Early community diagnosis of heart disease: a new model of care in Ireland for The Heartbeat Trust
THE HEARTBEAT TRUST
Early Community Diagnosis of Heart Disease – A New Model of Care in Ireland

*March 2014*
ABSTRACT

The objective of this project was to conduct a cost-effectiveness analysis (CEA) to evaluate a new community-based heart disease diagnostic service that is being offered on a trial basis by The Heartbeat Trust. This new outreach service was compared against the current hospital-based diagnostic service offered by the HSE on the basis of costs and utilities. It was decided that a Probabilistic Sensitivity Analysis (PSA) was the appropriate type of CEA to use for this project. This analysis should enable The Heartbeat Trust to determine whether their new service is cost-effective.
PREFACE

The Heartbeat Trust is a registered Irish charity that was formed in May 2004 to support the research and services of the St. Vincent’s Chronic Cardiovascular Disease Unit in Dublin. The main foci of the charity are:

- To raise public awareness of the risk of developing Cardiomyopathy and Heart Failure
- To develop improved strategies of detecting cardiomyopathy earlier in its development and prevent its' progression to Heart Failure.
- To enhance collaborative management between community and hospital based services of both people with and those at risk of developing cardiomyopathy and heart failure

The Trust supported St Vincent's Screening TO Prevent Heart Failure (STOP-HF) study which has gained international recognition. The aim of the study was to detect heart disease in at-risk patients without symptoms. They are now also supporting a trial to detect heart failure in patients with early signs of the disease through the use of community diagnostics, rapid (remote) specialist opinion and a new outpatient clinic to confirm suspected diagnoses.

This report succeeds in conducting a Probabilistic Sensitivity Analysis in Excel to determine whether or not the new outreach service supported by The Heartbeat Trust is cost-effective compared to current, usual care. The model was built in Excel and makes use of Bayesian and Monte Carlo methods.

This project was successfully completed thanks to the assistance and guidance offered by a number of people. Firstly, I would like to thank my supervisor Dr Cathal Walsh whose advice and support was invaluable over the course of this project. Secondly, I want to thank Dr Mark Ledwidge from The Heartbeat Trust whose knowledge and expertise in the area of heart disease was of great help in sourcing the information necessary to carry out this cost-effectiveness analysis. Finally, I would like to thank Dr Lesley Tilson from the National Centre for Pharmacoeconomics (NCPE) who assisted in formulating and defining the scope of the project.
THE HEARTBEAT TRUST
Early Community Diagnosis of Heart Disease

March 2014

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REFERENCES
1. INTRODUCTION

This chapter establishes the project background and the terms of reference for this study. It also provides a summary of the contents of the chapters that follow.

1.1. Project Background

The Heartbeat Trust targets three distinct groups of patients in the course of their heart failure prevention work, these are:

- Patients with established Heart Failure
- At-risk patients without symptoms
- Patients with early signs of the disease

The first group is addressed by St. Vincent’s Heart Failure Disease Management programme. Their landmark international study, St. Vincent’s Screening TO Prevent Heart Failure (STOP-HF) is aimed at identifying heart failure in the second group of patients.

They have recently turned their attention to identifying heart disease in the third group of patients. They are supporting a pilot project in a GP clinic in Gorey, Co. Wexford. At the beginning of this project, 100 patients had been evaluated. Currently, 500 plus patients have been evaluated and the trial is still ongoing. The main characteristic that identifies these patients is dyspnoea (shortness of breath) which can be an early symptom of heart disease.

The purpose of this project is to see if this new outreach service for heart disease diagnosis is more cost-effective than current, usual care in Ireland.

Outreach Service

When patients with dyspnoea present to the clinic in Gorey, a Brain Natriuretic Peptide (BNP) test is administered and based on the results of the test, patients are recommended for a remote echocardiogram or not. If a patient is recommended for an echocardiogram they will only have to wait between 1 – 4 weeks until the remote echocardiogram van visits the clinic. Based on the result of their echocardiogram they may or may not be referred for an outpatient visit. The wait time for the outpatient visit is between 1 – 4 weeks. During their outpatient visit, they may or may not be diagnosed with heart disease and they can then begin treatment if necessary.
**Usual Care**
Currently if a patient presents to a GP with dyspnoea, they are recommended for an outpatient appointment which can take up to 3 – 6 months. They will then be referred for an Echo which takes approximately 3 months. Finally, after a further 1 – 3 months, they will have a return outpatient visit where they will or won’t be diagnosed with heart failure. Due to the length of the expected time to diagnosis, patients run a real risk of undergoing an emergency admission to hospital which is both a costly and stressful experience. The wait times for usual care are based on the St. Vincent’s catchment area, however national wait times for an echocardiogram is approximately 20 months.

**Echocardiogram**
An echocardiogram is a non-invasive medical test that can take up to 25 minutes to administer. It involves recording moving images of a working heart from several different angles using sound waves in order to build up a clear picture of the heart. The purpose of the test is to assess how the heart is functioning, if the valves are opening normally and are not infected, to check for clots and finally to check for any fluid that may be surrounding the heart.

**BNP Test**
A Brain Natriuretic Peptide (BNP) test, also known as a B-type Natriuretic Peptide test is a test that checks the amount of BNP hormone present in a patient’s blood. BNP is secreted by the ventricles of the heart. Normally, only a low amount of BNP is found in your blood. But if your heart has to work harder than usual over a long period of time, for reasons such as heart failure, the heart releases more BNP, increasing the amount of BNP in the blood. Thus, it is a useful screening test for heart disease.

**Decision Tree Model**
It was decided from a reading of the literature (Cooper, K. et al., 2006) and through consultation with both my supervisor and client that a decision tree model was appropriate for this project. The tree has two main arms, one which represents the outreach service and the other which represents current usual care. There are two types of end nodes in this tree; Heart Disease diagnosis and GP Review. A GP Review end node indicates that heart failure has been ruled out and the patient is referred back to their GP for further investigation. Probabilities for each parameter were gathered from the outreach service trial and the literature. Probability distributions were then created for each parameter in the model.
1.2. Terms of Reference

To develop a Decision Tree in Excel to compare two models of heart failure diagnosis in Ireland, the traditional model and the proposed “community-based” approach.

