Commercial-in-Confidence

ACCESS ECONOMICS Pty Limited

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The value of diagnostic imaging

Report by Access Economics Pty Limited for

Australian Diagnostic Imaging Association

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TABLES

GLOSSARY OF ACRONYMS

AAA	abdominal aortic aneurysm
ABS	Australian Bureau of Statistics
ADIA	Australian Diagnostic Imaging Association
AMA	Australian Medical Association
AIHW	Australian Institute of Health and Welfare
AWE	Average Weekly Earnings
BMD	bone mineral density
CEA	Cost Effectiveness Analysis
CIS	Clinically Isolated Syndrome (of demyelination)
CDMS	Clinically Definite Multiple Sclerosis
CRT	controlled randomised trial
CT	Computerised Tomography
DALY	Disability Adjusted Life Year
DEXA (DXA)	Dual Energy X-ray Absorptiometry
DI	diagnostic imaging
DoHA	Department of Health and Ageing
DRG	Diagnosis Related Group
GDP	gross domestic product
HRQOL	health-related quality of life
ICER	Incremental Cost Effectiveness Ratio
IDK	internal derangement of the knee
MBS	Medicare Benefits Schedule
MRI	Magnetic Resonance Imaging
MS	multiple sclerosis
NSW	New South Wales
PBS	Pharmaceutical Benefits Scheme
PPMS	Primary Progressive Multiple Sclerosis
QALY	Quality Adjusted Life Year
RR	relative risk
RRMS	Relapsing Remitting Multiple Sclerosis
SDAC	Survey of Disability Ageing and Carers (ABS)
SPMS	Secondary Progressive Multiple Sclerosis
US	Ultrasound
USPSTF	United States Preventive Services Task Force
VSL	Value of a Statistical Life

VSLY	Value of a Statistical Life Year
WHO	World Health Organization
WTA	willingness to accept
WTP	willingness to pay
YLD	Years of healthy life Lost due to Disability
YLL	Years of Life Lost due to premature death

EXECUTIVE SUMMARY

This analysis investigates the cost effectiveness of various diagnostic imaging (DI) services, using a case study approach to assess the value of DI in terms of its contribution to enhancing health outcomes in Australia.

Methods

A list of six interventions was selected in conjunction with the Australian Diagnostic Imaging Association (ADIA) steering group, that provides a good mix of modalities and therapeutic areas. In each case the clinical pathway is clear and the tier of evidence is high to ensure robustness of the Cost Effectiveness Analysis (CEA). The interventions selected and their counterfactual comparators were:

- Dual Energy X-ray Absorptiometry (DEXA) scan to diagnose osteoporosis (and treat it with bisphosphonate and calcium therapy) versus no scan (and no treatment) in women aged 65-74 years, with the main benefit prevention of osteoporotic fractures;
- Magnetic Resonance Imaging (MRI) for diagnosis of internal derangement of the knee (IDK) versus arthroscopy, with the main benefit saving unnecessary surgeries while effectively treating the condition;
- Ultrasound (US) screening versus no screen in diagnosing abdominal aortic aneurysms (AAA) in males aged 70 years and older, with the main benefit being prevention of rupture and associated mortality;
- Mammography (X-ray) for breast cancer screening versus no screening in women aged 50-69 years, with the main benefit being early treatment better survival prognosis;
- MRI for diagnosing multiple sclerosis (MS) versus clinical diagnosis without MRI, which can generate the benefits of certainty and early treatment with interferons, which can delay onset and slow progression; and
- Computerised Tomography (CT) versus US and no CT in diagnosis of appendicitis, with the main benefit being early treatment where needed and avoidance of unnecessary surgery with better mortality and quality of life outcomes.

Literature and data investigation were conducted to estimate the sensitivity and specificity of the test, the probability of various outcomes (transition variables), and cost parameters. The DI instrument and its comparator were then evaluated using Markov modelling (TreeAge ProSuite 2007 Release 1.5) in terms of incremental cost effectiveness ratios (ICERs). ICERs compare the net cost of the intervention to the main outcome measure – the Disability Adjusted Life Years (DALYs) averted or Quality Adjusted Life Years (QALYs) gained.

Cost and benefits included in the CEAs comprised (to the extent possible in the analysis) net health system expenditures, productivity impacts, impacts on care services, other 'indirect' costs, the mortality burden (the Years of Life Lost due to premature death or 'YLL') and the disability burden (the Years of healthy life Lost due to Disability or 'YLD').

Findings

All of the DI interventions were very cost effective according to the World Health Organization (WHO) criterion (benchmark) of costing less that gross domestic product (GDP) per capita for each DALY averted or QALY gained (ie, <A$45,844/QALY in 2006-07). They are also thus naturally cost effective compared to two other common benchmarks – an

implicit $60,000/QALY benchmark used in the Department of Health and Ageing (DoHA, 2003) and the lower bound of the value of a statistical life year (VSLY) estimated in Access Economics (2008) of $155,409. Individual results for each DI intervention are presented in the table below, ranked by cost effectiveness.

Intervention	$/QALY gained or $/DALY averted
1. MRI vs. arthroscopy for diagnosing IDK	Dominates
2. CT and US vs no scan for diagnosing appendicitis	Dominates
3. Mammography for breast cancer screening vs. no screen (women 50-69 years)	$1,227
4. MRI for diagnosing MS vs. clinical diagnosis	$4,432
5. CT vs US for diagnosing appendicitis	$9,227
6. DEXA scan for diagnosing/treating osteoporosis vs no scan (women 65-74 years)	$25,802
7. US for diagnosing AAA (men 70+ years)	$28,993

Sensitivity analysis was performed for the decision tree models and in each case the cost effectiveness findings were robust when key transition variables or other parameters (eg, costs, disease weights, sensitivity and specificity of the tests) were changed.

Discussion

The analysis demonstrates the substantial contribution that DI makes to health outcomes in Australia – in priority health areas such as preventing injuries (fractures), musculoskeletal disease (knee derangement), cardiovascular disease (AAA), cancer (of the breast), neurological disease (MS) and digestive disease (appendicitis). Without these diagnostic techniques, a less optimal allocation of resources and health outcomes would be achieved. In the top two interventions above, health costs are higher and health outcomes worse without DI. In the other cases, Australians achieve better health outcomes very cost effectively as a result of DI.

Notably, all the DI interventions focus on prevention and early intervention, a policy priority in Australia. Many of the interventions analysed are already part of public health programs in Australia.

- For example, mammography is used in the BreastScreen program and, from April 2007, MRI is rapidly displacing arthroscopy to diagnose IDK (much of which is publicly funded) and additional funding has been provided for DEXA scans and treatment with alendronate for women with osteoporosis aged over 70 years.
- However, the analysis here suggests that DEXA scans and bisphosphonate therapy may be potentially cost effective for younger post-menopausal women also, if the full costs of fractures are taken into account, because of the high opportunity cost of informal care, which is not typically included in Australian government CEAs, due to the silo nature of funding programs. Similarly, CT vs US for appendicitis is shown to be less cost effective ($69,470/DALY averted) if productivity costs are excluded.
  - A recommendation is thus that the full economic costs of conditions (including the potential productivity losses of people with health conditions or their informal carers) are considered when assessing the cost effectiveness of potential public health programs.

- The analysis is particularly important in identifying the cost effectiveness of MRI in diagnosing MS and early pharmacological therapy, which is not yet established in Australia and could greatly enhance the health outcomes of over 16,000 Australians with MS.
- Other important novel findings are the value CT in diagnosing appendicitis and the value of US in diagnosing AAA for older men.

In conclusion, all the case studies demonstrate the value of DI services in cost effectively contributing to enhanced health outcomes in Australia. Further CEAs are recommended on a case by case basis to assess the value (including health and productivity gains) of extended public prevention and early intervention programs that utilise DI techniques, given the evidence from this analysis.

Access Economics
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1. INTRODUCTION

Access Economics was commissioned by the Australian Diagnostic Imaging Association (ADIA) to investigate the cost effectiveness of various diagnostic imaging (DI) services. The aim of the analysis was to assess the value of DI services in terms of their contribution to cost effectively enhancing health outcomes in Australia in particular areas.

1.1 GENERAL METHODOLOGY

A case study approach was adopted reviewing a selection of six interventions where the therapeutic pathways were relatively clear, so that cost effectiveness analysis (CEA) would be relatively easy and robust to map. For example, it is easier to conduct CEA as an evaluative tool in cases where a diagnosis is gained rather than in a case where a diagnosis is excluded as a result of the DI service.

The list of interventions was prepared in conjunction with the ADIA steering group. Access Economics acknowledges with appreciation the effort that the group invested to assist with identifying appropriate interventions and refining the clinical treatment pathways. The list provides a good mix of modalities and priority therapeutic areas – one 'injuries' (fractures), one musculoskeletal, one cardiovascular, one cancer, one neurological and one acute digestive system. In each case the clinical pathway is clear and the tier of evidence is high.

The results for each case study are summarised in the six chapters following:

- Chapter 2: Dual Energy X-ray Absorptiometry (DEXA) scan to diagnose osteoporosis (and treat it with bisphosphonate and calcium therapy) versus no scan (and no treatment) in women aged 65-74 years, with the main benefit prevention of osteoporotic fractures;
- Chapter 3: Magnetic Resonance Imaging (MRI) for diagnosis of internal derangement of the knee (IDK) versus arthroscopy, with the main benefit saving unnecessary surgeries while effectively treating the condition;
- Chapter 4: Ultrasound (US) screening versus no screen in diagnosing abdominal aortic aneurysms (AAA) in males aged 70 years and older, with the main benefit being prevention of rupture and associated mortality;
- Chapter 5: Mammography (X-ray) for breast cancer screening versus no screening in women aged 50-69, with the main benefit being early treatment better survival prognosis;
- Chapter 6: MRI for diagnosing multiple sclerosis (MS) versus clinical diagnosis without MRI, which can generate the benefits of certainty and early treatment with interferons, which can delay onset and slow progression; and
- Chapter 7: Computerised Tomography (CT) versus US and no CT in diagnosis of appendicitis, with the main benefit being early treatment where needed and avoidance of unnecessary surgery with better mortality and quality of life outcomes.

Each chapter commences by briefly describing the indication for which the DI instrument is being used as a diagnostic tool. Literature and data investigation is then reported in relation to the sensitivity and specificity of the test, the probability of various outcomes, and cost parameters. In each case the diagnostic tool is compared to a counterfactual or comparative diagnostic process, including no screening tool, a clinical diagnosis or a surgical investigation, for example.

The DI instrument and its comparator are then evaluated using Markov modelling to determine the differences in incremental cost effectiveness ratios (ICERs). ICERs compare the net cost of the intervention to the main outcome measure – the Disability Adjusted Life Years (DALYs) averted or Quality Adjusted Life Years (QALYs) gained. Some of the Markov models are simple decision trees and others are more complex iterative models (notably for breast cancer screening and diagnosis of AAA. All of the models are two-arm analyses except for the final (appendicitis) model which is a three-arm analysis.

Cost and benefits included in the CEA may comprise any of the following:

- net health system expenditures – eg, cost of the diagnostics and treatment, which may involve hospitalisations, pharmaceuticals, primary and specialist medical services, allied health and other health system costs;
- productivity impacts – for example, if people are absent from the workforce for a shorter period or remain in the workforce rather than dying prematurely;
- impacts on care services – for example, residential, community and informal care costs;
- other costs – for example, non-health aids, devices and home modifications, travel costs and so on; and
- the 'burden of disease' measured in DALYs or QALYs, comprising the mortality burden (the Years of Life Lost due to premature death or 'YLL') and the disability burden (the Years of healthy life Lost due to Disability or 'YLD').

1.2 PARTICULAR METHODOLOGICAL ASPECTS

The interventions are evaluation using CEA rather than cost benefit analysis, due to the particular issues involved in estimating gains in wellbeing (ie, lifespan and health-related quality of life – HRQOL), which is the main benefit for many health sector interventions. A discussion of the possible metrics for measuring the dollar value of healthy life is presented briefly below, but the non-financial metrics are used in this analysis, given the potential audience in the health sector.

1.2.1 VALUING LIFE AND HEALTH

Since Schelling's (1968) discussion of the economics of life saving, the economic literature has focused on **willingness to pay** (WTP) – or, conversely, willingness to accept (WTA) – measures of mortality and morbidity, in order to develop estimates of the **value of a 'statistical' life (VSL)** the **value of a 'statistical' life year (VSLY)**

Estimates may be derived from observing people's choices in situations where they rank or trade off various states of wellbeing (loss or gain) either against each other or for dollar amounts eg, stated choice models of people's WTP for interventions that enhance health or WTA poorer health outcomes or the risk of such states. Alternatively, risk studies use evidence of market trade-offs between risk and money, including numerous labour market and other studies (such as installing smoke detectors, wearing seatbelts or bike helmets etc),

The extensive literature in this field mostly uses econometric analysis to value mortality risk and the 'hedonic wage' by estimating compensating differentials for on-the-job risk exposure in labour markets, in other words, determining what dollar amount would be accepted by an individual to induce him/her to increase the possibility of death or morbidity by a particular percentage. Viscusi and Aldy (2002), in a summary of mortality studies, find the VSL ranges between US$4 million and US$9 million with a median of US$7 million (in year 2000 US

dollars), similar but marginally higher than the VSL derived from studies of US product and housing markets. They also review a parallel literature on the implicit value of the risk of non-fatal injuries.

Weaknesses in the WTP approach, as with human capital approaches to valuing life and wellbeing, are that there can be substantial variation between individuals. Extraneous influences in labour markets such as imperfect information, income/wealth or power asymmetries can cause difficulty in correctly perceiving the risk or in negotiating an acceptably higher wage in wage-risk trade off studies, for example.

Viscusi and Aldy (2002) include some Australian studies in their meta-analysis. Since there are relatively few Australian studies, there is also the issue of converting foreign (US) data to Australian dollars using purchasing power parity for an appropriate period.

Most recently, Access Economics (2008) undertook a meta-analysis of 244 studies (17 Australian and 227 international studies) between 1973 and 2007, to estimate the VSLY under a range of different assumptions and conditions. This study recommended that, where a VSLY is required for decision making, **an appropriate average VSLY for Australia is $252,014, with sensitivity analysis at $155,409 and $340,219.** This VSLY estimate is based on estimated VSL from the meta-analysis of $6.0 million, with the range in the health sector of $3.7 million to $8.1 million, discounted at 3.0% per annum over 40 years of remaining life expectancy. The study also concluded that the average is appropriate to apply to target populations of different ages, genders and ethnicities within Australia.

1.2.2 DALYs AND QALYs

In the last decade an alternative approach to valuing human life has been derived that is non-financial, where loss of wellbeing and premature mortality – called the 'burden of disease and injury' – are measured in terms of DALYs, with 0 representing a year of perfect health and 1 representing death. Other health states are attributed values between 0 and 1 as assessed by experts on the basis of literature and other evidence of the quality of life in relative health states. For example, the *disability weight* of 0.18 for a broken wrist can be interpreted as losing 18% of a person's quality of life relative to perfect health, because of the inflicted injury. Total DALYs lost from a condition are the sum of the mortality and morbidity components – the YLL and the YLD. This approach was developed by the World Health Organization (WHO), the World Bank and Harvard University and provides a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990, projected to 2020 (Murray and Lopez, 1996). Methods and data sources are detailed further in Murray et al (2001) and the WHO continues to revisit the estimates for later years.

The DALY approach has been adopted and applied in Australia by the Australian Institute of Health and Welfare (AIHW), with a separate comprehensive application in Victoria. Mathers et al (1999) from the AIHW estimated the burden of disease and injury in Australia in 1996, while Begg et al (2007) revisited the Australian estimates for the year 2003. The AIHW values DALYs equally for Australians of all ages, genders and ethnicities. The DALY approach has been successful in avoiding the subjectivity of individual valuation and is capable of overcoming the problem of comparability between individuals and between nations.

Note that a DALY is the reverse of a QALY, where 1 represents perfect health and 0 represents a health state perceived equivalent to death. Moreover, the disability weights for health impacts for DALYs are determined externally (by a panel of experts), while QALYs are generally based on metrics that place greater emphasis on the individual's perceived utility from their own different health states and thus may vary more across individuals.

The main problem (which is also a strength) with these approaches is that they are not financial and thus not directly comparable with most other cost and benefit measures. In public policy making, therefore, there is often the desire to apply a dollar conversion to ascertain the cost of an injury, disease or fatality or the value of a preventive health intervention eg, in cost benefit analysis. Such financial conversions tend to utilise WTP valuations as described above. An alternative approach in decision-making is to develop implicit or explicit benchmarks whereby an intervention is considered to be cost effective. A particular type of CEA is cost utility analysis, where the metric is 'dollars per DALY averted' or 'dollars per QALY gained'. Access Economics (2008) shows that such benchmarks for public financing purposes tend to be lower in the Australian health and transport sectors than the estimated average VSLY, which is in the interests of fiscal restraint.

1.2.3 INCREMENTAL COST EFFECTIVENESS AND BENCHMARKS

ICERs are calculated for each DI service relative to its comparator in terms of net dollars per QALY gained or net dollars per DALY averted.

- If financial benefits outweigh financial costs, an intervention is described as **cost-saving**.
- If the intervention saves costs and gains more QALYs (or averts more DALYs) relative to its comparator, it is described as **dominating** (and its comparator is **dominated**).
- If an intervention is more expensive than its comparator but gains more QALYs (or averts more DALYs), cost effectiveness benchmarks or other tools are needed to decide whether or not to pursue the intervention.
- If an intervention is less expensive but does gains fewer QALYs (or averts fewer DALYs), benchmarks or tools are also required, but change is often sticky in this direction.

Cost benefit analysis has an internal benchmark – the 'breakeven point' (ie, anything above this benchmark is a net benefit). CEA may use a variety of benchmarks to determine public financing thresholds (Access Economics, 2008) such as:

- gross domestic product (GDP) per capita ie, $45,844 in 2006-07 – in line with the WHO guidelines that interventions whose cost effectiveness is between one and three times GDP per capita per QALY gained (DALY averted) are cost effective and those less than GDP per capita per QALY gained (DALY averted) are very cost effective;[1]
- $60,000 – in line with the Department of Health and Ageing - DoHA (2003); or
- the VSLY of $252,014 or, conservatively, $155,409 – in line with the literature (see above and Access Economics, 2008).

1.2.4 MARKOV MODELS

While it is rather complex, Markov CEA analysis is a well-established and rigorous method of demonstrating the value of interventions. Markov chains (named after Andrey Markov) model a discrete-time stochastic process with the Markov property, namely that given the present state, the future states are independent of the past states. Alternatively stated, the present state description fully captures all the information that can influence the future

[1] http://www.who.int/choice/costs/CER_levels/en/index.html Average GDP per capita for the Western Pacific region is shown as US$27,534 with three times that shown as US$82,602 in the year 2000.

evolution of the process. Thus, given the present, the future is conditionally independent of the past.

At each time instant the system may change its state from the current state to another state, or remain in the same state, according to a certain probability distribution. The changes of state are called transitions, and the probabilities associated with various state-changes are termed 'transition probabilities'.

The parameters in the CEA were modelled using TreeAge Pro Suite 2007 Release 1.5.

1.2.5 DISCOUNT RATES

A discount rate is used to convert streams of benefits or costs into today's dollars. Choosing an appropriate discount rate for present valuations in cost analysis is a subject of some debate, and can vary depending on what type of future income or cost stream is being considered. For the modelling undertaken here, two important streams need to be discounted: financial costs (health system and indirect costs) and quality of life. For the latter, a real discount rate of 3% is used, while the former streams are discounted using discount rates appropriate to each cost (eg, wage inflation for productivity costs, consumer price index for aids and home modifications etc). Access Economics (2008) provides a more detailed description of discount rate use in CEAs and cost benefit analyses where valuing streams of healthy life are involved.

1.2.6 SENSITIVITY AND SPECIFICITY

Sensitivity and specificity are the most widely used statistics used to describe the performance of a diagnostic test.

- **Sensitivity** (probability of a positive test given appendicitis) refers to how good a test is at correctly identifying people who have appendicitis. Sensitivity ranges from 0 to 100%. For example if a CT scan correctly identified 27 out of 30 people who have appendicitis then its sensitivity would be 90%.
- **Specificity** (probability of a negative test given no appendicitis) on the other hand, is concerned with how good the test is at correctly identifying people who do not have appendicitis. For example if a CT scan correctly identified 57 out of 60 people who do not have appendicitis then its specificity would be 95%.

2. DEXA SCANS TO DIAGNOSE OSTEOPOROSIS

The first case study looks at the cost effectiveness of providing a DEXA scan (and bisphosphonate and calcium therapy) to diagnose osteoporosis vs no scan (and no treatment) in women aged 65-74.

2.1 MODEL PARAMETERS

2.1.1 OSTEOPOROSIS, BONE MINERAL DENSITY (BMD) AND DEXA

WHO defines osteoporosis as a 'disease characterised by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk' (WHO, 2003). Osteoporosis occurs when bone turnover increases and the rate of bone resorption exceeds that of bone formation, leading to loss of bone mass. Clinical diagnosis may be confirmed by:

1 The presence or history of osteoporotic fractures;
   - osteoporosis is currently usually discovered through occurrence of a low trauma fracture triggering an investigation by treating clinicians; or

2 The finding of low bone mass in the absence of fracture;
   - osteoporosis is defined as a deficit in BMD of 2.5 standard deviations or more below the young adult reference mean in postmenopausal Caucasian populations (Kanis, 1994), while osteopenia is a deficit in BMD of between 1 and 2.5 standard deviations below the young adult reference mean (Sambrook et al, 2002).

BMD is used as a measure of fracture risk with each standard deviation decrease in BMD being associated with an approximate twofold increase in the risk of fracture (Marshall et al, 1996).

The two major non-modifiable risk factors for osteoporosis[2] are age and female gender. Women are more likely to develop osteoporosis post menopause as the level of oestrogen, which is important for maintaining healthy bones in women, significantly decreases. The bones subsequently lose calcium and other minerals at a faster rate than that of pre-menopausal women.

DXA or DEXA is a widely used and thoroughly studied means of measuring BMD. Two X-ray beams with differing energy levels are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone.

The 2007 Medicare Benefits Schedule (MBS) approves a fee of $92.45 for Items 12306, 12309, 12312, 12315, 12318, 12321, 63328, although online Medicare data suggests that

[2] Other common risk factors for osteoporotic fractures (Nguyen et al, 2004) include family history of fracture; inadequate dietary calcium intake; sedentary lifestyle or physical inactivity; smoking; excessive alcohol intake; early or surgically induced menopause; short duration of reproduction lifetime (ie, late menarche and/or early menopause); gonadotropin-releasing-hormone agonist therapy; anorexia nervosa; low testosterone levels in men; vitamin D deficiency; low body weight; hyperthyroidism; and the use of corticosteroids.

benefits paid only averaged $76.93 per scan in 2006-07. Although Medicare benefits are not generally payable for bone density testing where the tests are used as a screening tool for osteoporosis, BMD tests for all patients aged 70 years and over have been covered by Medicare since 1 April 2007.[3] The Australian Medical Association's (AMA's) *List of Medical Services and Fees* recommends a fee of $192.00 for these items. According to online Medicare Statistics[4], 62% of radiology is bulk-billed. So the **average cost of a DEXA scan is estimated at $130.28** ($92.45 * 62% plus $192.00 * 38%).

2.1.2 PREVALENCE OF OSTEOPOROSIS IN AUSTRALIA

Osteoporosis has been considered under-diagnosed and under-treated in Australia since the early 1990s (Nguyen et al, 2004). Based on BMD it is estimated that 11% of men and 27% of women aged 60 years or older have osteoporosis, and another 42% of men and 51% of women would be considered osteopenic (Nguyen and Eisman, 1999). The Geelong Osteoporosis Study estimated 35.6% and 50.1% prevalence of osteoporosis for people aged 70-79 years and over 80 years respectively.

The 2004-05 National Health Survey conducted by the Australian Bureau of Statistics (ABS) showed 89,400 males and 496,400 females self-reporting osteoporosis (ABS, 2006a), based on whether they had 'ever been told' by a doctor or nurse. The ABS noted that 'presence of the condition is often not known or even suspected until medical diagnosis Results from this survey therefore expect to significantly under estimate the true prevalence of the condition.' (ABS, 2006b:55).

Comparing this self-report data with the clinically determined prevalence (27%) in women over 60 years estimated by Nguyen and Eisman (1999) suggests that the **prevalence of osteoporosis in women aged 65-74 is 25.5%** compared with the self-reported rate of 19.3%.

TABLE 2-1: PREVALENCE OF OSTEOPOROSIS IN AUSTRALIAN WOMEN, 2005

	55-64	65-74	75+
ABS (2006) self-reported osteoporosis	11.1%	19.3%	26.2%
Diagnosed estimates*	14.7%	25.5%	34.6%
Population (ABS census data)	1,087,899	715,077	751,660

* Derived by Access Economics based on relativities from the line above and population data from the line below, and Nguyen and Eisman (1999).

2.1.3 FRACTURE RISK AND THE CASCADE EFFECT

One in two Australian women and one in three men over the age of 60 have at least one fracture due to osteoporosis (Sanders et al, 1999).

[3] http://www.health.gov.au/internet/wcms/publishing.nsf/Content/diagnosticimaging-bd.htm

[4] The 62% parameter is used throughout this report based on September 2007 data from http://www.health.gov.au/internet/wcms/publishing.nsf/Content/3F0F7976502F1FE6CA25738D0081CFB9/$File/tableb7.pdf The formula (Bulk-billing rate * Medicare Fee + (1-BB rate) * AMA fee) may overstate the actual cost per unit as the rebate is 85% of the Fee and the AMA fee represents a maximum rather than an average. As such, the overall CEA is conservative and the results may be more favourable than suggested here.

