Real options theory applied to decision making in health care; a series of case studies

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Abstract

This thesis applies real options theory to case studies in health care. The aim is to establish the suitability of applying this technique, examine the implications of doing so, and outline methods through which real options analysis can be applied in practice. The concepts behind option valuation are established and current literature reviewed before introducing the theory of real options into decision making in health care. The first three case studies progress through the structure of financial options examining the call, put and compound options through application to a spectrum of decision problems faced by agents in health care. Firstly, watchful waiting is modelled as an option to defer therapeutic treatment using a call option framework. Secondly, the structure of the put option is used to model the option to defer removal of life support for patients in a coma. Thirdly, the strategy for technology approval adopted by the National Institute for Clinical Excellence is examined with appeal to compound option analysis. The fourth case study develops the work in two ways. The versatility of options analysis is developed by modelling underlying uncertainty with a combined Brownian motion / Poisson arrival evolutionary process, in preference to the single structures used in the previous case studies. Option premium is then shown to be a form of value of information relevant when information on uncertain variables can be observed through time. The usefulness of real options for analysing whether additional information is required is also considered. Within each study the three defining characteristics of financial options; uncertainty, irreversibility and an ability to defer, are discussed and explicitly addressed. The applications have led to some questions being asked of existing economic evaluation methodology, particularly with respect to the three characteristics. These issues are addressed as they are encountered and summarised within the concluding chapter.

Contents

List of tables

List of figures

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Declaration

I wish to draw attention to material in Chapter 4 concerning the option to defer therapeutic treatment that was presented at the Health Economics Study Group Meeting (January 2002), and material in Chapter 7 on the option to wait for additional information that was presented at the Health Economics Study Group Meeting (January 2003). The work presented within this thesis is entirely my own.

Chapter 1. Introduction

1.1 The notion of real options analysis

As individuals, most people will readily admit an enjoyment for having and making choices. We prefer to be in situations where we can make decisions, than situations where we are told what to do and how to do it. We value our options. Often we are even prepared to pay money in order to obtain more options.

Individuals are not the only groups of people to appreciate options. Business managers also abide by the silent rule of 'keeping your options open'. To expand production, build new factories, abandon failing products and downsize, are all options that face owners and managers of today's firms. Health care professionals, whether clinicians, health economists, General Practitioners (GP's), National Health Service (NHS) managers, health psychologists, policy makers, or decision making bodies such as the National Institute for Clinical Excellence (NICE), also face options. These include when and how to allocate a budget, whether to build a new ward, options over which patients take priority, when to begin treatment, and which drugs are preferable for a given ailment.

Options are continuously encountered, and actions taken today often prove to be ways of influencing options confronted tomorrow. Spending the majority of a budget early in the financial year reduces choices for spending later in the year, reducing future options. Current investment spending may alternatively provide positive side effects, creating options. Investment in a new laser creates the option to treat patients for a variety of problems including cervical cancer and glaucoma. Parting with the up-front costs necessary to build a hospital confers upon NHS managers the option to later expand the hospital creating, for instance, a dedicated eye unit or specialist transplant centre.

Recently authors have begun to realise the importance of trying to value options. The ability to accurately place a value on owning options may help in assessing how much we might be willing to pay to gain options, or how much compensation we require if options must be given up. Dixit and Pindyck (Dixit and Pindyck, 1994) have devoted considerable effort to surveying options facing firms, and how these might be valued. So as to highlight the difference between having an option and a choice, a very precise definition of an option has developed. When a decision must be made under conditions of uncertainty, irreversibility, and timing flexibility, then according to Dixit and Pindyck, there is an option.

Dixit and Pindyck are among a growing collection of authors who have recognised the similarities between this definition of every day options, and financial market options. The purchase of a financial options contract gives the owner the opportunity, or option, to perform a pre-specified stock transaction. Instead of options to invest, expand, defer and downsize, financial options are more restrictive, allowing only the purchase or sale of a pre-agreed quantity of a given stock, at a pre-arranged price. Buying the contract conveys the option. Options facing health care professionals are likely to be much more flexible than this, with a range of possible actions and differing payoffs to be received or paid when actions are undertaken (exercised). This similarity between financial options and current investments has lead authors to propose the use of financial option pricing techniques to value everyday options (Kester, 1984; Trigeorgis, 1999).

The analogy between financial options and commercial investments has gained increasing popularity among a variety of academics and is sufficiently widespread to have become a discipline in its own right; real options analysis (Amram and Kulatilaka, 1999). A real option is a proposed action that shares the characteristics of a financial option and that can be analysed by methods derived from financial option pricing techniques. This unites insights from finance with the peculiarities of everyday investments to create a dynamic decision making process applicable to a variety of decision problems.

Brennan and Schwartz (Brennan and Schwartz E S, 1985) and McDonald and Seigel (McDonald and Seigel, 1985) were among the first to apply option pricing techniques to valuing real investments. Their analyses considered the depletion of natural resources and valuation of firms respectively. Since early applications such as these the potential of real options analysis has been increasingly realised. More diverse subject areas are appealing to this "new" view of investment theory (Metcalf and Rosenthal, 1995).

Disciplines including environmental economics, private finance, and public sector economics have all embraced real options thinking. This has helped develop an understanding of issues such as optimal pollution control (Chao and Wilson, 1993), timber rotation (Plantinga, 1998), the handling of contagious diseases (Mahul and Gohin, 1999), and the benefits of research and development efforts (Pennings and Lint, 1997). Real options analysis has been able to explain observed phenomena that are inconsistent with existing decision techniques (Hasset and Metcalf, 1992), as well as aid handling of uncertainty (Sarker, 1999), enable incorporation of degrees of irreversibility (Tegene et al., 1999), and simplify consideration of the waiting alternative (Ingersoll and Ross, 1992). Trigeorgis (Trigeorgis, 1999) and Cheung (Cheung, 1993) provide reviews of early applications of real options thinking.

Health economics too may gain from considering these methods. The idea of applying financial techniques to health care is not new. O'Brien and Sculpher (O'Brien and Schulpher, 2000) suggested evaluating health technologies using portfolio theory. They examined the benefits of spreading funds over numerous projects to minimise the risk associated with budgetary allocations. The application of real options analysis to health care builds on such work. Section 2 of this chapter establishes the motivation behind application of real options analysis to decision making in health care while section 3 establishes the research aims of this thesis.

1.2 Motivations for applying real options analysis to decision making in health care

There have been few previous attempts to integrate real options thinking into decision making within the field of health care. Health economists use valuation methods that have evolved from discounted cash flow (DCF) techniques advocated by Fisher almost a century ago (Fisher, 1907). Most common are variants of net present value (NPV), which state that a potential investment should be pursued if the present value of benefits is equal to, or exceeds, the present value of costs. Valuing health benefits can be difficult and more recently economic evaluation literature has begun to account for society's willingness to pay for improvements in health outcome (Gold et al., 1996; Sloan, 1996). Amendments have, however, carried forward some of the problems inherent in traditional techniques (table 1). It is such limitations in existing methodology and practice that motivate an appeal to real options analysis. Since these shortcomings have been discussed in detail elsewhere (Paddock et al., 1988; MacCallum, 1987; Trigeorgis, 1993; MacCallum, 1987) only a brief summary is presented here.

Problems facing traditional analysis	Advantages provided by real options analysis
Now or never emphasis on decision making	Dynamic decision making process that explicitly considers the merits of deferral
Overlooking strategic reasons for investment	Option valuation assesses opportunities created and destroyed by current actions and does not automatically reject a project with NPV<0
Poor modelling of active management	Real options analysis takes a flexible view of uncertainty that incorporates managements ability to respond to anticipated and unanticipated events
Discounts rate issues	Hedging leads to risk neutral valuation
Implicit assumptions governing irreversibility	Explicitly considers the degree of reversibility and impact on decision-making

Table 1.1. Recognised problems facing decision techniques and how real options analysis mitigates these.

Current techniques tend to analyse projects at a single point in time and usually make an immediate decision. Deferral is not commonly considered and rejected projects are rarely reconsidered in the light of new information. Although increasing use of Bayesian analysis encourages re-estimation of project value, particularly when trials are expected to reveal information, there remains a tendency to examine projects at specific, predetermined points in time. Real options analysis is a dynamic decision-making process that explicitly considers deferral and reviews the status of projects when new information is revealed over time. Examining costs and benefits of deferral allows recommendations about the timing of actions and future reviews, advising not just *whether*, but *when* immediate action is optimal.

NPV methodology has been criticised for overlooking strategic reasons for investments (Hayes and Garvin, 1982). Rejecting projects with negative NPV fails to recognise potential strategic benefits, such as greater flexibility or learning effects, which are not easily valued. These projects may retrospectively be beneficial causing potentially favourable ventures to be rejected outright with the strict NPV based decision (Trigeorgis, 1990). Pharmaceutical research and development projects often suffer low NPV estimates due to the infrequency with which individual projects develop into profit making ideas. New surgical techniques might initially not be cost-effective due to high failure rates, but learning effects from continued practice may generate a cost-effective technique. Even projects deemed to have failed may contribute strategic value (McGrath, 1999). Real options analysis has been proposed as a way to capture this value (Slater et al., 1998).

NPV has also been accused of failing to account for the value of flexible and active management. Projects are analysed in period 0 using cash flow estimates given today's expectations to derive an optimal strategy. Decision trees combine sequential choices and events over numerous time periods enabling management strategies to respond to anticipated uncertainties. Detailed trees can be complex and computationally difficult to analyse, yet unanticipated events, to which managers will certainly react, are not modelled. Uncertainties in demand, running costs, technological developments, prices and disease progression mean projects rarely follow their expected path. Managers can respond by pursuing opportunities to expand, contract, abandon, or adjust the timing, input and output mixes, and progression rates of the project.

Possible managerial actions are options that define the structure of real option valuation. Combining this insight with a dynamic view of uncertainty allows options analysis to incorporate the effects of both anticipated and unanticipated events. Managerial flexibility is then explicitly modelled (Trigeorgis, 1999; Copeland and Keenan, 1998; Slade, 1998). Different aspects of the value of flexibility have been referred to in the real options analysis literature including managerial flexibility premiums (Cheung, 1993),(Trigeorgis, 1999) and timing or deferral value (McDonald and Seigel, 1986). In each case a premium is calculated that represents the value of flexibility. It is important to note that the real options premium is not a risk premium[1] and exists even for risk-neutral decision makers (Smith and McCardle, 1998). Although authors chose to emphasise different types and aspects of flexibility they refer to the same premium.

Traditional methods have sometimes made inappropriate adjustments for the timing of uncertain events with adhoc discount rates. Frequently a single discount rate is applied to an entire project, provoking debate over which is the most appropriate rate (Drummond et al., 1996). Within health care some researchers apply contrasting rates to costs and benefits. Smith and McCardle (Smith and McCardle, 1999) have argued that single rates are not suitable when complex projects encompass smaller staged investments whose risk structure is not the same as that of the overall project. In such circumstances varying rates may need to be applied according to the risk structure of sub-projects and correlation with the over all project. Real options analysis combines projects allowing risks to be hedged and a riskless position created that can be discounted using a risk-neutral rate (Coggins and Ramezani, 1998). This idea is at the centre of option pricing methodology (Jagle, 1999).

NPV based studies also make implicit assumptions, particularly concerning irreversibility (Baldwin, 1982). When reversibility is assumed all projects with expected NPV>0 are implemented immediately, as is currently the case. When projects have elements of irreversibility this forces decision makers to reflect

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[1] A premium paid by risk averse individuals to avoid a risky situation.

carefully before implementation because once introduced, such projects cannot be costlessly altered. The inherent ability to reverse most projects via incurring abandonment charges makes assumptions of complete irreversibility or reversibility inappropriate. Real options analysis recognises irreversibility as an important characteristic and explicitly highlights sources describing both initiation of inactive projects and abandonment of failing active projects.

Many practitioners believe that traditional techniques systematically undervalue some projects (Moyen et al., 1996) and managers appear to have acknowledged this through reluctance to consistently obey NPV signals (Nichols, 1994; Hanley, 2001). This suggests decision makers may be attempting to overcome some of the problems described here and may be receptive to new tools that attempt to correct these deficiencies. Whilst real options analysis cannot solve all the problems discussed, these methods help to highlight the issues and may work towards mitigating some (Slater et al., 1998; Deaves and Krinsky, 1998).

1.3 Setting out the research aims

Contrary to some belief, real options analysis is consistent with, and complements, existing evaluation methods (Smith and Nau, 1995; Smith and McCardle, 1998). Noticing this, Palmer and Smith (Palmer and Smith, 2000b) introduced the notion to decision making in health care. Their paper concentrates primarily on the ability of real options analysis to deal with uncertainties inherent in economic evaluation of health care technologies. The scope of real options extends potentially well beyond this.

The primary purpose of this thesis is to contribute to existing research by exploring the application of real options theory to decision problems in health care. This is achieved by seeking to answer a number of research questions that fall into three categories; is it theoretically appropriate to apply real options thinking to health care? Can real options analysis improve decision making in health care? Is it feasible to apply real options analysis to health care problems in practice? The questions are set out below:

Is it theoretically appropriate to apply real options thinking to health care?

- Are the defining characteristics of real options problems present in health care projects?
- Are the assumptions underlying real options analysis met in health care problems?
- Where assumptions are not met can the methods and assumptions be suitably adjusted?

Within the context of health care decision making, to what extent does real options analysis differ from existing methodology?

- Does real options analysis lead to different conclusions?
- Where different conclusions are reached, what implications does this have for decision making in health care?

Can real options thinking be feasibly applied in practice?

- Can the necessary variables be empirically estimated?
- Are the conclusions meaningful?
- Which areas are most suitable to analysis by real options?
- Which areas are not conductive to real options analysis?

In order to answer such questions, this thesis begins with a review of financial literature. This methodological and empirical appraisal discusses the theory behind option pricing and considers some valuation methods. Real options analysis is then introduced by demonstrating the analogy between exercising a financial option and initiating an investment project. The similarities and differences between the two are highlighted along with the variables required for valuation. Attempts to apply real options theory in practice are also discussed.

Having introduced this new research tool chapter three considers how these ideas apply broadly within economic evaluation and health care decision making. An examination is made contrasting real options analysis and conventional cost-effectiveness techniques as ways of assessing value. Examples are drawn from throughout the health care sector. It is not the intention to contribute to the technical content of real options analysis but to examine existing methods and assess their applicability within health care.

Chapters four through to seven each take a case study of interest. The fourth chapter considers watchful waiting as an option on therapeutic treatment and examines how the characteristics of the treatment decision align to a financial call option. A trinomial lattice framework provides the underlying structure for uncertainty in a hypothetical example. Contrastingly the concept of a put option is used in chapter five to look at the option to defer removal of life support for patients in a coma. This study uses a continuous Brownian motion model for uncertainty and discusses how options analysis can be used to advise both individual and group level treatment decisions.

The call and put option ideas are combined in chapter six which examines the National Institute for Clinical Excellence's compound option to approve and later retract approval of health care technologies. Within this study issues surrounding irreversibility are explicitly addressed as the ability to alter either a decision itself or its ramifications are discussed. Finally chapter seven considers the option to gather additional evidence, drawing parallels between option valuation and value of information analysis. The option to gather observational trial evidence is modelled using a combined Brownian motion / Poisson arrival process.

Each application considers whether the use of real options analysis alters our perspective of the area and whether there are implications for decision making. Chapter eight concludes by summarising the contributions made to the field of decision making in health care and discussing areas for further work.

Chapter 2. Real options in a real world

2.1 Financial options

2.1.1 Introduction

Real options analysis has evolved from financial option pricing theory as a potentially useful technique complementing traditional approaches to economic evaluation. Financial options analysis developed from the 1970s seminal work of Black, Scholes (Black and Scholes, 1973) and Merton (Merton, 1973). Today these techniques are used extensively to describe and price complex financial portfolios (Jarrow, 1999). Many authors summarise the basic properties of options and the theory behind their pricing. Brearly and Myers (Brearley and Myers, 1992), and Wilmott, Howison and Dewynne (Wilmott et al., 1995) both provide comprehensive introductions whilst Hull (Hull, 1997) gives a more advanced review. Authors such as Haug (Haug, 1998) concentrate on the practice of option pricing with detailed financial methods and formulae.

Real options analysis applies the financial theories to real projects that share the same characteristics as financial options. Within the framework of financial economics, options problems can be described in a clear, unambiguous manner. Relevant variables are specified within a written contract and usually concern publicly available information. Real world factors complicate these ideal financial circumstances. Although analogous, real options are harder to identify, describe, and analyse. Understanding financial options provides a basic underpinning from which to approach real option valuation. This chapter sets out the fundamentals of financial option pricing before formally introducing real options analysis.

2.1.2 Options have value

Purchase of a financial options contract confers the right to perform a specific future stock transaction. For instance a call option permits the holder to buy a fixed number of units of a given commodity (the underlying asset) at a specific price (exercise price), on or before a stated date (the exercise date). The owner has the right but not the obligation, to carry out the transaction. Whilst call options confer an entitlement to buy, put options confer a right to sell. Options also differ in their condition of exercise; options that may be exercised only on the exercise date are European options while those that may be exercised prior to this date are American options.

Whether an option is exercised depends on the exercise price (X) stated in the options contract, relative to the prevailing market price (S). Suppose an American call allows stock A to be purchased for £300. On the exercise date if the market price is £310 the option holder can exercise the option, buying at £300, and sell the stock on the market yielding a profit of £10. Exercise is optimal. If the market price were £250 the option holder will not want to exercise, preferring instead to purchase the stock from the market and allow the options contract to expire worthless. This gives a payoff of zero. The payoff, or intrinsic value, from optimally exercising the option is given by the maximum of the profit from exercising (S-X), or zero (equation 2.1).

$$\text{Intrinsic value (call)} = \max(S-X, 0) \qquad \textbf{(EQN. 2.1)}$$

Options that are profitable to exercise ($S-X>0$) are known as being "in the money". The more profitable is an option the "deeper" into the money it is. Options that are currently unprofitable ($S-X<0$) are "out of the money" and should not be exercised, whilst "at the money" refers to options whose exercise price is equal to the current market price ($S-X=0$).

Market price	Optimal action	Intrinsic value
£270	Allow option to expire	£0
£280	Allow option to expire	£0
£290	Allow option to expire	£0
£300	Exercise	£0
£310	Exercise	£10
£320	Exercise	£20
£330	Exercise	£30

Table 2.1. Intrinsic value for an American call option on the exercise date with exercise (strike) price of £300.

On the exercise date the market price might assume any value, each of which is associated with an optimal action. Table 2.1 gives intrinsic value for a plausible range of prevailing market prices. The option moves from being 'out of the money' to being 'in the money' at S=£300. An option will only be exercised when it is 'in the money', and so provides protection from losses. Figure 2.1 plots net benefit and intrinsic value, illustrating how the latter never falls below zero.

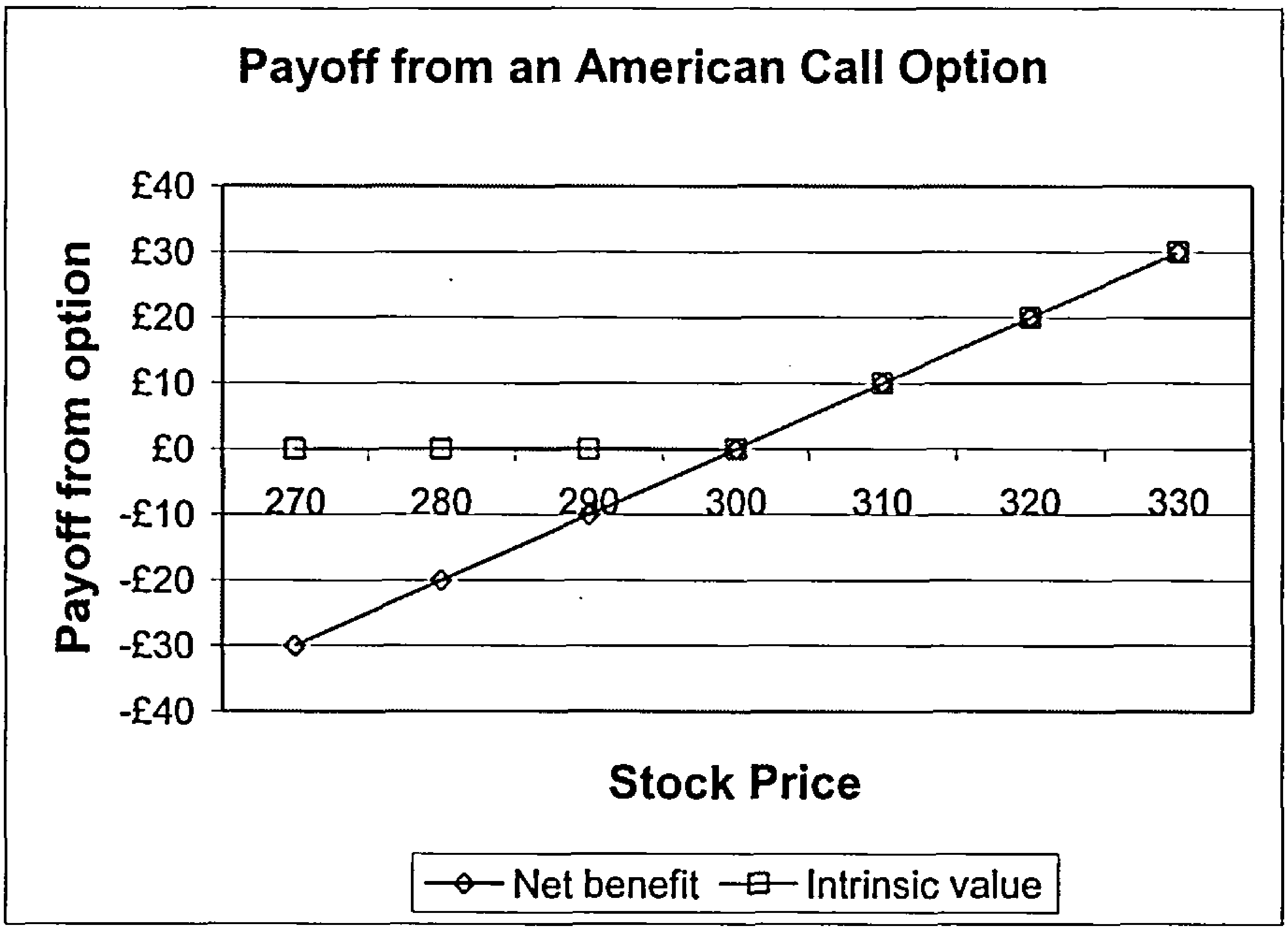

Figure 2.1. Net benefit and intrinsic value from an American call option with exercise price of £300, on the exercise date.

Put options operate just as call options but convey an opportunity to sell an asset in return for some fixed payment. A put option comes 'into the money' as market price falls below the exercise price leading to an intrinsic value [max(X-S, 0)] which mirrors that of the call option (equation 2.2). This similarity in structure gives rise to the put-call parity and allows put options to be priced using information from the call option[2].

$$\text{Intrinsic value (put)} = \max(X-S, 0) \qquad \textbf{(EQN. 2.2)}$$

Purchase of a financial option creates choices that, as with real choices facing health care decision makers, have value. One of the sources of value is the ability to react to changing circumstances whilst the option is still held, and means that options have benefits in excess of their intrinsic value. To see this consider the same American option one week before the exercise date. Suppose the option is currently 'out of the money'. History informs the investor that prices are volatile and trend upward over time. Although the option is not currently profitable knowledge of the price evolution process suggests that profits may be realised in the future, making the option valuable even when intrinsic value is zero. Option value exceeds intrinsic value because the former accounts for future information that is not part of the intrinsic value calculation. Figure 2.2 shows hypothetical option values.

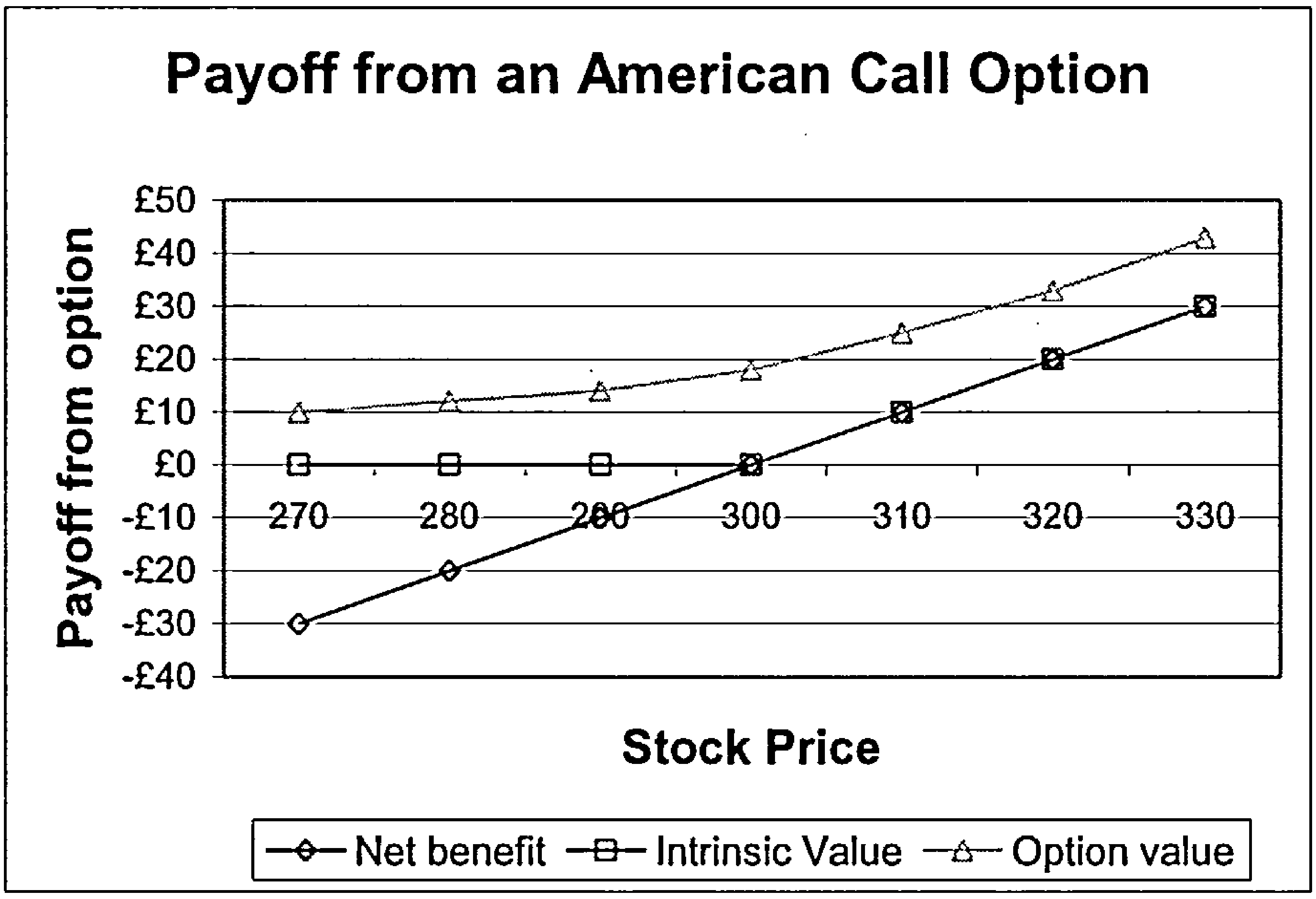

Figure 2.2. Graphical representation of option value, intrinsic value and net benefit from an American call option with exercise price £300.

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[2] A portfolio consisting of a put option and a stock has the same payoff as a call option (when the options have identical exercise prices) irrespective of the prevailing market price. To avoid riskless arbitrage the two portfolios must have the same price.

To see this numerically consider a situation in which an NHS manager must decide whether to purchase a new piece of equipment. The equipment requires up front purchase and installation costs (C = £20,000) and yields monetary benefits net of running costs in each of the following three years. Benefits depend on demand and may be high (H = £8,500) or low (L = £2,000). These states of nature occur with respective probabilities q and (1-q). The equipment is then scrapped for a salvage value (A = £2,000). If the investment must be considered today, the decision maker has a choice. Expected annual monetary benefits are [qH+(1-q)L]. Assuming q=0.45 gives an annual steam of £4,925 (0.45×8500+0.55×2000). A discount rate of 5% gives:

$$NB(1) = -C + \frac{(qH+(1-q)L)}{(1+r)} + \frac{(qH+(1-q)L)}{(1+r)^2} + \frac{(qH+(1-q)L)}{(1+r)^3} + \frac{A}{(1+r)^3} = -4862$$

The project is out of the money and would be rejected[3]. Suppose, like a financial option, the decision could be delayed for one period during which information is revealed. If a newer technology arrives demand falls:

$$NB(2) = \frac{-C}{(1+r)} + \frac{L}{(1+r)^2} + \frac{L}{(1+r)^3} + \frac{L}{(1+r)^4} + \frac{A}{(1+r)^4} = -12{,}216$$

Should a new technology fail to arrive demand is high:

$$NB(3) = \frac{-C}{(1+r)} + \frac{H}{(1+r)^2} + \frac{H}{(1+r)^3} + \frac{H}{(1+r)^4} + \frac{A}{(1+r)^4} = 4641$$

Decision makers would choose not to purchase if demand was low (intrinsic value = £0), but to purchase if demand was high (intrinsic value = £4641). Option value is therefore given by

$$NB^* = Option\ Value = (0.45 * 4641) + (0.55 * 0) = £2088$$

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[3] This now or never assessment of value is similar to intrinsic value under an option pricing approach. Intrinsic value has a minimum value of zero as the option will not be exercised if net benefit is less than zero.

Although waiting means postponing benefits, information is collected that potentially alters the adoption decision. In this case not only has the benefit of investment increased (NB(1)<NB*) by valuing the option to defer, but the possibility of deferral has changed the conclusion. Positive option value means the project is no longer rejected.

Option value indicates the market price for which options should be bought and sold and is usually calculated over a range of values for the underlying asset (figure 2.2). An option priced higher is over-priced and will not be purchased. An option priced lower is under-priced and would not be offered for sale. £2088 would be the market price for the option to defer purchase of equipment. Option value is bounded between intrinsic value and S, for a call option, or E, for a put option.

Once option value and intrinsic value are known, option "premium", the difference between the two for any given stock value, can be calculated. Option premium gives the value associated with owning an option in preference to a now or never choice, or the value of being able to defer[4]. In the numerical example the project is out of the money making option premium is equal to option value (Option premium = £2088 – 0 = £2088).

An option is always worth at least as much as an immediate choice (option premium ≥ 0) because information gained during deferral is potentially useful. This is the case despite payoff being limited to intrinsic value if and when investment actually occurs (option premium = 0). Once the decision becomes an immediate choice, as is the case when exercise occurs, either no additional information is expected or the anticipated information holds no extra value. Option premium falls to zero and deferral holds no further benefits.

Option value is influenced by numerous factors (table 2.2). Call options become profitable to exercise as stock price rises creating a positive relation between the

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[4] This terminology is consistent with Quigg (Quigg, 1993) and others, although Quigg discusses the premium as being relative to the total option value (option premium as a proportion of option value). Trigeorgis (Trigeorgis, 1999) refers to this same option premium as being a "time value".

price of the underlying asset and option value. The converse is true for put options. A longer maturity date (T) and time remaining to expiration (t) both serve to increase option value by extending the period for which the option is available and increasing the choices available to a decision maker. Uncertainty in the stock price (σ) also positively affects option value; as stock prices move with greater volatility, so the call (put) option holder benefits from more extreme upward (downward) price movements contributing to greater potential profits while losses are limited by the structure of intrinsic value.

Variable	**Call option**	**Put option**
Current value of stock (S)	Positive	Negative
Maturity date (T)	Positive	Positive
Time to expiration (t)	Positive	Positive
Stock value uncertainty (σ)	Positive	Positive
Exercise price (X)	Negative	Positive
Risk-free interest rate (r)	Positive	Negative
Dividend (δ)	Negative	Positive

Table 2.2. Spheres of influence on option value.

The payoff structures underlying intrinsic value (equations 2.1 and 2.2) cause larger exercise prices (X) to have a negative impact on call option value, and a positive impact on put option value. The interest rate (r) impacts option value through the exercise price. The greater is the risk-free rate the more the exercise price is discounted over time generating a smaller present value. This is beneficial for the call but detrimental to the put option.

Dividends cannot be earned until the stock itself is owned; the value of holding an *option* to purchase a stock is therefore reduced by dividend payments, increasing the incentive to exercise early. For a put option the incentive to exercise (sell the stock) is diminished because the value of possessing an *option* to sell, in preference to selling immediately, has risen.

Options are beneficial to own because they preserve flexibility. Their value is related to factors specific to the option contract (T, t, X), as well as market-based influences (S, σ, δ, r). Some pricing techniques used to establish the value of particular options are now examined.

2.1.3 Binomial option pricing techniques

Calculating option values has historically proven difficult because demand for these assets is derived; depending on the price of the underlying asset. Despite this, in 1973, Black and Scholes (Black and Scholes, 1973) had an important insight that allowed the value of certain types of option to be ascertained; the assumption of no arbitrage opportunities meant that manufactured portfolios could be used to establish option value. This section illustrates these ideas numerically using a call option whose underlying volatility follows a highly simplified structure. Section 2.1.3 examines the Black and Scholes' model.

Arbitrage opportunities exist when securities with equivalent risk and return structures are priced differently on the market. This allows trade that generates a risk-free profit. An arbitrage-free economy exists when all such opportunities are exhausted. If the risk and return structure of a security can be accurately described, then a composite portfolio may be constructed that exactly replicates this structure (the replicating portfolio). Shares of the underlying asset and a risk free asset can be combined to replicate the payoffs from an option[5]. Black and Scholes' insight was to recognise that since the option and the replicating portfolio share the same risk and return structure, within an arbitrage-free economy, they must also share the same price. Option pricing formulae use the replicating portfolio and no-arbitrage principles to specify a precise option value.

The payoff of an option is correlated with the current market price of the underlying asset. Continuously evolving prices over the lifetime of an asset complicates option pricing by requiring changes in the replicating portfolio. To illustrate the principles of option pricing without encountering this complexity a call option that expires in one period and whose underlying asset follows a binomial distribution is discussed. Binomial pricing techniques, first developed by Cox, Ross and Rubinstein (Cox et al., 1979a) are among the most intuitive of methods available to price options due to their simplification of asset volatility.

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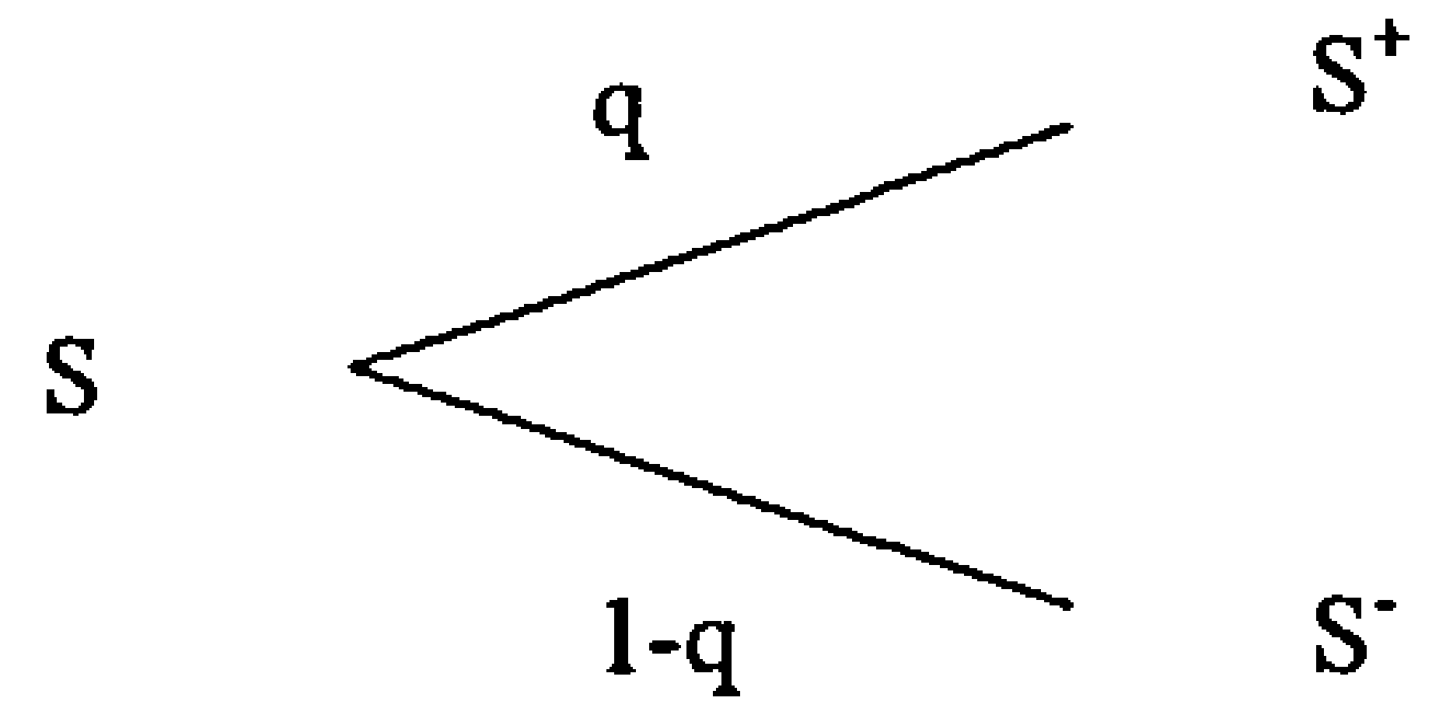
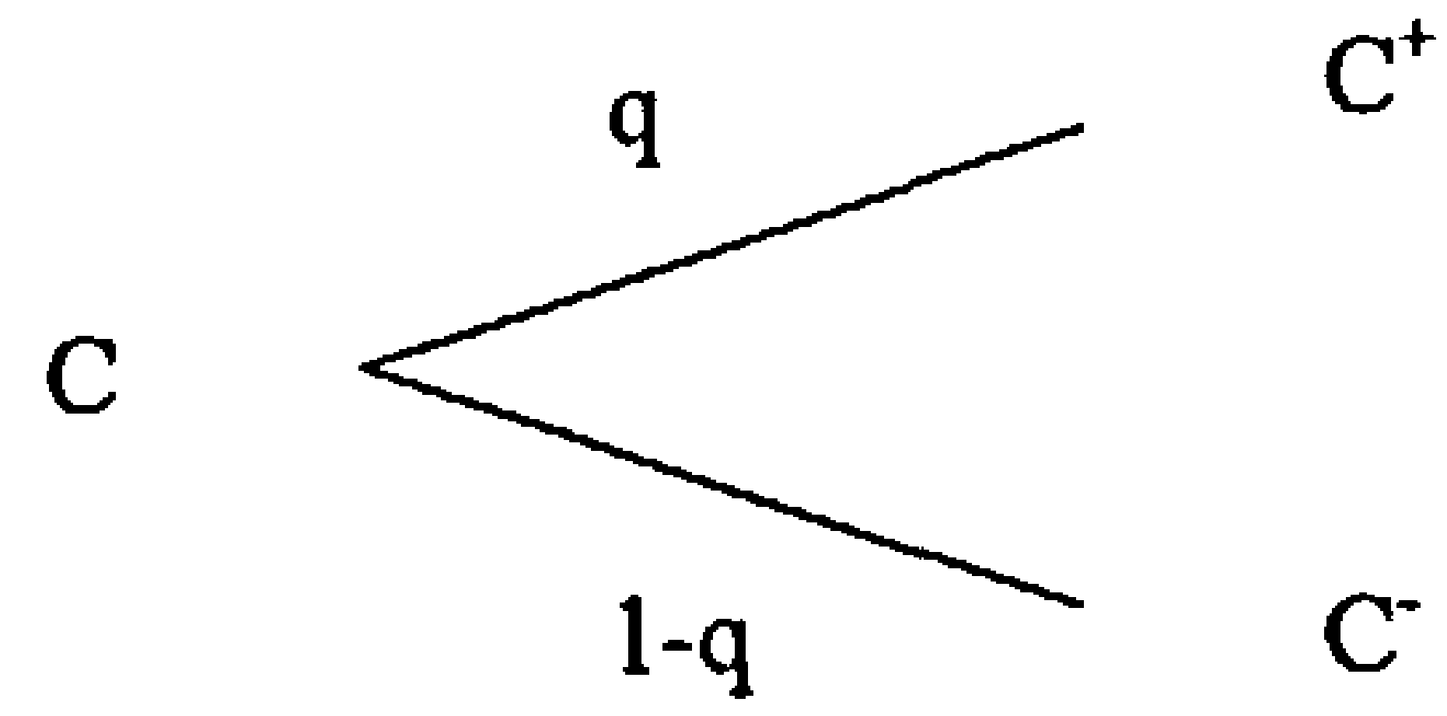
[5] Alternatively a hedging portfolio could be created that combines shares and options to replicate a risk-free return.

Rather than asset prices evolving continuously, the binomial model restricts movement to upward or downward jumps of pre-specified distance and probability in each discrete period.

Let the value of an underlying asset S, evolve according to a binomial distribution with probability q of increasing to S^+, and probability (1-q) of decreasing to S^- in the next period.



The value of a call option, C, written on this asset will move in a positively correlated way:



An investor can borrow £B at the risk free rate to contribute towards buying N units of the underlying asset. This portfolio can be adjusted via changes in N and B to replicate the returns of the option in any future state of nature[6]. Creating this portfolio occurs at a net out-of-pocket cost of N*S-B[7]. Since the portfolio and option have the same risk and return structure they must have the same current price:

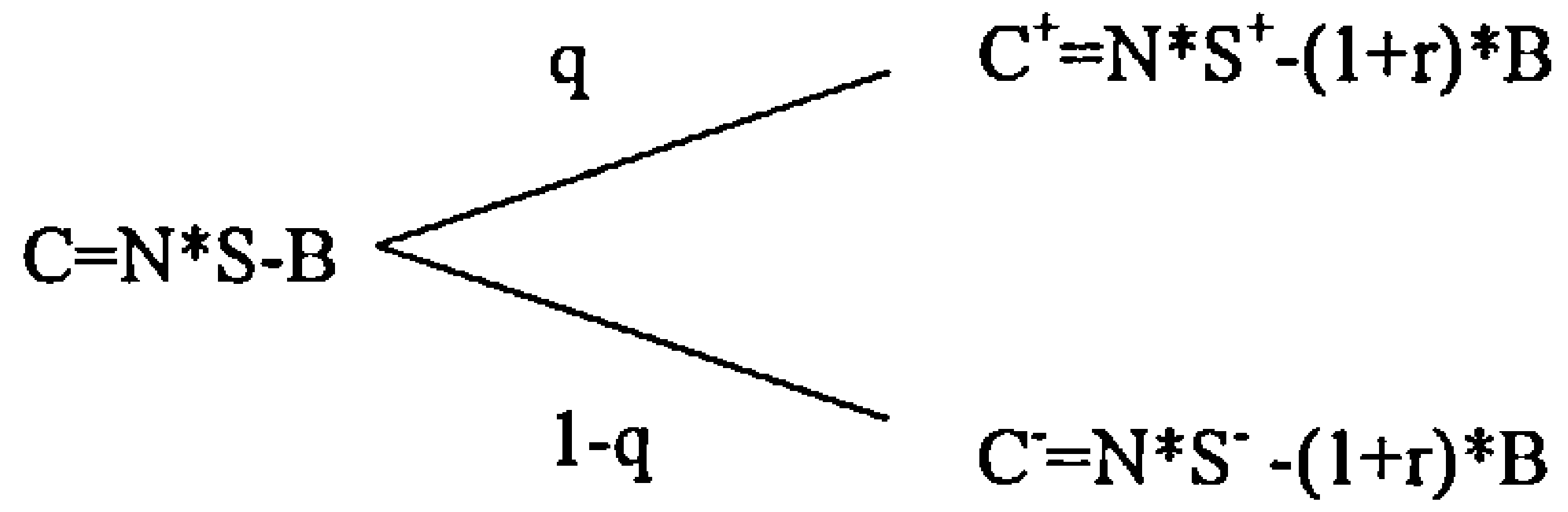
$$C = (N * S - B) \qquad \textbf{(EQN. 2.3)}$$

After one period the stock are sold and the loan repaid (both the principle B, and interest at rate r) giving a payoff of $NS^+-(1+r)B$, or $NS^--(1+r)B$, depending on the state of nature. The portfolio and option must also have the same future price:

---

[6] Alternatively a hedged portfolio could be created; sell short one call option and purchase N shares of the underlying asset. Capital gains / losses associated with the stock are exactly offset by gains / losses of the option and return on the portfolio is riskless, NS-C=B.

[7] For a put option the replicating portfolio consists of selling shares of stock and lending at the risk-free rate, P=-N*S+B.



This gives two simultaneous equations [$C^+=NS^+-(1+r)B$ and $C^-=NS^--(1+r)B$] that can be solved to obtain N[8], the number of shares required to create the replicating portfolio.

$$
\begin{aligned}
C^+ - C^- &= [NS^+ - (1+r)B] - [NS^- - (1+r)B] \\
C^+ - C^- &= NS^+ - NS^- \\
C^+ - C^- &= N(S^+ - S^-) \\
N &= \frac{C^+ - C^-}{S^+ - S^-}
\end{aligned}
\qquad \textbf{(EQN. 2.4)}
$$

N is given by the spread of future option values relative to the spread of future stock values. Rearranging either the upper or lower future value of the option gives the borrowing requirement, B, into which N can be substituted to give the requirement in terms of future values of the asset and option value:

$$C^-=NS^--(1+r)B$$

$$B = \frac{NS^- - C^-}{1+r}$$

$$B = \frac{S^-C^+ - S^+C^-}{(S^+ - S^-)(1+r)} \qquad \textbf{(EQN. 2.5)}$$

Finally substituting values for N and B (equations 2.4 and 2.5) into today's call price (equation 2.3) gives the current value of the call option[9].

---

[8] Known as the hedge ratio, or "delta" of the option.