- Collect data on costs, probabilities and utilities.
- Build Decision Tree to compare new model against existing model.
- Analyse output of Decision Tree and determine which model is most cost-effective.

1.3. Summary of Chapters

This report contains the following chapters:

- **Chapter 2**: Outlines the main conclusions of the project and contains the list of recommendations that resulted from them.
- **Chapter 3**: Contains a literature review based on the main concepts involved in this project.
- **Chapter 4**: Describes the approaches used in the modelling and the methodology behind it.
- **Chapter 5**: Outlines the model construction and details the distributions used to model parameters.
- **Chapter 6**: Examines the overall results of the model.
2. CONCLUSIONS AND RECOMMENDATIONS

This chapter contains the conclusions and recommendations of the project.

2.1. Conclusions

- The results of the PSA look promising for the new outreach service offered by the Heartbeat Trust. The probability of the new service being cost-effective at the threshold of €45,000 is 99.2%. (See Section 6.2)
- Altering the threshold would not make a serious change in the cost-effectiveness of the new service as shown from the cost-effectiveness acceptability curve. (See Section 6.1)
- A one-way sensitivity analysis of the model parameters highlighted the key parameters from each parameter type; probability, cost and utility. The large impact that these parameters had on the cost-effectiveness represents the huge uncertainty surrounding the data used in this model. (See Section 6.3)

2.2 Recommendations

- It is recommended that the decision maker carry out further analysis e.g. Budget Impact Analysis (BIA) to establish the feasibility of rolling this service out across Ireland.
- The decision maker should also be aware that there is huge uncertainty surrounding the parameters used in this model and should further evidence arise the decision should be revisited again.
3. LITERATURE REVIEW

This chapter contains a literature review that discusses topics relevant to this project.

3.1. Literature Review

This review is broadly based in the domain of health economics which is growing rapidly due to considerable interest from health providers around the world in assessing the cost-effectiveness of a medical intervention (O'Hagan, Stevens, 2001). The National Institute for Health and Care Excellence (NICE) in the United Kingdom was set up in 1999 and is now regarded as a world leader in the field of health economics. The Irish equivalent, the National Centre for Pharmacoeconomics was established in St. James' hospital in 1998. Both these organisations conduct economic evaluations of new and existing health technologies. From a reading of the literature, I hope to gain a better understanding of the types of analysis, methodologies and measures that those organisations are likely to use in the course of their work.

Economic Evaluation

There are three types of economic evaluations; cost-effectiveness analysis, cost-utility analysis and cost-benefit analysis. They differ in how they assess health benefits. Cost-effectiveness analysis would typically have use health benefits such as Life-Years Gained (LYG) but this is limited as it can only measure a single type of unit. In particular, health related quality of life (HRQoL) cannot be accounted for. Cost-utility analysis typically assesses health benefits in units known as Quality-Adjusted Life Years (QALYs). QALYs can account for survival benefits, e.g. a longer life, and improved HRQoL. Finally, cost-benefit analysis tries to convert health gains into monetary terms which can limit this type of analysis. According to Cooper et al., the most popular type of models of heart disease treatments are decision trees, Markov and state transition models. Decision trees are generally used for short term or acute interventions while the Markov and state transition models are more suited for modelling chronic or long term interventions (Cooper et al., 2006).

Dealing with Uncertainty in Cost-Effectiveness Models

There are many different types of uncertainty inherent in cost-effectiveness models; chance, heterogeneity, ignorance and parameter uncertainty (Spiegelhalter, et al., 2004, p.321). Of these four types of uncertainty, parameter uncertainty is the most widely discussed in the literature. An example of an inherently uncertain parameter would be the cost of an echocardiogram, this value will change from hospital to hospital and will even change over time. Sensitivity analysis is the conventional way to deal with this uncertainty. The values of each parameter can be varied one at a time (one-way sensitivity analysis) or together (multi-way sensitivity analysis) to assess their impact on cost-effectiveness. These are types of Deterministic Sensitivity Analysis, however O'Hagan et al. suggest that the most statistically
sound way to assess the uncertainty in a model is to carry out a Probabilistic Sensitivity Analysis (O’Hagan et al., 2003:40). PSA involves assigning appropriate probability distributions to model parameters and using Monte Carlo simulation to generate output. PSA is advantageous as it allows all parameters to vary simultaneously. The output from a PSA can be used to generate a cost-effectiveness acceptability curve. “The CEAC indicates the probability that the intervention is cost-effective compared with the alternative, given the data and for a given value of the maximum acceptable ratio (λ)” (Fenwick et al., 2005). It is useful aid for decision makers in the area of health economics and other applied studies.

Comparison Measure for Interventions
A popular measure for comparing two types of health interventions is the incremental cost-effectiveness ratio. The ICER is defined as “the cost per unit increase in effectiveness by adopting treatment option T2 rather than T1” (Spiegalhalter et al., 2004, p.308). This can be presented in the following formula:

\[
ICER = \frac{Cost_2 - Cost_1}{Utility_2 - Utility_1}
\]

ICERs represent the incremental cost per additional unit of outcome. This could be the cost per patient treated, cost per QALY gained or any other type of quantifiable health gain. As the ICER becomes smaller the new treatment 2 is considered to be more cost-effective than treatment 1. ICERs can take values below zero and this may indicate that the new treatment represents a cost saving as well as being cost-effective. The mean ICER value of an intervention is typically compared to a predetermined threshold. O’Hagan and Stevens define this threshold as the cost that decision makers are willing to accept in order to increase the effectiveness of the treatment applied by one unit (O’Hagan et al., 2001). There is no formal threshold in Ireland but the Department of Health and Children have agreed to reimburse most drug interventions with an ICER of less than €45,000 per QALY gained. Threshold values will vary from country to country, for example in the UK, the threshold is set at £20,000.