There is increasing policy emphasis on prevention of the 'first fracture' since an important factor for future osteoporotic fractures is an initial vertebral or non-vertebral fragility fracture (Ross et al, 1991). Once one fracture has occurred, the chances of having another fracture are much higher compared to someone who has not had any. This is called the 'cascade effect'. The literature varies in relation to the exact extent of the increased risk, which also depends on type of fracture, number of prior fractures, age and severity of osteoporosis. In line with the whole body of evidence, the risk of any subsequent fracture once a first fracture has occurred is approximately fourfold (Klotzbuecher et al, 2000; Johnell et al, 2001; Marshall et al, 1996; Nevitt et al, 1999; Cuddihy et al, 1999). In terms of time and risk profile, the evidence from Phillips and Braddon (2004) shows fracture risk for any fracture increasing from 0.25% for post-menopausal women over 60 with no osteoporosis or fracture, to 4.2% with osteoporosis and no fracture, and then to 12% for osteoporosis and at least one existing fracture, over a five year period.

Access Economics (2006b) estimates annual osteoporotic fracture risk in the 60+ population from hospitalisation data as 1.3% (0.7%-1.9%). This estimate is used as the population risk in the 65-74 age group in this analysis (since this age group had about the same prevalence of osteoporosis as the 60+ group, and since there is sensitivity analysis around this parameter anyway). **For people with osteoporosis, the annual risk of osteoporotic fracture is thus 5.1%** (1.3%/25.5% = 5.1%), since ostoeoporotic fracture does not occur in people without osteoporosis.

2.1.4 MORTALITY AND MORBIDITY FROM FRACTURES

Osteoporotic fractures, commonly of the hip, spine, humerus, forearm and wrist, are typically sustained with little or no antecedent trauma (Nguyen et al, 1993). However, morbidity from fractures includes pain, deformity, being bed-ridden; reductions in independence and activities of daily living (Nevitt et al, 1998); fear of falling; anxiety; social isolation and emotional disturbances such as depression (Salkeld et al, 2000). Fractures are associated with excess rates of nursing home admissions (Cumming et al, 1997) and reduced quality of life; hip fractures can be particularly disabling, with complications that, as with other fractures, can result in death (Center et al, 1999; Cauley et al, 2000).

All major osteoporotic fractures are associated with a twofold increase in age-adjusted mortality in women and a threefold increase in men (Randell et al, 2000). The relative risk (RR) of mortality is estimated to be 60% higher in women with vertebral fracture than in women without one (Ismail et al, 1998). The probability of death in the first year after a hip fracture is estimated at 10–20% (Cummings et al, 1998; Cooper et al, 1993; Cumming et al, 1997). Approximately half of the survivors are disabled and need help with activities of daily living, or even require long-term nursing care (Sernbo and Johnell, 1993; Beatriz and Perry, 1994).

Access Economics (2006b:30) estimated the one-year mortality risk due to a fracture as 4% in the 60+ female population with fracture, and this risk is included in the modelling. Ten years of life are assumed to be lost per death, given life expectancy for the 65-74 cohort. The disability weight for YLD is estimated as 0.266 based on the AIHW estimate for a vertebral column fracture (Mathers et al, 1999:201). The weight is thus estimated as 4%*10+0.266 = 0.666 per fracture on average.

Including mortality and morbidity impacts, a fracture is estimated to cost **0.666 DALYs** on average in the modelling.

2.1.5 TREATMENT OF OSTEOPOROSIS

Treatments are available that prevent accelerated bone loss, slow the deterioration of the bone's microarchitecture and reduce the subsequent risk of fractures (Sambrook et al, 2002). There is a broad range of pharmacotherapies for osteoporosis, from over-the-counter medications such as calcium and vitamin D, to oestrogen therapy, newer medications such as the Selective Estrogen Receptor Modulators and bisphosphonates.

Bisphosphonates, given orally usually once-daily or once-weekly, are currently a common treatment for people with osteoporosis, with three bisphosphonate generic compounds marketed in Australia – alendronate, disodium etidronate and risedronate – of which approximately 95% dispensed are paid for through the Pharmaceutical Benefits Scheme (PBS). In calendar year 2005, there were 67,860 people initiated on bisphosphonates and 211,930 people continuing bisphosphonate therapy, for a total of 279,790 Australians taking bisphosphonates in 2005 (Access Economics, 2006b:10). PBS access previously required a pre-existing fracture; however, from 1 April 2007 alendronate became available on the PBS for patients with osteoporosis aged 70 years and over who are at high risk of fracture as measured by a BMD test.[5]

Treatment of osteoporosis with bisphosphonates has been shown to be effective in reducing the risk of fracture by approximately 50% in women with osteoporosis with and without a pre-existing fracture (Liberman et al, 1995; Black et al, 1996; Harris et al, 1999; Access Economics, 2006b; Sambrook et al, 2002). Bisphosphonates are only recommended for people with osteoporosis and have not been shown to reduce fracture risk in women or men with normal BMD or with osteopenia and no history of fracture (Sambrook et al, 2002). **The relative fracture risk for those with osteoporosis receiving bisphosphonates as 0.50.**

The average cost of a bisphosphonate prescription under the PBS is estimated as $55.91 to Government (Access Economics, 2006b:22-23), with the cost per person to the Government estimated as $670 per annum[6] and to the individual estimated as $56.40 (12 times the $4.70 co-payment per script). **The bisphosphonate annual treatment cost is thus $726.40.**

Calcium therapy for post-menopausal women has had mixed results, as calcium alone cannot usually prevent bone loss. However, with vitamin D it has been shown to be efficacious (eg, Trivedi et al, 2003) and is commonly prescribed, frequently in combination with bisphosphonates, for older populations with a poor diet who may also be in residential care, is often recommended as best practice and these costs are consequently also included in the cost of treatment for those diagnosed with osteoporosis in this analysis. **The cost of Calcium and Vitamin D together is estimated as $100.96 per annum[7].**

[5] http://www.health.gov.au/internet/wcms/publishing.nsf/Content/diagnosticimaging-bd.htm

[6] http://www.health.gov.au/internet/wcms/publishing.nsf/Content/E14AAF411525C4F2CA257273007F98B2/$File/Alendronate.pdf

[7] Unpublished estimates of DVA annual treatment costs, which triangulates well with web prices for these over-the-counter supplements.

This brings the total pharmacotherapy cost (ie, bisphosphonates, calcium and Vitamin D) to **$827.36 per annum**

2.1.6 COSTS OF FRACTURE

Access Economics (2006b) estimated a range of financial costs of osteoporotic fracture, which are presented in Table 2-2 and briefly outlined below:

- greater health system utilisation, including acute hospitalisation, admission to residential aged care and rehabilitation;
  - hospitalisation costs were calculated from AIHW data;
  - residential aged care costs were based on 14% post-fracture admission rates and an annual cost of $48,671 in 2005;
  - rehabilitation costs were based on a bottom-up costing comprising elements compiled by medical specialists for the proportion (50%) receiving some form of post-fracture rehabilitation;
- loss of productivity in the paid and voluntary workforce (eg, capacity to care for a spouse or significant other);
  - this was calculated using the average employment rates in the 65-74 age group and average weekly earnings (AWE) from ABS data;
- the value of the increased need for personal care and household services provided either by informal family carers or by formal sector community care services;
  - the 2003 ABS Survey of Disability Ageing and Carers (SDAC) data reported that 35,300 informal primary carers (7.4% of all primary carers in Australia) provide care for people with osteoporosis as their main disabling condition (ie, post-fracture, since pre-fracture osteoporosis is not disabling);
  - Access Economics (2005a) analysed this large group of Australian care recipients with a severe or profound core activity limitation from osteoporosis and estimated the value of the care provided in the community setting, using ABS data and the net present value of the opportunity cost of care for the three years following the fracture; and
- greater need for aids, equipment or home modifications, largely to enhance mobility (eg, walking frames and sticks), with these costs calculated from ABS data from the SDAC on utilisation rates together with market prices.

TABLE 2-2: AVERAGE COST PER FRACTURE PER ANNUM, 2005 AND 2007 ($)

	2005	2007
Hospitalisation	4,908	5,278
Residential aged care	6,814	7,327
Rehabilitation	3,001	3,227
Sub-total health costs	*14,723*	*15,833*
Productivity loss	331	361
Care (informal and community)	17,452	19,058
Aids and home modifications	62	66
Sub-total indirect costs	393	427
Total cost per annum per fracture	**32,568**	**35,318**

Source: Access Economics (2006b) estimates for 2005 inflated to 2007 by health cost inflation (3.7%pa) for the health costs; nominal wage growth (4.5%pa) for productivity and carer losses and consumer price inflation (2.5%pa) for aids and home modifications.

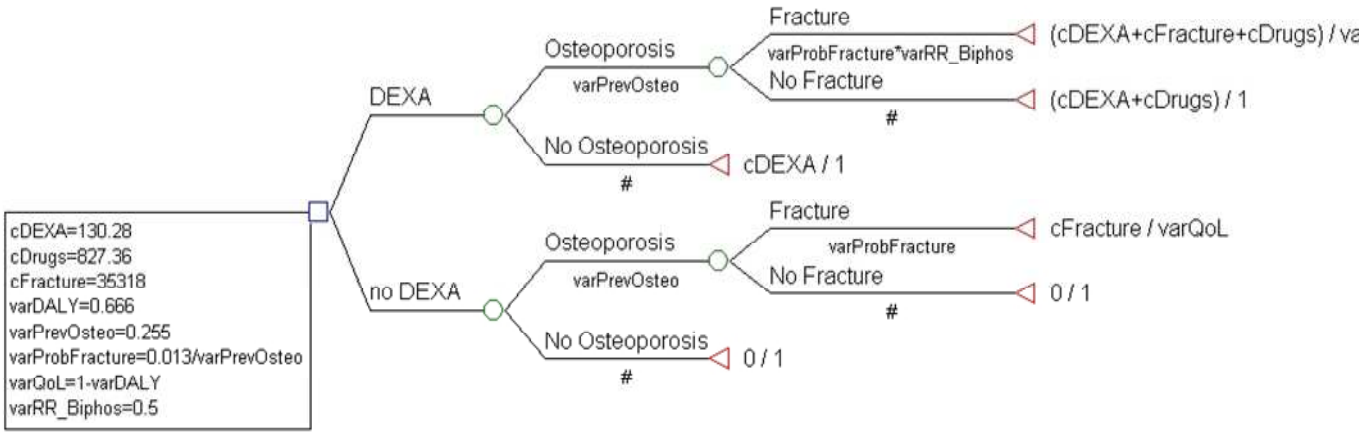
Total financial costs per annum per fracture are thus modelled as **$35,318 per annum**.

2.2 RESULTS

2.2.1 BASE CASE RESULTS

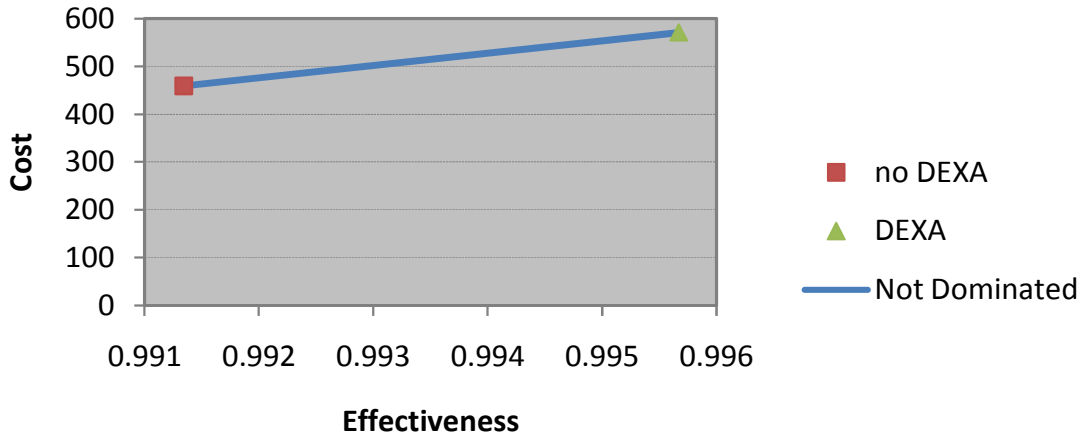
The base case was modelled with the parameters and pathways shown in Figure 2-1.

FIGURE 2-1: DEXA SCANS: MARKOV MODEL PATHWAYS



The ICER of the DEXA scan pathway in the base case was **$25,802/QALY** compared to the no-scan pathway. The DEXA scan cost $571 per person with 0.0043 DALYs (0.9957 QALYs) after one period while the no-scan scenario cost $459 per person with 0.0087 DALYs (0.9913 QALYs).

FIGURE 2-2: DEXA SCANS: CEA RESULTS



The DEXA scan is thus considered a cost effective intervention to scan and treat older Australian women (65-74 years). This aligns with the policy decision last April to provide Australian Government funding for this purpose, including an extra $135.3 million through Medicare for BMD testing over five years.[8]

2.2.2 SENSITIVITY ANALYSIS

Sensitivity analysis was conducted in relation to key parameters, notably:

- prevalence of osteoporosis – low (14.7%) and high (34.6%) relative to base of 25.5% (keeping the fracture rates constant at 5.1% untreated and 2.55% treated);
- the fracture rate – low (0.7%) and high (1.9%) relative to base of 1.3%;
- the RR of fracture reduction – low risk reduction (0.75) and high risk reduction (0.25) relative to 0.50 (base);
- cost per fracture – low rate (health costs only ie $15,833) relative to $35,318 (all); and
- disability weight – low (0.5) and high (0.8) relative to 0.666 (base).

A summary of the impacts on the ICER is provided in Table 2-3, relative to the base case of $25,802/QALY.

8 http://www.health.gov.au/internet/wcms/publishing.nsf/Content/E14AAF411525C4F2CA257273007F98B2/$File/Alendronate.pdf

TABLE 2-3: SENSITIVITY ANALYSIS ON ICER OF DEXA SCANS FOR OSTEOPOROSIS ($/QALY)

Sensitive parameter	Low	High
Osteoporosis prevalence	47,993	17,847
Fracture rate	93,372	908
RR of fracture (bisphosphonate therapy)	104,634	Dominates (cost saving)
Cost per fracture	55,059	Na
Disability weight	34,368	21,480

The sensitivity analysis showed the greatest sensitivity to the RR of fracture. This is interesting as there was no additional protection modelled from the calcium and vitamin D therapy, although this supplementary therapy may in fact may offer more than the 50% protection afforded by bisphosphonate monotherapy (Trivedi et al, 2003). Conversely, lack of adherence to bisphosphonate therapy would reduce the protective effect (Access Economics, 2006b).

The results for osteoporosis prevalence sensitivity and fracture rate sensitivity underscore that DEXA scans and associated treatment are more cost effective in older age groups, where both prevalence and risk of fracture are higher. The policy decision in relation to Australians aged 70 years and older makes sense in this context, concluding that there is 'no evidence of clinical value of bone densitometry as a general screening tool'.[9] That said, this analysis suggests that the threshold age might be a little lower, particularly if indirect costs are included in the analysis as we have done here. If only health system costs are considered, cost effectiveness of 65-74 year olds is lower at $55,059/QALY, underscoring the importance of including full economic costs, not just those in one silo, in cost effectiveness analyses.

All the sensitivity analysis results maintained the cost effectiveness of the DEXA pathway relative to no scan, with variation of the ICER from cost saving to $104,634/QALY.

[9] http://www.health.gov.au/internet/wcms/publishing.nsf/Content/diagnosticimaging-bd.htm 'General' is assumed to mean 'all age groups' here.

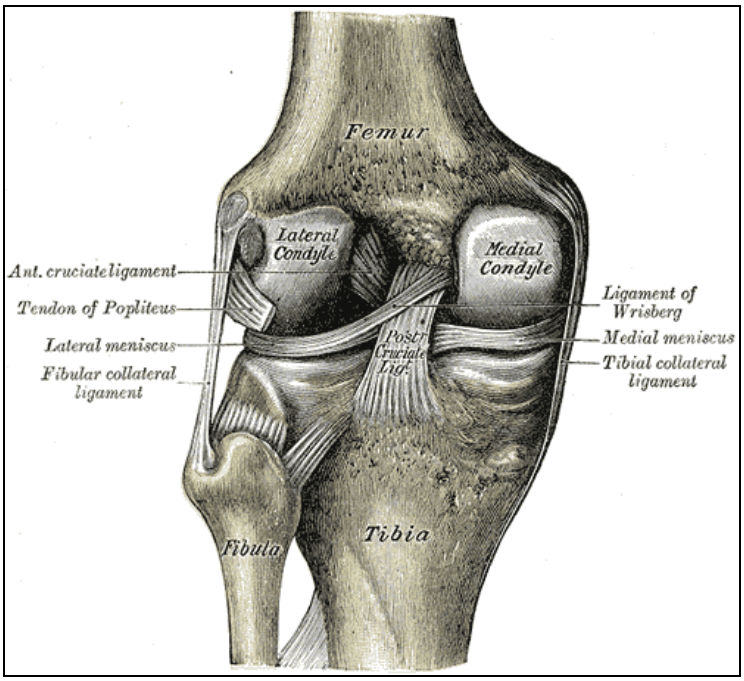
3. MAGNETIC RESONANCE IMAGING TO DIAGNOSE IDK

3.1 WHAT IS IDK?

IDK is the term used to cover a group of disorders involving disruption to the normal functioning of the ligaments or cartilages (menisci) of the knee joint.

The normal knee joint has two collateral ligaments, two cruciate ligaments and two semilunar cartilages (menisci). Any of these may be involved in a derangement, some being more easily damaged than others. In some instances more than one structure is disrupted.

FIGURE 3-1: ANATOMY OF THE KNEE



Source: Gray (2004).

Physical trauma is the cause of the vast majority of IDKs, frequently from participation in contact or other sports (such as football, ice hockey, netball, basketball, hockey, tennis, badminton, squash or skiing). The majority of acute knee injuries result from a valgus and/or twisting strain. Most commonly, they involve the medial joint structures and the anterior cruciate ligament – for example, when an athlete is hit from the lateral side and the knee is driven medially. Meniscus tears occur when substantial rotational stresses are applied to the flexed knee.

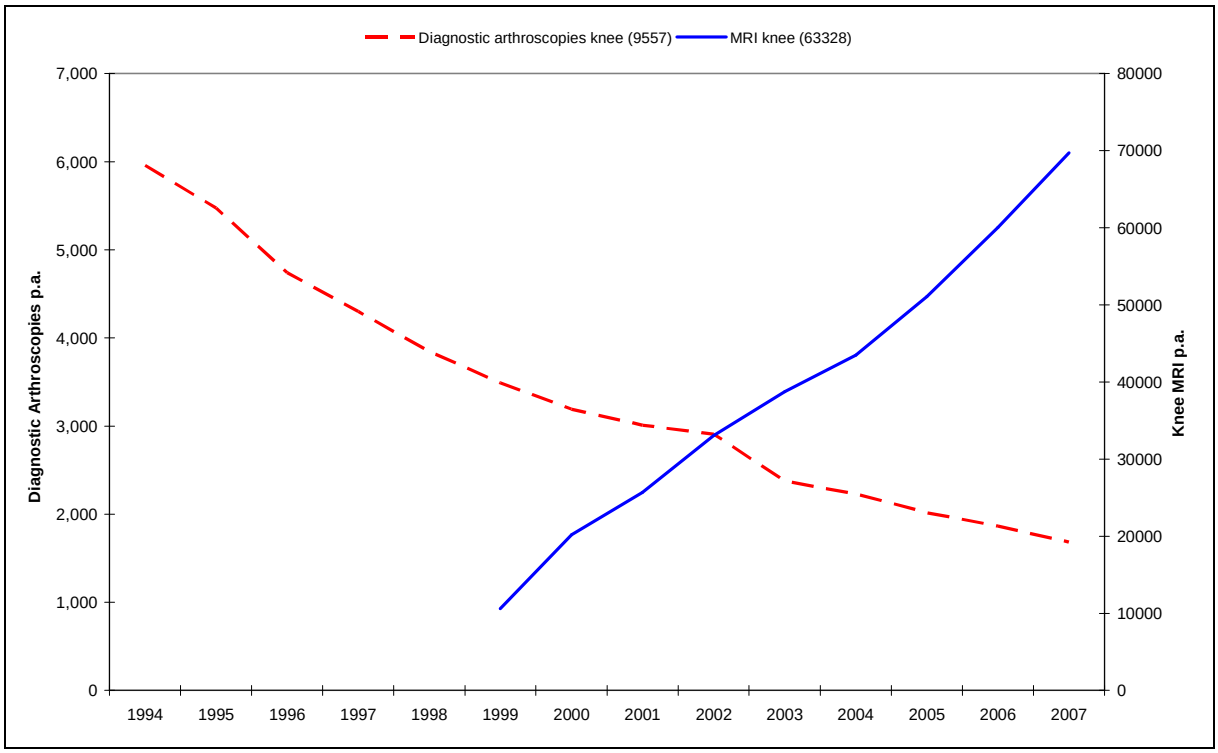
In Australia, AIHW data[10] show that, in the five years to 2004-05, meniscus injuries accounted for 73% of all IDKs. Moreover, 76% of these injuries were to the medial meniscus rather than to the lateral meniscus.

[10] http://www.aihw.gov.au/cognos/cgi-bin/ppdscgi?DC=Q&E=/ahs/principaldiagnosis9899-0405 AIHW National Hospital Morbidity Database.

3.2 DIAGNOSIS OF IDK

Clinical findings at physical examination in patients with abnormalities of the knee may be unable to determine whether the patient requires corrective surgery. In such cases, doctors may need to use other diagnostic modalities to inform the selection of appropriate treatments. Although diagnostic arthroscopy is an invasive and relatively high cost procedure, proponents point to its accuracy and to the surgeon's ability to diagnose and treat abnormalities with a single intervention. However, if diagnostic arthroscopy reveals no abnormality or only minor lesions, then patients may have been subjected to unnecessary surgery - with its associated risks[11]. Thus, orthopaedic surgeons are increasingly turning to MRI as a non-invasive means of diagnosing knee problems. As can be seen in Figure 3-2 below, MRI is rapidly replacing arthroscopy as a diagnostic tool for knee injuries.

FIGURE 3-2: TRENDS IN KNEE INJURY DIAGNOSIS: ARTHROSCOPY AND MRI



Source: MBS Statistics Online (http://www.medicareaustralia.gov.au/statistics)

Arthroscopy is considered to be the gold standard for diagnosis, and has been modelled as such in this exercise - that is with 100% accuracy for both sensitivity and specificity.

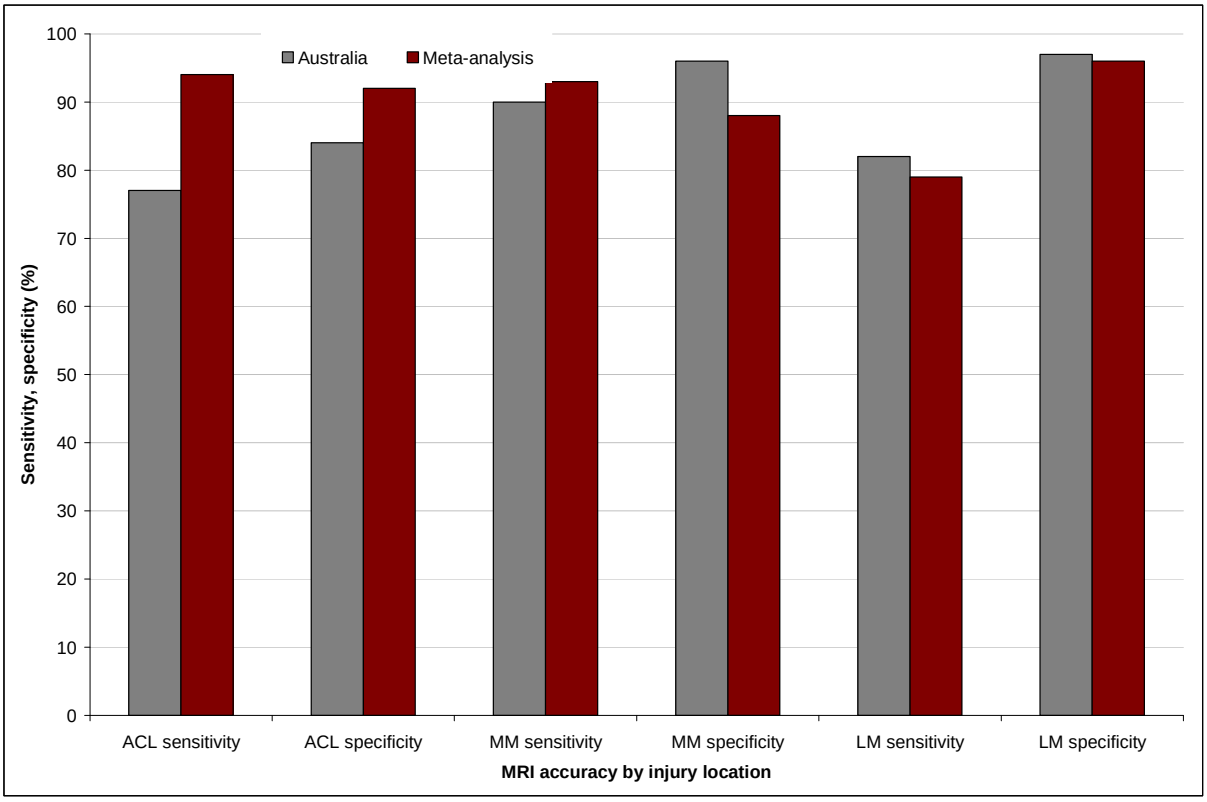
- However, Quinn and Brown (1991) have called into question the use of arthroscopy as the gold standard, noting that there are areas of the knee, such as the posterior horn of the medial meniscus, and the posterior cruciate ligament, that are usually not visualised at arthroscopy. Hence, when arthroscopy indicates an apparent false negative from MRI, in some cases these may actually be false-positives from arthroscopy. Any actual inaccuracies of arthroscopy would increase the cost effectiveness of MRI reported in this exercise.

