Exceptional Returns

The Value of Investing in Health R&D in Australia II

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CONTENTS

FIGURES

TABLES

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GLOSSARY OF ACRONYMS

ABS	Australian Bureau of Statistics
AD	Alzheimer's Disease
AIHW	Australian Institute of Health and Welfare
AMD	Age related macular degeneration
ASIR	age specific incidence rate
ASMR	Australian Society for Medical Research
ASRC	Australian Standard Research Classification
B/C	benefit/cost
CRC-VT	Cooperative Research Centre for Vaccine Technology
CSL	Commonwealth Serum Laboratories
CSMO	clinically significant macular oedema
DALY	Disability Adjusted Life Year
DM	diabetes mellitus
DR	diabetic retinopathy
GAS	Group A Streptococci
GBD	Global Burden of Disease
GDP	gross domestic product
GERD	gross expenditure on R&D
HPV	human papillomavirus
ICT	Information and Communication Technology
LIPID	Long-Term Intervention with Pravastatin in Ischaemic Disease
NVG	neovascular glaucoma
NPV	net present value
OECD	Organization for Economic Cooperation and Development
PNP	private non-profit
R&D	research and development
RFCD	research fields, courses and disciplines (R&D classification)
ROI	return on investment
SEO	socioeconomic objective (R&D classification)
(S)SCI	(Social) Science Citation Index
STSS	streptococcal toxic shock syndrome
UK	United Kingdom
US	United States
VLP	virus like particle
VSL(Y)	Value of a Statistical Life (Year)
WHO	World Health Organization
WTP	willingness to pay
YLD	Years of healthy life Lost due to Disability
YLL	Years of Life Lost due to premature death

ABSTRACT

Economic benefit of health research and development (R&D)

- Australian health R&D expenditure between 1992-93 and 2004-05 is estimated to return a net benefit of approximately $29.5 billion. For the average dollar invested in Australian health R&D, $2.17 in health benefits is returned, with a minimum of $0.57 and maximum of $6.01.
- The annual value to Australians of gains in wellbeing (from all sources, not just Australian R&D) are over $100 billion for females and over $270 billion for males by 2045.
- Australian health R&D expenditure is estimated to be 1.1% of the global expenditure on health R&D. The proportion of world health returns attributable to Australian R&D is approximately 3.04%.
- Health R&D provides returns to Australia of 117%, exceeded only by mining (159%) and wholesale/retail (438%) of sectors considered.

Gains in wellbeing

- Australia is becoming a healthier nation with life expectancy one of the highest in the world.
- For Australia, approximately 1.34 million Disability Adjusted Life Years (DALYs are a measure of a year of healthy life lost) will be averted in 2023 relative to 1993 levels, 839,000 by males and 497,286 by females.

Expenditure on health R&D

- Australia spent $2.8 billion on health R&D in 2004-05 (0.38% of gross domestic product – GDP) ranking in the middle of comparable countries in the Organization for Economic Cooperation and Development (OECD). New Zealand (NZ), The Czech Republic and Japan spend less relative to GDP while the United Kingdom (UK), United States (US), Germany, France, Denmark and Canada spend more, of the ten countries studied.
- Cancer was the leading area of non-business clinical research ($233 million), followed by cardiovascular and neurological disorders. The highest average annual growth rate of this R&D between 1992-93 and 2004-2005 was in arthritis, bone and joint disorders (17%) and infectious diseases (13%).
- Universities performed 44% of health R&D, businesses 26%, private non-profit (PNP) organisations 16% and government institutions 14%. The public sector thus performed 58% and the private sector 42%.
- The majority of health R&D since 1992-93 has been undertaken in clinical R&D, which increased from $413 million to $1.43 billion (an average growth rate of 12% annually).

Potential impacts (case study examples)

- The development of Gardasil to vaccinate against 70% of cervical cancer has potential returns in terms of wellbeing of around 2.5:1.
- Prevention or delay of vision loss associated with diabetes, or vision gain through intensive hyperglycaemic control means 4,111 fewer people with visual impairment by 2025 representing savings of $7.6 billion (in 2008 prices).

- Decreasing incidence of Alzheimer's disease by 5% through Australian R&D will result in savings of $10.3 billion by 2050. Over half of these savings would be in the residential care sector.
- The value of a Group A Streptococci (GAS) vaccine could provide health benefits valued at $319.7 million per year, of which $78.4 million would be realised by indigenous Australians.

Focus

- The greatest burden of disease currently is from cancer (19% of Australia's total), followed by cardiovascular disease (18%). The major burden is from mortality associated with these two diseases. Non-fatal diseases also play a significant and increasing role in the burden of disease and the years of healthy life lost due to disability. An emphasis for the future should be reducing disability within the population.
- Composition of burden of disease changes across age with greatest burden up to age 40 years from mental disorders and injuries; after age 40, cancer is the leading cause until age 75 where cardiovascular disease takes over.
- Australia has a comparative advantage in health R&D given levels of discovery, publications and citations. In addition to the 'good international citizen' arguments, there are therefore weighty economic reasons for sustaining and enhancing health R&D investment.

Context

- The returns presented in the 2003 ASMR *Exceptional Returns* report found a mean B/C ratio of 2.4 with a minimum of 1.0 and a maximum of 5.0. These returns were derived by retrospectively comparing the estimated gains in any year with the research spend in that same year. This report captures the lag between R&D and its benefits and finds a mean B/C ratio of 2.17 with a minimum of 0.57 and a maximum of 6.0.

EXECUTIVE SUMMARY

This report estimates the economic value of health R&D in Australia, updating the Access Economics (2003) *Exceptional Returns* report for the Australian Society for Medical Research (ASMR) in light of recent increases in health R&D expenditures. These increases are reflected in Australian Bureau of Statistics (ABS) data, and the analysis also includes sensitivity analysis, benchmarking of the rates of return and case studies of four specific examples of the wellbeing returns to health R&D.

Methods

The major return on investment (ROI) from health R&D is the gain in wellbeing achieved from lowering mortality rates and associated morbidity, relative to what they would otherwise have been (ie, in the absence of the R&D). Gains in Australian wellbeing were estimated from 1993 to 2023 by the Australian Institute of Health and Welfare (AIHW, Begg et al, 2007). Wellbeing was measured using burden of disease methodology, which is non-financial. The metric of wellbeing is the Disability Adjusted Life Year (DALY), which comprises both a mortality component (Year(s) of Life Lost due to premature death, YLLs) and a morbidity component (Year(s) of healthy life Lost due to Disability, YLDs).

The value of the DALYs averted relative to 1993 levels was converted to a dollar equivalent using willingness to pay (WTP) estimates of the value of a statistical life (year) (VSL/Y). Access Economics recently undertook a literature investigation and meta-analysis for an Australian Government client to determine the most appropriate estimate of the average VSLY in Australia (Access Economics, 2008). The meta-analysis included 244 studies (17 Australian and 227 international studies) between 1973 and 2007, and recommended that, where a VSLY is required for decision making, an appropriate average for Australia in 2006 prices is $252,014. This is higher than the VSLY used in Access Economics (2003) and was, additionally, converted to 2008 dollars by multiplying by two years of inflation (2.9% in each year, from the Access Economics Macroeconomic model). This resulted in a base case VSLY of $266,843 with lower and upper bounds of $164,553 and $360,238.

Naturally, not all the potential future gains in wellbeing as estimated by the AIHW are due to Australia's own R&D. The methodology estimates the proportion due to research as opposed to other factors (eg, public health awareness and preventive programs such as 'Slip Slop Slap' or 'Quit', screening and early intervention initiatives, the public subsidy of drugs and interventions through the Pharmaceutical Benefits Scheme and the Medicare Benefits Schedule, and so on). Based on the factors identified in Access Economics (2003), this proportion is re-estimated as 50% (30% to 70%) for R&D.

The other important parameter is the proportion of wellbeing gains due to R&D that can be attributed to Australia's own R&D rather than that outside our borders. In Access Economics (2003) this was estimated as 2.5% for Australian health R&D, reflecting that Australia 'punches above our weight' given our world population share of 0.3% (Wills, 1998). In this report the estimate is 3.04%, based on recent bibliometric evidence from the Department of Education, Science and Training (DEST). This higher global contribution seems reasonable given that Australia's expenditure on health R&D has increased in recent years.

Expenditure on health R&D was estimated for the period 1992-93 to 2004-05, the only years for which there are available Australian Bureau of Statistics (ABS) data (two-yearly, on a socioeconomic objective – SEO basis).

The ROI analysis compared the value of the wellbeing gains projected to occur with a 40-year lag from the expenditure year, to take account of lags in R&D translation into benefits, and the long period for which benefits from R&D may continue to be realised. Thus the total benefits over (fiscal years) FY2033-2045 relative to FY1993 were compared with the expenditures over FY1993-2005. This is a slightly different approach from Access Economics (2003) in relation to lags, as it projects forward rather than retrospective analysis, although since the AIHW projections are based on historical trends there is considerable similarity in the method. To retain the 40-year period used in Access Economics (2003) implicitly assumes that most of the value of the benefits of R&D are captured within this period. In reality many benefits may be more prolonged (eg, we continue to benefit from polio vaccines). The methodology may also be conservative because it only includes the value of wellbeing gains that accrue to the individual as benefits.

- Other health sector benefits of averting DALYs accrue to governments (eg, health expenditures saved), to firms (to the extent that they bear part of the productivity losses associated with disease and injury) and to the rest of the society (eg, the value of informal care from family and friends).
- Outside the health sector there are also benefits, such as the commercial gains to firms and the economy of producing preventive and therapeutic interventions. A good example is the cervical cancer vaccine (Gardasil®) developed and produced in Australia that is exported worldwide.