The STOP-HF Randomised Trial
The Heartbeat Trust has already been involved in a successful study that provided collaborative care to patients on the basis of their BNP test results (Ledwidge, M. et al., 2013). 1374 patients were randomly assigned to a control group (677) and an intervention group (697). The intervention group was then screened using a BNP test and collaborative care was provided to 263 patients. The results of the study demonstrated a reduction in newly diagnosed HF, asymptomatic left ventricular dysfunction, and emergency cardiovascular hospitalizations in the intervention group. This was the first study of its kind that used a BNP test to screen for heart failure. The new outreach service that this project is concerned with also uses a BNP test to screen for heart failure.
4. PROBABILISTIC MODELLING

This chapter contains information related to the techniques used in this project.

4.1. Probabilistic Sensitivity Analysis

Probabilistic Sensitivity Analysis (PSA) is the standard method of running a cost-effectiveness analysis. This approach is used by Irish agencies such as the Health Information and Quality Authority (HIQA) and the National Centre for Pharmacoeconomics (NCPE). The National Institute for Health and Care Excellence (NICE) in the United Kingdom also recommends the approach undertaken in this project. NICE is the NCPE’s equivalent in the United Kingdom and would be recognised as one of the leaders in the field of health economics. In PSA, probability distributions are assigned to the model parameters to represent the uncertainty in each value.

4.2. Bayesian Methods

Using probability distributions to model all sources of uncertainty in a statistical model is one of the characteristics of a Bayesian method. Therefore, our PSA uses a Bayesian approach. Bayesian methods are widely used in the field of health economics. In contrast to frequentist statistics where probability is seen as being derived from long run frequency distributions, the Bayesian viewpoint sees probability as a degree of belief in a hypothesis. One of the advantages of Bayesian methods is the ability to incorporate prior belief into a model, either in the form of expert opinion or information from previous relevant studies. Combining the data with the prior distribution gives us the posterior distribution from which we can make inferences about a parameter or proposition.

4.3. Decision Trees

Decision tree models are widely used in cost-effectiveness analysis. They are very easy to understand which is advantageous in the multidisciplinary field of health economics. They consist of branches and three types of nodes; decision, random and end nodes. Decision nodes represent a situation where a decision must be made. Random nodes represent an event where the outcome is uncertain. End nodes can be thought of as all the possible consequences of each decision.
4.4. Monte-Carlo Methods

Monte-Carlo methods are a common technique used in probabilistic sensitivity analysis. The technique was first used by scientists working on the atom bomb; it was named after a famous casino in Monaco, the Monte Carlo. They are a broad class of computational algorithms that make use of repeated random sampling to obtain numerical results. In this case our decision tree model was simulated 10,000 times in order to determine if the new service is more cost-effective than the current service. Monte-Carlo simulation allows all the model parameters that have inherent uncertainty to vary independently and therefore it will produce both extreme and conservative outcomes as well as everything in between. A Monte-Carlo simulation turns a deterministic model into a stochastic one.

4.5. Incremental Cost-Effectiveness Ratio

The Incremental Cost-Effectiveness Ratio is the ratio of the difference in cost of a new treatment compared to an alternative to the difference in utility of the new treatment compared to the same alternative treatment.

\[
ICER = \frac{Cost_1 - Cost_2}{Utility_1 - Utility_2}
\]

This ratio can be useful in determining if a new treatment is cost effective or not. A treatment is regarded as cost effective if the mean ICER from the analysis is less than some predetermined threshold. Thresholds can vary by country, in the United Kingdom, the threshold is set at £20,000 but treatments up to £30,000 are also considered. In Ireland, treatments up to €45,000 are considered. However it must be noted that, some treatments over the threshold have been implemented while treatments that have an ICER of less than the threshold, are not guaranteed implementation.

4.6. One-Way Sensitivity Analysis of Parameters

This type of analysis is useful in determining which parameters have the largest effect on the outcome variable, in this case the ICER. To run this analysis all parameters are set to their base values, the model is run and the ICER is recorded. Then, each parameter is adjusted in turn, with the effect on the ICER being recorded each time. Usually, a low and a high value are tried for each parameter. The results can be displayed in a tornado diagram that is useful for highlighting the most important parameters. The main disadvantage of this analysis is that it cannot detect interactions between parameters as they are varied independently.

4.7. Software

The model will be built and analysed in Microsoft Excel. Excel is a widely used and powerful tool that is very suitable for this type of project.
5. **MODEL**

This chapter describes the model and distributions used within this analysis.

5.1. **Construction**

There is no native functionality in Excel that allows the user to automatically construct decision trees. Therefore, it was necessary to design and construct the tree manually. The Excel file contains four sheets:

- Decision_Tree
- Costs
- Utilities
- Monte_Carlo

**Stage One**

The first task involved designing the tree; several drafts of the tree were exchanged with the client before a final design was decided upon. The tree was then constructed in Excel using probabilities supplied by the client and with rough estimates of the cost and probability parameters. The decision tree has only one decision node, whether to diagnose the patient through the new or existing service. The rest of the nodes were random nodes, terminating in end nodes. I attached the cost and utility parameters to their respective end nodes and I assigned the probability parameters to the appropriate arms. This model was of very little use as the cost and utility parameters were little more than guesswork and there was no uncertainty captured within the model.

**Stage Two**

The first step to improving the model involved sourcing cost and utility information from the outreach service trial and the literature to create better estimates for those parameters. Probability distributions were assigned to model parameters on the basis of their mean and variance. This turned our deterministic model into a stochastic one, where a parameters value is randomly drawn from a distribution representing it. The distributions used are explained in Section 5.2. and their implementation in Excel is discussed in Appendix D.
Stage Three

The final stage of this model involved implementing a Monte Carlo simulation of the model. This involved running the model 10,000 times and recorded the results each time. The results that were recorded were the expected cost and expected utility for both services. Those results were used to get the incremental cost, the incremental utility and the Incremental Cost Effectiveness Ratio (ICER). The ICER values can be used to establish if the new service is cost-effective or not.

5.2. Distributions Used

The uncertainty inherent in the model parameters was implemented by assigning probability distributions to each parameter. Different distributions were used for each type of parameter and these are discussed below.

Beta Distribution

Beta distributions were used to model probability parameters that have two outcomes. They are well suited for this as they return a value between 0 and 1 and also the shape parameters $\alpha$ and $\beta$; represent the number of successes and failures respectively. Utilities were almost modelled as Beta distributions as they are typically values between 0 and 1 with 1 being perfect health and 0 being death. Negative utility values can occur (i.e. states worse than death) however they need not be considered in this model.