[11] Munshi et al (2000) note that the rate of complications for arthroscopy is under 2.5%, and that such complications are fairly minor, mainly relating to bruising and other healing difficulties. Accordingly, this model does not account for complications.

- Similarly, Suarez-Almazor et al (1999), argue that there are 'false positives' from diagnostic arthroscopy. They note that there are many 'therapeutic' arthroscopies that are widely performed by surgeons, but not proven to be effective, such as debridement, plica excision, and synovectomy. In such cases, had an MRI been carried out rather than a diagnostic arthroscopy, the patient would probably not have undergone surgery.

Oie et al (2003) conducted a meta-analysis of the performance of MRI for the menisci and cruciate ligaments, and concluded that MRI was a 'highly accurate diagnostic tool'. While this study included a wide range of countries, there were no Australian data. However, in a recent study, Challen et al (2007) found very similar levels of accuracy for MRI use in a major Australian hospital (Figure 3-3). While there is no apparent systemic difference between the two studies, because the Challen study is particular to Australia and more recent, it has been used for sensitivity and specificity parameters in this CEA. As noted above, the menisci account for 73% of IDKs, and the medial meniscus 76% of these. Moreover, sensitivity and specificity for the medial meniscus are not outliers relative to the lateral meniscus or anterior cruciate ligament parameters. **Hence, MRI sensitivity (90%) and sensitivity (96%) for the medial meniscus have been used in the modelling as a proxy for these parameter estimates for all IDKs.**

FIGURE 3-3: ACCURACY OF MRI FOR KNEE DIAGNOSTICS



Source: Oei et al(2003) for 'Meta-analysis'; Challen et al (2007) for 'Australia'.
ACL = anterior cruciate ligament, MM = medial meniscus, LM = lateral meniscus.

3.3 COST DATA

3.3.1 MRI

The MBS approves a fee of $403.20 for 'Magnetic Resonance Imaging: derangement of the knee or its supporting structures' (Item 63328). Private scans are considerably more expensive. The AMA's *List of Medical Services and Fees* recommends a fee of $1,195 for 'Magnetic Resonance Study of one region of the body, or two contiguous regions' (Item OP200). According to online Medicare Statistics[12], 62% of radiology is bulk-billed. Thus, the **average cost of an MRI is estimated at $704.08** ($403.20 * 62% plus $1,195.00 * 38%).

3.3.2 ARTHROSCOPY

Casemix data for 2004-05[13] show that the average cost of an arthroscopy procedure in a public hospital was $2,365.72 (Drug Related Group - DRG Group I24Z). However, in contrast to MRI, arthroscopies conducted in private hospitals are somewhat cheaper than their public counterparts. The last time Casemix data were collected for private hospitals (2002-03), their arthroscopies were only 58.1% of the public hospital cost that year. Applying the same ratio to the 2004-05 public costs gives an estimated private cost of $1,375.36 in that year. Weighting this by the Casemix public / private separations ratio (65.9%:34.1%) gives an average cost of $2,028[14]. Multiplying this by the average health inflation rate for the period 2000 to 2005 (3.7% per annum), to bring arthroscopy costs to 2006-07 prices, gives a final estimate of $2,103 for all arthroscopies.

The next step is to separate the average cost of diagnostic and therapeutic arthroscopies. Both forms of arthroscopy are procedurally much the same. Both are forms of surgery that require hospitalisation, an operating theatre, anaesthesia, and both require significant recovery time. In fact, as Suarez-Almazor et al (1999) point out, it can be difficult sometimes to differentiate between the two operations. However, therapeutic arthroscopy will require some additional use of surgeon's time above that of diagnostic arthroscopy. The MBS lists a fee of $241.20 for 'knee, diagnostic arthroscopy of' (Item 49557). The most common therapeutic arthroscopy (MBS Item 49561: menisectomy including osteoplasty or chondroplasty) - which accounts for three-quarters (75.5%) of all therapeutic arthroscopies - has a scheduled fee of $595.65. (That is, a cost difference of $354.45).

MBS online data show that in 2006-07 there were nearly 35 times as many therapeutic arthroscopies for knees (53,873) as there were diagnostic arthroscopies (1,683) ie, only 3.1% of therapeutic arthroscopies are preceded by diagnostic arthroscopies. The respective shares in total arthroscopies, together with the difference in cost, can be used to calculate the cost of **diagnostic arthroscopy as $1,759** and the cost of **therapeutic arthroscopy as $2,114.**[15]

[12] See footnote 4.

[13] http://www.health.gov.au/internet/wcms/publishing.nsf/Content/Casemix-1. 2004-05 was latest available at time of writing (December 2007).

[14] =$2,365.72*65.9% plus $1,375.36*34.1%

[15] 1,759*3% + 2,114*97% = 2,103 and 2,114-1,759 = 354, rounded.

3.3.3 TIME COSTS

Suarez-Almazor et al (1999), using cost ratios and a methodology not dissimilar to that employed here, found that, using health system costs only, there was no great advantage to using MRI for diagnosis. Hence, health system costs alone may not be sufficient to explain why, in practice, diagnostic arthroscopies are seldom used any more. The authors concluded that time costs provided the explanation. The average patient undergoing an arthroscopy (diagnostic or therapeutic) has to have a full week off work. In contrast you can almost fit in an MRI during your lunch break – the scan itself can take as little as 15 minutes – and there are no after-effects. For this exercise, 2½ hours is allotted, to allow for administrative time.

Figures supplied by ABS[16] show that AWE in 2006 were $1,045, with an average hourly rate of $26.13. Thus, for the average worker, the time cost of an MRI is $65.31, and the time cost of an arthroscopy is $1,045. Allowing for the fact that at current participation and unemployment rates[17], 62.4% of the working age population is in paid employment, and valuing the leisure time of everyone else at 30% of the average wage[18], then **the time costs are $48.13 for an MRI and $770.15 for an arthroscopy.**

- There is also a waiting period for elective surgery in public hospitals. The AIHW reports that in 2005, the average wait for elective surgery in Australian public hospitals was 48 days. As around two-thirds of all surgeries are conducted in public hospitals, the model assumes an average wait of one month for diagnostic arthroscopy. However, once the diagnostic arthroscopy has been performed, there is no waiting period for therapeutic surgery (ie, it is done in the same operation)
- Conversely, there do not appear to be significant waiting times for DI, even in public hospitals. However, there is then an assumed month waiting for therapeutic surgery. Thus, under both modes, the time between clinical diagnosis and therapeutic surgery (if needed) is assumed to be the same – one month – and netted out for simplicity.

3.4 MODEL AND RESULTS

The parameters were modelled using TreeAge Pro 2007. The model follows a decision tree (rather than a multiple stage Markov chain) as events occur within a short time interval. The time frame between diagnostic and therapeutic arthroscopy is instantaneous, and that between an MRI diagnosis and surgery should also be reasonably short.

Probably less than one third of knee injuries will require further diagnostic assistance (either MRI or arthroscopic) after clinical consideration. A study by Bryan et al (2001) found that **knee specialists made a correct diagnosis (clinically) in 72% of cases**. Assuming that the correct diagnoses are concentrated at either end of the spectrum, this leads to an approximate division of cases between:

- injuries that can be clinically determined not to need surgery (36%);

[16] *Employee Earnings and Hours, Australia (2006)*, ABS Cat No 6306.0

[17] http://www.abs.gov.au/ausstats/abs%40.nsf/mf/6202.0

[18] According to traditional microeconomic theory (in particular the work of Gary Becker in the 1960s), people will work until they are indifferent between the marginal value of the income earned relative to the personal value of the leisure sacrificed. However no-one else tends to value the individual's leisure similarly. The typical approach to overcome this problem is to value leisure time at a discounted proportion of earnings which takes into account taxes that reduce the effective income from work and restrictions on the amount of time that can be used for work (for both biological and governmental regulation reasons).

- injuries that are clinically uncertain / require further diagnosis (28%); and
- injuries that can be clinically determined to need surgery (36%).

Intuitively, the more likely it is that surgery would be necessary, the more effective it is to go straight to arthroscopy, as the diagnostic arthroscopy would proceed seamlessly to therapeutic all in the same operation – whereas if MRI demonstrated surgery was necessary, the patient would have to undergo two separate procedures. Conversely, however, given MRI is cheaper in terms of both time and money, MRI will be more effective where the probability of surgery is lower.

The **null hypothesis modelled is that there is a 50% a priori likelihood that the patient does in fact have an injury that will necessitate surgery**. While this is the default probability, an MRI study by Ruwe et al (1992) found that 51.4% of patients – who would otherwise all have had arthroscopies – did not need surgery (so 50% is potentially conservative).

3.4.1 QUALITY OF LIFE

Therapeutic arthroscopy is assumed to be fully effective whichever diagnostic pathway is undertaken[19]. Thus, the patient will have full health at the end of the process. While Australian burden of disease publications have no knee-specific estimates, Mathers et al, 1999 suggested a disability weighting of 0.06 for 'Other musculoskeletal disorders' (based on the Dutch weight for chronic low back pain), which includes IDK. We have conservatively assumed that, in the absence of surgery, the average patient would live with IDK for (at least) a further ten years[20]. **That is, surgery will improve the patient's health by (at least) 0.60 QALYs.**

Diagnostic arthroscopy, as an invasive procedure, also inflicts disability costs on the patient, albeit temporarily. Wu et al (2003), in a study of HRQOL for postoperative patients (the majority of whom had knee operations), found a mid-point estimate of 30.9 using SF-12 index scores. This represents a 38.2% reduction in HRQOL against an equivalent age and gender population norm score of 50. Thus, **for the week it takes an average patient to recover from diagnostic arthroscopy, the disability weight used in modelling is 0.007** (=.382 /52).

Because of the high sensitivity of MRIs, in 90% of cases, if an IDK requiring surgery is present it will be detected. However, in the 10% of cases where the injury is present but not detected, the assumption is that symptoms will persist and the patient will ultimately be referred for therapeutic surgery. That is, under the MRI pathway, in all cases where IDK is present, the patient will eventually undergo therapeutic arthroscopy. However, in the case of false negatives, the patient is assumed to have to put up with an additional six months of disability from their IDK before their GP is convinced the initial diagnosis was incorrect and a booking for surgery is made. **Thus, the healing of 0.60 QALYs is reduced by half a year of disability (that is 0.03 QALYS) to 0.57 QALYS.**

[19] There will be some pain and loss of mobility from therapeutic surgery. These are not included as this analysis is focused on the competing diagnostic modes, rather than therapy impacts (which are the same across modes).

[20] As people with IDK are relatively young and thus likely to live considerably longer than ten years, future QALY gain has not been discounted.

3.4.2 MARKOV MODEL PATHWAYS

Where no IDK is present, MRI will correctly diagnose 96% and the model assumes that the **4% of patients who receive false positives will be referred for unnecessary (diagnostic) surgery.** Under the diagnostic arthroscopy pathway, as both sensitivity and specificity are assumed to be 100%, there will be no unnecessary surgeries, and no cases of false negatives[21]. This may be conservative, since Suarez-Almazor (1999) observed that in practice there may be unnecessary surgery following diagnostic arthroscopy.

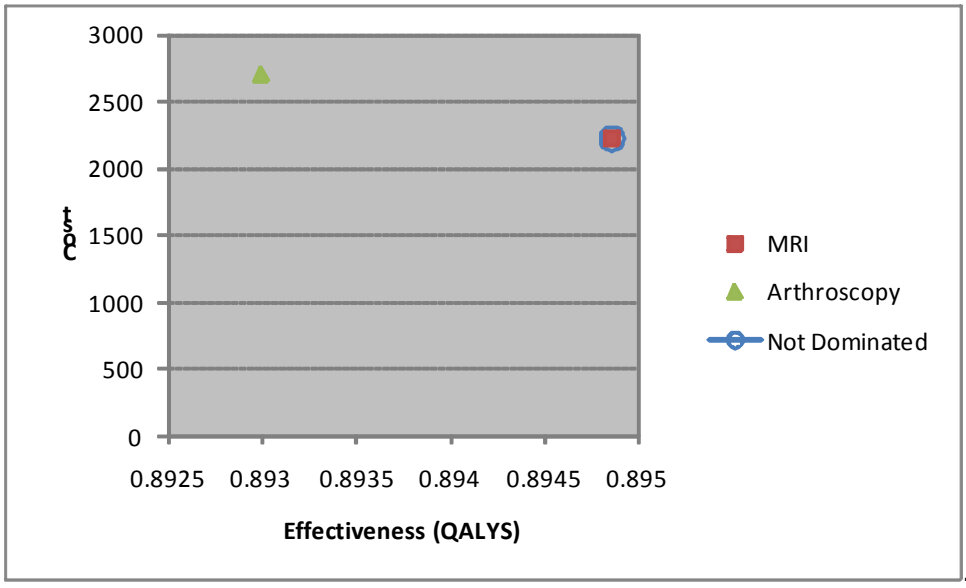
3.4.3 RESULTS

In cases where IDK is present, arthroscopy is quite cost effective, at $4,683/QALY (Table 3-2)[22] and cheaper than MRI ($6,163/QALY)[23] (Table 3-3). However, in cases where IDK is not present, under arthroscopic diagnosis the average cost is $2,529 for no QALY gain together with a loss of 0.007 QALYs after allowing for a post-surgery week of pain and immobility. Under MRI, the cost is only $854[24] and there are fewer QALYs lost, with only 4% false positives at 0.007 QALYs of postoperative disability each.

Overall, the expected cost under the arthroscopy pathway is $2,707, and the expected gain is 0.293 QALYs, for a cost effectiveness of $9,328 per QALY. The expected cost under the MRI pathway is $2,245, and the expected gain is 0.295 QALYs, for a cost effectiveness of $7,613 per QALY.

In terms of incremental cost effectiveness, as MRI is both cheaper and saves more QALYs. As Figure 3-4 below shows, MRI thus dominates arthroscopy.

FIGURE 3-4: COST EFFECTIVENESS OF MRI VS. ARTHROSCOPY



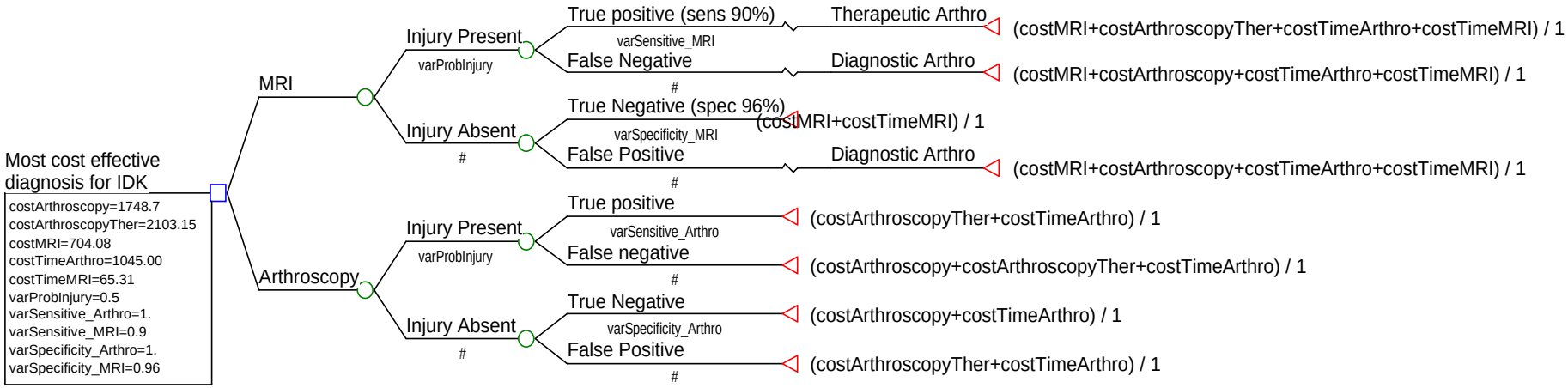
[21] Both these false positive and false negative arms have been included in the model for schematic completeness, but assigned a probability of zero.

[22] $2,884 spent for 0.593 QALYs gained.

[23] Weighted average of MRI true +ve ($6,132;45%) and MRI false –ve ($6,459; 5%).

[24] Weighted average of MRI true –ve ($752; 48%) and MR false +ve ($3,282, 2%)

TABLE 3-1: IDK DIAGNOSIS AND TREATMENT DECISION TREE



CostArthroscopy = cost of diagnostic arthroscopy, CostArthroscopyTher = cost of therapeutic arthroscopy, costMRI – cost of MRI, costTimeArthro = cost of time spent recovering from arthroscopy (diagnostic &/or therapeutic), costTimeMRI = cost of time taken for MRI scan, varProbInjury = probability of injury requiring surgery, varSensitive_Arthro = diagnostic arthroscopy sensitivity, var_Sensitive_MRI = MRI sensitivity, varSpecificity_Arthro = diagnostic arthroscopy specificity, varSpecificity_MRI = specificity MRI.

TABLE 3-2: COST EFFECTIVENESS OF IDK DIAGNOSIS USING ARTHROSCOPY

Injury	(prob)	Diag Outcome	(prob)	Surgery cost	Time cost	DI cost	Sum Cost	DALYs averted	DALYs caused	Net DALYs averted	(prob)	$/DALY averted (1st year)
		True +ve	*100%*	$2,113.78	$770.15	-	$2,883.93	0.60	-0.007	0.593	*50.0%*	$4,863
IDK present	*50%*	False -ve	*0%*								*0%*	
IDK absent	*50%*	True -ve	*100%*	$1,759.33	$770.15	-	$2,529.48	0	-0.007	-0.007	*50.0%*	N/A
		False +ve	*0%*								*0%*	
Overall							**$2,706.71**			**0.023**		**$9,328**

TABLE 3-3: COST EFFECTIVENESS OF IDK DIAGNOSIS USING MRI

Injury	(prob)	Diag Outcome	(prob)	Surgery cost	Time Cost	DI cost	Sum Cost	DALYs averted (1st year)	DALYs caused	Net DALYS averted	(prob)	$/DALY averted (1st year)
		True +ve	*90%*	$2,113.78	$818.28	$704.08	$3,636.14	0.60	-0.007	0.593	*45.0%*	$6,132
IDK present	*50%*	False -ve	*10%*	$2,113.78-	$48.13	$704.08	$3,636.14	0.57	-0.007	0.563	*5.0%*	$6,459
IDK absent	*50%*	True -ve	*96%*	$-	$48.13	$704.08	$752.21	0	0	0	*48.0%*	N/A
		False +ve	*4%*	$1759.33	$818.28	$704.08	$3,281.70	0	-0.007	-0.007	*2.0%*	N/A
Overall							**$2,244.77**			**0.026**		**$7,613**

3.4.4 SENSITIVITY ANALYSIS

As MRI already dominates arthroscopy under the base case, a variety of scenarios were modelled that were unfavourable to MRI, to ascertain whether this finding would change.

- Under Scenario 1, the sensitivity and specificity of MRI were reduced to the lowest in the range from the Australian and meta-analysis results shown in Figure 3-3. Challen et al (2007) found that the MRI's sensitivity and specificity for anterior cruciate ligaments were 77% and 84% respectively.
- In Scenario 2, time costs were not included, which removes any disadvantage to arthroscopy from its causing a week of being laid up.
- Scenario 3 increases the probability of injury to 64% -the upper boundary of where a clinician may possibly still call for further diagnosis, rather than sending the patient straight to surgery.
- Finally, Scenario 4 assumes that rather than two-thirds of patients getting MRIs at public hospitals, two thirds go to private clinics instead, with the result that average costs increase by $190 to $890.

As Table 3-4 shows, while the numbers vary considerably across scenarios, in all cases but one, MRI continues be both cheaper and to avoid more DALYs than arthroscopic diagnosis.

- In Scenario 1, the lower sensitivity and specificity mean that, while MRI is still cheaper, it reduces marginally fewer DALYs (0.001) than does arthroscopy. As the ICER in this scenario is over $600,000/QALY, MRI would not be chosen under a typical WTP of $60,000/QALY. That said, these sensitivity and specificity ranges apply for anterior cruciate ligament injuries, which account for less than 1% of IDKs.

TABLE 3-4: MRI VS. ARTHROSCOPY COST AND EFFICACY SCENARIOS FOR IDK DIAGNOSIS

Scenario	Cost difference	Difference in DALYS averted	ICER
0. Base Case	-$462	0.002	dominates
1. MRI Sensitivity 77% Specificity 84%	-$311	-0.001	$608,176
2. Not include time costs	-$140	0.002	dominates
3. Prob injury 64%	-$122	0.000	dominates
4. Public Private MRI split reversed	-$272	0.000	dominates

4. ULTRASOUND SCREENING FOR ABDOMINAL AORTIC ANEURYSMS

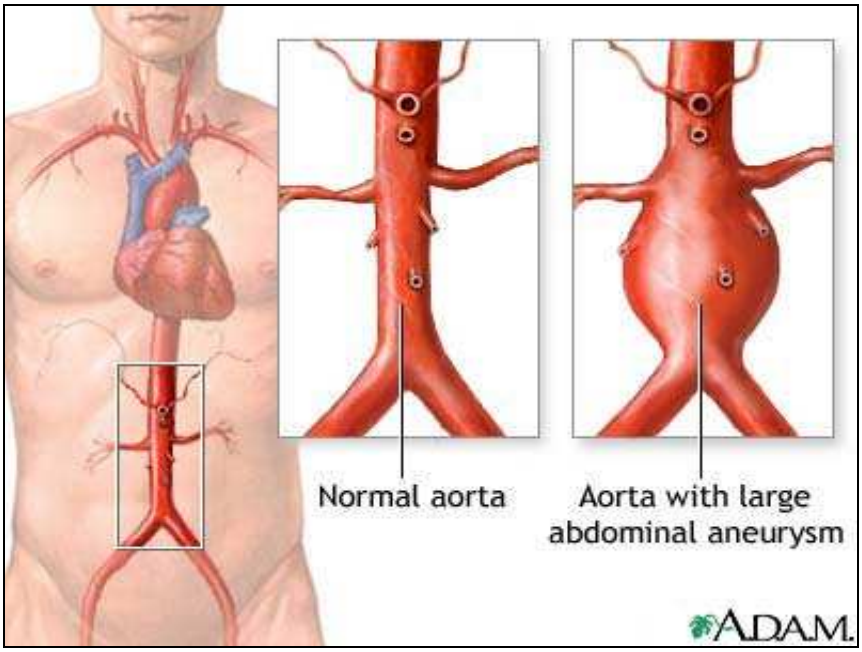
This case study looks at the cost effectiveness of US screening versus no screen for AAAs, targeting males aged 70+.

4.1 BACKGROUND

The abdominal aorta is the main artery supplying blood to the lower part of the body. It is the body's largest blood vessel and in addition to its role as a conduit, the aorta is an elastic capacitance vessel, which reduces the functional work of the heart's left ventricle.

An AAA occurs when the lining in the wall of abdominal aorta becomes weakened and expands in size[25] (see Figure 4-1). The most common location for the AAA is below the area where the aorta supplies blood to the kidneys and above where it divides to supply blood to the pelvis and legs.[26] The abdominal aorta is usually around 2 cm in diameter, by definition an AAA is present when the diameter of infrarenal aorta exceeds 3 cm (Johnston et al 1991).

FIGURE 4-1: ANATOMY OF THE ABDOMINAL AORTA



AAAs develop slowly over many years and are often symptomless until they rupture. Usually the larger the aneurysm, the greater is the risk of its rupture, which is high when an

[25] This caused by a degenerative process that results in the decline in the elasticity and dispensability of the aortic wall. Biomechanical forces from the pressure of the blood being pumped through the aorta cause expansion at the site of weakness.

[26] In some cases, the aneurysm can extend to include one or both of the iliac arteries (the arteries that supply blood to the pelvis and legs).

aneurysm exceeds 5.5 cm in diameter (Lederle et al 2002a).[27] A ruptured AAA causes life-threatening internal haemorrhaging and has a high mortality rate even with prompt treatment: 80% for patients reaching hospital; and 50% for those undergoing surgery for emergency repair (Cosford PA, Leng GC 2007). In 2005 (the latest year when cause of death data are available from the ABS), there were 707 male deaths from AAA with rupture in Australia.

The incidence of AAA increases in men rapidly after 55 years of age and peaks at age 80. Among women, the incidence increases rapidly after 70 years of age and peaks at age 90. Males are 5 times more likely than females to be affected (AIHW 2006). The frequency is much higher in smokers than in non-smokers. Other risk factors include hypertension, family history, infection, trauma, arteritis, cystic medial necrosis and connective tissue disorders.

4.1.1 TREATMENT

Generally, treatment for an AAA depends on its size and location and the patient's general health. A "watch-and-wait" approach is usually taken for AAAs that are detected, but are small (a diameter of between 3 and 5.5 cm). Patients with small AAAs can be safely monitored with US and don't require surgery until the risk of rupture outweighs the risk of surgery. Elective surgery is usually recommended for patients with aneurysms bigger than 5.5 cm in diameter and for aneurysms that rapidly increase in size (>0.5 cm/year) (Lee 2007). The goal is to perform surgery before further complications or symptoms develop.

There are two types of surgical treatment. One involves replacing the damage section of the abdominal aorta with a synthetic tube. This can be performed either as open abdominal surgery or laparoscopically. The other procedure uses an endovascular stent graft (endograft) which is inserted via catheters that are threaded up the groin area through small incisions.

4.2 AAA SCREENING WITH US

Given AAAs usually remain asymptomatic and undetected until they rupture, when it becomes a catastrophic event, there has been interest in population screening to detect, monitor and repair AAAs before complications can occur.

Screening abdominal US in asymptomatic individuals is an accurate test, with **95% sensitivity and near 100% specificity** (Fleming et al 2005). A number of international controlled randomised trials (CRTs), and one in Western Australia, have used abdominal US to screen for AAA in a target population. A meta analysis by the US Preventive Services Task Force (USPSTF) of these trials showed a RR reduction of 43% in AAA-related deaths from screening with US (OEPC 2005).

The comparison of AAA screening in Australian men aged 70+ and no screening was modelled using TreeAge Pro 2007. The model was constructed using data obtained from a range of internal, domestic and international sources.