[9] Solving for the current value of the call option.

$$C = NS - \frac{NS^- - C^-}{1+r} = \frac{NS(1+r) - NS^- + C^-}{1+r} = \frac{\frac{C^+-C^-}{S^+-S^-}[S(1+r) - S^-] + C^-}{1+r}$$

$$Define \quad \rho = \frac{S(1+r) - S^-}{S^+ - S^-}$$

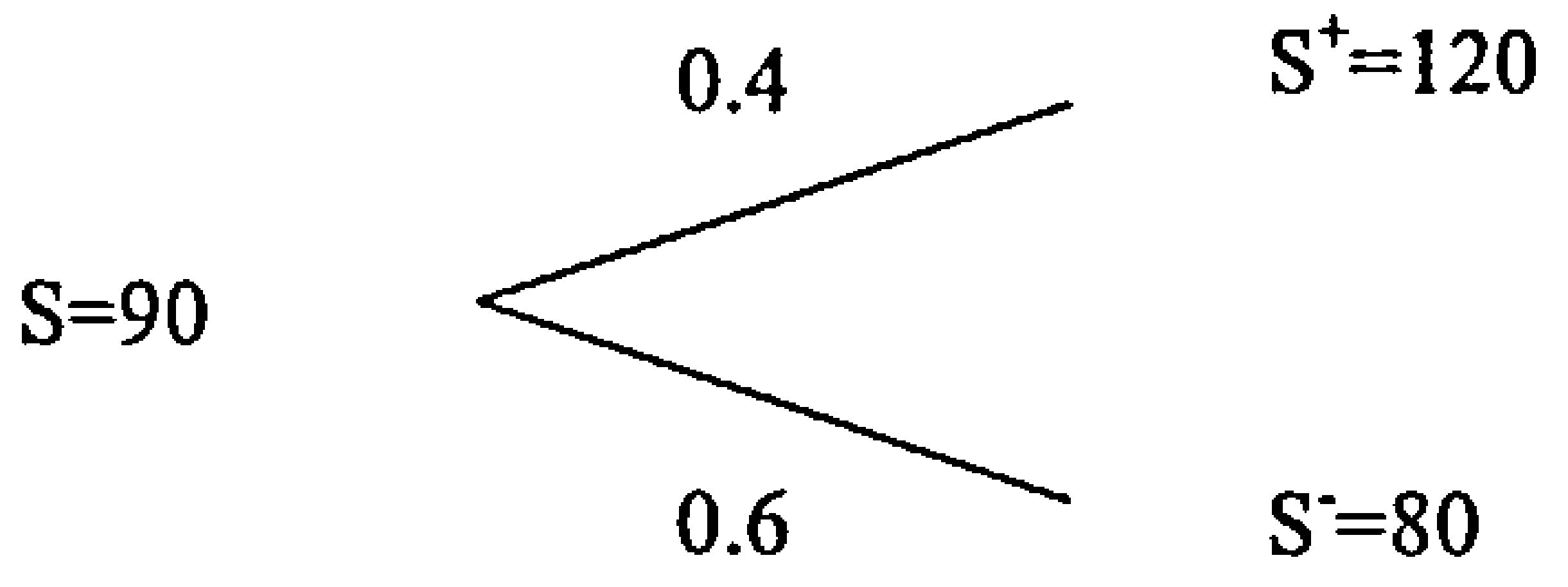
$$C = \frac{\rho(C^+ - C^-) + C^-}{1+r} = \frac{\rho C^+ + (1-\rho)C^-}{1+r}$$

$$C = \frac{\rho C^{+} + (1-\rho)C^{-}}{1+r} \qquad \textbf{(EQN. 2.6)}$$

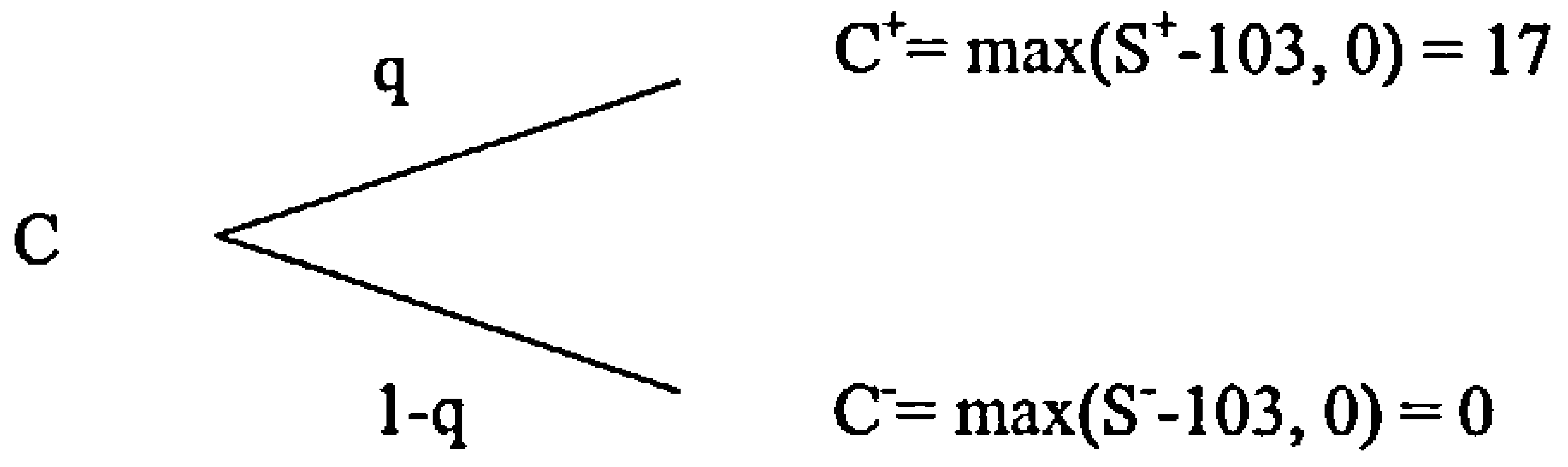
where ρ (interpreted as the risk neutral probability of a rise in stock price[10]) is given by:

$$\rho = \frac{(1+r)S - S^{-}}{S^{+} - S^{-}} \qquad \textbf{(EQN. 2.7)}$$

Given future values of the stock price (and thus future values of the call option) and a risk free interest rate, current call option value can be determined. Notice that the actual probability (q) of a rise in stock price, and investors' attitudes to risk, have no role in option pricing. Applying option valuation techniques is best illustrated with a numerical example. Suppose an asset whose current stock price is £90 follows a binomial distribution with probability 0.4 of rising to £120 and 0.6 of falling to £80.



A call option specifies that the asset may be purchased with exercise price £103 next period. The option will be exercised for a profit of £17 if price rises and allowed to expire worthless if price falls.



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[10] In a risk-neutral world all assets earn the risk free rate. The expected return on a stock, where ρ is the probability of a price rise, is the risk-free rate: $(1+r)S = \rho S^{+} + (1-\rho)S^{-}$. Rearranging; $\rho = (S(1+r) - S^{-})/(S^{+} - S^{-})$, the weight applied to future rises in option pricing.

Incorporating this information into equations 2.6 and 2.7, with the assumption of a 5% risk free interest rate, gives:

$$\rho = \frac{(1+r)S - S^-}{S^+ - S^-} = \frac{1.05*90-80}{120-80} = 0.3625$$

$$C = \frac{\rho C^+ + (1-\rho)C^-}{1+r} = \frac{(0.3625*17)+(0.6375*0)}{1.05} = 5.8690$$

The market price of £5.87 provides a single point on the option pricing line corresponding to current asset price. Deriving a complete option pricing line for a plausible range of stock prices requires a continuum of such calculations.

Although this example is highly simplified and apparently unrepresentative of reality, the structure is quite useful and has, for instance, been developed to value multi-option investments (Trigeorgis, 1991), petroleum projects (Ekern, 1988) and a mine property (Kelly, 1998). Stock prices can only 'move' in one of three directions at any point in time; upward, downward or no change. Using a trinomial (figure 2.3) rather than binomial lattice, where the relative probabilities assigned to future prices reflect observed fluctuations, can improve the accuracy of the model. A stock price observed to rise more often than fall might have 0.6 probability of rising and 0.2 for both remaining constant or falling during any given period. Childs and Triantis (Childs and Triantis, 1999) have used a trinomial lattice to evaluate interacting research and development projects. Application of these methods has been further extended with a pentanomial lattice to assess the influence of product life cycles on the option to alter capacity (Bollen, 1999).

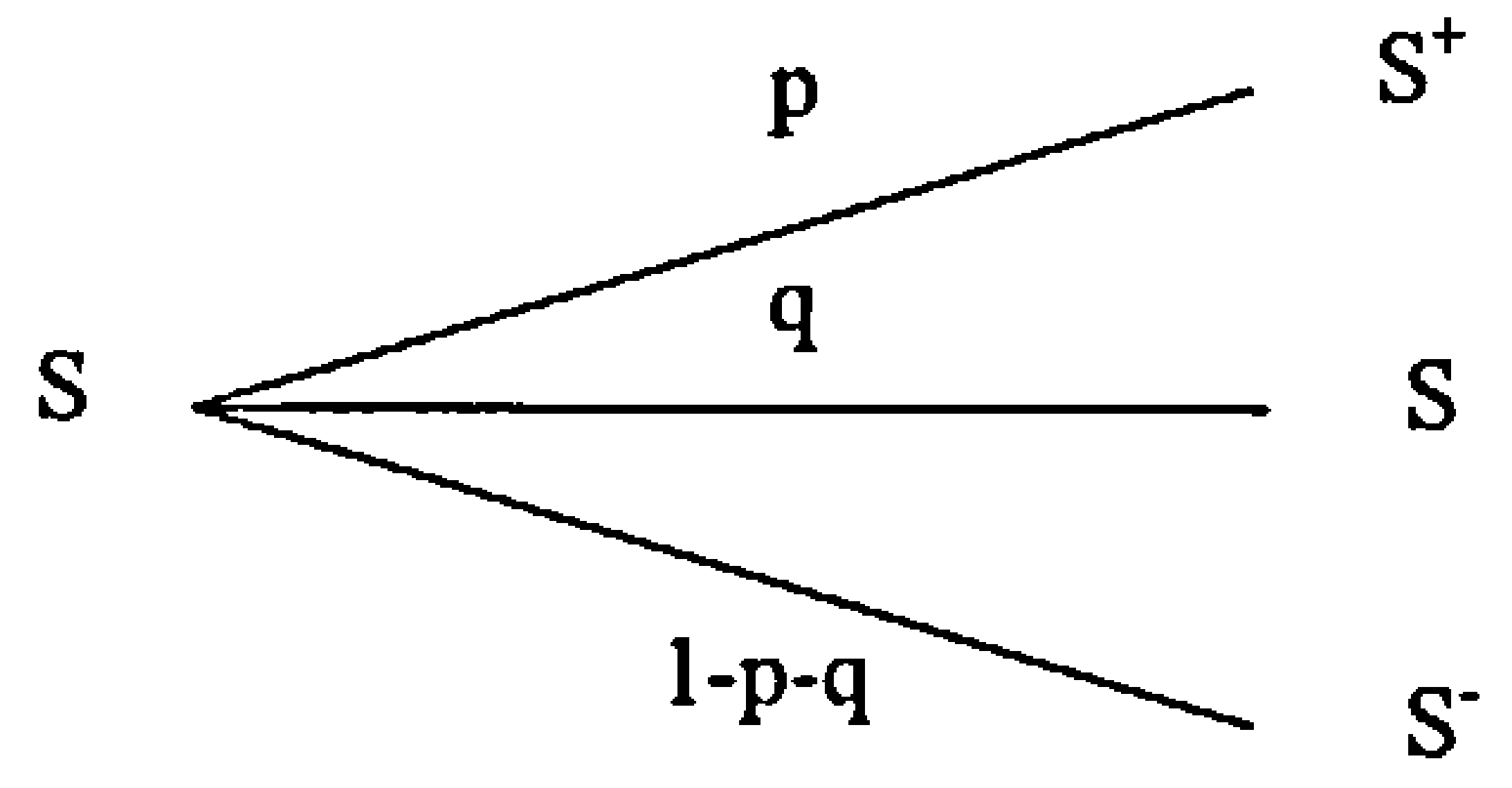

Figure 2.3. A single period trinomial lattice

Some authors have introduced a tendency away from a symmetric structure to "tilting" lattices (Tian, 1999). In this case branches of the lattice are organised to create an upward bias to prices. For trinomial lattices unchanged movements become moderate upward movements and the remaining two branches create respectively greater and less extreme movements. Where stock prices are observed to fall over time the lattice may be biased downwards.

The binomial example given is limited to a single period (n=1). Multi-nomial models are usually extended to many periods. A binomial lattice of 4 periods allows price to assume up to[11] 16 (2^4) values in the last period. An option that expires in one year modelled as a 12 period binomial lattice with each period representing one month allows up to 4096 (2^{12}) prices in the final period. Increasing the number of periods and reducing the time associated with each (eg. 52 periods = one week per period) improves the reality of the model as prices evolve more quickly and take on a greater range of values. To price multi-period options valuation occurs the expiration date by summing possible (j=0,...,n) option values (multiplied by their relative probabilities) to find the expected terminal option value. Backward induction and discounting are used to find current option value:

$$C = \frac{\sum_{j=0}^{n} \frac{n!}{j!(n-j)!} p^j (1-p)^{n-j} \max(u^j d^{n-j} S - E, 0)}{(1+r)^n} \qquad \textbf{(EQN. 2.8)}$$

Where $\frac{n!}{j!(n-j)!} p^j (1-p)^{n-j}$ is probability that price will rise j times in n periods, each with risk neutral probability p, and $\max(u^j d^{n-j} S - E, 0)$ is the associated call value at expiration, taking account of the probability of up (u) and down jumps (d). Kamrad (Kamrad, 1995) has used multi period lattices to value manufacturing and mining production.

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[11] Assuming lattice branches do not recombine.

Binomial models can be framed to approximate continuous models by creating infinitesimally short periods and simultaneously generating an infinitely large number of periods. Whilst multi-period call, put, American and European options can be modelled, complexity comes at a price. Sophisticated models can loose their transparency and may become difficult to handle with solutions requiring computer assistance. Programs in Excel or programming languages such as Fortran can be written to find option values and optimal exercise dates. Cox, Ross and Rubinstein (Cox et al., 1979b) have shown that when continuous time is approximated and specific values for u, d and p are chosen, as $n \rightarrow \infty$, the discrete binomial formula above converges to the continuous-time Black and Scholes model. Yoshimoto (Yoshimoto and Shoji, 1998) for instance, uses a binomial approximation to find the optimal rotation age for a forest stand. The Black and Scholes formula is a continuous time model, attractive for its computational efficiency and direct relationship to the hedging ideology in pricing simple options. It is discussed in the following section.

2.1.4 Black and Scholes option pricing

Black and Scholes created a mathematical formula to value options written on non-dividend paying assets whose prices follow a lognormal distribution. This formulation encompasses ideas that prices are continuous rather than discrete, do not fall below zero, and that lower and higher prices face a smaller probability of occurrence. Black and Scholes made some strong assumptions in addition to the arbitrage-free economy:

- Capital markets are perfect
- Short sales are permissible
- Securities are infinitely divisible
- Securities are continuously tradable
- Any amount may be borrowed or lent at the risk-free rate
- There are no transaction costs
- No dividends are payable

These assumptions allow the replicating portfolio principle to theoretically be applied accurately and continuously at no cost throughout the life of the option. The assumption of no dividends was made for simplicity and was later relaxed for known dividend payments (Black 1975) and for dividends expressed as a continuous compounded yield (Merton 1973).

To value a European call option Black and Scholes considered the probability (given current price) that on the exercise date stock price exceeds the exercise price, prompting exercise to occur. Using arbitrage arguments a hedging portfolio (B=NS-C) is constructed, where C and S, are continuous variables. The model describes continuous application of the hedging portfolio; since S is constantly changing, N and B must be continuously adjusted to maintain equivalence between the hedging portfolio (NS-C) and risk free borrowing (B). Using Ito's Lemma for finding the derivative of non-smooth functions, Black and Scholes derived a partial differential equation (PDE) that must be satisfied by the value of the option:

$$\tfrac{1}{2}\sigma^2 S^2 C''(S) + rSC'(S) - C'(t) - rC = 0 \qquad \textbf{(EQN. 2.9)}$$

This is subject to an exercise condition, lower, and upper boundary. For a call option these are respectively; C=max(S-E,0), if S=0 then C=0, and $\frac{C}{S}$ approaches unity as S approaches infinity[12]. For a call with exercise price E, Black and Scholes showed option value to be:

$$C(S,t,E) = SN(d1) - Ee^{-rt}N(d2) \qquad \textbf{(EQN. 2.10)}$$

where

$$d1 = \frac{\ln(S/E) + (r - \frac{1}{2}\sigma^2)t}{\sigma\sqrt{t}}$$

$$d2 = d1 - \sigma\sqrt{t}$$

---

[12] The European put option faces equivalent boundary conditions.

$N(\cdot) =$ Cumulative standard normal distribution function

Since dividends are assumed absent in the Black and Scholes' model, and an American option without dividends is never exercised early, the pricing of an American call is identical to a European call. The value of a European put may be ascertained either directly or via the put-call parity:

$$P(S,t,E) = -SN(-d1) + Ee^{-rt}N(-d2) \qquad \textbf{(EQN. 2.11)}$$

Valuation of an American put requires a further condition to check whether the discounted value of the option at any node is exceeded by the value from early exercise. For this there is then no closed-form solution given a finite time to maturity. Various numerical techniques can be used to obtain an approximation. The Black and Scholes formula can be used to confirm the nature of influences on option value discussed earlier (table 2.2).

Some authors including Luehrman (Luehrman, 1998) have tabulated Black and Scholes option values. Analysts can use an adjusted volatility parameter ($\sigma/\sqrt{t}$) and stock price relative to the present value of the exercise price ($S/(Ee^{-rt})$) to consult tables presenting option value relative to stock price. Trigeorgis (Trigeorgis, 1999) provides option values for the adjusted volatility parameter between 0.05 and 1, and for the relative current asset price between 0.5 and 2.5.

Despite the attractiveness of a comprehensive formula there exist some problems. 'Long Term Capital Management' used the formula extensively to identify under-priced options and engage in profitable arbitrage. Success prevailed until a severe downturn in the US stock market meant that the cost of creating hedging portfolios exceeded the funds available, and the company collapsed. This example demonstrates how transaction costs assumed negligible in the model, can make continuous hedging difficult if not impossible to carry out, and that prices may not conform to the random walk specification underlying option pricing. Evidence also exists that the formula carries some systematic biases in the pricing of call options. Bhattacharya (Bhattacharya, 1980) has demonstrated that although present, such biases are not generally operationally significant. The Black and Scholes' model remains a commonly used formula for pricing options.

Several developments have extended the basic Black and Scholes model. The Garman-Kohlhagen (Garman and Kohlhagen, 1983) model prices European options on foreign currency, Margrabe (Margarbe, 1978) developed a theoretical model for the right to exchange one asset for another – the exchange option, and Geske (Geske, 1979) created a model to price options on options – the compound option. This particular piece of work paved the way for pricing other kinds of option, including American call options on dividend paying stocks (Roll, 1977), and options on the maximum and minimum of two risky assets (Stulz, 1982). An important break through was pricing of options where the underlying asset price is subject to abrupt jumps (Merton, 1976). This was previously difficult due to the challenge of hedging such jumps, and proved important for pricing real options whose underlying assets may not be subject to continuous evolutionary processes.

Progress in pricing financial options has eventually led to developments in pricing real options. Theories that have allowed financial analysts to price ever more complex combinations of assets, derivatives, interest rates and exchange rates have gradually transferred to pricing options to invest, abandon, exchange, and alter scale, that prevail in the real sector.

2.2 Real Options

2.2.1 Creating the analogy between financial and real options

Real options analysis is based around the idea that some investment projects closely resemble financial options. Here the application of financial techniques to valuation of real options is explored. In particular this section examines the circumstances surrounding, characteristics underlying, and parameters appropriate for valuing different types of option.

A financial option is bought on a market and the owner must decide when, if at all, the option should be exercised subject to a fixed exercise date. Stock price uncertainty, payment of any dividends, and the exercise price and date influence optimal exercise. These factors encompass elements of uncertainty, irreversibility and an ability to defer. Variables are observed and monitored, and a decision rule, 'exercise when keeping the option open (deferring) is no longer more valuable than killing the option (exercising immediately)', is adopted. If an investment opportunity is equivalent to a call option, initiating the investment can be thought of as 'exercising an option to invest'. Many of the characteristics underlying financial options also exist for 'real options' (table 2.3).

	Financial option	**Real option**
Acquiring option	Purchased	Purchased / conferred / created
Factors affecting value	Dividends, Exercise price, date	Interim payment, Investment cost, time horizon
Underlying uncertainty	Stock price	Net present value
Source of irreversibility	Once exercised the option no-longer exists	Sunk costs, some actions and their implications cannot be altered, or are costly to alter
Ability to defer	Subject to exercise date	Subject to endogenous and exogenous influences

Table 2.3. Characteristics of financial and real options.

An investor must decide at what point, if any, to initiate a project. On approval investment costs are incurred and the option to invest at a later date is killed. To help inform the exercise decision a range of variables are observed including current asset price (if the project produces a commodity), or present value (if the project produces a service or similar untraded benefits). The costs and benefits of deferring are weighed and a decision rule is created: 'Invest when the benefits of keeping the option to invest alive no longer exceed the benefits gained from killing the option and commencing the investment'. In other words, invest when the present value of expected cash flows is sufficiently high relative to the investment cost.

Financiers confront a fixed and known exercise date. Real projects may or may not face an explicit deadline although there is usually some implied time horizon and some deadlines may be stochastic. Investment deadlines might be imposed internally by managers, or by investment opportunities naturally disappearing. Alternatively timing constraints may be due to external constraints such as patents or competitive forces. Since real options are unlikely to have a single fixed date on which to exercise, they are more akin to American rather than European options. Option pricing methods have also been adapted to value opportunities with no expiry date (McDonald and Seigel, 1986).

Many real options do not have a fixed exercise price; investment costs may evolve. Sources of fluctuations may again be external (input prices), or internal (related to project scale). This poses little of a challenge to the analogy and can be accounted for graphically through either a shift or pivot in the intrinsic value curve. For instance, in the case of investment cost being positively related to project value intrinsic value will slope upward more steeply. Trigeorgis (Trigeorgis, 1999) describes a model with stochastic investment cost.

Financial options are described in formal contracts where the structure of the problem is stated, and relevant variables clearly specified. The contract sets out unambiguously the terms (exercise price and date etc) that bind relevant parties, ruling out debates concerning whether the option exists, who owns it, who has the right to exercise, or when the option expires. Financial outcomes such as price can be unquestioningly observed leading to a transparent exercise decision.

The explicitness of financial options does not always transfer to the real sector. Since formal contracts do not exist, real options must be forcibly identified, are often harder to describe, and outcomes may be the subject of some debate. Important in defining and identifying real options therefore, are the characteristics underlying the decision problem. Option problems, whether real or financial, are characterised by uncertainty, irreversibility, and an ability to defer (figure 2.4).

These factors, and the interactions between them, are central to identifying and understanding real options problems. Some authors emphasise one factor (usually uncertainty) over the others but for an option to exist all three must be present. Since real options are not expressed within formal contracts, examining a project for these factors is a reliable way to recognise a real options problem and is used to explore the case studies presented in later chapters.

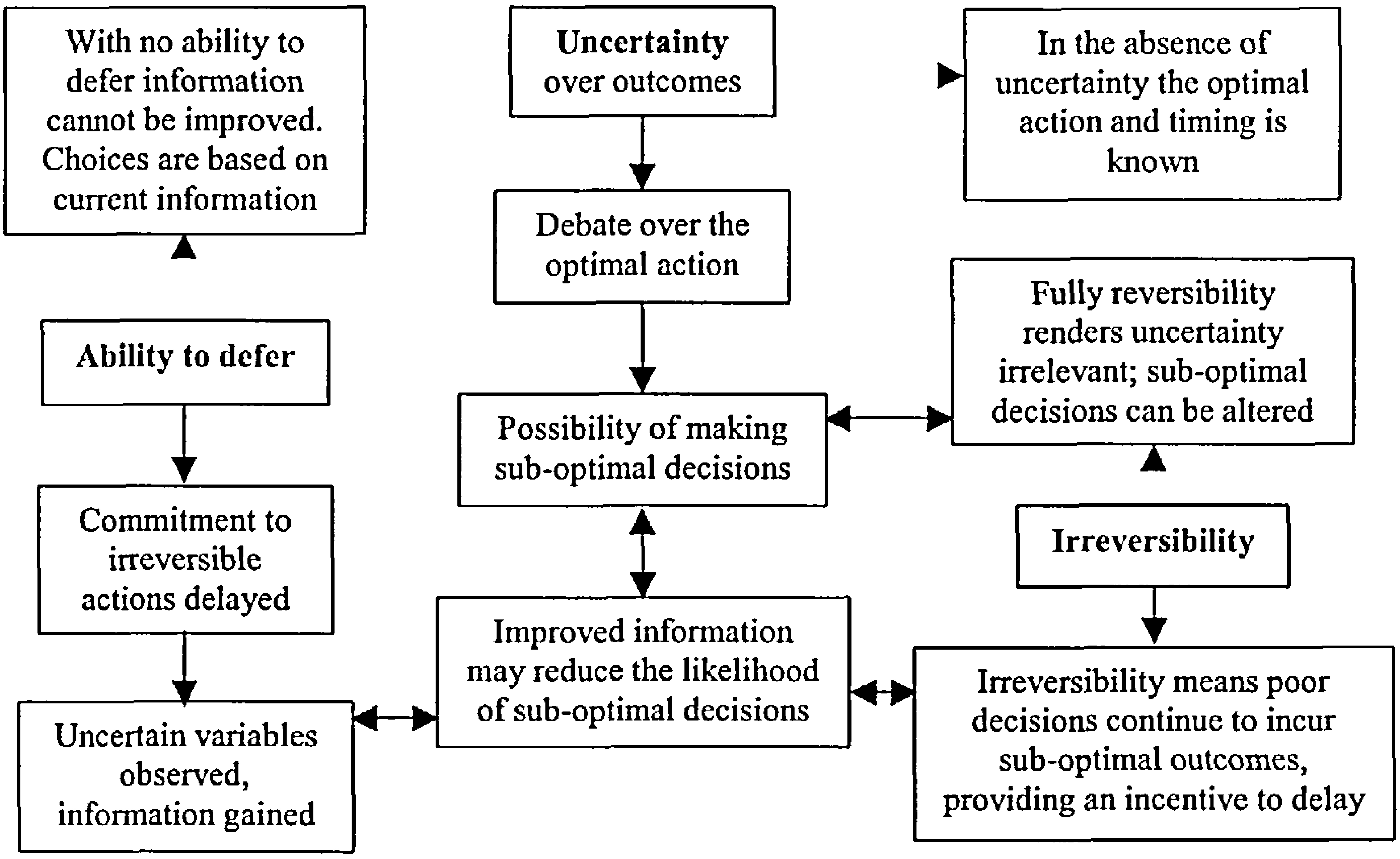

Figure 2.4. Interactions between uncertainty, irreversibility and the ability to defer.

Although discussion has centred upon the option to invest as being analogous to the call option real options analysis encompasses more than just investment projects. A firm might consider options to expand, temporarily close, reopen, permanently close, or switch inputs and outputs. In the real options literature growth options, abandonment options, options to exit and switching options have been used to assess these circumstances. Compound options may also exist in the real sector. For instance current research and development provides an option on product development which in turn provides the option to market, and expand or abandon production depending on market conditions. The following section considers the pricing of real options.

2.2.2 Pricing real options

Pricing real options requires identification and estimation of variables previously recognised as influencing option value. Table 2.4 summarises these variables, their interpretation from a real options perspective, and comments on their measurement. The precise variables required to value an option depend on the model used, but follow this general format.

Call option	Real option	Source and measurement
Spot price (S)	Present value of expected cash flows (V)	Estimated cash flow given current expectations of the future. Evolves with the realisation of uncertain events and interim cash flows.
Variance in stock value (σ^2)	Variance in expected value over time (σ^2)	Volatility caused by numerous sources of uncertainty including prices, disease progression, effectiveness of a therapy.
Exercise price (X)	Investment cost (I)	Estimate of upfront development costs, may vary over time.
Time to expiration (T)	Time until investment opportunity disappears (T)	Timing constraints imposed either internally or externally including government, progress of patient, availability of funds, competitive pressures, expiry of patents, political pressures. May be stochastic.
Risk-free interest rate (r)	Risk-free interest rate (r)	Observed
Dividend (δ)	Payout rate (δ)	Periodic cash flows resulting from the project or denied / paid while deferring. For instance costs incurred whilst deferring

Table 2.4. Variables required for real option valuation.

The assumptions underlying real option valuation are similar to those for financial options but with some additions. Early real options applications used contingent claims valuations methodology that transfers hedging arguments to the real sector. Assumptions that the underlying source of uncertainty was tradable and that a well-developed derivatives market exists ensure hedging can be carried out. The majority of applications therefore concerned projects where a tradable commodity was produced such as mining of natural resources (Brennan and Schwartz E S, 1985; Paddock et al., 1988).

Whilst the original aim was to value traded assets the models can equally well be applied to projects whose underlying source of uncertainty is not traded (Benaroch and Kauffman, 1999). Applications have increasingly moved in this direction with analysis of research and development (Angelis, 2000) and environmental investment decisions (Cortazar et al., 1998). In these cases the assumptions of contingent claims are inappropriate (Slade, 1998) and dynamic programming techniques are used, which examine the stopping and continuation value of an option and consider a decision maker's willingness to hold the option until the following period.

McDonald and Seigel (McDonald and Seigel, 1986) developed a basic model of real option pricing addressing the issue of when to pay a sunk cost I, in exchange for a project of value, V. This represents an optimal stopping problem for the decision maker. He / she must choose when to exercise (stop) the option in return for a flow of uncertain benefits. In their model the value of the investment V, evolves according to a geometric Brownian motion.

$$dV = \alpha \ V \, dt + \sigma \ V \, dz \qquad \textbf{(EQN. 2.12)}$$

The underlying random variable V changes each period *dt* with some drift α subject to a known and constant variance σ^2. Brownian motion is a Markov process; future values of the diffusion process depend only on the current value. The term *dz* is an increment from a Weiner process such that the probability distribution of a change in any time interval is independent of any other time interval, and has changes that are normally distributed with variance growing linearly with the time horizon.

The optimal stopping problem maximises the value of the *investment opportunity,* F(V). Investment at time t provides payoff $V_t - I$, where I is the investment cost. The decision maker maximises the expected present value of investment at time t, subject to the evolution of V:

$$F(V) = \max \varepsilon[(V_t - I)e^{-\rho t}] \qquad \textbf{(EQN. 2.13)}$$

Where ε is the expectations operator, t is the future time (currently unknown) when the investment is made, and ρ is the discount rate. To obtain a finite investment date the constraint $\alpha < \rho$ is imposed. Without such a constraint the value of the investment project would grow more quickly than it is discounted over time. Larger t would always increase project value creating an incentive for continuous deferral. An optimal exercise date would not exist. The difference ρ -

α is defined as δ, the payout rate[13]. The payout rate causes a project to grow at a slower rate than the market discount rate and is akin to a dividend (table 2.4).

The most lucid case exists when $\sigma = 0$. With this assumption the value of the project at time t is given by $V(t) = V_0 e^{\alpha t}$ (where $V(0) = V_0$). If investment occurs at time τ, the value of the investment opportunity becomes:

$$F(V) = (Ve^{\alpha\tau} - I)e^{-\rho\tau} \qquad \textbf{(EQN.2.14)}$$

Equation 2.13 considers the future unknown value achieved when investment occurs and discounts back. Equation 2.14 incorporates the current known project value, asserts a growth rate of αt, until investment occurs at τ, and discounts back. Maximisation over time requires that the first derivative be set to zero and the second derivative be negative:

$$\frac{dF(V)}{d\tau} = -(\rho - \alpha)Ve^{-(\rho-\alpha)\tau} + \rho Ie^{-\rho\tau} = 0 \qquad \textbf{(EQN. 2.15)}$$

This corresponds to equating the marginal benefit ($\alpha Ve^{-(\rho-\alpha)\tau}$) and marginal cost ($\rho(Ve^{-(\rho-\alpha)\tau} + Ie^{\rho\tau})$) from waiting and leads to the optimal exercise date τ^*:

$$\tau^* = \max\left\{\frac{1}{\alpha}\log\left[\frac{\rho I}{(\rho-\alpha)V}\right], 0\right\} \qquad \textbf{(EQN. 2.16)}$$

If τ^* is 0 the optimal exercise date is now. Positive values of τ^* indicate how far into the future one should wait before investing. For $\tau^*=3$ the investment should be undertaken three periods from the current time period.

With no uncertainty if $\alpha \leq 0$, V(t) will remain constant or fall as time elapses. The optimal strategy becomes adopt immediately if $V \geq I$ and never adopt otherwise. When $0 < \alpha < \rho$ immediate investment is optimal only when $\tau^*=0$. From equation 2.16 this requires that V exceeds some threshold level V* where:

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[13] Some times referred to in real options literature as a convenience yield.

$$V^* = \frac{\rho}{\rho-\alpha} I > I \qquad \textbf{(EQN. 2.17)}$$

Since ρ>α, $\frac{\rho}{\rho-\alpha} > 1$, and V* necessarily exceeds I. For values of V ≥ V*, $\frac{1}{\alpha}\log[\frac{\rho I}{(\rho-\alpha)V}]$ is less than zero. τ*=0 and immediate investment is optimal. For V<V*, a positive deferral period exists because $\frac{1}{\alpha}\log[\frac{\rho I}{(\rho-\alpha)}]>0$. Relative growth ($e^{\alpha T}$) and discounting ($e^{-\rho T}$) cause expected present value to increase over time so that in some future period V will sufficiently exceed I (V*>I), leading to investment. The value of the investment opportunity in this case is found by substituting the optimal timing τ* (equation 2.16) into the value of the investment opportunity (equation 2.14):

$$F(V) = [\alpha I/(\rho-\alpha)][(\rho-\alpha)V/\rho I]^{\rho/\alpha} \qquad \textbf{(EQN. 2.18)}$$

Table 2.5 summarises these explicit decision rules and option value for different assumptions concerning project growth and intrinsic value.

Assumption	**Intrinsic value**	**Action**	**Option value, F(V)**
$\alpha \leq 0$	If V < I	Never invest	0
$\alpha \leq 0$	If V ≥ I	Invest immediately	V-I
0< $\alpha < \rho$	If V ≥ V*	Invest immediately	V-I
0< $\alpha < \rho$	If V< V*	Defer	$[\alpha I/(\rho-\alpha)][(\rho-\alpha)V/\rho I]^{\rho/\alpha}$

Table 2.5. Decision rules from real options analysis when σ=0.

When no growth is expected (α≤0) option value is equal to intrinsic value [max(V-I,0)], otherwise option value exceeds this leading to a positive option premium [F(V)-max(V-I,0)]. Larger expected growth generates greater option value, and option premium, creating a stronger incentive to defer. Figure 2.5 plots option value for different levels of α showing this relationship whilst reinforcing the similarity between real and financial option value. The decision threshold V* is shown as the first value of V (above V=I=1) at which option value equals intrinsic value or equivalently when option premium falls to zero.

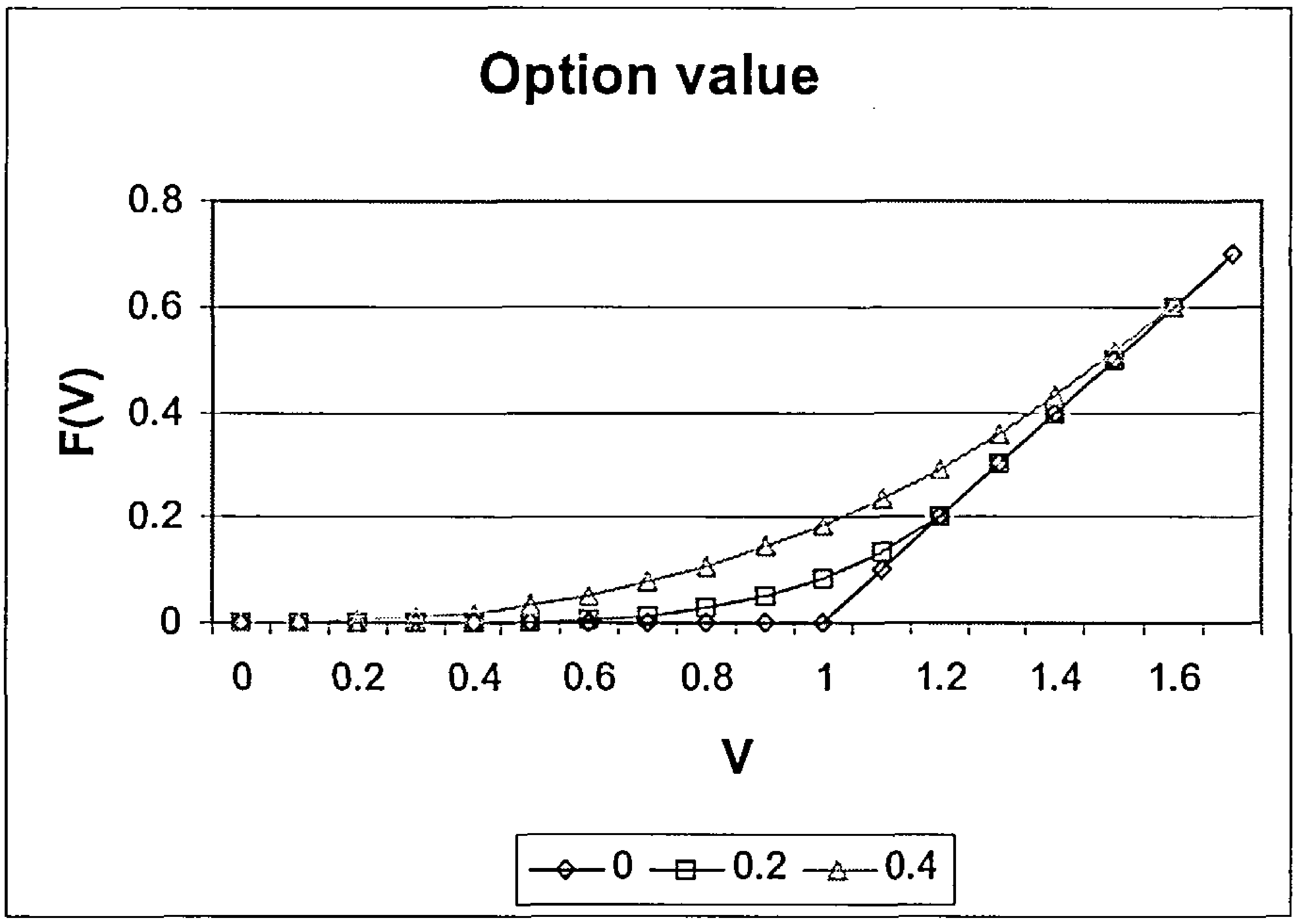

Figure 2.5. Option value for four levels of project growth (α=0, 0.2, 0.4) where I=1, and σ=0.

The decision thresholds and functions for option value derived above relate to the case of no uncertainty. Figure 2.5 therefore illustrates that option value can exceed intrinsic value even in the absence of uncertainty demonstrating that option premium is not a risk premium. Most projects do have some degree of uncertainty.

The solution to the theoretical case where $\sigma > 0$ follows a logic similar to the reduced case. A Bellman equation encompasses information about the stopping value (intrinsic value) and the continuation value (future value) of a real option, asserting that over any time interval prior to investment total expected return is equal to expected capital appreciation. The optimal action maximises the sum of these two components. When $\sigma > 0$, dynamic programming techniques use this concept to solve the stopping problem defined by exercise of an option. Dixit and Pindyck (Dixit and Pindyck, 1994) demonstrate the use of Ito's Lemma[14] to expand the Bellman equation and derive a second order partial differential equation (PDE) that must be satisfied by the value of the investment opportunity,

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[14] A mathematical tool for computing the derivative of non-continuous random functions

F(V). This is the stochastic equivalent to equation 2.15 which maximises in the deterministic case:

$$\tfrac{1}{2}\sigma^2 V^2 F''(V) + \alpha V F'(V) - \rho F(V) = 0 \qquad \textbf{(EQN. 2.19)}$$

F'(V) and F''(V) represent the first and second derivatives of F(V) with respect to V. By satisfying the PDE, F(V) conforms to the intuitive constraint that the value of the investment opportunity must equal the maximum of the continuation or stopping value. A set of Boundary conditions must also be satisfied that limit F(V) and identify the solution V*.

$F(0) = 0$ Absorbing barrier

$F(V^*) = V^* - I$ Value matching condition **(EQN. 2.20)**

$F'(V^*) = 1$ Smooth pasting condition

The absorbing barrier provides a lower boundary on F(V), stating that should project value fall to zero, the investment opportunity will be worth nothing. Both will remain worthless due to the stochastic process governing V. The value matching condition holds at V*, equating the value of the investment opportunity with the value of immediate action V-I. The free boundary, V*, and the region of V for which the PDE is valid, are endogenous and as yet unknown, and are identified using the smooth-pasting condition. At V* the two arguments of the Bellman equation not only equate but meet tangentially. If this were not the case then over some small waiting period, either the stopping payoff or the continuation payoff would rise more rapidly and immediate exercise would not be optimal, an improvement in payoff would be possible by exercising at a different time point.

Finding F(V) requires solving the PDE subject to the boundary conditions. To comply with the absorbing barrier F(V) takes the form:

$$F(V) = AV^{\beta} \qquad \textbf{(EQN. 2.21)}$$

where β is the known constant:

$$\beta = \tfrac{1}{2} - \alpha/\sigma^2 + \sqrt{\left[\alpha/\sigma^2 - \tfrac{1}{2}\right]^2 + 2\rho/\sigma^2} > 1 \qquad \textbf{(EQN. 2.22)}$$

Substituting the first derivative of F(V), arranged for A into the value matching condition to find V* and putting this back in to the solution for A gives V* and A in terms of β and I alone:

$$V* = \frac{\beta}{\beta - 1} I \qquad \textbf{(EQN. 2.23)}$$

$$A = (V* - I)/(V*)^{\beta} = (\beta - 1)^{\beta-1}/(\beta^{\beta} I^{\beta-1}) \qquad \textbf{(EQN. 2.24)}$$

The value of the investment opportunity and the optimal investment rule are provided by equations 2.21 and 2.23 respectively. These solutions are equivalent to equations 2.17 and 2.18 in the deterministic case and along with equations 2.22 and 2.24 provide sufficient information for decision makers to make informed choices within a real options framework. The presence of uncertainty means the timing threshold t* cannot be solved for directly in the stochastic case leading to some debate over project timing.

Since $\rho > \alpha$ and $\beta > 1$, both the deterministic and stochastic solutions for V* involve a multiplier attached to I that exceeds 1. In both cases therefore, the optimal investment threshold V* exceeds the cost of the investment, I, leading to a decision threshold that conflicts with traditional decision-making (V=I). Since V* necessarily exceeds I, real options analysis always supports deferral when NPV based techniques recommend immediate action.

McDonald and Seigel (McDonald and Seigel, 1986) describe a real option that is available in perpetuity and achieve closed form intuitive results. Since many real options have timing constraints and other complications such as staged developments and capabilities to contract and expand the project in response to market conditions, methodology has progressed to incorporate these factors. As project descriptions become increasingly complex closed form analytical solutions may be unattainable and numerical methods are required. As authors consider broader applications alternative models including lattices that incorporate investment deadlines have become popular. Authors have extended and enhanced the primary works exploring a range of options based techniques that encompass varying levels of sophistication. The following section discusses some applications of real options theory.

2.2.3 Review of the application of real options

Applications of real options analysis have developed in terms of depth (addressing more complex problems), breadth (focussing on wider types of problem including options to abandon and switch) and scope (increasing the variety of fields to which real options is applied). This review considers all aspects paying particular attention to the last since this thesis falls into the category of increasing scope.

Early applications of real options theory centred on problems with a single source of traded uncertainty and significant upfront costs. This helped emphasise the similarity between financial and real options and meant that investments in resource extraction industries were especially prominent because a commodity is sold. For instance, Tourinho (Tourinho, 1979) considered depletion of natural resources while Paddock et al. (Paddock et al., 1988) focussed on petroleum reserves. This theme has continued into recent applications with Frimpong (Frimpong and Whiting, 1997) and Cortazar (Cortazar and Casassus, 1998) looking at the value of an existing mine and expansion respectively, and Imai (Imai and Nakajima, 2000) performing options analysis of an oil refinery project.

Significantly, many early applications focus on valuing projects in isolation and treating options independently. Real life investments are rarely this simple, often involving exercising a string of connected options or simultaneously exercising interacting, or compound, options. As early as 1989, Dixit (Dixit, 1989) tackled joint consideration of firms' entry and exit decisions. Hypothetical examples were used to explore the relationship between price thresholds triggering entry and exit.

Dixit highlighted the wide appeal of the results; "ranging from foreign trade to job search...witness the great reluctance of university deans to approve new faculty positions in departments that experience a surge of students."

Trigeorgis performed several analyses using compound options. In 1991 (Trigeorgis, 1991) a log transformed binomial numerical analysis, capable of modelling option interactions, demonstrated results consistent with previous attempts to value American abandonment options by Myers and Majd (Myers and Majd, 1990). Later work looked at interactions between options for multi-option investments (Trigeorgis, 1993) and examining leases with complex options built in (Trigeorgis, 1996). More recent work in this area includes sequential ordering of interrelated projects (Childs et al., 1998), interdependencies between toll road infrastructure projects (Rose, 1998), optimal timing and spread of phased rollout projects (Pennings and Lint, 2000), and sequentially staged investments (Majd and Pindyck, 1987).

Methodological improvements in the depth of real options analysis, including pricing compound interacting options and projects based on multiple sources of uncertainty, permitted the breadth of real options applications to develop. Investment opportunities came to be considered as strategic growth options (Kester, 1984; Kulatilaka and Perotti, 1998). In particular Hevert (Hevert et al., 1998) considered the impact of interest rates on the value of growth options. Perhaps more importantly projects other than investments gained increasing attention. Margarbe's (Margarbe, 1978) financial work on options to exchange assets encouraged work on options to switch inputs and outputs. Options to contact/expand production, timing options (Farzin et al., 1998), options to scrap (Moretto, 1996a), or abandon (Pennings and Lint, 2000; Myers and Majd, 1990), and options to temporarily and permanently shut down (McDonald and Seigel, 1985) have all been the subject of analysis.

Whilst early applications maintained the solid analogy to finance, increasing breadth promoted the similarities between finance and projects from wider fields where uncertainty, irreversibility and an ability to defer are present. Applications have become particularly prominent in environmental sectors where the characteristics are especially evident. Uncertainty can be associated with prices of naturally occurring resources such as wood, in which case irreversibility may be the time and cost to replace a forest stand and the ability to defer the decision to harvest might be infinite. Authors examine specialised themes including climate policy (Conrad, 1997a; Plantinga, 1998), forest management (Thorsen, 1999), strategic development of agricultural land (Tegene et al., 1999) and crop management (Khanna et al., 2000).