The probability estimates were not supplied with figures for their variance so a coefficient of variation of 0.1 was used to estimate the variance. Beta distributions were then created in Excel using the mean and variance. The literature reported standard deviation figures for the utility values so Beta distributions were created for them from those figures. The formula for the coefficient of variation is below:

$$Coefficient\ of\ Variation = \frac{Standard\ Deviation}{Mean}$$

LogNormal Distribution

LogNormal distributions are widely used for modelling costs because they are positively skewed and cannot take values less than zero. Similar to the probability parameters, only estimates of the costs’ means were reported so a coefficient of variation of 0.1 was used to estimate the standard deviation of the LogNormal distributions.
5.3. **Adjustments and Limitations**

This section briefly discusses the adjustments and limitations of the model.

**Differing Amount of Diagnoses**

The probabilities for the outreach service arm were taken from the trial and for a cohort of 100 people, 26 could be expected to be diagnosed. The probabilities from the existing service were taken from UK data and for a cohort of 100 people 32 could be expected to be diagnosed; 12 of which would be diagnosed after and emergency admission.

To accommodate this, the client felt it was appropriate to decrease the number of diagnoses in the existing service pathway to 26 by reducing the number of diagnoses in the emergency arm from 12 to 6. This has the effect of improving the cost-effectiveness of the existing service.

**Utility Values**

The basis for the utility values used in the model was taken from the literature (Dyer et al., 2010). The values used were 0.78 with a standard deviation of 0.18 for patients with mild heart failure and 0.51 with a standard deviation of 0.21 for patients with severe heart failure. Patients that underwent an emergency admission had utility values that were based on the severe heart failure figures while patients that didn’t experience an emergency admission were assigned utility values that were based on the figures for mild heart failure. However utility values within these groupings were increased or decreased depending on the expected time it took to reach each end node and if the patient’s utility was expected to be better or worse than the base case. Close consultation with the client was necessary to ensure that these values were fair.

**Patient Frailty**

Initially when the model was run first, the probability and utility parameters all made separate calls to RAND(). This resulted in a very wide spread of ICER values because the same patient (i.e. a single simulation) might end up, by chance, with a high utility through the existing service route and a low utility for the outreach service route. We felt this was unreasonable as the same patient would be expected to have roughly the same utility no matter which diagnostic service they used. To adjust for this we made a single call to RAND() which we termed as a patient’s frailty which was used to draw values from the utility parameters’ distributions and another call to RAND() which was used to draw from the probability parameter distributions. A patient’s frailty can be thought of as adjusting for a patient’s pre-existing condition. The cost parameters were allowed to vary independently as there is no reason to assume that they are correlated.
6. RESULTS

This chapter contains a discussion on the results of the CEA. The results are presented in graph format for readability.

6.1. Cost-Effectiveness Acceptability Curve

Cost-Effectiveness Acceptability curves show the probability that a new service is more cost-effective than the existing service for a range of different threshold values. It can be interpreted as the probability that the ICER is less than each threshold value. In Ireland, interventions with an ICER up to €45,000 are considered. It is not clear from the graph but the probability of The Heartbeat Trust’s new outreach service being more cost-effective than current usual care is 0.992. Even at a threshold of -€10,000 (i.e. a saving of €10,000) this new service has a probability of cost-effectiveness of 0.6981. This graph provides strong evidence that the new service will be cost-effective.

![Cost-Effectiveness Acceptability Curve](image)

FIGURE 6.1.1 – Cost-Effectiveness Acceptability Curve
6.2. Incremental Cost Effect Scatterplot

The Incremental Cost-Effectiveness Scatterplot plots the ICER’s obtained from the PSA on a graph with the incremental utility on the x-axis and the incremental cost on the y-axis. The red line represents the threshold of €45,000 that is used in Ireland. This plot is very informative from a cost-effectiveness viewpoint.

The top-left quadrant corresponds to the domination of the existing service over the new outreach service. This means that the new service is more costly and less effective than the existing service. As can be seen from the graph, there are almost no points in this quadrant.

The bottom-right quadrant represents domination of the new outreach service over the existing service. Points in this region mean that the new service is less costly and more effective in utility terms than the existing service. The top-right and bottom-left quadrants are split by the threshold line, any point below the line is deemed cost-effective.

On this graph, 99.2% of the points fall in the regions that are deemed cost-effective. This means that the new service has a 99.2% probability of being cost-effective compared to the existing service. This graph is ideal for decision making as it presents clear evidence that the new service will be cost-effective.
6.3. One-Way Sensitivity Analysis of Parameters

When the decision tree model was run deterministically, with all values set to their point estimates the resulting ICER was -€12,198. Each parameter was then set to a low and high value in turn and the effect on the ICER was recorded. Bars to the right of the base value of -€12,198 represent a reduction in cost-effectiveness, while bars to the left represent an increase in cost-effectiveness. The graphs are split up by parameter type and parameters are ordered from top-to-bottom according to the size of their effect on the ICER. The parameters are on the y-axis and the ICER values are on the x-axis.

The low value was taken as the value at 0.025 in the parameters distribution. The high value was taken as the value at 0.975 in the parameters distribution. It should also be noted that the variances associated with the probability parameters’ distributions was at least an order of magnitude smaller than the variance associated with either the cost or utility parameter distributions.

Probability Parameters

From the graph, it is clear that the main driver of cost-effectiveness for the probability parameters is the probability of being referred and attending an outpatient appointment in the existing service. This makes sense because if the patient does not make it to their appointment, they will be admitted to hospital through an emergency admission which is an expensive process. The more patients undergo emergency admissions in the existing service arm, the more cost-effective the new treatment appears.

![Probability Parameters Tornado](image)

FIGURE 6.3.1 – Probability Parameters Tornado
Cost Parameters

By far, the most important cost parameters from a cost-effectiveness viewpoint are the cost of an emergency admission with heart failure and the cost of an emergency admission without heart failure. This is expected as emergency admissions are expensive and they also have a low utility score attached to them. Also the patient’s condition has obviously deteriorated significantly if an emergency admission was necessary. Higher emergency admission costs would make the new service even more appealing.