An Excel model was used to estimate the net present value (NPV) of the net benefit streams as well as the ROI and the Benefit/Cost (B/C) ratio for health R&D undertaken over 1992-93 to 2004-05, which were benchmarked in terms of:

- historical benchmarks and comparisons in expenditure since 1998-99 in light of the recommendations of the 'Wills' Review of Health and Medical Research in 1998, which marked somewhat of a turning point in terms on focus on health R&D in Australia;
- international benchmarks – with data from the Organization for Economic Cooperation and Development (OECD) used to compare health R&D expenditure in Australia with that in comparable OECD countries including the UK, Canada, the US, western Europe, Japan and Korea; and
- benchmarks in other sectors of the Australian economy, in terms of expenditures and rates of return – notably manufacturing, mining, wholesale and retail trade and in agriculture.

The final aspect of the analysis was to present four case study examples of the value of health R&D in Australia, specifically in the therapeutic areas of diabetes, dementia, cancer, and indigenous health.

Gains in wellbeing

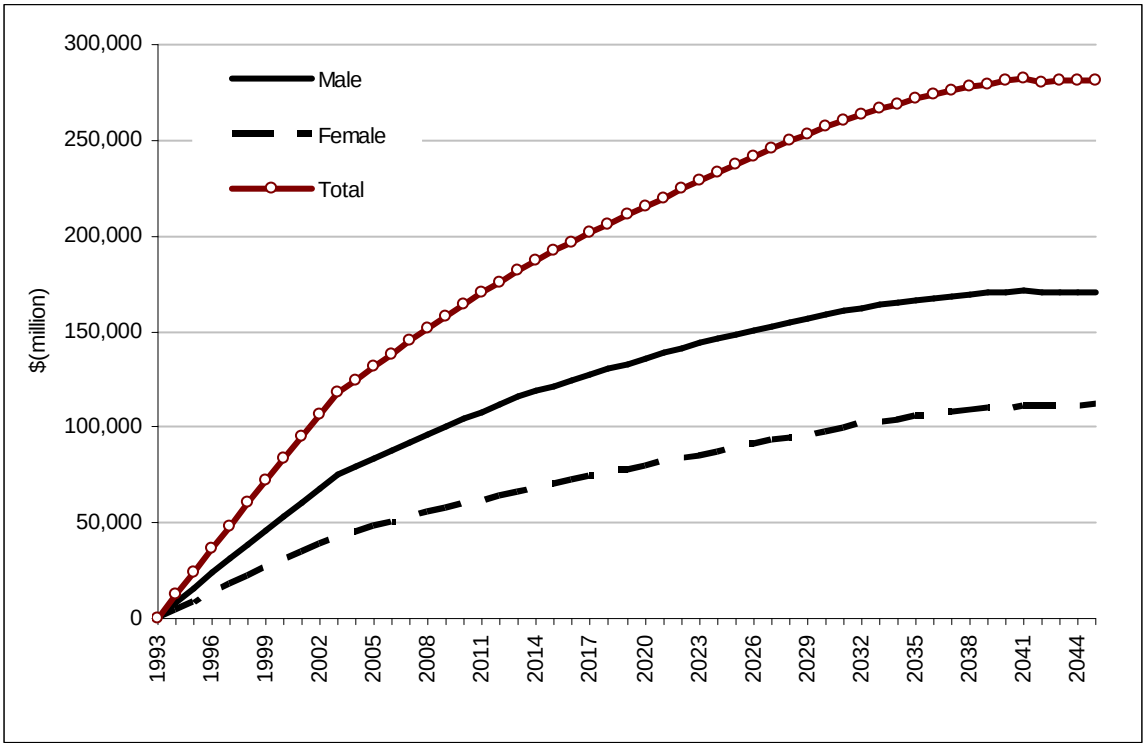
For Australia, nearly 1.34 million DALYs are estimated to be averted in 2023 relative to 1993 burden of disease levels (in terms of DALYs per 1,000 population). Of these, 839,000 DALYs are averted by males and 497,286 by females, primarily reflecting higher expected benefits to males in the future in relation to cardiovascular disease, cancer, chronic respiratory disease, injuries, and endocrine and metabolic disorders.

Notably – there are wellbeing *losses* projected in the future for acute respiratory infections, diabetes mellitus, nervous system and sense disorders, musculoskeletal disease and oral conditions – as well as mental disorders for females and, for males, infectious and parasitic diseases. These conditions are those where disability is the main source of disease burden rather than premature mortality. Together with the increasing overall proportion of Australia's burden of disease that is due to YLD rather than YLL, this suggests that a prime emphasis of

health R&D in the future should also be on reducing disability within the Australian population.

Applying the VSLY to the total number of DALYs averted, **the annual value to Australians of gains in wellbeing expected to result from all impacts on health** (not just Australian R&D) **are over $100 billion for females and over $270 billion for males by 2045** (see chart below).

ANNUAL VALUE OF DISCOUNTED GAINS IN WELLBEING, BY GENDER, 1993-2045



Source: Access Economics.

Expenditure on health R&D in Australia

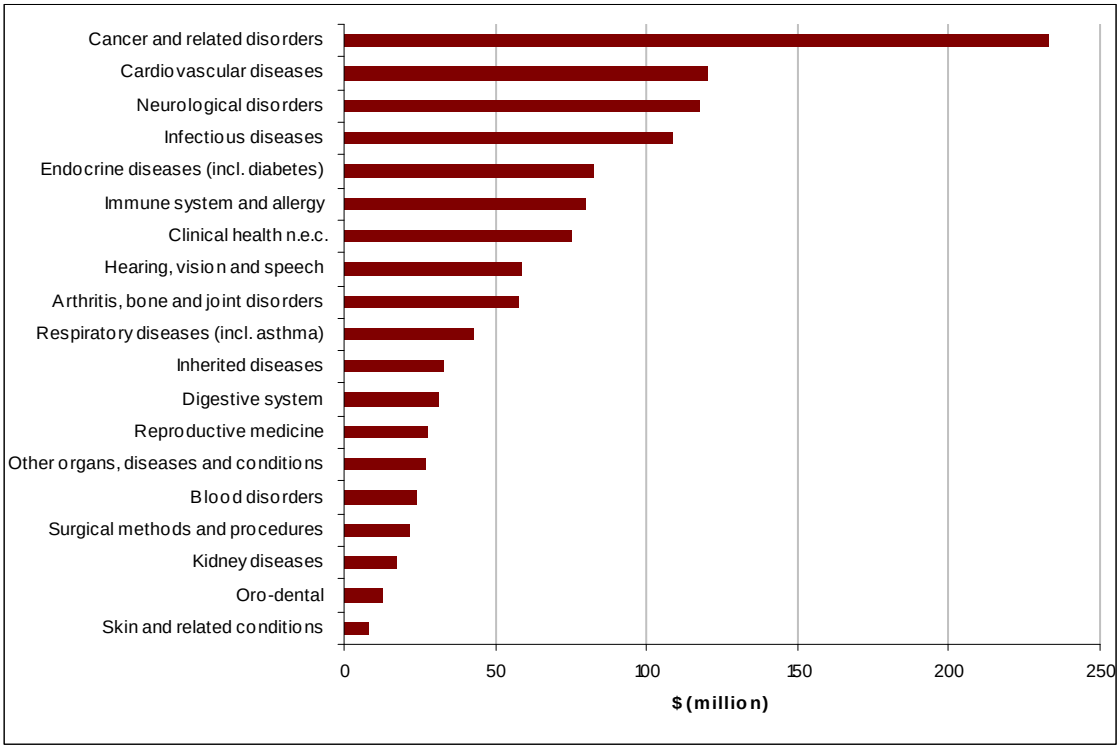
In 2004-05, **$2.8 billion was spent on health R&D in Australia** – Australian Standard Research Classification (ASRC) SEO subdivision 730000 Health.

- Around 44% of health R&D was performed by higher education facilities, 26% by business, 16% by private non-profit (PNP) organisations and 14% by Government facilities.
- Although the Commonwealth sector performs the least amount of health R&D, most of the funding comes from the Commonwealth government. In 2004-05, the Commonwealth contributed around $1.4 billion of funds across all five sectors. The majority of this spending went to higher education facilities (79%) while business received the lowest amount of funding (2%). The business sector spends the second highest amount of funds on health R&D and, not surprisingly, most of these funds are spent on R&D undertaken by business. Overseas funding accounts for around $121 million (4%) of Australian health R&D spending, of which the majority is performed by the PNP sector.
- The majority of health R&D since 1992-93 has been undertaken in clinical research, which has increased from around $413 million to $1.43 billion at an average annual growth rate of 12%. R&D expenditure on human pharmaceutical products and public health had similar expenditures in 2004-05 with $548 million and $536 million spent

respectively, although the average annual growth rate for the former was larger at 15% compared to 12%. Health and support services (which includes medical and health sciences prior to 2000-01) had the lowest expenditure in 2004-05 at $250 million and the lowest average annual growth rate at 12%.

- Of non-business clinical R&D (business data were not available by class), around $233 million was spent on cancer, which was nearly double the expenditure for cardiovascular disease at $120 million. The smallest class of expenditure in 2004-05 was for skin and related conditions, at around $8 million (see chart below).

TOTAL NON-BUSINESS CLINICAL R&D (SEO) EXPENDITURE, BY CLASS, 2004-05



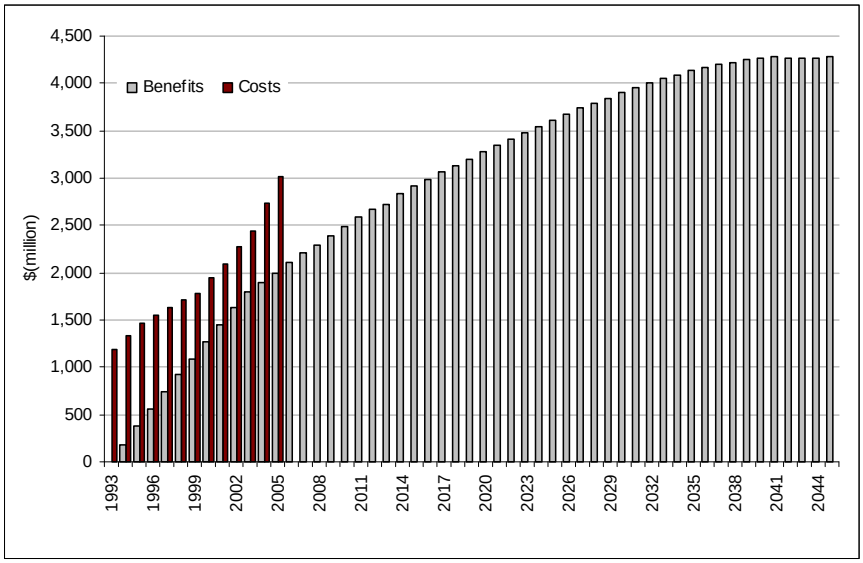
Source: Access Economics, based on ABS data.