Hasset (Hasset and Metcalf, 1992) and Chao and Wilson (Chao and Wilson, 1993) develop pollution concerns. The former takes the individual's perspective with regards to purchasing energy saving appliances while the latter assumes the perspective of a firm purchasing emission allowances. Both conclude that waiting generates improved information that provides an incentive to defer irreversible investments. This creates inertia against environmentally friendly efforts both at the individual and firm level.

Environmental policy has been examined by Kocagil (Kocagil and Eduardo, 1996), who looked at the impact of new environmental standards on the mining industry, and Conrad (Conrad, 1997a), who considered a government's option to introduce policies to slow global warming. Both use hypothetical examples to analyse policies of pollution abatement. Conrad uses Brownian motion to model mean temperature drift and volatility to serve as the underlying source of uncertainty. The author uses two evolutionary processes to represent environmental impact before and after implementation of preventative policies. A trigger temperature for adoption of policies was found to be 15.54 °C. Given current forecasts the authors suggest this is unlikely to be reached within two decades of the analysis being carried out. In this instance real options analysis recommended deferring action to slow global warming.

Conrad has also contributed to real options applications within the field of forest management. Albers (Albers, 1996) had previously considered the option to develop tracts of tropic rainforest, identifying elements of uncertainty (future forest value), irreversibility (the loss associated with deforestation) and the ability to defer (waiting before commencing development). Conrad's contribution (Conrad, 1997b) assesses the relative benefits of preserving a stand of old-growth coast redwood, and abandoning the forest in favour of selling the wood. The amenity value of the forest as a function of visit rates is modelled as the underlying source of uncertainty with timber prices assumed constant. Conrad solves for a trigger amenity value required to justify preservation.

Forestry has received considerable attention. Plantinga (Plantinga, 1998) investigated optimal time to harvest, Yoshimoto (Yoshimoto and Shoji, 1998), optimal rotation age, and Thorsen (Thorsen, 1999), establishment of new forest stands. Such analyses typically use future stand values or wood prices as the underlying source of uncertainty and highlight an irreversible investment (sunk cost and loss of the forest). Whilst Plantinga favours Brownian motion to describe uncertainty in future stand values Yoshimoto prefers a binomial approximation to model future wood prices. Thorsen looks at implications of policies to influence investor behaviour, and concludes not only that subsidies to induce afforestation must increase, but that the extent of the increase depends on the nature of the subsidy. Analyses such as this suggest potential ramifications for policy design in other areas including health care.

Whilst most applications of real options analysis fall within broad categories such as resource extraction, forestry related, and technology adoption there have been an increasing number of novel applications. Burda (Burda, 1995) applies option pricing techniques to assess individuals' decisions to migrate. Uncertainty is discussed in the context of income in the home and new countries, with migration involving unrecoverable costs that can be postponed almost indefinitely. This work may have implications for the wider labour market, in particular mobility of workers in sectors such as nursing. Grenadier (Grenadier, 1995) uses options theory to value lease contracts incorporating options to renew and cancel leases with payments contingent on asset use. Saphores (Saphores, 2000) considers optimal introduction of measures to curb pest populations, and Mahul (Mahul and Gohin, 1999) similarly looks at optimal timing of animal disease control policies. Review of such applications prompts potential applications within the health care arena, in this case control of contagious disease and immunisation programmes.

The majority of applications are of a theoretical nature with numerical analysis often based on hypothetical figures to illustrate important concepts and maintain transparency, although some authors (Thorsen, 1999) have used historical prices and observed volatility to calculate optimal thresholds. Whilst real options analysis has spread widely in some areas in recent decades, the limited scope and lack of empirical applications are arguably due to the mathematical complexity of many real options models. Several articles and books, for instance Luehrman (Luehrman, 1998) and Copeland and Antikarov (Copeland and Antikarov, 2001), have pursued non-technical explanations and discussion aimed at applying real options theory in practice, to help over come this problem.

This thesis aims to expand the scope of real options by applying the technique to several decision making problems encountered within health care. No attempt is made to contribute to the mathematical content of real options analysis; instead existing models are used within case studies to illustrate the analogy between financial and health care options, and to demonstrate some key results and implications for decision making of using the real options approach. Chapter 4 examines the watchful waiting decision, chapter 5 analyses the option to defer removal of life support technology for comatose patients, chapter 6 considers the National Institute for Clinical Excellence's option to approve new and existing technologies, and chapter 7 looks at option value as a value of deferred information in the context of using clinical trials to gather addition evidence. Prior to this some alternative notions of option value are discussed in order to clarify the definition of option value used within this thesis.

2.2.4 Alternative notions of option value

Discussion thus far has centred on a specific interpretation of option value; the value of projects characterised by uncertainty, irreversibility and an ability to defer, as ascertained using financial option pricing techniques. This notion of option value might be referred to as a 'production type' option value since production related activities are usually the subject of interest. In parallel with this two schools of thought concerning what shall be termed ‘consumption type’ options have developed. One school makes reference to option value, the other to quasi-option value.

Weisbrod (Weisbrod, 1964) initiated a debate when he considered that individuals might be willing to pay a price for assured access to an environmental resource. In particular he referred to consumers who have an option to visit Utah’s Wasatch mountain range. He argued that when there is uncertainty over their future demand and exogenous future supply of the natural resource, consumers place a value on owning the option to visit in future and are willing to pay to preserve this option. Weisbrod raised the issue that if no formal mechanism exists to charge potential users for this benefit, their option values would not be incorporated into private decision making concerning the future of the resource.

Weisbrod’s ideas lead to some confusion with different interpretations of his work developing into two contrasting schools of thought. Cicchetti and Freeman (Cicchetti and Freeman, 1971) believed option value related to the relationship between maximum willingness to pay for an option and expected value of ownership. If option price is the individual’s maximum willing to pay for an option guaranteeing the right to consume future benefits, then option value is the difference between this and the expected value of consumer surplus derived from actually consuming the benefits. If this is true consumer surplus underestimates economic benefits. Cicchetti and Freeman argued that option value exists predominantly as a result of risk averse behaviour and is limited to positive values.

Schmalensee (Schmalensee, 1972) used a similar framework to Cicchetti and Freeman to derive a more general result concluding that option value might be positive or negative depending on the characteristics of the problem and individual preferences. Since Schmalemsee was not optimistic about accurate measurement of preferences he advised option value be assumed zero for applied studies. Bohm (Bohm, 1975) reinforced conclusions concerning the sign of option value but in so doing challenged Schmalemsee’s risk aversion assumption and recommendation for applied work. Subsequent work has contributed to both arguments with numerous authors seeking to explain and reconcile the apparently conflicting results (Bishop, 1982; Anderson, 1981). There now appears consensus that option value can be positive or negative depending on the preferences and assumptions underlying uncertain variables (Freeman, 1984).

Meanwhile Henry (Henry, 1974), and Arrow and Fisher (Arrow and Fisher, 1974), simultaneously developed an alternative interpretation of Weisbrod's work. Their quasi-option value focussed on irreversibility. When a project is irreversible (for instance results in irreversible destruction of an ecosystem or requires irrecoverable investments), waiting for information prior to making a commitment may be valuable. These authors argued that independently of risk aversion, cost benefit analysis that omits this value of information is biased against environmental preservation.

Conrad (Conrad, 1980) believed that quasi-option value was equivalent to the expected value of perfect information when deferral reveals complete information, and the expected value of information when deferral reveals only partial information. Hanemann (Hanemann, 1989) later pursued this line of thinking arguing that option value was distinct from, but bounded by the unconditional value of information. In Hanemann's opinion quasi-option value existed conditional on no irreversible action being undertaken and therefore was a conditional value of information.

This school of thought developed with inclusion of information functions to model information arrival through time (Batabyal, 1997), and challenges to the assumption of total irreversibility via inclusion of an 'irreversibility cost' (Zhao and Zilberman, 1999). Efforts to measure quasi-option value include Greenley (Greenley et al., 1981) who used contingent valuation to assess option value for water quality and recreation on the South Platte River, and Smith (Smith et al., 1983) who measured willingness to pay for water pollution control. Both concluded that option value was significant accounting for 40% of reported consumer surplus (Greenley) and 50% of stated willingness to pay bids (Smith). Ha-Duong (Ha-Doung, 1998) considers climate policy choices, defining option value to be variation in expected value of future information between two strategies of aggressive and moderate emissions abatement. Option value was shown to be positive and around 50% of the cost of abatement.

Hanemann (Hanemann, 1984) made an important contribution to the field when he showed that the two interpretations, option value and quasi-option value could be reconciled. Hanemann demonstrates that the Arrow-Fisher-Henry (AFH) quasi-option value can be measured in two ways and that the Schmalensee-Bohm (SB) option value represents the difference between these measures. He suggests the reason for the difference is that the two interpretations deal with different aspects of decision-making under uncertainty. AFH is concerned with dynamic, temporal resolution of uncertainty whilst SB is a static measure. This is consistent with Smith (Smith, 1983) who had previously suggested "the apparently contradictory conclusions of several earlier studies are largely due to a reflection of differences in these studies' characterisation of the behavioural decision process".

Fisher (Fisher, 1997) later provides commentary that forges links between these consumption based option values and financial option value, using simple versions of the two models to demonstrate equivalence. 'Consumption' and 'production' type option value both involve decision making under uncertainty requiring knowledge of underlying sources of uncertainty, information gained through time, and details of the exercise decision. Differences seem to be a matter of perspective, underlying assumptions and valuation methods. Most importantly production type options use valuation methods derived from financial option pricing to establish value. It is these techniques and their applicability to health care that form the basis of this thesis.

A final perspective of option value has arisen from consideration of future choices and the impact of current decision making on availability of choices. Rosenhead (Rosenhead, 1992) recommends that decision makers should select alternatives today in order to optimise the choices available in future periods. Whilst this is similar in nature to considering deferral in real options techniques, Rosenhead does not propose financial option pricing techniques as a way to establish value.

Chapter 3. Real options in health care.

3.1 Introduction

Most current research in health economics fails to acknowledge the option like characteristics of many health care related decisions (table 3.1). For instance pharmaceutical companies have options to research, clinically test, and develop new compounds, hospital budget holders have options to invest in new equipment, or increase the prevalence of existing equipment. The decision to exercise such options is surrounded by uncertainty, and requires irreversible commitment in terms of time, money, exposure to risk and confronting potentially costly side effects. There is also the possibility of deferral, although in some cases this may be limited.

Decision maker	Option	Type
Patient	• Option to purchase private health insurance • Option to comply with prescribed drugs • Option to defer surgery	• Invest • Abandon/continue • Defer
Managers	• Option to alter hospital capacity, ward size	• Expand/contract
GP	• Option to prescribe medication • Option to switch medication	• Invest • Switch
Childbearing mother	• Option to have a caesarean • Option over anaesthetic	• Switch • Switch
National Institute for Clinical Excellence	• Option to approve a drug, procedure, device	• Invest / switch
Pharmaceutical company	• Option to research, market test and release now compounds	• Invest/expand/ contract/abandon
Policy makers	• Option to initiate waiting list reduction measures, campaign to increase supply of nurses	• Invest
Clinical trial manager	• Option to alter the size of study arms or length of trial	• Switch/extend/ contract

Table 3.1. Options in health care.

Consider a patient facing surgical amputation for a foot ulcer. The option to amputate is owned by the physician in consultation with the patient. Uncertainty exists over progression of the untreated ulcer. If self-healing occurs amputation is unnecessary, if rapid deterioration occurs amputation is essential to reduce spreading. Amputation is not guaranteed to successfully halt ulcer growth leading to additional uncertainty surrounding post-surgery progression. Adverse side effects from surgery and the patient's ability to cope with post surgery disabilities are further sources of uncertainty. Amputation has health (infection, risks from general anaesthetic) and mobility (relearning basic mobility) costs for the individual as well as financial costs that provide sources of irreversibility. Deferral provides information on spread or rate of healing. In the event that self-healing occurs amputation is avoided. If this is not the case immediate surgery may have reduced (though perhaps not eliminated) the likelihood of spreading, and may have reduced the severity of amputation compared to amputation following deferral. The consultant has an option on immediate surgery akin to a financial call option.

Real options are embedded throughout the health care sector. Accounting for option like characteristics can have implications for decision making and as a result affect the optimal allocation of resources. This chapter examines the three defining characteristics and establishes their importance for decision making within the health care context. This helps demonstrate the equivalence between financial options and real health care options and justifies the application of option pricing models to supplement existing economic evaluation methodology.

Sections 3.2 considers existing decision making techniques. Section 3.3 examines the role of uncertainty (section 3.3.1), irreversibility (section 3.3.2) and the ability to defer (section 3.3.3) in health care decision-making problems. Section 3.4 compares the valuation methods underlying classical economic evaluation in health care and real options analysis. This section demonstrates that when projects are compared like for like the two methodologies give the same assessment of value. This means that it is differences in the assumptions governing valuation that cause the contrasting results and conclusions of real option valuation. Section 3.5 brings these aspects together.

3.2 Economic evaluation in health care

Potentially unlimited demand for health care services, limited supply of resources and the lack of market prices as a method of allocation mean that other mechanisms are required to distribute health care funds among competing uses. Optimal allocation of resources requires comparison of projects either against some exogenously stated criterion or against alternative projects. For a single project, having assumed a specific perspective, possibly that of society or the National Health Service, and identified a study time horizon, economic evaluation examines costs and benefits. Analysis by net present value (NPV) allows projects of unequal length, or those with high start up costs in contrast to prolonged running costs to be compared. A project is implemented if the present value of benefits exceeds costs (equation 3.1) or equivalently if NPV exceeds zero (equation 3.2). B_t and C_t are respectively periodic monetary benefits and costs; r is an appropriate discount rate.

$$\sum_{t=1}^{T} \frac{B_t}{(1+r)^t} > \sum_{t=1}^{T} \frac{C_t}{(1+r)^t} \qquad \text{(EQN. 3.1)}$$

$$NPV = \sum_{t=1}^{T} \frac{B_t}{(1+r)^t} - \sum_{t=1}^{T} \frac{C_t}{(1+r)^t} > 0 \qquad \text{(EQN. 3.2)}$$

Future costs and benefits however, are rarely certain and the handling of uncertainty has attracted much attention in economic evaluation literature (Briggs and Gray, 1999). First order uncertainty concerning the probability that a given event will occur, such as whether an individual will become infected with a contagious disease, or whether a drug is effective, is typically incorporated using expected values. A treatment that may be very effective, with benefits of £150, moderately effective, with benefits of £100, or barely effective with benefits of £40, with respective probabilities 0.2, 0.5, and 0.3, has an expected benefit of £92 [0.2(150)+0.5(100)+0.3(40)]. Having obtained expected NPV sensitivity analysis is frequently used to assess the effects of changes in base case parameter values on the outcome of interest. Two-way sensitivity analysis demonstrates interactions by altering inputs simultaneously.

Second order uncertainty exists when there is uncertainty not only over the outcome of an event but also the probability associated with each potential outcome. The probability of developing a disease and costs of factor inputs may be subject to second order uncertainty. Probability distributions can be assigned to variables using Monte Carlo Simulation (Doubilet et al., 1985) that lead to a related distribution surrounding the outcome measure. Expected value for the project under consideration will depend on the distributions chosen to represent uncertainty, and whether pessimistic, optimistic, expected or median base case values are used.

Methods for handling uncertainty may help the understanding of a project and improve the extent to which a model reflects reality but do not necessarily help in decision making. Uncertainty may result in an inability to demonstrate statistical significance meaning that an analysis fails to show a difference (greater than that expected by chance) between two alternatives. In addition there are no guidelines for choosing between projects of contrasting risk and return structures such as where a greater point estimate is associated with a larger confidence interval that contains lower possible outcomes. Claxton (Claxton, 1999) has argued in favour of using expected values only for decision making, and reserving estimates of uncertainty to help establish priorities for research and the reduction of uncertainty.

Although cost-benefit methodology works in principle, few health-care related benefits accrue in monetary form. This has led to different types of economic evaluation each with contrasting aims; cost minimisation, cost-effectiveness/utility, and net- benefit analyses. Cost minimisation examines projects of equivalent outcome selecting the alternative with minimum resource use. This is most useful when outcomes are comparable.

Cost-effectiveness analysis examines costs per unit of a specific outcome measure such as the number of adverse outcomes avoided or number of successful outcomes. Cost-utility analysis enables broader comparisons to be made. Outcomes are described in units such as life years saved, quality adjusted life year gained, and disability years avoided that account for quality as well as quantity of life affected by a given treatment. Cost utility calculates the cost per unit of outcome and also marginal cost per unit of additional outcome in order to derive an incremental cost-effectiveness ratio (ICER) (equation 3.3). Dominated alternatives that cost more and provide fewer benefits, and extendedly dominated alternatives (dominated by some combination of other actions) are removed from consideration. The remaining therapies can be ranked with greater benefit being available at increased cost (see (Karlsson and Johannesson, 1996)).

$$ICER_a = \frac{C_a - C_b}{B_a - B_b} = \frac{\Delta C}{\Delta B} \qquad \textbf{(EQN. 3.3)}$$

Choosing between the alternatives requires, whether implicitly or explicitly, some valuation of society's willingness to pay for an additional unit of health benefit (λ). Alternatives are selected in order up to and including the regime with the largest ICER compatible with this willingness to pay (equation 3.4). Goeree (Goeree et al., 1999) uses this evaluation methodology to assess cost effectiveness of strategies to treat Gastro-oesophageal reflux disease. Authors have suggested obtaining willingness to pay valuations from court payout decisions, previously implemented programmes (league tables), and conjoint analysis (O'Brien et al., 1998; O'Brien and Gafni, 1996) studies.

$$ICER_a = \frac{C_a - C_b}{B_a - B_b} \leq \lambda \qquad \textbf{(EQN. 3.4)}$$

Some drawbacks exist within the cost utility framework. Negative, 0 and undefined ratios pose potentially large problems. For instance negative ratios may result from either a cost or benefit reduction, which have opposing implications for decision making. Costs and benefits must be accurately specified within ratios as the impact of misplacing a value as the numerator or denominator can be large.

Cost-benefit analysis values health outcomes in monetary units to calculate net benefit. Society's willingness to pay for a health outcome (λ) is explicitly used to convert ratios into net benefits[15], which can be expressed either in monetary units (equation 3.5) or in units of effectiveness (equation 3.6)[16]. Programmes are chosen in order of incremental net benefit subject to budgetary constraints.

$$\lambda(B_a - B_b) - (C_a - C_b) \geq 0 \qquad \textbf{(EQN. 3.5)}$$

$$(B_a - B_b) - \tfrac{1}{\lambda}(C_a - C_b) \geq 0 \qquad \textbf{(EQN. 3.6)}$$

Advantages of the net benefit approach include avoidance of problems associated with ratios, easier calculation of confidence intervals and the ability to compare outcomes from a broader spectrum of projects. Outcomes expressed in monetary units can be compared to any program where outcomes can similarly be assigned monetary value. This is particularly useful for governments responsible for decision making over a range of departments including health and education.

There has been extensive work in recent years to explore the advantages of a net benefit approach (Stinnett and Mullahy, 1998) including demonstrating equivalence with cost-effectiveness ratios (Phelps and Mushlin, 1991). Advances in this field include construction of cost-effectiveness acceptability curves that plot the probability of a project being cost-effective for a range of estimates for willingness to pay. This in turn has prompted discussion of the consequences of making wrong decisions, and the value of acquiring further information. Drummond has summarised both methods for economic evaluation and implementation of these methods in practice (Drummond et al., 1997; Drummond and McGuire, 2001).

Within the general framework for economic evaluation and decision making in health care there is much to debate. This thesis concentrates on aspects relevant to real options analysis taking the structure as given[17]. Real options analysis requires

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[15] A cost-benefit analysis in the true sense would use the willingness to pay of gainers and losers from a project, whilst the net benefit approach typically uses a single societal willingness to pay.
[16] Given as either net monetary benefit or net health benefit.
[17] Some health economics literature uses the terminology 'financial option appraisal' to refer to monetary valuation and comparison of treatment alternatives, for instance Batra (Batra, 2001). This is not the same as the real options theory presented within this thesis. Similarly Bala (Bala et

a monetary valuation of projects and is therefore applied within, and comparable to, the net benefit approach. The remainder of this chapter looks at the treatment of uncertainty, irreversibility and the ability to defer within traditional methods and considers how real options analysis might contribute to the ways in which they are handled.

3.3 The defining characteristics of decision making

3.3.1 Uncertainty

This section looks at uncertainty in financial markets and contrasts this to uncertainty in health care decision making. Smith (Smith, 1983) provides a systematic framework from which to examine uncertainty, arguing that three questions should be considered;

(1) What is the source of the uncertainty?
(2) How is the uncertainty in decision making ultimately resolved?
(3) Does decision making permit progressive learning to incorporate new information that may resolve some of the uncertainty?

These questions can be developed to provide a complete characterisation and understanding of uncertain variables;

(1) What sources of uncertainty are relevant to the current decision?
    (1.1) Who is affected by uncertainty and thus who's perspective important?

(2) Can uncertainty be resolved at all?
    (2.1) Is uncertainty resolved naturally over time?
    (2.2) Must uncertainty be actively resolved?
    (2.3) Are costs incurred in observing new information?
    (2.4) Can the uncertainty ever be fully resolved?

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al., 1999) has referred to a patient's (consumption type) option value from having treatments available to them. These benefits were estimated empirically and do not necessarily equate to financial option value.

(3) Can new information be incorporated into the decision model?
  (3.1) Does irreversibility prevent actions being altered to account for new information?
  (3.2) Can information be incorporated at some cost?
  (3.3) Can barriers to incorporating information be reduced via further decision making and the creation of flexibility?

In finance an option has a single source of uncertainty (price process, interest rate, exchange rate). For a call option current knowledge and future expectations governed by an evolutionary price process influence the owner's incentive to exercise. As prices evolve they reveal information that is freely available each period. Perfect information is available each period when price is revealed. Despite this tomorrows price remains uncertain; uncertainty is never fully resolved. Where price history is believed to influence future prices, random walks with drift have been used to characterise uncertainty. In this case new information is continually being incorporated into the model and used to alter predictions for the future. When no drift is used history is judged to be irrelevant, information may affect the current exercise decision but is not used to predict future prices. While exercise is deferred new information can be costlessly incorporated into the decision-making process, following exercise, irreversibility prevents this.

Whilst answers to the questions for financial options are reasonably straightforward this is not necessarily the case for real projects. Health care decisions cover a broad range of investment and disinvestment opportunities with multiple sources of uncertainty often relevant to a single decision problem[18]. Relevant sources include financial based prices (of inputs such as disposables or labour) and costing data (capital overheads, bed costs), and physical based disease progression (growth of cancer, spread of contagious disease), responses to treatment, and risk reductions. Projects whose value is sensitive to price variables are most likely to reflect simple financial options. Where multiple sources are present Monte Carlo simulation can be used to combine uncertainties as inputs

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[18] Options with multiple sources of uncertainty are termed Rainbow options

into a single output such as net benefit. Copeland and Antikarov (Copeland and Antikarov, 2001) demonstrate the use of Monte Carlo simulation within real options analysis.

Prices and costs in the real sector behave much like prices in the financial sector evolving over time with new information widely available. Disease incidence, prevalence and status within an individual also evolve through time with current values observable and future values unknown. By contrast however, costs may be incurred when observing information relevant to health care decisions. Expensive patient tests, population surveys, and studies of resource use may be required to observe detailed information. Other sources of uncertainty such as safety, efficacy and cost-effectiveness may require specific actions such as clinical trials to improve information.

In most instances as with financial price variation, uncertainty is never fully resolved, although real sources of uncertainty may be correlated through time. A patient who has deteriorated continuously throughout the previous 10 periods is increasingly less likely to begin recovery in the following period. For coma patients there is a strong link between time spent in a coma and the likelihood and degree of recovery (Council on Scientific affairs and council on Ethical and judicial affairs, 1990).

Information arrival can be incorporated into real options models in many ways. A stochastic Markov process such as Brownian motion might be relevant when changes in a variable are continuous, independent and normally distributed with mean zero and variance increasing linearly with the time interval. When the lower limit of the variable is zero, such as with prices or health status, using the logarithm (as in the Black and Scholes formula) may be appropriate. When history is believed important, a more generalised Wiener process with non-zero drift and alternative volatility parameter may be suitable. A Poisson specification is appropriate when information is expected to arrive at discrete, though uncertain points in time. Modelling information arrival will depend on what is known, or believed to be true of the evolutionary process.

Health care decisions can involve irreversibility that limits the ability to incorporate new information. Altering plans in response to information can be costly and some actions themselves cannot be reversed (such as amputation) rendering additional information, when available, effectively worthless. Responses to uncertainty and information evolution therefore depend on the degree of irreversibility characterising a decision.

3.3.2 Irreversibility

While irreversibility is inherent in exercise of a financial option, continuous deferral maintains a position of flexibility that allows new information to influence decision making. Once exercise occurs it cannot be reversed, even if poorer than anticipated outcomes result. The ability or inability to improve good, and mitigate poor outcomes can be used to define the extent of irreversibility. The less costly are such actions the lower the degree of irreversibility. In financial markets further shares, options and futures might be bought and sold in an attempt to mitigate losses.

Several sources of irreversibility affect the attractiveness of real projects (Gershbach, 1997). Investment under uncertainty literature focuses on an inability to recuperate some or all sunk costs (Dixit and Pindyck, 1994), and the degree of difficulty in restoring a previous state altered by some decision has also been discussed (Fanai and Burn, 1997). Manipulation of anticipated and unanticipated outcomes (Fanai and Burn, 1997) and the associated cost (Zhao and Zilberman, 1999) is emphasised in literature that considers irreversibility as a selection criterion for projects. Actions in health care can fall into all three categories.

Sunk costs are incurred in capital investments, patient surgery, and research and development but are particularly relevant to infrastructure decisions including development of a new hospital or ward. This form of irreversibility is most significant when benefits do not accrue until the entire investment is complete, such as following surgery. This type of irreversibility is commonly encountered.

Having been initiated most project strategies can be altered (at some cost) to influence outcomes. Unanticipated changes in demand could prompt disposal or purchase of technologies, unpopular policy decisions can be altered at some political cost and altering a patient's drug regime may induce withdrawal effects or new side effects that then impose costs. These strategy alteration costs create inertia against changing the initial decision policy, even when the original plan reveals lower than expected rates of return.

Finally some actions themselves are physically irreversible. This kind of irreversibility is most prominent in environmental sectors (Viscusi, 1988) where, for example, destruction of the ozone layer cannot be reversed. Within health care the decision to terminate care for a patient whose life is preserved solely through life support technology is irreversible. This source of irreversibility also relates to aids sufferers where the receipt of current treatment regimes diminishes the benefits or in some cases precludes the use of future technologies with greater potential to improve well-being. Decisions to surgically amputate also face irreversibility. This form of irreversibility can also exist when a decision is deferred. For instance deferring treatment may allow a disease to have some irreversible impact and deferring approval of an efficacious treatment may permit existing patients to be managed suboptimally.

The degree of irreversibility encountered in a health related decision increases with sunk costs, strategy alteration costs and the inability to physically reverse actions. Any scrap value gained when technologies are decommissioned or projects abandoned, reduces irreversibility. Despite these clear sources of irreversibility there is little explicit discussion of irreversibility in the majority of health economic evaluations. Real options techniques can contribute to existing methodology by encouraging explicit discussion of irreversibility as well as providing a means of analysis. Basic real options models assume complete irreversibility in the sense that projects have upfront costs that cannot be recuperated and no ability to reverse is included. This is appropriate for modelling options such as the removal of life support. Exploring and modelling future options created or by the exercise decision incorporates degrees of irreversibility.

3.3.3 Deferral

When a decision is surrounded by uncertainty, and there is some degree of irreversibility, deferral becomes a relevant alternative to immediate action. In practice existing decision-making techniques employ a now or never framework; projects with positive NPV are accepted, and rejected projects are not necessarily reconsidered in light of new information. Real options analysis provides a framework within which deferral can be assessed and compared with immediate action. The similarities between deferral of financial and real projects, and incorporating deferral are considered here.

Discussion of the ability to defer must encompass the length of deferral (and the extent to which this is understood / known by relevant parties), information potentially available from deferral, and the costs associated with observing this information. The maximum deferral period is stated explicitly for financial options by the exercise date and is fixed at the time of purchase. For American options exercise may occur any time prior to the exercise date so the remaining deferral period is always known with certainty. Information in the form of prices are revealed freely each period and can be incorporated into decision making until such time as exercise occurs.

The deferral period for real investments can take a number of forms including indefinite postponement, limited periodic postponement (waiting x periods), or waiting subject to additional analysis being completed or specific information becoming available. The option to remove life support may be deferred almost indefinitely whilst a patient awaiting transplant surgery faces a limited deferral period. Deferral might be limited by factors such as budget constraints. Funding for a project may only be guaranteed for a year, or leasing arrangements may constrict time available. The end of an NHS financial year signifies an exercise date. Negative attitudes to deferral of health improvement measures, expressed for instance as complaints about waiting lists may generate shorter exercise dates, despite longer deferral being potentially beneficial for some patients.

Health care options are likely to have stochastic exercise dates. For instance a patient might receive watchful waiting; a regime whereby some (usually invasive) treatment is deferred pending information on disease status. Watchful waiting is only relevant either before the disease enters some irreversible state (or has some irreversible impact), or the patient becomes unfit for surgery (or is believed to no longer benefit), or the patient dies from alternative causes. Given differing disease progression both within and between individuals, the ability to defer will change over time for a given patient, and vary between patients. Contrasting beliefs about disease progression may even create different perceptions of the ability to defer for a given patient at a given point in time.

Although deferring financial options reveals freely observable price information deferral itself can have a cost. An investor will always defer exercise of a non-dividend paying stock because information is available at no cost. When dividends are payable deferring exercise delays receipt of dividend payments imposing a cost on deferral. The investor must weigh the relative costs and benefits from deferral to make a decision.

Multiple sources of uncertainty underlying real options means deferral can reveal broader types of information. Prices (drugs, devices), demand and supply conditions, disease prevalence and incidence, and individual disease status might all be monitored. Information relevant to health care decision making is unlikely to be freely observable. For patient-level decisions monitoring disease progression may involve costly tests, such as magnetic resonance imaging, that provide an incentive for early exercise. Costs incurred in deferral and observing information must be weighed against the benefits (delay investment cost, improved information) in order to assess the desirability of deferring action. When the cost of deferral exceeds the benefits exercise is optimal.

Deferral is introduced into decision tree structures by including a waiting alternative branch at the trunk of the tree. Cost-effectiveness of deferral is calculated by comparing discounted expected costs and benefits of deferral (option value) to those of immediate action (net benefit), (figure 3.1).

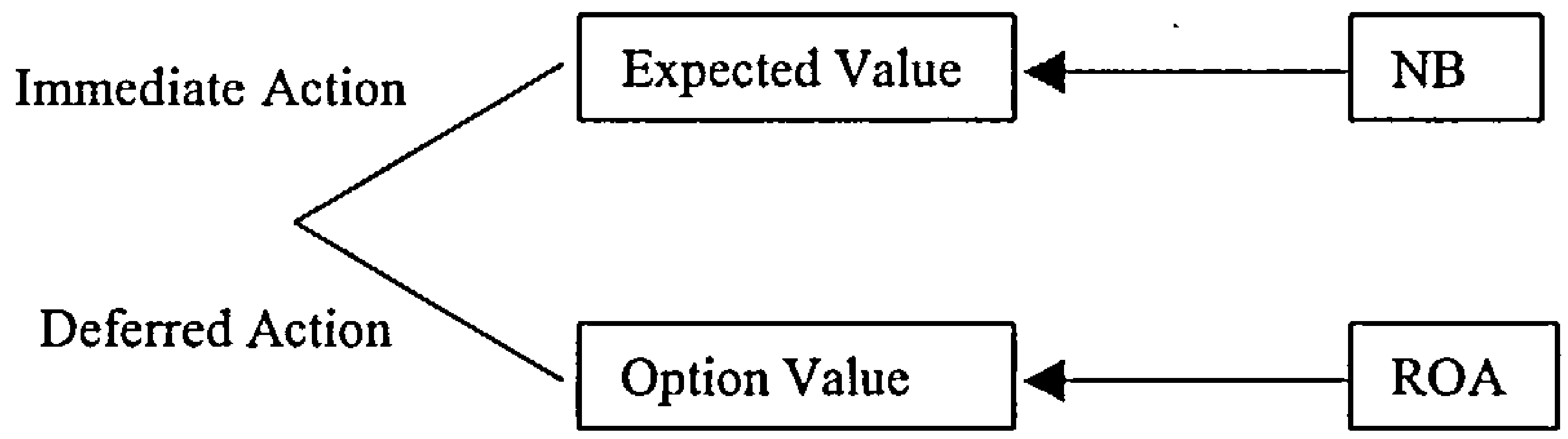

Figure 3.1. Comparing immediate action and deferred action.

When deferral is introduced there must exist some way for information to improve during the period of waiting; otherwise there is no incentive to defer. This is achieved by modelling events such as price changes or disease progression following the decision to defer and prior to the following decision node. In this way revisions are made to the available information set and can influence the decision of interest. Real options analysis therefore allows decisions to be conditioned not only on today's information but also anticipation of tomorrow's information and information that may be revealed in every future period for which deferral is a possibility.

3.4 Comparison of valuation methods

Whilst real options analysis makes explicit the treatment of uncertainty, irreversibility and the ability to defer within economic evaluation, the principles underlying valuation remain consistent with those of traditional methodology. As such, it is differences in the way the three factors are perceived and modelled that generate conflicting results and conclusions. In the very unlikely case that a real options approach and traditional economic evaluation lead a project to be compared like for like, identical assessments of value are obtained. Chapter 2 section 1.1 illustrated how net present value techniques can be used to estimate option value when deferral is modelled fully. This example assumed a very simple structure for uncertainty. When uncertainty, and therefore risk, is dealt with appropriately in net present value the two methods again give consistent results. This can be seen through the use of a simple numerical example.

Section 1.2 in chapter 2 valued an option whose payoffs were related to the price of a stock. Uncertainty was modelled using a binomial structure that allowed future payoffs to rise or fall with respective probabilities q=0.4 and (1-q)=0.6. Exercise of the option was assumed irreversible and there was an ability to defer exercise for one period. Figures 3.2 and 3.3 re-illustrate this problem, where C is the value of the option and S is the value of the underlying stock.

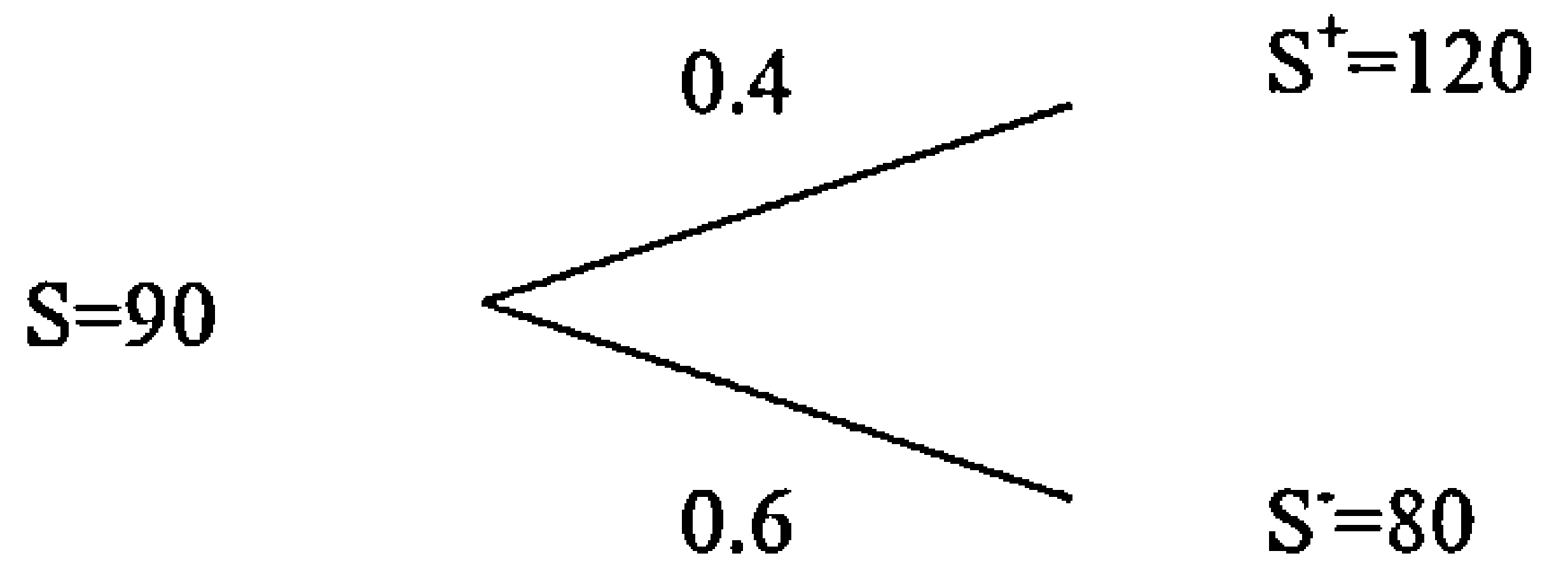

Figure 3.2. Hypothetical asset underlying a call option

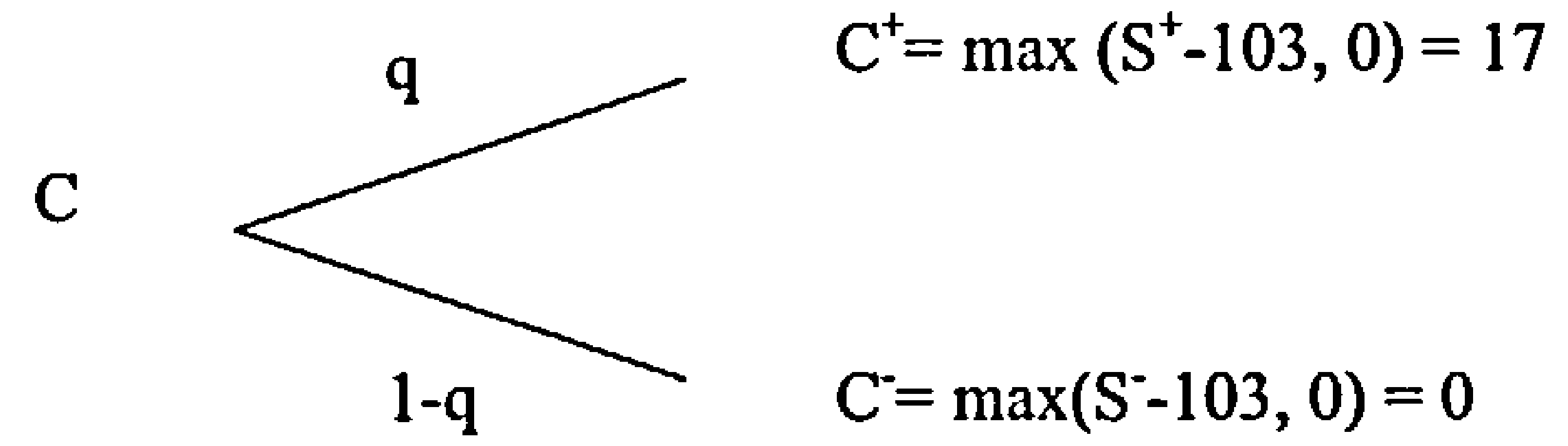

Figure 3.3. Hypothetical call option

Suppose this option relates to a decision faced by the National Institute for Clinical Excellence who have an option to approve a drug for treatment of Alzheimers disease. Real options analysis suggests that a portfolio is created that combines the option and the stock such that the payoffs from the portfolio are equal irrespective of whether stock price and option value increase or decrease over time. This previously enabled current option price to be estimated using equations 2.6 and 2.7.

$$p = \frac{(1+r)S - S^-}{S^+ - S^-} = \frac{1.05*90-80}{120-80} = 0.3625$$

$$C = \frac{pC^+ + (1-p)C^-}{1+r} = \frac{(0.3625*17)+(0.6375*0)}{1.05} = 5.8690$$

These equations valued the project using a risk-neutral probability that a positive outcome would result, and so discounted payoffs at the risk-free rate establishing option value of £5.87. Conventional valuation techniques would have valued the same project using the actual probability of a positive outcome and discounted at a risk-adjusted rate. This reflects the implicit risk that the decision maker must face and so will be greater than the risk-free rate. The risk-adjusted rate of return (r^A) for the option can be calculated by estimating the return on a portfolio with an equivalent risk and return structure. A portfolio can be created using a risk free investment (B) and N shares of the underlying stock to recreate the payoffs of the option (NS-B). The current and expected future payoff from this portfolio, and the actual probability of a positive event occurring, can be combined to estimate the expected return on the portfolio and so the return on the option (equation 3.7)[19].

$$1+r^A = \frac{q(NS^+ - B(1+r)) + ((1-q)(NS^- - B(1+r)))}{(NS - B)}$$

$$1+r^A = \frac{(0.4*(0.425*120-1.05*32.38)) + (0.6*(0.425*80-1.05*32.38))}{(0.425*90)-32.38} = 1.159$$

(EQN. 3.7)

Calculating option value using actual probabilities and a risk-adjusted rate gives an identical value for the option:

$$C = \frac{qC^+ + (1-q)C^-}{1+r^A} = \frac{(0.4*17)+(0.6*0)}{1.159} = 5.8690$$

Net present value methods value a risky project and so require a risk-adjusted discount rate. Different aspects of the same project can face contrasting risks, necessitating multiple discount rates within a single project. If the appropriate risk-adjusted rates of return were known a priori the two valuation methods would have resulted in identical assessments of value for the option faced by NICE.

Real options analysis values a riskless project by using the principle of hedging to ensure that the payoffs from holding a portfolio (that incorporates the option) are the same in any future state of the world. When valuing such a project the risk-neutral discount rate is appropriate. If all risks within a project are hedged in this way the risk-neutral discount rate can be used to discount costs and outcomes

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[19] Calculation of the number of shares required (N) and amount of risk free borrowing (B) are given in chapter 2 section 1.2.

relevant to the entire project. This also allows the project to be valued without appeal to subjective assessments of, and preferences towards, risk.

In order to create the portfolio used to replicate option payoffs and generate a risk-free return some other investment, portfolio of investments or financial instrument must be identified that offsets the risk and return structure of the investment opportunity of interest. Although seemingly difficult this task should be put into context; within a large public health care system where a variety of investment projects at both patient and system level are undertaken each year each with contrasting risk exposures, there exist vast possibilities for creating portfolios. Booth for instance (Booth and Walsh, 2001) has examined hedging payoffs from rental income in the housing market. Perhaps a greater issue is that real options analysis requires an efficient market for risk (to allow hedging). However, for net present value analysis to be carried out accurately the same assumption is required to enable calculation of risk-adjusted rates of return.

This section has illustrated some important aspects of real option valuation relating to the treatment of risk. Whilst these issues are very relevant to the practice of economic evaluation, the focus of this thesis lies elsewhere, in the approach to valuation that a real options analysis encourages. This includes the approach to recognising, understanding and appreciating the importance of uncertainty, irreversibility and the ability to defer, and explicit modelling of these factors.

The example presented in this section has demonstrated that when projects are compared like for like option pricing and traditional techniques provide the same assessment of value for an investment opportunity. Any discrepancy in value therefore reflects differences in the way the project is described and modelled under the two approaches. Real options analysis adopts a dynamic structure for uncertainty, explicitly identifies types and degrees of irreversibility, and rigorously analyses deferral. It is these attitudes towards some of the key drivers of value that generate differences in valuations obtained within a real options framework and a conventional economic evaluation.

The case studies presented within the remainder of this thesis explore situations where options analysis might be applied within economic evaluation of health related decisions and show that some very different conclusions can be reached.

3.5 Conclusions

Many economic agents operating within the field of health care face choices that are akin to options. Since such decisions share the defining characteristics of financial options; uncertainty, irreversibility, and an ability to defer, it seems appropriate to use financial option pricing techniques as a valuation method. Real options analysis can be applied within the existing net benefit framework. The contrasting ways in which real options analysis perceives and models uncertainty, irreversibility and the ability to defer generate differences between the results and conclusions of the two approaches.

The challenge facing health economists is to identify real options in health care; an arena where formal option contracts do not exist. Having recognised problems whose analysis may be improved through explicit consideration of the three underlying factors a further challenge is to adapt existing option pricing models to account for peculiarities defining the health related decisions. The remainder of this thesis assesses four potential applications; the option to defer immediate therapeutic treatment, the decision to defer removal of life support, the option to approve technologies and treatments for use on the NHS, and the collection of trial data to improve information.

Chapter 4. Should we wait and see? The real options approach to watchful waiting.

4.1 Introduction

Within clinical areas where disease progression is slow and conventional therapies do not dramatically extend either quantity or quality of life, watchful waiting may be a relevant treatment alternative. Watchful waiting describes a patient management strategy in which immediate curative treatment is not given. Instead the patient undergoes a period of close observation in which periodic check ups permit illness progression to be monitored. Given this ability to defer, if uncertainty and irreversibility also characterise the decision to begin treatment, real options analysis may justifiably be used to assess such patient management strategies.

This chapter considers the methodological and practical suitability of applying real options analysis to a decision-making problem in which deferral is already considered a relevant alternative. Having discussed watchful waiting in section 2, section 3 explores how deferral is currently incorporated into decision making and the contribution of real options analysis. Section 4 sets out watchful waiting as an 'option to treat', examining the characteristics of the decision problem and parameters required for valuation. Section 5 provides a hypothetical example assessing watchful waiting as a treatment alternative for patients with abdominal aortic aneurysms, and explores the implications and consequences of employing real options analysis. Concluding remarks and broader implications are the subject of section 6.

4.2 Watchful waiting as a treatment alternative

During watchful waiting[20] patients undergo assessments that provide information valuable for the final treatment decision. Watchful waiting is an active strategy implying a conditional treatment decision, not a policy in which an ailment is left to deteriorate unchecked, or where a placebo therapy is given, and should be distinguished from time spent on a waiting list. Uncertainty over outcome, associated risks (complications, infections, side effects), and high financial costs of immediate treatment all provide motivations for deferral. Deferring allows data on population, sub-group, and individual cost-effectiveness to be collected from on-going trials, or monitoring disease progression. These sources of information contribute to making the decision of when to commence immediate treatment for a defined (group of) patient(s). When deferral reveals that treatment is unnecessary, perhaps due to self-healing, the potential adverse effects of immediate action are avoided.