FIGURE 6.3.2 – Cost Parameters Tornado
Utility Parameters

The utility parameters were adjusted differently than the other parameters. They were all set to low and then to high simultaneously. It is clear for Figure 6.3.3 that even if we grossly underestimated or overestimated the utility values, the outreach service is still cost effective.

FIGURE 6.3.3 – Utility Parameters Tornado
All Parameters

This final graph includes all the parameters used in the model. It is obvious from the graph that the cost and utility parameters have a greater effect on the ICER value than the probability parameters. This reflects the larger uncertainty (i.e. variance) surrounding the cost and utility parameters as they are allowed to vary to quite extreme values in comparison to the probability parameters.

FIGURE 6.3.4 – All Parameters Tornado
APPENDIX A

ORIGINAL PROJECT OUTLINE

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<td>Cathal Walsh</td>
</tr>
</tbody>
</table>

Client Background

The Heartbeat Trust (www.heartbeat-trust.org) was founded in May 2004 and supports research and specialist services in the Heart Failure Unit in St Vincent’s University Hospital Group. The major work is focused on heart failure prevention, understanding myocardial fibrosis and connected healthcare.

Project Background

The Heartbeat Trust’s heart failure prevention work has been directed at three distinct types of patients: first, patients with well-established heart failure who have had at least one hospitalisation event; second, at-risk patients without symptoms; third, patients with early signs of the disease.

Amongst the first group of patients, the St Vincent’s Heart Failure Disease Management programme has shown dramatic reductions in hospitalization and improved outcomes. In the second group of patients, the St Vincent’s Screening TO Prevent Heart Failure (STOP-HF) project has shown that it is possible to reduce heart failure (HF) and major cardiovascular events by more than 40% (p<0.01) in a landmark international study. Our efforts are now directed at providing a new service for patients in the community with early stages of heart failure. The diagnosis is difficult for General Practitioners to make without access to specialist diagnostics and opinions. The waiting times for outpatient appointments for non-urgent cases ranges from 6 months to more than 4 years around the country.
Client Requirement

In a pilot project, the Trust is supporting out-reach diagnostics in a General Practice in Gorey, Co. Wexford. Using community diagnostics, rapid (remote) specialist opinion and a new outpatient clinic to confirm suspected diagnoses, the numbers of patients being evaluated in hospital is significantly reduced and the time to diagnosis is dramatically cut. More than 100 patients have been evaluated in the pilot phase of this community diagnostic clinic. This project will model the time and cost to diagnosis in the new service compared with current usual care.

What is involved for the student?

The student will work with the Trust team to develop an economic model that compares current usual care with the new out-reach service in terms of costs and time to correct diagnosis. Support will be available from the pilot general practice. Standard HSE costs will be used where available and assumptions around other costs will be justified. The medical literature will be used to model the risk of hospitalisation when diagnosis (and treatment) is delayed and information on standard outpatient waiting times for cardiology outpatient appointments in 3 selected hospital locations in Ireland will be used for comparison. The student will carry out sensitivity analyses using key cost drivers (e.g. P/Consultant/Specialist nurse time, Cardiac Technician time and Imaging costs, blood tests, consumables, travel etc). A business case will be made for roll out of the new clinic locally and nationally. The ideal candidate will have experience working with spreadsheet models in Excel.
APPENDIX B

INTERIM REPORT

Project: Early community diagnosis of heart disease – a new model of care in Ireland
Client: Heartbeat Trust
Student: Maurice McCole
Supervisor: Cathal Walsh

Review of Background and Work to Date

The Heartbeat Trust is a registered charity in Ireland that was formed in 2004 to support the services and research at the St Vincent’s Chronic Cardiovascular Disease Unit, Dublin. In a pilot project, the Trust is supporting out-reach diagnostics in a General Practice in Gorey, Co. Wexford. Using community diagnostics, rapid (remote) specialist opinion and a new outpatient clinic to confirm suspected diagnoses, the numbers of patients being evaluated in hospital is significantly reduced and the time to diagnosis is dramatically cut. More than 100 patients have been evaluated in the pilot phase of this community diagnostic clinic. This project will model the time and cost to diagnosis in the new service compared with current usual care.

The following work has been completed to date:

- Met with the client to discuss the scope of the project and determined that a decision tree model is suitable for this analysis
- Conducted an initial literature review around the health economics of heart failure assessment
- Requested the cost, utility and probability information necessary to model the problem
- Created initial decision tree in Excel with estimated probabilities
Terms of Reference

To develop a Decision Tree in Excel to compare two models of heart failure diagnosis in Ireland, the traditional model and the proposed “community-based” approach.

- Collect data on costs, probabilities and utilities.
- Build Decision Tree to compare new model against existing model.
- Analyse output of Decision Tree and determine which model is most cost-effective.

Further Work

Christmas: Completion of Decision Tree in Excel.

January: Carry out cost-effectiveness evaluation.

February/March: Report writing.

Conclusions

There are no conclusions to be made at this point. All conclusions will be made after completion of the cost-effectiveness analysis.
APPENDIX C

MICROSFOT EXCEL INFORMATION

Formulae Used

This section will detail the various formulae that were used in the construction and analysis of the model.

Sum
This function adds all the numbers in a range of cells. The formula is: “=SUM(range)”.

Average
This function returns the arithmetic mean of a range of cells. The formula is: “AVERAGE(range)”.

Standard Deviation
This function estimates the standard deviation based on a sample (i.e. a range of values). The formula is: “=STDEV.S(range)”.

Natural Logarithm
This function returns the natural logarithm of a number. The function is “=LN(number)”.

Inverse Logarithm
This function returns the inverse of the lognormal cumulative distribution function of x, where ln(x) is normally distributed with parameters Mean and Standard Deviation. The formula is “=LOGNORM.INV(Probability, Mean, Standard Deviation)”.

Absolute Values
This function returns the absolute value of a number, a number without its sign. The formula is “=ABS(number)”.