Net benefits, ROI and Benefit/Cost ratio

The projected net benefits from health R&D over the period 1992-93 to 2004-05 are estimated as $29.5 billion, representing an average net benefit of around $2.3 billion per year. The ROI is around 117%, which means that a dollar invested in Australian health R&D is estimated to return an average net health benefit valued at $1.17. To put it another way, the B/C ratio is 2.17, which means that a dollar invested in Australian health R&D returns $2.17 in health benefits.

Expenditure has increased substantially since 1993, reaching just over $3.0 billion (in 2008 prices). Similarly, benefits have also been increasing since 1993 but at a decreasing rate. The annual benefit stream from gains in wellbeing and the cost stream associated with Australian health R&D are shown in the next chart.

BENEFIT AND COST STREAMS FROM AUSTRALIAN HEALTH R&D, 1993 TO 2045

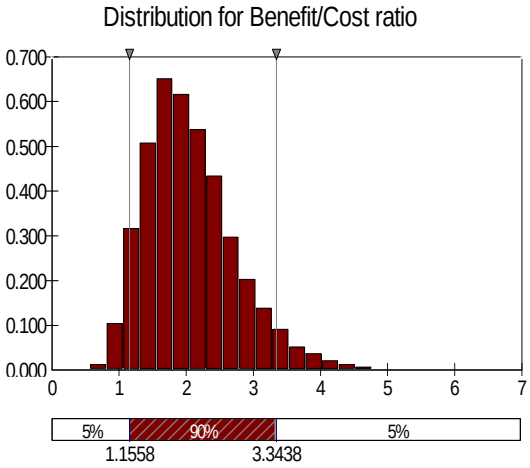


Sensitivity analysis

A sensitivity analysis was undertaken using a Monte Carlo simulation to investigate how the net benefits, ROI and B/C ratio change with different assumptions regarding inputs used within the model. This helps account for uncertainty and provides an indication of confidence in the results. The inputs that were investigated included:

- the VSLY (a gamma distribution around $266,843);
- the delay in benefits from R&D (a discrete distribution at 20, 30, 50 and 60 years compared to 40 years);
- the proportion of Australia health gains attributed to world R&D (a triangular distribution around 50% - bounded at 30% and 70%); and
- the proportion of world R&D gains attributed to Australian R&D (a triangular distribution around 3.04% - bounded at 2% and 4%).

Even though there is large uncertainty surrounding the inputs, there is a 90% chance that the net benefits from Australian R&D lie in the range $3.9 billion to $59.1 billion that the ROI from Australian R&D is between 15.6% and 234.4% and the B/C ratio is in the range 1.16 to 3.34.



The B/C ratio is estimated as 2.17 (90%CI 1.16 to 3.34, min 0.57, max 6.01). This compares with 2.4 (min 1.0, max 5.0) in the 2003 analysis. The slight decline largely reflects the increased expenditures on health R&D in the interim together with lower expected future gains as the disability burden of the chronic diseases of ageing are projected to increase in coming decades, despite the contribution of R&D.

Benchmarking

It should be noted that there is a wide variation in methodologies and assumptions when making benchmarking comparisons intersectorally and internationally.

Historical: **Australia's health R&D expenditure has increased substantially since the Wills review in 1998**. Compared to historical benchmark at that time of around $1.7 billion, R&D reached $2.8 billion in 2004-05, an average growth rate of around 12% per year. This real growth has occurred across all sectors (although highest in the business sector) and across all areas (health and support services, clinical R&D and public health R&D) except for human pharmaceutical products.

International: **Australia ranks in the middle of comparable countries with health R&D** expenditure estimated as 0.38% of GDP[1] (Organization for Economic Cooperation and Development – OECD, 2007). New Zealand, The Czech Republic and Japan spend less relative to GDP, while the UK, US, Germany, France, Denmark and Canada all spend more, of the ten countries studied.

Sectoral: **The ROI for health R&D is higher than the average ROIs for R&D in other sectors**. According to Shanks and Zheng (2006), the ROI for health R&D of 117% is higher than the market and manufacturing sectors (each around 50%) and agriculture (around 24%), but lower than the mining sector (159%) and the wholesale and retail trade sector (a very high 438%). The health R&D ROI is also higher than the average gross rate of return presented within the Productivity Commission (2007) review (65% to 85%).

Case study examples

To place the modelling in the context of real world examples, four studies were reviewed based on R&D activity translating into wellbeing gains.

- Gardasil is a vaccine against certain types of human papillomavirus (HPV) which is founded on research breakthroughs initiating from Australia, notably by Professor Ian Frazer at the University of Queensland and his fellow researcher, the late Dr Jian Zhou – in collaboration with other bodies including Commonwealth Serum Laboratories (CSL) Australia, the US Cancer Research Institute, the University of Rochester (New York) and Merck Sharp & Dohme.
  - Using an average lifetime cost per incident and actively prevalent case of cancer averted of $1.63 million, 1,701 such cases per annum in Australia, 50% of benefits attributable to R&D, 60% coverage by the vaccination program and 13% of the R&D component due to Australian (as opposed to overseas) research based on royalty attribution, yields an attributable benefit of $63 million per annum, which (compared to $8.5 million per annum in costs) yields a B/C ratio of 7.5:1. Taking into account that benefits occur 37 years in the future are valued at

[1] The OECD estimate is a little higher than the ABS estimate, which is closer to 0.3% of GDP.

less than a third of the value of an event occurring now, in NPV terms, the B/C ratio may be closer to 2.5:1 than 7.5:1. The calculation does not take account the cost of the immunisation program or the availability of alternatives, and another caveat is that cervical cancers have yet to demonstrate long term efficacy. That said, the potential benefits worldwide are the saving of 225,000 lives each year worldwide.

- For diabetes, the example is from trial data on intensive hyperglycaemic control in bringing about a reduction in visual impairment from diabetic eye diseases. The major eye diseases associated with diabetes are diabetic retinopathy (DR), cataract and neovascular glaucoma (NVG).
  - Extending intensive blood glucose treatment to those whose diabetes is currently not controlled (around 28% of people with treated diabetes) will result in a significant reduction in diabetic eye disease and hence in visual impairment and associated deaths (eg, falls, accidents). By 2025, it is projected that there would be 4,111 fewer people with visual impairment than in the base case and 18,850 DALYs averted (a NPV increase of around $7.6 billion in 2008 prices).
  - Moreover, there are additional benefits from treating blood glucose that flow from reducing other (non ophthalmic) complications of diabetes, such as reduced risks to kidney, and heart disease, and reduced risk of amputation, nerve damage, and stroke. Although these have not been quantified in the modelling here, they represent a significant benefit from intensive glucose control as studied in these R&D trials.
- For Alzheimer's disease (AD), the example models the potential gains from R&D that could delay the onset of dementia.
  - If incidence of AD could be reduced by 5% through Australian R&D, then over the period 2005-2010, cumulative savings of $195 million would be realised - $10.3 billion over 2005-2050.
  - If incidence of AD could be reduced by 50% through Australian R&D, then over the period 2005-2010, cumulative savings of $1.97 billion would be realised - $104.9 billion over 2005-2050.
  - Over half of these savings (an estimated 57%) would be in the health and residential care sector.
- Development of a vaccine for Group A streptococci bacteria, currently commencing Phase I trials, has potential wellbeing gains in terms of deaths averted worth around $319.7 million, of which $78.4 million would be realised by indigenous Australians.
  - This may be conservative given the scale of other benefits, such as morbidity and hospitalisations averted.
  - Such vaccination R&D aligns well with the Rudd Federal Government commitment to preventive health and to removing the mortality gap between indigenous and non-indigenous Australians.

Health R&D can be seen as an investment in wellness with exceptional returns. The corollary is that public finance should be strategically targeted to cost-effective high priority R&D areas. This report has shown that on average every dollar invested in the future health challenges of demographic ageing in Australia is likely to be recouped as highly valued healthspan, and in most cases, many times over. Health R&D remains an exceptional investment, with exceptional returns.

Access Economics
23 May 2008

1. INTRODUCTION

Access Economics was commissioned by the Australian Society for Medical Research (ASMR) to estimate the economic value of health R&D in Australia, updating the 2003 *Exceptional Returns* report in light of recent increases in health R&D expenditures reflected in Australian Bureau of Statistics (ABS) data, and including benchmarking and case studies. This report represents the deliverable, clearly presenting the methodological underpinnings of the analysis and surrounding the findings with sensitivity analysis.

1.1 BACKGROUND

Access Economics (2003) developed a methodology to assess the historical returns on investment to health R&D in Australia over the period 1960-1999 in our previous report for ASMR – *Exceptional Returns: The Value of Investing in Health R&D in Australia.*

The methodology for that report essentially estimated the life expectancy and quality of life gains experienced by Australians over the 40-year period, in terms of reductions in disability adjusted life years (DALYs), and placed a dollar value on these gains using the concept of the value of a statistical life (VSL) from the willingness to pay (WTP) literature. Only a proportion of these gains can be attributed to Australian R&D, so the analysis depended critically on two parameters:

1 the proportion of gains attributable to R&D rather than other factors, such as improvements in environmental factors (eg, sanitation) or public policies (eg, health awareness or promotion programs); and

2 the proportion of gains attributable to Australian health R&D rather than health R&D from overseas.

Sensitivity analysis thus surrounded the analysis to account for potential uncertainty in relation to these parameters. The dollar value of the gains attributable to health R&D was then estimated and compared to the annual expenditure on Australian health R&D (both public and private) estimated from ABS data.