The growing quantity of studies in this area, including economic evaluations, testifies to the increasing recognition that deferring aggressive therapy can be an appropriate, and in some cases, cost-effective treatment alternative (Chodak, 1994; Steinberg et al., 1998). To assess deferral Johansson (Johansson, 1994) followed 233 patients with early stage prostate cancer between March 1977 and February 1984. Patients younger than 75 were randomised to deferred treatment or radiation therapy. Risk of progression and death was found to be high in grade III compared to grades II and I tumours, suggesting watchful waiting may be most appropriate for patients in the latter groups.

More recently Warner and Whitmore (Warner J and Whitmore Jnr W F, 1994) analysed 75 of 4000 prostatic cancer registrations who were managed expectantly for at least one year following diagnosis. In the majority of patients, local progression preceded distant metastasis, leading the authors to conclude that "short periods of observation may be permissible if such prove useful in estimating tumour growth rates".

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[20] Also referred to as intelligent watchful waiting (Horowitz, 2000) and expectant management (Zhao and Kling, 1998).

Decision making for patients with prostatic cancer is not alone in drawing attention to the deferral alternative. Early therapy versus watchful waiting has previously been assessed for glue ear (Maw et al., 1999; Bennett et al., 1998), small abdominal aortic aneurysms (Katz and Cronenwett, 1994) (Valentine et al., 2000), mild chronic hepatitis C (Wong and Koff, 2000), solitary pulmonary nodules (Dietlein M. et al., 2000), and acute bacterial rhinosinusitus (American Academy of Family Physicians, 2001). Conclusions vary according to illness, severity, patient age, methods of observation used in the waiting period, and compliance (Wong and Koff, 2000). Deferral has also been considered for hormone therapy (Anderson, 1981).

Whynes (Whynes, 1995) developed a framework for identifying optimal times of transfer between watchful waiting programmes and intervention. This study looks specifically at watchful waiting that terminates due to spontaneous medical improvement rather than situations in which medical deterioration provokes aggressive therapy. Structuring the decision to swap treatments as a cost minimisation problem, Whynes identifies that increases in the probability of recurrence after auto-resolution, the probability of remaining unresolved, and the cost of a watchful waiting programme relative to immediate therapy, reduce optimal times of transfer, effectively curtailing the deferral period.

When assessing cost-effectiveness of watchful waiting, current decision technologies have not generally acknowledged that deferring preserves the option to commence immediate treatment in future should the disease begin to deteriorate significantly. In failing to account for this source of value, existing decision criterion may arrive at mistaken conclusions with regards the attractiveness of watchful waiting. The following section considers deferral in decision making.

4.3 Incorporating deferral into decision making

When diseases progress quickly patients may suffer detrimental long-term effects or become unfit for surgery making deferral an inappropriate course of action. The decision maker must evaluate whether watchful waiting is a cost-effective alternative, and when immediate treatment should start for a given individual (or group of individuals) with identified risk factors. Mechanisms used to assess deferral in decision making are therefore important.

Wong et al (Wong and Koff, 2000) considered cost-effectiveness of watchful waiting versus immediate therapy for mild chronic hepatitis C. Using clinical trial data and data from published sources the authors considered the relative merits over a twenty-year period of biopsy every three years compared to immediate antiviral therapy. Those patients randomised to watchful waiting were subsequently treated with combination therapy (ribavirin and interferon) for 24 weeks if biopsy revealed cirrhosis or moderate hepatitis. Markov simulation was used to estimate prognosis beyond the capacity of the trial. With a 5% discount rate for costs and survival, the incremental cost-effectiveness ratio for immediate therapy was $13,500, and had extended dominance over watchful waiting. In this instance high repeated costs ($1,033) of observing information (biopsy detecting the clinical state of the liver), and the inability of this therapy to prevent future hepatitis C, meant deferral was not optimal for patients with baseline characteristics.

The waiting alternative has been evaluated using decision tree analysis. Introducing deferral requires including a branch in addition to branches representing immediate treatments (figure 4.1). When watchful waiting is chosen observed disease progression can influence the treatment decision. Costs and benefits associated with watchful waiting are likely to differ from those associated with immediate therapy causing expected cost-effectiveness of the strategies to differ.

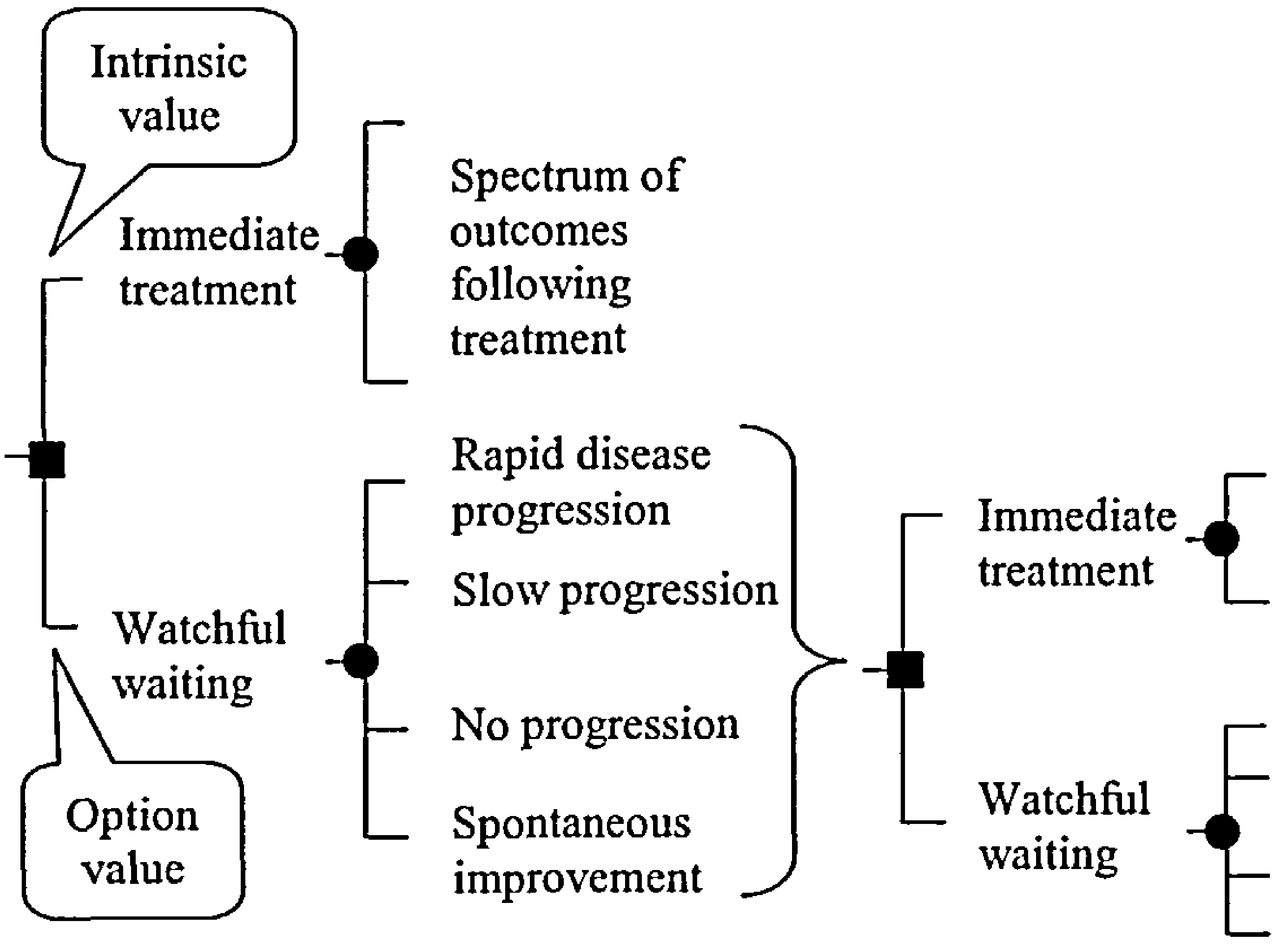

Figure 4.1. Decision tree for a single immediate action that can be implemented now or deferred.

Dietlein et al (Dietlein M. et al., 2000) used this style of analysis to assess cost-effectiveness of varying treatments for management of solitary pulmonary nodules. Watchful waiting was compared to transthoracic needle biopsy, exploratory surgery, and positron emission tomography. When 100% nodule growth was observed by computer tomography (CT) during an observation period, the patient was referred for immediate exploratory surgery. Observation continued for two years with regular CT checks. Mean values for variables used in the analysis were obtained from medical literature. At baseline values the alternatives involving immediate action lead to improved health outcomes at a higher cost. When the probability of malignancy was small (0.1-0.7) even the most cost-effective immediate therapy had an ICER that exceeded the stated willingness to pay for a life year saved (50 000 EUR). For this range of probabilities watchful waiting was declared the preferred strategy.

Despite the attractiveness of this intuitive and logical approach some drawbacks exist. Williams (Williams, 1997) illustrates both the beauty and limitations of decision trees through describing a reasonably complex technology adoption problem. Although not a watchful waiting study Williams' work demonstrates some of the generic problems associated with modelling deferral.

When multiple treatments are available, each of which might be deferred, the complexity far exceeds that of the stylised example in figure 4.1. A single deferral alternative can create a continuum of outcomes from evolving variables. Following initial deferral, immediate action or further deferral may occur; the basic structure of the decision tree is repeated. Each opportunity to defer causes a geometric increase in the number of branches, whether occurring from different deferred treatments or multiple opportunities to defer the same treatment. This complexity is immediately apparent in Williams' work. Williams' 'buy now' tree contains 55 possible outcomes. Introducing deferral in each of the four periods generates an *additional* 90 outcomes.

When a decision problem encompasses numerous uncertain variables such as disease progression, fitness to treat, and costs of treatment, deferral may reveal information on each. This complexity affects the transparency of decision models complicating both analysis and interpretation of results. Such 'bushyness' has been reduced using state transition models, such as Markov modelling, to summarise uncertain variables. These models use transition probabilities to determine movements between disease states over consecutive time cycles. Although useful in simulating events that recur over time, and so potentially appropriate for considering deferral, Markov modelling is not commonly used for this purpose.

In Williams' hypothetical example the initial problem description is relatively simple with no uncertainty in demand or benefit to patients, and only four periods. Despite the simplifying assumptions there is sufficient complexity to prompt questions concerning what is learnt over time and the motivation for deferral. Answers are not apparent in Williams' work yet these are essential questions that must be understood and answered if deferral analysis is to provide useful conclusions. Through explicitly considering deferral and its interaction with uncertainty and irreversibility, real options analysis provokes answers to questions such as these. It is predominantly evolution of information on disease progression, the uncertainty surrounding treatment, and potential irreversibility of treatment side-effects that makes watchful waiting a viable treatment alternative.

Finally, existing methodology commonly models a current (static) perception of uncertainty defined by a probability distribution over outcomes. Real options analysis considers of how this perception changes during deferral. For instance, the mean of a distribution of interest, such as growth rate of an aneurysm may increase through time[21]. In terms of decision trees, uncertain events have a family of distributions; each member represents uncertainty in a given time period. Real options analysis thereby models a dynamic perception of uncertainty. Despite this apparent added complexity, real options analysis sits well within the decision tree framework. Immediate action is assessed according to standard techniques and summarised by expected net benefit. Deferral is assessed using real options analysis that estimates option value. The two valuations are compared and the action with greatest value is the preferred strategy.

4.4 Watchful waiting as an option on treatment

4.4.1 The real options problem

Deferring the decision to actively treat a patient is akin to an American call option; exercise can be deferred for some period of time and involves paying some 'cost' in return for a stream of benefits. Demonstrating the analogy between financial options and the option to treat requires consideration of the characteristics defining the two decision problems, and parameters necessary for valuation. Here we concentrate on the option to defer treatment for abdominal aortic aneurysms (AAA's).

Optimal treatment for patients presenting with AAA's involves surgical repair of those likely to rupture and shorten life expectancy, whilst avoiding unnecessary surgery in patients who would otherwise die of unrelated causes Katz (Katz et al., 1992). Currently, for aneurysms smaller than 5cm the risk of rupture is relatively low causing some debate about whether immediate elective repair is necessary (Katz and Cronenwett, 1994). This fuels arguments in favour of watchful waiting.

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[21] Basic real options models assume a constant variance, although changing variance may be incorporated using numerical methods.

Clinicians must decide on a treatment management strategy for presenting patients who can be treated immediately or be managed with watchful waiting (figure 4.2).

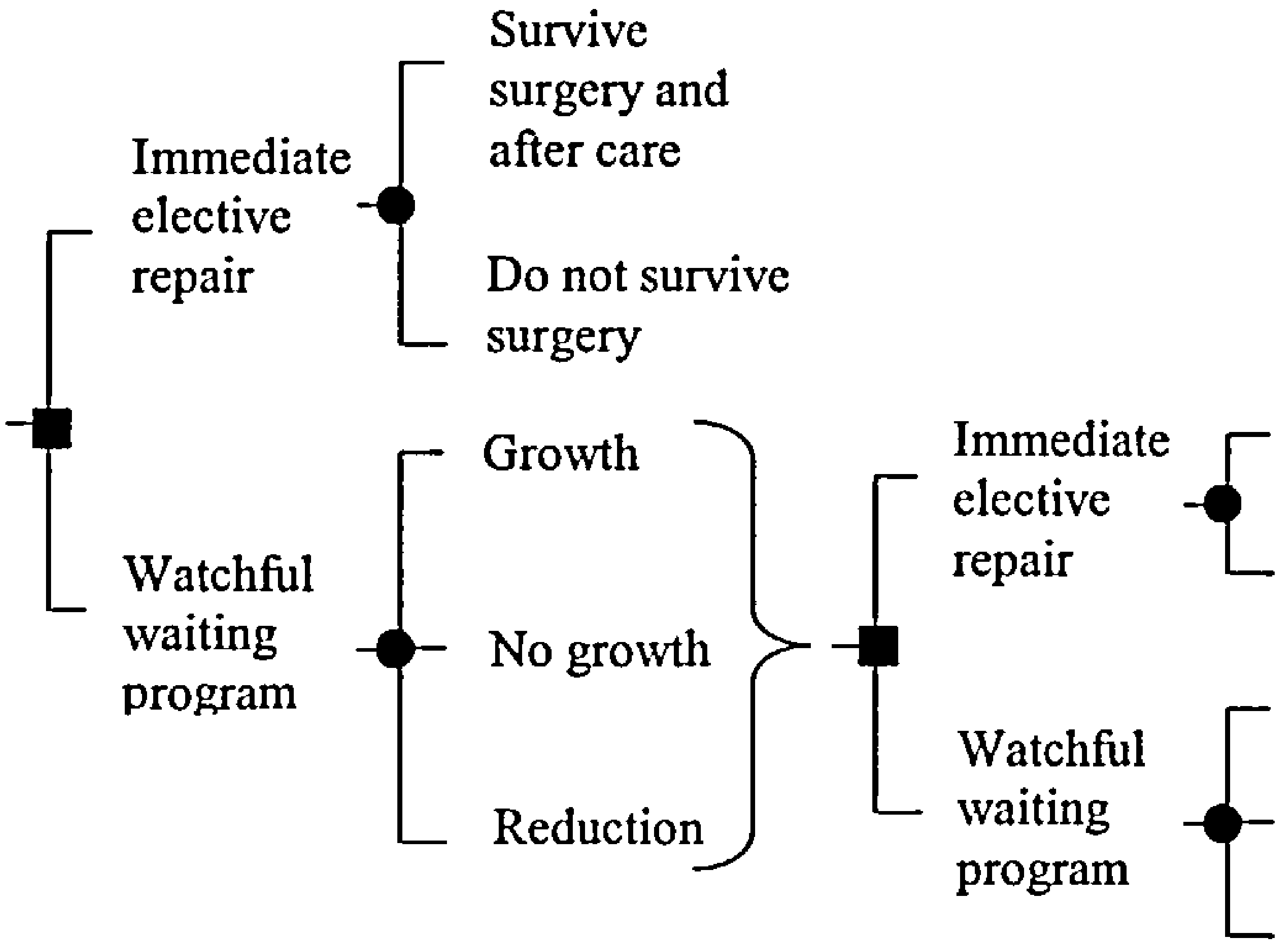

Figure 4.2. Management of a patient presenting with an abdominal aortic aneurysm.

To receive the benefits of deferred stock purchase decision-making bodies such as individuals or firms, must first purchase an option. Real options such as the option to defer treatment are rarely purchased on a market, instead they are usually conferred to patients and clinicians through previous actions. In the case of watchful waiting the treatment option may be conferred via early screening, which identifies potential problems before they become self-evident. Although the methods of obtaining financial and real options differ, once owned, the similarities become apparent (table 4.1).

	Financial option	**Real option to defer immediate treatment of abdominal aortic aneurysms**
Decision maker	Owner of option	Clinician in conjunction with patient and family
Source of option	Purchased	Conferred endogenously through previous investment in screening technology and surgical development, and exogenously via gradual disease progression and early presentation by individual
Dominant source of uncertainty	Stock price	Underlying disease progression; rate of growth in aneurysm
Information gained by deferral	Changes in stock price	Absolute growth / shrinkage, and rate of change
Source of irreversibility	Exercise price	Cost of surgical reparation, associated risks and their costs. Patient becoming unfit for surgery
Ability to defer	Limited by exercise date	Will vary between diseases and patients. Limited by aneurysm growth and factors rendering the patient unfit for surgery. Influenced by treatments available.

Table 4.1. Characteristics defining the option to defer treatment for abdominal aortic aneurysms.

A financial investor must decide on what date, prior to the option expiring, exercise is optimal. Waiting allows information gathering on stock price uncertainty but also defers the benefits of owning stock, such as capital appreciation and dividends. The clinician must decide when commencing surgical repair is optimal. Immediate action is more costly than deferral and brings risk of operative mortality (primarily cardiac risk). Uncertainty over aneurysm growth generates uncertainty over whether immediate surgery is always necessary. Waiting allows information gathering on severity of disease but defers potential benefits of immediate treatment including improved health status. Deferral may be cheaper, but is associated with risk of rupture and death both of which are positively related to aneurysm size and growth rate. Some patients may become medically unfit for surgery during a deferral period.

The three defining characteristics of financial options are present in the option to defer treatment. The ability to defer is inherent to the problem, and as with a financial option, is limited. The exercise date cannot, however, be agreed when the decision problem is first considered; the point at which an option to defer treatment no longer exists is stochastic, influenced by factors such as the growth rate of the aneurysm and the patient becoming unfit for surgery.

Financial and health care options both have sources of uncertainty. On deferring exercise of a financial option, the price of the underlying asset is observed. Real options usually have multiple sources of uncertainty. For watchful waiting, in addition to uncertainty over aneurysm growth, uncertainty may exist over a patient's ability to respond, fight back, and cope, in addition to unrelated health problems occurring. These sources of uncertainty combine to create a state of well-being that evolves over time. Clinicians observe information on disease progression and well-being each period. Disease specific measures such as growth rate of a tumour or aneurysm, and prostate specific antigen levels, or generic scales such as blood pressure, self-rated quality of life or expected remaining QALYs, may be used to measure well-being.

Despite knowing historical price variation, the random walk evolution of stock prices means that financiers can never predict future prices. Although this is true in essence for real options more emphasis is usually placed on historical observations as current and historic values are more likely to be predictors. With health care options, particularly deferred treatment, the passing of time increases available information upon which a decision to exercise is conditioned. A clinician may observe a relatively large aneurysm that would normally undergo immediate repair. Following a period of deferral, the absence of diameter growth may alter the clinician's recommendation. Observed rapid growth of a small aneurysm may likewise alter a prior opinion to defer treatment.

Financial options are irreversible in the sense that exercise involves paying the exercise price. Watchful waiting defers some treatment, usually surgery, which involves extensive sunk costs in the form of bed costs, surgeon and anaesthetist costs, and the cost of disposables. Immediate action also involves physical sources of irreversibility such as side effects of surgery. Deferral of treatment for localised prostate cancers for instance, defers the possible irreversible effects of impotence and incontinence, not to mention risk of infection, or worse; death. Deferring amputation likewise provides an example of irreversibility. Where the deferred treatment is medical rather than surgical commencing some drug regimes may create irreversibility due to withdrawal effects. Unlike the financial case deferral can involve irreversibilities for health care related options. When watchful waiting leads the patient to be come unfit for surgery, deferral has had irreversible effects.

While similarities between financial options and the option to defer treatment exist, applying option-pricing techniques to health care requires identifying variables that relate to the parameters used in financial formulae (table 4.2). The parameters actually used in an application will depend on the pricing method chosen but are closely related to those given.

Parameter	**Financial option**	**Real option to defer immediate treatment of abdominal aortic aneurysms**
Current value of source of uncertainty	Spot price (S)	Current estimated expected benefit from surgical repair
Estimate of uncertainty	Variance in stock value (σ^2)	Uncertainty surrounding expected benefit of surgical repair over time
Cost of exercising option	Exercise price (X)	Cost of surgical repair (anaesthetics, antiseptics, disposables, bed costs, surgeon costs). Will remain fairly constant over life of option
Date before which option must be exercised	Exercise date (T)	Date when aneurysm ruptures or patient becomes unfit for surgical repair
Cost associated with deferral	Dividend (δ)	Costs of tests used to gather information. Uncertainty, worry and pain for the patient

Table 4.2. Parameters used in financial option pricing techniques and their counterparts for the option to defer treatment for abdominal aortic aneurysms.

Stock price provides the source of uncertainty underlying the majority of financial options. Spot price and associated volatility give the relevant information for pricing formulae. Shares have value, prices, because they confer a future stream of benefits. Price therefore effectively represents the current value of these streams. The analogy in health care is the present value of a project that, once initiated, confers a stream of cash flows. For the option to defer treatment, the present benefit from surgical repair and associated volatility through time (as disease progresses) must be estimated.

The sunk cost of surgical repair represents the cost of exercising the treatment option, and the exercise date is found by estimating the date when the aneurysm will rupture or the patient will become otherwise unfit for surgery.

Dividends are paid to stockholders but are not received by holders of options. Deferring exercise of a call option delays receipt of dividends creating an implicit cost to deferral. Deferring exercise of a treatment option can involve more explicit costs; specifically the cost of observing patient information. Observing aneurysm progression involves detailed tests and scans such as ultrasound with significant costs. These costs are assumed absent in financial models where prices can be observed freely, but can be incorporated into option pricing as implicit dividends.

The similarities in structure between holding and exercising financial and health options and the ability to approximate financial variables suggests that health care decision problems such as the deferred treatment option are amenable to real options analysis. The following section considers a hypothetical numerical example.

4.4.2 Numerical example

Clinicians must choose management strategies for patients who present with an aneurysm and are suitable for either immediate elective repair or watchful waiting. The decision to beginning immediate treatment is conditional upon the clinicians information on aneurysm size and expected growth, and given by results from scans, and observations taken during deferral.

An aneurysm is assumed to be able to grow, remain constant, or reduce in size with the same probabilities and to the same extent during each deferral period. A patient who improves during the first period and deteriorates the following period faces the same outcome as if they remained unchanged for two consecutive periods. The patient is monitored at regular intervals, with ultrasound or computed tomography scanning used to supply information on aneurysm size and growth rate. Immediate surgical repair is carried out when the diameter of the aneurysm reaches some threshold size[22].

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[22] Katz 1994 uses 6 monthly observations and a treatment triggering threshold of 5cm.

A model based on real world data would estimate the health benefit of immediate surgery using knowledge of the current size and growth of the aneurysm, risk of rupture, risk of becoming unfit for surgery, and surgical risk. Monte Carlo simulation could be used to combine these sources of uncertainty into a measure of well-being, and convert well-being into net benefit using society's willingness to pay for a unit of health outcome (figure 4.3). Since the sources of uncertainty evolve, monetary benefit also evolves revealing information through time, just as a price variable. For the purposes of the example expected benefit is assumed to be $20,000.

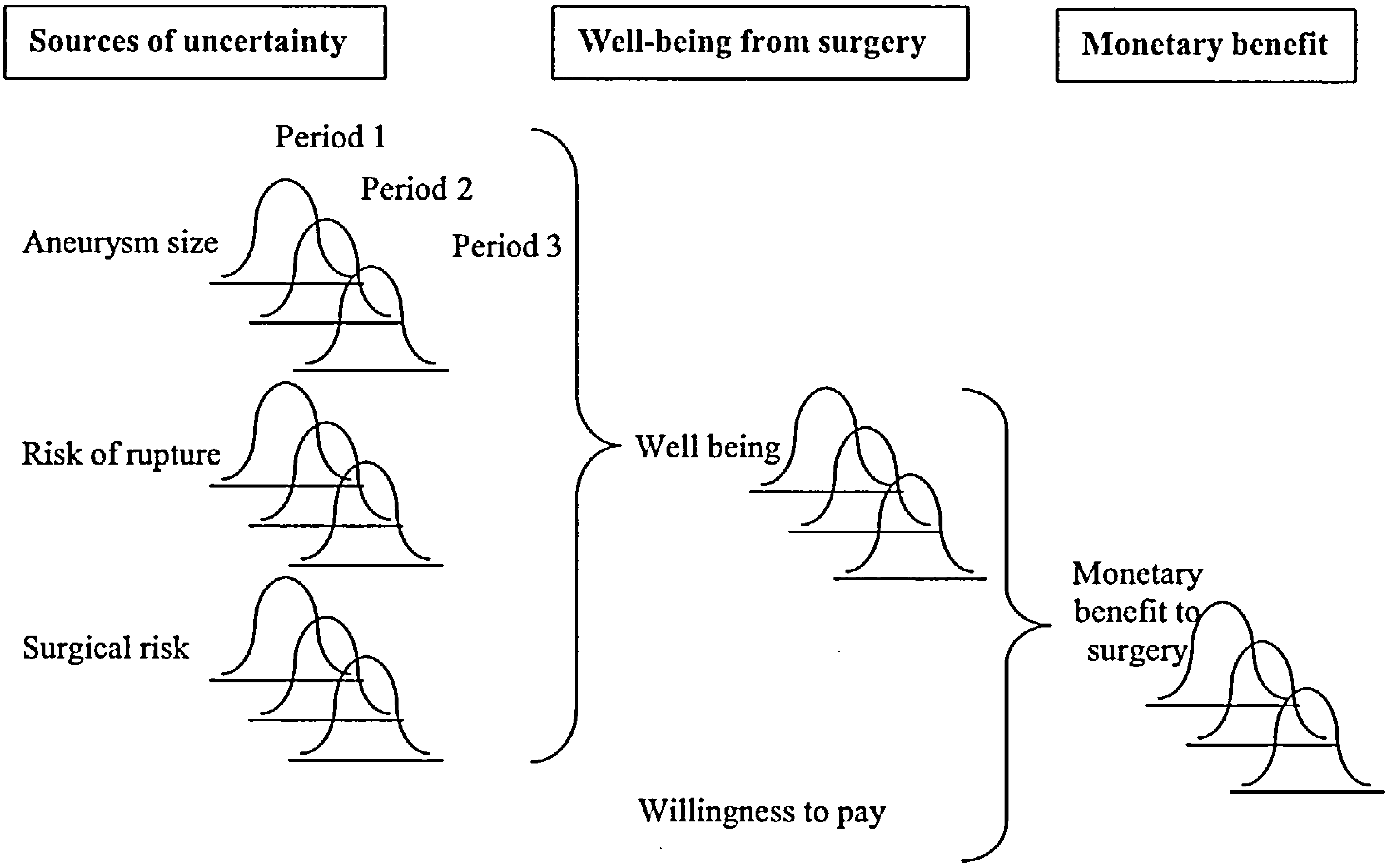

Figure 4.3. Combining sources of uncertainty to derive evolving net benefit from surgery.

Monetary benefit is assumed to follow a trinomial distribution dominated by the trinomial structure of aneurysm growth in each period. Joining trinomial periods in a repetitive, expanding manner creates a lattice representing progress of the patient over successive periods. As biomedical state is truly a continuous variable parameters are chosen to approximate a continuous time diffusion process. Following Trigeorgis (Trigeorgis, 1991) the total deferral period (T) is divided into N intervals of length dt such that T=N*dt. As dt tends to zero the trinomial converges to a continuous distribution. Trigeorgis demonstrated estimation of binomial state and time variables to guarantee stability of the discrete time approximation.

Immediate treatment is assumed to be deferrable for up to one year (T=1)[23]. The patient then becomes unfit for surgery and the option to treat expires. Observations are made on a monthly basis (N=12). The incremental cost of each monitoring session involving abdominal ultrasonography, above the cost associated with a physician visit, is assumed to be $261[24]. In contrast to the analogous stock dividend, this cost is assumed to be independent of evolving monetary benefits.

The current cost of elective AAA surgery including disposables, clinician time, and bed costs is assumed to be $24,020 (Katz and Cronenwett, 1994). Although currently not cost-effective (net benefit = $20,000-$24,020=-$4,020), net benefit fails to account for the option to treat at some point in the future, when treatment may have become cost-effective. Framing the problem as an option to defer treatment, $20,000 is the current estimate of the uncertain variable and $24,020 is the exercise price. An annual riskless discount rate of 6% is used. A volatility parameter dictates the evolutionary process of expected benefits from surgery. 25% volatility results in a trinomial structure with approximately a 0.25 probability of rising or falling by 10%, and 0.5 probability of remaining unchanged (figure 4.4).

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[23] In practice the length of the ability to defer is stochastic. The use of a constant is a simplifying assumption that facilitates analysis but does not affect the principle results.

[24] Cost estimates based on figures presented in Katz (Katz and Cronenwett, 1994).

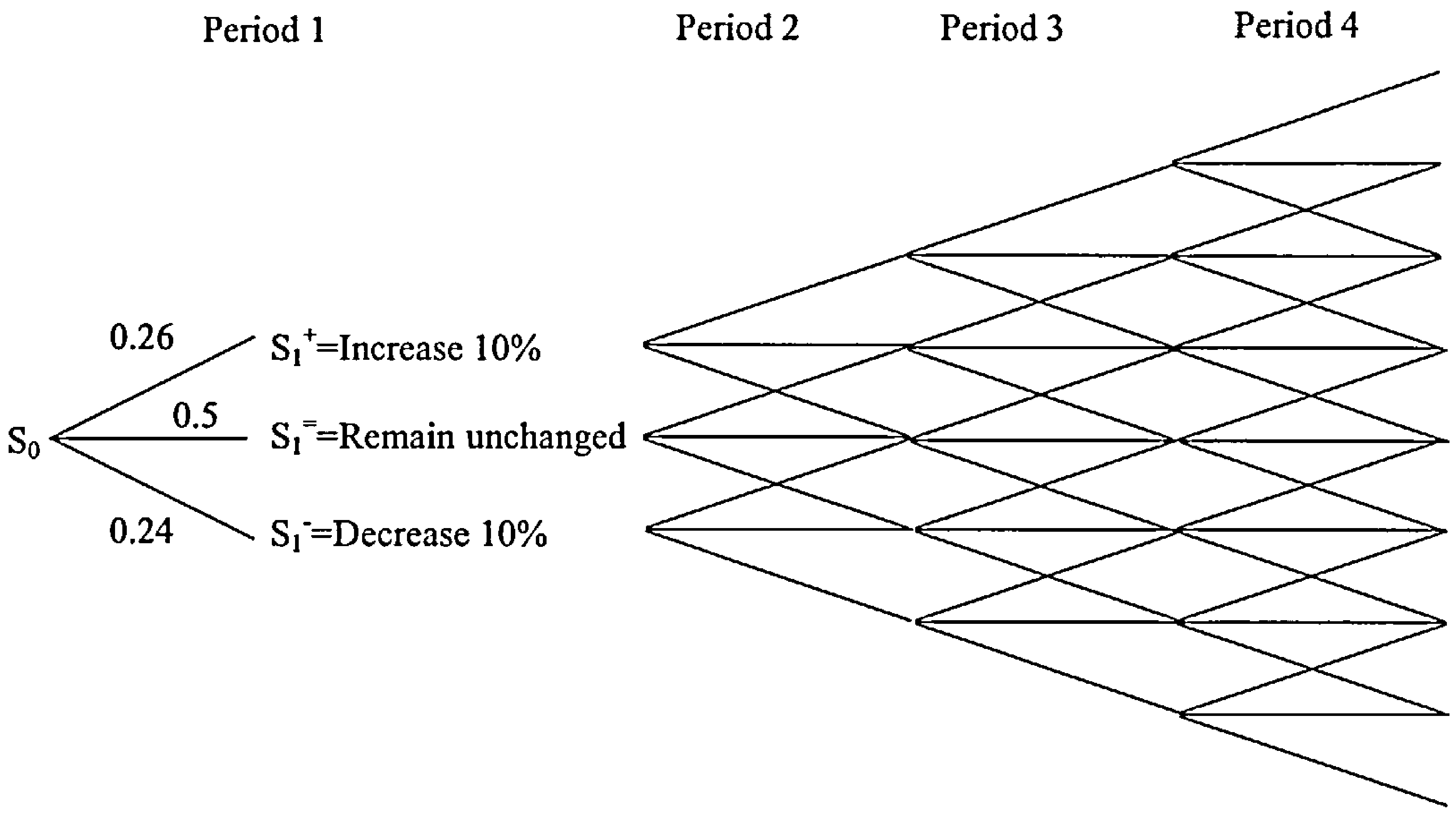

Figure 4.4. Recombining trinomial lattice showing the evolution of net benefit.

Fortran code (see appendix) based on an algorithm by Haug (Haug, 1998) and adjusted for observation costs is used to project monetary benefits through time until the exercise date. After each deferred month a decision node permits immediate treatment to commence. This allows exercise at any point up to one year from the time of initial deferral. Final period option values are calculated and backward induction applied to compare deferral with immediate action in the penultimate period and thus calculate option value for this period. The code moves recursively through the trinomial lattice, deriving option values for each period until the present is reached. Current option value is then compared to the expected benefit of immediate action.

4.4.3 Results

Given the base case parameter estimates (table 4.3) the current value of the option to defer immediate treatment is $954, despite negative net benefit (-$4020). If these estimates were true in practice for an individual, deferral would be the appropriate strategy. In practice a patient with negative net benefit would be assigned to a watchful waiting regime rather than 'rejected' outright (as with a proposed investment project). Negative net benefit would therefore confirm the conclusion that immediate action is not appropriate.

Parameter	Base case value
Time to expiration (in years) (T)	1
Number of periods (N)	12
Riskless rate (r)	0.06
Current expected benefit (S)	$20,000
Treatment cost (X)	$24,020
Volatility parameter (V)	25%
Observation cost (F)	$261

Table 4.3. Base case parameters for the option to defer treatment for abdominal aortic aneurysms.

Expected benefit from immediate action differs over time for a given individual, and between individuals. Table 4.4 gives option value and net benefit for a plausible range of expected benefits. Examining the range permits direct comparison of the decision rules resulting from the two methodologies.

Expected Benefit	Option Value	Net Benefit
15,000	75.37	-9020
16,000	143.6	-8020
17,000	269.18	-7020
18,000	418.06	-6020
19,000	674.79	-5020
20,000	954.22	-4020
21,000	1358.31	-3020
22,000	1770.42	-2020
23,000	2336.08	-1020
24,000	2901.75	-20
25,000	3575.83	980
26,000	4292.29	1980
27,000	5025	2980
28,000	5861	3980
29,000	6698	4980
30,000	7557	5980
31,000	8474	6980
32,000	9392	7980

Table 4.4. Option value and net benefit for a range of expected benefits for the option to defer treatment for abdominal aortic aneurysms.

Net benefit analysis presents a dichotomous decision rule to accept or reject immediate treatment, identified by the level of benefits where net benefit equals zero. In this case patients with monetary benefit in excess of $24,020 receive immediate treatment. Those patients, failing to meet this criterion either join a watchful waiting program or receive no further attention, though no distinction is made[25], and no optimal deferral time is suggested. Two patients with little clinical difference where one just meets the criterion and the other falls slightly below can receive opposing management strategies. Real options analysis presents a trichotomous decision structure: immediate action, watchful waiting or no action. Patients on the borderline are still managed differently but their strategies are likely to be more compatible.

The contrasting decision structures mean there are four regions of possible conflict or agreement, over the range of expected benefits, between real options and net benefit decision making (figure 4.5); Below expected benefit of $17,000 (region 1) both techniques reject immediate treatment. Real options denies admission to a watchful waiting because the option to wait is worth so little, and net benefit analysis does not distinguish those on deferral and those refused further treatment. Between $17,000 and $24,020 (region 2) option value exceeds zero supporting deferral. While net benefit rejects immediate treatment there is no formal criterion to recommend the waiting program. After $24,020 (region3) net benefit becomes positive recommending immediate treatment whilst option valuation conservatively continues to support deferral. Finally above $28,500 (region 4), when the marginal benefit from the two outcome measures becomes equal, both methodologies advise immediate treatment.

The regions of most interest are those where real options analysis potentially alters the preferred treatment strategy. In regions 1 and 2 options analysis differentiates patients who would benefit from deferral and those for whom deferral holds no long-term benefit. Traditional techniques, with their dichotomous decision structure cannot make this distinction. This causes potential differences in the way patients are treated. A patient placed on a waiting scheme by traditional decision-making might be more cost-effectively managed with no further treatment (or observation) if the benefit to surgical repair in the future is very small.

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[25] If the analysis concerned a treatment decision in which deferral is not routinely considered or waiting programs are not in place the patient would receive no further treatment.

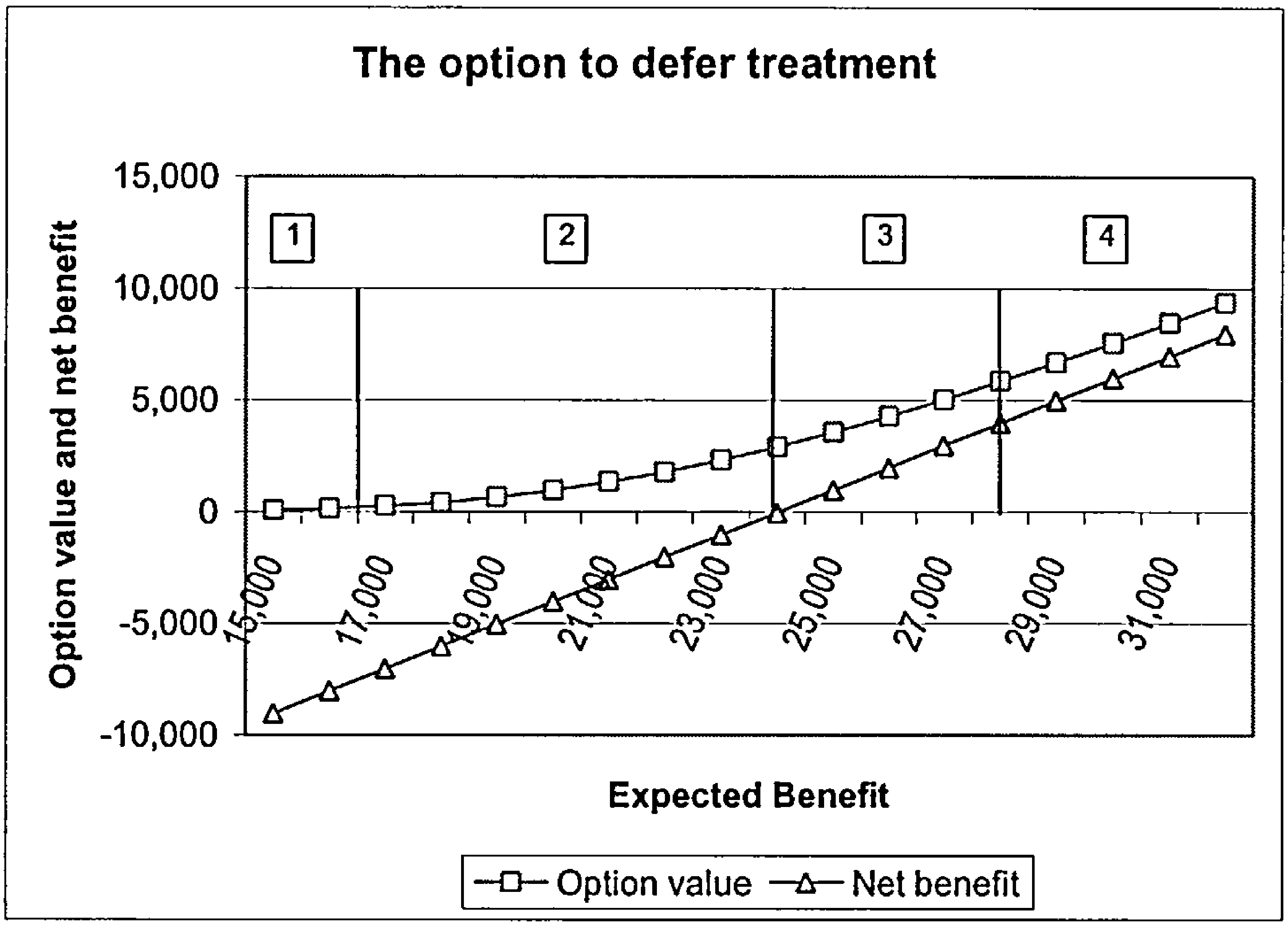

Figure 4.5. Graphical representation of option value and net benefit for a range of expected benefits for the option to defer treatment for abdominal aortic aneurysms.

Patients falling into region 3 would receive immediate surgery according to net benefit but enter deferral if option value is used. If some of these patients progress to no longer need repair, the patients themselves are spared unnecessary surgery, and fewer people await surgery in the long run reducing pressure on waiting list. For these conclusions to hold, clinical measures must be able to accurately describe patients in terms of their benefit from immediate treatment and the way this variable evolves through time. This ensures only suitable patients undergo watchful waiting. In addition the period of time between watchful waiting ending and actually receiving treatment must be short. If this is not the case, the option to treat may expire whilst the patient queues for immediate treatment.

Changes in parameter values affect option value and the desirability of deferral (table 4.5). Bivariate sensitivity analysis is used to explore the impact of T and N since a longer time to expiration is usually associated with more observational periods. N is increased in-line with T to keep the deferral period (dt) at one month[26]. As the time to expiration increases from six months (T=0.5, N=6) to two and a half years (T=2.5, N=30) option value increases for a given level of monetary benefits. A longer time to expiration allows expected benefits to evolve for an extended period, permitting self-healing or deterioration to become more pronounced over the life of the option. The positively skewed payoff structure of options prevents poorer payoffs being realised (choosing not to treat patients in which self-healing occurs) and the positive payoffs (from treating very ill patients) increase option value.

Timing between stages of a disease is crucial if watchful waiting is to be considered a relevant treatment alternative. When diseases progress quickly patients remain suitable for watchful waiting for a very short period of time. Observations must be frequent to detect the optimal timing of treatment prior to the option becoming unavailable. Diseases with slower progression make more suitable watchful waiting candidates since observations can be less frequent, without risk of losing the option. Exploring different times to expiration for a given patient, to find the expiration date at which immediate action becomes optimal, can give an indication of the optimal deferral period. For instance, if the expected time to expiration is two years, and analysis for 6 months suggests deferral is optimal but analysis for one year recommends immediate action, then a clinician can reasonably comfortably defer treatment for 7/8 months. Perhaps in the early periods observation can even occur less frequently.

Time to expiration (years)	Number of time periods	Option value	Discount rate	Option value	Volatility	Option value
0.5	6	333.5	0.02	748.7	0.1	76.8
1	**12**	**954.2**	0.04	847.1	0.15	305.1
1.5	18	1566.8	**0.06**	**954.2**	0.2	625.3
2	24	2151.8	0.08	1070.3	**0.25**	**954.2**
2.5	30	2709.4	0.1	1195.6	0.3	1353.8

Table 4.5. Sensitivity analysis for the option to defer treatment for abdominal aortic aneurysms. Base case values displayed in **bold.**

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[26] Changing N or T alone influences the degree to which the model approximates the continuous evolutionary process.

Univariate analysis is used to assess the effect of the discount rate and volatility. The costs involved in surgery are incurred at some point in the future. The discount rate therefore has a positive impact on current option value.

Volatility has a positive impact for reasons similar to the time to expiration; greater volatility allows more extreme movements in monetary benefit of which the positively skewed valuation system takes advantage. Figure 4.6 shows the impact on option value of increasing volatility from 15% to 25%. Altering volatility in this way causes the upward and downward movements in monetary benefit each period to increase from 6% to 10%, and causes the whole option valuation curve to shift vertically.

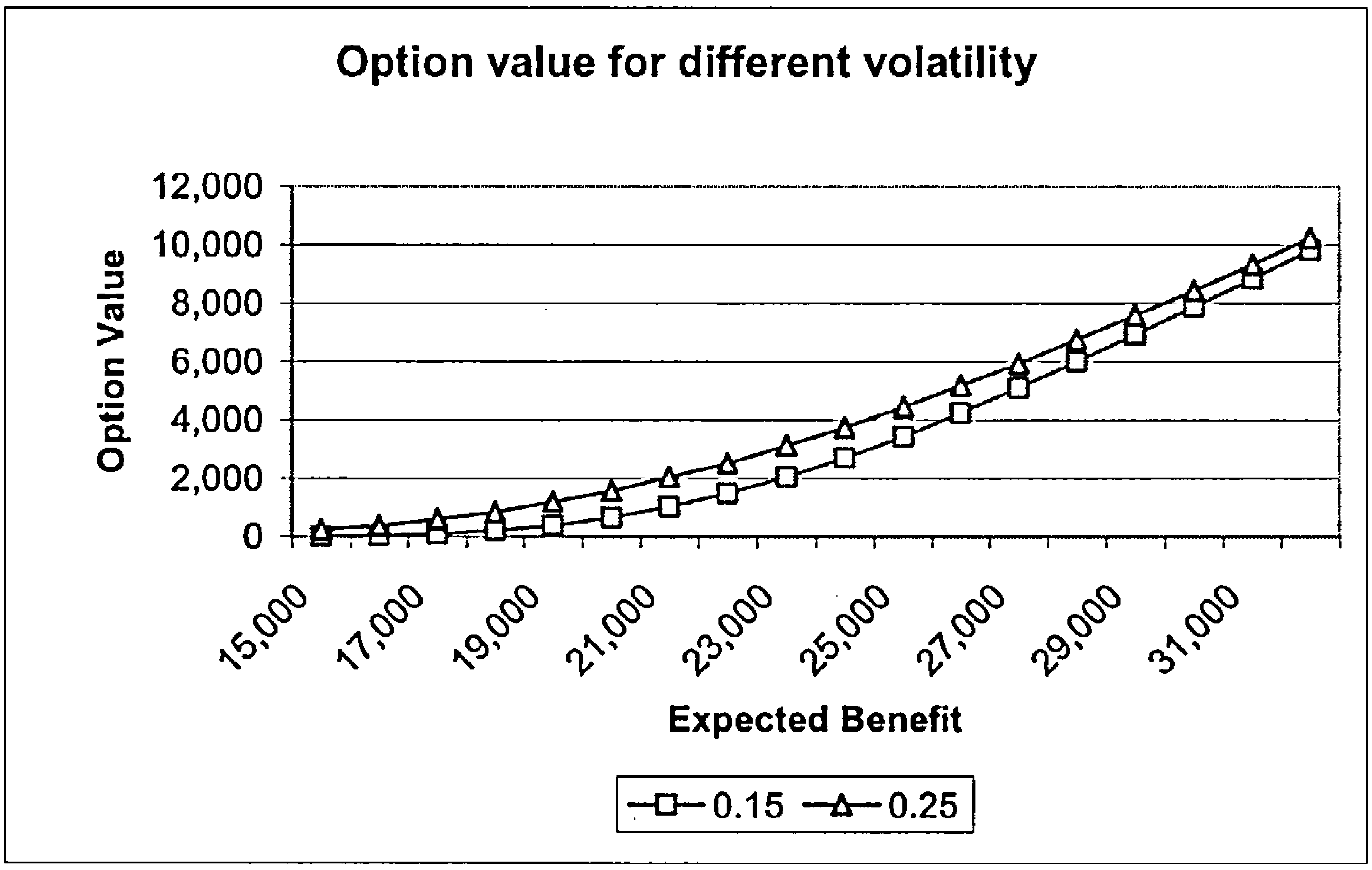

Figure 4.6. Effect of volatility on option value for a range of expected benefits for the option to defer treatment for abdominal aortic aneurysms.