[27] It is estimated in Lederle et al 2002a that AAAs with aortic diameter of 5.5-5.9cm have a 9.4% chance of rupture, 6.0-6.9 cm a 10.2% chance and 7+cm a 32.5% chance. This compares with a chance of rupture of 0.30% for 3.0-3.9 cm and 1.00% for 4.0-5.4cm.

4.2.1 PREVALENCE OF AAA IN AUSTRALIA, 2005

The prevalence of AAAs found in population-based abdominal US screen studies form various countries is about 4% to 9% (OECP 2005). In the Western Australian CRT, prevalence was found to be 7.2% for aortic diameter greater than 3.0 cm and 0.5% for diameter greater than 5.5 cm (Norman et al 2004). Separately, in a screening study of 126,696 US veterans, 97% of whom were male, the prevalence of AAA was 1.99% at 55-59 years, 4.75% at 65-69 years, and 5.95% in 75-79 years (Lederle et al 2002).

Disaggregated estimates of AAA prevalence by age and size have been estimated by Access Economics. Total prevalence among the target group was calculated as the mid-point between the various international trials (6.5%). Table 4–1 shows the active prevalence (numbers and rates) in men aged 55+ for Australian in 2005.

TABLE 4–1: PREVALENCE OF AAA IN AUSTRALIAN MEN, 2005

	3.0 - 3.9 cm		4.0 - 5.4 cm		5.5+cm		Total	
Age	Rate	Persons	Rate	Persons	Rate	Persons	Rate	Persons
55-59	2.0%	12,500	1.0%	5,957	0.2%	1,400	3.2%	19,857
60-64	3.4%	16,116	1.6%	7,680	0.4%	1,805	5.4%	25,601
65-69	4.8%	18,018	2.3%	8,587	0.5%	2,018	7.6%	28,623
70-74	5.4%	16,164	2.6%	7,703	0.6%	1,811	8.6%	25,677
75-79	6.0%	14,968	2.9%	7,133	0.7%	1,677	9.5%	23,778
80+	6.0%	15,442	2.9%	7,360	0.7%	1,730	9.5%	24,532
Total 55+	**4.1%**	**93,207**	**2.0%**	**44,420**	**0.5%**	**10,441**	**6.5%**	**148,068**

Source: OEPC (2005), Norman et al (2004), and Access Economics estimates.

4.2.2 MORTALITY DUE TO AAA IN AUSTRALIA, 2005

Data on mortality due to AAA was sourced from the ABS. Access Economics further disaggregated mortality by stage and by age. This disaggregation process took in account the following information.

- Aortic diameter size is the greatest predictor of AAA rupture, and it was determined in the literature review that the annual incident risk of rupture by aortic diameter was 0.3% for 3.0-3.9 cm, 1.0% for 4.0-5.4 cm (OEPC 2005) and an average of 17.4% for 5.5+ cm (Lederle et al 2002a).
- The operative mortality for open surgical repair of an AAA is 4.2%, with nearly one third of all patients undergoing this procedure suffering fatally from other complications (such as cardiac or pulmonary). The operative mortality for endografts is 1.7% with a further 18.0% suffering fatal complications (OEPC 2005).
  - The weighted average of mortality from surgical repair was estimated at 25.2%, this was triangulated with ABS data on the number of deaths from AAA (707) and the data from DoHA on the number of surgical repairs performed (2796) in 2005, giving an average mortality of 25.3%.
- The type of surgical procedure is dependent on patient condition and whether the AAA is intact or has ruptured. Approximately 2/3 of patients with intact AAAs undertake the endostent procedure, due to being unsuitable for open repair. Open repair is only suitable for younger, more fit patients or where the AAA has ruptured, while it has a higher operative mortality rate, it is the only cure.

- Additionally, the prevalence of AAA peaks at around 80 years of age, and almost all (88% of) deaths from ruptured AAAs occur in men older than age 65 years and younger than age 80 years.

Table 4–2 below shows mortality due to AAA by age and stage.

TABLE 4–2: MORTALITY DUE TO AAA IN AUSTRALIA, 2005

Age	3.0 - 3.9 cm Persons	4.0 - 5.4 cm Persons	5.5+cm Persons	Total Persons
55-59	0	0	0	0
60-64	4	6	25	35
65-69	12	19	76	106
70-74	19	31	126	177
75-79	34	53	217	304
80+	9	15	61	85
Total 55+	**78**	**124**	**505**	**707**

Source: ABS (2007), USPSTF (2007), and Access Economics estimates.

4.2.3 PROBABILITY OF DIAGNOSIS WITHOUT US

The condition is almost entirely asymptomatic and diagnosis usually occurs incidentally during examination for other conditions. As such, an assumption was made that the ordinary probability of an individual with an AAA being diagnosed with the disease is estimated based on the probability of rupture at each stage.

The estimated progression rate of AAAs was based on studies that have shown that the incidence rate for new AAAs in a period of 10 years is low, ranging from 0% to 4%, and that none of the incident AAAs exceeded a diameter of 4.0 cm. A conservative approach was then taken using a maximum likely progression rate, this was the annualised rate of 4.0 cm over a ten year period or 0.4% per annum.

4.2.4 COSTS OF US FOR DIAGNOSIS

The total cost of US screening has been calculated by combining the public and privately funded components of US scans.

- The November 2007 MBS approves a fee of $111.30 for an US scan of the abdomen (item 55036).
- Private USs are more than double the public fee. The AMA's *List of Medical Services and Fees* recommends a fee of $290 for the same service (OA085).

According to online Medicare Statistics,[28] 62% of radiology is bulk billed. Thus**, the average cost of a US scan is estimated at $179.21** ($111.30*62% plus $290*38%).

4.2.5 COST OF TREATMENT – AORTIC REPAIR

An AAA can be repaired either by open abdomen surgery or by an endovascular procedure as detailed above. The cost of these procedures has been calculated based on DoHA data on public and private hospital casemix data by DRG.

[28] See footnote 4.

- Casemix data for 2004-05[29] shows that the average cost of an open repair procedure and an endovascular procedure, with and without complications in a public hospital was $15,112. Inflating this to 2006-07 by the average health inflation rate for the period 2000 to 2005 (3.7%) gives a public hospital cost of $16,251.
- The last time Casemix data was collected for private hospitals (2002-03), the cost of the same procedures, with and without complications[30] was $10,053. Inflating this to 2006-07 by health inflation gives a private hospital cost of $11,671.

Combining the public and private hospital costs, based on the number of hospital separations for aortic repair 57.8% (public) and 42.2% (private), **this equates to an average cost of AAA repair of $14,326 in 2006-07**.

4.2.6 QUALITY OF LIFE

Finally, the **quality of life following aortic repair** is also taken into account. This is the inverse of the disability weight of AAA (0.349) available from the AIHW (Mathers et al, 2007) providing a value of 0.651. The disability weight is divided by 12 to account for the length of time taken to full recovery after surgery.

4.3 MODEL AND RESULTS

4.3.1 THE MARKOV MODEL

Figure 4-2 presents a considerably simplified representation of the Markov model tree. All individuals who are screened generate a per person health system cost for the US ($179.21). Individuals are only screened once in the model.

Those individuals that are diagnosed with AAA of diameter 5.5+ cm go on to generate an additional health system cost of treatment ($14,326) for surgical aortic repair. Additionally, the treatment costs are also allocated to those with AAAs that rupture at each stage of the disease. A disability weight of 1-(0.349/12) is applied per each surgical aortic repair,.

Table 4–3 contains a summary of the key parameters used in the model.

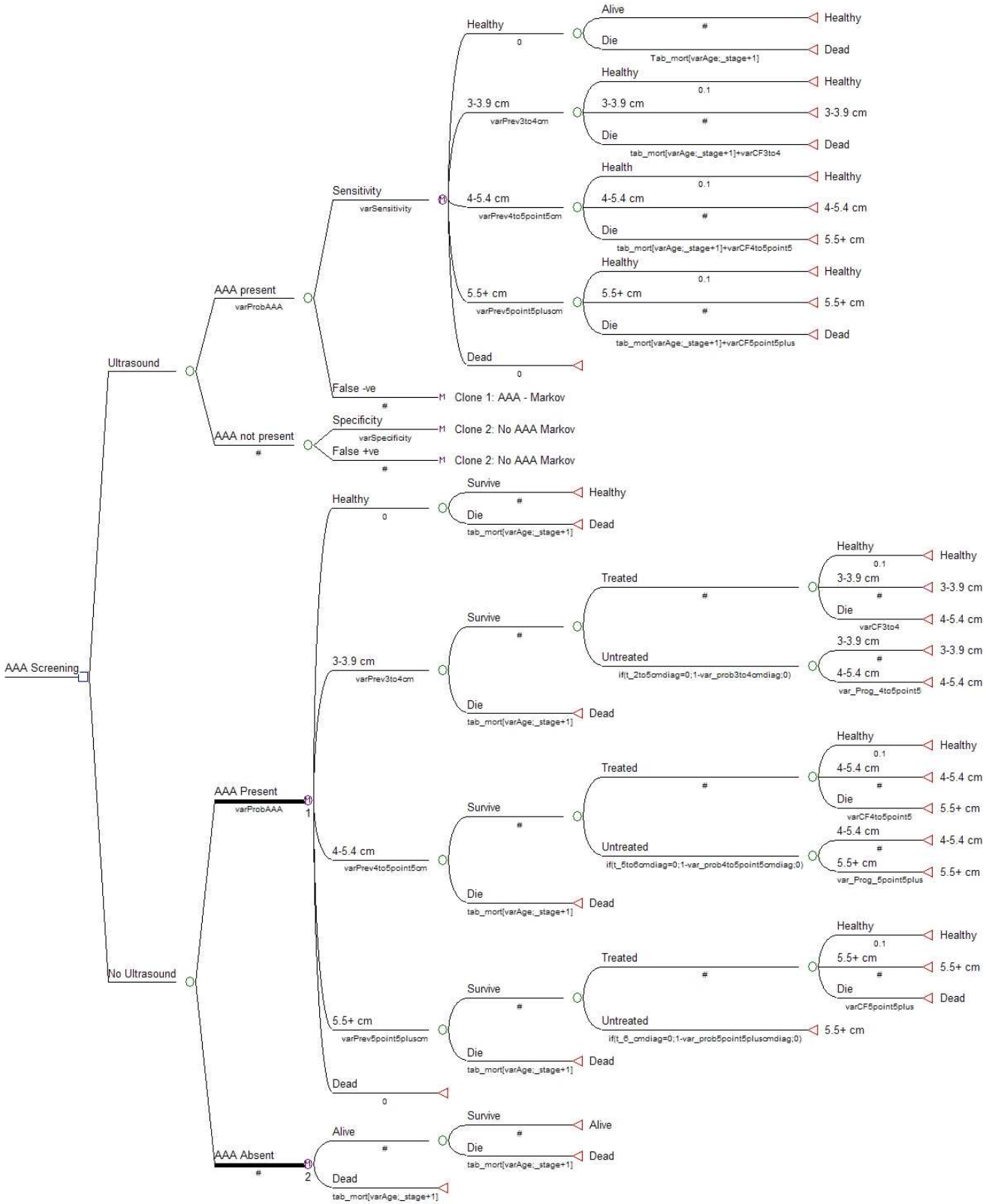
[29] http://www.health.gov.au/internet/wcms/publishing.nsf/Content/Casemix-1. 2004-05 was latest available at time of writing (December 2007).

[30] Complications associated with surgery for aortic repair was estimated at 25.39%, and without complications at 74.61% for both private and public.

TABLE 4–3: SUMMARY OF KEY MODEL PARAMETERS

Item	Variable name	Healthy	3.0 - 3.9 cm	4.0 - 5.4 cm	5.5+ cm
Ultrasound cost	cScreen	$ 179.21	$ 179.21	$ 179.21	$ 179.21
Treatment cost	CHealthSystem	$ -	$ 14,316.47	$ 14,316.47	$ 14,316.47
BoD	varQoL	0.000	0.971	0.971	0.971
Distribution of AAA	VarPrev	0.0%	63.0%	30.0%	7.0%
Progression	var_Prog			29.6%	29.6%
Case fatality	varCF		0.1%	0.3%	4.9%
Probability of diagnosing AAA in absence of screening	var_probdiag		1.2%	2.7%	44.5%
Sensitivity of ultrasound	varSensitivity	95.0%			
Specificity of ultrasound	varSpecificity	100.0%			
Discount rate of health spending	disHealth	3.0%			
Discount rate for the quality of life	disQoL	3.0%			

FIGURE 4-2: SIMPLIFIED MARKOV MODEL TREE, AAA SCREENING

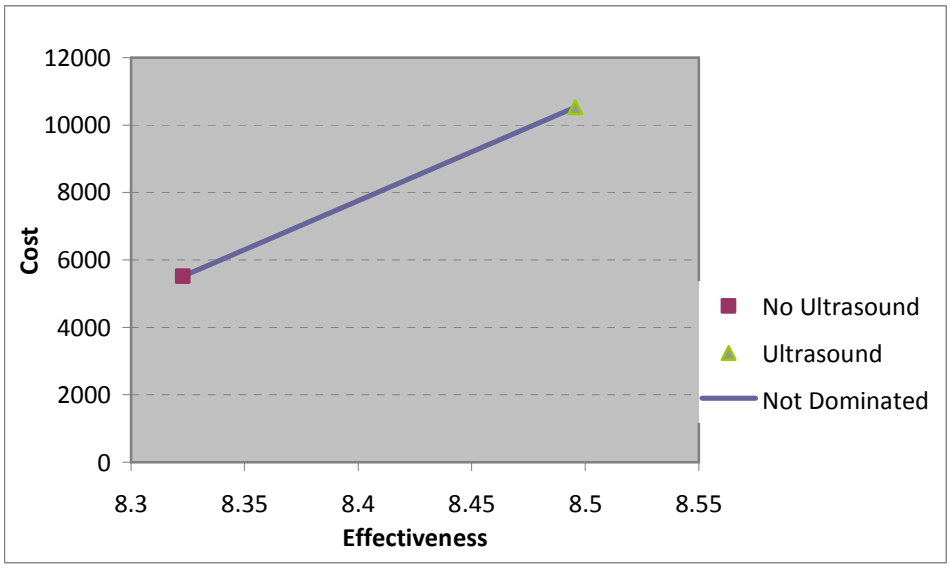


MODELLING RESULTS

The cost effectiveness of abdominal US for AAA screening in men aged 70+ is compared with no screening. A Monte Carlo Microsimulation is used to calculate an expected value by traversing individuals through the model according to the defined probabilities.

The Microsimulation results suggest while abdominal US for AAA screening is more costly than no screening, it is also more effective (Figure 4-3).

FIGURE 4-3: COST EFFECTIVENESS OF ABDOMINAL US FOR AAA SCREENING VERSUS NO SCREENING



For Australia, the ICER of the US screening pathway was **$28,993/QALY** compared to the no-screen pathway. This is based on the results that the US scan cost $10,524 per person with 8.495659 QALYs while the no-scan comparison cost $5,515 per person with 8.322896 QALYs.

While the abdominal US for AAA is considered a cost effective intervention to scan and treat Australian men aged 70 years and over, cost effectiveness AAA screening has come under considerable discussion in the literature. A number of options have been put forward to improve cost effectiveness, including selective targeting of the population (limiting maximum age), and isolating individuals with significant risk factors. For example, it was noted in one article that the increased presence of comorbid conditions for people aged 75 years and older decreases the benefits from screening. Additionally, screening AAA would most benefit those how have a reasonably high probability of having an AAA, such as those who smoke or that have a family history.

5. MAMMOGRAPHY (X-RAY) FOR BREAST CANCER SCREENING

5.1 BACKGROUND

5.1.1 THE NATURE OF BREAST CANCER

Cancer describes a range of diseases in which abnormal cells proliferate and spread out of control. Under normal circumstances, cells grow and divide to form new cells as the body needs then – when cells die, new cells grow and replace them. However sometimes this biological process goes wrong, new cells form when the body does not need them and old cells do not die when they should. These excess cells can form a mass of tissue known as a tumour or neoplasm. Tumours can be benign (non cancerous) or malignant (a cancer).

Cancer can develop from most types of cells in different parts of the body, and each cancer has its own pattern of growth and spread. While some cancers remain in or on the body for years without showing any symptoms, others can grow, invade and spread rapidly and may be fatal in a short period of time (AIHW, 2007). Proximity to other vital organs is also an important factor in natural progression and treatment.

Breast cancer starts in the ducts or lobules of the breast. Cells lining the ducts or lobules can grow out of control and develop into cancer. Breast cancer found while still confined to the ducts or lobules of the breast is called pre-invasive breast cancer. The most common types are ductal carcinoma in situ and lobular carcinoma in situ (The Cancer Council NSW, 2006).

Most breast cancers are found when they are invasive. This means the cancer has spread outside the ducts or lobules of the breast into surrounding tissue. There are several types of invasive breast cancer. The International Association of Cancer Registries (Esteban et al, 1995) defines breast cancer by the following stages:

- **Localised breast cancer:** contained in the breast but may have spread to one or more lymph nodes in the armpit.
- **Regional breast cancer:** may have spread to places near the breast, such as the chest (including the skin, muscles or bones of the chest), regional lymph nodes but has not spread to other parts of the body.
- **Metastatic/distant breast cancer:** the cancer cells spread from the breast to other areas of the body, such as the bones, liver or the lungs and distant lymph nodes. Characterised by discontinuous metastasis.

5.1.2 AETIOLOGY

The precise causal mechanisms of breast cancer are not known, however a number of risk factors for the disease have been identified including age, personal or family history of breast cancer, hormones and menstrual history (including age at menopause), breast density, and lifestyle factors such as obesity, alcohol consumption and cigarette smoke exposure. Regular physical activity and child bearing are protective factors (ie, risk reducing) for breast cancer.

5.1.3 BREAST CANCER IN AUSTRALIA

Breast cancer is the most frequently diagnosed cancer in females in Australia and is also the leading cause of cancer deaths in women. The number of new cases of breast cancer among females increased from 5,318 (80 per 100,000 women) in 1983 to 11,788 (112 per 100,000 women) in 2003 (AIHW, 2007b). Although the number of deaths attributable to breast cancer has increased from 2,040 in 1983 to 2,719 in 2005, the age-standardised mortality rate has decreased from 16.8 to 12.7 deaths per 100,000 women, with the risk of mortality due to breast cancer falling from 1 in 52 to 1 in 67 (AIHW, 2007b), reflecting improvements in treatment options.

5.1.4 BREAST CANCER DETECTION

Breast cancer can be detected though a number of methods and it is usually through a sequential combination of these that changes to the breast are confirmed as breast cancer. Primary detection methods include breast self-examination and physical examination of the breasts and lymph nodes under the arm by a physician. If an abnormality is detected, breast imaging is usually undertaken via either US or mammography. US uses soundwaves to construct a picture of the breast, enabling the physician to identify the presence of a tumour and, in some cases, whether it is benign or malignant. **A mammogram is a low dose x-ray of the breast, allowing the identification of both benign and malignant neoplasms.**

If imaging detects an abnormal area of tissue in the breast, a biopsy is usually taken for pathological examination. If breast cancer is confirmed, further testing may be undertaken to assess the extent of the cancer and determine whether it has spread to other parts of the body.

5.1.5 TREATMENT

Treatment for early stage localised breast cancer aims at removing the cancer itself and destroying any cancerous cells that may have spread to other parts of the body. This usually involves breast conserving surgery followed by radiotherapy or mastectomy (surgical removal of all or part of the breast). Treatment for advanced metastatic breast cancer involves systematic therapies that enter the bloodstream and destroy or control cancer throughout the body. These include chemotherapy, hormone therapy and biological therapy and are often undertaken in conjunction with radiotherapy. As well as attempting to control the cancer, these treatments centre around providing palliative care to reduce symptoms and improve quality of life of the individual.

5.2 BREAST CANCER SCREENING WITH MAMMOGRAPHY

5.2.1 MAMMOGRAPHY IN AUSTRALIA

A fundamental component of breast cancer control is the use of screening mammography to enable early detection of breast cancer. According to the National Breast Cancer Centre, women whose cancer is diagnosed before it has spread outside the breast have a 90% chance of surviving five years. The five year survival rate drops to 20% if the cancer spreads to other parts of the body before diagnosis. It is generally accepted that cancers detected early may be treated more conservatively and that these women have a higher likelihood of survival.

A nationwide breast cancer screening program is undertaken by BreastScreen Australia, jointly funded by the Commonwealth and state and territory governments. The Program targets women aged 50–69 years for screening once every two years and aims to have 70% or more of women aged 50–69 years participating in screening over a 24 month period. All recruitment activities undertaken by BreastScreen Australia specifically target women in this age group, although women aged 40–49 years and those over 70 years may also use the service.

5.2.2 EFFICACY OF MAMMOGRAPHY

Screening mammography detects breast cancers earlier than those detected symptomatically, and so mammographically detected breast cancer tends to have a better prognosis. Mammogram has been consistently demonstrated to reduce the risk of mortality due to breast cancer in a range of international studies.

- In a set of extensive randomised trials in Sweden (Nystrom et al, 2002), screening for breast cancer with mammogram has been shown to result in a 16% reduction in breast cancer mortality in women aged 50 to 59 (RR=0.84; 95% CI:0.70-1.01) and a 33% reduction in women aged 60 to 69 (RR=0.67; 95% CI=0.53-0.84).
- Results from the first 10 years of the mammography service screening program in Copenhagen reveal a 25% reduction in breast cancer mortality in women aged 50 to 71 (RR=0.75; 95% CI:0.63 to 0.89) compared with what would be expected in the absence of screening (Olsen et al (2005).
- Data presented by the Swedish Organised Service Screening Evaluation Group (2006), pertaining to 6,231 deaths among a population of over 500,000 showed that screening with mammography resulted in a 39% reduction in mortality in women aged 40 to 69 (RR=0.61; 95% CI:0.55-0.68).
- In a report based on 11 years' data from the Helsinki screening program, Anttila et al (2002) found a 19% reduction in mortality in the screened cohort (RR=0.81; 95% CI: 0.62-1.05).

5.3 MODELLING MAMMOGRAPHY FOR BREAST CANCER SCREENING IN WOMEN AGED 50 TO 69

As with the other Markov models presented in this report, the comparison of mammography for breast cancer screening in women aged 50 to 69 and no screening was undertaken using TreeAge Pro 2007. The model was populated using population and mortality data from Access Economics' in-house demographic model, AE-DEM, which is based on the most recently released ABS data. From this framework, the model was constructed using data obtained from a range of sources. This section briefly outlines the data and parameters applied in the model.

5.3.1 ACTIVE PREVALENCE OF BREAST CANCER IN WOMEN AGED 50 TO 69

Active prevalence in any given year is the cumulative number of cancer patients diagnosed prior to that year and who have not yet died, but on the basis of probability will die from their cancer (thus will require health care for active cancer now or in the future). Estimates of active prevalence of breast cancer were calculated in Access Economics (2006a) and have been adopted in the modeling undertaken here. Table 5-1 shows the active prevalence (numbers and rates) in women aged 50 to 69 for Australian in 2005.

TABLE 5-1: ACTIVE PREVALENCE OF BREAST CANCER IN AUSTRALIAN WOMEN, 2005

Age	Prevalence (rates)	Prevalence (persons)
50-54	0.2666%	1,791
55-59	0.4238%	2,627
60-64	0.4238%	1,982
65-69	0.4578%	1,780

Source: Access Economics (2006a).

5.3.2 MORTALITY DUE TO BREAST CANCER IN WOMEN AGED 50 TO 69

Data on mortality due to breast cancer in women aged 50 to 69, by stage of the disease, was sourced from the Cancer Institute NSW (Table 5-2). While the AIHW publishes data on mortality due to breast cancer in Australia, this does not distinguish between disease stages and as such was insufficient for the purposes of the modelling undertaken here. The AIHW mortality data did, however, provide an important source of verification for the Cancer Institute data used and as Table 5-2 below shows, the overall mortality rates from the two sources are relatively similar.

TABLE 5-2: BREAST CANCER MORTALITY, WOMEN AGED 50-69, 2003-2005 (RATE PER 100,000)

Age	CI local	CI regional	CI metastatic	CI Overall
50-54	39.9	9.3	18.4	39.9
55-59	56.9	11.6	25.4	56.9
60-64	68.3	16.9	30.1	68.3
65-69	72.4	22.6	26.9	72.4

Source: Cancer Institute (CI) NSW; AIHW (2007b).

5.3.3 BREAST CANCER PARAMETERS

Probability of diagnosis

The ordinary probability of an individual with breast cancer being diagnosed with the disease is estimated based on breast cancer incidence data sourced from the Cancer Institute NSW. At some stage, all individuals with breast cancer will be diagnosed. Consequently, the rate of diagnosis of breast cancer at the local and regional stage is calculated as the proportion of total incident cases of the disease (ie local, regional and metastatic cases combined) which were local or regional, respectively. At the metastatic stage, the rate of diagnosis is assumed to be 100%. Table 5-3 shows the parameters adopted in modelling.

TABLE 5-3: PROBABILITY OF DIAGNOSIS BY STAGE OF BREAST CANCER

Stage	Probability of diagnosis
Local	59.1%
Regional	87.1%
Metastatic	100%

Source: Access Economics based on Cancer Institute NSW data.

Undiagnosed progression

The progression of breast cancer is a complex function of many factors and is not readily able to be established from the literature in a form adequate for modelling. To circumvent this issue, consultation was undertaken with oncology specialists including Oncology ACT, the Cancer Council NSW and the NSW Cancer Institute. Based on these discussions, it is assumed that, over a 12 month period, 33% of those with undiagnosed localised breast cancer progress to the regional stage and 66% of those with undiagnosed regional breast cancer progress to the distant stage.

Survival and progression following diagnosis

If an individual with breast cancer survives five years after diagnosis, they are assumed in the model to be 'cured' of the disease. As such, the probability of an individual with breast cancer being 'cured' is determined based on the five-year survival rates for each cancer stage.