A similar approach has been adopted in relation to this project noting that the ABS data on health R&D are now available over a longer period (although fewer disaggregated data are made publicly available) and there are some minor changes to the methodology and parameters.

- Notably, the second parameter above (the proportion of gains attributable to Australian health R&D rather than overseas health R&D) has been reassessed in this analysis based on more recent data, increasing from 2.5% in 2003 to 3.04% in 2008 (Section 4.2.2). This higher global contribution seems reasonable given that Australia's expenditure on health R&D has ramped up substantially in recent years.
- In addition, the value of a statistical life year (VSLY) has also been revised upwards in the intervening period, with a broad-ranging meta-analysis used to determine the parameter based on Access Economics (2008), including upper and lower bound estimates (Section 2.3.1).
- In addition, previous estimates were based on historical comparisons with gains in 1998-99 (relative to 1960) compared to expenditure on health R&D in 1998-99. In this analysis, projections of the burden of disease from the Australian Institute of Health and Welfare (AIHW) are now available for the years 1993, 2003, 2013 and 2023, so these have been utilised to compare the gains in wellbeing projected 40 years into the

future (relative to 1993) with the investments in health R&D between 1992-93 and 2004-05 (Section 4.3). This refinement in methodology is also now sensitivity tested at 20 and 60 years, and a more sophisticated sensitivity analysis is undertaken in this updated study, utilising probability distributions of inputs to determine the 90% confidence interval of the outputs (Sections 4.1 and 4.4).

- As such, the returns presented in the 2003 report of a mean benefit/cost (B/C) ratio of 2.4 with a minimum of 1 and a maximum of 5 were derived and presented a little differently from the presentation in this report. There is nonetheless a high level of comparability, with the slight decline in the mean B/C ratio due to the substantial ramp up in health R&D expenditure (the denominator) over recent years, without a commensurate (yet) projected increase in benefits, since the DALY projections are based on 2003 data. There is thus some element of flux in the current calculations and further estimates of the returns in 5-10 years would be worthwhile for comparative purposes, using a similarly based method.

1.2 STRUCTURE OF THIS REPORT

The report is structured along the lines shown below.

- Chapter 2 estimates the gains in wellbeing from DALYs averted, by analysing mortality and morbidity from 1993 to 2023 for Australia, using burden of disease projections from the AIHW. Projections of years of life lost due to premature death (YLL) and years of healthy life lost due to disability are analysed historically and in the future by cause, and gains in wellbeing relative to 1993 are then estimated, with decomposition of the various DALYs averted by gender and cause. Since the burden of disease methodology is non-financial, the value of the wellbeing gained is converted to a dollar equivalent using WTP estimates of the VSLY. As noted above, Access Economics recently undertook a literature investigation and meta-analysis for an Australian Government client to determine the most appropriate estimate of the average VSLY in Australia (Access Economics, 2008), and presents the rationale and range identified from that review in this chapter.
- Chapter 3 presents expenditure on health R&D in Australia from the ABS, which is available for the period 1992-93 to 2004-05. Summary data are presented by who performed the R&D – Commonwealth, state/territory, higher education, private non profit (PNP) or business – and by who financed it – Commonwealth, state/territory, PNP, business or overseas. Trends in expenditure are presented in overall R&D by socioeconomic objective (SEO) as well as clinical non-business expenditure by 'class' (therapeutic area).
- Chapter 4 summarises the methodology for comparing the wellbeing gains with the expenditures on health R&D, including treatment of lags and sourcing the parameter estimates for the proportion of gains due to R&D and those due to Australian rather than overseas R&D (based on Australia's share of global R&D expenditure and our share of publications). The formulae for modelling the net present value (NPV) of the net benefit streams is presented, followed by the results (outputs) of the modelling in terms of net benefits, return on investment and the B/C ratio for R&D undertaken over 1992-93 to 2004-05. Benefits are also presented by cause and sensitivity analysis is undertaken on the key parameter drivers, namely:
  - the VSLY;
  - the delay in benefits from R&D;
  - the proportion of Australia health gains attributed to world R&D; and
  - the proportion of world R&D gains attributed to Australian R&D.

The chapter concludes by noting that the methodology does not include benefits other than wellbeing gains, and by listing some other additional potential benefits.

- Chapter 5 presents benchmarking analysis in terms of:
  - historical benchmarks and comparisons in expenditure since 1998-99 light of the recommendations of the 'Wills' Review of Health and Medical Research in 1998, which marked somewhat of a turning point in terms on focus on health R&D in Australia;
  - international benchmarks – with data from the Organization for Economic Cooperation and Development (OECD) used to compare health R&D expenditure in Australia with that in comparable OECD countries including the UK, Canada, the US, western Europe, Japan and Korea; and
  - benchmarks in other sectors of the Australian economy, in terms of expenditures and rates of return – notably manufacturing, mining, wholesale and retail trade and in agriculture.
- Chapter 6 provides four case study examples of the value of health R&D in Australia, specifically in the therapeutic areas of cancer, diabetes, dementia and indigenous health. This is achieved by reviewing evidence where specific R&D activities have led to (or could possibly lead to) mortality reductions and enhancements in quality of life in the future.
- Chapter 7 provides a summary of the previous chapters and draws conclusions and recommendations.

2. GAINS IN WELLBEING

Australia is becoming a healthier nation. Higher incomes, education, and improved health care have increased the life expectancy of Australians to the second highest in the world (behind Japan). However, measuring gains in wellbeing is not just about living longer, it is also about living healthier. As such, measuring the gains in wellbeing of a population must take into account both the change in mortality and the change in morbidity.

In order to measure the gains in wellbeing over time, this study has used a framework known as a 'burden of disease' analysis. This was originally developed by the World Bank in its Global Burden of Disease and Injury study to inform global health planning and has been subsequently widely used and improved (by Access Economics and others) in a number of Australian and international settings. The methodology and its application to this study are discussed below.

2.1 METHOD FOR QUANTIFYING GAINS IN WELLBEING

Burden of disease analysis aims to calculate the size and impact of health problems derived from disease and injury across a population. It uses measured incidence, prevalence, duration, mortality, and morbidity for an exhaustive and mutually exclusive set of major diseases and injuries to quantify a summary measure of population health known as Disability Adjusted Life Years (DALYs). An estimated dollar value of a DALY is then applied to the total number of DALYs in a population to derive an economic value of disease and injury to the total population.

The DALY extends the concept of potential years of life lost due to premature death to include equivalent years of 'healthy' life lost by virtue of being in states of poor health or disability. In brief, DALYs for a disease or health condition are calculated as the sum of the years of life lost due to premature mortality (YLL) in the population and the years of healthy life lost due to disability (YLD) for incident cases of the health condition[2]. This can be represented by:

DALY = YLL + YLD

As a DALY incorporates loss of life (YLL) and loss of non-fatal healthy life (YLD), it is a summary measure of the loss of 'perfect health' from different diseases and injuries. The life lost due to premature mortality is calculated by subtracting age at death as a result of the disease or injury from the life expectancy under perfect health (which is 82.5 years in females and 80 years in males). Calculating the loss of healthy life due to non-fatal health conditions (YLD) requires estimation of the incidence of the health condition (disease or injury) in the specified time period. For each new case, the number of years of healthy life lost is obtained by multiplying the average duration of the condition (to remission or death) by a severity weight that quantifies the equivalent loss of healthy years of life due to living with the health condition. The severity weight is based on a social value and ranges between zero and one, with one being the most severe disability. Years lost due to disability (YLD) can be represented as follows:

YLD = I*D*L

[2] The concept of a DALY is described in detail in the WHO's Global Burden of Disease study (GBD) (Murray and Lopez, 1996).

Where I is the number of incident cases in the reference period, D is the disability weight (in the range 0–1) and L is the average duration of disability (measured in years). With discounting at rate r to account for positive time preference (ie, valuing healthy life today more than healthy life in the distant future), the formula for calculating YLD becomes:

YLD = I*D* [1 - exp(- rL)] / r

YLDs are proportional to incidence multiplied by duration, which may approximately equal the prevalence of the condition in a particular year.

The burden of disease and injury approach and the employment of DALYs was initially adopted and applied in Australia by AIHW to determine the burden of disease and injury (or loss of wellbeing) in Australia. Mathers et al (1999) estimated the burden of disease and injury in Australia in 1996, while Begg et al (2007) revisited the Australian estimates for the year 2003. However, the Australian studies depart from the GBD methodology in two important areas. This includes:

- the GBD study discounted DALYs using age weights that gave higher weight to a year of life in young and mid-adult years, and lower weight to a year of life at very young and older years. The Australian studies do not use age weights; and
- the GBD study did not attempt to deal with the effects of comorbidities on YLD estimates for individual diseases. The Australian study adjusts YLD estimates for comorbidities between mental disorders and between physical disorders at older ages.

In order to ensure the net benefit estimates from Australian health R&D calculated within this study are comparable to the burden of disease studies undertaken by the AIHW, projections of DALYs between 1993 and 2023 from the most recent report on the burden of disease and injury in Australia (Begg et al, 2007) have been used. The methodology that was used to project DALYs by Begg et al (2007) is discussed in the next section.

2.1.1 ESTIMATING PAST, PRESENT AND FUTURE WELLBEING IN AUSTRALIA

The complete epidemiology of a disease is ultimately a function of only three parameters, which includes the incidence (the hazard of getting the disease), remission (the 'hazard' of being cured from having the disease) and case-fatality (the hazard of dying as a consequence of having the disease). For most chronic diseases, cause-specific mortality is influenced by only two of these—incidence and case-fatality—with remission having little if any role. It follows, therefore, that any epidemiological parameter of interest for a chronic disease can be 'back-cast' from a point in time for which the complete epidemiology of that disease is known simply by making assumptions about the relative contribution of incidence and case fatality to the observed changes in mortality.

This idea also applies to projections, provided one is willing to make predictions about cause-specific mortality into the future. As cause-specific mortality is a reliable and consistently recorded source of information on changes in disease frequency in many cases, cause-specific mortality is a sound starting point for projecting the epidemiology of a disease.