Superimposing net benefit would indicate that regions 2 and 3 (optimal deferral, formal watchful waiting scheme, according to real options analysis) together account for a greater range of monetary benefits. The point at which option value exceed zero occurs at a lower monetary benefit and the point at which deferral is suspended in favour of immediate treatment occurs at a greater monetary benefit. Potentially more patients therefore face the possibility of altered management strategies as a result of using option valuation. This has implications for the length of waiting lists for treatment, and the numbers of patients recommended for watchful waiting.

The responses to model parameters described here are consistent with predictions based on behaviour in financial models.

4.5 Conclusions

Wong et al's study of watchful waiting versus immediate therapy for mild chronic hepatitis C uses standard techniques to calculate cost per QALY and concludes that watchful waiting is not optimal. Incorporating the option value of deferral may lead to waiting being cost-effective in some cases where it is not currently. Failing to accurately account for option value may result in sub-optimal treatment decisions. This chapter has attempted to correct this potential deficiency by applying real options analysis to an area where deferral is already considered a relevant treatment alternative.

The similarity between financial options and the option to defer treatment are apparent at an intuitive level; uncertainty, irreversibility and the ability to defer characterise both forms of option. This chapter has shown how the real options model can also incorporate factors specific to the watchful waiting decision. For instance the speed of disease progression enters through changes in the volatility parameter, the costs of aggressive therapy are stated explicitly in the exercise price, and observation costs incurred during the waiting period are considered as an implicit dividend.

Within this application, some challenges to the analogy were encountered. Initially, simple financial options have a single source of uncertainty. The value of the option to defer treatment is influenced by disease progression, currently available treatments, risk of rupture and surgical risk. Closer examination of financial markets reveals options written on more than one asset suggesting that multiple sources of uncertainty are not so uncommon[27]. The use of Monte Carlo simulation that is increasingly used within health care evaluations means this problem is more apparent than real. The simulations allow sources of uncertainty to be combined as inputs into a single output whose uncertainty underlies the payoff of the option.

A further strain to the analogy is the ability of the exercise price, surgery costs, to vary. Financial option contracts clearly state terms of exercise including the predetermined exercise price. Although surgical costs are not likely to be highly volatile they are unlikely to remain constant over a prolonged period. This issue has been addressed by Trigeorgis (Trigeorgis, 1999) who finds closed form solutions for options with stochastic exercise prices following continuous diffusion processes. The trinomial technique employed here can be altered to account for treatment costs varying over time. This would involve assigning an evolving distribution akin to that for expected benefit. The complexity of the model would be greatly increased.

Data collection issues pose a problem to the application of real options analysis in practice. Currently data on disease progression, particularly aneurysm growth, is collected with a static perspective so net benefit estimates supply information on cost-effectiveness for the current period and do not take a dynamic view of uncertain parameters. In explicitly recognising uncertainty, irreversibility and the ability to defer, real options analysis asks about their precise influences on the decision. This requires a projection of uncertainty into the future that in turn requires regular, periodic measurements of uncertain variables today. Clinical trials monitor data periodically but intervals tend to be uneven, extending as the trial progresses (eg. 1 month, 3 month, 6 month observation points). Ideally adoption of real options methodology requires existing practice be altered to meet these data requirements[28]. Some authors, for instance Capozza (Capozza and Li, 2001) have tested theoretical models with empirical data, this would also be required for the true applicability of real options analysis to be ascertained.

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[27] Such option have been called Rainbow options in the real options literature (Copeland and Antikarov, 2001).

[28] Few applications of real options theory progress to empirical analysis predominantly because of data requirements.

Here a trinomial option pricing approach has been used to value the watchful waiting alternative. Choice of valuation technique can be important in determining the extent to which a model represents the decision problem of interest. Although advances continually arise in financial option pricing there can be some delay in making techniques suitable for real options analysis. Many option pricing techniques involve complex differential equations with no closed-form solutions, making the use of numerical techniques and programming inevitable. This can potentially lead to problems for the transparency of analyses and generates a trade off between simplifying the real option to suit basic valuation techniques and accepting detailed financial valuations that strain the analogy. As a result there are few real options applications that use empirical data and detailed valuation techniques to assess prominent decisions. Multinomial methods have proven popular because they represent a compromise between technical accuracy and transparency.

The multi-nomial methods presented here might be used to address several decision problems within health care. Any decision that can potentially be deferred, whether treatment of an individual, developing and releasing a new pharmaceutical, or considering a society wide initiative to promote a vaccination programme, can theoretically be analysed using real options theory. The versatility of the multi-nomial structure, incorporating many time periods and the ability to manipulate the probability and extent of upward and downward movements in uncertain variables, means this type of model can support a wide variety of applications.

The aim of this exploratory study was to attempt to establish a methodological and conceptual justification for the use of real options analysis within an area of health care where deferral is already considered relevant. This chapter has used standard techniques to demonstrate that real options analysis may be applied to health care decision making, and to fail to do so may introduce bias into evaluations where deferral is potentially viable. Future applications of real options analysis to deferred treatment may demonstrate that watchful waiting is beneficial in areas where consensus views waiting as detrimental, or where watchful waiting has previously not been considered. In particular the period of deferral between regular screening sessions such as with cervical smear, and the optimal timing of release from hospital to care in the community might be analysed.

Chapter 5. The option to preserve life for patients in a coma

5.1 Introduction

Initiating life support for comatose patients creates an option to defer removal of that support akin to an American put option. This confers the chance of later recovery. Exercising the option and withdrawing life support technology eliminates future treatment possibilities and the patient's opportunity to regain consciousness. The current option has implications for later available options and decisions. Option valuation provides a framework to evaluate options available to decision makers at a given point and their impact for future decision making.

Rosenhead (Rosenhead, 1992) has highlighted the importance of strategically managing options, emphasising the use of robustness analysis to examine beneficial and detrimental opportunities. Amram and Kulatilaka (Amram and Kulatilaka, 1999) refer to the 'discipline' of real options when discussing the relationship between the set of options currently available and those available, or potentially available, in the future. For instance, a pharmaceutical company researching treatments for cancer creates options to produce and market successful compounds. This in turn generates an option to expand or contract production depending on revealed market conditions.

While health care evaluations report expected economic return as a measure of desirability, evaluating cost and benefits for the purpose of creating and destroying options is not usually considered. This chapter applies real options theory to the option to remove life support, an area where deferral, an important source of maintaining options, is not explicitly considered. The ability to alter and manipulate future option sets is shown to be an important source of value. Section 2 considers creation and destruction of options in health care, drawing on examples from throughout the sector and narrowing to focus on the option to defer removal of support. Section 3 reviews the financial put option and the real options theory equivalent; the abandonment option. Section 4 models removal of life support as a perpetual abandonment option. A hypothetical example is presented. Section 5 concludes.

5.2 Creating and destroying options in health care

At any point in time a decision maker has a number of choices. For instance, a National Health Service manager must choose how much of a budget to allocate to each speciality, an intensive care team must decide whether to dedicate equipment to an existing or new patient. Such option sets might be significantly affected by current actions. For instance if 75% of a spending budget is consumed within the first 3 months of the financial year then severe limitations are imposed for the remaining months. Initial spending has reduced the available options set.

Research and development efforts provide clear examples of creating future options in health care. Clinical trials and cost-effectiveness analyses may demonstrate that a new treatment is equally effective as current therapies, increasing the number of treatments available for a given ailment. Development of new technologies and extending use of existing technologies enables detection of new disease areas and better understanding of, and treatments for, known disease areas. Incurring costs to improve knowledge and understanding today unlocks options available for treating illnesses in future. This mirrors the way purchase of an option today confers the choice to defer exercise tomorrow.

Some ventures have a less evident impact on options. Early investment in pioneer technologies brings the option to upgrade cheaply and adapt more quickly as newer and better versions emerge, or switch to similar technologies once staff receive initial training (Grenadier and Weiss, 1977; Moretto, 1996b). Previous research and experience in new surgical techniques gradually enables patients to choose between invasive and less invasive modes of treatment such as medical or surgical management; kidney dialysis or kidney transplant. These choices have only developed through sequential decisions taken within the health care industry that have periodically extended available options.

Whilst these are examples of option creation, the same events can often be the source of destroying options. Investments requiring upfront expenditure prevent funds being allocated elsewhere, reducing the options available. Consumption of one drug may preclude use of another, such as treatments for aids. The decision to amputate a limb may limit the life choices available to a patient. Since acting now destroys options, deferring action is an important way to maintain options. For instance, deferring purchase of a technology preserves the option to do so later and perhaps confers an option to invest in a newer. improved model.

Consider the option to defer removal of life support. Coma may arise following a variety of insults to the brain. Physical injury, nutritional deficiency, poisoning, stroke and the effects of degenerative diseases may all result in cognitive loss. In this state the body retains only the ability to perform vegetative functions and cannot survive without sufficient nutritional and bodily support. With help such as simple feeding, nutrition, bathing, ventilation and circulatory assistance (Singer and Grant, 1999) patients may live for months or years (Council on Scientific affairs and council on Ethical and judicial affairs, 1990). For some patients the only semblance of life may be sleep-awake cycles, for others, sporadic responses to internal and external stimulus may occur and manifest themselves in displays of emotion, such as smiling and crying.

Despite current cognitive loss there is a possibility that after some uncertain period of time the patient will spontaneously improve sufficiently to regain consciousness and some degree of normal life. Practice has revealed however, that patients may remain severely disabled and enjoy only a low quality of life. In some cases, given the limited prognosis (The Multi-Society Task Force on PVS, 1994) of the patient and continuing high resource costs, (Kaufman and Lipton, 1992) decision makers may choose to terminate life support and allow the patient to die. The ethical issues inherent in end-of-life decision making contribute to the debate over whether and when to withdraw treatment (Meisel et al., 1999).

Incurring the financial expense necessary to initiate life support is analogous to purchasing a perpetual option to defer removal of support, and preserve life until the option is exercised. The option is purchased if the expected value of ownership exceeds the price, which in this case includes the costs of introducing the patient to the intensive care unit, linking them to support technology and associated nursing care. Once bought, the option to remove care can be deferred almost indefinitely. Exercising the option and ending treatment destroys the option to recover removing all the patient's future lifetime options, and destroys the option to remove support at a later date should the patient fail to improve. Deferring removal preserves the option to withdraw life-sustaining technologies prolonging the patient's opportunity to spontaneously recover.

Conventional decision theory would, in principle, calculate cost-effectiveness of treatment withdrawal using expected discounted cost and benefits (Chalfin et al., 1995). The benefits to withdrawing treatment are resource savings, and the costs are potential Quality Adjusted Life Years (QALYs) forgone. Previous economic analyses in this area, however, have concentrated primarily on cost (Sailly, 1994). In addition, existing analyses consider the attractiveness of an immediate, now or never, action. To the author's knowledge the ability to wait before removing life support, the information potentially conferred, and the option preserved have not been explicitly addressed.

An initial examination of the withdrawal decision suggests there are similarities with an American put. Option pricing techniques that value the option to defer removing support and associated maintenance, rather than destruction, of future options, may help in understanding and analysing this decision problem. Since deferral is a relevant alternative for intensive care patients, particularly when information about recovery is lacking, (Council on Scientific affairs and council on Ethical and judicial affairs, 1990) option analysis seems an especially relevant valuation tool.

5.3 Real option theories of abandonment

Whilst an option to defer immediate treatment delays initiating a project with uncertain future outcomes, the option to defer removal of life support brings an end to an ongoing project. Removing life support efforts takes an active project and terminates the uncertain benefit flows, periodic QALYs gained and discounted future potential QALYs, in favour of an inactive status; allowing the patient to die. Real options analysis refers to the termination of active projects, which are analogous to put options, as abandonment options. This section reviews the financial and real theories relevant to pricing the option to remove life support.

Put options are options to sell, rising in value as stock price falls. Exercise occurs when current market stock price falls below the contracted exercise price, and a payoff equal to the difference between the two is received, making intrinsic value a mirror image of the equivalent call option. Akin to call options, by allowing the holder to exercise only when stock price falls, the option provides protection from losses. Even when an option is not currently profitable, knowledge of the volatile price evolution process reassures investors that profits may be made at some future date. While the option is still held there exist choices and a chance to benefit from price falls that no longer exists once the option is exercised. For these reasons the put option has value in excess of intrinsic value, making the option valuable to the holder even when intrinsic value is zero (figure 5.1).

A put option must be bought on a market. Abandonment options exist only once an investment has been made; a project is initiated by incurring set up costs that act as the purchase price of the option. While the put option is held, the owner is entitled to a stream of dividend benefits associated with stock ownership. The owner of a real project realises a stream of payoffs that last only as long as the project is in operation. Options convey a right with no associated obligation, and in tune with this, the owner of the investment programme has the right to abandon his investment should the payoffs prove less than desirable.

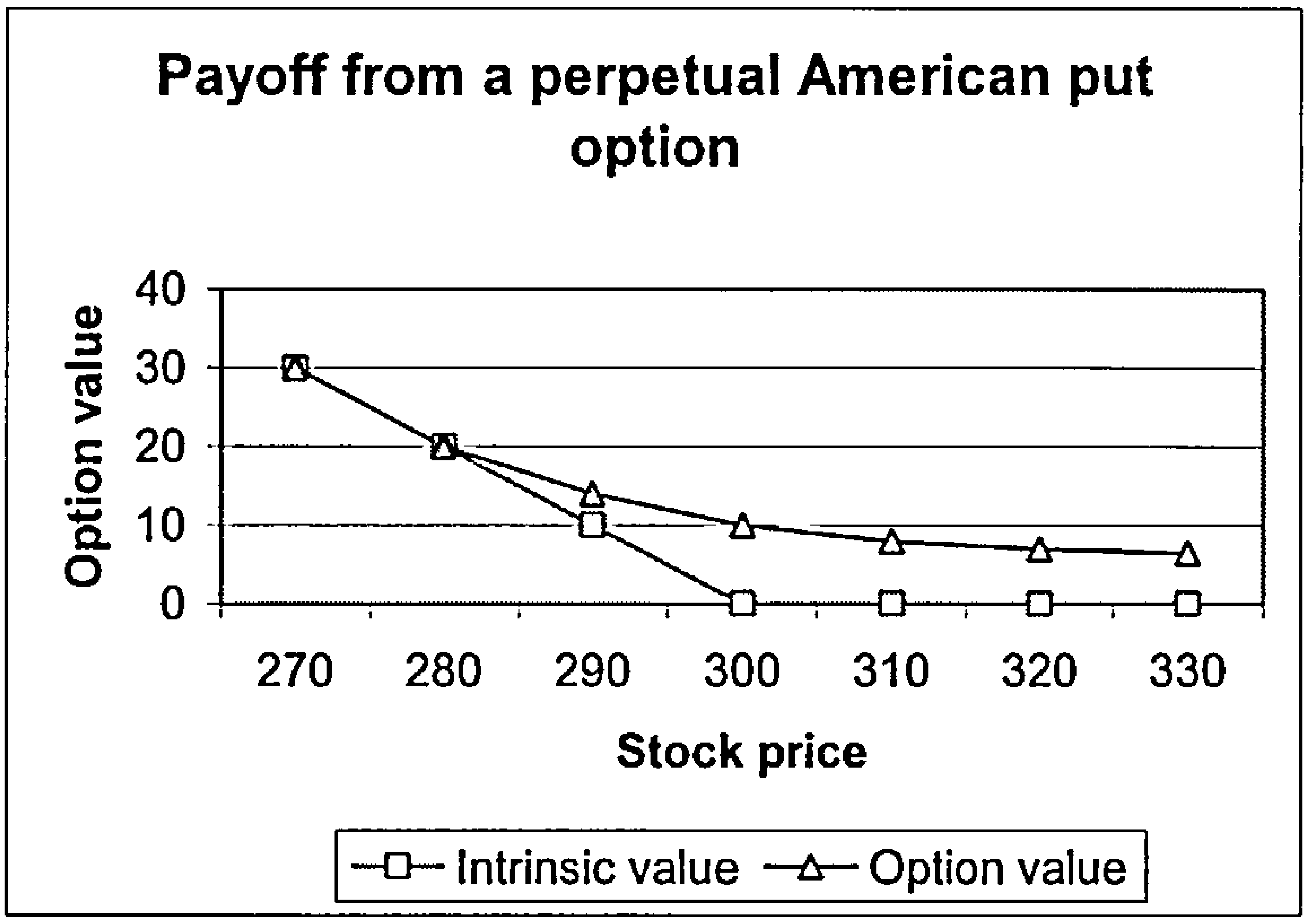

Figure 5.1. Intrinsic value and option value for a perpetual American put option with exercise price £300.

On exercise the put owner receives a single payoff (exercise price) and stops receiving both capital gains and dividends. When profits fall below some threshold level, exercise of the option to terminate the project occurs. Abandonment involves sale of assets in return for a single lump sum payoff (scrap or abandonment value) and an end to the stream of payoffs associated with ownership. Losses are then limited to any fixed costs associated with abandoning the project creating a kinked payoff structure akin to intrinsic value.

Numerous authors have recognised the similarities between put options and abandonment of real projects. McDonanld and Siegel (McDonald and Seigel, 1985) provide one of the earliest attempts to value firms with an option to shut down, examining the impact of variable output price on the value of the option. More recently Berger (Berger et al., 1996) considered valuation of generic abandonment options and Alvarez (Alvarez, 1999) analysed optimal exit of firms facing demand uncertainty. In this study exit is recommended only when the value of future productive options is less than the value of irreversibly exercising the exit option. Alvarez notes that this may lead to continued production when net cash flows are negative. At a micro level Moretto (Moretto, 1996a) examines individuals' car scrapping decisions illustrating how irreversibility and uncertainty combine to lengthen the period of ownership, increasing deferral.

The majority of abandonment option applications either value a firm currently possessing abandonment options, or consider a micro level decision of whether or not to abandon a single project. The latter category usually attempts to identify some abandonment threshold beyond which the project should be terminated. For instance Conrad (Conrad, 1997b) identifies the cut wood price threshold beyond which an old-growth forest, currently used for amenity value, should be abandoned and the resulting wood sold off. Similarly Myers and Majd (Myers and Majd, 1990) determine option values and optimal abandonment schedules for generic projects. These authors also explore the impact of deterministic and stochastic scrap values. This seems an appropriate stance from which to investigate the option to defer removal of life support technology.

5.4 The option to defer removal of life support

5.4.1 The real options problem

Initiation and termination of life support technology respectively create and destroy the option to preserve life. Termination of support may become a viable choice if the possibility of the patient regaining consciousness is very small or if severe disability would result. The decision to abandon life support efforts may be made immediately or deferred (figure 5.2). Immediate removal of support efforts kills the option to remove support at a later date should the patient fail to improve. Deferral maintains this option. Comparing the values associated with each of the two decisions therefore identifies the incremental value of deferral (option premium), and so the value associated with owning and maintaining the current option.

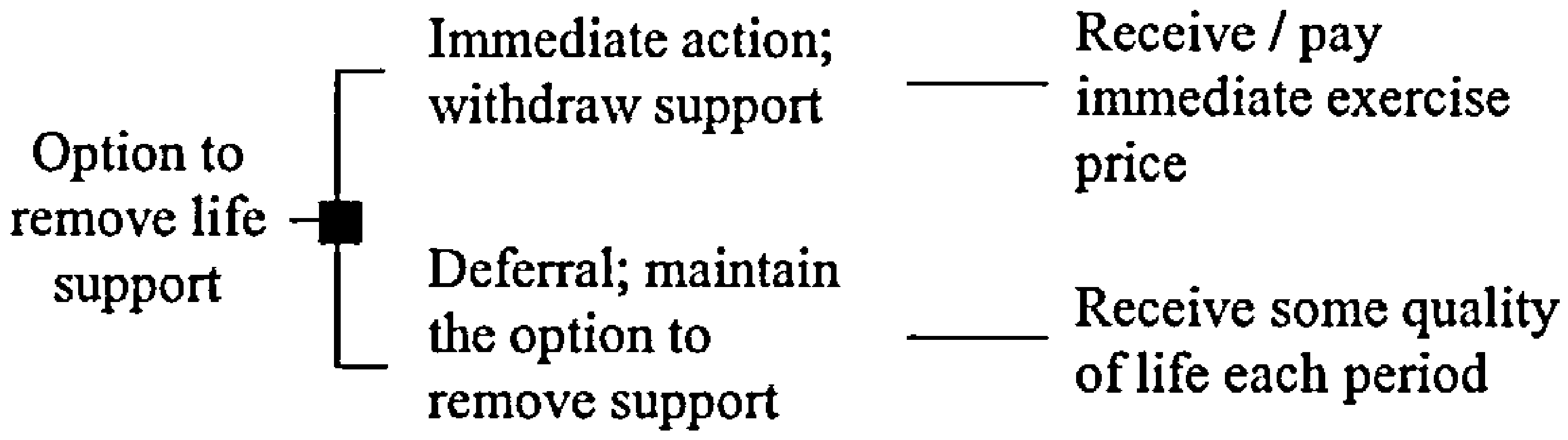

Figure 5.2. The option to defer removal of life support

As with the option to defer immediate treatment, for the application of real options analysis to be justified in practice, the characteristics of the option to remove support must identify with the characteristics of the put option (table 5.1). In this unusual instance the option owner, the decision maker, is not the party directly affected by the source of uncertainty, the patient. The decision to exercise is taken by the intensive care unit doctor in discussion with the patient's family, and in the interests of the unconscious patient.

	Financial option	**Real option to defer removal of life support**
Decision maker	Owner of option	Clinician in conjunction with patient's relations
Source of option	Purchased	Conferred through the starting and continuing life support
Dominant source of uncertainty	Stock price	Underlying biomedical state of the patient
Information gained through deferral	Changes in stock price	Individual level information on well-being, rate of change
Source of irreversibility	Exercise price	Death of patient, costs involved in termination of support
Ability to defer	Limited by exercise date	Limited only by the patient naturally dying or regaining consciousness

Table 5.1. Characteristics defining the option to defer removal of life support.

Having been conferred through starting life support the value of the removal option depends on sources of uncertainty that evolve whilst exercise is deferred. The dominant source of uncertainty is the vegetative patient's well-being measured by their biomedical state and converted into QALYs. Deferring removal provides QALY benefits for the patient whilst still unconscious (dividend type payouts) as well as potential future QALYs in the event of recovery. These are transformed to monetary benefits using an estimate of society's willingness to pay for a unit of health outcome, for input into a real options model.

Further sources of uncertainty include: relatives gaining some non-monetary rewards while removal of support is deferred (although an element of certainty and perhaps relief may also be gained when immediate action is pursued); the lack of clarity concerning predictions of recovery and, in the face of recovery, quality of life regained; disagreement between health care professionals as to whether a patient is emerging from a vegetative state due to lack of tests to detect patient inner awareness (Hollerback et al., 1995); the emergence of technological advances that may induce improvement; and the value from transplanted organs.

Whilst all these factors are relevant, to focus on the structure of the decision, elements of uncertainty about recovery and the value of organ transplantation form the core of the analysis. This enables a stylised example to be created that resembles the financial put option whilst maintaining sufficient simplicity to allow transparent interpretation of the model. The evolution of a composite variable defines the uncertainty underlying the decision problem. With this in mind information is gained each period about the patient's continuously drifting biomedical state and associated possibility for future recovery. This information may be measured using the Glasgow Coma Score (GCS), and would need to be converted into monetary terms. The data would then feed into the final exercise decision.

Irreversibility is particularly prominent in this example, not only are costs incurred in the event of removing support but ultimately once supporting machines and care are removed, and loss of life confirmed, a life is lost. Dixit and Pindyck (Dixit and Pindyck, 1994) suggest that an abandonment option is "realistic if a live project has some tangible or intangible capital that disappears quickly if a project in not kept in operation." This is particularly true of a patient's life lost when preservation efforts are discontinued.

Finally, deferral is inherent in the decision to remove support. Deferral maintains the option for later abandonment whilst allowing continued monitoring and reassessment. In practice life support is often continued for many months and sometimes even years. Although discussion of the *option to initiate* life support may seem attractive, the inability to defer this decision makes a real options approach inappropriate. The option to invest in life saving technology as a way to create options to treat future seriously ill patients might, however, be discussed.

Application of real options theory requires similarities in valuation parameters as well as decision structure. Whilst the parameters required to value a particular option are highly dependent on the valuation technique used, generic variables can be discussed (table 5.2).

Variables describing uncertainty, the current estimate and volatility are given by the expected benefit from preserving life (dictated by uncertain QALYs), and associated volatility through time. When assessments of comatose patients are made, classification is usually via scores such as the Glasgow Coma Score (GCS), Glasgow Outcome Scale (GOS), the Acute Physiology, Age, and Chronic Health Evaluation (APACHE) II and III and the Simplified Acute Physiology Score (SAPS). The Glasgow Outcome Scale, for instance, identifies five categories of outcome; good recovery, moderate disability, severe disability, vegetative and dead. Whilst scores give a reasonable indication of well-being including information on motor functioning, verbal response, eye opening and pupilliary light reflex, they do not provide accurate quality of life assessments. This currently hinders the application of option pricing techniques.

Parameters	**Financial option**	**Real option to defer removal of life support**
Current value of source of uncertainty	Spot price (S)	Current expected benefit from preserving life
Estimate of uncertainty	Variance in stock value (σ^2)	Uncertainty surrounding expected benefit over time
Immediate cost/benefit of exercising option	Exercise price (X)	Immediate monetary benefit / cost associated with removing support. Eg. Benefit of transplantable organs
Date before which the option must be exercised	Exercise date (T)	Date when patient dies naturally and option to remove support is no longer available
Benefit associated with deferral	Dividend (D)	Expected benefit from QALYs gained each period net of periodic costs

Table 5.2. Parameters commonly used in financial option pricing and their counterparts for the option to defer removal of life support.

Degree of detail in case studies of comatose and vegetative patients is a barrier to estimating uncertainty. Of those observational studies examining well-being, occurrences of death and regaining consciousness are relatively well documented. Whilst some studies provide information on survival, degree of recovery, and death, the timing of events is often lacking (Kaplan 1999). Bastos and Bricolo (Bastos P G et al., 1993) for instance, provide one-year final outcomes. Some studies aggregate outcomes combining death with vegetative state, or vegetative state with survival (Facco E et al., 1998) making reinterpretation of data impossible.

Studies providing sufficiently detailed information tend to concentrate on the first month of coma. For instance Bassetti (Bassetti et al., 1996) considers patients who remained comatose for more than 6 hours following cardiac arrest. Of 60 patients 13 (27%) died within the first 3 days and 31 (65%) died the following month. Of the 12 patients who regained consciousness (20%), the only details given are that 11 awoke in the first week. This lack of detail poses severe problems for a real options analysis that requires periodic estimates of well-being.

A put option realises value on exercise. The option to defer removal of support may provide value from exercise through donation of suitable organs such as heart, lungs, kidneys, livers and corneas that aid recovery of other patients. Costs may, however, be incurred in removal of support, such as the cost of additional physician support. The balance of these influences will determine whether the final exercise price is a cost or benefit. Although a cost paid on exercise does not align completely to the financial model, the structure of the decision remains the same; if payoffs from continuing the project are sufficiently poor, then paying some cost to end the project becomes worthwhile. This may be the case in many real options applications.

A patient's natural death or spontaneous recovery determine the exercise date for the removal option. While financial options generally have a given exercise date, valuation as a perpetual option, as is most appropriate in this case, is not unusual for real options. If a patient was older, impact of the time to maturity might be explored using a finite binomial / trinomial approximation.

Finally, in contrast to the call option, deferring exercise of a put option is associated with receipt of dividends. Preserving life has dividends in the form of QALYs gained each period for which the patient remains alive. Maintaining life through external support, however, involves use of high technology machines, beds, continuous nursing care, drugs and nourishment. Estimates of cost per bed day, for instance, range between £1000-£1800 (Singer and Grant, 1999). Such costs should be offset against positive interim payments.

5.4.2 The model

Since well-being of patients can improve, remain unchanged, or deteriorate each period, trinomial valuation initially seems appropriate. Several factors make this specification unsuitable in practice. Patients remaining vegetative are often assessed according to a probability of death score (Cho et al., 1995). This is informed by observed data such as the patient's response to pain (Somosonary Evoked Potentials (SEPS)), spontaneous breathing, Glasgow Coma Score (GCS), Acute Physiology, Age, and Chronic Health Evaluation (APACHE III) system probability of death, and in some cases blood glucose levels. Most commonly, assessments are made on entry to, and exit from, the intensive care unit. Despite the varsity of assessments, data on vegetative state patients is not yet sufficiently detailed, in terms of frequency, to inform a trinomial model. The probability of moving between states in any given time period and absolute changes in well-being cannot currently be estimated with sufficient confidence for inclusion in a model.

Given these difficulties, and the effectively perpetual nature of the option, a geometric Brownian motion infinite horizon model is used. In this process, the underlying random variable *Q*, the expected benefit gained from deferral and life preservation, changes continuously each period *dt* with some drift, α, subject to a known and constant variance, σ^2;

$$dQ = \alpha Q\, dt + \sigma Q\, dz \qquad \textbf{(EQN. 5.1)}$$

This process assumes that the current value of the project is known and that future values are log-normally distributed with variance growing linearly with the time horizon. The parameter *dz* is a Weiner process, a random variable drawn from a normal distribution with mean zero and variance *dt*. Figure 5.3 demonstrates the relationship between Brownian motion and the discrete multinomial process by illustrating the evolution of expected benefit.

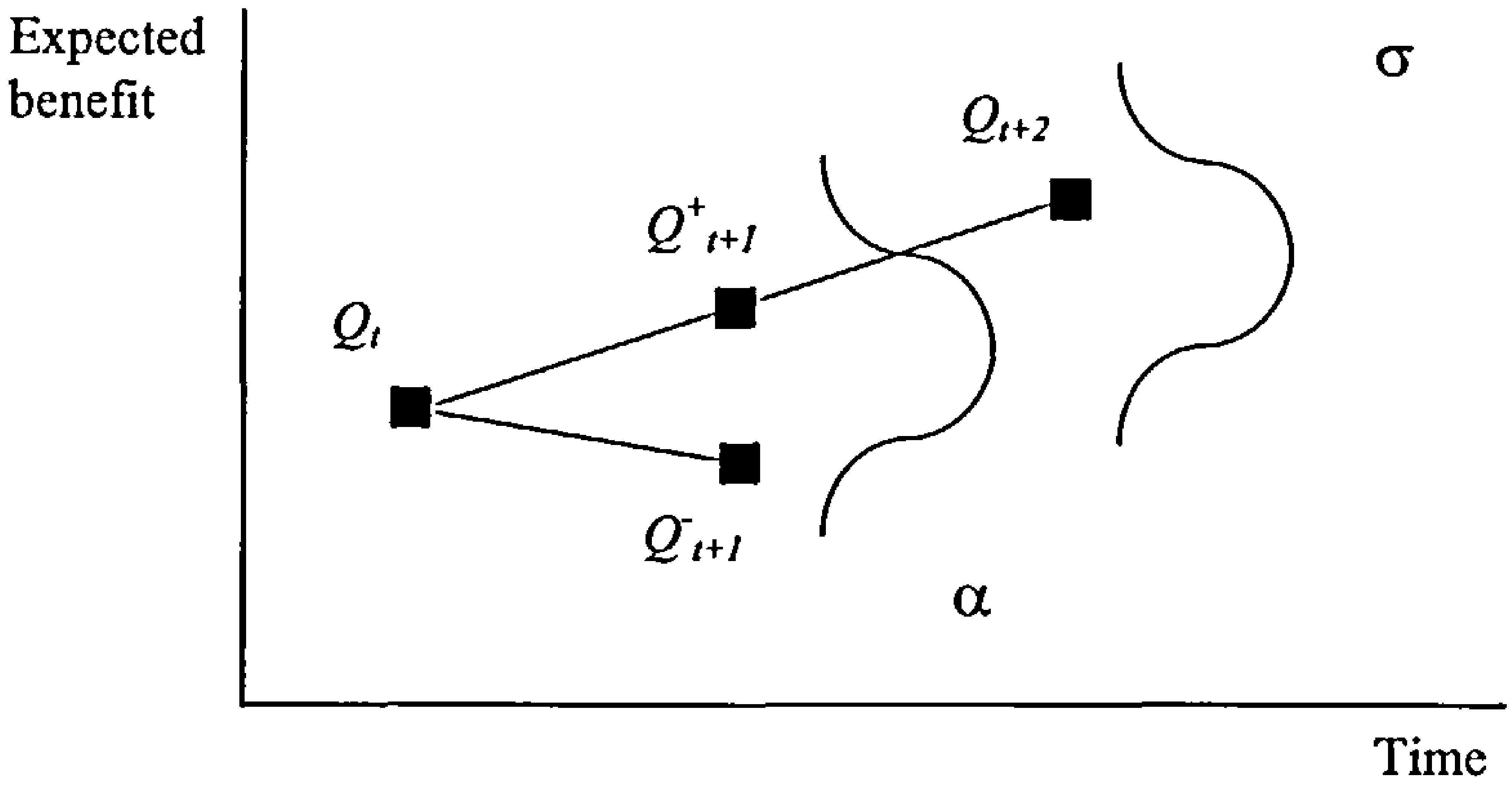

Figure 5.3. The evolution of expected benefit determining α and σ for the Weiner process.

Myers and Majd (Myers and Majd, 1990) use this specification to solve a general abandonment problem employing methodology initially used by Merton (Merton, 1973) to find a partial differential equation (PDE) for abandonment value. This formulation has also been used by Conrad (Conrad, 1997b) to value the option to preserve old-growth forest. Brownian motion is predominantly used in applications where the underlying source of uncertainty is a commodity price that can be reasonably modelled with a log normal distribution. Expected benefit is restricted to positive values since death represents the lowest benefit to preserving life, at a value of zero[29]. In addition, the majority of patients face a relatively low benefit to survival and fewer patients face a fair to good prognosis. Brownian motion therefore seems appropriate.

Brownian motion requires specification of α and σ in place of probabilities and degrees of up and down movements. If the probability of regaining consciousness dominates expected benefit, the latter may drift downwards as time spent unconscious elapses, resulting is a negative value for α. Both the trend and variance are assumed known with certainty although sensitivity analysis may be used to demonstrate the impact of different parameter values.

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[29] Vaulation studies have actually shown that some health states can be considered worse than death. For simplicity it is assumed that death is a boundary state with a utility value of zero.

Whilst the infinite horizon Wiener process is commonly used in real options applications it is one of many possible specifications for underlying uncertainty. For instance a Poisson jump may more accurately represent the probability of spontaneously regaining consciousness. Although expected benefit may be subject to discontinuous jumps resulting from sudden changes in biomedical state, the current formulation is chosen for the way the continuous Weiner process mimics a patient's continuously drifting biomedical state.

The value of the removal opportunity, V(Q), consist of two elements, entitlement to expected benefit from continued life and the option to remove support should the patient's prognosis, and so expected benefit, fall to very low levels. Whilst the option is still available net cash flows are received each period $[(Q - C)dt]$ equal to the difference between expected benefit of remaining alive (Q) and the cost of maintaining support (C). While expected benefit follows the evolutionary process, the daily cost of patient related care in an intensive case unit is assumed to be fixed at £592 (Kemna, 1993).

The value of the removal or disinvestment opportunity must satisfy a partial differential equation (equivalent to Equation 2.19 for the investment opportunity) that Dixit and Pindyck (Dixit and Pindyck, 1994) show to be;

$$\tfrac{1}{2}\sigma^2 Q^2 V''(Q) + \alpha Q V'(Q) - rV(Q) + Q - C = 0 \qquad \textbf{(EQN 5.2)}$$

Dixit and Pindyck illustrate that the general solution is:

$$V(Q) = B_1 Q^{\gamma_1} + B_2 Q^{\gamma_2} + Q/\delta - C/r \qquad \textbf{(EQN 5.3)}$$

The discount rate for costs and benefits are given respectively by r and δ. The last two terms of equation 5.3 give the value of pursuing life support efforts forever, irrespective of the health status. The first two terms value the option to remove support at some point in the future. The likelihood of removal becomes extremely small as Q tends to infinity suggesting the value of the removal option should approach zero as Q becomes large. To achieve this B_1 is set to zero leaving:

$$V(Q) = B_2 Q^{\gamma_2} + Q/\delta - C/r \qquad \textbf{(EQN. 5.4)}$$

Where B_2 is a constant yet to be determined and γ_2 is given by:

$$\gamma_2 = \tfrac{1}{2} - \alpha/\sigma^2 - \sqrt{[\alpha/\sigma^2 - \tfrac{1}{2}]^2 + 2\delta/\sigma^2} < 0 \qquad \textbf{(EQN. 5.5)}$$

Dixit and Pindyck use this formulation as part of a combined firm entry and exit decision strategy identifying complementary entry and exit price thresholds. Here the exit decision is the focus of attention and appropriate exit boundary conditions are derived to ensure a solution exists (equations 5.6-5.8). These limit the value of the option to withdraw support, and link the values and derivatives of deferring removal and immediate removal, when immediate withdrawal occurs.

Absorbing barrier: $V(Q = \infty) = 0$ **(EQN. 5.6)**

Value matching condition: $V(Q_L) = E - (Q/\delta - C/r)$ **(EQN. 5.7)**

Smooth pasting condition: $V'(Q_L) = 1$ **(EQN. 5.8)**

The option to remove support exists while the patient remains alive. When the patient resumes consciousness the option to remove support is no longer relevant and becomes worthless. The absorbing barrier (equation 5.6) states that the value of the removal opportunity falls to zero as expected benefit from deferral becomes infinitely large.

Intuitively, whilst expected benefit remains above some threshold (Q_L), removal is deferred and the option preserved. When expected benefit falls below this threshold removal becomes optimal. The value of the removal opportunity V(Q) is valid only above this lower expected benefit threshold. At the removal threshold society pays / receives the lump-sum quantity, E, (assumed to be a receipt of £10,000) to terminate the periodic cashflows $(Q - C)dt$. The value matching condition (equation 5.7) ensures the value of the option and immediate action are equal at the abandonment threshold Q_L.

Whilst the value matching condition identifies a feasible set of thresholds, the smooth pasting condition (equation 5.8) identifies the optimal decision point by ensuring the marginal value of deferring and removing are equal.

Applying the smooth pasting condition to the value of the removal option $V(Q)$ and rearranging gives B_2:

$$B_2 = (1-\delta^{-1})/(\gamma Q^{\gamma-1})$$ **(EQN. 5.9)**

Substituting this into the value matching condition yields:

$$B_2 Q^{\gamma} + Q/\delta - C/r = E - (Q/\delta - C/r)$$ **(EQN. 5.10)**

$$\frac{1-\delta^{-1}}{\gamma Q^{\gamma-1}} Q^{\gamma} + Q/\delta - C/r = E - (Q/\delta - C/r)$$ **(EQN. 5.11)**

Solving yields the optimal threshold Q_L, the lowest value of expected benefit consistent with the patient receiving continued support:

$$Q_L = (E + \frac{2C}{r})(\frac{\delta\gamma_2}{\delta - 1 + 2\gamma_2})$$ **(EQN. 5.12)**

Q_L may be used to find B_2 at the decision threshold, $B_{2(L)}$. Q_L and $B_{2(L)}$ are used to find the value of the removal option V(Q) given in equation 5.4:

$$V(Q) = B_2 Q^{\gamma_2} + Q/\delta - C/r$$ **(EQN. 5.4)**

Sensitivity analysis can be used to explore the effect of changing base case parameter estimates.

5.4.3 Results

For the base case scenario, expected benefits are assumed to drift downwards at 2% per year (α=-0.02) with a constant volatility of 15% (σ=0.15). Periodic costs of £592 per day and upfront benefits to ending support of £10,000 are used. Costs are discounted at 6% and benefits at 2% in accordance with economic evaluation practice. A period of one month is used to illustrate the model (table 5.3).

Parameter	**Basecase parameter values (monthly)**
Drift in expected benefit (α)	-0.0106
Variance in expected benefit (σ)	0.0125
Discount rate for costs (r)	0.0116
Discount rate for benefits (δ)	0.0106
Periodic costs of maintaining support (C)	£16,576
Benefits from ending life support (E)	£10,000

Table 5.3. Base case parameter values for the option to defer removal of life support.

An Excel spreadsheet is used to calculate the optimal threshold (Q_L), the value of the removal option [V(Q)], and the net benefit of immediate removal [$E-(Q/\delta - C/r)$]. For base case parameter values the optimal removal threshold occurs when expected benefits reach £10,120 (Q_L=£10,120). For any given patient currently receiving support, when their monthly expected benefit from preserved life falls below £10,120, life prospects have become so poor that removing support is optimal. A patient above this threshold should have removal of support deferred.

Figure 5.4 shows option value and net benefit over a range of expected benefits encompassing the threshold Q_L. A patient to the left of the decision threshold would have support removed immediately, and a patient to the right would receive continued support. For an investment option there is an implicit assumption that the project is not active, suggesting the threshold has yet to be reached but that project value is rising to induce action. This renders deferral relevant below the threshold. For the current case the opposite implicit assumption exists; that the 'project' is active and expected value is yet to fall sufficiently to induce action. Therefore, in this instance deferral is relevant above the threshold and the decision maker looks for decreasing expected benefits through time to trigger action.

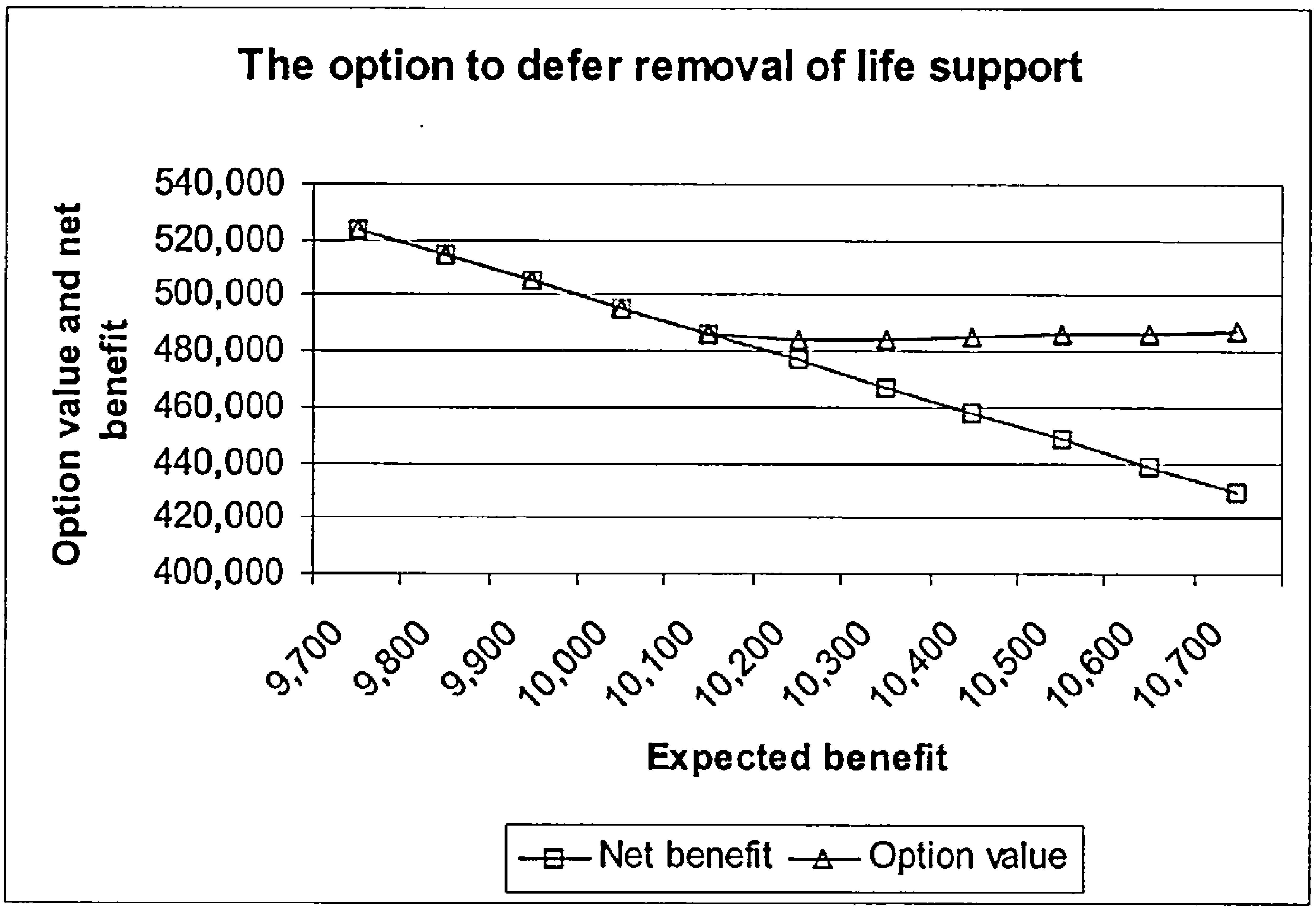

Figure 5.4. Option value and net benefit for the option to defer removal of life support.