Five-year survival rates are also used in the model to capture the progression of diagnosed breast cancer. Once diagnosed, efficacious treatment ensures that progression is significantly slower than in undiagnosed cases, and in some instances remission occurs. This is modelled implicitly, with the high probability of survival in the earlier stage of disease ensuring that these individuals remain in the model and progress through the stages.

Survival data for breast cancer by extent of disease at diagnosis were obtained by special request from the NSW Cancer Institute for the years 1999-2003 (Table 5-4). Survival rates for Australia are assumed to be the same.

TABLE 5-4: SURVIVAL PROBABILITIES BY STAGE OF BREAST CANCER, NSW, 1999-2003

Year	Overall	Localised	Regional	Distant	Unknown
0	1.000	1.000	1.000	1.000	1.000
1	0.975	1.000	0.988	0.714	0.929
2	0.949	0.998	0.950	0.594	0.867
3	0.924	0.988	0.913	0.522	0.818
4	0.903	0.979	0.882	0.463	0.775
5	0.884	0.970	0.854	0.407	0.734

Source: NSW Cancer Institute special request.

5.3.4 MAMMOGRAPHY SCREENING PARAMETERS

Accuracy of mammography

The accuracy of mammography depends on sensitivity, the probability of mammography detecting breast cancer given that the individual has breast cancer, and specificity, the probability of mammography confirming no breast cancer given that the individual has no breast cancer. The range of estimates of sensitivity and specificity in the literature is wide. Table 5-5 presents a cross section of estimates from the Australian and international literature.

TABLE 5-5: SENSITIVITY AND SPECIFICITY OF MAMMOGRAPHY

Reference	Location	Age group	Sensitivity	Specificity
Elmore et al	United States	N/R	75.0%	92.3%
Anttila et al	Finland	50-59	58.0%	N/R
Kavanagh et al	Australia	40 and older	75.6%	94.9%
Banks et al	United Kingdom	50-64	86.6%	96.8%
Miller et al	Canada	50-59	56.0%^	N/R
AIHW (2007c)*	Australia	50-69	78.6%	92.3%

N/R: Not reported. ^Results from biennial screening. *BreastScreen results.

For the purposes of the model, the sensitivity and specificity observed in Australia's BreastScreen program were adopted as these represent an accurate reflection of the efficacy of mammography in Australian conditions.

Costs of mammography

The per person cost of screening using mammography was estimated based on data from Australia's BreastScreen program, provided via a special data request from the AIHW (Table 5-6 below).

TABLE 5-6: EXPENDITURE ON BREASTSCREEN, $2005 PER PERSON

	50-54	55-59	60-64	65-69
BreastScreen	38	38	38	24

AIHW: Special data request.

5.3.5 THE COSTS OF BREAST CANCER IN AUSTRALIA

5.3.5.1 HEALTH SYSTEM COSTS OF BREAST CANCER IN AUSTRALIA

The health system costs relating to breast cancer in Australia were previously estimated by Access Economics (2008 forthcoming; 2006), based on expenditure data obtained from the AIHW for the health system costs of treating invasive breast cancer in Australia.

Briefly, the per person expenditure on breast cancer includes: spending on hospitals (admitted and non-admitted patients), high-level residential care, out-of-hospital expenditure (GP services, imaging, pathology and referrals to specialists), pharmaceutical costs and other costs (other health professionals and research) as well as the cost of recent cancer initiatives such as the *Better treatment for cancer patients: radiation oncology services initiative* and *Investing in Australia's health: Strengthening Cancer Care* initiative. It does not, however, include health system expenditure associated with long-term side-effects of cancer treatment (for example, ongoing heart, lung or hearing problems due to chemotherapy or radiotherapy). The methodology used by the AIHW classifies expenditure on treatment of these adverse side effects to other disease codes (eg, heart, lung or hearing codes).

Table 5-7, below, presents the per patient treatment costs used in the modelling. Note that available data do not provide sufficient detail to model these costs by the stage of breast cancer and, as such, health system costs are modelled as invariant with disease stage. That is, every individual with breast cancer, regardless of the stage of disease, incurs a given cost for treating breast cancer. Implicit within this, although relatively minor, is the additional cost

generated as a result of the screening program, such as unnecessary investigations in those falsely diagnosed with breast cancer. For CEA, this method is likely to produce a conservative estimate if expenditure in fact increases with severity, as might be expected.

TABLE 5-7: HEALTH SYSTEM COST OF TREATING BREAST CANCER, $2005 PER PERSON^

Age group	$2005
50-54	22,923
55-64	21,656
65-69	22,721
All ages	24,564

^ Excludes screening costs.

Source: Access Economics based on AIHW expenditure data.

5.3.5.2 INDIRECT FINANCIAL COSTS OF BREAST CANCER IN AUSTRALIA

Indirect financial costs are all those that are not direct health system costs, outlined above, nor intangible costs – the loss of health and wellbeing due to breast cancer. These include productivity losses resulting from absenteeism and reduced labour force participation, costs associated with informal care, out of pocket expenses, deadweight losses associated with increased economic transfers and funeral costs.

- **Productivity costs:** these may be short term, such as time away from work to attend medical appointments or receive medical care, or long term, including reduced ability, or total inability to continue to participate in paid and/or unpaid work.
- **Costs of informal care**: informal carers are those who provide care outside the established health system, often family or friends of the individual with breast cancer. While informal care is provided free of charge, it is not free in an economic sense, as time spent caring is time that cannot be directed to other activities such as paid work, unpaid work or leisure. As such, informal care is a use of economic resources.
- **Out of pocket costs:** individuals with breast cancer also incur additional costs as a result of their disease such as costs of aids and modifications and the cost of travel and accommodation associated with seeking treatment.
- **Deadweight losses:** transfer payments — taxation and welfare payments — represent a shift of consumption power from one group of individuals in the community to another, affecting the distribution of resources, rather than the amount of resources available. While the payments themselves do not represent an economic cost, there are costs associated with administering the taxation and welfare systems, and in addition, there are distortions to consumption and work choices associated with transfer payments, which diminish the available resources in the economy.
- **Other indirect financial costs**: Other financial costs not included in health system expenditure include: The National Respite for Carers program, the community based palliative care and other palliative care services.

Table 5-8 presents a breakdown of the indirect financial costs associated with breast cancer in Australia. Detailed methodology for estimating the magnitude of these costs can be found in Access Economics (2008 forthcoming; 2006). Costs that are incurred by those with breast cancer regardless of whether the disease is terminal are presented on a cost per person (with breast cancer) basis and applied to all those with breast cancer at each stage. Those costs that are only incurred if the individual dies from breast cancer are modelled on a per death basis, for every death that occurs in the model due to breast cancer.

TABLE 5-8: SUMMARY OF INDIRECT FINANCIAL COSTS OF BREAST CANCER, $2005 PER PERSON

Age	Short term productivity costs (per person)	Long term productivity costs (per person)	Cost of informal care (per person)	Out of pocket expenses (per person)	Other indirect financial costs (per death)	Dead weight losses (per person)	Additional funeral costs (per death)
50-54	2,314	247,531	1,056	2,648	1,663	26,813	2,153
55-59	1,504	116,780	1,056	2,648	1,663	14,508	1,843
60-64	827	37,948	1,056	2,648	1,663	7,486	1,525
65-69	89	9,466	1,056	2,648	1,663	4,127	1,212

Sources: ABS (2006a), ABS (2006b) and calculations by Access Economics.

5.3.6 OTHER PARAMETERS

Disability weights

The disability weights adopted for quantifying the quality of life impacts of breast cancer in Australia are based on the Dutch weights presented in the AIHW *Burden of disease and injury in Australia* publication (Mathers et al, 2003) (and also used in the AIHW *Burden of disease and injury in Australia 2003* publication (Begg et al, 2007). After adjusting the published weights to reflect the staging of the disease, the following weights have been applied to the model:

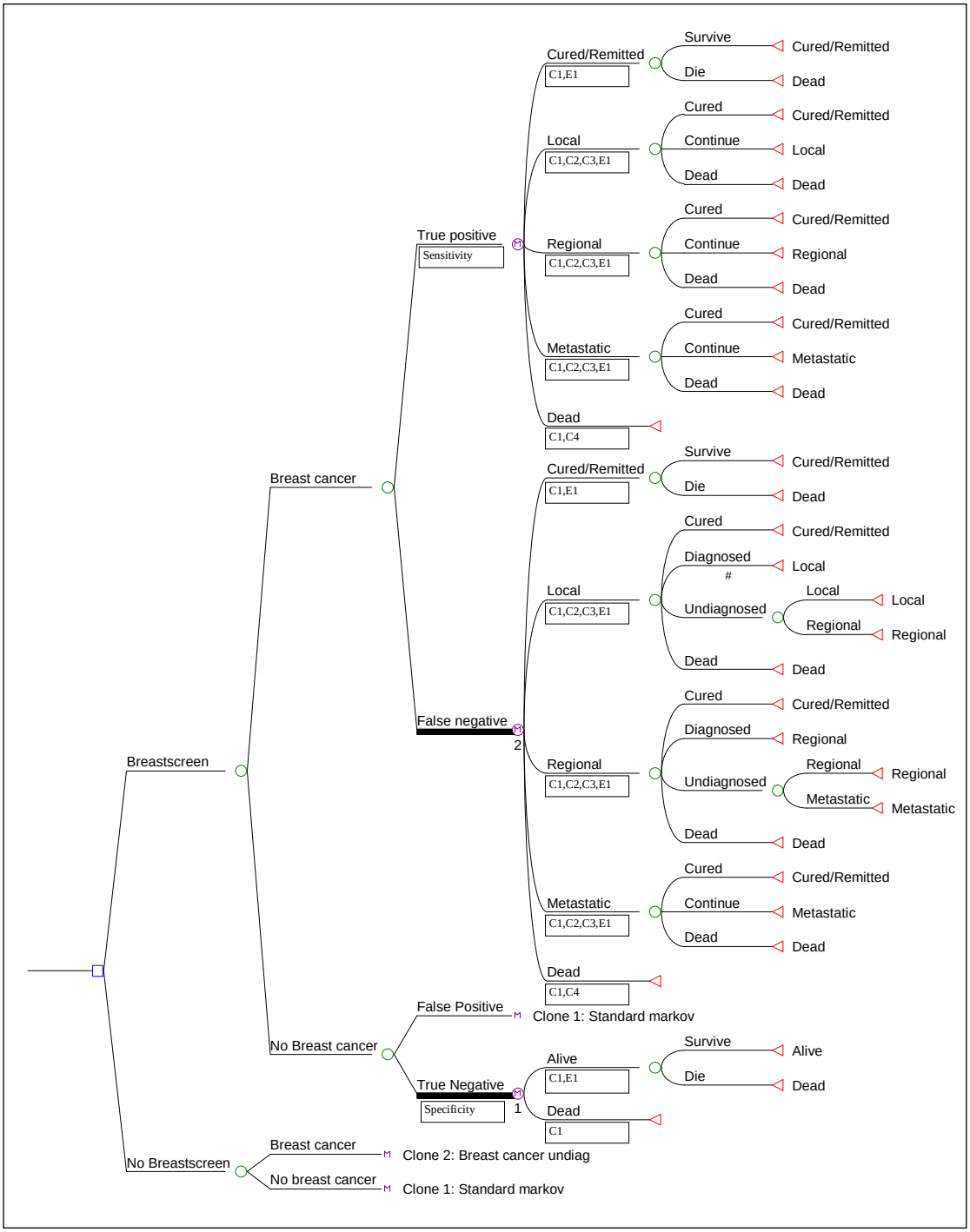
- localised breast cancer: 0.26;
- regional breast cancer: 0.69; and
- metastatic breast cancer: 0.81.

5.4 MODEL AND RESULTS

5.4.1 THE MARKOV MODEL

Figure 5-1 presents a considerably simplified representation of the Markov model tree. All individuals who are screened incur the per person costs of BreastScreen, with those diagnosed with breast cancer then incurring costs of treatment including direct (health system) and indirect costs. Additional costs, as outlined above, are incurred if the disease is fatal. Health outcomes are determined by the disability adjusted utility at each stage of the disease.

FIGURE 5-1: SIMPLIFIED MARKOV MODEL TREE, BREAST CANCER SCREENING



5.5 MODELLING RESULTS

This section analyses the cost effectiveness of mammography for breast cancer screening in women aged 50-69 compared with no screening. The technique used to conduct this analysis is a Monte Carlo Microsimulation. The Monte Carlo Microsimulation calculates an expected value by traversing individuals through the model according to the defined

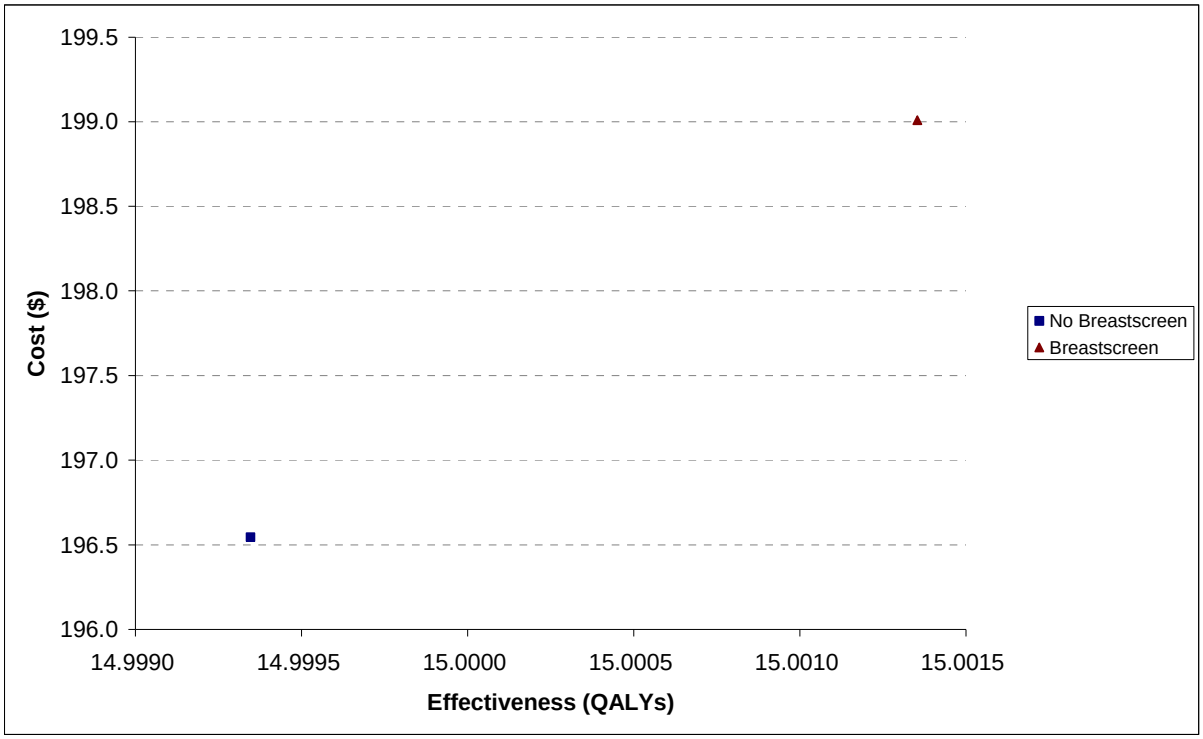
probabilities. The cost and benefits obtained per individual are summed over the course of the Monte Carlo Microsimulation with a mean value calculated from all the trials.

Two distinct Monte Carlo Microsimulations were run, one which included only the health system costs of breast cancer and another which included total economic costs (ie, both health system costs and indirect costs). Many cost effectiveness analyses do not included indirect costs, hence the former of these modelling exercises presents a good measure for comparison with other international studies. The inclusion of indirect costs better captures the true cost of breast cancer in Australia and hence the true cost effectiveness of mammography.

5.5.1 HEALTH SYSTEM COSTS ONLY

The Microsimulation results suggest for the scenario with health system costs only (i.e. no indirect costs) suggest that mammography for breast cancer screening is cost effective compared with no screening (Figure 5-2). While mammography is more costly than no screening, it is also more effective. With an ICER of $1,227/QALY, mammography may be considered very cost effective relative to all international benchmarks. Simple cost effectiveness ratios for no mammography and mammography are $13.10 and $13.26 respectively.

FIGURE 5-2: COST EFFECTIVENESS OF MAMMOGRAPHY FOR BREAST CANCER SCREENING VS. NO SCREENING



For the vast majority of individuals (97.21%) from the microsimulation, the cost of mammography is more than no mammography and the effectiveness (measured in terms of QALYs gained) is less than no mammography (Table 5-9). Overall, for society, the effectiveness of mammography exceeds that of no mammography indicating that the gains of those who benefit from mammography far outweigh the losses of those who do not. When taken with Figure 5-2, mammography is clearly cost effective relative to no mammography.

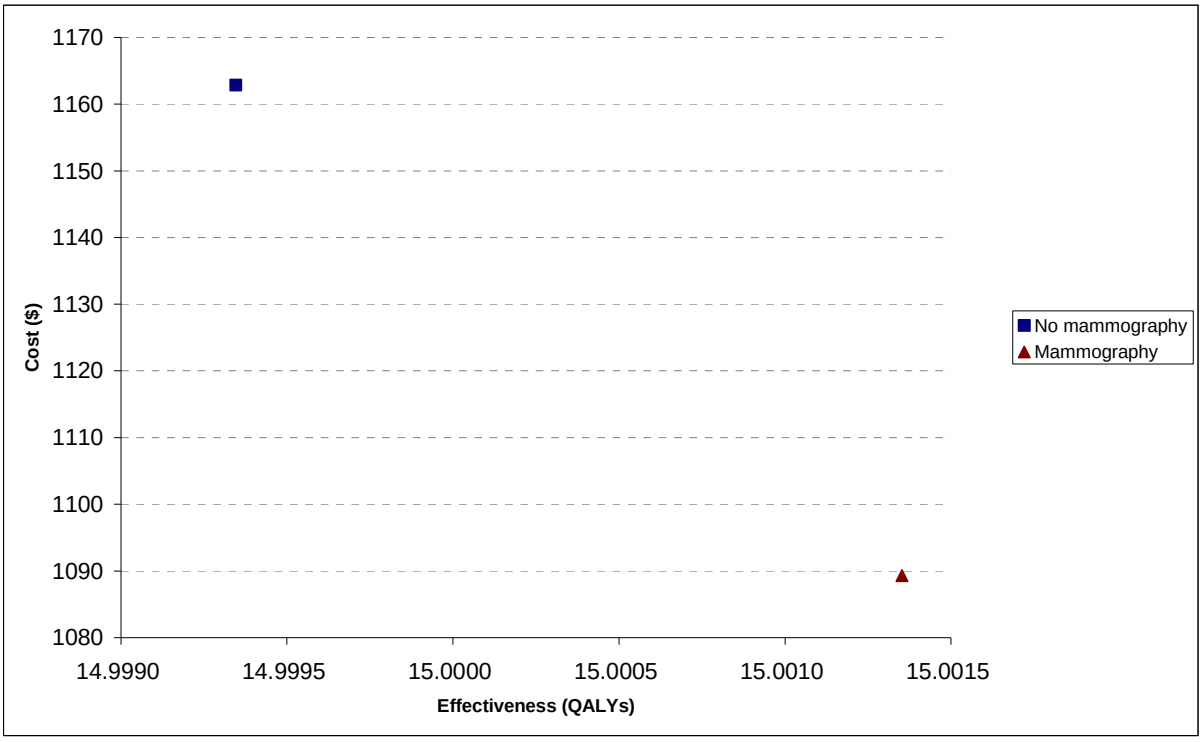
TABLE 5-9: ICER DISTRIBUTION FOR MAMMOGRAPHY VS. NO MAMMOGRAPHY SCREENING

Inc Eff	Inc Cost	ICER	# Points	Per cent
IE>0	IC<0	Superior	4,952	0.23%
IE>0	IC>0	<60,000	53,595	2.50%
IE<0	IC<0	<60,000	1,325	0.06%
IE<0	IC>0	Inferior	2,087,629	97.21%

5.5.2 TOTAL ECONOMIC COSTS

With the inclusion of indirect costs, the cost effectiveness of mammography improves further as the costs averted through the early detection breast cancer increase. In fact, when the total economic costs of breast cancer are considered, mammography is actually cost-saving – that is, mammography is both less costly and more effective than no screening (Figure 5-3).

FIGURE 5-3: COST EFFECTIVENESS OF MAMMOGRAPHY FOR BREAST CANCER SCREENING VERSUS NO SCREENING, TOTAL ECONOMIC COSTS



6. MRI FOR DIAGNOSING MS

6.1 BACKGROUND

6.1.1 WHAT IS MS?

Multiple Sclerosis (MS) is a chronic, relatively common and incurable disease that randomly attacks the central nervous system (brain and spinal cord).

In MS, the inflammation, breakdown and loss of myelin (which insulates nerves) disrupts the conduit of electrical impulses to and from the brain, producing the unpredictable symptoms of MS. Symptoms may vary and include: extreme tiredness (fatigue), tingling, numbness, impaired vision, loss of balance and muscle coordination, slurred speech, tremors, stiffness, bladder and bowel problems, difficulty walking, problems with memory and concentration, mood swings and, in severe cases, partial or complete paralysis. The sites where myelin is lost (plaques or lesions) appear as hardened ('sclerotic' or scarred) areas: in people with MS these scars appear at different times and in different areas of the brain and spinal cord. The term 'multiple sclerosis' means, literally, *many scars*.

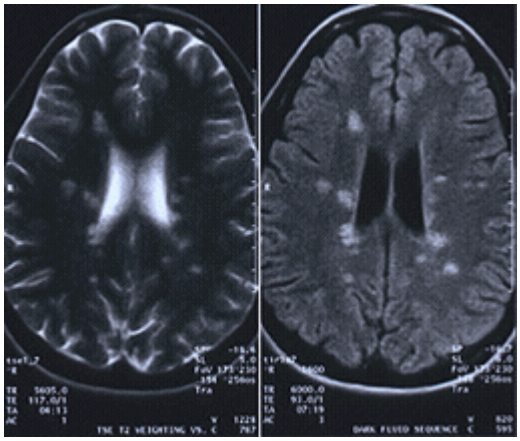
Progression and onset: The progress, severity and specific symptoms of the disease cannot be predicted. 70% of cases begin between 20 and 40, with the average age being 30 and the peak incidence occurring in the mid-twenties, although rare individuals as young as 2 and as old as 75 have developed it. There are two distinct patterns of prognosis (Patwardhan et al, 2005):

- **Relapsing/remitting (RRMS):** About 80% of people with MS have a form in which neurological symptoms and signs typically evolve over a period of several days, stabilise, and then often improve spontaneously within weeks.
  - However, over time, signs and symptoms of central nervous system dysfunction persist after relapses, or progression occurs between relapses; this pattern is called **secondary progressive (SPMS)**.
- **Primary progressive (PPMS)**: In about 20% of patients, a progressive course is apparent from onset.

6.1.2 SENSITIVITY AND SPECIFICITY OF MRI CF TRADITIONAL DIAGNOSIS

The peculiar nature of MS makes the diagnostic process complex, requiring a combination of neurological exams, medical and laboratory tests and imaging to eliminate other possible disorders and confirm MS. Other diseases to exclude in the differential diagnosis include vascular disease, spinal cord compression, vitamin B12 deficiency, central nervous system infection (eg, Lyme disease, syphilis), and other inflammatory conditions (eg, sarcoidosis, systemic lupus erythematosus, Sjögren's syndrome) (Calabresi, 2004).

For many patients with MS the first presentation is a Clinically Isolated Syndrome (CIS), a single clinical episode of demyelination. Not all people with a CIS develop MS, and **this analysis models a 50% likelihood of developing MS if presenting with clinically-assessed CIS symptoms**. MRI with gadolinium contrast, especially during or following first presentation, can be helpful in providing evidence of lesions in the brain and spinal cord. A second MRI scan may be useful at least three months after the initial attack to identify new lesions and provide evidence of dissemination over time (Calabresi, 2004). Newer MRI technologies have added greatly to diagnostic capacity (see scan reproduction following).



MS diagnosis with advanced Open MR system, image courtesy of Siemens Medical Systems T2 image on the left and newer Turbo-FLAIR image on the right.[31]

Depending on the number and location of findings, MRI can vary greatly in terms of sensitivity and specificity in the diagnosis of MS. This is especially true of PPMS, which may not show the classic discrete lesions of RRMS.

Traditionally, diagnosis of MS generally required the demonstration of clinical activity that was disseminated in both time and space. With MRI techniques, Frohman et al (2003) concluded from the evidence that MS disease activity could be demonstrated in 50% to 80%[32] of patients at the time of the first clinical presentation. Prospective studies have shown that the presence of such lesions predicts future conversion to Clinically Definite MS (CDMS) from a CIS, once alternative diagnoses are excluded at baseline.

Other studies have drawn similar conclusions, with a few listed below.[33]

- Brex et al (2001) studied the positive predictive value, sensitivity, and specificity of MRI indices for the development of MS after one year from two MRI examinations obtained three months apart from people with an initial CIS, with a clinical assessment after one year. Contrast enhancing lesions at both time points were the most predictive indices for developing MS (positive predictive value 70%) but had low sensitivity (39%). The combination of T2 lesions at baseline with new T2 lesions at follow up had the best overall positive predictive value (53%), sensitivity (83%), and specificity (76%).
- In 2001 the International Panel on Diagnosis of MS formalised the inclusion of MRI and made other refinements to formulate what are now called the 'McDonald criteria' for

[31] Description and picture reproduced from www.imaginis.com/ multiple-sclerosis/mri-and-ms.asp

[32] The finding of three or more White Matter lesions on a T2-weighted MRI scan (especially if one of these lesions is located in the PeriVentricular region) is a very sensitive predictor (>80%) of the subsequent development of CDMS within the next 7 to 10 years. Moreover, the presence of two or more Gadolinium (Gd)-enhancing lesions at baseline and the appearance of either new T2 lesions or new Gd enhancement on follow-up scans are also highly predictive of the subsequent development of CDMS in the near term. By contrast, normal results on MRI at the time of clinical presentation makes the future development of CDMS considerably less likely (Frohman et al, 2003).