The method used by Begg et al (2007) to estimate the past, present and future DALYs in Australia between 1993 and 2023 involved a number of separate analytical or computational steps. A brief outline of the overall approach is presented below.

- Baseline models for over 170 diseases and injuries for Australia in 2003 were developed as part of the core set of analyses for the present study.
- Trends in observed all-cause mortality rates over the period 1979 to 2003 were analysed and projected into the future using a simple log-linear Poisson regression

model. Cause-specific mortality data were collapsed into 51 groups of conditions and a multinomial logistic regression was used to determine the contribution of each group to the all-cause mortality. These models were then used to estimate the cause-specific structure of mortality (by age group and gender) based on mortality rates from all causes.

- For mostly fatal conditions, each baseline disease model was extrapolated backwards and forwards in time based on assumptions about the relative contribution of incidence and case-fatality to changes in mortality.
- Baseline models for mostly non-fatal conditions were extrapolated based on assumptions about changes in incidence only. The complete epidemiology of each was then estimated separately in a fully dynamic model that accounted for changes in all-cause mortality as well as changes in incidence and case-fatality (where appropriate) so that incidence, prevalence and duration by age, gender and cause were described over the past as well as into the future.

Among the causes analysed, cardiovascular disease, cancers, chronic obstructive pulmonary disease, diabetes, alcohol-related conditions, road traffic accidents, falls, suicide and homicide showed significant mortality trends. Mortality trends for cancers, chronic obstructive pulmonary disease, diabetes, alcohol-related conditions, road traffic accidents, falls, suicide and homicide were assumed to be fully due to changes in incidence. Incidence trends for these causes were therefore adjusted to reflect changes in mortality over the projection period, with case-fatality being held constant.

The majority (58%) of the drop in cardiovascular mortality observed in England and Wales was due to a drop in incidence and the remaining 42% due to a reduction in case-fatality. The same proportions were assumed to apply in Australia to all cardiovascular disease over the projection period.

For Type 2 diabetes, the approach taken was to translate historical trends in body mass index into expected changes in diabetes incidence following the risk attribution methods described in the WHO Comparative Risk Assessment project. As information on trends in case-fatality rates among people with diabetes was scarce, an assumption was made that at least half the mortality in these people is due to vascular causes and subject to the same factors that influence cardiovascular disease mortality more generally. The result of using an increasing body mass index and a decreasing case-fatality was a large increase in the incidence and prevalence of Type 2 diabetes in the future.

Due to lack of survey data, no mortality trends were assumed for the main conditions that are largely non-fatal, which include mental health, hearing loss, vision loss and musculoskeletal disorders. This is not a big issue as mortality trend data is not particularly relevant for conditions that are largely non-fatal.

The burden of disease and injury in the past, present and future derived from the above methodology are represented in Begg et al (2007) by a standardised rate ratio. This is the growth rate of DALYs after the effect of population ageing has been removed. The standardised rate ratio used to estimate DALYs between 1993 and 2023 for males and females at the cause level are shown in Table 2-1. Growth was projected from an initial starting point in 2003 so the ratio for 2003 is one for all disease and injury categories (ratios for 1993 were 'back-casted').

Table 2-1 shows that for most diseases it is projected that the burden will decrease. For example 'Infectious and parasitic diseases' is expected to decline from 1 to 0.99 (or 1%) for males and from 1 to 0.85 (or 15%) for females between 2003 and 2023. However for some diseases, the burden is expected to increase. For example, 'Diabetes mellitus' is expected to

increase from 1 to 1.32 (or 32%) for males and from 1 to 1.40 (or 40%) for females between 2003 and 2023, which is representative of the expected increase in risk factors, notably obesity.

As data on the growth rate of DALYs were only available for four time periods (1993, 2003, 2013, and 2023) linear projections were used to fill in the data gaps. Furthermore, Begg et al (2007) only projected DALYs up to 2023, whereas the benefits from health R&D in this study were measured beyond this period. Consequently linear projections were used to estimate DALYs up to 2045.

TABLE 2-1: STANDARDISED RATIO OF DALYS, 1993 TO 2023

	Males				Females			
	1993	2003	2013	2023	1993	2003	2013	2023
Infectious and parasitic diseases	0.93	1.00	1.02	0.99	0.99	1.00	0.93	0.85
Acute respiratory infections	0.67	1.00	1.00	1.00	0.61	1.00	1.00	1.00
Maternal conditions	0.00	0.00	0.00	0.00	1.09	1.00	1.03	1.02
Neonatal causes	1.32	1.00	0.80	0.68	1.00	1.00	0.82	0.71
Nutritional deficiencies	1.12	1.00	1.03	1.02	1.03	1.00	0.99	0.98
Malignant neoplasms	1.20	1.00	0.85	0.70	1.16	1.00	0.88	0.74
Other neoplasms	1.03	1.00	0.83	0.68	0.94	1.00	0.89	0.81
Diabetes mellitus	0.87	1.00	1.15	1.32	0.89	1.00	1.18	1.40
Endocrine and metabolic disorders	1.88	1.00	1.08	1.03	0.89	1.00	1.16	1.31
Mental disorders	1.03	1.00	1.01	0.99	0.99	1.00	1.01	1.01
Nervous system and sense organ disorders	0.96	1.00	1.02	1.03	0.96	1.00	1.03	1.05
Cardiovascular disease	1.56	1.00	0.69	0.48	1.51	1.00	0.74	0.53
Chronic respiratory disease	1.22	1.00	0.83	0.73	1.04	1.00	0.96	0.93
Diseases of the digestive system	1.01	1.00	0.81	0.71	1.03	1.00	0.85	0.75
Genitourinary diseases	0.97	1.00	0.97	0.96	0.97	1.00	0.98	0.95
Skin diseases	1.00	1.00	1.00	0.99	1.00	1.00	1.00	0.99
Musculoskeletal diseases	0.98	1.00	1.03	1.05	0.97	1.00	1.02	1.02
Congenital anomalies	1.11	1.00	0.84	0.74	1.19	1.00	0.84	0.72
Oral conditions	0.99	1.00	1.02	1.03	0.98	1.00	1.01	1.02
Ill-defined conditions	1.70	1.00	0.83	0.73	1.31	1.00	0.93	0.89
Injuries	1.16	1.00	0.91	0.79	1.08	1.00	0.89	0.76
All causes	**1.18**	**1.00**	**0.90**	**0.81**	**1.11**	**1.00**	**0.93**	**0.87**

Source: Begg et al (2007).

The final issue with projecting total DALYs is the changing composition of the Australian population. Greater incomes, improved health care, healthier lifestyles, and decreased fertility are resulting in population ageing. As the prevalence and incidence of disease and injury is closely linked with ageing, the expected changes in the Australian population need to be taken into account when estimating total DALYs for a population. Within this study, DALY growth rates (as represented by the standardised ratio of DALYs) were multiplied by population projections (at the five year age cohort level) derived from the Access Economics Demographic Model. This provided a total DALY estimate by age, gender and cause for each year between 1993 and 2045 (see Section 2.3).

2.2 LOSS OF WELLBEING BY CAUSE

2.2.1 TOTAL LOSS OF WELLBEING

Projections of DALYs using the standardised ratios require a starting point of total DALYs (or total loss of wellbeing) in the population. The starting point used by Begg et al (2007) was the DALYs per 1,000 population 2003, shown in Table 2-2.

TABLE 2-2: DALYS PER 1,000 POPULATION, BY GENDER AND CAUSE, 2003

	Males	Females	Persons
Infectious and parasitic diseases	2.77	1.74	2.25
Acute respiratory infections	1.74	1.83	1.79
Maternal conditions	0.00	0.21	0.11
Neonatal causes	1.93	1.55	1.74
Nutritional deficiencies	0.15	0.47	0.31
Malignant neoplasms	26.78	23.48	25.12
Other neoplasms	0.47	0.63	0.55
Diabetes mellitus	7.84	6.63	7.23
Endocrine and metabolic disorders	1.47	1.40	1.44
Mental disorders	16.78	18.47	17.63
Nervous system and sense organ disorders	14.86	16.60	15.73
Cardiovascular disease	25.57	22.12	23.83
Chronic respiratory disease	10.02	8.77	9.39
Diseases of the digestive system	2.90	2.93	2.92
Genitourinary diseases	2.85	3.70	3.28
Skin diseases	1.00	1.04	1.02
Musculoskeletal diseases	4.48	6.12	5.31
Congenital anomalies	1.90	1.44	1.67
Oral conditions	1.16	1.31	1.23
Ill-defined conditions	0.45	0.68	0.57
Injuries	13.12	5.55	9.31
All causes	**138.2**	**126.7**	**132.42**

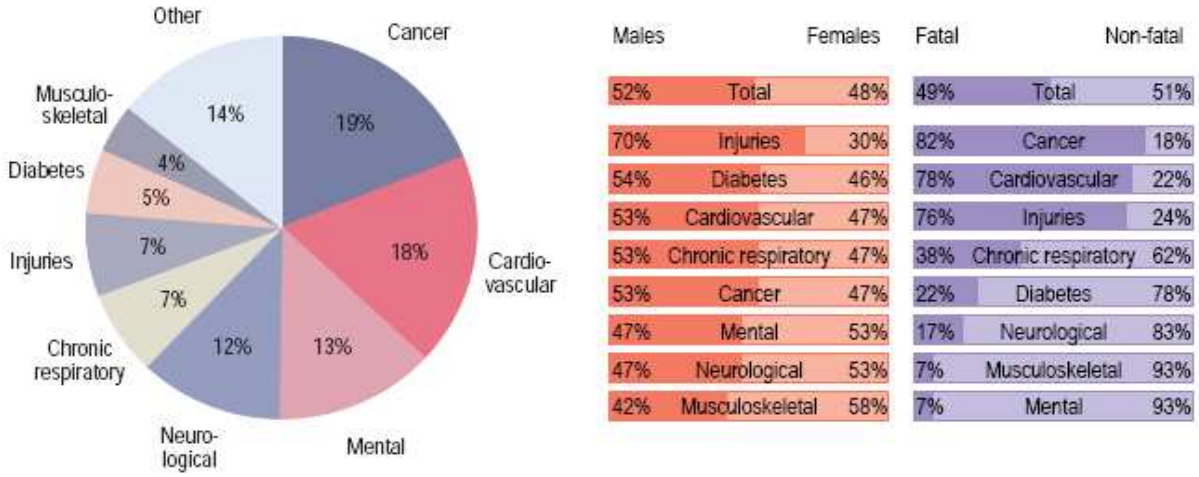
Source: Begg et al (2007).