The value of a financial put option tends towards zero as stock price increases. This is not evident in this real option. The value of the option to defer removal comprises option value and the value of continuing support infinitely (equation 5.3). As expected benefit increases the latter component dominates causing option value to rise again. In practice there would exist an upper threshold such that a patient with expected benefits exceeding the trigger would regain consciousness and the upper portion where option value begins to rise would become invalid.

Real options analysis suggests that removal of life support should be deferred until the expected value from preserving life falls below Q_L =£10,120. If the decision to remove support is considered as a now or never decision, characteristic of existing decision techniques, removal occurs when the payoff from removal (E) equals the value from continued support ($Q/\delta - C/r$). Net benefit is given by $E-(Q/\delta - C/r)$ and the level of benefits where net benefit equals zero identifies the removal threshold. Rearranging for this level of expected benefits *(Q_{L^*})* gives:

$$Q_{L^*} = \delta(E + \frac{C}{r}) \qquad \textbf{(EQN. 5.13)}$$

With traditional techniques that do not account for the value of maintaining the removal option, immediate abandonment would occur when expected benefit falls below £15,253 per month (Q_{L^*} = £15,253).

Consistent with existing applications of real options analysis the two decision thresholds do not coincide. For the option to defer removal of life support the real options decision threshold is below that of traditional decision making. For a given patient, standard cost-effectiveness analysis would recommend treatment withdrawal more readily than real options analysis. Real options analysis therefore allows the well-being of the patient to deteriorate further before treatment withdrawal is recommended, theoretically ensuring that the patient is supported for longer in intensive care.

Real options analysis has provided a more conservative criterion. This conclusion suggests there may exist large deviations in the amount of time for which life preservation efforts are sustained when the two decision rules are compared. Palmer and Smith's work (Palmer and Smith, 2000a) confirms that for reasonable parameter values applied to an option to invest in a new health technology, the two decision criteria can differ substantially, reinforcing this conclusion.

In addition patients with expected benefit between the two thresholds would be treated differently under the two methodologies. A patient with an expected benefit of £12,000 would have their care removed in conventional decision making but would receive continued support under a real options approach. If budgetary allocations in this area are based on historical patterns, this result suggests that an insufficient quantity of resources may be allocated to intensive care units for patients to be treated optimally. If current treatment decisions are actually determined by the availability of resources, which may be the case in some trusts, then there may exist some scope for optimal reallocation of resources.

The value of maintaining a flexible position (keeping the option to remove support in preference to taking immediate action and losing the option) is given by the difference in value between deferring and acting immediately. This incremental value of deferring, or option premium, captures the value of maintaining rather than destroying future available options, and so places a value on flexibility. The optimal threshold Q_L can also be identified as the first value of expected benefit at which this option premium falls to zero. Where the options premium is positive (above Q_L), possessing future choices is more valuable than immediate action and deferring removal is appropriate. Where the option premium is equal to zero (below Q_L) possessing future options holds no extra value and immediate removal is appropriate. The decision thresholds for real options and net benefit analyses differ precisely because of this ability to account for future options.

5.4.3 Sensitivity analysis

For a given patient the value of the option to defer removal of support is determined by their characteristics, which influence parameter estimates. Individual patients with different risk factors will have different option values that alter the relative attractiveness of maintaining their life support, and preserving their recovery option. For instance patient age is an important predictor of coma outcome since very young and very old patients historically face greater risk of failing to regain consciousness, when compared to middle age persons (Coggins and Ramezani, 1998). Age may affect the evolution of well-being, causing expected benefit to deteriorate more quickly in the very old and very young. Figure 5.5 shows option value for a middle aged person (α=-0.02) compared to an older person (α=-0.04).

Reducing the drift in expected benefits increases option value for the removal opportunity. This gives the seemingly perverse result that a middle aged person deteriorating less slowly will have a higher removal threshold; optimal removal of support occurs at a higher threshold than for the older person (middle aged Q_L = £10,120, older person Q_L = £9,930).

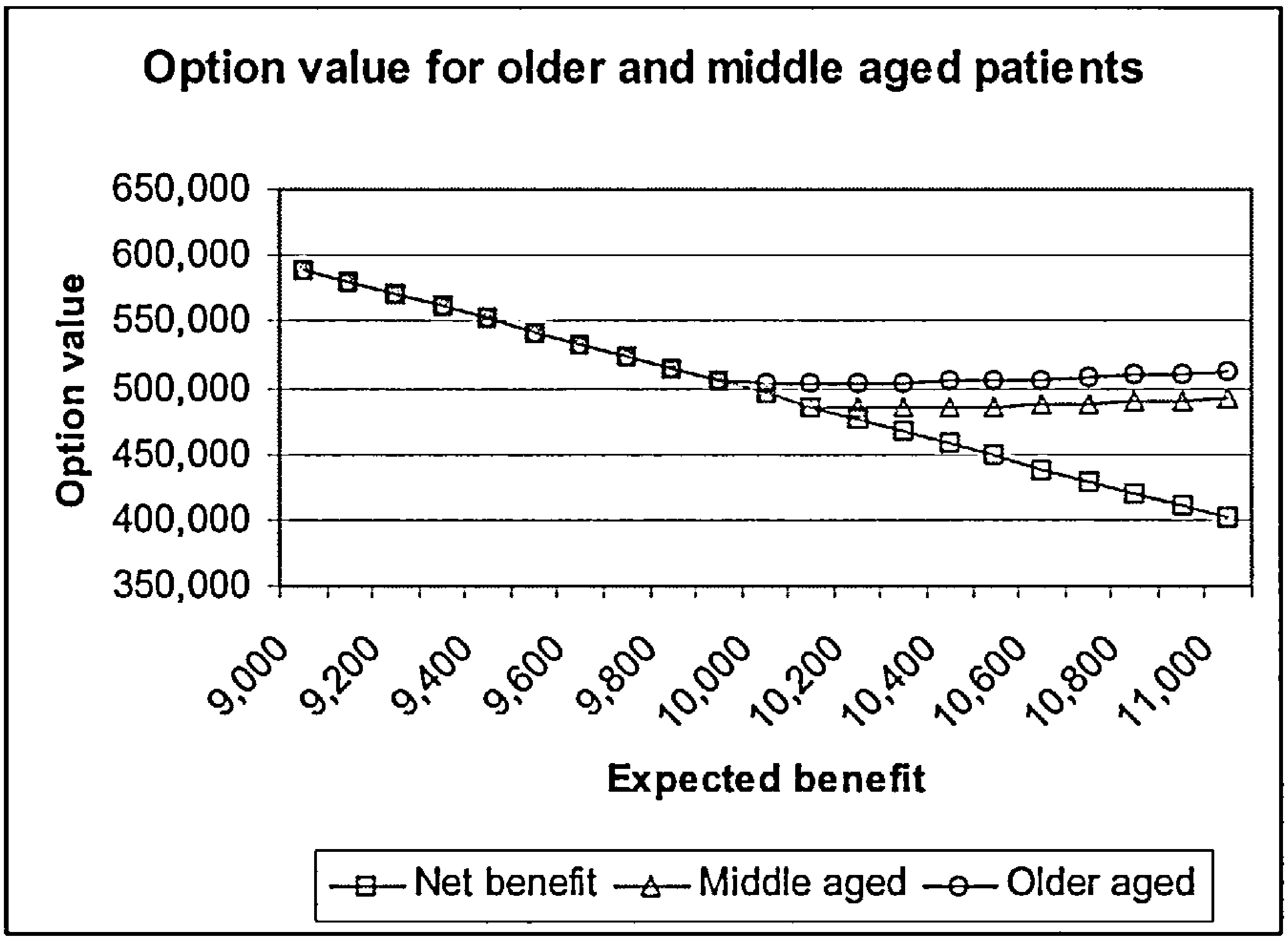

Figure 5.5. Option value for middle versus older aged patients

To understand this, consider the put option. When stock price falls more quickly potentially greater profits are made, the option is worth more, and exercise occurs more readily. With the option to defer removal of support a patient deteriorating quicker releases their organ donation sooner, presents a smaller resource commitment over the duration of deferral (because they are expected to die more quickly), and most importantly following deferral for such a patient exercise will require sacrificing fewer expected benefits. These influences exert a positive influence on option value causing exercise to occur less readily. Older patients are therefore likely to receive more prolonged support.

Although the older patient receives care until a lower threshold is reached, in practice the speedier deterioration may cause the threshold to be reached sooner and support to be continued for a shorter period of time. This conclusion is consistent with Sarkar (Sarker, 1999) who argued that although trigger thresholds for investment options are more conservative using real options analysis investment often occurs sooner. In addition older persons may start from a lower initial level of expected benefit and may therefore be closer to their removal threshold.

The cause of the coma; traumatic, non-traumatic or degenerative disease, has also been identified as an important indicator of outcome (The Multi-Society Task Force on PVS, 1994). Patients entering the state due to a degenerative disease will face less uncertainty over their outcome. This difference in uncertainty means a trauma patient (perhaps $\sigma=0.15$) has a different decision threshold to a patient suffering neurological problems (perhaps $\sigma=0.05$). Increased uncertainty means the monetary benefit of deferring removal deteriorates in a more volatile way, increasing the possibility of future improvement. This generates greater option value causing a lower removal threshold. The trauma patient will have removal of support deferred for a longer period of time if equal average rates of deterioration (α) between the patients are assumed.

Attitudes towards time preference impact on option value because deferring and keeping opportunities available in future is a key part of real options analysis. Discounting costs and benefits at a greater rate, placing less value on future outcomes, affects both the value of immediate removal and the value of deferred action. Since future outcomes have less weight option value is diminished creating pressure for the optimal threshold to increase, and prompting treatment withdrawal to occur more readily. The value of immediate action meanwhile is enhanced because the present value of QALYs sacrificed when support is removed falls, causing the decision threshold to fall. The value of deferred action is diminished whilst the value of immediate action is enhanced. Since time preference has altered to favour current outcomes the second influence dominates causing an aggregate fall in the optimal removal threshold.

Changing the exercise price similarly has a significant impact. A patient entering coma following acute trauma may have more value as an organ donor than a patient suffering long-term degenerative effects. In some cases net costs may be incurred in the process of removing support detracting from the put option analogy (potentially where a patient has no value as a donor). Reducing the value of any benefit to removing support reduces the optimal decision threshold. Where a patient presents less value or creates a cost when removal of support occurs, this action is deferred for longer. A patient who has a high value of transplantable organs perhaps because they can save another patients life may therefore face a more stringent decision criterion. Taking the irreversible action to remove future life options for the current patient generates future options for alternative patients. This lowers the value of flexibility for the current patient.

Individual patient characteristics have an impact on the value of deferring removal of life support, and so influence the timing of treatment withdrawal. Where maintaining future choices for the current patient is not valued highly relative to immediate actions that reduce or create flexibility elsewhere, the removal threshold is high, encouraging removal to occur more readily.

5.5. Conclusions

5.5.1 Applying real options analysis: the option to remove support

The termination of life support is viewed here as a current action that significantly affects the availability and desirability of future choices accessible to the clinician. Removal of life support efforts is a decision influenced by uncertainty, and extensive irreversibility. Since the action can be deferred, the removal opportunity becomes an option to defer removal and can be analysed using financial option pricing techniques. Real options analysis places emphasis on the ability to defer taking the irreversible removal decision, in a situation where deferral is inherent yet not usually considered. Explicit appraisal of deferral allows a value to be placed on future flexibility. Although valuing deferral is in principle possible using current decision theory, the discipline of real options addresses this issue explicitly. This enhances transparency in the approach to valuing flexibility.

This application has shown that the ability to defer removal is valuable and sensitive to patient characteristics. As a result characteristics affect the real options decision threshold and directly influence decisions governing treatment; in theory each patient would have a unique treatment removal trigger and homogenous treatment recommendations are ruled out. Real options analysis has shown that capturing the effects of creating and destroying future flexibility is important. Failing to account for this source of costs and benefits may lead to a misstatement of the value of an action, and misguided decision making. In particular, the value of preserving a life is understated; leading to fewer resources than optimal being allocated to this speciality.

This case study centred on an example involving total irreversibility, this is unlikely to be the case for many real options. Usually investment and disinvestments opportunities have sunk costs that constitute irreversibility but the projects themselves and associated outcomes can be altered (although usually at some cost) once initiated. Degrees of irreversibility can be accounted for within the real options framework by redefining the value matching condition, and modelling multiple interacting options.

Extensive data requirements make applying the model presented here difficult in practice. Making this operational requires an estimate of the expected drift and variance of monetary benefit gained by deferral. For this, Quality of Life scales are essential, although patient assessment tools such as the Glasgow Coma score or the APACHE III scale supply important well-being data, they do not provide sufficiently detailed information to develop the necessary picture of expected benefit over time. For instance, mortality prediction models usually provide one-off assessments whilst options analysis requires ongoing assessments at regular intervals. Data frequency such as that shown by Chang (Chang, 1988), who tracked daily Apache II scores and used trend analysis to predict probability of death, would be required on an extensive and ongoing basis.

Data requirement issues exist in parallel with other barriers to implementation. Acceptance of net benefit arguments is a prerequisite that necessitates an explicit statement of policy makers' willingness to pay for health outcomes. The trade-off between methodologically accurate valuation models and maintaining simplicity such that options can still be solved analytically is an additional consideration. Data issues however, require a change in current practice and so perhaps pose the greatest obstacle.

5.5.2 Wider implications

This chapter has applied the principles of financial put-option pricing theory to assess cost-effectiveness of treating coma patients. Both the real options theory of abandonment and the concept of explicitly valuing future opportunities have wider appeal within health care.

The theory of abandonment options might be used by pharmaceutical companies to assess timing of production downsizing in response to uncertain demand, or the optimal abandonment time of a novel compound for which a lack of efficacy has been demonstrated. Outputs from hospitals might be examined to recommend optimal closure of out-dated wards in favour of newer facilities. On a micro level patients consuming specific drugs might be monitored. Well-being reaching some lower threshold indicates the optimal timing to end the regime or switch (abandon and reinvest) to an alternative. Within each of these potential applications the presence of uncertainty, some degree of irreversibility, and an ability to defer, supports the use of financial techniques.

The idea of valuing future opportunities is particularly useful to assess desirability of current investment opportunities. Purchase of life saving equipment and research into life saving techniques create options to initiate life support. When merging with another company, a pharmaceutical may be interested in future opportunities created by the merger in addition to current firm value. In other words, decision makers are just as interested in the option premium, the value of future flexibility, as in intrinsic value and option value. Research and development projects are especially important for their effects on future capabilities. These examples assume the perspective of creating rather than destroying options but any decision that involves a resource commitment destroys options.

This chapter has used a continuous diffusion process to model the evolution of patient well-being. This format could be used in many patient level decisions in addition to macro level choices. For instance, medical and surgical management may be compared by modelling well-being following each course of action. Continuous processes are also appropriate when the underlying source of uncertainty is a price or cost such as the price of a pharmaceutical or price charged for health related services (perhaps dental or chiropody services).

The purpose of this chapter was to apply real options within an area where deferral is not explicitly considered. A Brownian motion continuous diffusion process was used to value the flexibility lost when the option to defer removal of life support technology is exercised. Such flexibility has been shown to be valuable and should be acknowledged when decisions are made, irrespective of whether a choice creates or destroys future opportunities. The specific research problem identified is to specify and estimate relevant parameters. With this achieved the real options model can become operational.

Chapter 6. Real options analysis and technology assessment within the NHS.

6.1 Introduction

In 1997 the UK government set up the National Institute of Clinical Excellent (NICE) to assess the desirability of health-care related technologies. NICE respond to requests by the Department of Health for guidance on the usage of a variety of new and established technologies. Current evidence, incorporating information on clinical effectiveness, cost effectiveness, and wider implications to the National Health Service (NHS), is assessed to generate recommendations for appropriate use.

When performing an appraisal, NICE face an option to approve the given technology. Granting approval creates an option to alter this decision at a later date (an alteration option). This is analogous to a compound financial option where exercise of an initial option confers the ability to exercise a second. Both decisions are characterised by uncertainty in cost-effectiveness estimates, an ability to defer and some degree of irreversibility, suggesting further similarities with the compound option.

Analysing technology appraisal as a compound option to approve and later retract may have implications for the initial guidance recommendation, particularly when current evidence is lacking or inconclusive. Complementary decisions to reduce irreversibilities may also be promoted. This chapter explores the methodological reasoning underlying, and implications resulting from, the application of financial option pricing techniques to the appraisal of health technologies. Having examined the role and decision-making capabilities of NICE in section 2, section 3 considers financial compound options analysis and section 4 considers real compound options, drawing parallels to decision making within NICE. Section 5 develops a model for the option to approve and later retract. This is evaluated in section 6 using a numerical example. Section 7 concludes.

6.2 The role of NICE and current decision making

Since its creation in 1997, NICE has been involved in appraising numerous technologies for use within the NHS of England and Wales. A technology, for the purposes of NICE, has a broad interpretation including medical devices, procedures and medicines. Examples of appraisals include cartilage transplantation for defective knee joints (Guidance issue No. 16), wisdom teeth removal (No. 1), and prescription of pharmaceuticals for management of patients suffering from Motor Neuron Disease (No. 20).

Within the process of appraisal, NICE explore current evidence on areas such as cost, clinical effectiveness, equity implications and budgetary impacts[30]. This involves taking account of submissions from manufacturers, literature reviews of published material, and consultation from medical experts and patient representation groups. Having synthesised relevant evidence, guidelines are formulated. For example, the process has resulted in guidance on the use of nicotine replacement therapy (NRT) for smoking cessation (No. 39). In this case guidance recommends medication be prescribed for patients with an expressed desire to quit. Guidelines sometimes specify patient groups for whom the advice is appropriate, such as those of a certain age or with particular risk factors. For instance, NRT should not normally be prescribed if a patient has received this therapy within the past 6 months and failed.

The UK is not alone in attempts to introduce economic considerations into technology appraisal. Australia led the way in requesting economic evidence to support applications for reimbursement. The Australian Medical Services Advisory Committee (MSAC) invites applications for review and follows a structured process that results in a statement of recommendation presented to the

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[30] Details of NICE, technologies currently under appraisal, previously appraised and issued guidance can be found on the website; http://www.nice.org.uk.

health minister. Since this scheme, countries including Portugal, Finland and Denmark have created similar committees. NICE is one of the youngest bodies assessing economic evidence on health related technologies.

Currently within the UK, NICE guidance is viewed as relatively irreversible. Irreversibility may encompass an inability to recuperate sunk cost, abandonment expenses required to alter the decision itself and avoid adverse repercussions, or a physical inability to alter the decision and repercussions. Despite the existence of review dates where previous recommendations are assessed in the light of new information, political pressures and physical costs generate considerable irreversibility for technology approval. As technologies increasingly come up for review and guidelines are altered, political resistance may fall reducing the degree of irreversibility.

Australia assumes a more flexible approach in the adoption decision, acknowledging possible reversal in their initial recommendation statement. Where evidence is inconclusive or insufficient MSAC have recommended interim approval. In 1999 endoluminal grafting for abdominal aortic aneurysms was given approval although ongoing data collection was recommended with review as soon as possible due to insufficient evidence. Also in 1999 directional, vacuum assisted breast biopsy was granted interim funding with the condition that costs be continually investigated. Evaluation of near patient cholesterol testing using cholestech LDX, brachytherapy for treatment of prostate cancer, and deep brain stimulation for symptoms of Parkinson's disease have all received similar recommendations. For the latter two, review was required within three years of the initial approval date.

Acknowledging potential for reversibility reveals a similarity between decisions facing NICE and decisions to exercise compound financial options. Appraisal of new and existing health technologies creates an option to defer approval. The decision to exercise is surrounded by uncertainty in cost-effectiveness estimates, and exercise can usually be deferred, and is partially irreversible. Importantly, exercise in principle creates an option to alter, or defer altering, the original recommendation. As a technology is subject to more research and is used in a wider context, and on a prolonged basis, information may become available that either supports or contradicts the initial approval decision. When newly available information alters the desirability of the technology, NICE can exercise their option to alter the treatment guidance. This may take the form of extended or retracted coverage, or reversing their initial decision by withdrawing the technology altogether.

NICE face two sequentially linked options; the option to approve, and the option to alter that decision. Both elements of the decision problem are characterised by uncertainty, some degree of irreversibility, and an ability to defer. The sequential interaction of these decisions resembles a compound financial option and supports the use of option pricing techniques to evaluate the initial approval decision. These techniques encourage the reversal decision to be discussed ex-ante. The following section examines the analogy more closely, looking at the theory surrounding compound options and how this relates to the current application. This section also highlights existing examples of real compound options analysis.

6.3 The compound option

Compound options consist of any combination and number of simple call and put options. A financier may own a call option on a call option. The first call is an option to defer purchasing the second. Exercise confers the second option, which in turn confers the opportunity to defer purchasing some underlying asset.

Compound options analysis is not new in the real options arena. Dixit and Pindyck (Dixit, 1989) provide an early study modelling interrelated decisions, examining entry and exit decisions of a firm given uncertain prices. The authors treat idle and active firm status as call options on each other and identify a pair of trigger prices that induce entry and exit. Entry provides active status and confers the option to exit, whilst exit makes a firm idle and confers the option to enter. Noting that these thresholds differ from thresholds identified using standard techniques, Dixit and Pindyck use their solutions to explain hysteresis.

Sunnevag (Sunnevag, 1998) looks at exploration licensing strategy for non-renewable resources. Exploration is evaluated as a compound call option on a further call option to develop the resource. In this case the options are owned by relevant licence granting authorities that respond to uncertainty in resource prices. Valuation is based on a binomial lattice with the development option expiring in 20 years (50 periods each of 0.4 years). Sunnevag investigates optimal timing of exploration and development.

Work in this area has been furthered by Trigeorgis (Trigeorgis, 1996) who valued complex multi-option leases, accounting for a series of exercise prices, non-proportional dividends and interaction effects. In addition, Rose (Rose, 1998) has presented a methodology specifically to value interaction effects between embedded options, examining a tollroad infrastructure project. Underlying risk factors were simulated using Monte Carlo methods leading to the conclusion that option value may account for more than half of market value for complex interacting real options. Pennings (Pennings and Lint, 2000) has considered market entry as a compound option on phased roll out of a product. Pennings examines the optimal rate and global position of the phased roll out as endogenous actions to reduce uncertainty.

In addition to addressing compound options, real options analysis has been used to evaluate the impact of varying degrees of irreversibility; an integral part of the compound real option. Tegene (Tegene et al., 1999) and Hodge (Hodge, 1984) both study irreversible development of agricultural land. The former discusses future returns from agriculture and urban use as the dominant sources of uncertainty. The decision to sell the land for development is analysed as irreversible exercise of an option. Hodge focuses on the uncertain value of preservation and discusses irreversibility in the form of expected opportunity loss from a given choice. Degrees of irreversibility are examined by altering the time taken for information, necessary to identify and correct errors, to become available.

Zhao (Zhao and Zilberman, 1999) introduces an irreversibility cost. Within this paper, which considers natural resource development, the author distinguishes types of irreversibility, categorising technical and economic irreversibility. Finally Fanai, (Fanai and Burn, 1997) defining irreversibility as the "degree to which...anticipated and unanticipated impacts on a project can be mitigated", explicitly adopts the degree of irreversibility as a selection criterion.

6.4 The compound option to approve and later retract

In the case of technology approval NICE have an option to approve which involves selecting one of three choices; reject the claim for approval immediately, approve immediately, or defer making the approval commitment until some future date. NICE observe expected benefit to inform the approval decision. Exercising the option to approve is akin to a compound American call option. On exercise (irreversible) upfront costs are incurred to approve a technology with uncertainty future health benefits. The option to alter the approval guidance, which includes the option to reverse the decision and withdraw approval, is also conferred.

The reversal option is only conferred once the option to approve is exercised and is akin to an American put option. In finance, exercising a put means giving up dividends and price appreciation in return for some positive price. In the real sector exercise of a put or abandonment option is usually with the aim of preventing or ending a stream of negative payments and occurs at some cost. Exercising the opportunity to reverse the approval decision may involve incurring political costs in return for ending the stream of uncertain benefits. When appraising a new or existing technology NICE own an American call on an American put. Figure 6.1 illustrates this compound approval option in decision tree format. Although the tree is structured as a collection of sequentially faced decisions and events, observation of uncertain expected and realised benefit occurs continuously and underlies the entire tree.

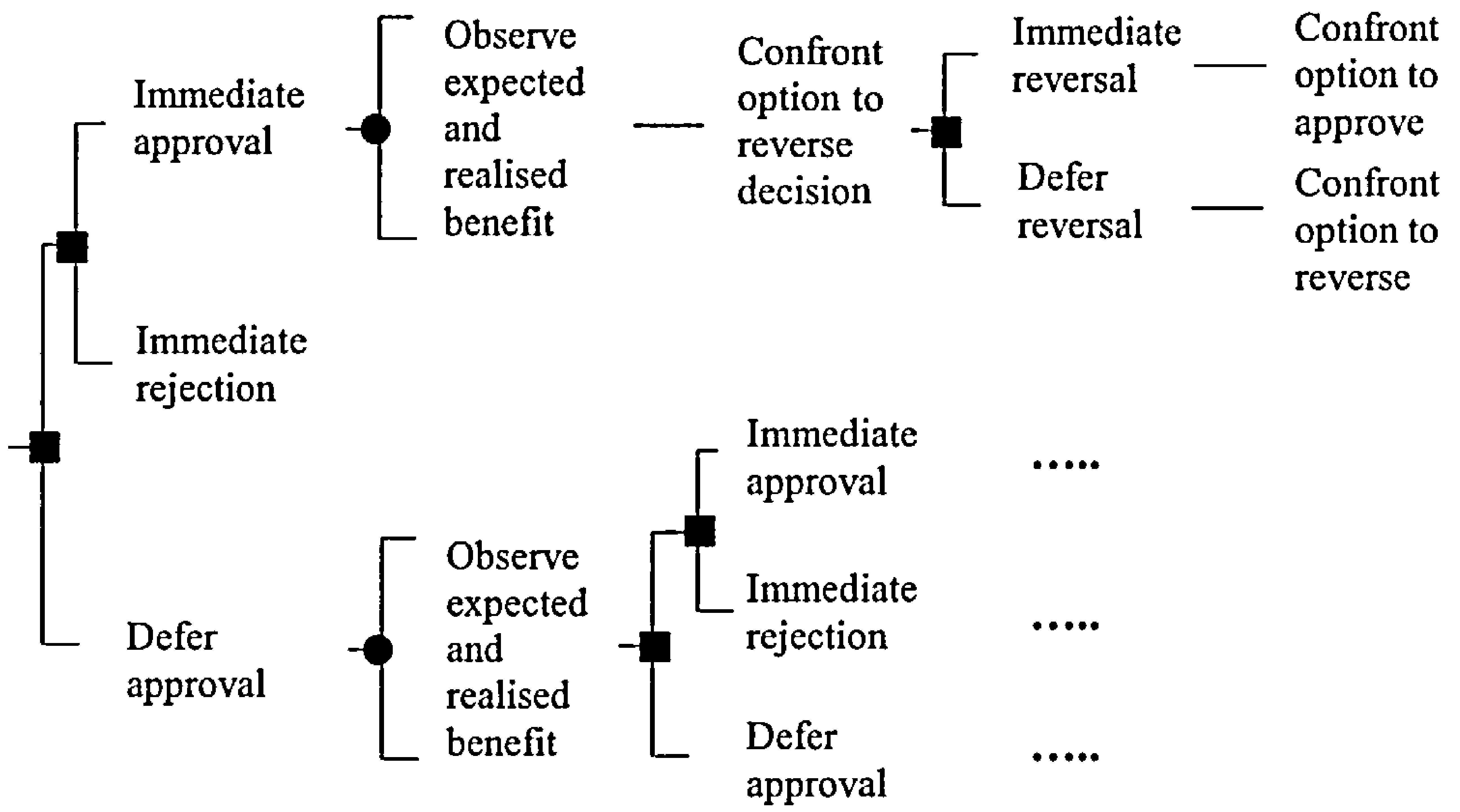

Figure 6.1. Decision tree illustrating the compound option to approve a technology.

The two elements of the compound real option can be compared to the characteristics of financial options (table 6.1) to assess similarities in structure. Both options are owned by NICE. The opportunity to approve is conferred by the nature of NICE as a decision-making body and exogenous agents pursuing research and development activities that generate technologies. The alteration option is conferred only through exercise of the approval option. In both cases uncertainty surrounds expected cost-effectiveness of immediate exercise and deferred action. With reference to this, information on clinical benefit, cost, and cost-effectiveness becomes available over time. Both options have some degree of irreversibility in the form of upfront costs associated with exercise, and both decisions can be deferred.

	Option to approve	Option to alter decision
Decision maker	NICE	NICE
Source of option	Conferred exogenously via actions of firms (R&D), and appraisals process	Conferred endogenously via decision to approve
Nature of option	Call - Investment	Put - Abandonment
Dominant source of uncertainty	Expected cost-effectiveness	Realised health gain and future expected cost-effectiveness
Information gained through deferral	Information on cost and effect from ongoing randomised controlled and pragmatic trials, and case study observations from increased use	Information on cost and effect from ongoing randomised controlled and pragmatic trials, and case study observations from increased use
Source of irreversibility	Cost of issuing guidance, training practitioners in use of technology	Political and physical costs of altering adoption decision
Ability to defer	Limited by NICE, arrival of new technologies, or public pressure. May be known with certainty, entirely stochastic, or dependant on arrival of additional information	Limited by NICE, arrival of new technologies, or public pressure. May be known with certainty, entirely stochastic, or dependant on arrival of additional information

Table 6.1. Characteristics describing the compound option.

The parameters required to value the compound option are identical to those required for stand alone options because the structure and underlying source of uncertainty are the same (table 6.2). For the compound case two exercise prices (investment and abandonment costs) and, if applicable, two maturity dates are required. The exercise cost of adopting comprises the expense of appraising, creating, and disseminating guidelines as well as technological set up costs and associated training requirements. The exercise cost of altering is likely to be political. Although unique exercise dates may exist for each option, determined by both endogenous and exogenous factors, formal deadlines may not exist. Periodic benefit lost before the technology is adopted or received once approval has occurred represents the dividend found in financial models.

Parameters	**Compound option to approve a technology**
Current value of source of uncertainty	Expected benefit of approving (V)
Estimate of uncertainty	Uncertainty surrounding expected benefit (σ^2)
Cost of exercising call	Cost incurred in development, dissemination and adoption of guidelines (I)
Cost of exercising put option	Costs incurred in reversing decision (E)
Dates before which options must be exercised	Date before which NICE must make decisions (T_1, T_2). Formal deadlines may not exist
Benefits of exercising / costs of deferral	Periodic benefits received once approval occurs (δ)

Table 6.2. Parameters used to value the compound option to approve a health technology.

Given the wider appeal of compound options methodology, and the similarities between the underlying financial problem and the compound option to approve new and existing technologies, the application of financial techniques to this area seems appropriate. The following section develops a model and numerical example to develop this analogy further.

6.5 The model

Many real options valuation techniques, including multinomial lattice methods, make the assumption of complete irreversibility. This usually takes two forms. Firstly, projects have large up front costs that cannot be recuperated. Secondly, provision to end projects that have turned out less effective than anticipated is not often incorporated into modelling. Complete, or perfect, irreversibility rarely exists in practice so real option models must be adapted to account for differing degrees of irreversibility. Compound options analysis provides a way to achieve this through incorporating the opportunity to change decisions, and the costs of doing so.

The compound option to approve and later reverse approval consists of two elements; an investment type option and an abandonment type option. The underlying source of uncertainty, expected benefit, is assumed to follow a geometric Brownian motion diffusion process (equation 6.1).

$$dV = \alpha\, V\, dt + \sigma\, V\, dz \qquad \textbf{(EQN. 6.1)}$$

Current expected benefit is known with certainty. Future values change each period *dt* with some drift α subject to a known and constant variance σ^2. *dz* is the increment on the Weiner process[31]. This formulation assumes the option is available infinitely and once investment occurs benefits accrue in perpetuity.

The components of the compound option are considered in turn. For the first element of the compound option NICE must decide, given the evolution of expected benefit, when (if ever) to exercise their option to approve. This amounts to choosing when to incur an irreversible sunk cost I, to approve, generate, and disseminate guidelines in order to benefit from the technology. The optimal action and timing is found by maximising the value of the investment opportunity $F_0(V)$. This comprises a continuation value (value from maintaining the option) and a stopping value (value from immediate investment).

The optimal stopping problem is solved using dynamic programming techniques to maximise the sum of the components of the optimal stopping problem. The valuation model follows methods used by Dixit and Pindyck (Dixit and Pindyck, 1994) who show that the investment opportunity, $F_0(V)$, must satisfy a second order partial differential equation (PDE):

$$\tfrac{1}{2}\sigma^2 V^2 F_0''(V) + \alpha V F_0'(V) - \rho F_0(V) = 0 \qquad \textbf{(EQN. 6.2)}$$

$F_0'(V)$ and $F_0''(V)$ represent first and second derivatives of $F_0(V)$ with respect to V, and the subscript '0' refers to the fact that investment is yet to occur. The risk free discount rate is given by ρ. By satisfying the PDE, the value of the investment opportunity F(V), is always equal to the maximum of the continuation or stopping value. The solution has a functional form:

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[31] Chapter 2 discusses the Weiner process in more detail.

$$F_0(V) = A_0 V_0^{\beta_0} \qquad \text{(EQN. 6.3)}$$

where A_0 is a constant yet to be determined and β_0 is the known constant:

$$\beta_0 = \frac{1}{2} - \frac{\alpha}{\sigma^2} + \sqrt{\left(\frac{\alpha}{\sigma^2} - \frac{1}{2}\right)^2 + \frac{2\rho}{\sigma^2}} > 1 \qquad \text{(EQN. 6.4)}$$

This solution is valid only over the interval during which investment has yet to occur, and the project remains inactive. If investment is found to become optimal at some upper threshold V_H, $F_0(V)$ will be valid in the range $(0, V_H)$.

Whilst expected benefits are received each period they arrive at a constant cost C per period. Whilst continuing to hold the option to alter their approval decision, NICE hold an active project with operating benefits (V-C) accruing each period for which approval remains optimal. In the complete irreversibility case an investment threshold[32] can be obtained analytically[33] that relates to the cost per period (C) incurred once approval is given:

$$V^* = \frac{\beta}{\beta - 1} C \qquad \text{(EQN. 6.5)}$$

Completely irreversible models usually contrast expected discounted operating benefits with upfront investment costs. Comparing marginal cost to marginal benefit (expected benefit per period) is more appropriate when a project can later be reversed and continual monitoring is required[34]. The optimal threshold can be used with the functional form (equation 6.3) and a smooth pasting boundary condition to determine A:

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[32] To distinguish the complete and partial irreversibility models the approval threshold in the complete irreversibility model is referred to as V*, and in the partial irreversibility model as V_H.

[33] Given an absorbing barrier and appropriate value matching and smooth pasting boundary conditions (see Chapter 2 section 2.2; equations 2.19-2.24).

[34] When a project is fully irreversible an investment threshold is more likely to be obtained that relates expected discounted operating benefits to upfront sunk cost. Actual operating revenues are effectively irrelevant once the project is initiated since the project is fully irreversible. Here, for comparability with the reversible scenario, a threshold is generated that relates periodic expected benefits to periodic costs.

$$A=\frac{V^{*}-C}{V^{*\beta_0}}=\frac{(\beta_0-1)^{\beta_0-1}}{\beta_0^{\beta_0}C^{\beta_0-1}} \qquad \text{(EQN. 6.6)}$$

The solution for the simple option, for a given set of parameter values, may be compared against the solution for the compound option in order to assess the impact of accounting for degrees of irreversibility. When there is incomplete irreversibility the adoption option must be solved simultaneously with the reversal option.

To introduce the compound element of the option, the value of the active project must be considered. Having granted approval expected benefits of the technology (V-C) continue forever or until the decision is altered. The value of the alteration opportunity associated with the active project must satisfy a second order partial differential equation, which closely reflects that facing the inactive project:

$$\frac{1}{2}\sigma^2V^2F_1''(V)+\alpha VF_1'(V)-\rho F_1(V)+V-C=0 \qquad \text{(EQN. 6.7)}$$

The subscript '1' indicates that investment has occurred. The additional term (V-C), representing periodic operating profits of the active project, leads to a difference in functional form for the solution:

$$F_1(V)=A_1V_1^{\beta_1}+\left(\frac{V}{\delta}-\frac{C}{r}\right) \qquad \text{(EQN. 6.8)}$$

The terms δ and r are the discount rates applied to benefits and costs respectively. As before A_1 is a parameter yet to be determined. β_1 is given by:

$$\beta_1=\frac{1}{2}-\frac{\alpha}{\sigma^2}-\sqrt{\left(\frac{\alpha}{\sigma^2}-\frac{1}{2}\right)^2+\frac{2\rho}{\sigma^2}}<0 \qquad \text{(EQN. 6.9)}$$

The first term of equation 6.8 values the abandonment option whilst the second two terms provide the discounted value of the live project if the firm must continue to operate forever. The reversal threshold is valid only once initial investment has occurred, and whilst the project remains active. If reversal becomes optimal at a lower abandonment threshold V_L, the solution will be valid for benefits above this threshold; $F_1(V)$ will be valid in the range (V_L, ∞).

The thresholds, V_H and V_L, together form part of the solution to the compound adoption decision faced by NICE. As with simple options, at the thresholds, value matching and smooth pasting boundary conditions link the values and derivatives of the two opportunities, enabling the complete solution to be derived.

The approval opportunity is given up at a cost of I in order to obtain the reversal opportunity. Therefore, at V_H the value of the approval opportunity must be equal to the value of the reversal opportunity less the cost (I) of creating that opportunity (equation 6.10). This gives the value matching condition for investment. In addition the incremental values of both opportunities for a small change in expected benefits must be equal (equation 6.11), the smooth pasting condition.

$$F_0(V_H) = F_1(V_H) - I \qquad \textbf{(EQN. 6.10)}$$

$$F_0'(V_H) = F_1'(V_H) \qquad \textbf{(EQN. 6.11)}$$

On altering the adoption decision, NICE regain the initial option to adopt the technology of interest, at a cost of E. At V_L the value of the reversal opportunity must equal the value of the approval opportunity less this cost (E) associated with reversing the decision (equation 6.12). Again the derivatives of the two functions must equate (the smooth pasting condition (equation 6.13)).

$$F_1(V_L) = F_0(V_L) - E \qquad \textbf{(EQN. 6.12)}$$

$$F_1'(V_L) = F_0'(V_L) \qquad \textbf{(EQN. 6.13)}$$

Rewriting the four boundary conditions using the values for the two options, F_0 (V) and $F_1(V)$, yields 4 equations in 4 unknowns; V_L, V_H, A_0 and A_1.

$$-A_0V_H^{\beta_0} + A_1V_H^{\beta_1} + \frac{V_H}{\delta} - \frac{C}{r} = I \tag{EQN. 6.14}$$

$$-\beta_0A_0V_H^{\beta_0-1} + \beta_1A_1V_H^{\beta_1-1} + \frac{1}{\delta} = 0 \tag{EQN. 6.15}$$

$$-A_0V_L^{\beta_0} + A_1V_L^{\beta_1} + \frac{V_L}{\delta} - \frac{C}{r} = -E \tag{EQN. 6.16}$$

$$-\beta_0A_0V_L^{\beta_0-1} + \beta_1A_1V_L^{\beta_1-1} + \frac{1}{\delta} = 0 \tag{EQN. 6.17}$$

The simplicity of the basic model does not transfer due to the highly non-linear nature of the equations, and a closed form analytic solution is not possible. Numerical methods must be employed to simultaneously solve the four equations to obtain values for the 4 unknowns.

Dixit (Dixit, 1989) uses this formulation to evaluate a proposed investment in a mine. He shows that a unique solution exists that is economically intuitive because the thresholds satisfy the natural progression $0 < V_L < V_H < \infty$. In the following section numerical methods are employed to solve the adoption and reversal decisions for a hypothetical technology assessment.

6.6 The option to approve drugs for epilepsy

6.6.1 Numerical example

In October 2003 NICE anticipates publication of their guidance from the wave six appraisal of newer drugs for epilepsy in adults and children. Assume that until approval is granted the drugs are not supplied by the health service. NICE have an option to approve which involves selecting one of three choices; reject the claim for approval immediately, approve immediately, or defer making the approval commitment until some future date. The reversal option is conferred when the option to approve is exercised. NICE can explicitly identify the pair of transitional approval and reversal decision thresholds referring to expected benefit per treatment, V.

Suppose current expected benefit per treatment is £8 evolving through time according to patients' capacity to benefit at 3% (α=0.03) with 10% volatility (σ=0.1). Discount rates of 2% for benefits and 6% for costs are applied, consistent with existing economic evaluation practice. The costs of granting approval and generating guidelines are initially set to £200 (I) with reversal costs at 50% of this (E =£100), the constant costs (C) borne by the health service per treatment are £7 (table 6.3). The values have been scaled downwards from likely true values in order to maintain ease of identifying a solution. With this in mind approval and reversal costs might be interpreted as average costs per patient treated.

Parameter	Base case parameter values
Drift in expected benefit (α)	0.03
Variance in expected benefit (σ)	0.1
Discount rate for costs (r)	0.06
Discount rate for benefits (δ)	0.02
Approval costs (I)	£200
Periodic costs of technology (C)	£7
Reversal costs (E)	£100
Risk neutral discount rate	0.05

Table 6.3. Base case parameter values for the compound option to approve and later reverse approval of a technology.

UTS Software, TK Solver release 4 is used to calculate the constants (β_0, β_1) and simultaneously solve the 4 equations (6.14 – 6.17) for the functional form parameters (A_0, A_1), and optimal thresholds (V_L, V_H). The package employs a modified Newton-Raphson iterative procedure to converge on the four solutions. For each iteration TK Solver uses either initial guesses (for the first iteration only) or previous solutions as inputs into the model. The problem is solved repeatedly until error terms are reduced below a given tolerance. Manually substituting the final solutions into the four equations confirms that an accurate solution has been identified. While accurate for parameter values within given ranges, the model is not sufficiently robust to solve for all combinations of inputs, particularly where high investment costs are required.

For the parameter estimates summarised in table 6.3 the approval (V_H) and alteration (V_L) thresholds were found to be £18.28 and £0.31 respectively (table

6.4). These values satisfy the intuitive constraint $0 < V_L < V_H < \infty$. The epilepsy drugs should be approved when expected benefit reaches £18.28. NICE would then exercise the option to reverse their decision only once expected benefit falls to £0.31. Although a seemingly large differential exists between the thresholds they should be interpreted with reference to current expected benefit (£8) and cost (£7) per treatment. Palmer and Smith (Palmer and Smith, 2000b) have previously shown that for reasonable parameter values an investment threshold can exceed investment cost by a factor of 3.7. The current example suggests periodic benefits should exceed periodic costs by a factor of 2.6 for approval to occur.

Variable	Estimate
β_0	1.53
β_1	-6.53
A_0	7.004
A_1	0.001
V_H	£18.28
V_L	£0.31

Table 6.4. Solutions for the compound option to approve and later reverse approval of a technology.

Given current expected benefit of £8, if NICE were considering the problem for the first time they would not approve the drugs. If the drugs had previously been approved, NICE would not reverse this decision.

The thresholds differ in structure and value to those derived under conventional investment theory. Equating marginal revenue with marginal cost suggests approval and reversal as expected benefits respectively rise above and fall below the £7 periodic cost. This leads to a single decision rule triggering exercise of both options, rather than the pair identified by real options analysis. The single decision rule introduces the potential for oscillation between approval and withdrawal decisions with very small changes in expected benefit or parameter estimates. This means possibly unnecessary investment and abandonment costs might be repeatedly incurred.

The real options approval threshold is significantly higher, and the reversal threshold significantly lower, than the £7 periodic cost of maintaining the option. This analysis therefore generates more conservative decision criterion for both types of option, reducing the possibility for oscillation in the optimal decision. The conservatism reflects the explicit handling of irreversibilities with real options modelling.

The result that thresholds are more conservative is not specific to the numerical example demonstrated here. Examining the investment threshold in the presence of perfect irreversibility (equation 6.5) helps illustrate the generality of the conservative criterion. V^* is related to costs and β. Equation 6.4 shows that β exceeds one; it follows that $\beta/(\beta-1)$ also exceeds one resulting in a decision rule V^* that necessarily exceeds costs. V^* exceeds C because immediate investment kills the option to invest at a later date. This is an implicit opportunity cost to investment, which is incorporated into real options analysis. When varying degrees of irreversibility are introduced, although the option to approve is lost, it can be regained later at some cost; the reversal cost. The implications of the degree of irreversibility are considered in the following section.

Parallel arguments are true for an abandonment option considered in isolation. When simple options are combined to form a compound option the respective decision thresholds become connected. The result is two conservative decision criteria.

The high value of V_H, more than twice the periodic cost, indicates reluctance of the decision maker to commit to an expensive and partially irreversible venture. Similarly the low value of V_L represents the decision maker's reluctance to incur expenses to abandon a venture that may later prove beneficial, especially when re-approval at a later date is also costly. Maintaining the status quo keeps future opportunities alive without having to incur sunk costs. Continuing to supply a drug even when it has been shown not to be cost-effective keeps open the option of later withdrawal or alteration to usage guidance without incurring large costs.

The boundaries (V_L, V_H) define a region of inertia within which current expected (£8) benefit falls. Within this area, if approval has previously been granted the drugs will continue in circulation, but if approval has not yet occurred, or has been withdrawn, the drugs shall remain unapproved. This provides an intuitively reasonable explanation for observed behaviours. For instance decision makers may not react immediately with changes in decisions following new information on expected benefit. This may indicate that expected benefit has not altered sufficiently to reach a decision threshold.

Given knowledge of whether approval has yet been given, current expected benefit, and the direction and extent of change over time, NICE can assess the likelihood of future approve or retraction, and anticipate future need for announcements, guidance, and improved information. For instance, suppose epilepsy drugs have not yet been approved, expected benefit is £14, and analysts anticipate a rise over time due to more accurate drug targeting. NICE should defer approval, but predicting an improvement in cost-effectiveness, should plan to review evidence after some period of time. Larger values of α indicate quicker arrival at the required threshold and suggest the need for earlier review.