Random Numbers
This function returns a random number greater than or equal to 0 and less than 1 with each value over the range being equally likely. It does not take any arguments. The formula is: “=RAND()”.

Page C.1.
Countif
This function counts the number of cells in a range that meet the given condition. The formula is: “=COUNTIF(range, condition)”.  

Beta Distribution
This function returns the inverse of the cumulative beta probability distribution. The function requires three arguments a probability, an alpha and a beta value. The values of alpha and beta determine the shape of the Beta distribution. The formula is: “=BETA.INV(Probability, Alpha, Beta)”.  

Data Tables
A data table was used in this project to carry out the Monte Carlo simulation. The data table recorded the expected cost and expected utility of both diagnosis services 10,000 times. These values were then used to produce various graphs and determine the cost-effectiveness of the outreach service.
APPENDIX D

MODEL IMPLEMENTATION IN EXCEL

This section of the appendix details how the distributions were implemented in Excel and how the one-way sensitivity analysis was carried out.

How the distributions were implemented in Excel

Beta Distribution

The BETA.INV() function was used to implement the Beta distributions in Excel for the probability and utility parameters. As mentioned before in Section 5.2 the probability estimates were not supplied with a variance or standard deviation so a coefficient of variation of 0.1 was used to get a value for the variance. Standard deviation values were reported with the utility parameter means.

Once, all parameters had a mean and a variance, it was necessary to use formulae derived from the mean and variance formulae for the Beta distribution to get values for the shape parameters $\alpha$ and $\beta$. The derived formulae are below:

$$\alpha = \text{mean} \left( \frac{\text{mean}(1 - \text{mean})}{\text{Variance}} - 1 \right)$$

$$\beta = \alpha \left( \frac{1}{\text{Mean} - 1} \right)$$

The next step was to enter the following formula (“=BETA.INV(p_frailty,[@Alpha],[@Beta])”) into the realisation column to generate values from the Beta distributions in each row. As mentioned in Section 5.3 p_frailty represents a call to RAND().

![FIGURE D.1 – Example for Beta Distribution](image)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Point Estimate</th>
<th>Variance</th>
<th>Alpha</th>
<th>Beta</th>
<th>Realisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>p_hb_echo_referral</td>
<td>0.6</td>
<td>0.0036</td>
<td>39.4</td>
<td>26.26667</td>
<td>633995244</td>
</tr>
</tbody>
</table>

LogNormal Distribution

Similar to the probability parameters, a coefficient of variation of 0.1 was used with the cost parameters to get a figure for the standard deviation. Then it was just a matter of plugging them into the following formula:

<table>
<thead>
<tr>
<th>Events</th>
<th>Realisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>bnp_test</td>
<td>28.61560772</td>
</tr>
</tbody>
</table>

FIGURE D.2 – Example for LogNormal Distribution

Page D.1.
How the one-way sensitivity analysis of parameters was conducted in Excel

The one-way sensitivity analysis was done in the “Tree – Results” workbook. The model inputs were all set to their point estimates and each parameter was varied in turn at a low and then a high value. The low and high values were set in A10 and A12 in the “Decision_Tree” worksheet as shown in the Figure D.3 below.

![FIGURE D.3 – Low and High values for One-Way SA](image)

Those values were then used to draw values from the probability distribution of each parameter.

<table>
<thead>
<tr>
<th>Beta Distribution Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameters</td>
</tr>
<tr>
<td>p_hb_echo_referral</td>
</tr>
<tr>
<td>p_hb_outpatient_visit</td>
</tr>
<tr>
<td>p_hb_heart_failure_diagnosis</td>
</tr>
</tbody>
</table>

![FIGURE D.4 – Example for Low and High value draws from parameter probability distributions](image)

The model was run first with all values at their nominal values and the base ICER was recorded. Then, each parameter was varied in turn and the new ICER was recorded in the “One-Way SA” worksheet.

<table>
<thead>
<tr>
<th>Base ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Low</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>p_hb_echo_referral</td>
<td>-11460.57133</td>
<td>-13033.9</td>
</tr>
<tr>
<td>p_hb_outpatient_visit</td>
<td>-11852.95877</td>
<td>-12568.3</td>
</tr>
<tr>
<td>p_hb_heart_failure_diagnosis</td>
<td>-12062.73031</td>
<td>-12274.5</td>
</tr>
</tbody>
</table>

![FIGURE D.5 – Example for One-Way Sensitivity Analysis results](image)
APPENDIX E

EXPLANATIONS AND INSTRUCTIONS FOR SPREADSHEETS

The Google Drive link provided in Appendix F, accesses a folder called “THE HEARTBEAT TRUST” which contains two Excel workbooks:

- Tree – Model
- Tree – Results

The “Tree-Model” workbook contains the stochastic decision tree model as well as all the necessary inputs. It also contains the results from the Monte Carlo simulation. The “Tree-Results” workbook contains a deterministic version of the decision tree that was necessary for the one-way sensitivity analysis. The results of the Monte Carlo simulation are analysed and graphed in this workbook. Graphs are also produced for the one-way sensitivity analysis.

Tree – Model Workbook

Decision Tree Sheet
This sheet contains the decision tree model, a sample of which is shown in Figure E.1 below. Each branch of the tree has a probability associated with it that is drawn from the appropriate parameter’s Beta distribution that can be seen in Figure E.3.

![Decision Tree](image.png)

FIGURE E.1 – Decision Tree
The decision tree probabilities are multiplied along the branches and the result is stored in the Probabilities column in Figure E.2 below. Values for the Costs and Utilities columns are drawn from the appropriate distributions in the “Costs” and “Utilities” sheets. The expected cost and expected utility values are calculated by multiplying the Probabilities column value by the Costs and Utilities column values respectively. These columns are then summed for each pathway (i.e. outreach service and current service) in order to understand the expected cost and utility associated with each decision pathway.