Table 2-2 shows that the loss of wellbeing in Australia in 2003 was not uniform across the population. Males had a greater burden of disease rate, with the total DALY per 1,000 males in the Australian population being around 138 compared to females at 127. Furthermore, the rates across causes were highly variable, ranging from 0.11 for maternal conditions for all persons to 25.12 for malignant neoplasms. There is even greater variation in starting point DALYs when the data are investigated by cause and by age (at five year age cohorts)

In terms of the total DALYs in 2003, Figure 2-1 shows that the greatest burden of disease on the Australian population was from cancer, which accounted for around 19% of the total burden. This was closely followed by cardiovascular disease, accounting for around 18% of the total burden. The majority of the burden from cancer and cardiovascular disease is from the mortality associated with these conditions. However, non-fatal health outcomes also play a significant part in the total burden of disease. Mental disorders and neurological and sense disorders account for around 25% of the total burden even though the contribution of

mortality in these disorders is relatively low. Together with the increasing proportion of the burden that is due to YLD rather than YLL, this suggests that a prime emphasis of health R&D should also be on reducing disability within the Australian population.

FIGURE 2-1: DALYS BY BROAD CAUSE GROUP, 2003



Source: Begg et al (2007). Disability Adjusted Life Years (DALYs) are a measure of a year of healthy life lost.

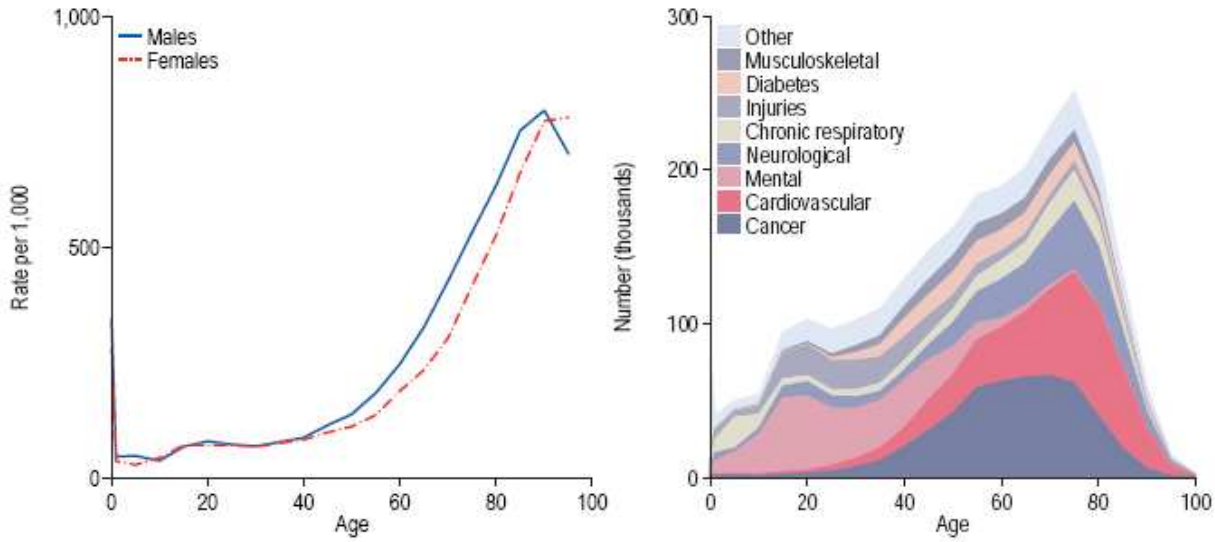
The distribution of the total burden of disease and injury between males and females is almost equal, with males contributing around 52% of the total burden. However the distribution of DALYs between males and females across causes is different. Males account for a greater burden for injuries, diabetes, cardiovascular disease, chronic respiratory disease and cancer, while females account for a greater burden for musculoskeletal disorders, mental disorders and neurological and sense disorders.

The distribution of DALYs within the Australian population in 2003 was skewed towards the older age brackets. Figure 2-2 shows DALYs by age and broad cause. DALYs per 1,000 people slightly increases for males and females between birth and age 40. However exponential growth in DALYs per 1,000 people starts to occur just after 40, with a slightly higher growth in males. By the age of around 90, DALYs per 1,000 people peaks and is similar for males and females.

However, Figure 2-2 shows that total DALYs rise steadily across ages until a peak at around the age of 75. This is because the total number of people within each age cohort starts to decrease at an increasing rate from about the age of 70. Even though the people in older age cohorts would be experiencing a larger burden of disease per capita (as evident from the DALYs per 1,000 for each age cohort), there are less people in these age cohorts.

The composition of the burden of disease also changes across age. For example, the majority of the burden of disease up to the age of 40 is from mental disorders. Injuries also play a large part. After the age of 40, cancer starts to become the leading cause of disease burden, until around the age of 75, where cardiovascular disease takes over.

FIGURE 2-2: DALYS BY AGE, 2003



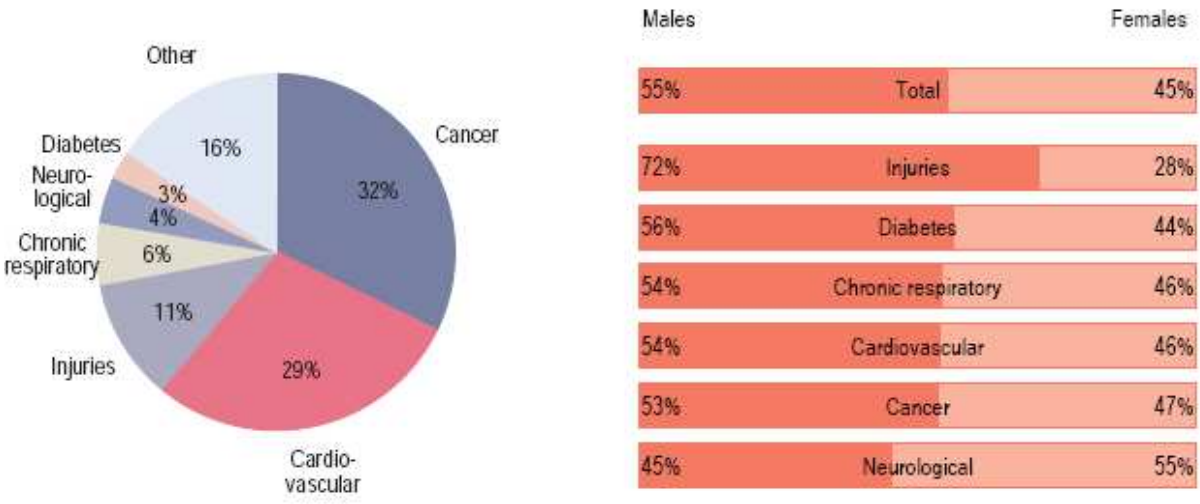
Source: Begg et al (2007).

2.2.2 LOSS OF WELLBEING DUE TO YLL AND YLD

The contribution to the total loss of wellbeing from YLL was 49% in 2003. Figure 2-3 shows that the majority of YLL burden (72%) was due to deaths resulting from cancer, cardiovascular disease and injuries. Males account for around 55% of the total YLL, and a high 72% of the YLL from injuries. The leading causes of mortality burden for males were ischaemic heart disease, lung cancer, suicide and self-inflicted injuries, stroke, and colorectal cancer, while for females the leading causes were ischaemic heart disease, stroke, breast cancer, lung cancer, and colorectal cancer (Begg et al, 2007).

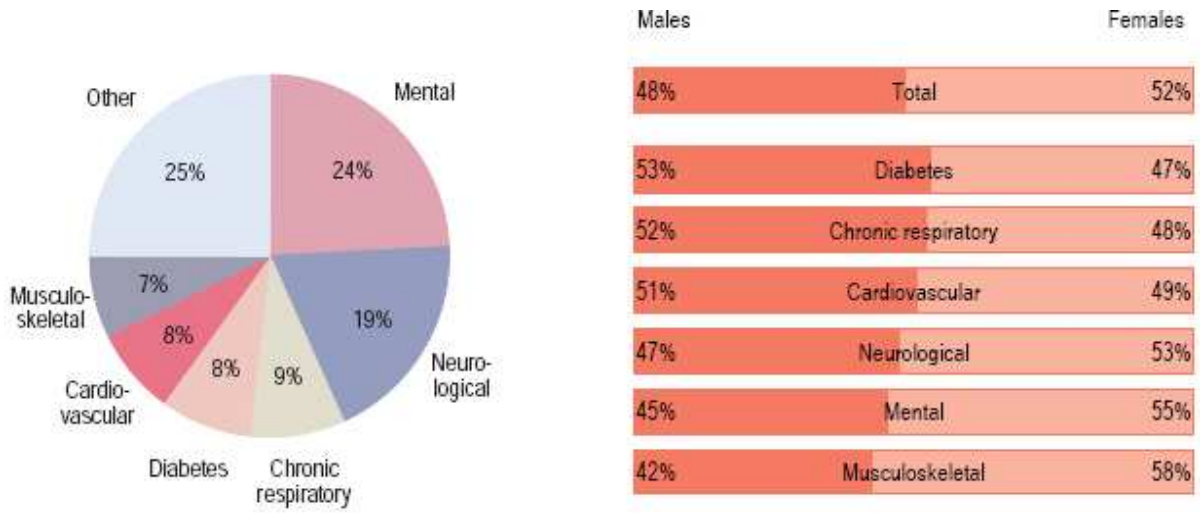
The contribution to the total loss of wellbeing from YLD was 51% in 2003. Figure 2-4 shows the three main causes – mental disorders, neurological and sense disorders and chronic respiratory disorders (together 52% of YLD). Unlike YLL, females experience the higher share of YLD (also 52%). The leading causes of non-fatal burden for males were anxiety and depression, type 2 diabetes, adult-onset hearing loss, asthma and dementia, while for females the leading causes were anxiety and depression, type 2 diabetes, dementia, asthma and ischaemic heart disease (Begg et al, 2007).