When evaluating multiple technologies whose evidence is insufficient, expectations for the future can be used to prioritise the timing of reviews and appeals. Real options analysis can be used to justify the timing of re-examinations of current evidence, reducing the likelihood of ad hoc reviews set at future dates with no apparent explanation.

NICE may be concerned about differentiation among patient groups with contrasting characteristics and risk factors. Existing guidance has frequently made such distinctions. For instance, April 2001 guidance for treatment of patients who have experienced a myocardial infarction (MI) identifies three groups of patients; those with prior MI who do not have heart failure, those with prior MI who have diabetes, and those with prior MI who do have heart failure. The precise guidance depends on which group an individual falls in to.

Within the real options model individual characteristics may cause patient groups to differ with respect to their current expected benefit, drift and volatility over time. Guidance issue may even be more irreversible for some groups than others. A group of patients who, in the public perception, are believed to benefit greatly are likely to have greater political irreversibility costs (E). Due to interactions within the model this raises the initial investment threshold. Such differences generate contrasting decision thresholds between groups, allowing guidance to be tailored to a sub-group of interest.

Similarly, every technology considered will have unique characteristics. Differences may exist in current expected benefits that evolve through time, with their associated drift and volatility, as information on disease incidence, prevalence and cost-effectiveness becomes available. Irreversibility in the form of sunk costs of approval and withdrawal may vary between technologies, in addition to ongoing treatment costs. Each technology will, therefore, have exclusive approval and reversal threshold that depend on the characteristics of the technology and the patients receiving treatment.

Finally NICE may be interested in the arrival of trial based data that could impact on current expected benefit or its evolution. If a trial is known to be reporting soon and the release of data is anticipated to reduce uncertainty, these effects can be incorporated into the model and their effect on the decision thresholds observed. Alternatively NICE may choose to defer the approval decision pending release of additional information.

Through this variety of mechanisms real options analysis can contribute to understanding and evaluating decisions faced by NICE with respect to new and existing health care technologies.

6.6.2 Assessing the impact of irreversibility

Existing economic evaluation techniques make implicit assumptions with regards to the irreversibility of decisions. Actions are usually considered irreversible in the sense that upfront costs are sunk, and actions to alter or reverse decisions are rarely considered. Real options analysis highlights irreversibility and makes assumptions explicit, opening them to academic debate. Analysis of simple investment and abandonment options assume perfect irreversibility. Analysis of compound options, which examine interrelated sequential actions, allows varying degrees of irreversibility to be considered. In the current example, irreversibility enters the analysis through three factors; the existence of the reversal option, which allows the initial decision to be reversed, sunk costs of making the initial decision, and sunk costs incurred when the reversal option is exercised.

To examine the impact of being able to reverse a decision, the investment threshold given partial irreversibility, V_H can be compared to the threshold generated in a model of complete irreversibility V* (equation 6.5)[35].

$$V^* = \frac{\beta}{\beta - 1} C \qquad \textbf{(EQN. 6.5)}$$

From table 6.4, the β applying to the simple adoption option, β_0, is 1.53. β/(β-1) is therefore given by 2.89 suggesting the perfectly irreversible approval threshold is reached when expected benefits exceed costs by a factor of 2.89. Given a cost level of £7, approval is not announced until expected benefits reach £20.23, £1.95 greater than the partial irreversibility model (V_H = £18.28). When analysing technologies with greater irreversibility NICE are therefore advised to be more conservative in their initial approval recommendation.

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[35] Comparison of option values under complete and partial irreversibility may also seem appealing. However, this comparison requires using only a subset of the partial irreversibility model because option value depends the active/idle status of the firm. This is inappropriate due to synergies existing between the components. Since the approval threshold for the partial irreversibility model incorporates influences from the reversal decision, this latter comparison is valid.

Extensive irreversibility may surround the approval decisions of national programmes that have high public profiles such as issuing free contraceptives or advising regular cervical smear testing; approval or even the existence of either programme might be seen as irreversible. The higher approval threshold causes NICE to be more cautious, deferring for longer periods of time when analysing such programmes. When prioritising potential treatments, real options analysis lends greater support to investments with potential for reversibility.

The sunk cost irreversibility metrics, I and E, also affect the decision-making thresholds. Increases in E and I amplify irreversibility, creating inertia against exercise. Dixit and Pindyck (Dixit and Pindyck, 1994) illustrate how this raises the investment, and reduces the reversal thresholds, widening the region of inertia. In the numerical example presented here doubling the approval cost from £100 to £200 increases the approval threshold from £12.51 to £18.28, and reduces the reversal threshold from £0.32 to £0.31. An effect is felt on the reversal threshold since exercising the option to reverse recreates the initial approval option and so allows the possibility of re-approval. This requires incurring I for a second time. Altering reversal costs has significantly less impact on both thresholds. This is predominantly because, if incurred at all, E is faced in the future. Discounting effects within the model cause the two types of cost to affect their 'own' threshold more strongly, and cause more immediate effects to be greater. Table 6.5 summarises influences on the thresholds.

Influence	Effect on V_H	Effect on V_L
Ability to reverse	Negative	-
I	Positive	Negative
E	Positive	Negative
C	Positive	Positive
σ	Positive	Positive

Table 6.5. Factors influencing the decision thresholds for the compound option to approve and later reverse approval of a technology.

Explicitly recognising and analysing the effects of irreversibility can contribute to decision making within NICE. Suppose NICE is considering approving one of two substitute drugs. Having been prescribed, withdrawal of compound A is associated with extensive side effects that make reversing the approval decision costly, both on an individual level and politically. Compound B is initially more expensive to approve and prescribe due to training costs required by staff providing the medication. The relative attractiveness of the two compounds is not immediately apparent. Real options analysis can be used to assess relevant sources of irreversibility; informing immediate adoption decisions as well as longer run strategies for technology adoption, collection of additional information, and prioritising areas where actions to reduce irreversibility might be useful.

6.7 Conclusions

This chapter has structured technology approval decisions by NICE as exercise of a set of compound options, analogous to a portfolio of financial call and put options. For contingent choices to be analysed in this way exercise of one option must automatically confer a related choice. In this case technology approval confers an option to renege, altering the initial guidance. Both the approval and reversal decisions are characterised by the same underlying sources of uncertainty, some degree of irreversibility, and an ability to be deferred.

The focus of this application has been the implications for health care decision making of incorporating option pricing techniques, specifically attitudes towards and methods for incorporating, partial irreversibility. This chapter has used dynamic programming and numerical techniques to solve the approval problem for two distinct, yet complementary, decision criteria. Although successful for the range of base case parameter values used, the iterative solver employed is not robust to large changes in these values. Further work is required to improve the power of the solution procedure and mathematical tractability.

Conventional investment theory has a single investment / disinvestment threshold identified by marginal revenue equating to marginal cost. Within a volatile economy this can lead to successive and potentially unnecessary investment and disinvestment decisions. Real options analysis recognises sequentially linked investment and disinvestment decisions and identifies two complimentary decision thresholds generating a region of inertia that reduces the potential for oscillating decision making. The criteria are unique to the technology of interest for the patient group under consideration. Within the bounds of this region inactive projects remain silent and active projects continue in operation. Dixit (Dixit, 1989) has argued that such inertia, which might be viewed as a cause of hysteresis and evidence of a sluggish economy, is actually the result of firms' dynamic and strategic thinking.

Applying real options analysis has emphasised the need for explicit discussion of irreversibility. In practice health care projects display varying different forms and degrees of irreversibility. NHS infrastructure projects involve heavy up front sunk expenditures and research efforts require initial spending in addition to prolonged commitment. Surgical operations often cannot be reversed at all and political costs may prove an important consideration in many strategy decisions. Outside of the NHS pharmaceutical companies may face irreversibilities linked to development and clinical testing of new drugs, and private health insurance companies face difficulty reversing previous commitments to finance certain treatments. Irreversibility has not yet received attention within health economics literature in proportion to its importance in decision making. Real options analysis may help to redress this problem.

The understanding of irreversibility provided by real options analysis can be used to influence current actions, not only with respect to the decision of interest but also with respect to influencing future irreversibilities. Actions might be taken today on the basis that they reduce future costs of reversing decisions, rather than because of high expected returns. For instance, the political costs of reversing an approval decision might be reduced by action taken now to promote the idea of temporary approval pending additional information. In the case of insufficient information, contracts might be drawn up such that the company submitting a drug for approval agrees to incur reversal costs should temporary approval be granted, and this turns out to be a poor decision[36].

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[36] NICE have, in essence, embraced this idea in their guidance for treatment of patients with Multiple Sclerosis. An evaluation of current treatments did not demonstrate cost-effectiveness. NICE/Department of Health have therefore approved the drugs but have set up a risk sharing scheme. This scheme aims to reduce the costs to the NHS should treatments fail to be sufficiently cost-effective. Payments to the pharmaceutical companies are reduced if realised average cost per

On a broader perspective, advocating temporary and flexible nursing contracts may reduce the irreversibility of increasing staffing during winter months when pressure is greatest. Upfront thought about the sources and impact of irreversibility can help avoid irreversible situations being encountered, promote action to reduce irreversibilities, and shape longer run decision strategies.

Additional work is needed in this area to assess the suitability of applying compound options analysis in practice. Whilst every effort has been made to create an intuitive example that encompasses real world effects, bringing empirical data into such a theoretical model will inevitably create difficulties. Perhaps the greatest challenge is to collect sufficient data at regular intervals to provide reliable estimates for the mean and variance of expected benefit and its progression through time.

Compound options analysis has been applied here to address partial irreversibility within the health care arena. There are many broader issues for which this theory may be relevant. In essence compound option analysis is applicable to any situation in which multiple decisions interact sequentially. This is the case for staged development of new hospitals or where building a general ward creates an option to treat increasing numbers of patients. Adoption of new technologies, which require specialist training, may create options to switch between similar technologies requiring comparable skills, or upgrade to newer technologies as they become available.

To conclude, this chapter has considered the application of compound options analysis to the health care sector to address partial irreversibility. This has required an amalgamation of the underlying principles of previous chapters that have considered call and put options independently. In this case study the compound option to approval and later reverse approval of health technologies has been analysed and decision criteria for the two complementary exercise

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Qaly exceeds some pre-agreed level. This measure acknowledges and takes account of irreversibilities potentially faced by NICE in their decision to approve. Details of the guidance and the risk sharing scheme are available on the NICE website: http://www.nice.org.uk/article.asp?a=27673 decisions generated.

Chapter 7. The option to wait for more information: option value and the value of information.

7.1 Introduction

Methods of incorporating uncertainty into economic evaluation of health technologies have been debated for some time. Techniques to help understand, present and evaluate uncertainty have included single, multi-way and probabilistic sensitivity analysis, scenario and threshold analysis, and the use of confidence intervals and cost-effectiveness acceptability curves (Briggs and Gray, 1999). Value of information analysis has developed as a tool that places a value on uncertainties within a model and has been proposed as a way to prioritise efforts to reduce uncertainty. The expected value of perfect information (EVPI) defines a maximum willingness to pay for research efforts that provide information relevant to the decision.

Real option theories consider decisions under uncertainty and are relevant when choices can be deferred, and deferral is associated with learning more about uncertain variables. Analysing the opportunity to wait for information as an option to defer, allows option premium (difference between option value and intrinsic value) or the incremental value of deferral, to be estimated. This places a numerical estimate on the value of waiting for additional information. Option premium is therefore a form of value of information that can be compared to the expected value of perfect information. This may have implications both for the way uncertainty is perceived and the way research budgets, aimed at reducing uncertainty, are allocated.

This chapter explores the relationship between these two measures of value of information. Section 2 considers existing work on value of information in economic evaluation and develops a stylised example concerning information gained from a clinical trial to illustrate relevant concepts. Section 3 discusses deferral as a way of gaining information, and estimates the incremental value of deferral. Section 4 makes the distinction between actively seeking and independently observing information and identifies a relationship between option premium and the expected value of perfect information. The analogy between real and financial options is reiterated in section 5 where a combined Brownian motion / Poisson information arrival function is created to model the option to wait for additional information. Applications to health care and implications for decision making are examined. Section 6 concludes.

7.2 Value of information in economic evaluation

When a decision is made in the presence of uncertainty there is some possibility that an alternative, other than that with the greatest expected net benefit, offers a greater payoff retrospectively. Information collected prior to the decision being made can improve the probability of making an ex-post optimal decision. Uncertainty is therefore costly, and information is valuable for this reason. In the extreme, perfect information on parameters of interest may be sought.

The expected value of perfect information (EVPI)[37], measures the value of information by considering the probability of making a sub-optimal decision (based on prior information) and the implications of doing so. EVPI is estimated by calculating the difference in expected payoff between a decision made with perfect information and one made in the presence of uncertainty. Discussion of the concept of EVPI and its usefulness within health care have developed from statistical decision theory (Raiffa and Schlaifer, 1959; Pratt et al., 1995). Lapin (Lapin, 1994) gives a non-technical introduction both to the idea and calculation of EVPI. In practice, value of information analysis has been applied to a variety of areas including engineering (Howard, 1966) and food safety (Hammitt and Cave, 1991).

Clinical trials are designed to improve current evidence concerning effectiveness, providing greater information for clinicians, GP's and policy makers faced with

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[37] EVPI is mathematically equivalent to, and is sometimes referred to, as expected opportunity loss.

choosing between competing technologies. Whilst gathering information is beneficial, it is also costly; trials and research and development consume large proportions of research budgets. EVPI defines the maximum potential improvement in payoff available as a result of improved information and, therefore, places a bound on the achievable benefit from collecting evidence. As a result EVPI has been used to identify an upper boundary on the willingness to pay for research activities within health care (Claxton and Posnett, 1996). EVSI (expected value of sample information) has likewise been used to define the potential benefits from clinical trials that sample effectiveness for a subset of the population (Claxton and Posnett, 1996).

The EVPI concept has been increasingly applied to methodological work within health care, both as a form of sensitivity analysis and as a way of prioritising research proposals. Felli (Felli and Hazen, 1998) discusses the relative merits of various measures of decision sensitivity including probabilistic sensitivity analysis, and introduces EVPI as a possible alternative. Three case studies were used to show that EVPI supersedes the other measures for suitability in assessing the impact of uncertainty, and tractability when multiple sources of uncertainty exist. The author also mentions EVPI as an upper limit on the value of information gained from sampling or diagnostic testing.

Claxton (Claxton, 1999) argues the irrelevance of sensitivity analysis for current decision making favouring comparison of expected values based on prior information. EVPI and EVSI are then reserved for the complementary decision of whether additional information is required. From a policy point of view the value of additional information becomes an aid to prioritising future research agendas.

In addition to these predominantly theoretical papers, an increasing number of authors have estimated value of information[38] (VOI) in practice. Bartell (Bartell et al., 2000) examined specific risk management applications of genetic biomarkers for patients with occupational Chronic Beryllium Disease (CBD),

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[38] Since EVPI is considered an unattainable theoretical construct, work has developed around 'value of information'. This considers variables on which information might feasibly be gathered.

and Dakins (Dakins et al., 1996), has estimated EVPI and EVSI for environmental remediation efforts to reduce polychlorinated biphenyl sediment contamination.

Within the health care sector Meltzer (Meltzer, 2001) considers the decision to treat prostate cancer comparing three strategies; watchful waiting, radical prostatectomy and the optimal decision with perfect information on the average rate of progression. Melzer calculates that perfect information improves the expected value of treating each patient by US $6400 compared to making an optimal decision with prior information. Aggregating to estimate population EVPI yielded an estimate of US $21 billion, which far exceeds the cost of a proposed experiment that provides information on the likelihood that cancer is aggressive. Value of information analysis has also been used in other areas including the decision to adopt a new pharmaceutical for the treatment of Alzheimer's disease (Claxton et al., 2001).

The classical concept of EVPI can be illustrated through a hypothetical example. The National Institute for Clinical Excellence (NICE) may find it useful to estimate value of information when assessing new and existing technologies for use within the NHS. Suppose a new technology has been submitted for assessment and NICE must make an approval or rejection decision. The decision is assumed to be fully irreversible. Once approved the technology confers uncertain monetary benefits each period in perpetuity. For simplicity the decision is characterised only by first order uncertainty, which is resolved by a trial that reports towards the end of the current period. If an improvement in cost-effectiveness is demonstrated expected benefits per period are £1000. If a reduction is shown, benefits per period are £40. The prior belief is a 0.5 probability that the trial will improve (or deteriorate) periodic monetary benefit. Upfront irreversible costs of approval are assumed to be £2000 (figure 7.1) encompassing the costs of generating and disseminating guidelines.

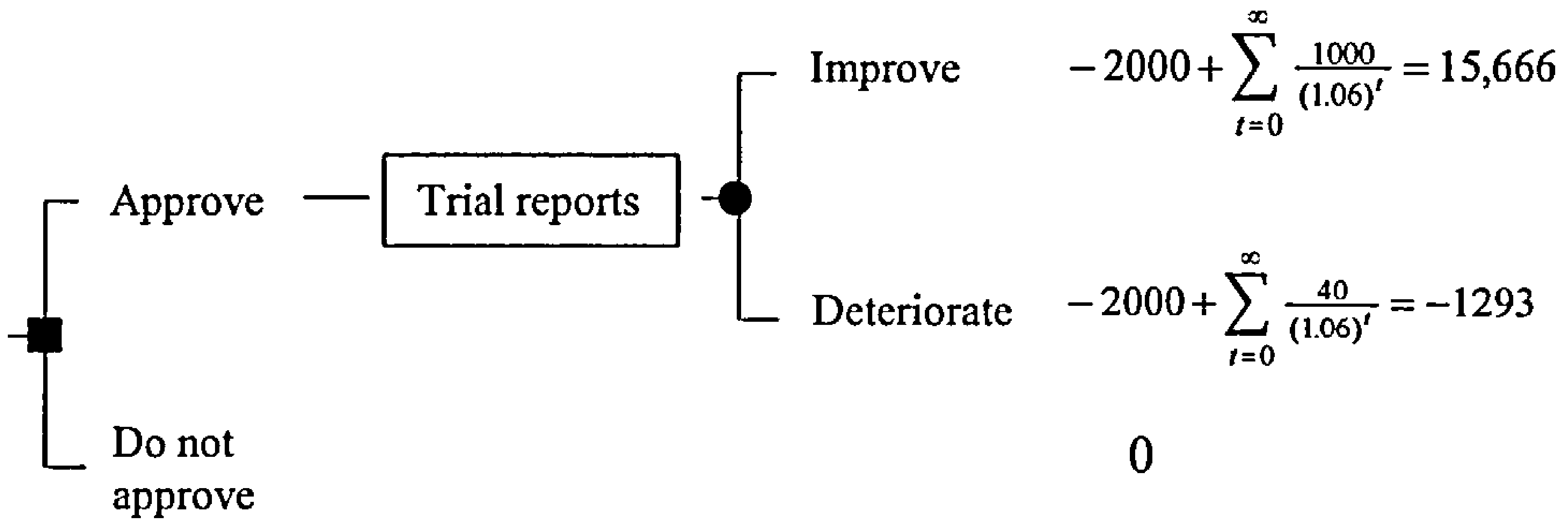

Figure 7.1. The decision to approve a technology

With a discount rate of 6% the optimal decision is to adopt the technology with a net benefit of £7187 (equation 7.1).

$$\text{Net benefit} = -2000+\sum_{t=0}^{\infty}\frac{0.5*1000+0.5*40}{(1.06)^t} \qquad \textbf{(EQN. 7.1)}$$

-2000+9187

7187

EVPI is calculated by considering immediately, the best retrospective decision. In this case approval should only be granted in the event that an improvement in cost-effectiveness occurs. The difference in payment between this and expected net benefit is EVPI. The classical approach to value of information assumes no delay in receiving information, and in this example additional information provided by the trial would improve expected payoff by £646 (equation 7.2). This represents the decision-makers maximum willingness to pay to obtain the research results immediately.

EVPI = Payoff under certainty – Payoff under uncertainty

$$0.5\left[\sum_{t=0}^{\infty}\frac{1000}{(1.06)^t}-2000\right]-\left[-2000+\sum_{t=0}^{\infty}\frac{0.5*1000+0.5*40}{(1.06)^t}\right] \qquad \textbf{(EQN. 7.2)}$$

7833-7187

646

Although simple, using a single source of first order uncertainty, this stylised example illustrates relevant concepts for comparison with a real options model. The approval decision is characterised by uncertainty and irreversibility and can be considered an option if immediate action can be deferred. The option to defer approval is considered below.

7.3 Option value as a value of information

Exercising the option to approve a technology is akin to an American call option on a dividend paying stock. Taking advantage of the ability to defer allows information on sources of uncertainty to be gained during the waiting period. This can be incorporated into assessments about whether irreversible decisions with uncertain outcomes should be pursued. In that VOI and option pricing both examine the impact and value of improved information on current decision making, they are alike.

Intrinsic value is the benefit associated with immediate action under an option pricing approach. Option value is the benefit associated with a deferred decision made in light of new information available during the period of deferral. The difference, option premium, is the incremental value of being able to defer and gather information, and equates to a value of deferred information.

Suppose the National Institute for Clinical Excellence (NICE) face an option to defer approval for one year. In the intervening period the trial discussed previously will publicly report additional cost-effectiveness evidence revealing all information relevant to the decision. The probability and absolute payoff associated with improved or deteriorated cost-effectiveness remain the same. NICE must estimate intrinsic value and option value in order to make a decision (figure 7.2).

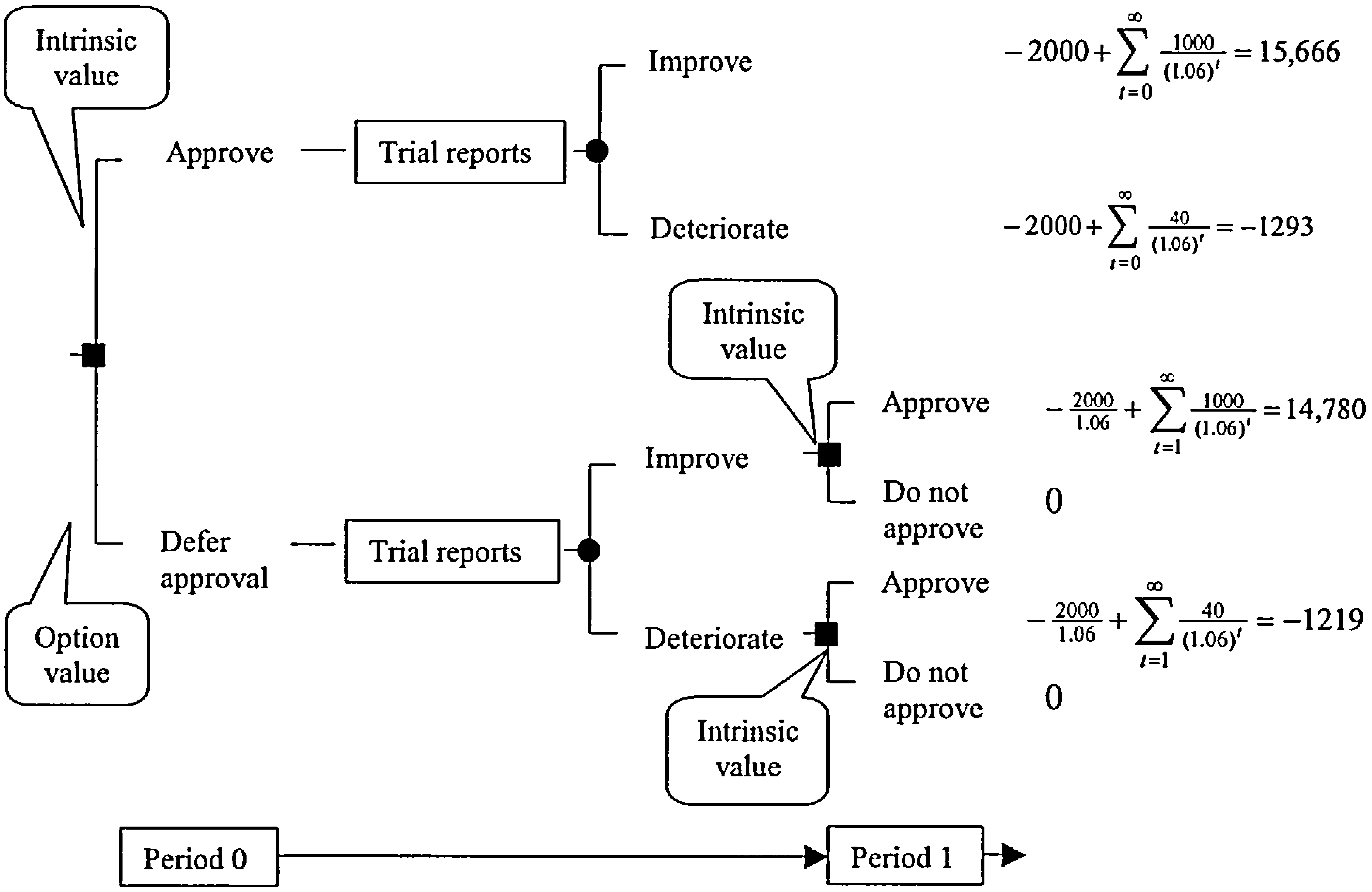

Figure 7.2. The decision to approve or defer approval of a technology

If immediate approval occurs the irreversible costs are incurred upfront. Combining this with the 0.5 probability of receiving beneficial or detrimental cost-effectiveness evidence gives an intrinsic value estimate equal to net benefit under a traditional approach[39].

$$\text{Intrinsic value} = \quad -2000+\sum_{t=0}^{\infty}\frac{0.5*1000+0.5*40}{(1.06)^t} \qquad \textbf{(EQN. 7.3)}$$

$$-2000+9187$$

$$7187$$

If deferral is chosen, the trial reports prior to the decision being made. In this case irreversible costs and potential benefits are both delayed for one period. Real options analysis must weigh the relative gain from information against the gains and losses from delayed action. Once the trial has reported the decision maker can assess the relative desirability of approving given the additional trial

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[39] Intrinsic value = max(net benefit, 0). If net benefit is negative no action would be taken and intrinsic value would be 0. Net benefit and intrinsic value only equate when net benefit is positive.

based information. On the exercise date the option to approve is exercised only if intrinsic value is positive. If the trial reports improved cost-effectiveness the optimal action is to approve (£14,780). Conversely, if the trial reports poor cost-effectiveness the optimal action is not to approve (£0) (see figure 7.2). Following deferral, approval will only be granted if the trial demonstrates positive results. Current option value providing the expected value of deferral is given by:

$$\text{OV} = 0.5\left[\sum_{t=1}^{\infty}\frac{1000}{(1.06)^t}-\frac{2000}{1.06}\right] \quad \textbf{(EQN. 7.4)}$$

$$0.5[16667-1886.8]$$

$$7390$$

The difference between option value and intrinsic value, option premium, gives the incremental value of deferral, and places a value on the information revealed during the waiting period;

$$\text{Option premium} = \text{Option value} - \text{Intrinsic value}$$

$$0.5\left[\sum_{t=1}^{\infty}\frac{1000}{(1.06)^t}-\frac{2000}{1.06}\right]-\left[-2000+\sum_{t=0}^{\infty}\frac{0.5*1000+0.5*40}{(1.06)^t}\right]$$

(EQN. 7.5)

$$7390-7187$$

$$203$$

Option premium may be interpreted as the maximum willingness to pay to gain information available during deferral. In this case deferral is optimal while the cost of observing information remains less than £203. When waiting provides perfect information on all sources of uncertainty relevant to the decision, as in this instance, EVPI and option premium both value obtaining perfect information. Since the two VOI estimates are based on the same underlying principles, intuition suggests they should equate. This example demonstrates a situation in which a difference exists. Deeper consideration reveals the reasons for this difference.

EVPI is the value associated with having perfect information available instantaneously (at t=0). Option premium differs from EVPI due to timing effects introduced into the decision tree by considering deferral. The real options framework ensures that option premium accounts for both the way in which, and time at which, information becomes available. In addition, the effects of delayed receipt of benefits and spending on sunk costs are incorporated. Since the negative influence (deferred benefits) dominates, and receipt of perfect information is delayed, option premium (£203) is less than EVPI (£646). Without deferral and discounting influences in the calculation of option premium, the two estimates of value of information coincide. (The same is true if EVPI is adjusted for delayed arrival of information)[40].

Some authors, outside of the health economics arena, have discussed theoretical circumstances and identified examples where option premium is equivalent to EVPI. This occurs particularly within 'consumption type options' where a consumer has an option to visit a site of outstanding natural beauty. In such examples the key sources of uncertainty are usually the individual's own preferences and whether the site still exists on the exercise date. For an individual with an option to visit a threatened natural park, deferral reveals both whether the park still exists, and whether the individual prefers to visit on the day of decision making. Information on the two sources of uncertainty is fully revealed, leading EVPI and option premium to equate if timing effects are accounted for. Smith (Smith et al., 1983) and Greenley (Greenley et al., 1981) have independently estimated option value for water quality improvements.

Within a similar context Conrad (Conrad, 1980) has claimed that quasi-option value is equivalent to the expected value of information and that option value

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[40] The difference between EVPI and OP resulting from timing effects raises questions concerning the validity of using EVPI, which assumes information is instantaneously available, to assess the relative benefits of competing research proposals. Evidence from research is often not available for some time. When EVPI or EVSI is used as a willingness to pay for information and there are competing projects that might provide relevant evidence but at different times, presumably our willingness to pay for evidence should be adjusted for the expected timing of information arrival? Whilst relevant to the research priorities debate, and raising serious issues concerning the methodological interpretation and usefulness of VOI, this is a topic for future study and such questions are not the primary concern here.

equates to the expected value of *perfect* information[41]. This is intuitively sound in the consumer framework where deferral reveals complete information about preferences and future supply. Conclusions with respect to the relation between EVPI and option premium hinge on beliefs about sources of uncertainty and assumptions regarding resolution of information through time.

Although EVPI and option premium can coincide this is not necessarily, or even usually, the case. The example considered above of NICE approving health related technologies defines a special case in which deferral provides perfect information about all sources of uncertainty relevant to the decision. The following section explores the more general case in which deferral provides only partial information, calculating the expected value of improved, rather than perfect information.

7.4 Actively seeking and independently observing information

Deferral may reveal information on factors such as disease incidence and prevalence, whether competing drugs become available, or on an individual basis, disease progression. Cost-effectiveness analyses include variables such as efficacy, and trial based cost information for which data might only be obtained through positive actions. For instance, NICE may have felt there was insufficient information to make an immediate decision and may not have expected a trial to report further evidence in the near future. In this case deferral alone may not confer sufficient information for a decision to be made. Rather than simply deferring to benefit from exogenously available information revealed over time, NICE may consider taking positive steps to actively improve information. For instance, they may think about commissioning a trial to improve evidence.

The extent of information revealed over time in practice will depend on the nature of uncertainty impacting on the decision and costs associated with collecting information. Prices of drugs, interest rates, actions of competitors introducing substitute technologies, some costs, and disease progression can be

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[41] Chapter 2 examines the difference between these interpretations of option value.

reasonably well observed through time as they are revealed independently of any actions regarding the decision of interest. Evidence on factors such as effectiveness within a given population subset, or side-effects of a novel drug can only be discovered through specific, and usually costly, activities that are endogenous to the decision of interest.

Whilst EVPI refers to complete information on both types of variable, option premium is relevant for valuing information on variables that evolve stochastically through time. Uncertain variables may be categorised according to whether information must be actively sought, or simply observed. Where at least some variables are active, deferral cannot reveal complete information. In these cases option premium is necessarily less than EVPI[42]. More accurately option premium (OP) becomes a subset of EVPI (figure 7.3). This distinction creates cause to clearly define willingness to pay for information gained from different sources: option premium defines a maximum willingness to pay to observe exogenous information sources such as literature reviews, meta-analyses, or patient observations and test[43].

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[42] This distinction of value of information for different types of variable is similar to calculating partial EVPI of variables of interest (see (Fenwick et al., 2000)), although with option premium variables are purposefully categorised according to whether information on them becomes available though time.

[43] When there are no synergies or correlations between active and passive variables, the difference EVPI-OP, or active value of information (AVOI), gives a willingness to pay for positive actions including commissioning generic research, specific safety and efficacy trials, and cost-effectiveness analyses.

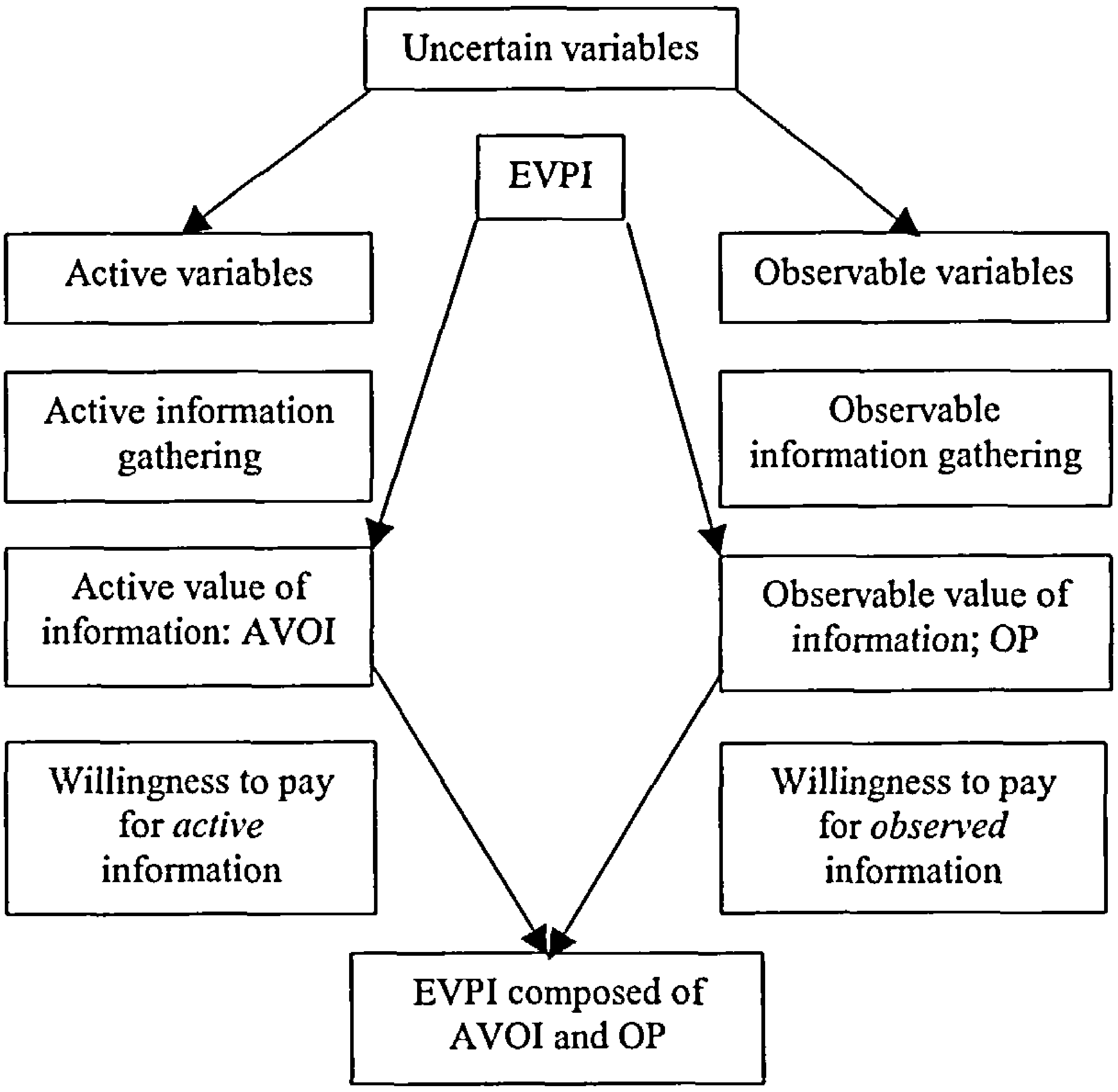

Figure 7.3. Distinguishing actively sought and exogenously observed information

Similar observations with regard to value of information and option value have been made previously outside of the health economics arena. Hanemann (Hanemann, 1989) has talked about option premium being "distinct from but bounded by value of information in the overall problem". Fisher and Hanemann (Fisher and Hanemann, 1990) consider option value as a conditional value of information (conditional on retaining an option to preserve or develop) and view expected value of perfect information as an unconditional value of information, and Gersbach (Gershbach, 1997) makes the distinction between actively sought information and uncertainty that is resolved only by the passage of time, using passive versus active terminology.

For any given decision, if immediate action is optimal option premium will equal zero and EVPI will comprise active value of information only; there is no incentive to wait. When waiting is preferable, option premium affects our attitudes towards data collection and should be explicitly estimated to help inform both the initial adoption decision and the complementary decision of whether to gain additional information. The following section derives a model of stochastic information arrival.

7.5 A model of information arrival

7.5.1 The model

Uncertainty plays an important role in the decision concerning when, and indeed whether, to approve the drug, and whether to commission research that improves information. Irreversibility also surrounds the approval decision: approval is a costly activity requiring dedicated time, and costs of generating and disseminating guidance. Potential political ramifications, especially if the approval decision is against popular opinion, or turns out to be poor in the light of mounting evidence, provide further sources of irreversibility. The ability to defer is inherent in any decision to approve a new or existing technology. The presence of these characteristics confirms the appropriateness of modelling the opportunity to defer approval as a real option.

Whilst information on uncertain variables may evolve continuously, such as with prices or disease progression, sporadic events may occur that generate one off, discrete shocks in the information set. These events result in discontinuous changes in expected payoff. Shocks may include interim results of a trial becoming available, a patient becoming unfit for surgery, infections following surgery, or launch of a novel drug that affects cost-effectiveness of an existing compound. Combining a Brownian motion process with a Poisson arrival process enables information to evolve in this manner.

Suppose NICE is considering approval of a new drug used to treat a specific disease. Expected benefit evolves continuously due to changing incidence and prevalence with drift α and variance σ^2. The possibility of a trial reporting means there is some probability λdt each period that V will change as a result of the Poisson arrival, causing an increment of dq. Expected benefit from immediate treatment (V) follows a combined evolutionary process.

$$\frac{dV}{V} = \alpha dt + \sigma dz + dq \qquad \text{(EQN. 7.6)}$$

The mean arrival rate, λ, varies between 0, representing no event or trial, and 1 representing a trial reporting each time period. $1/\lambda$ indicates the mean time between arrivals[44]. If a trial is expected once every three years ($1/\lambda = 3$) the mean arrival rate is 1/3. When an event occurs q changes by some proportion ϕ[45] ($0 \leq \phi \leq 1$) (equation 7.7). If $\phi > 0$ stochastically arriving trial results have a positive influence on V, the opposite occurs if $\phi < 0$. If $\phi = 0$ events have no impact and the combined process reverts to Brownian motion. Following an event, V resumes the Brownian motion evolutionary process, until another occurs.

$$dq = \begin{cases} 0 \text{ with probability: } (1-\lambda)dt \\ \phi \text{ with probability: } \lambda dt \end{cases} \qquad \text{(EQN. 7.7)}$$

Given this specification the average rate of change in expected benefit over any time period is $\alpha + \lambda\phi$. Increasing either the likelihood or impact of an event alters the rate of change in V. Incorporating the Poisson element also has an impact on the variance of V. Although variation is mostly due to the continuous evolution, when an event occurs, it has a large impact. Dixit and Pindyck (Dixit and Pindyck, 1994) show that variance consists of two parts; one resulting from the Brownian motion influence when no event occurs, and the other from the Poisson influence.

$$\text{Variance(V)} = \sigma^2 V^2 dt + \lambda \phi^2 V^2 dt$$

When considering this formulation Dixit and Pindyck (Dixit and Pindyck, 1994) used a version of Ito's lemma specifically for finding the differential of the

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[44] λ is assumed fixed reflecting the idea that NICE would have some expectation governing the arrival time of information although λ may be incorporated as a stochastic variable if there is no evidence concerning information arrival.

[45] In the following model ϕ is assumed to be a fixed proportion of expected benefit although in reality ϕ may be a random variable.

combined evolutionary process to identify a partial differential equation that must be satisfied by the value of the investment opportunity, F(V)[46]:

$$\tfrac{1}{2}\sigma^2 V^2 F''V + (r-\delta)VF'(V) - (r+\lambda)F(V) + \lambda F[(1-\phi)V] = 0$$

For action to occur at a finite point in time the growth rate of uncertain benefits α, must be less than the rate r at which they are discounted. The difference r-α is given by δ and represents dividend type payments. F'(V) and F''(V) represent the first and second derivatives of F(V) with respect to V. By satisfying the PDE, F(V) conforms to the intuitive constraint that the value of the investment opportunity must equal the maximum of the continuation (value from deferring) or stopping value (value from exercising). The partial differential equation is subject to an absorbing barrier, value matching condition and smooth pasting condition[47]. Finding F(V) requires solving the PDE subject to the boundary conditions. To comply with the absorbing barrier F(V) takes the form $F(V) = AV^{\beta}$ where β is the solution to a non-linear equation:

$$\tfrac{1}{2}\sigma^2 \beta(\beta-1) + (r-\delta)\beta - (r+\lambda) + \lambda(1-\phi)^{\beta} = 0 \qquad \textbf{(EQN. 7.8)}$$

Numerical methods are required to find β but once achieved, the parameter A can be estimated and the immediate action threshold, V*, identified. Option value and option premium, both at the critical threshold and the current value of V, can also be determined. Vonnegut (Vonnegut, 2000) has used similar combined evolutionary methods to assess investment in emerging economies. This study used Poisson events to reflect structural economic changes, allowing events to impact both positively and negatively on expected value.

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[46] This is the stochastic equivalent (accounting for the Poisson event) to the deterministic case presented in chapter two (equation 2.15) where the value of the investment opportunity is maximised over time.

[47] The boundary conditions are the same as those of the stand-alone Brownian motion model (equation 2.20).

7.5.2 Numerical example

The key uncertainties within the model are whether and/or when a trial reports evidence and the effect this has on cost-effectiveness. Assume that the trial, on publication of results, demonstrates a fall in the cost-effectiveness of the compound under consideration by NICE, causing a *downward* jump in payoff. The Poisson event then has a negative impact on the evolutionary process defining cost-effectiveness.

$$\frac{dV}{V} = \alpha dt + \sigma dz - dq \qquad \textbf{(EQN. 7.9)}$$

In particular, assume the abrupt Poisson jump causes expected benefit to fall to zero, reducing payoff by 100% (ϕ=1). Due to zero being an absorbing state in the Brownian motion process expected benefit remains at zero[48]. This renders the option worthless. In this case λ defines a maximum ability to defer before the option becomes worthless[49]. In reality the effects from the trial would not be known and there would also be uncertainty on prior parameter estimates and implications for posterior estimates where Bayesian analysis is used.

The assumptions serve to simplify the analysis allowing analytic solutions to be obtained, and although seemly restrictive, numerous health economic applications conform to such a specification. Patients participating in a watchful waiting regime usually have some disease whose progression evolves continuously. Adverse events may occur that render immediate treatment less effective. For instance, the patient may experience some co-morbidity. In the extreme a patient may become unfit for surgery, making the value of immediate treatment, and thus the option, zero.

Further examples include a firm with an option to market a drug whose price will evolve continuously. The Poisson event 'a competitor releases a dominant drug'

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[48] This is would not necessarily be the case for alternative evolutionary processes.

[49] This formulation effectively allows an exercise date to be incorporated in to the perpetual Brownian motion diffusion process.

may make the payoff from marketing the current drug fall to zero. Coma patients also conform to this model. The uncertain events that a patient either dies naturally or regains consciousness render the option to defer removal of support worthless because this is no longer a relevant alternative.

In the case where $\phi=1$ Dixit and Pindyck show that equation 7.8 simplifies to a quadratic, from which β can be determined;

$$\beta=\tfrac{1}{2}-(r-\delta)/\sigma^2+\sqrt{\left[(r-\delta)/\sigma^2-\tfrac{1}{2}\right]^2+2(r+\lambda)/\sigma^2} \qquad \textbf{(EQN. 7.10)}$$

This differs from models without the combined Poisson element in the addition of λ which serves as a positive influence on β. V^* and A are then given by;

$$V^*=\frac{\beta}{\beta-1}I \qquad \textbf{(EQN. 7.11)}$$

$$A=\frac{V^*-I}{V^{*\beta}} \qquad \textbf{(EQN. 7.12)}$$

and option value can the be obtained from the functional form;

$$F(V)=AV^{\beta} \qquad \textbf{(EQN. 7.13)}$$

Assume that the expected benefit from approval is currently 1.1[50] and improves at a rate of 1% per period with associated volatility of 20%. Suppose also that one period is equal to one year, and that on average a trial will report after 6 years (λ=0.167). If these estimates are combined with a discount rate (6%), and an investment cost normalised to 1 for illustrative purposes, option value can be estimated. A summary of these base case estimates is given in table 7.1.

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[50] Chosen to be 10% larger than the cost of approval for illustrative purposes.

Parameter	Base case parameter value
V	1.1
α	0.01
σ	0.2
ϕ	1
I	1
r	0.06
λ	0.167

Table 7.1. Base case parameter values for the option to deferral approval in order to improve information

Option premium at the optimal investment threshold V*, at the current level of expected benefit, and at the point where traditional techniques advocate approval (V=I) can then be obtained to illustrate the value of observed information.

7.5.3 Results

Given the base case parameter estimates (table 7.1) the net benefit of immediate approval is 0.1 (1.1 –1 = 0.1), while the option to defer approval is worth 0.1668 (table 7.2).

Parameter	Calculation	Base case result
ß	Equation 13	3.628
A	Equation 15	0.118
Option value F(V)	Equation 10	0.1668
Net benefit	V-I	0.1
Option premium	F(V)-max[(V-I),0]	0.0668
V*	Equation 14	1.38

Table 7.2. Base case solutions for the option to defer approval in order to improve information

When traditional techniques overlook deferral they suggest approval should be granted immediately (NB>0). Real options theory recommends deferral in order to gain observable information on evolving expected benefit (OV>NB). This ability to wait adds 0.0668, or 67% to the value of the approval opportunity, suggesting additional information is worth this amount. Figure 7.4 shows option value and net benefit for a range of expected benefits.