[33] This brief list is not intended to be exhaustive, but appears to be fairly representative after a cursory review of the literature. Sensitivity analysis models other potential parameters than the conclusions drawn from this short handful of studies.

diagnosis (McDonald et al, 2001).[34] The McDonald criteria have been widely used and tested in a variety of research settings relative to clinical criteria previously used.

- Dalton et al (2002) compared the McDonald criteria and the previous Poser Criteria for CDMS. At three months, 20 of 95 (21%) patients had MS with the McDonald Criteria, whereas only seven of 95 (7%) had developed CDMS. After one year, the corresponding figures were 38 of 79 (48%) and 16 of 79 (20%), and after three years, they were 29 of 50 (58%) and 19 of 50 (38%). The development of MS with these MRI criteria after one year had a high sensitivity (83%), specificity (83%), positive predicative value (75%), negative predictive value (89%), and accuracy (83%) for CDMS at three years. Use of the new McDonald criteria more than doubled the rate of diagnosis of MS within a year of presentation with a CIS.
- Tintore et al (2003) followed 139 patients with CIS for three years, with brain MRI within three months of their first attack and again 12 months later. At 12 months, 11% had CDMS according to Poser Criteria compared to 37% with McDonald Criteria, of whom 80% developed a second clinical episode within a mean follow-up of 49 months. The new criteria showed a sensitivity of 74%, specificity of 86%, and accuracy of 80% in predicting CDMS. One year after symptom onset, more than three times as many patients with CIS were diagnosed with MS using McDonald criteria.
- In 2006, the McDonald criteria were modified using a less stringent definition for Dissemination In Space and a new T2 lesion after three months for Dissemination In Time (Swanton et al, 2006). Modified and McDonald criteria were both highly specific (>90%) but the modified criteria were more sensitive (77% v 46%) and more accurate (86% v 73%), relative to CDMS by Poser criteria at three years of follow-up.

These findings are summarised in the table below, with the modelled differences in sensitivity (82% cf 34%) and specificity (84% cf 35%) between MRI and traditional diagnosis after one year highlighted in the bottom rows. The ratio of MRI to traditional is based on the average of 2.42:1 after one year. The same ratio is assumed to apply to specificity as for sensitivity.

TABLE 6-1: SENSITIVITY AND SPECIFICITY OF MRI CF TRADITIONAL DIAGNOSIS OF MRI

	Sensitivity	Specificity	Criteria
Swanton et al (2006)	**77%,46% baseline**	**>90%**	Modified McDonald & McDonald criteria vs Poser at 3yrs
Frohman et al (2003)	**>80% baseline**	Na	>=3 White Matter lesions on a T2-weighted MRI scan + Gd cf clinical @7yrs
Dalton et al (2002)	21% cf 7% 3mths 38% cf 20% 1 yr 58% cf 38% 3yrs		McDonald cf Poser criteria
	83% baseline	**83%**	McDonald criteria cf Poser at 3 yrs
Tintore et al (2001)	37% cf 11%, 1yr		McDonald cf Poser
	74% baseline	**86%**	McDonald cf Poser at 4yrs
Brex et al (2001)	**83% baseline**	**76%**	T2 lesions @ baseline & new T2 lesions @ followup cf clinical at 1 yr
McDonald et al (2001)	65%, 3mths	94%	Abnormal baseline MRI
	93%, 1 yr	**83%**	Abnormal baseline MRI
Modelled	**82%**	**84%**	**MRI best practice**
	34%	**35%**	**Traditional clinical**

[34] Essentially, they allow for the second attack in time to be defined by a new lesion appearing on MRI. Also, the MacDonald criteria allow the dissemination in space to be established on the basis of either 9 typical white matter lesions on MRI or 1 enhancing lesion. If cerebrospinal fluid studies show increased immunoglobulin G values or oligoclonal banding, the presence of only 2 typical MRI lesions satisfy the dissemination-in-time criteria.

6.1.3 COST OF MRI AND TRADITIONAL DIAGNOSES

The MBS approves a fee of $492.80 for 'Magnetic Resonance Imaging: scan of head and cervical spine for demyelinating disease of the central nervous system' (Item 63125). The AMA's *List of Medical Services and Fees* recommends a fee of $1,195 plus $142 for use of gadolinium (which is assumed to be used in diagnosing MS). According to online Medicare Statistics[35], 62% of radiology is bulk-billed. Thus, the **average cost of an MRI is estimated at $813.60** ($492.80 * 62% plus $1,337 * 38%). It is assumed that two MRI scans with gadolinium are required to make a diagnosis in the first year.

6.1.4 ADVANTAGES OF MRI DIAGNOSIS AND EARLIER TREATMENT

Evidence now strongly suggests that the most destructive changes from MS in the brain occur very early on in the disease process and may cause considerable damage even before symptoms begin. Earlier diagnosis with new MRI technology, together with access to evolving treatments, offers the promise of more effective early intervention strategies for MS (Frohman et al, 2003). Many experts are now urging treatment after a first episode of RRMS (a CIS) using disease-modifying agents, particularly where specific findings from advanced MRI techniques can help determine which patients are at highest risk for progression. Quality primary and specialist (neurologist) care are very important to comprehensive and effective management of MS. Many therapeutic and technological advances are helping people with MS lead more productive lives by modifying the underlying disease course as well as by providing learning strategies to help them cope with the many changes brought on by the disease. As such, treating patients early on can save money over time by preventing severe disability (Access Economics, 2005b). Wilson and Islam (2007) conclude:

> *'Radiologically, the use of MRI is revolutionising the investigation, diagnosis, and even the treatment of MS. Usually, MRI is the only imaging modality needed for imaging patients with MS, and it far surpasses all other tests with respect to its positive predictive value. Cerebrospinal fluid analysis for oligoclonal banding or Immunoglobulin G levels is no longer routine in the investigation of MS, although this test may be of use when MRI is unavailable or MRI findings are non-diagnostic.'*

The main pathway providing evidence for better outcomes due to earlier diagnosis is the pharmacological pathway, notably interferons and other disease-modifying agents. Since 1996 four medications (Betaferon, Copaxone, Rebif and Avonex) have been approved in Australia and are available under the PBS for RRMS. They can help to lessen the frequency and severity of MS attacks, reduce the accumulation of lesions in the brain, and have also been shown to slow the progression of disability. It is not clear if interferons and other standard RRMS treatments help those with SPMS. Mitoxantrone and other immunosuppressant (eg, cyclophosphamide, methotrexate and cladribine) may delay relapse and progression in SPMS although they can have toxic side effects. No treatments have been proven yet to slow PP MS, although there are studies using interferons and glatiramer. In addition to the medications above, there is a wide range of therapies available to treat symptoms of MS such as spasticity, pain, fatigue and weakness, bladder dysfunction and depression.

[35] See footnote 4.

Data from the PRISMS (Prevention of Relapses and Disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis) and EVIDENCE (EVidence for Interferon Dose-response: European North American Comparative Efficacy) studies showed that 74% of people taking Rebif 44 mcg had no disease progression at two years compared to 63% of patients taking placebo as well as fewer brain lesions.[36] Thus implies that at 2 years, 37% of people would have naturally progressed but treatment slowed this to only 26%. This represents a 41% slowing in the rate of progression, which was similar to findings demonstrated in the BENEFIT (Betaseron in Newly Emerging Multiple Sclerosis for Initial Treatment) placebo-controlled trial and a subsequent open-label follow-up study. The BENEFIT studies measured disability progression by the Expanded Disability Scale Score (EDSS) and found that interferon beta-1b reduced the risk of progression to CDMS at two years by 46-50% compared to placebo. Also, after three years of follow-up, patients who had received interferon beta-1b at the outset had a 41% lower risk of progression to CDMS compared with patients who were started on the drug later.

The average of the trial evidence suggests that progression with treatment is an estimated **12.8% per annum while without treatment it is 18.5% per annum**. The slowing of progression provides benefits in terms of saving quality of life and saving indirect costs, which are estimated in the next section.

6.2 MODEL PATHWAYS AND PARAMETERS

6.2.1 TREATMENT COSTS

Access Economics (2005b) estimates the cost of pharmaceuticals for people with MS. The lion's share of these expenditures is on the new generation interferons, and the average expenditure per person with MS in 2005 was $4,502. Note this is an *average* expenditure across all people with MS (ie, not the drug treatment cost per annum); even though some (eg, people with PPMS or SPMS) may not be receiving this pharmacotherapy, in the model the desired parameter is the 'average' person so there is no need for adjustment to this average cost**. Inflated to 2007 prices at average health inflation of 3.7% per annum provides a 2007 estimate of early intervention treatment costs of $4,842 per person per year**. The interferon cost may be lower than this, as the Pharmaceutical Benefits Pricing Authority (2006) estimated the average price of interferon drugs to the Government as $1,178.34 in 2005-06 (33,642 scripts costing $39.6 million in total). The treatment cost is thus subjected to sensitivity analysis in the modelling, with the lower bound at $1,272.20 (ie, (1,178.34+4.70)*1.037^2) and the upper bound calculated to be equidistant from the mean. This variation reflects that the average treatment cost might also be seen to include other therapies in addition to interferon treatment, potentially.

The annual costs of treatment are modelled over 20 years as follows:

- For people with early diagnosed MS (true positives), the treatment costs are modelled as the net present value of 20 years of treatment at $4,842 (base case) per person per annum with a discount rate of 3% per annum, ie $72,030 in 2007 dollars.
- For people with later diagnosed MS (false negatives), the treatment costs are modelled as the net present value of 18 years of treatment at $4,842 (base case) per person per annum starting in Year 3, with a discount rate of 3% per annum, ie $62,766 in 2007 dollars.

[36] http://www.mslifelines.com/rebif/guide/effectiveness.jsp

- For people without MS who receive an incorrect early diagnosis of MS (false positives), treatment costs are modelled as the net present value of 2 years of treatment at $4,842 (base case) per person per annum discontinued in Year 3, with a discount rate of 3% per annum, ie $9,264 in 2007 dollars.
- For people without MS (true negatives), the treatment costs are modelled as zero.

6.2.2 FINANCIAL COSTS OF MS

Access Economics (2005b) also estimated other costs of MS, including:

- health system expenditures due to the disease itself, that treat the disease rather than that delay progression, notably hospital inpatient stays, residential care accommodation, GP and specialist visits, allied health services and health care overheads – derived from AIHW data;
- productivity losses – derived from ABS and the Australian MS Longitudinal Study on reduced work hours, temporary absences from work, early retirement and premature death (people with MS have an estimated seven-year shorter life expectancy relative to Australians without MS);
- the value of formal community care and informal care – derived from data from the Australian MS Longitudinal Study, showing 12.3 hours per week of informal care required per person and $432 per person with MS of formal community care per annum on average;
- aids and home modifications for people with MS, including walking aids, wheelchairs, special kitchen and hygiene items, ramps, car and home adaptations – from the Australian MS Longitudinal Study; and
- deadweight losses arising from taxation revenue forgone and welfare payment transfers.

TABLE 6-2: AVERAGE COST PER PERSON WITH MS PER ANNUM, 2005 AND 2007 ($)

	2005	2007
Health system costs	3,961	4,260
Other, indirect costs	28,891	31,550
Total cost per annum per person	**32,852**	**35,810**

Source: Access Economics (2005b) estimates for 2005 inflated to 2007 by health cost inflation (3.7%pa) for the health costs; nominal wage growth (4.5%pa) for the indirect costs which were largely productivity and care costs.

Total financial costs per annum per person with MS are estimated as **$35,810 per annum** in 2007 prices

The impact on the costs of MS of earlier diagnosis and treatment is to delay their onset, which is modelled in proportion to the delay in progression of the disease severity. The modelling suggests that on average people would naturally progress to reach the average financial costs of MS by about Year 7 with no treatment but would reach the average SPMS at Year 10 if they are treated from first CIS. After year 10 the financial costs are modelled to stabilise. **Over 20 years the net present value of the two streams would be $422,271 for the early treated stream and $572,018 for the later treated stream.**

However, these financial costs are **only included in the sensitivity analysis**, in the interests of conservatism in the base case.

6.2.3 QUALITY OF LIFE IMPACTS

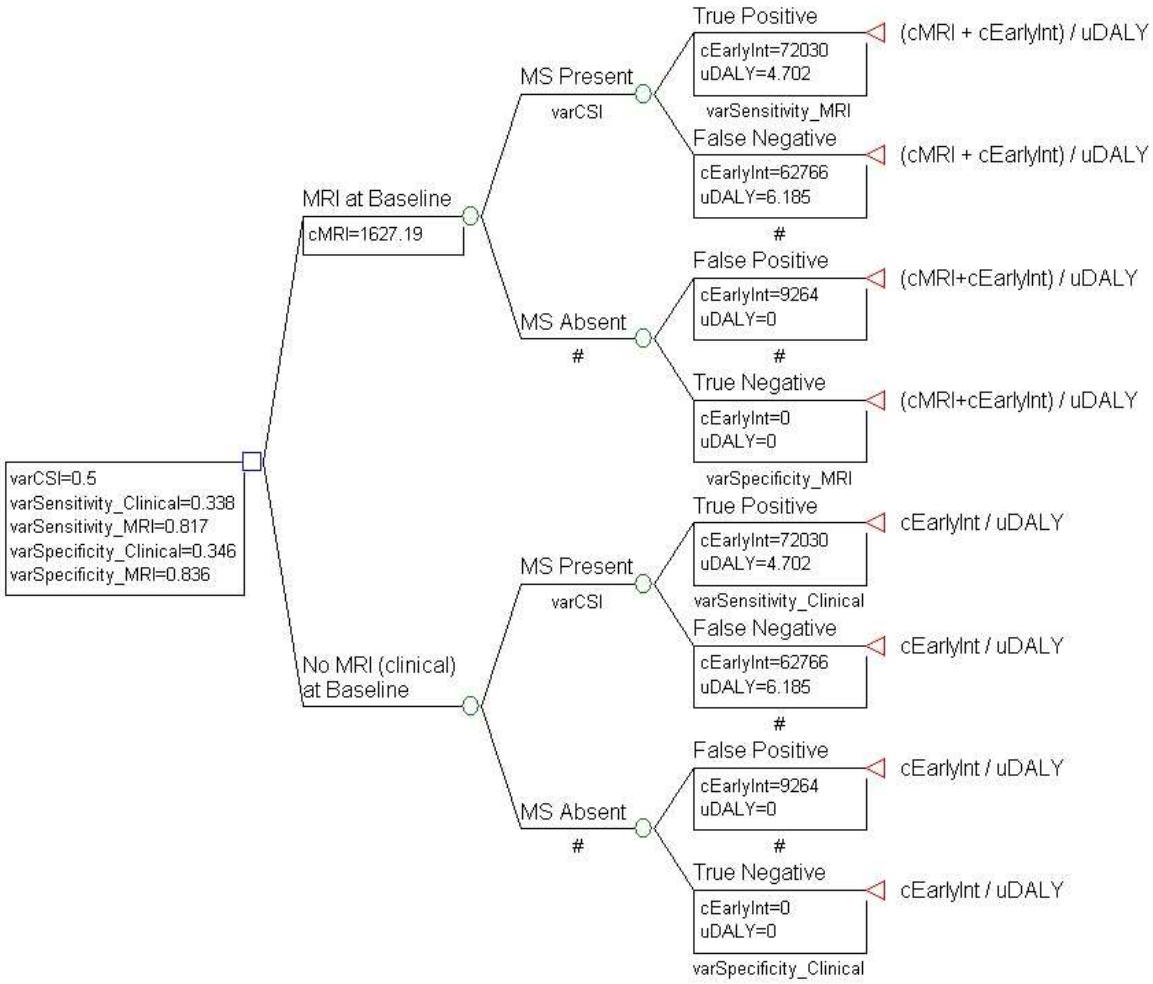
The AIHW (Mathers et al, 1999; Begg et al, 2007) estimate the disability weight associated with RRMS as 0.33 and with SPMS and PPMS as 0.67.

As with the non-treatment financial costs of MS in the previous section, the impact on the quality of life of people with MS of earlier diagnosis and treatment is to delay the impact of symptoms, which is modelled in proportion to the delay in progression of the disease severity. The modelling suggests that on average people would naturally progress to reach SPMS (0.67) at about Year 17 with no treatment but would only reach this SPMS level of disability at Year 25 if they were treated from first CIS. **Over 20 years the net present value of the two DALY streams would be 4.70 DALYs for the early treated stream and 6.18 DALYs for the later treated stream.**

6.2.4 THE MARKOV MODEL

Figure 6-1 presents the Markov model tree.

FIGURE 6-1: MARKOV MODEL TREE, MRI FOR DIAGNOSING MS



6.3 RESULTS

6.3.1 BASE CASE REULTS

The ICER of the MRI diagnostic pathway in the base case was **$4,432/DALY** averted compared to the no-scan pathway. The MRI pathway cost $37,553 per person with 2.487 DALYs after one period while the no-scan scenario cost $35,978 per person with 2.842 DALYs.

FIGURE 6-2: MRI FOR MS DIAGNOSIS: CEA RESULTS ($/DALY)

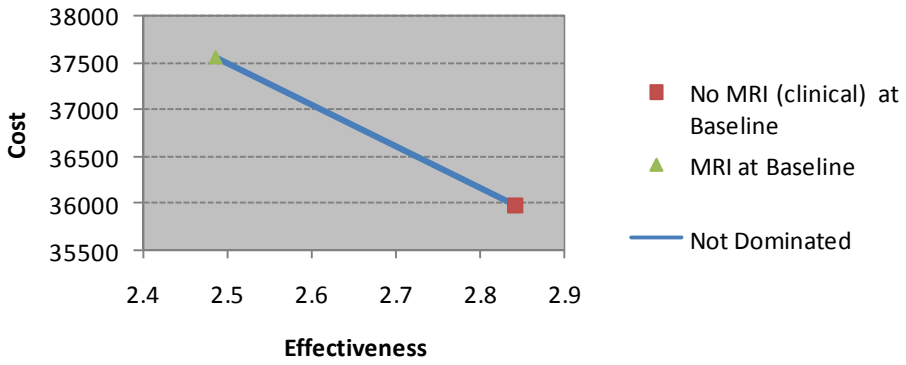


Figure 6-2 slopes downwards in this case because the Markov model was necessarily built to model DALYs averted over a long time period rather than QALYs gained in a shorter time horizon. Shorter time periods are more appropriate for acute conditions such as aortic aneurysm, IDK treatment, breast cancer and even osteoporotic fracture (where the maximum impacts were smaller risks over 10 years) – compared to chronic progressive diseases where the probable outcomes are disabling and last 20 or more years.

The MRI scan is thus considered a very cost effective intervention to diagnose MS in Australia if associated with early access to interferon therapies.

6.3.2 SENSITIVITY ANALYSIS

Sensitivity analysis was conducted in relation to key parameters, notably:

- chance of having MS at CIS presentation – low (25%) and high (75%) relative to base of 50%;
- sensitivity and specificity of MRI – low (60% for both at one year) relative to base of 81.7% and 83.6% respectively;
- sensitivity and specificity of clinical diagnosis – high (40% for both at one year) relative to base of 33.8% and 34.6% respectively;
- drug treatment costs – low ($1,272.20) and high ($8,410.86) relative to base of $4,842);
- natural progression rates – low (10%) and high (25%) relative to base of 18.5%; and
- inclusion of other financial costs of MS – $422,271 over 20 years for early treated cases and $572,018 over 20 years for later-treated cases, relative to base case where these costs were not included.

A summary of the impacts on the ICER is provided in Table 6-3, relative to the base case of $4,432/DALY averted.

TABLE 6-3: SENSITIVITY ANALYSIS ON ICER OF MRI FOR MS ($/QALY)

Sensitive parameter	Low	High
Probability of MS at CIS	$4,432	$4,432
Sensitivity and specificity of MRI	$6,233	na
Sensitivity and specificity of clinical diagnosis	na	$4,976
Early intervention treatment costs	$4,541	$4,323
Natural progression rates	$6,274	$3,995
Inclusion of financial costs of MS	na	Dominates (cost saving)

The sensitivity analysis showed the greatest sensitivity to the inclusion of the financial costs of MS. If these were included, the MRI diagnostic option would dominate clinical diagnosis, with gain of net present value of costs averted over 20 years of $34,298 in 2007 prices, as well as wellbeing gains of 0.3553 DALYs averted.

There was little sensitivity in the results to substantial changes in early intervention treatment costs, sensitivity and specificity parameters or to assumed natural progression rates (keeping the relative protective effect of interferon treatment constant). Changing the probability of MS at CIS did not affect the results at all, due to the symmetry of the 'payoffs' in each pathway.

All the sensitivity analysis results maintained the high cost effectiveness of the MRI pathway relative to no scan, with variation of the ICER from substantially cost saving to only $6,274/QALY.

7. COMPUTED TOMOGRAPHY TO DIAGNOSE APPENDICITIS

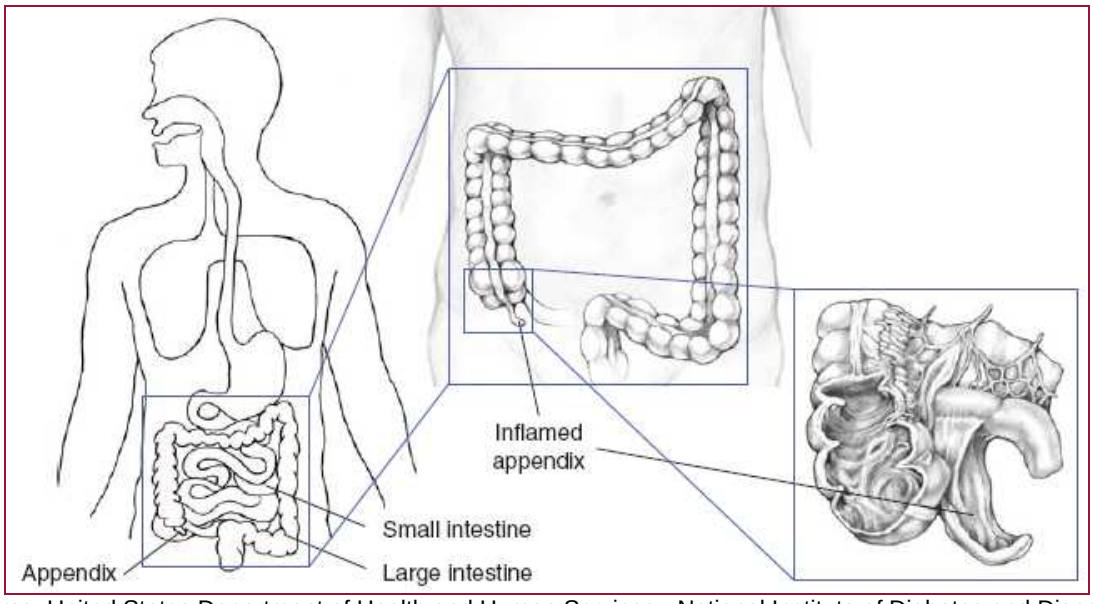
7.1 AETIOLOGY AND TREATMENT

The appendix is a small, tube-like structure or appendage that is joined to the first part of the large intestine, also called the colon. The appendix is located in the lower right side of the abdomen. It has no known function and its removal does not appear to cause any changes in digestive function.

Appendicitis is an inflammation of the appendix. Food or faecal matter can become lodged in the narrow tube of the appendix, leading to a blockage that may then become infected with bacteria. Once appendicitis begins there is no effective medical therapy. As a result, it becomes a medical emergency and usually needs to be treated (surgically) within hours of the inflammation occurring. When treated promptly, most patients recover without problems. If treatment is delayed, the appendix can burst, causing infection and even death.

Appendicitis is the most common indication for emergency abdominal surgery in Australia (Weston et al, 2005). However, the diagnosis of appendicitis remains relatively difficult.

FIGURE 7-1: ANATOMY OF THE APPENDIX



Source: United States Department of Health and Human Services - National Institute of Diabetes and Digestive and Kidney Diseases.

The common symptoms of appendicitis initially include the rapid onset of abdominal pain followed by nausea and vomiting. This is followed by localised pain in the right lower quadrant of the abdomen, often with rebound tenderness and pain upon cough. Finally, an elevated white blood cell count and low-grade fever typically occur. A significant proportion of patients (around one third) do not necessarily have these typical symptoms, leading to delayed or missed diagnosis (Weston et al, 2005). In addition, a number of other conditions can mimic the clinical presentation of appendicitis, making a concrete diagnosis difficult.

Appendicitis is treated by surgery to remove the appendix – called an appendectomy. The operation may be performed through a standard small incision in the right lower part of the

abdomen, or it may be performed using a laparoscope, which requires three to four smaller incisions. The appendix is almost always removed, even if found to be normal. Surgical treatment of acute appendicitis is generally a highly successful medical intervention.

7.2 DIAGNOSTIC TOOLS

Conventional assessment of appendicitis includes a thorough physical examination and careful consideration of the symptoms and the patient's history. However, if the diagnosis is not clear then diagnostic tools are needed. These procedures are widely available in Australia but are considered to be 'in addition' to the conventional clinical assessment (Weston et al, 2005). The most commonly used tools include CT and US.

7.2.1 COMPUTED TOMOGRAPHY

CT is a fast, non-invasive procedure using X-rays to generate cross-sectional images, secondary to the rate of radiation absorption of different tissues. CT scanning has advantages over other methods of imaging the appendix, as it is able to visualise the entire appendix. A diagnosis of acute appendicitis is generally made when the appendix measures greater than 6mm in diameter, the lumen is not filled with air or enteric material, and there is evidence of inflammation.

7.2.2 ULTRASOUND

US is a non-invasive technique involving the emission of high-frequency sound waves from a transducer into the underlying tissues, from where sound is reflected in accordance with tissue density, allowing an image to be viewed in real time. The procedure is dependent on the skill and experience of the operator of the US apparatus to interpret results, and poor technique may compromise its diagnostic accuracy.