<table>
<thead>
<tr>
<th>Costs</th>
<th>Utilities</th>
<th>Probabilities</th>
<th>Ex[Cost]</th>
<th>Ex[Utility]</th>
</tr>
</thead>
<tbody>
<tr>
<td>358.5504559</td>
<td>0.642785071</td>
<td>0.211230357</td>
<td>75.73674094</td>
<td>0.13577572</td>
</tr>
<tr>
<td>358.5504559</td>
<td>0.667368954</td>
<td>0.047941139</td>
<td>17.18931734</td>
<td>0.031994428</td>
</tr>
<tr>
<td>165.5766755</td>
<td>0.738858452</td>
<td>0.298704375</td>
<td>49.45847744</td>
<td>0.220700252</td>
</tr>
<tr>
<td>98.57647004</td>
<td>0.851271321</td>
<td>0.442124128</td>
<td>43.58303586</td>
<td>0.376367591</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>1.00</td>
<td><strong>185.9675716</strong></td>
<td><strong>0.764837991</strong></td>
</tr>
</tbody>
</table>

FIGURE E.2 – Example of Decision Tree End Nodes
The Beta Distribution table below has formulae in the Variance, Alpha, Beta and Realisation columns. The variance is calculated using a coefficient of variation and the alpha and beta values are calculated using the formulae in Appendix D. The realisation column contains a BETA.INV() function that returns a value from a Beta distribution. If you want to change a Beta distribution, you have the option of entering the mean (i.e. point estimate) and variance or you can enter the alpha and beta values directly. The realisation column will automatically update correctly.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Point Estimate</th>
<th>Variance</th>
<th>Alpha</th>
<th>Beta</th>
<th>Realisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>p_hb_echo_referral</td>
<td>0.6</td>
<td>0.0036</td>
<td>39.4</td>
<td>26.26667</td>
<td>0.557875872</td>
</tr>
<tr>
<td>p_hb_outpatient_visit</td>
<td>0.5</td>
<td>0.0025</td>
<td>49.5</td>
<td>49.5</td>
<td>0.464568392</td>
</tr>
<tr>
<td>p_hb_heart_failure_diagnosis</td>
<td>0.866666667</td>
<td>0.007511111</td>
<td>12.46667</td>
<td>1.917949</td>
<td>0.81502156</td>
</tr>
<tr>
<td>p_tr_outpatient_referral</td>
<td>0.77</td>
<td>0.005929</td>
<td>22.23</td>
<td>6.64013</td>
<td>0.718284784</td>
</tr>
<tr>
<td>p_tr_outpatient_referral_hf_diagnosis</td>
<td>0.220779221</td>
<td>0.000487435</td>
<td>77.7013</td>
<td>274.2399</td>
<td>0.20495285</td>
</tr>
<tr>
<td>p_tr_emergency_admission_hf_diagnosis</td>
<td>0.391304348</td>
<td>0.001531111</td>
<td>60.47826</td>
<td>94.07729</td>
<td>0.363408345</td>
</tr>
</tbody>
</table>

FIGURE E.3 – Beta Distribution Parameters

If you wish to change the coefficient of variation, it is located in cell A5. The frailty cell contains the function =RAND() and this is used to generate realisations from Beta distributions in the sheet.

<table>
<thead>
<tr>
<th>Coefficient of Variation</th>
<th>Frailty</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>0.240657865</td>
</tr>
</tbody>
</table>

FIGURE E.4 – Coefficient of Variation and Frailty
Costs Sheet

The second sheet in this workbook is the “Costs” sheet and the cost parameters for the model are stored here. The Mean is calculated by taking the natural logarithm of the cost estimate column, then the mean and coefficient of variation is used to calculate the standard deviation. If you wish to change a cost value, simply change the required Cost Estimate cell and the rest of the table will update automatically.

![Events Mean Standard Deviation Cost Estimate](data:image/png;base64,iVBORw0KGgoAAAANSUhEUgAAAIoAAADkCAYAAAAWgk29AAAAGXRFWHRTb2Z0d2FyZQBBZG9iZSBJbWFnZVJlYWR5ccllPAAAAiSURBVHheUIx耳5QaB5JkC0KUAAAABJRU5ErkJggg==)

**FIGURE E.5**

The top table in this sheet, Figure E.6, has the realisation values that are used in the model. They are created using the Log.INV() function with parameters taken from the appropriate row in Figure E.5.

![Events with LogNormal Distribution](data:image/png;base64,iVBORw0KGgoAAAANSUhEUgAAAIoAAADkCAYAAAAWgk29AAAAGXRFWHRTb2Z0d2FyZQBBZG9iZSBJbWFnZVJlYWR5ccllPAAAAiSURBVHheUIx耳5QaB5JkC0KUAAAABJRU5ErkJggg==)

**FIGURE E.6**

![Events with LogNormal Distribution](data:image/png;base64,iVBORw0KGgoAAAANSUhEUgAAAIoAAADkCAYAAAAWgk29AAAAGXRFWHRTb2Z0d2FyZQBBZG9iZSBJbWFnZVJlYWR5ccllPAAAAiSURBVHheUIx耳5QaB5JkC0KUAAAABJRU5ErkJggg==)
Utilities Sheet

The Utilities worksheet houses the utility values used in the model. The alpha and beta values are calculated using the formulae in Appendix D. The point estimates and variances are based on the values in Figure E.7. To adjust the utility distributions, you can either enter the alpha and beta values directly or enter the mean and variance values.

<table>
<thead>
<tr>
<th>Dyer et al., 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure Severity</td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>Severe</td>
</tr>
</tbody>
</table>