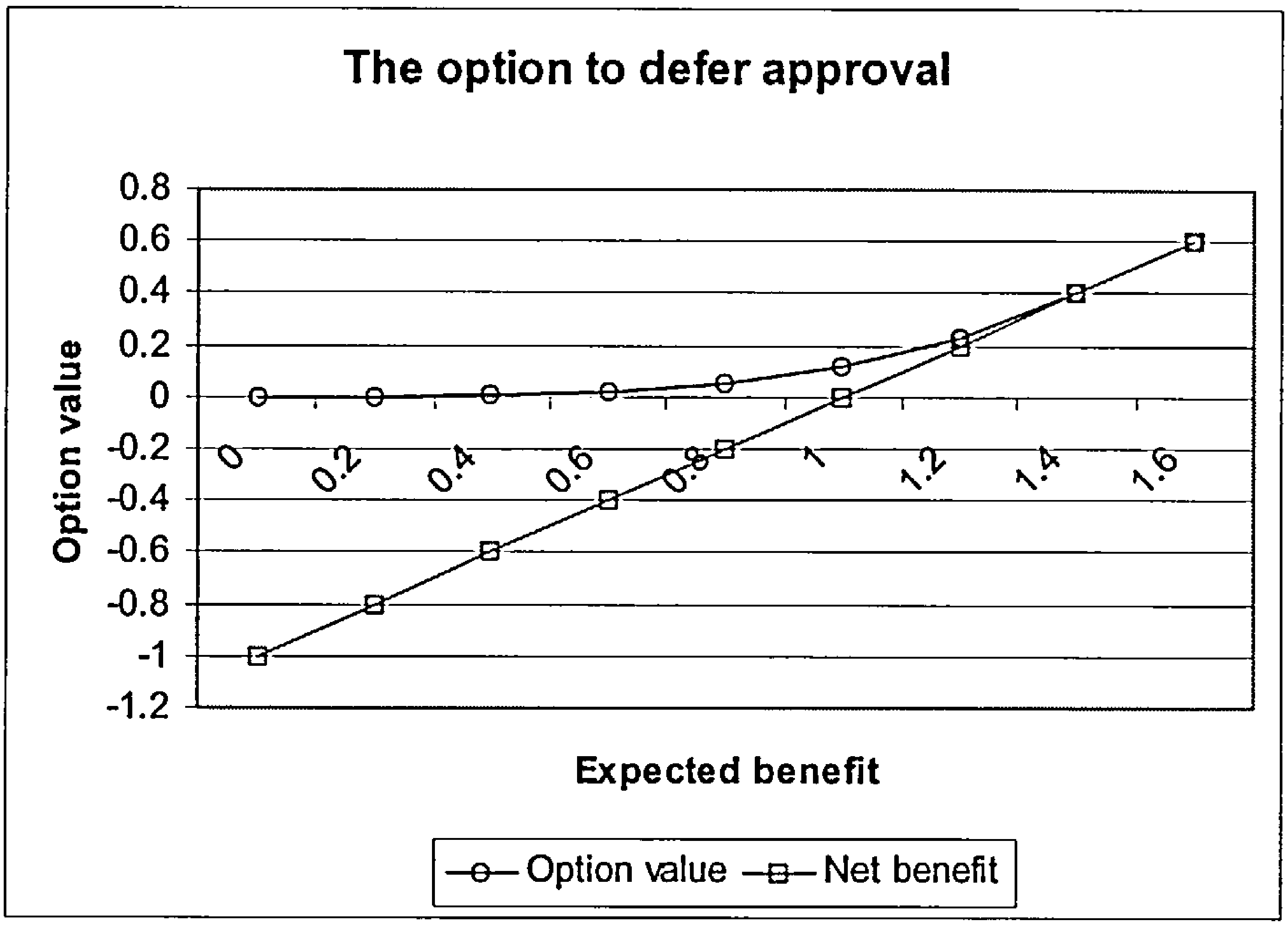

Figure 7.4. Intrinsic value and option value for a range of net benefits for the option to defer approval in order to improve information.

Option value assumes a minimum of zero when net benefit from immediate action is very negative. Consequently real options analysis would suggest that approval neither be given now nor deferred. Although net benefit does not become positive until expected benefit exceeds the investment cost (V=1), option value becomes positive at approximately V=0.4. This indicates positive gains from additional information. Option value becomes equal to net benefit at the real options investment threshold V*=1.38, indicating immediate action should be pursued. In this case the gains from deferral and information gathering no longer exceed the gains from immediate action.

From the real options analysis perspective, a new drug or technology is rejected outright if expected benefits are less than 0.4. Deferral is recommended once expected benefits exceed this level (but remain less than V*), and immediate approval is given when expected benefit exceeds 1.38. Within this range of expected benefit, deferral is optimal suggesting that observable information is valuable.

Under traditional techniques a technology is approved when expected benefit equates to the irreversible investment cost (V=1). This threshold is appropriate if deferral is not feasible. A technology with net benefits just smaller would be rejected whilst one with net benefit just greater would be approved; opposing decision rules despite the potentially very small actual difference between technologies[51]. Real options analysis circumvents the perversely polarised treatment of relatively similar projects by placing a high value on observable information, and recommends that the adoption decisions for both technologies be deferred. Waiting may reveal differences in cost or effect that enable technologies to be distinguished methodically on cost-effectiveness grounds.

The incremental value of deferral (option premium) can also be used to identify the decision threshold and estimate a maximum willingness to pay for observable information. Option premium is plotted for a range of expected benefits (figure 7.5). Until option value becomes first becomes positive option premium remains at zero. Net benefit here is so poor that even positive additional information is unlikely to influence the rejection conclusion. This makes exogenously observed information effectively worthless and immediate rejection optimal. At V=V* option value becomes equal to intrinsic value and option premium is again zero. The decision is undertaken immediate precisely because the action is sufficiently desirable that additional information holds no further benefits.

Between the two limits (V=0.4 and V=V*=1.38) option premium assumes positive values. In this region observing exogenous information relevant to the decision of interest has some benefit, and so waiting becomes optimal. If current expected benefit is 1.2, option value is 0.23 and option premium is 0.03. The willingness to pay to observe information amounts to 13% (0.03/0.23) of the value of the option. While the costs of observing information do not exceed this level, observational research including literature reviews and meta-analyses, is efficient.

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[51] Confidence intervals surrounding the point estimate may well include 0, suggesting no significant difference between technologies.

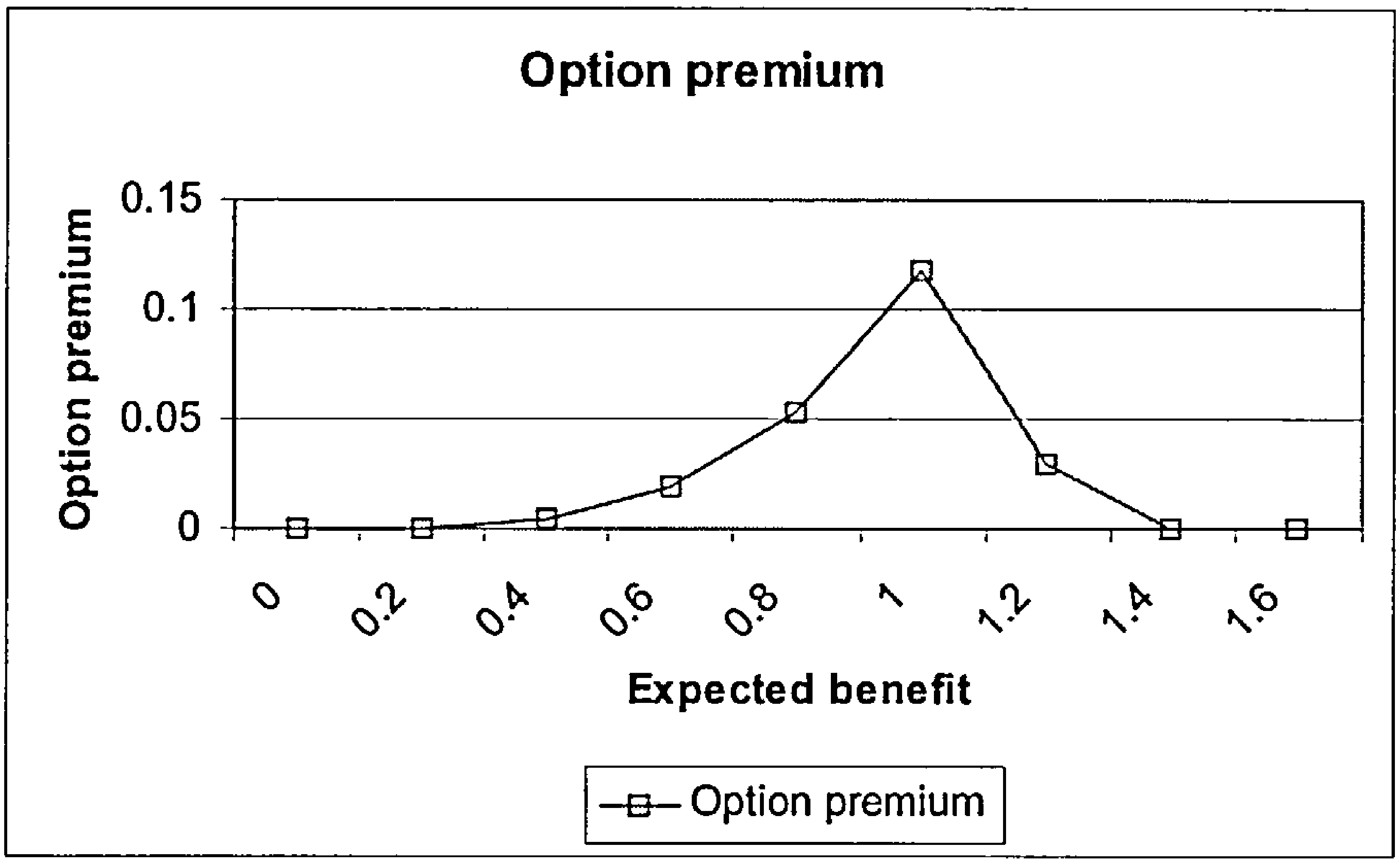

Figure 7.5. Option premium for a range of expected benefits for the option to defer approval in order to improve information.

At V=I=1 the difference between option value and intrinsic value is greatest and so option premium is at a maximum (0.118), observational data is at its most valuable and deferral is most strongly supported. This point coincides with the decision-making threshold adopted by traditional methodology so that at the exact value of expected benefit where standard techniques change from rejection to approval, real options analysis most strongly advocates waiting. This represents a significant change in decision making. If confidence intervals are used to supplement expected values, when expected benefit is 1 (V=1) a 90% confidence interval may well include 0 suggesting no significant positive benefit to immediate approval. This knowledge helps support the recommendation of deferral. Once V* is reached a confidence interval is less likely to include the possibility of no significant difference.

The shape of the option premium curve emphasises the similarities between option premium and EVPI. Both represent a maximum value to collecting specific types of information. They are based on the same underlying principles and when graphed over a range of expected benefits both assume the same shape. Consistent with classical value of information, observable information is most valuable when the immediate decision is marginal. In both cases information becomes less valuable as the difference in payoff between the optimal decision and the next best alternative increases. Traditional and real options techniques therefore agree that additional information is most valuable when a close call exists between alternatives, although real options analysis then recommends deferral, enabling collection and incorporation of additional evidence.

7.5.4 Sensitivity analysis

Whilst real options analysis is useful for analysing the approval decision of a single technology in isolation, sensitivity analysis helps examine the impact of different characteristics belonging to multiple technologies. Option premium is responsive to the expected arrival rate of the Poisson event λ. If a trial is expected to report in 20 years (perhaps referring to a cancer technology currently undergoing initial research and development) the rate of arrival is 0.05. An increased rate suggests trials are expected to report more frequently (perhaps representing technologies undergoing phase one and two testing). Figure 7.6 plots the effect on option premium of three arrival rates; 0.05, 0.1, 0.2 equivalent to trials reporting every 20, 10 and 5 years.

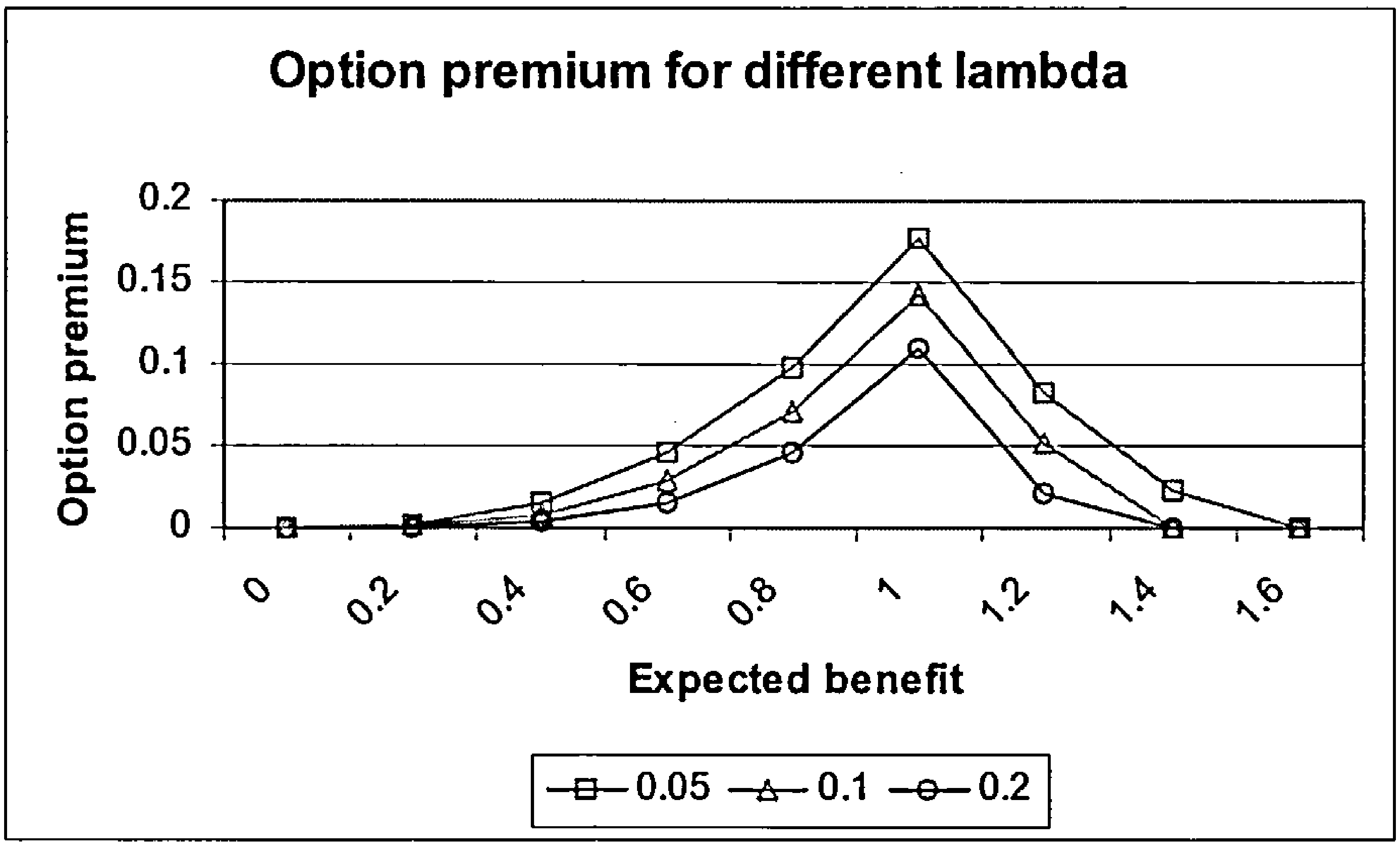

Figure 7.6. The effect of different Poisson arrival rates over a range of expected benefits.

Increasing the expected arrival rate of information reduces option premium for each level of expected benefit. As information arrives more frequently uncertainty is resolved quicker reducing the benefit to further deferral. With respect to decision making, option premium first becomes positive at a higher expected benefit, and returns to zero (identifying V*) at a lower expected benefit reducing the range of benefits for which deferral is optimal.

Comparing two technologies requesting approval with the same underlying characteristics but differing in the expected arrival of information, the technology with a trial reporting sooner will have a lower V* threshold. If the expected benefit of the two technologies starts from the same level and continues to increase at the same rate, approval will occur sooner. This generates a preference towards technologies with results reporting sooner. The alternative technology however, has greater value of observational data suggesting more extensive efforts may be pursued to obtain further information. This may encourage efforts to speed information arrival such as commissioning reviews, or encouraging interim results.

Uncertainty also enters the model through variance in the continuous element of the information evolution function, σ. Greater uncertainty is associated with larger option premium (figure 7.7) for all values of expected benefit. If changes in disease incidence and prevalence or the costs of using a technology cause increased uncertainty, the value of observing exogenously available information will increase. This reduces the threshold that recommends deferral in preference to rejection and increases the immediate approval threshold. Deferral is therefore optimal over a greater range of expected benefits.

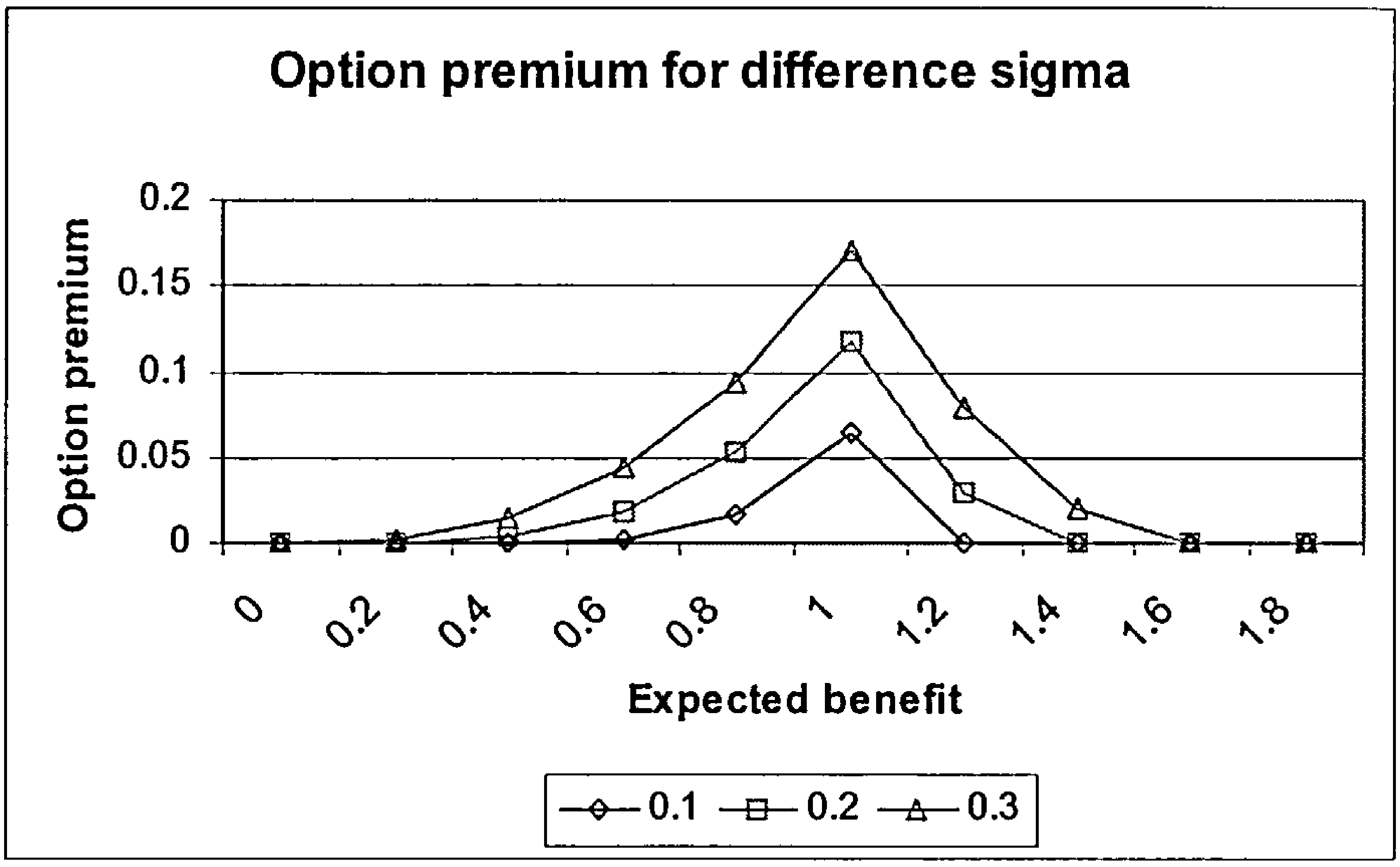

Figure 7.7. The effect of different sigma over a range of expected benefits

When competing technologies are being assessed, if neither is suitable for immediate approval NICE can consider the benefits from gathering additional information to help inform a future decision. More importantly, NICE can combine analysis on continuous and one off sources of uncertainty and information arrival to compare the relative merits of waiting to observe evidence on each of the technologies. This may be useful when one technology is surrounded by greater uncertainty but additional evidence is expected sooner.

This example has assumed a single source of first order uncertainty that is resolved with the passing of time. It is rare that time alone will provide all the information relevant to a decision of interest and often specially commissioned trials are necessary. Suppose EVPI for this decision problem was 0.55, half the value of expected benefit. For the prior level of expected benefit (V=1.1) deferral was recommended and option premium was 0.067. Willingness to pay for a new trial providing further evidence is 0.483 (0.55-0.067)[52], 12% less than the willingness to pay for complete information on all variables. In addition if this estimate is used to determine whether a particular research proposal should be carried out, the expected timing of information arrival from that proposal should be acknowledged.

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[52] This assumes there are no interactions between exogenously observed information and actively sought information

Although option premium and EVPI are based on the same underlying principles they refer to opposing types of variable; those revealing information over time and those on which evidence must be actively sought. If the value of observing information is ignored in this example, EVPI overstates the maximum willingness to pay for research activities by 13.9% (0.067/0.483)[53]. When thinking in practice about population EVPI and commissioning of trials to improve evidence, 13% represents a large difference in funding. The greater is option premium as a proportion of EVPI the more EVPI potentially overestimates the maximum willingness to pay for active research. If EVPI is used as a means of allocating budgets without accounting for option premium, a misallocation of resources may result, with less money than optimal going towards observational efforts.

7.6 Conclusions

This chapter has developed the breadth of real options applications in health care moving from the individual decision-making perspective concerning patients or technologies, towards implications for collecting future evidence and associated budgetary implications. This has been achieved by reconsidering value of information theory from a real options perspective. The application has lead to three important developments; enabled improved modelling of information arrival, provided an insight into the implications of the timing of information arrival, and demonstrated the benefits of valuing information available exogenously to the decision of interest.

Brownian motion and Poisson arrival processes were combined to create a dynamic evolution of information function. Combining the processes improves the modelling capabilities of real options. Specifically, Brownian motion, which assumes variables evolve continuously in perpetuity allowing options to be infinitely deferred, is adjusted to account for sporadic one-off events. This allows

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[53] This assumes that EVPI is calculated using perfect information on all variables. In practice EVPI has usually been estimated on variables for which information can feasibly be sought.

models to account for numerous events including competitor actions, infection following surgery, and death. Whilst used here to describe continuous disease and discrete exogenous trial influences on expected cost-effectiveness, this model is likely to describe many decision-making problems within the field of economic evaluation in health care. Some alternative applications have been discussed.

Furthermore, introducing a Poisson event that reduces the value of the option to zero at a stochastic time point creates an exercise date by effectively defining a maximum deferral period. The option must be exercised prior to this date else it becomes worthless. Decay of machinery, competitive forces, and the finite nature of life similarly impose flexible timing constraints on actions and their payoffs. Adjusting the expected arrival rate of the first event allows the average time horizon to be altered to reflect the deadline of the project under analysis. This allows a broader range of projects, those with prominent but uncertain exercise dates, to be modelled using a continuous diffusion process rather than a multinomial approximation.

This chapter has also sought to contribute to value of information literature in health care. In particular the timing of information arrival has been considered. EVPI estimates the value of perfect information available instantaneously. When comparing potential research projects it is important to acknowledge that information received in five or ten years time is not as valuable as information received instantaneously. This should be reflected in our willingness to pay for a given project.

In addition, a methodological distinction has been made between option premium and the expected value of perfect information. Where perfect information can be observed over time, and adjustments are made for timing, the two are equal. In the general case where deferral reveals information on a subset of variables option premium is less than EVPI. The distinct yet complementary elements of EVPI leads to a categorisation of variables as being observational or active in nature, depending on how evidence concerning the variable must be sought.

Deferral is useful if variables on which information is naturally revealed over time are present within a decision problem.

Variables may at times create conflict in their classification; in particular classification may change over time. Cost-effectiveness estimates may be improved through initiating a trial or by waiting for existing trials to report. The former constitutes positive actions and forms part of active value of information while the latter demonstrates information gained from deferral. When NICE commission a trial to improve evidence they are taking actions motivated by active variables. As the trial begins to report the same uncertainty is revealed by observation. Decision makers must decide whether active resolution is necessary; this is determined by their assessment of exactly how much, and what quality of evidence may be gained by deferral.

Using a combined information function absolute and relative option premium have been estimated for a hypothetical example. The absolute value gives the maximum willingness to pay for observational evidence. This includes allocating funds to reviewing existing medical evidence such as literature reviews and meta-analyses, and at a patient level, observing progress through means such as clinical observation, MRI, CT and biopsy. Option premium relative to EVPI has broader, policy level implications. In particular relative option premium should be used in conjunction with EVPI to ensure efficient allocation of resources dedicated to reducing uncertainties.

The model used to illustrate these concepts has required some assumptions, particularly those facilitating an analytic solution. This limitation is acknowledged, and can be overcome with the use of numerical techniques and detailed computer programming. Here the emphasis has remained firmly on illustrating the principles behind, and implications of, using real options theory to value observable information. There are several developments that naturally follow from this work. Perhaps the most important is calculating option premium in practice. Although fraught with difficulties including estimating volatilities through time, once achieved, observational research efforts can be subject to the same theoretical economic assessment as positive research efforts. Further work may also be carried out on the extent of interaction between observable and actively sought information so that information might be obtained in the most efficient manner.

This chapter has reconsidered value of information literature from a real options analysis perspective. Through taking a dynamic view of uncertainty, and modelling information evolving during a period of deferral this application has highlighted the importance of the timing of information arrival and the distinction between observational and active variables. These insights may have implications both for the current decision of whether to pursue a given project and the complementary decision of whether to collect additional evidence. This chapter has therefore shown that real options analysis may have an influence beyond current decision making.

Chapter 8. Conclusions: real options analysis, a useful tool?

8.1 Introduction

Real options analysis has become increasing well established since the development of financial option pricing in the 1960s, and its application to real investment projects beginning in the 1970s. The tool has brought innovative ways to evaluate the uncertainty, irreversibility and timing flexibility that characterise many decision problems. Developments in financial valuation and growing awareness of the limitations of traditional techniques have encouraged hypothetical real options applications to become detailed analyses of topical decision problems. In addition, greater use of computer programmes to calculate option values has made the tool increasingly accessible. To this end authors from varied backgrounds have begun using real options theory.

This thesis has built on two stands of growing literature; the broadening real options literature, and health economic evaluation methodology. This is achieved by establishing a motivation for, and assessing the suitability of, applying financial option pricing techniques to the evaluation of health care related projects. Several case studies, encompassing a range of decision-making scenarios faced by health care professionals have been analysed using real options methodology. For each study the theoretical and practical justification for employing options analysis has been assessed, and the implications of doing so discussed.

Chapter one identified a set of research aims to provide a logical, coherent structure from which to approach the case studies. In the process of exploring the research aims this thesis has made three significant contributions to existing literature. Firstly, the reasons for proposing the use of real options analysis, and the methods for doing so are established. Secondly, the implications with respect to decision making are shown. Thirdly, underlying these two contributions, real options theory is used to identify and make explicit, assumptions that are currently made implicitly within traditional techniques. Real options analysis demonstrates the importance of these assumptions and opens them to critical review. Section 2 considers these contributions in greater detail. Section 3 outlines areas for future research. Concluding thoughts are presented in section 4.

8.2 Research contributions

8.2.1 Motivations and methods for the application of real options analysis

Financial options provide an opportunity with no associated obligation to perform a prespecified action subject to agreed conditions. The first set of research questions explore the extent to which health care decisions fit within this framework. The questions emphasise the structure of decision making in real and financial environments and assumptions underlying option valuation. The review in chapter 2 showed that exercise of a financial option is a choice made under conditions of uncertainty, irreversibility, and timing flexibility. Examples presented throughout this thesis demonstrate that these characteristics feature in many health care decisions. The four studies identified sources of uncertainty, types and degrees of irreversibility, and factors enhancing and limiting the ability to defer.

Uncertainty has received considerable attention in economic evaluation literature. Discussions encompass estimation, presentation, and methods for dealing with uncertainty, as well as allocating resources to resolve uncertainty. Irreversibility and the ability to defer have received considerably less attention. Real options analysis highlights the characteristics as three equally significant interacting forces, encouraging detailed consideration of each. This makes the analogy between real and financial options explicit. The fundamental role of these characteristics makes them central to many conclusions and implications, and it is assumptions with respect to these factors that are sometimes made implicitly within existing evaluative frameworks.

The case studies also examined and confirmed that the variables required for option pricing are present in health care options. Usually variables transfer readily between financial and real models. Where differences occur these have been dealt with on an individual basis. For instance, chapter four noted the existence of observation costs that are assumed non-existent in financial modelling, and treated these as implicit dividends.

Part of the motivation for using real options theory has come from recognised limitations in existing methodology. Real options analysis has been used to highlight some of these. While problems cannot necessarily be solved, recognition and discussion through the application of option pricing techniques is an important process towards understanding and addressing these limitations. Several areas have been discussed:

- Now or never decision-making dominating the practice of economic evaluation[54].
- Lack of clarity over assumptions governing irreversibility.
- Ad hoc discounting.
- Ignoring strategic reasons for investment.
- Inability to value active management.

Deferral can be addressed by current techniques: the now or never tendency is a problem of practice rather than methodology with deferral often receiving insufficient attention to assess whether it is appropriate. Real options analysis focuses on whether waiting is relevant, and what may be gained during a period of waiting, explicitly challenging the now or never tendency. Information on disease progression, incidence, prevalence, efficacy and cost-effectiveness, prices, and actions of competitors may be revealed over time. Highlighting variables that reveal information illustrates potentially unforeseen gains and losses exposing important influences on the decision of interest

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[54] Except in areas where deferral is the key decision of interest such as watchful waiting.

Within the case studies, different timing horizons and information arrival processes have been illustrated. The American formulation of health care options was recognised and applied throughout. The binomial was used to provide an exact deadline for the option to defer treatment in a discrete framework whilst Brownian motion examples modelled infinite time horizons in a continuous framework. Taking a restricted version of the combined Brownian motion / Poisson model allowed a compromise between the extremes. Covering these possibilities gives confidence that real options analysis can be applied to model deferral in many health care decision problems.

Irreversibility has particularly been over looked in economic evaluation. Real options analysis raises the issue and presents ways in which to identify and integrate it into decision making. Degrees of irreversibility are incorporated partly via sunk costs and scrap values but more importantly by the structure of the model itself. Developing a simple option generates perfectly irreversible decisions. Degrees of reversibility are modelled when compound options, that allow choices to reverse decisions or mitigate outcomes, are built in. Chapter six emphasised the ability to model irreversibility within a real options framework by analysing the option to approve and later retract approval of health technologies.

Within economic evaluation discount rates are applied and justified with appeal to NICE guidelines where a difference between rates applied to costs and benefits is advocated. The lack of methodological reasoning underpinning either the choice of, or distinction between, rates generates an area of debate. Within an options problem events are described by their risk neutral, rather than actual probability of occurrence, allowing the entire decision problem to be discounted by the risk-free rate. This provides an alternative to arbitrary section of rates.

Discounted cash flow techniques have been criticised for failing to recognise strategic reasons for investment by rejecting projects whose net present value falls below zero. Strategic value includes benefit derived from creating future choices, such as development of novel compounds by pharmaceutical companies that create opportunities to market and later expand production. Research and development efforts are pursued predominantly for strategic reasons. Applying real options analysis to decision making in health care requires a dynamic specification for uncertainty. This raises the possibility that although not immediately attractive, projects may be sufficiently profitable at a later date, and allows strategic value to be recognised through deferral rather than rejection of projects that initially seem unattractive. This idea has been embraced throughout this thesis by use of the trichotomous decision rule in each case study.

Real options analysis offers improved assessment of the value of active management. Decision trees enable some reaction to anticipated events yet a full description of actions covering the entire length of a project generates a complex tree whose analysis borders on impossible. Unanticipated events that affect project value, by their very nature, cannot be incorporated. Real options analysis provides a flexible approach to uncertainty. Decisions and events are combined in a similar manner but dynamic uncertainty is incorporated that allows expected benefit to diverge from its predicted path. This formulation permits influences from both anticipated and unanticipated sources of uncertainty and reactions to these from management.

Within each case study multiple sources of dynamic uncertainty and structures for the resolution of information over time were combined to influence option payoffs. A discrete trinomial lattice allowing well-being to improve, deteriorate, or remain unchanged was illustrated for the option to postpone treatment. Continuous Brownian motion models were presented to assess the options to remove life support and approve new technologies, and a combined Brownian motion / Poisson jump structure was used to assess value of information in a health economics framework. The breadth of applications considered, joined with the coverage of uncertainty formulations demonstrates the versatility of real options concepts.

Real options analysis addresses some of these limitations by combining the rule of maximising immediate payoff with particular explicit attitudes and assumptions towards dealing with uncertainty, irreversibility and the ability to defer.

The methods for applying option techniques have been presented in some detail within the case studies and have shown how specific ideas about these factors can be integrated into analysis of health care related options. Decisions normally undertaken on a now/never basis have been challenged and deferral proposed, sources of irreversibility highlighted and incorporated, and volatility estimated to reflect multiple sources of both static and dynamic uncertainty.

By identifying weaknesses of existing techniques and addressing these with the strengths of option pricing methodology, this thesis has shown how real options analysis can create a coherent framework within which to evaluate health care decision problems.

8.2.2 Implications of applying real options analysis

The second set of research questions examines the implications of broadening real options applications to health care and includes the extent to which new conclusions are offered. The central role of uncertainty, irreversibility and timing flexibility means real options analysis contributes most to decision making where these characteristics have not previously been fully considered.

The most prominent difference between results from real options and traditional evaluation is the trichotomous decision structure incorporating deferral. The ability to defer decisions thus provides great potential for altered decisions. Any proposed action can be accepted immediately, rejected immediately, or deferred either indefinitely or for a specific period of time. The case study on watchful waiting illustrated instances where a patient recommended for immediate curative treatment by traditional decision techniques would be placed on a formal watchful waiting programme given real options analysis. Likewise, when NICE is making approval decisions, options analysis emphasises the possibility of delaying approval or recommending temporary approval.

The absolute attractiveness of deferral and range of expected benefits for which deferral is optimal is influence by uncertainty. The watchful waiting study demonstrated the increased range of benefits for which deferral is chosen when uncertainty increases and the corresponding decrease in attractiveness of immediate action. Low deferral costs, including costs of observing information, and greater growth in expected benefits have a similar impact. For any set of parameter estimates, option premium is necessarily greatest when net present value is zero. Analysing the option to wait for additional information demonstrated that the value of information gained from observational efforts is largest, and waiting therefore most valuable, when current decision techniques first advocate immediate action. Real options analysis is more likely to provide contrasting results and conclusions when uncertainty is high, observation costs are low, and the immediate decision is marginal.

The approach to handling uncertainty makes two further contributions to decision analysis; allowing for anticipated and unanticipated uncertain events and encouraging dynamic rather than static formulations. Both these influences can alter the optimal decision by changing the absolute attractiveness of deferral and incremental value relative to immediate action. The latter observation enables real options analysis to contribute to value of information literature. Chapter seven discussed how deferral reveals exogenously available information and why option premium can be interpreted as a partial value of information. In addition to having implications for the attractiveness of immediate action, option premium was shown to have potential ramifications for the complementary decision of whether to collect further information. This in turn can affect the way research budgets are allocated.

The option owned by NICE to approve and later retract approval of a health technology illustrated how varying degrees of irreversibility can be incorporated into decision making. Modelling an option to reverse decisions at some cost, reduced the threshold which triggered technology approval, making immediate action more likely, and deferral optimal over a smaller range of benefits. This conclusion can have implications for patient prioritisation. Patients with lesser irreversibility, perhaps whose potential side effects from surgery are easier or cheaper to correct, may receive treatment sooner. Through effects such as these, real options analysis also emphasises that actions to improve flexibility can be as important as immediate value maximisation strategies.

The combined impact of these aspects and most striking result of real options analysis is the creation of the threefold decision structure and associated effect on the threshold triggering immediate action. These effects potentially lead to significant differences between recommendations made by tradition forms of analysis and those provided under real options analysis.

8.2.3 Highlighting assumptions made implicitly within existing evaluation techniques

The previous two sections have shown how uncertainty, irreversibility and an ability to defer can have a significant impact on how a decision problem is modelled and the results of an analysis, leading to implications for decision making. When assumptions with respect to these factors are made implicitly, inaccurate modelling and biased conclusions can result. Moreover, assumptions should be open to critical review and debate, something that is not possible when they are made implicitly with little thought or attention given to their significance for decision making.

Few economic evaluations explicitly recognise and discuss the extent to which any decision is already reversible, or could be made reversible by future coordinated activities. Employing real options analysis to promote explicit discussion is an important step towards clarifying the role of irreversibility. Value of information used to set future research priorities suggests information gained will be incorporated into the decision strategy at a later date. Aspects of irreversibility may prevent this altogether or, more likely, generate costs of doing so. Upfront, explicit discussion of irreversibility can help recognition of such issues before an initial decision is made. Previous sections have shown this can have serious implications for if, and when, actions are pursued.

In contrast much focus has been placed on uncertainty. In particular distinctions have been made between first order and second order uncertainty. Although probability distributions are used to describe second order uncertainty these distributions, which usually consist of current mean and variance estimates, are static. Real options analysis has promoted a dynamic view of uncertainty by asking how event probabilities change through time, making evident the static assumption of tradition analyses. This has implications for immediate decision making as well as value of information and future decision making.

The ability to defer is generally only examined if deferral is the key decision of interest, otherwise an implicit assumption is made either that waiting is not possible or that this alternative holds no benefit (or cost). Again there are potential implications for decision making.

Using real options analysis to assess decision problems in which these factors are present has highlighted areas where assumptions are made implicitly within existing techniques and encouraged explicit critical discussion of these factors. Only through formally identifying such assumptions and considering them openly can their applicability and relevance to a decision problem be assessed. More importantly where explicit consideration concludes that an assumption is inappropriate, discussion can be initiated to adjust for this. Real options analysis has been used here to challenge existing assumptions particularly those concerning uncertainty, irreversibility and the ability to defer, and in some cases propose alternatives.

8.3 Further work

Whilst much has been achieved within this thesis, the application of an existing technique to a new area inevitably creates extensive areas for future research. These include examining a broader range of health related projects developing valuation methods to account for the increasingly diverse characteristics of these projects. Primarily due to data collection issues and timing constraints, analysis here has been theoretical in nature. A key development is, therefore, analysis of an empirical decision problem. The decision of interest would need to be confirmed as an options problem and well specified with ample data to support the application. Variables relevant to real options analysis would have to be identified perhaps using formats suggested within this thesis. Once appropriate models are identified they could be populated using information available from published literature or observed sources such as population incidence and prevalence or disease progression.

Creating an empirical example poses many problems for analysts. Lander 1998 (Lander and Pinches, 1998) details some of the issues faced when using real options analysis in practice. Chapter 4 examined an option to defer therapeutic treatment and found that many factors influence well-being including disease progression, ability to cope with effects of disease, confounding factors and subjective quality of life. Each factor must be observed through time at regular intervals to provide data to estimate a volatility parameter. This may imply changes in the current practice of data collection. Data is usually collected at strategic time points, perhaps 1 week, 1 month and 3 months following start of the trial. For drift and variance parameters to have a meaningful role within the model periods must be of equal length implying observations on a weekly or monthly basis for the duration of observation. Alternative specifications for the resolution of information may not have such extensive requirements.

When there are multiple sources of uncertainty Monte Carlo simulation can be used to combine these sources into a single monetary value required for input into the real options model. This requires estimating those sources of uncertainty that will dominate, driving the evolution of uncertainty and resolution of information through time. Observations can be used as a basis to estimate and extrapolate expected growth in net benefit due to immediate and deferred action, and generate estimates of volatility through time.

Such an example would demonstrate both the positive aspects and problems encountered when applying real options analysis in practice. In particular if immediate and deferred action were compared, the potential impact on decision making could be irrevocably displayed.

Further research includes extending the breadth of applications within health care. This thesis has detailed four applications yet a far wider area might benefit from real options thinking. Chapter four examined a decision problem in which deferral is already considered relevant. Similar deferral analysis might be applied to assess different timings between preventative screening sessions for patients with contrasting risk factors. For example real options analysis might be used to analyse whether women who become sexually active at a younger age, or who have had numerous partners should be encouraged receive cervical smear tests on a more frequent basis.

Chapter 5 discussed the option to defer removal of life support efforts emphasising the role of irreversibility. Options analysis may be particularly relevant for assessing the merits of genetic screening (and disclosing genetic information) where there is perfect irreversibility of information disclosure. All surgery potentially involves irreversibility; transplant and amputation present poignant examples. Where one treatment precludes the use of another, such as drugs that should not be used in conjunction, irreversibility is present and a real options approach can be considered.

The option to approve and later retract approval of a technology for use within the NHS (the subject of chapter 6) assumed a policy level perspective. In other domains options analysis has been used to retrospectively assess the success of policy decisions such as the impact of subsidies. In a similar way payment mechanisms for GP's or incentive compatible reimbursement might be considered.

In addition to broadening applications within health care, as the theory of real options develops and use becomes more widespread there will need to be empirical tests assessing option valuation. For instance, once created, evolution of information functions will need to be verified perhaps using regression analysis. Chapter 7, for instance, thought about the use of a combined Brownian motion and Poisson evolutionary process. The ability of this function to describe the events of interest would need to be assessed. In addition, the way in which new information is incorporated in to decision models should be explored. In particular the use of Bayesian analysis that assesses the relative importance of prior and newly available information and combines them to generate posterior estimates should be investigated as a tool to enhance real options analysis.

Future research also includes ways to make real options techniques more accessible. Traditionally options analysis has involved cumbersome dynamic equations or mathematically challenging finite difference methods. Improvements in computing techniques are making this easier but can lead to confusion and the creation of a black box of understanding around the methods. Wider use of spreadsheets and Monte Carlo simulation techniques to model and combine uncertainties improves the openness of real options analysis in a way that is increasingly acceptable to health services researchers. Improved accessibility will also prove important for dissemination; an issue that must be confronted if real options techniques are to be incorporated into decision making as standard practice.

8.4 Concluding thoughts

This thesis has applied real options analysis to decision making within health care. Case studies on options to defer therapeutic treatment, defer removal of life support, approve new and existing health technologies, and gather information have been considered. Comparing the structure of decision making between financial options and the health care examples provided theoretical justification for the application of real options analysis. Within the studies this thesis has established that options are valuable and should be included in decision analytic modelling when uncertainty, irreversibility and an ability to defer characterise the decision.

A variety of types and combinations of options and their potential contributions to decision making have been considered. This includes both call and put options, which are the core building blocks of financial decision making; all portfolios of financial options consist of some combination of these two blocks.

The real equivalents; investment and abandonment opportunities, are the building blocks of real options analysis. Within the first two case studies these types of option were considered in turn, and their applicability within health care examined. The third case study combined the blocks to build a portfolio. From this basis theoretically any portfolio of investment and disinvestments decisions within the health care context, that are characterised by uncertainty, irreversibility and an ability to defer, can be examined. The final case study demonstrated that real options theories may be used to analyse and reinterpret important issues within the domain of health economics. The foundations for wider application of financial option pricing techniques within health care have been established.

Appendix: trinomial option pricing program

This program is written in Fortran.

```
C
C     Trinomial Tree
C
        IMPLICIT REAL*8 (A-H,O-Z)
        DIMENSION OVALUE(2000)
     2
        LOGICAL CALLFLAG, american
        CHARACTER*16 NAME
C
C
      T = 1.5
      N = 18
      R = 0.06
      B = 0.06
      S = 20000
      X = 24020
      V = 0.2
      F = 261
      Callflag = .true.
      American = .true.
C
C
      Z = -1
      If(callflag) z = 1
      DT = T/N
      U = exp(v*dsqrt(2*dt))
      D = exp(-v*dsqrt(2*dt))
      UX = exp(v*dsqrt(dt/2))
      DX = exp(-v*dsqrt(dt/2))
      AX = exp(b*dt/2)
      PU = ((ax-dx)/(ux-dx))**2
      PD = ((ux-ax)/(ux-dx))**2
      PM = 1 - PU - PD
      Df = exp(-r*dt)
      P = PM+PU+PD
C
      Do 3  ITER = 1,31
            S = ITER*1000+14000
C
C
      Do 10 i = 0,2*n
            ovalue(i) = 0
            mn = n*2 - n - i
            if(mn.lt.0) mn = 0
            in = i - n
            if(in.lt.0) in = 0
            ovalue(i) = z*((s-f)*u**in*d**mn-x)
            if(ovalue(i).lt.0) ovalue(i) = 0
10    continue
C                       Line 50
C
```

```
      Do 20 j = n-1,0,-1
            Do 30 i = 0,j*2
            If(american) goto 25
C
C     European
C
            ovalue(i) = (pu*ovalue(i+2)+pm*ovalue(i+1)
     1         +pd*ovalue(i))*df
            goto 30
C
C     American
C
25          mn = j*2 - j - i
            if(mn.lt.0) mn = 0
            in = i - j
            if(in.lt.0) in = 0
            tt1 = z*((s-f)*u**in*d**mn-x)
            tt2 = (pu*ovalue(i+2)+pm*ovalue(i+1)
     1         +pd*ovalue(i))*df
            ovalue(i) = tt1
            if(tt2.gt.tt1) ovalue(i) = tt2
30             continue
20     continue
C
      Write(6,*) 'S=', S
      Write(6,*) 'option value=', ovalue(0)
      If(iter.gt.1) goto 3
      Write(6,*) 'T=', T
      Write(6,*) 'N=', N
      Write(6,*) 'R=', R
      Write(6,*) 'B=', B
      Write(6,*) 'X=', X
      Write(6,*) 'V=', V
      Write(6,*) 'U=', U
      Write(6,*) 'D=', D
      Write(6,*) 'PU=', PU
      Write(6,*) 'PD=', PD
      Write(6,*) 'PM=', PM
      Write(6,*) 'P=', P
      Write(6,*) 'F=', F
      Write(6,*) '---------'
C
3     continue
      Stop
      End
```

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