The focus of this analysis is to compare the performance and cost effectiveness of CT versus other ways to diagnose appendicitis – including US.

- This is particularly relevant in designing the most appropriate diagnosis and treatment protocol especially in light of the difficulty in accurately detecting appendicitis.

The analysis is done by sourcing relevant effectiveness, cost and other parameters and modelling them using a diagnosis and treatment decision tree in TreeAge Pro 2007.

7.2.3 PERFORMANCE OF CT AND COMPARISON WITH US

Table 7-1 presents the sensitivity and specificity results of a number of studies comparing CT with US. **While both diagnostic tools are generally effective in diagnosing appendicitis, CT is a clearly superior tool, having a greater accuracy in nearly all the studies considered.**

The sensitivity and specificity parameters for this analysis have been sourced from Weston et al (2005), an Australian review and comprehensive meta-analysis which compared CT against US. **It shows a sensitivity and specificity of CT of 97% and 95% respectively, which compares favourably against a lower sensitivity and specificity for US of 87% and 93%.**

- However, as noted in the review, the practical application of these findings needs to be balanced against the cost and availability of CT compared to US. The relevant cost parameters are considered in the next section.

TABLE 7-1: SENSITIVITY AND SPECIFICITY OF CT COMPARED TO US FOR DIAGNOSING APPENDICITIS

Author, date and country	Patient group	Study type (level of evidence)	Outcomes		Key results
Balthazar EJ et al 1994 USA	100 patients aged 15-82 years	Prospective study	Sensitivity of US = Sensitivity of CT = Specificity of US = Specificity of CT =	76% 96% 89% 91%	CT was superior to US in evaluating patients suspected of having acute appendicitis
Pickuth et al 2000 Germany	120 patients aged 8-81yrs.	Prospective study	Sensitivity of US = Sensitivity of CT = Specificity of US = Specificity of CT =	87% 95% 74% 89%	Unenhanced spiral CT is more accurate than US in patients suspected of having acute appendicitis
Horton DH et al 2000 USA	89 patients aged 18-65 years	Prospective randomised study	Sensitivity of US = Sensitivity of CT = Specificity of US = Specificity of CT =	76% 97% 90% 100%	Non-contrast CT scan is the superior diagnostic modality
Wise SW et al 2001 USA	100 patients >18yrs old	Prospective patient study	Sensitivity of US = Sensitivity of CT = Specificity of US = Specificity of CT =	32-62% 71-96% 71-89% 73-92%	CT had significantly better diagnostic performance than US
Poortman P et al 2003 Netherlands	199 patients aged 3-89 years	Prospective patient study	Sensitivity of US = Sensitivity of CT = Specificity of US = Specificity of CT =	79% 76% 78% 83%	CT was not superior to US in the diagnosis of acute appendicitis
Weston et al 2005 Australia	Systemic review and meta analysis	Systemic review and meta analysis	Sensitivity of US = Sensitivity of CT = Specificity of US = Specificity of CT =	87% 97% 93% 95%	CT has better sensitivity and specificity than US. Application of these findings would need to evaluate the better diagnostic performance of CT against its cost and availability
Keyzer C et.al 2005 Belgium	94 patients aged 16-81 years	Prospective patient study	Sensitivity of US = Sensitivity of CT = Specificity of US = Specificity of CT =	77% 87% 87% 92%	No difference in diagnostic performance, however, more inconclusive images were obtained with US
Johansson EP et al 2007 Sweden	304 patients aged 2-94 years	Retrospective study	Sensitivity of US = Sensitivity of CT = Specificity of US = Specificity of CT =	83% 91% 98% 94%	Diagnostic accuracy was high for US as well as for CT. US was better for diagnosing positive findings, while CT was better for excluding diagnosis of appendicitis

7.3 COSTS OF DIAGNOSIS AND TREATMENT

7.3.1 CT

The cost of CT has been calculated by combining the public and privately funded components of CT screening.

- The November 2007 MBS approves a fee of $250 for a CT scan of the pelvis (iliac crest to pubic symphysis) without intravenous contrast medium (item 56409).
- Private CT scans are more than double the public fee. The AMA's *List of Medical Services and Fees* recommends a fee of $580 for the same service (OD305).

According to online Medicare Statistics[37], 62% of radiology is bulk billed. Thus, **the average cost of a CT scan is estimated at $375.40** ($250*62% plus $580*38%).

7.3.2 ULTRASOUND

Similarly, the total cost of US combines the public and privately funded components of US scans.

- The November 2007 MBS approves a fee of $111.30 for an US scan of the abdomen (item 55036).
- Private USs are more than double the public fee. The AMA's *List of Medical Services and Fees* recommends a fee of $290 for the same service (OA085).

Applying the 62% rate, the **average cost of an US scan is estimated at $179.21** ($111.30*62% plus $290*38%).

7.3.3 APPENDECTOMY

As outlined, appendicitis is treated surgically through an appendectomy. The cost of an appendectomy has been calculated by using public and private hospital Casemix data by DRG from DoHA. These data encompass a wide range of costs including: Medical; Nursing; Non Clinical; Pathology; Imaging; Allied; Pharmacy; Critical Care; Operating room; and Emergency Department costs.

- Casemix data for 2004-05[38] shows that the average cost of an appendectomy procedure in a public hospital was $4,500 (DRG G07B). Inflating this to 2006-07 by the average health inflation rate for the period 2000 to 2005 (3.7%) gives a public hospital cost of $4,839.16.
- The last time Casemix data were collected for private hospitals (2002-03), the cost of an appendectomy procedure was $2,463.00. Inflating this to 2006-07 by health inflation gives a private hospital cost of $2,859.23.

Combining the public and private hospital costs equates to an **overall average cost of appendectomy of $3,955.84 in 2006-07**. This is based on the public and private hospital

[37] See footnote 4.

[38] http://www.health.gov.au/internet/wcms/publishing.nsf/Content/Casemix-1. 2004-05 was latest available at time of writing (December 2007).

separations shares for appendectomy of 55.4% compared to 44.6%, respectively – sourced from the DoHA National Admitted Patient Care Collection.[39]

7.4 OTHER PARAMETERS

As well as the cost parameters outlined above other parameters are relevant to the analysis.

- The **probability of having appendicitis** is taken into account. This has been defined as the probability of appendicitis when patients with existing abdominal pain are referred to a specialist for further testing. Data from Krasna (2000) indicated that 42% of referred patients had appendicitis. This is consistent with data from the meta-analysis performed in Australia by Weston et al (2005).
- Because of the uncertainty around diagnosing appendicitis, an **additional GP consultation (or follow-up)** is factored into the diagnosis and treatment pathway (see below). As the overwhelming majority of total Medicare GP claims are for Item 23 ('Level B') consultations, this is assumed to be the case for appendicitis. Taking into account bulk-billing rates and AMA recommended fees[40], the average cost per encounter is $38.52 (Table 7-2).

TABLE 7-2: APPENDICITIS FOLLOW-UP CONSULTATION COSTS

GP Costs	Cost per encounter	Bulk billing rate (%)
Standard Consultation of 20 minutes (MBS item 23)	$32.80	77.3
Private fee	$58.00	22.7
Average cost	**$38.52**	

Source: MBS Online: http://www.health.gov.au/internet/mbsonline/publishing.nsf/Content/Medicare-Benefits-Schedule-MBS-1.

- The **mortality rate of people with appendicitis** is also important to assess cost effectiveness. Using data from Begg et al (2007) *Burden of disease and injury in Australia 2003*, there were 24 deaths due to appendicitis in 2003 and an annual incidence of 26,170. This allows us to calculate a mortality rate of 0.092%[41] over all appendicitis pathways that result in death, although the probability of death is assumed to vary by pathway depending on the likelihood that the patient receives an accurate diagnosis and effective treatment.
- The **quality of life with appendicitis** is also taken into account. This is calculated as unity minus the disability weight of appendicitis (0.463) available from the AIHW (Mathers et al, 1999), providing a value of 0.537. Consistent with Mathers et al 1999, this reduction in quality of life is assumed to have an average two-week duration over all appendicitis pathways that do not result in death, although the severity is assumed to vary by pathway, again depending on how quickly the patient receives an accurate diagnosis and effective treatment.

[39] http://www.health.gov.au/internet/wcms/publishing.nsf/Content/NAPPC-data_2004-05. 2004-05 was latest available at time of writing (December 2007).

[40] All bulk-billing percentages are from Medicare Online Statistics for the last quarter (September 2007) - http://www.healthconnect.gov.au/internet/wcms/publishing.nsf/Content/medstat-sep07-tables-b.

[41] Incidence rather than prevalence was used as appendicitis is a short-term condition which does not usually persist for the whole year. As a result, the prevalence of appendicitis in 2003 was a much lower 1,002 people (Begg et al, 2007). Therefore, incidence provides a more realistic picture of the impact of appendicitis.

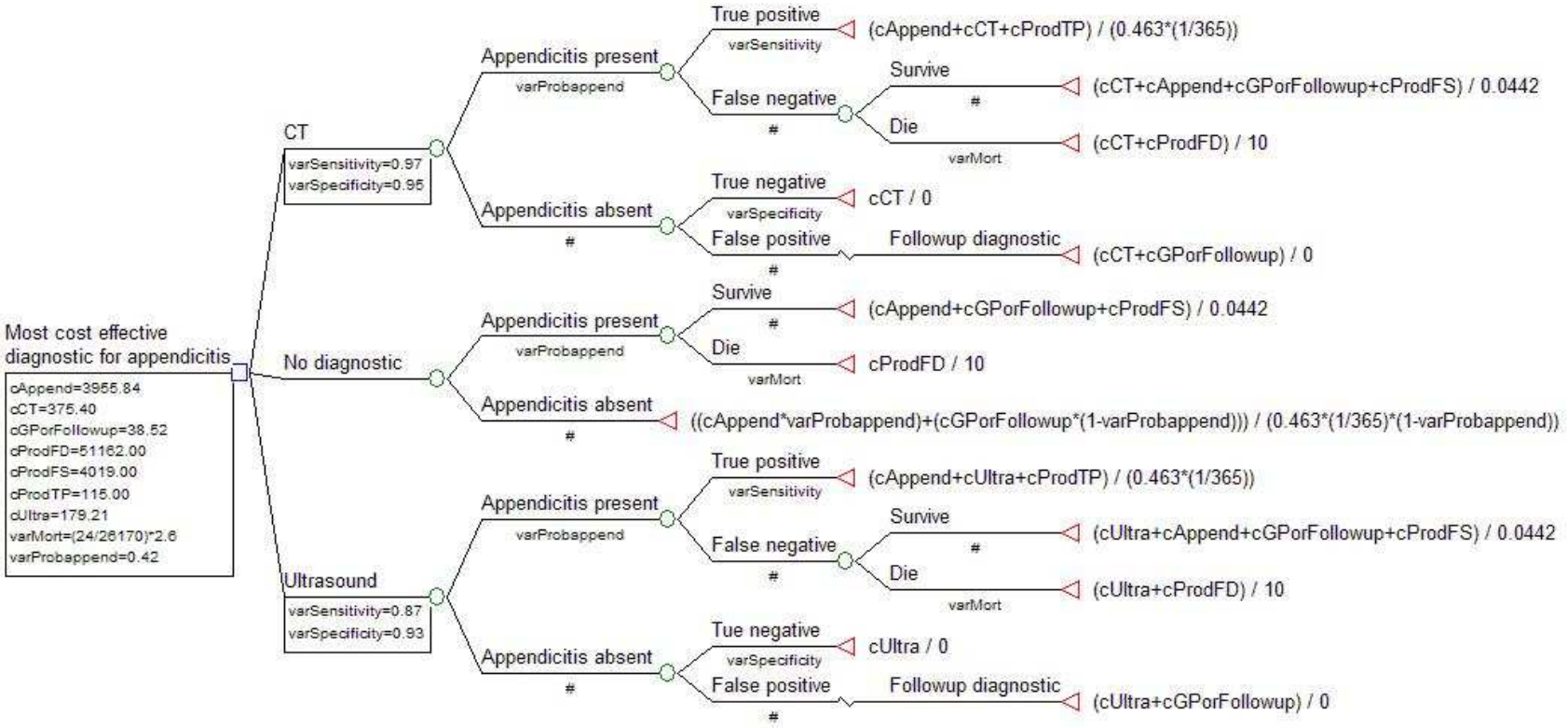
- **Productivity losses** are also estimated based on the age-gender profile of employment, AWE and deaths from appendicitis in Begg et al (2007) – which shows 20.8% of deaths in the 25-64 year group, 12.5% in the 65-74 group and 66.7% in the 75+ group – and the average life expectancy remaining for each cohort.

7.5 MODEL AND RESULTS

7.5.1 THE MARKOV MODEL

The parameters described above were modelled using Tree Age Pro 2007. The model follows a decision tree (rather than a multiple stage Markov chain) as events occur within a single time interval, given that the time between diagnosis of appendicitis and its treatment is usually a matter of hours (Figure 7-2).

FIGURE 7-2: APPENDICITIS DIAGNOSIS AND TREATMENT DECISION TREE[42]



[42] Descriptions of variables in the decision tree include: cAppend = cost of appendectomy; cCT = cost of CT; cFollowup = cost of a follow-up consultation; cProdFD = productivity costs for if the patient dies; cProdFS = productivity costs if the patient survives; cProdTP = productivity costs if true positive; cUltra = cost of US; varMort = mortality rate of people with appendicitis; varProbappend = probability of having appendicitis; varQAL_append = quality of life following appendicitis; varSensitivity (CT) = sensitivity of CT; varSpecificity (CT) = specificity of CT; varSensitivity (US) = sensitivity of US; varSpecificity (US) = specificity of CT; and # = 'inverse' of variable in directly opposite branch (eg, for a probability, the 'inverse' is unity minus that probability). These variables are defined in Sections 7.3, 7.4 and 7.5

The model begins with a decision point, whether to send the patient for a CT scan, a US diagnostic, or whether to have no diagnostic (a proxy for the conventional assessment of appendicitis).

- **For a CT scan**, the model applies the probability of having appendicitis to the sensitivity and specificity of CT. This determines how a patient progresses and whether the test is a true negative or false positive.
  - If the CT scan accurately diagnoses a true positive, the appendicitis is successfully dealt with and the patient proceeds to lose the equivalent of 0.463 QALY for one day only (ie, 0.0013), reflecting temporary pain from the appendicitis itself and the surgery. The costs associated are the cost of the CT scan and appendectomy. The productivity loss is estimated as $115, based on the age-gender profile of employment and AWE.
  - If the CT scan accurately diagnoses a true negative, the only cost is the CT scan.
  - If the CT scan is inaccurate and a false negative results then the patient can either survive or die depending on the mortality rate of any appendicitis.
    - If they survive their quality of life is diminished (the relativity is determined as 0.0442 so that overall the disability weight is 0.0178=0.463/26) and there are costs associated with the CT scan, a follow-up visit as their pain continues where the decision to operate is made, and then the appendectomy cost. Moreover, their productivity losses are in the same proportion as their loss of QALYs, relative to the true positive case ($4,019). Delay may lead to a ruptured appendix and associated chronic infection, reflected in the quality of life and productivity losses.
    - If they die then their quality of life is zero for the remaining life expectancy of their cohort (derived as around 10 years from the age-gender profile or appendicitis deaths in Begg et al, 2007). The cost of the CT scan is incurred but, since they died, they are assumed to have not have made it to the hospital for an appendectomy in time, and to have received no follow-up. Their productivity loss is estimated as the net present value of their expected future income streams lost ($51,162) taking into account employment rates, age, gender, AWE and life expectancy.
  - If the CT scan is inaccurate and a false positive results then the patient lives with a full quality of life and no productivity losses but incurs the cost of the scan as well as a follow-up visit to reconcile the CT result with the (lack of) symptoms, and to decide not to operate.
- **For an US scan**, the process is identical to the one for CT described above – except that the US scan sensitivity, specificity, and cost variables are applied.
- Finally, **for no diagnostic**, the model applies the probability of having appendicitis.
  - For the 42% of people where appendicitis is present, the patient may either survive or die depending on the mortality rate of any appendicitis (the model solves the probability of death as 0.238% in this pathway, reflecting poorer prognosis due to less chance of correct diagnosis and appendectomy).
    - For those who survive, the costs are assumed to comprise a GP visit, the appendectomy cost, a productivity loss of $4,019 and QoL loss of 0.0442 as above for false negatives.
    - For those who die, the costs are ten years of lost life and $51,162 in productivity losses, as above.

- For the 58% of people where appendicitis is absent, the patient is assumed to have a 58% chance of receiving a follow-up visit and, for those not followed up, a 42% chance of unnecessarily having surgery. Quality of life losses are minimal (0.0007) reflecting the latter group's discomfort from surgery but not from appendicitis. There are no attributed productivity losses.

7.5.2 RESULTS

The modelling in this CEA uses DALYs averted rather than QALYs gained as the outcome measure.

The results from the TreeAge decision tree model (Figure 7-3 and Figure 7-4) indicate that the no diagnostic approach is the most costly yet least effective approach – significantly influenced by the inclusion of productivity costs. CT and US are closely related in terms of costs; however, CT is clearly more effective being associated with a better (lower) DALYs outcome of 0.003 versus 0.010 at a probability of appendicitis of 1.

FIGURE 7-3: APPENDICITIS DIAGNOSIS COSTS

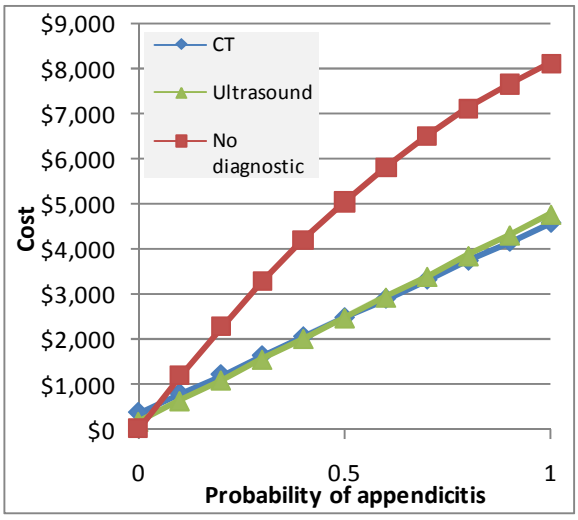
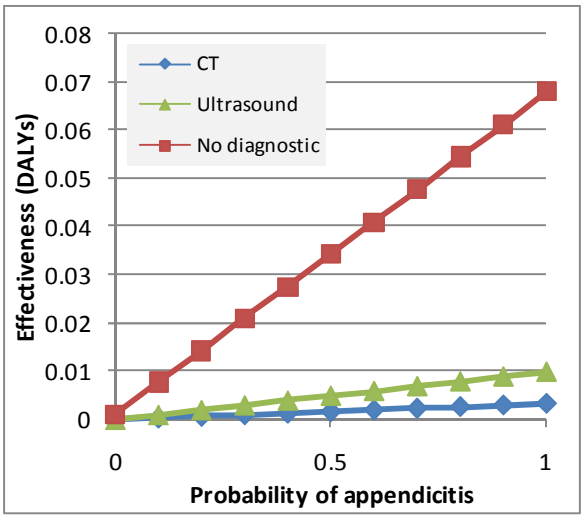


FIGURE 7-4: APPENDICITIS DIAGNOSIS EFFICACY



These results are derived by changing the probability of having appendicitis from 0 to 1, noting that of course in reality it is not possible to accurately know the probability of appendicitis for any particular individual with abdominal pain referred to a specialist. Hence when cost and effectiveness are plotted against each other, the likely outcome for each diagnostic pathway is clearer (Figure 7-5).

FIGURE 7-5: COST VERSUS EFFECTIVENESS

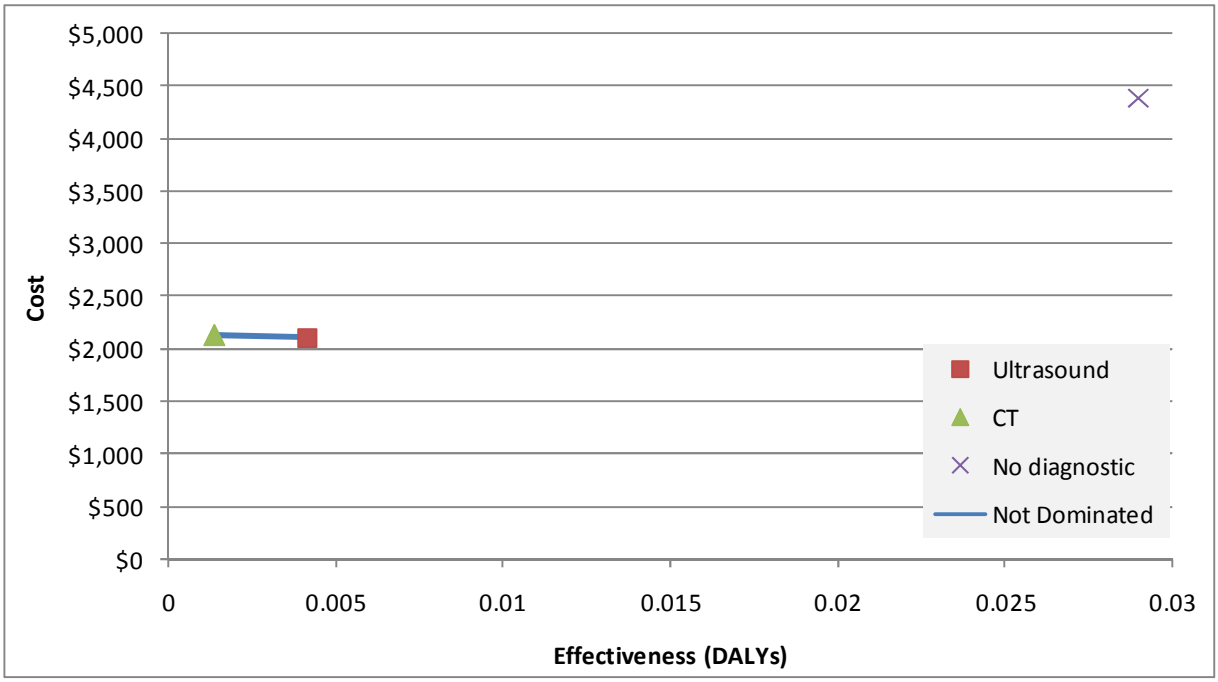


Figure 7-5 confirms that the no diagnostic approach is clearly dominated by the diagnostic tools. The no diagnostic pathway is associated with the highest costs of $4,385 per person yet has the highest DALYs (0.03). The US pathway has a much lower cost of $2,111 per person and a significantly lower 0.004 DALYs. While CT has a slightly higher cost of $2,137 per person, it is associated with only 0.001 DALYs. In fact the ICER for CT is $9,227/DALY and as such it is a cost effective intervention relative to US.

The robustness of these results is tested by performing a sensitivity analysis of the probability of having appendicitis. A low scenario of 32% and a high scenario of 52% are trialled (relative to a baseline of 42%) (Figure 7-6 and Figure 7-7).

FIGURE 7-6: COST VS. EFFECTIVENESS (LOW PROBABILITY OF APPENDICITIS)

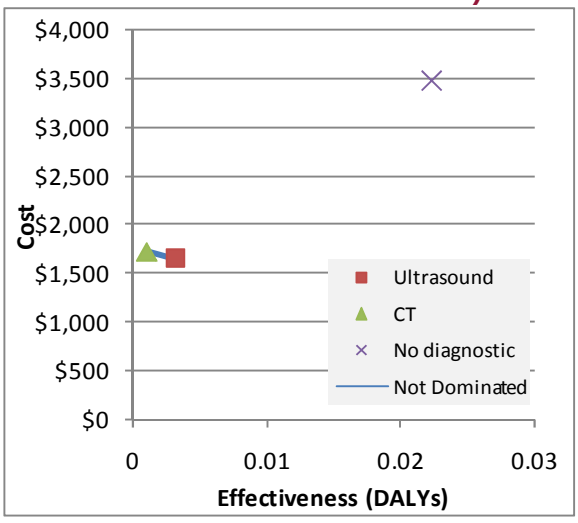
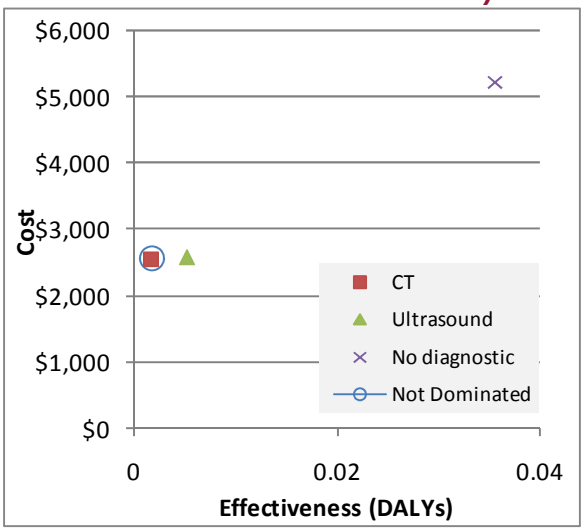


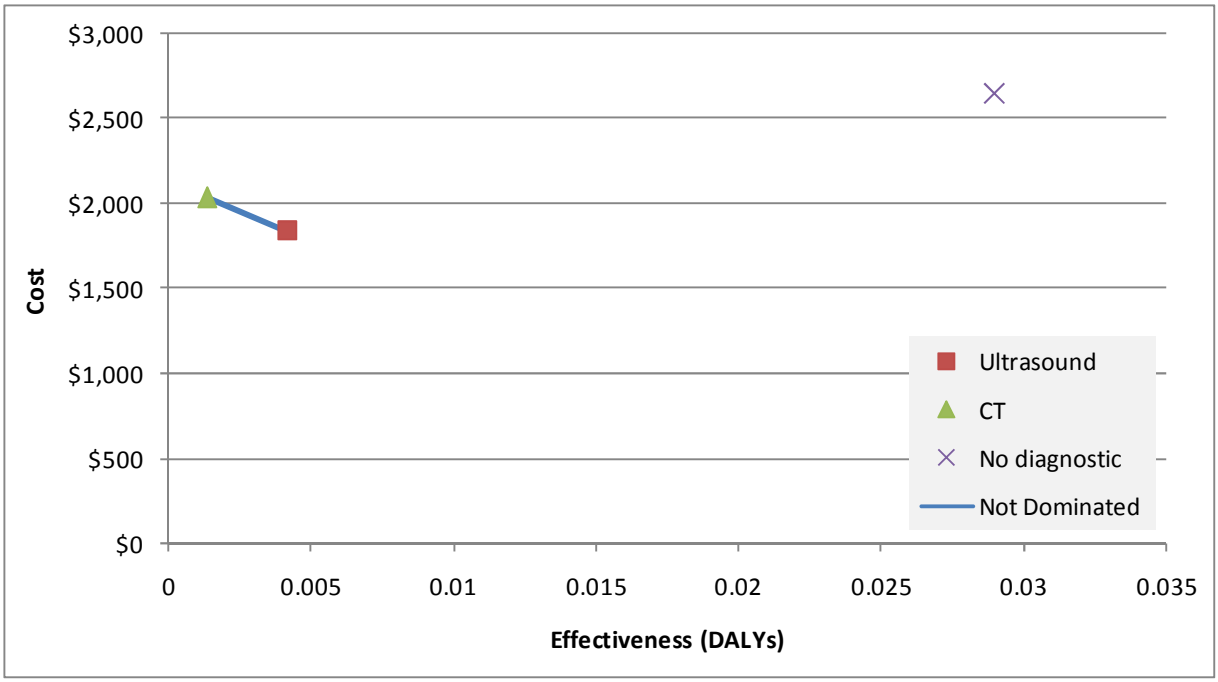
FIGURE 7-7: COST VS. EFFECTIVENESS (HIGH PROBABILITY OF APPENDICITIS)



Both figures above confirm the relationship presented in Figure 7-5 – with CT and US dominating the no diagnostic, and CT being a cost effective intervention. As the likelihood of appendicitis increases so does the cost effectiveness of CT such that, at a probability of appendicitis of 52%, CT dominates both US and the no diagnostic approach (having a cost of $2,556 per person with 0.002 DALYs).