FIGURE 2-3: YEARS OF LIFE LOST (YLL), BY BROAD CAUSE, 2003



Source: Begg et al (2007).

FIGURE 2-4: YEARS LOST DUE TO DISABILITY (YLD), BY BROAD CAUSE, 2003



Source: Begg et al (2007).

2.3 TOTAL GAINS IN WELLBEING

Total gains in wellbeing can be represented by the reduction in DALYs from a base case. In this study, the base case was total DALYs for 1993, which was constructed by 'back-casting' total DALYs from 2003 across age, gender and cause using the standardised ratio of DALYs and population for 1993. The total aversion of DALYs per annum was then calculated by subtracting the DALYs at 1993 levels from DALYs projected using the standardised ratio of DALYs together with population projections from Access Economics' Demographic Model. Within the model, gains in wellbeing were calculated for every other year between 1993 and

2042 using linear projections. The gains in wellbeing for 2003, 2013, and 2023 are shown in Table 2-3.

TABLE 2-3: DALYS AVERTED RELATIVE TO 1993, BY CAUSE AND GENDER, 2003, 2013, 2023

	Males			Females		
	2003	2013	2023	2003	2013	2023
Infectious and parasitic diseases	-1,933	-3,010	-2,388	-175	1,259	3,498
Acute respiratory infections	-5,739	-7,516	-9,963	-7,192	-9,199	-11,785
Maternal conditions	0	0	0	194	140	179
Neonatal causes	6,081	10,970	14,957	0	3,089	5,515
Nutritional deficiencies	175	161	218	143	220	308
Malignant neoplasms	53,699	123,129	224,935	38,100	83,468	153,924
Other neoplasms	140	1,245	2,861	-381	388	1,233
Diabetes mellitus	-10,205	-27,536	-53,948	-7,387	-23,839	-50,914
Endocrine and metabolic disorders	12,943	14,542	18,954	-1,555	-4,670	-8,926
Mental disorders	4,999	3,749	8,175	-1,854	-4,068	-4,358
Nervous system and sense organ disorders	-5,946	-11,676	-17,692	-6,714	-14,742	-24,150
Cardiovascular disease	143,448	298,776	490,252	114,234	224,205	373,282
Chronic respiratory disease	22,003	48,614	77,367	3,542	8,521	14,280
Diseases of the digestive system	290	7,378	13,873	889	6,625	12,814
Genitourinary diseases	-856	0	486	-1,118	-447	1,059
Skin diseases	0	0	137	0	0	153
Musculoskeletal diseases	-896	-2,774	-4,708	-1,860	-3,773	-4,524
Congenital anomalies	2,067	5,724	8,780	2,749	5,690	8,563
Oral conditions	-115	-409	-628	-264	-470	-716
Ill-defined conditions	3,143	4,327	5,274	2,137	2,886	3,447
Injuries	20,870	37,557	62,418	4,471	12,393	24,406
All causes	244,169	503,250	839,360	137,957	287,676	497,286

The aversion of DALYs generally increases out into the future for males and females. This suggests that despite population increases and ageing, total DALYs are expected to be less than 1993 levels overall.

However, for some conditions the aversion of DALYs is negative for males and females in the future, such as acute respiratory infections, diabetes mellitus, nervous system and sense organ disorders, musculoskeletal disorders and oral conditions. This can be interpreted as an increase in the burden of disease due to an increase in incidence and the population at risk.

For other conditions, DALYs increase for one gender but decrease for the other. This occurs for infectious and parasitic diseases, endocrine and metabolic disorders, and mental disorders. For infectious and parasitic disease, males are expected to experience an increase in the burden of disease, whereas females are expected to experience a decrease. This is because the rate of decline in the disease for males is much less than for females (see Table 2-1) and the population growth for males at risk is faster than for females.

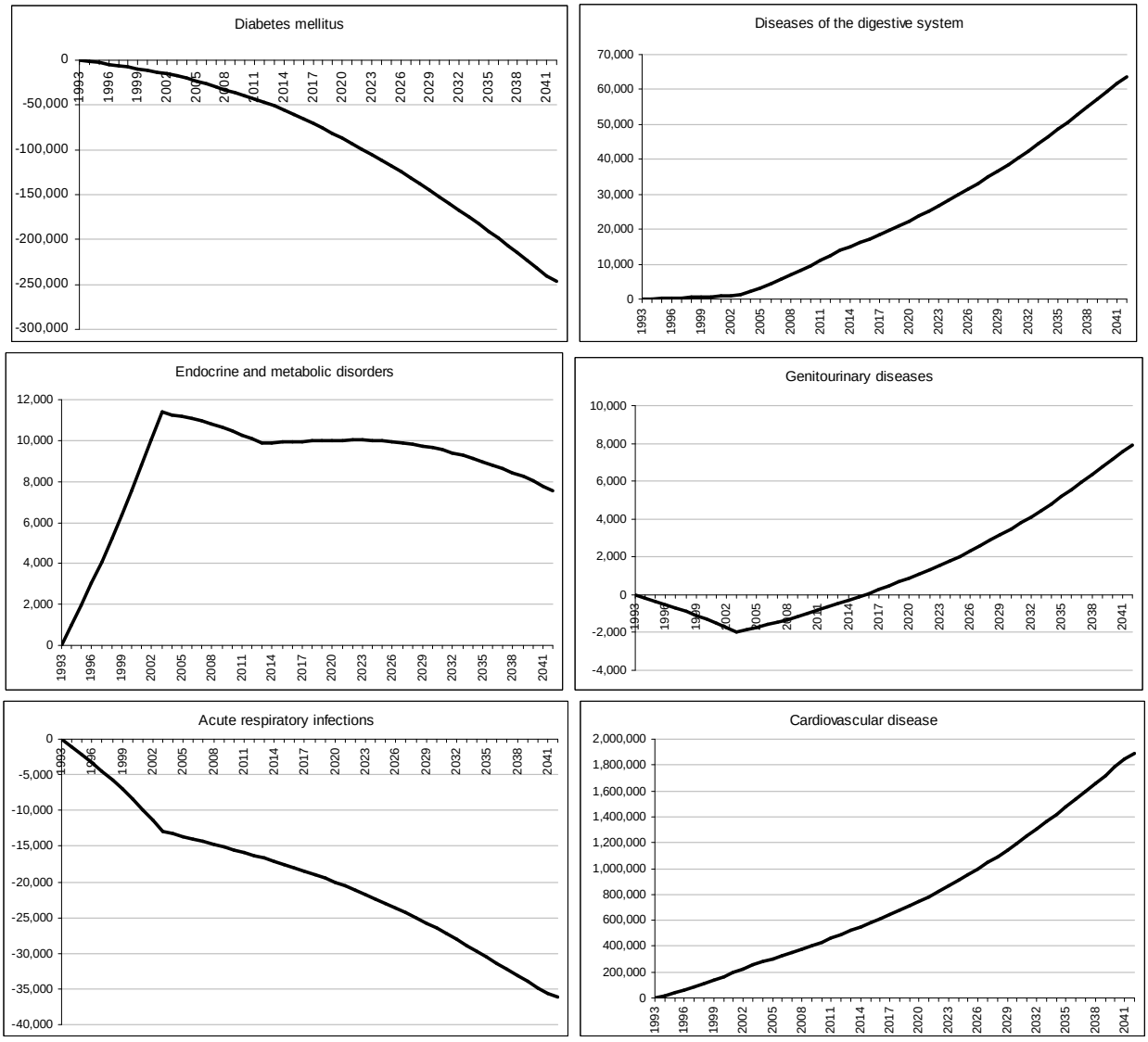
For endocrine and metabolic disorders, males are projected to experience a decrease in the burden of disease whereas females are projected to experience an increase. This is because

endocrine and metabolic disorders are relatively high in the base case for males. For example, the standardised ratio of DALYs presented in Table 2-1 is 1.88 for males compared to 0.89 for females.

For mental disorders, males are projected to experience a decrease in the burden of disease, whereas females are projected to experience an increase. This is because the burden of disease for males is relatively high in the base case compared to females. This is exemplified by the fact that the female population at risk of mental disease is also growing faster than the male population at risk.