FIGURE E.7 - Utility Values from an Academic Paper

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Point Estimate</th>
<th>Variance</th>
<th>Alpha</th>
<th>Beta</th>
<th>Realisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNP_Test - GP_Review</td>
<td>0.90</td>
<td>0.0324</td>
<td>1.6</td>
<td>0.177777778</td>
<td>0.999999648</td>
</tr>
<tr>
<td>BNP_Test - Remote_Echo - GP_Review</td>
<td>0.85</td>
<td>0.0324</td>
<td>2.49490741</td>
<td>0.440277778</td>
<td>0.998905334</td>
</tr>
<tr>
<td>BNP_Test - Remote_Echo - OPD_Visit - HF_Diagnosis</td>
<td>0.78</td>
<td>0.0324</td>
<td>3.35111111</td>
<td>0.945185185</td>
<td>0.979226032</td>
</tr>
<tr>
<td>BNP_Test - Remote_Echo - OPD_Visit - GP_Review</td>
<td>0.80</td>
<td>0.0324</td>
<td>3.15061728</td>
<td>0.787654321</td>
<td>0.987772141</td>
</tr>
<tr>
<td>EA - HF_Diagnosis</td>
<td>0.51</td>
<td>0.0441</td>
<td>2.38</td>
<td>2.286666667</td>
<td>0.814197843</td>
</tr>
<tr>
<td>EA - GP_Review</td>
<td>0.60</td>
<td>0.0441</td>
<td>2.66530612</td>
<td>1.776870748</td>
<td>0.886861542</td>
</tr>
<tr>
<td>OPD_Visit - Hospital_Echo - HF_Diagnosis</td>
<td>0.75</td>
<td>0.0324</td>
<td>3.59027778</td>
<td>1.196759259</td>
<td>0.962836695</td>
</tr>
<tr>
<td>OPD_Visit - Hospital_Echo - GP_Review</td>
<td>0.80</td>
<td>0.0324</td>
<td>3.15061728</td>
<td>0.787654321</td>
<td>0.987772141</td>
</tr>
</tbody>
</table>

FIGURE E.8 – Utility Beta Distribution Parameters
Monte Carlo Sheet

This sheet stores the results from the Monte Carlo simulation in a data table.

<table>
<thead>
<tr>
<th>Simulation</th>
<th>Ex[Cost]_1</th>
<th>Ex[Utility]_1</th>
<th>Ex[Cost]_2</th>
<th>Ex[Utility]_2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>168.6989789</td>
<td>0.976229798</td>
<td>1231.886328</td>
<td>0.89444289</td>
</tr>
<tr>
<td>2</td>
<td>151.6204698</td>
<td>0.971531073</td>
<td>2064.396754</td>
<td>0.8941738</td>
</tr>
<tr>
<td>3</td>
<td>364.2895111</td>
<td>0.873810566</td>
<td>1077.20228</td>
<td>0.68419553</td>
</tr>
<tr>
<td>4</td>
<td>200.0289311</td>
<td>0.757675246</td>
<td>2061.070259</td>
<td>0.580914353</td>
</tr>
<tr>
<td>5</td>
<td>190.0518682</td>
<td>0.966315782</td>
<td>892.8080047</td>
<td>0.89209659</td>
</tr>
<tr>
<td>6</td>
<td>175.0464923</td>
<td>0.971816342</td>
<td>5620.530528</td>
<td>0.835358417</td>
</tr>
<tr>
<td>7</td>
<td>135.5024145</td>
<td>0.988751693</td>
<td>2246.597601</td>
<td>0.92144219</td>
</tr>
<tr>
<td>8</td>
<td>245.9150951</td>
<td>0.968715257</td>
<td>6136.071377</td>
<td>0.863928144</td>
</tr>
<tr>
<td>9</td>
<td>287.2787804</td>
<td>0.982011706</td>
<td>1451.656245</td>
<td>0.91551939</td>
</tr>
<tr>
<td>10</td>
<td>168.5645196</td>
<td>0.703642466</td>
<td>1332.119943</td>
<td>0.495793794</td>
</tr>
</tbody>
</table>

**FIGURE E.9 – Results from Decision Tree**

The results are used to produce the following table in Figure E.10 that will be used to create graphs in the Tree – Results workbook.

<table>
<thead>
<tr>
<th>Incremental Cost</th>
<th>Incremental Utility</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1063.187349</td>
<td>0.081786908</td>
<td>-12999.481</td>
</tr>
<tr>
<td>-1912.776284</td>
<td>0.077357274</td>
<td>-24726.521</td>
</tr>
<tr>
<td>-712.9127693</td>
<td>0.189615036</td>
<td>-3759.7903</td>
</tr>
<tr>
<td>-1861.041328</td>
<td>0.176760893</td>
<td>-10528.581</td>
</tr>
<tr>
<td>-702.7561364</td>
<td>0.074219192</td>
<td>-9468.6578</td>
</tr>
<tr>
<td>-5445.484036</td>
<td>0.136457924</td>
<td>-39905.957</td>
</tr>
<tr>
<td>-2111.095187</td>
<td>0.067309503</td>
<td>-31363.999</td>
</tr>
<tr>
<td>-5890.156282</td>
<td>0.104787112</td>
<td>-56210.694</td>
</tr>
<tr>
<td>-1164.377465</td>
<td>0.066492316</td>
<td>-17511.459</td>
</tr>
<tr>
<td>-1163.555423</td>
<td>0.207848673</td>
<td>-5598.0893</td>
</tr>
</tbody>
</table>

**FIGURE E.10 – Calculation of ICER values from Decision Tree results**
**Tree – Results Workbook**

The Tree-Results workbook also has decision tree, costs and utilities sheets as they were needed for the one-way sensitivity analysis explained in Appendix D. The results of the Monte Carlo simulation from the Tree – Model workbook can be found in the ICE Scatterplot and the CEAC sheets, along with the respective graphs and the necessary workings to create them. If you want to run the model again, you will need to re-run the model in the Tree-Model workbook and then copy and paste the results into the ICE Scatterplot and CEAC sheets.

**One-Way Sensitivity Analysis**

The rest of the sheets in the workbook, “One-Way SA”, “Cost_Param”, “Prob_Param”, “Utility_Param” and “Short_Param_NAMES” all deal with the one-way sensitivity analysis. The “One-Way SA” sheet contains the workings for the analysis and the “Short_Param_NAMES” sheet serves as a legend that matches the shortened names that appear on the graphs with their full name. The other sheets contain tornado diagrams of the on-way sensitivity analysis results.
APPENDIX F

EXCEL WORKBOOK

Workbook Access

The workbooks are available in my TCD google drive and can be accessed at:

http://goo.gl/QyGehf

If there is difficulty accessing the workbooks, I can be contacted at: mccole@tcd.ie.

Drive Contents

<table>
<thead>
<tr>
<th>No.</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tree - Model</td>
</tr>
<tr>
<td>2</td>
<td>Tree - Results</td>
</tr>
</tbody>
</table>
References