The robustness of the findings is further tested by assuming productivity costs are zero (Figure 7-8). Under this scenario, the no diagnostic pathway is still dominated by the diagnostic tools (particularly CT). The US pathway again has the lowest cost of $1,844 per person and a significantly lower 0.004 DALYs. CT has a slightly higher cost of $2,038, and is associated with a more significantly lower 0.001 DALYs. The ICER for CT is now a higher $69,470/DALY and it is now borderline in cost effectiveness. While this scenario is useful to illustrate the importance of the relatively high productivity costs associated with appendicitis, it should be noted that these costs should not be ignored – particularly where a person with appendicitis is adversely affected or dies through lack of screening by either US or CT.

FIGURE 7-8: COST VERSUS EFFECTIVENESS (NO PRODUCTIVITY COSTS)



In conclusion, both CT and US dominate the no diagnostic approach.

Further, CT scans are cost effective relative to US. This makes the use of CT a sensible option for the diagnosis of appendicitis.

REFERENCES

Access Economics (2005a) *The economic value of informal care,* Report to Carers Australia, August.
http://www.accesseconomics.com.au/publicationsreports/showreport.php?id=6&searchfor=2005&searchby=year

Access Economics (2005b) *Acting Positively: Strategic implications of the economic costs of multiple sclerosis in Australia,* Report to Multiple Sclerosis Australia, Winter.
http://www.accesseconomics.com.au/publicationsreports/showreport.php?id=7&searchfor=2005&searchby=year

Access Economics (2006a) *Cost of Cancer in NSW*, Report for the Cancer Council of NSW, June.
http://www.accesseconomics.com.au/publicationsreports/showreport.php?id=144&searchfor=2006&searchby=year

Access Economics (2006b) *Breaking point: The economic cost of not adhering to bisphosphonate treatment for osteoporosis*, Report for Roche Products Pty Limited and GlaxoSmithKline, November.
http://www.accesseconomics.com.au/publicationsreports/showreport.php?id=109&searchfor=2006&searchby=year

Access Economics (2008 forthcoming) *Economic analysis of chemoprevention of breast cancer*¸ Report for the Cancer Institute NSW, expected release in March.

Access Economics (2008) *The Health of Nations: Estimating the average value of a statistical life year in Australia*, Report for the Office of the Australian Safety and Compensation Council, Department of Employment and Workplace Relations, January.

Anttila A, Koskela K, Hakama M (2002) 'Programme sensitivity and effectiveness of mammography service screening in Helsinki, Finland' *Journal of Medical Screening,* 9(4):153-158.

Australia Institute of Health and Welfare (2005) *Health system expenditure of disease and injury in Australia, 2000-01*. Second edition. AIHW Cat No HWE 28, (Health and Welfare Expenditure Series No 21), Canberra.

Australia Institute of Health and Welfare, Australasian Association of Cancer Registries (2007a) *Cancer in Australia: an overview, 2006* AIHW Cat No CAN 32, Canberra.

Australian Bureau of Statistics (2005a) *Australian Labour Market Statistics*, Cat No 6105.0, October 2005.

Australian Bureau of Statistics (2005b) *Employee earnings, benefits and trade union membership*, Cat No 6310.0, August.

Australian Bureau of Statistics (2006a) *National Health Survey 2004-05: Summary of Results*. Cat No 4364.0, Canberra.

Australian Bureau of Statistics (2006b) *National Health Survey* 2004–05*: Users Guide - Electronic*. Cat No 4363.0.55.001, Canberra.

Australian Bureau of Statistics (2007) '3303.0 - Causes of Death, Australia, 2005', Australian Bureau of Statistics.

Australian Bureau of Statistics (2007) *Causes of Death, Australia, 2005*, Cat No 3303.0.

Australian Institute of Health and Welfare (2006) *Heart, stroke and vascular diseases, Australian Facts: 2004,* AIHW Cat No CVD 27, Canberra:

Australian Institute of Health and Welfare (2006). Heart, stroke and vascular diseases, Australian Facts: 2004. AIHW Catalogue no. CVD 27. Canberra:

Australian Institute of Health and Welfare (2007b) *Australian Cancer Incidence and Mortality (ACIM)* Books, AIHW, Canberra.

Australian Institute of Health and Welfare (2007c) *BreastScreen Australia monitoring report 2003–2004* AIHW Cat No CAN 31, Canberra.

Balthazar EJ, Bernard AB, Yee J, Megibow AJ, Roshkow J, Gray C (1994) 'Acute Appendicitis : CT and US Correlation in 100 patients' *Radiology* 190(1):31-5.

Beatriz JE, Perry HM (1994) 'Age-related osteoporosis' *Clin Geriatr Med* 10:575–577.

Begg S, Vos T, Barker B, Stevenson C, Stanley L, Lopez AD (2007) *Burden of disease and injury in Australia 2003*, AIHW PHE 82 Canberra, April.

Black DM, Cummings SR, Karpf D et al (1996) 'Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures' *Lancet* 348:1535–1541.

Brameld K, Holman D, Threlfall T, Lawrence D, De Klerk N (2002) 'Increasing active prevalence of cancer in Western Australia and its implications for health services' *Australian and New Zealand Journal of Public Health*, 26(2):164-169.

Brex PA, Miszkiel KA, O'Riordan JI, Plant GT, Moseley IF, Thompson AJ, Miller DH (2001) 'Assessing The Risk Of Early Multiple Sclerosis In Patients With Clinically Isolated Syndromes: The Role Of A Follow Up MRI' *J Neurol NeuroSurg Psychiatry* 70(3):390-3.

Bryan S, Weatherburn G, Bungay H, Hatrick C, Salas C, Parry C, Field S, Heatley F (2001) 'The cost effectiveness of magnetic resonance imaging for investigation of the knee joint' *Health Technology Assessment* 5(27).

Calabresi PA (2004) 'Diagnosis and Management of Multiple Sclerosis' *Am Fam Physician* 70:1935-44.

Cauley JA, Thompson DE, Ensrud KC, Scott JC, Black D (2000) 'Risk of mortality following clinical fractures' *Osteoporos Int* 11(7):556-61.

Center J, Nguyen T, Schneider D, Sambrook P, Eisman J (1999) 'Mortality after all major types of osteoporotic fracture in men and women: an observational study.' *Lancet* 353:878–82.

Cooper C, Atkinson EJ, Jacobsen SJ, O'Fallon M, Melton LJ (1993) 'Population-based study of survival after osteoporotic fractures.' *Am J Epidemiol* 137:1001–1005.

Cosford PA, Leng GC (2007) 'Screening for abdominal aortic aneurysm', *The Cochrane Database of Systematic Reviews* 4.

Cosford PA, Leng GC (2007) 'Screening for abdominal aortic aneurysm', The Cochrane Database of Systematic Reviews 2007 Issue 4.

Cuddihy MT, Gabriel SE, Crowson CS et al (1999) 'Forearm fractures as predictors of subsequent osteoporotic fractures.' *Osteoporosis Int* 9:469-475.

Cumming RG, Nevitt MC, Cummings SR (1997) 'Epidemiology of hip fractures.' *Epidemiol Rev* 19:244–257.

Cummings SR, Black DM, Thompson DE et al (1998) 'Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures.' *JAMA* 280:2077-2082.

Dalton CM, Brex PA, Miszkiel KA, Hickman SJ, MacManus DG, Plant GT, Thompson AJ, Miller DH (2002) 'Application Of The New McDonald Criteria To Patients With Clinically Isolated Syndromes Suggestive Of Multiple Sclerosis' *Ann Neurol* 52(1):47-53.

Department of Health and Aged Care (1999) 'Endoluminal grafting for abdominal aortic aneurysm', Medicare Services Advisory Committee Final assessment report.

Department of Health and Aged Care (1999) *Endoluminal grafting for abdominal aortic aneurysm*, Medicare Services Advisory Committee Final assessment report.

Department of Health and Ageing (2003) *Returns on investment in public health: An epidemiological and economic analysis*, Report to the DoHA by Applied Economics.

Elmore J, Armstrong K, Lehman C, Fletcher S (2005) 'Screening for Breast Cancer' *JAMA,* 293(10): 1245-1256.

Esterban D, Whelan S, Laudico A, Parkin D (eds) (1995) *Manual for Cancer Registry Personnel* IARC Technical Report No 10, Lyon.

Fleming C, Whitlock EP, Beil TL, Lederle FA. (2005) 'Screening for abdominal aortic aneurysm: a best-evidence systematic review for the U.S. Preventive Services Task Force'. Ann Intern Med. 2005;142:203-11

Frohman EM, Goodin DS, Calabresi PA, Corboy JR, Coyle PK, Filippi M, Frank JA, Galetta SL, Grossman RI, Hawker K, Kachuck NJ, Levin MC, Phillips JT, Racke MK, Rivera VM, Stuart WH (2003) 'The Utility Of MRI In Suspected MS: Report Of The Therapeutics And Technology Assessment Subcommittee Of The American Academy Of Neurology' *Neurology* 61(5):602-11.

Gray H (2004) *The Anatomy of the Human Body* 39th edition, CV Mosby, New York.

Harris ST, Watts NB, Genant HK et al (1999) 'Effects of risedronate treatment on vertebral and non-vertebral fractures in women with established osteoporosis.' *JAMA* 282:1433–1452.

Horton MD, Counter SF, Florence MG and Hart MJ (2000) 'A Prospective Trial of Computed Tomography and Ultrasonography for Diagnosing Appendicitis in the Atypical Patient' *Am J Surgery* 179(5):379.

Ismail AA, O'Neil TW, Cooper C et al (1998) 'Mortality associated with vertebral deformity in men and women: results from the European Prospective osteoporosis Study (EPOS).' *Osteoporosis Int* 8:291-297.

Johansson EP, Rydh A, Riklund AK (2007) 'Ultrasound, Computed Tomography, and Laboratory Findings in the Diagnosis of Appendicitis' *Acta Radiologica* 48(3):267-273.

Johnell O, Oden A, Caulin F and Kanis JA (2001) 'Acute and long-term increase in fracture risk after hospitalisation for vertebral fracture' *Osteoporosis International* 12:207–214.

Johnston KW, Rutherford RB, Tilson MD, Shah DM, Hollier L, Stanley JC (1991) Subcommittee on Reporting Standards for Arterial Aneurysms, Ad Hoc Committee on Reporting Standards, Society for Vascular Surgery and North American Chapter, International Society for Cardiovascular Surgery Journal of Vascular Surgery 13:(3):452-458.

Johnston, K.W. Rutherford, R.B. Tilson, M.D. Shah, D.M. Hollier, L. and Stanley J.C. (1991) Subcommittee on Reporting Standards for Arterial Aneurysms, Ad Hoc Committee on Reporting Standards, Society for Vascular Surgery and North American Chapter, International Society for Cardiovascular Surgery Journal of Vascular Surgery 1991. 13: (3) 452-458.

Kanis JA (1994) 'Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO Study Group.' *Osteoporosis Int* 4:368-381.

Kavanach A, Giles G, Mitchell H, Cawson J (2000) 'The sensitivity, specificity, and positive predictive value of screening mammography and symptomatic status' *Journal of Medical Screening,* 7(2):105-110.

Keyzer C, Zalcman M, Maertelaer VD, Coppens E, Bali MA, Gevenois PA, Gansbeke DV (2005) 'Comparison of US and Unenhanced Multi-Detector Row CT in Patients Suspected of Having Acute Appendicitis' *Radiology* 236(2):527-34.

Klotzbuecher CM, Ross PD, Landsman PB et al (2000) 'Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis.' *J Bone Miner Res* 15:721-739.

Krasna IH (2000) 'Abdominal Pain and Appendicitis: Is There a Difference in Referrals Between HMO Pediatricians and Private Pediatricians?' *Journal of Pediatric Surgery* 35(7):1084-1086.

Lederle FA, Johnson GR, Wilson SE, Chute EP, Hye RJ, Makaroun MS et al (2002) 'The aneurysm detection and management study screening program: validation cohort and final results' Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators *Archives of Internal Medicine* 160(10):1425-1430.

Lederle, F.A. Johnson, G.R. Wilson, S.E. Chute, E.P. Hye, R.J.and Makaroun, M.S. et al (2002) 'The aneurysm detection and management study screening program: validation cohort and final results' Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators Archives of Internal Medicine 2000. 160: (10) 1425-1430.

Lederle, F.A. Johnson, G.R. Wilson, S.E. Chute, E.P. Hye, R.J.and Makaroun, M.S. et al (2002a) 'Rupture rate of large abdominal aortic aneurysms in patients refusing or unfit for elective surgery' JAMA 2002, 287: 2968-72.

Lee D (2007) 'Abdominal Aortic Aneurysm', available on line at **http://www.medicinenet.com/abdominal_aortic_aneurysm/article.htm**.

Lee, D (2007) 'Abdominal Aortic Aneurysm', available on line at **http://www.medicinenet.com/abdominal_aortic_aneurysm/article.htm**.

Liberman UA, Weiss SR, Broll J et al (1995) 'Effect of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis.' *N Engl J Med* 333:1437–1443.

Marshall D, Johnell O, Wedel H (1996) 'Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures.' *BMJ* 312:1254-1259.

Mathers C, Vos T, Stevenson C (1999) *The burden of disease and injury in Australia,* AIHW Cat No PHE17, Canberra.

McDonald WI, Compston A, Edan G, Goodkin D, Hartung HP, Lublin FD, McFarland HF, Paty DW, Polman CH, Reingold SC, Sandberg-Wollheim M, Sibley W, Thompson A, van den Noort S, Weinshenker BY, Wolinsky JS (2001) 'Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis' *Ann Neurol* 50:121-7.

Miller A, Bains C, To T, Wall C (1992) 'Canadian National Breast Screening Study: 1. Breast cancer detection and death rates among women aged 40 to 49 years' *CMAJ,* 149:1477-1488.

Munshi M, Davidson M, MacDonald P, Froese W, Sutherland K (2000) 'The efficacy of magnetic resonance imaging in acute knee injuries' *Clinical Journal of Sport Medicine* 10:34-39

Murray C, Lopez A (1996) *The Global Burden of Disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020,* Volume 1, Global Burden of Disease and Injury Series, Harvard: Harvard School of Public Health.

Murray C, Lopez A, Mathers C, Stein C (2001) *The Global Burden of Disease 2000 Project: aims, methods & data sources*, Discussion Policy Paper No 36, WHO, November.

Nevitt AW, Vida F, Kozarek RA, Traverso LW, Raltz SL (1998) 'The association of radiographically detected vertebral fractures with back pain and function: a prospective study.' *Ann Intern Med* 128(10):793-800.

Nevitt MC, Ross PD, Palermo L, Musliner T, Genant K, Thompson DE (1999) 'Fracture intervention trial research group. Association of prevalent vertebral fractures, bone density, and alendronate treatment with incident vertebral fractures: Effect of number and spinal location of fractures' *Bone* 25(5):613-619.

Nguyen T, Center J, Eisman J (2004) 'Osteoporosis: under-rated, under-diagnosed and under-treated.' *Med J Aust* 180:S18–22.

Nguyen T, Sambrook PN, Kelly P et al (1993) 'Prediction of osteoporotic fractures by postural instability and bone density.' *BMJ* 307:1111-1115.

Nguyen TV, Eisman JA (1999) 'Risk factors for low bone mass in elderly men', pp335-362 in Orwoll ES ed (1999) *Osteoporosis in men*. Academic Press, San Diego.

Norman P, Jamrozik K, Lawrence-Brown M, Le M, Spencer C, Touhy R, Parsons R, Dickinson J (2004) 'Population based randomized controlled trial on impact of screening on mortality from abdominal aortic aneurysm', *BMJ*.

Norman, P, Jamrozik K, Lawrence-Brown, M, Le, M, Spencer, C, Touhy, R, Parsons, R, Dickinson, J (2004) Population based randomized controlled trial on impact of screening on mortality from abdominal aortic aneurysm', BMJ.

Nystrom L, Andersson I, Bjurstam N, Frisell J, Nordenskjold B, Rutqvist L (2002) 'Long-term effects of mammography screening: updated overview of the Swedish randomised trials' *Lancet*, 359:909-19.

Oei EH, Nikken JJ, Verstijnen AC, Ginai AZ, Myriam Hunink MG (2003) 'MR imaging of the menisci and cruciate ligaments: a systematic review' *Radiology* 226:837–48.

Olsen A, Njor S, Vejborg I, Schwartz W, dalgaard P, Jensen M, Tange U, Blichert-Toft, Rank F, Mouridsen H, Lynge E (2005) 'Breast cancer mortality in Copenhagen after introduction of mammography screening: cohort study' *BMJ,* doi:10.1136/bmj.38313639236.82

Oregon Evidence-based Practice Center (2005) 'Primary Care Screening for Abdominal Aortic Aneurysm' U.S. Department of Health and Human Services, Agency for Healthcare Research and Quality.

Oregon Evidence-based Practice Center (2005) *Primary Care Screening for Abdominal Aortic Aneurysm*' US Department of Health and Human Services, Agency for Healthcare Research and Quality.

Patwardhan MB, Matchar DB, Samsa GP, McCrory DC, Williams RG, Li TT (2005) 'Cost of multiple sclerosis by level of disability: a review of literature' *Multiple Sclerosis* 11:232-239.

Pharmaceutical Benefits Pricing Authority (2006) Annual Report for the year ended 30 June 2006, Commonwealth of Australia, available on http://www.health.gov.au/internet/wcms/publishing.nsf/Content/D54934A7E75638F6CA2572170082946F/$File/pbpa%20annual%20report%202006.pdf

Phillips P, Braddon J (2004) 'Osteoporosis – diagnosis, treatment and management' *Australian Family Physician* 33(5):111-119.

Pickuth D, Heywang-Kobrunner S, Spielmann RP (2000) 'Suspected Acute Appendicitis: Is Ultrasonography or Computed Tomography the Preferred Imaging Technique?' *Eur J Surgery* 166(4):315-9.

Poortman P, Lohle PNM, Schoemaker CMS, Oostvogel HJM, Teepen HJLJM, Zwinderman KAH, Hamming JP (2003) 'Comparison of CT and Sonography in the Diagnosis of Acute Appendicitis: A Blinded Prospective Study' *AJR Am J Roentgenol*; 181(5):1355-9.

Quinn SF, Brown TF (1991) 'Meniscal tears diagnosed with MR imaging versus arthroscopy: how reliable a standard is arthroscopy?' *Radiology* 181:843–847.

Randell AR, Nguyen TV, Sambrook PN, Eisman JA (2000) 'Deterioration in quality of life following hip fracture: a prospective study.' *Osteoporosis Int* 11:460-466.

Report of the New South Wales Chief Health Officer (2006) *Cardiovascular disease Aortic aneurysm deaths and hospitalisations,* AIHW.

Report of the New South Wales Chief Health Officer (2006), Cardiovascular disease Aortic aneurysm deaths and hospitalisations, AIHW.

Ross PD, Davis JW, Epstein RS, Wasnich RD (1991) 'Pre-existing fractures and bone mass predict vertebral fracture in women.' *Ann Intern Med* 114: 919-923.

Ruwe P, Wright J, Randall R, Lynch K, Jokl P, McCarthy S (1992) 'Can MR Imaging effectively replace diagnostic arthroscopy?' *Radiology* 183(2).

Salkeld G, Cameron ID, Cumming RG, Easter S, Seymour J, Kurrle SE, Quine S (2000) 'Quality of life related to fear of falling and hip fracture in older women: a time trade off study.' *BMJ* 320(7231):341-6.

Sambrook P, Seeman E, Phillips SR, Ebeling PR (2002) 'Preventing osteoporosis: outcomes of the Australian Fracture Prevention Summit.' *Medical Journal of Australia* 176(8S):1-16.

Sanders KM, Nicholson GC, Ugoni AM et al (1999) 'Health burden of hip and other fractures in Australia beyond 2000. Projections based on the Geelong osteoporosis Study.' *Med J Aust* 170:467-470.

Schelling (1968) 'The life you save may be your own' in SB Chase (ed) *Problems in public expenditure and analysis*, Brookings Institution, Washington DC, p127-162.

Sernbo I and Johnell O (1993) 'Consequences of a hip fracture: a prospective study over 1 year.' *Osteoporosis Int* 3:148–153.

Suarez-Almazor M, Kaul P, Kendall C, Saunders L, Johnston D (1999) 'The cost effectiveness of magnetic resonance imaging for patients with internal derangement of the knee' *Int J Technology Assessment in Health Care* 15(2):392-405.

Swanton JK, Fernando K, Dalton CM, Miszkiel KA, Thompson AJ, Plant GT, Miller DH (2006) 'Modification Of MRI Criteria For Multiple Sclerosis In Patients With Clinically Isolated Syndromes' *J Neurol NeuroSurg Psychiatry* 77(7):830-3.

Swedish Organised Service Screening Evaluation Group (2006) 'Reduction in breast cancer mortality from the organised service screening with mammography: 2. Validation with alternative analytic methods' *Cancer Epidemioogyl Biomarkers & Prevention,* 15(1) 52-56.

The Cochrane Library (2007) *Screening for Abdominal Aortic Aneurysms Saves Men's Lives* National Institute for Clinical Excellence, UK.

The Cochrane Library, National Institute for Clinical Excellence, England (2007) 'Screening for Abdominal Aortic Aneurysms Saves Men's Lives'.

Tintore M, Rovira A, Rio J, Nos C, Grive E, Sastre-Garriga J, Pericot I, Sanchez E, Comabella M, Montalban X (2003) 'New Diagnostic Criteria For Multiple Sclerosis:

Application In First DeMyelinating Episode' *Neurology* 60(1):27-30.Cancer Council NSW (2006) 'Understanding breast cancer – breast cancer explained' *Information for patients family and friends,* The Cancer Council NSW, Woolloomooloo.

Trivedi DP, Doll R, Tee Khaw K (2003) 'Effect of oral four monthly vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community randomised double blind controlled trial' *BMJ* 326:469-474.

United States Department of Health and Human Services - National Institute of Diabetes and Digestive and Kidney Diseases (2004) *Appendicitis*, National Digestive Diseases Information Clearinghouse.

US Preventative Task Force (2005) 'Screening for Abdominal Aortic Aneurysms: Recommendation Statement', *Annuals of Internal Medicine*, 142(3):198-202.

US Preventative Task Force (2005) 'Screening for Abdominal Aortic Aneurysms: Recommendation Statement', Annuals of Internal Medicine, Vol 142, Issue 3, pp 198-202.

Viscusi WK, Aldy JE (2002) *The value of a statistical life: a critical review of market estimates throughout the world* Discussion Paper No 392, Harvard Law School, Cambridge MA, November, accessed 4 September 2005 www.law.harvard.edu/programs/olin_center/

Weston AR, Jackson TJ, Blamey S (2005) 'Diagnosis of appendicitis in adults by ultrasonography or computed tomography: A systematic review and meta-analysis' *International Journal of Technology Assessment in Health Care* 21(3):368–379.

Wilson J, Islam O (2007) 'Brain, Multiple Sclerosis' *EMed WebMD* available at http://www.emedicine.com/RADIO/topic461.htm#section~radiograph

Wise SW, Labuski MR, Kasales CJ, Blebea JS, Meilstrup JW, Holley GP, LaRusso SA, Holliman J, Ruggiero FM, Mauger D (2001) 'Comparative Assessment of CT and Sonographic Techniques for Appendiceal Imaging' *Am J Roentgenol* 176(4):933-41.

World Health Organization (2003) *Prevention and management of osteoporosis: Report of a WHO Scientific Group*. WHO Technical Report Series No 921, Geneva.

Wu C, Naqibuddin M, Rowlingson A, Lietman S, Jermyn R, Fliesher L (2003) 'The effect of pain on health-related quality of life in the immediate postoperative period' *Anesth Analg* 97.