 (0.64-0.88) |
| 5 | 0.78 (0.66-0.90) | 0.73 (0.51-0.87) |

*Table C.5: Matching Criteria between Donor and Recipient*

| Donor Blood group | Recipient Blood group | Donor weight | Recipient weight |
|---|---|---|---|
| A+ = 32% | A+ = 36% | <50kg=24% | <50kg=22% |
| A - = 8% | A - = 10% | 50-59kg=38% | 50-59kg=40% |
| AB+ = 2% | AB+ = 6% | 60-69kg=25% | 60-69kg=24% |
| B+ = 14% | B+ = 2% | 70-79kg=8% | 70-79kg=9% |
| B - = 3% | B - = 0% | >79kg=5% | >79kg=5% |
| 0+ = 33% | 0+ = 43% | | |
| 0 - = 8% | 0 - = 3% | | |

# Appendix D: Validation Graphs (LiverSim)

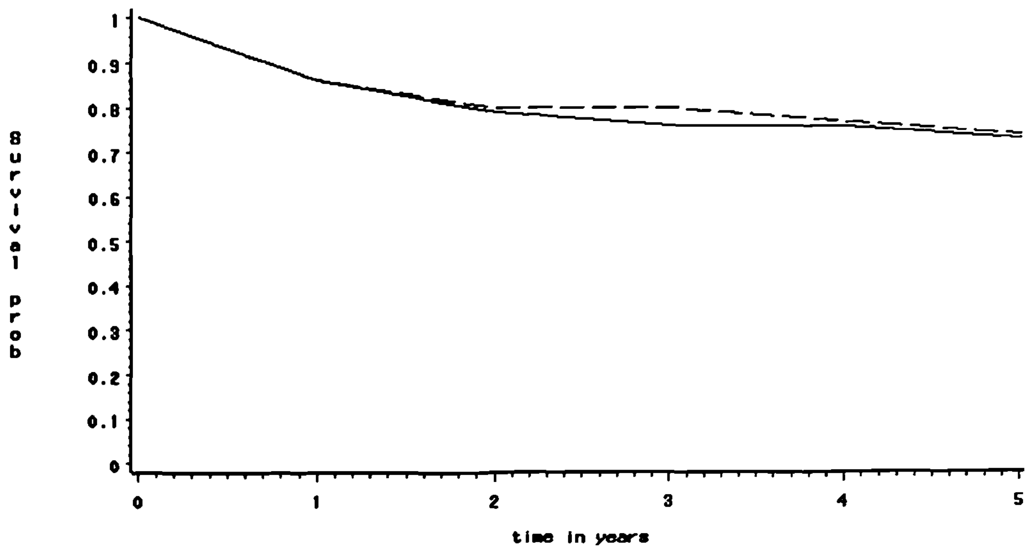



*Figure D.1: Survival for ALD Patients*

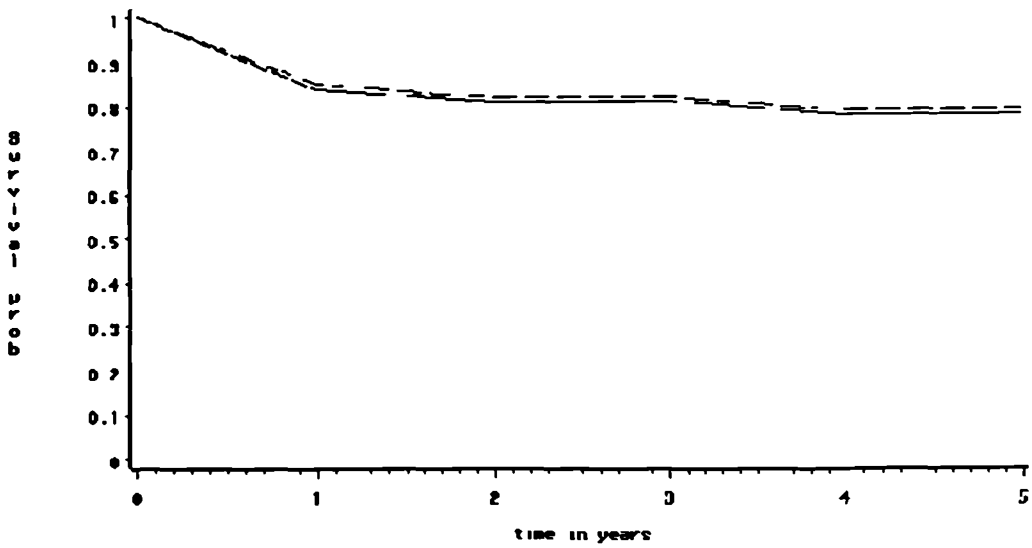



*Figure D.2: Survival for PBC patients*

Simulated ( ------------ ) Actuarial (————— )

# Appendix E: Results of Sensitivity Analysis (LiverSim)

*Table E.1: Sensitivity Analysis*

| Parameter values | Policy | Costtx (£) | Costld (£) | Survtx (yr.) | Survld (yr.) | ICER (£) |
|---|---|---|---|---|---|---|
| Survival discounted at 6% | High wait | 59086 | 24185 | 3.76 | 1.09 | 13072 |
| | Low wait | 57667 | 22686 | 3.61 | 1.00 | 13403 |
| | High age | 54725 | 16907 | 3.71 | 0.96 | 13752 |
| | Low age | 57382 | 25694 | 3.82 | 1.13 | 11780 |
| | High PI | 57613 | 18952 | 3.91 | 1.03 | 13424 |
| | Low PI | 59520 | 24078 | 3.73 | 1.13 | 13632 |
| | Groups | 59100 | 32777 | 4.02 | 1.11 | 09046 |
| Survival discounted at 10% | High wait | 59086 | 24185 | 3.57 | 1.09 | 14073 |
| | Low wait | 57667 | 22686 | 3.42 | 1.00 | 14455 |
| | High age | 54725 | 16907 | 3.52 | 0.96 | 14773 |
| | Low age | 57382 | 25694 | 3.63 | 1.12 | 12625 |
| | High PI | 57613 | 18952 | 3.71 | 1.03 | 14426 |
| | Low PI | 59520 | 24078 | 3.55 | 1.12 | 14585 |
| | Groups | 59100 | 32777 | 3.48 | 1.11 | 11107 |
| Costs undiscounted | High wait | 64652 | 26210 | 4.12 | 1.1 | 13400 |
| | Low wait | 63293 | 25206 | 3.97 | 1.01 | 12867 |
| | High age | 60014 | 18421 | 4.07 | 0.96 | 13374 |
| | Low age | 63892 | 28140 | 4.18 | 1.14 | 11761 |
| | High PI | 63370 | 20428 | 4.26 | 1.03 | 13295 |
| | Low PI | 65329 | 26594 | 4.09 | 1.14 | 13131 |
| | Groups | 65124 | 35127 | 4.02 | 1.12 | 10344 |
| Costs discounted at 10% | High wait | 55040 | 21849 | 4.12 | 1.1 | 10990 |
| | Low wait | 53781 | 19926 | 3.97 | 1.01 | 11438 |
| | High age | 51249 | 13981 | 4.07 | 0.96 | 11983 |
| | Low age | 53257 | 22930 | 4.18 | 1.14 | 09976 |
| | High PI | 53675 | 15569 | 4.26 | 1.03 | 11798 |
| | Low PI | 55683 | 21725 | 4.09 | 1.14 | 11511 |
| | Groups | 55057 | 29893 | 4.02 | 1.12 | 08677 |
| Lower CI for post-transplant survival | High wait | 58134 | 23287 | 3.95 | 1.1 | 12227 |
| | Low wait | 56237 | 21928 | 3.81 | 1.01 | 12253 |
| | High age | 52894 | 17100 | 3.90 | 0.96 | 12175 |
| | Low age | 55419 | 24982 | 3.99 | 1.14 | 10680 |
| | High PI | 55218 | 18982 | 4.07 | 1.03 | 11920 |
| | Low PI | 56723 | 23952 | 3.92 | 1.14 | 11788 |
| | Groups | 56937 | 32777 | 3.83 | 1.12 | 08915 |
| Higher CI for post-transplant survival | High wait | 59086 | 24185 | 4.33 | 1.1 | 10805 |
| | Low wait | 57667 | 22686 | 4.19 | 1.01 | 11000 |
| | High age | 54725 | 16907 | 4.28 | 0.96 | 11391 |
| | Low age | 57382 | 25694 | 4.40 | 1.14 | 09720 |
| | High PI | 57613 | 18952 | 4.45 | 1.03 | 11304 |
| | Low PI | 59520 | 24078 | 4.28 | 1.14 | 11287 |
| | Groups | 59100 | 32777 | 4.22 | 1.12 | 08491 |

*Table E.2: Summary Results: Mean of 25 Simulations (150 Patients)*

| Policy | Costtx (£) | Costld (£) | Survtx (yr.) | Survld (yr.) | ICER (£) | 95% CI (£) |
|---|---|---|---|---|---|---|
| High wait | 59275 | 23803 | 4.12 | 1.08 | 11691 | 11195-12187 |
| Low wait | 59180 | 24919 | 3.96 | 1.08 | 11915 | 11508-12323 |
| High age | 59543 | 22170 | 4.11 | 1.06 | 12323 | 12067-12579 |
| Low age | 55248 | 23953 | 4.20 | 1.08 | 10032 | 09830-10234 |
| High PI | 59536 | 23533 | 4.09 | 1.13 | 12195 | 12282-12826 |
| Low PI | 57673 | 21000 | 4.07 | 1.15 | 12554 | 11941-12449 |
| Groups | 57964 | 31123 | 4.01 | 1.07 | 9106 | 08928-09283 |