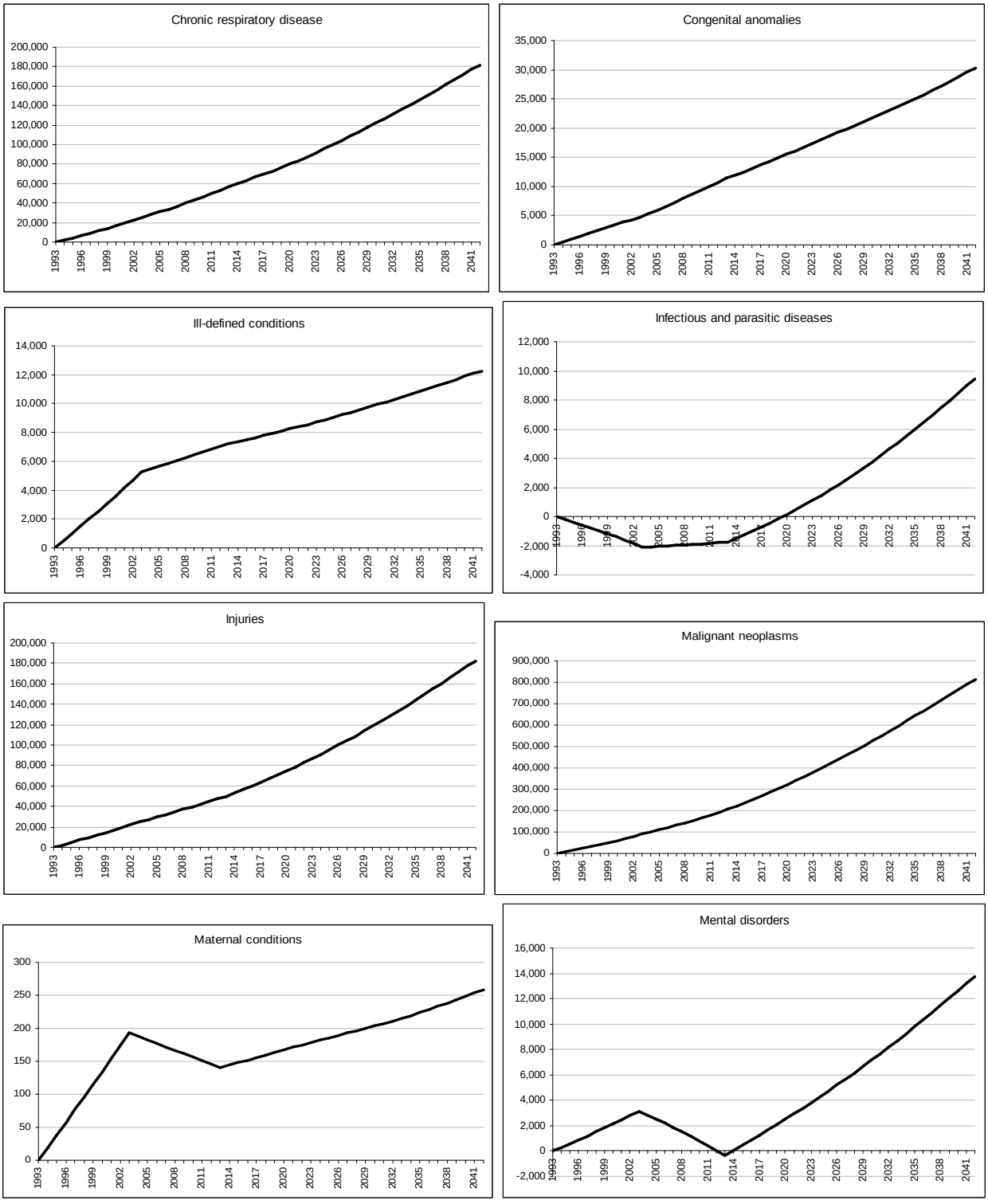
The gains in wellbeing by cause (projected total number of DALYs averted) between 1993 and 2042 are shown in Figure 2-5, Figure 2-6, and Figure 2-7. These are the projections of DALYs minus the DALYs for 1993 and are used to calculate the total value of gains in wellbeing and the net benefits from health R&D in Australia.

FIGURE 2-5: DALYS AVERTED, BY CAUSE, 1993-2042



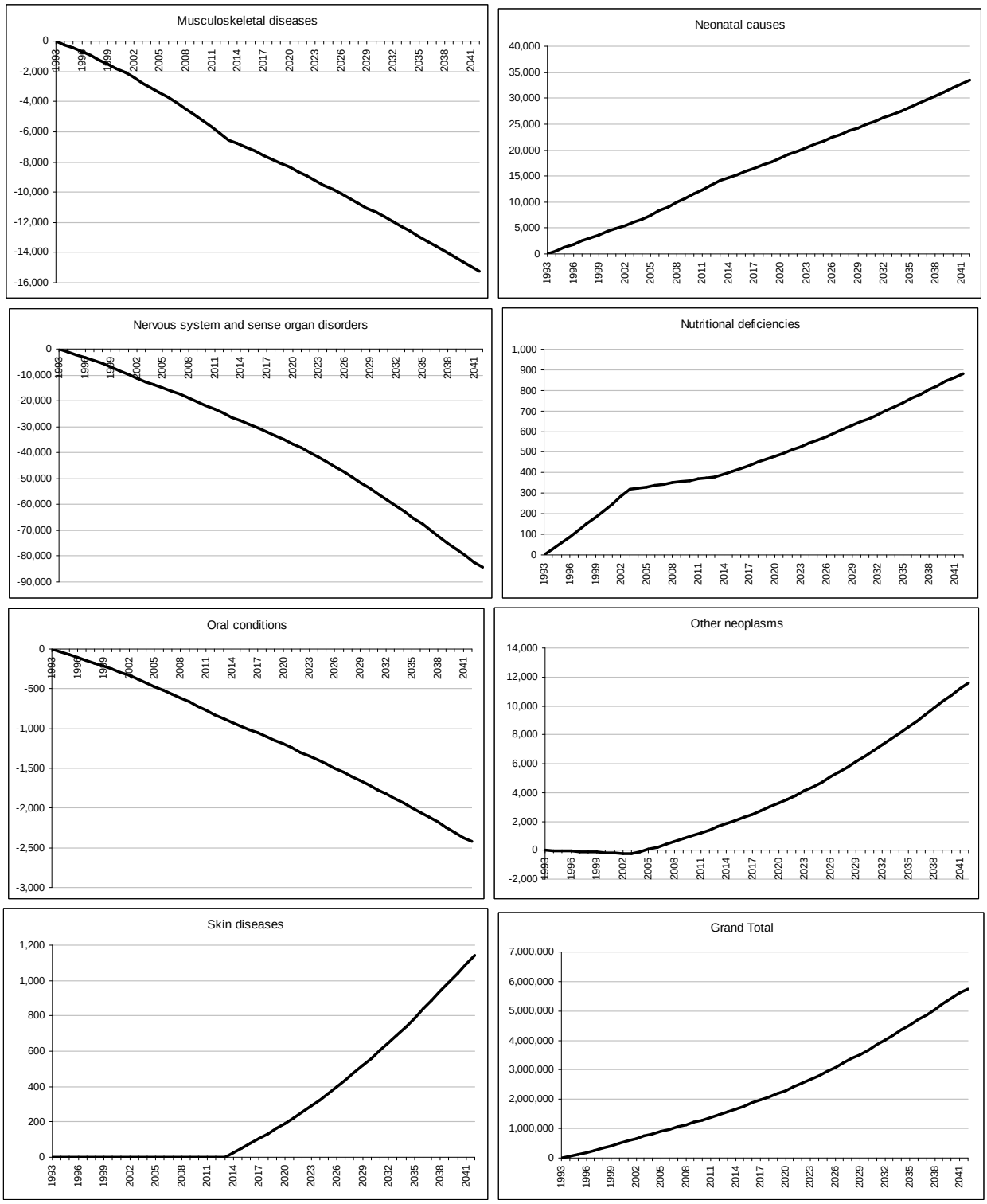
Source: Access Economics.

FIGURE 2-6: DALYS AVERTED, BY CAUSE, 1993-2042 (CONTINUED)



Source: Access Economics.

FIGURE 2-7: DALYS AVERTED, BY CAUSE, 1993-2042 (CONTINUED)



Source: Access Economics.

2.3.1 THE VALUE OF GAINS IN WELLBEING

The value of gains in wellbeing was calculated by multiplying the total number of DALYs averted per year by the Value of a Statistical Life Year (VSLY).

In the past, many economists and policy makers argued that it was not possible to place a value on human life. Despite the difficulties in measurement, most economists and public policy makers recognise that, given the scarcity of resources for public projects and the consequent need for efficient allocation, if such valuations are not made explicitly then they will be made implicitly through decisions about which projects proceed and the funding accorded to competing projects.

The terminology 'statistical' life evolved in an attempt to distinguish the value of the life of an anonymous or unknown individual from the life of a known or particular person, since identified lives are sometimes perceived to be of more value than unidentified ones.[3] While there are different definitions based on different approaches to measurement that could be discussed in more detail, it is more important to note that the value of a unit (year) of healthy life is the relevant variable for decision-making.

The Value of a Statistical Life (VSL) can be measured using different approaches including traditional productivity approaches and 'willingness to pay' (WTP) approaches.

Productivity approaches to measuring the VSL or VSLY are based on the expected earnings of the individual (lost production).

- Frictional approaches are appropriate to measure productivity losses in the short term or in situations of a relatively large unemployment pool.
- Human capital approaches are appropriate in the longer term in economies like Australia operating at near full employment.

However, the loss of human life is viewed as more than earnings, incorporating both the value of unpaid work and the utility value of leisure. As such, the human capital valuation is a lower bound on the VSLY.

To take account of the value of unpaid work and leisure, a hybrid or mark-up approach has been adopted in some cases where the value is estimated as 30% or 40% of the value of earnings. Other early approaches to valuing life included the discounted consumption approach, the implicit value approach, the insurance value approach and the court award approach.

Willingness to pay (WTP) approaches to valuing human life have been the focus of the literature on the economics of life saving since the 1960s. WTP assumes that a person's utility depends on their income and their health, although the complexities of the interactions are not always taken into account. The person's WTP, with their available income, to avoid a risk to their healthy life (including a certain risk) can then be translated mathematically into an estimate of their VSL/VSLY. There are two empirical methods of determining VSL/VSLY using WTP:

- stated preference valuation (contingent valuation or choice modelling) methods; and
- revealed preference (hedonic) valuation methods.

Stated preference methods do not infer values from actual real world decisions, but are hypothetical. Revealed preference studies are generally considered superior to measure individual WTP as they are based on real world empirical, binding market transactions. Compensating (hedonic) wage studies, for instance, use information on people's job choices to estimate WTP for job risk changes.

[3] We note that in a policy setting, anonymous valuation may not always be the correct perspective from which to make an assessment – eg, when target populations are small. The terminology may thus not be appropriate.

A literature search conducted by Access Economics (2008) identified VSL estimates from 244 'western' studies (17 Australian and 227 international studies) between 1973 and 2007. Estimates were analysed by sector, country, methodology and age of study, with simple analysis as well as meta-analysis performed. Converted into 2006 Australian dollars, VSL estimates ranged from $0.1 million to $117 million, with a mean of $9.4 million and a median of $6.6 million. Sector-specific medians ranged from $3.7 million to $8.1 million. A meta-analysis yielded an average VSL of $6.0 million, with a range of $5.0 million to $7.1 million based on exclusion sensitivity analysis.

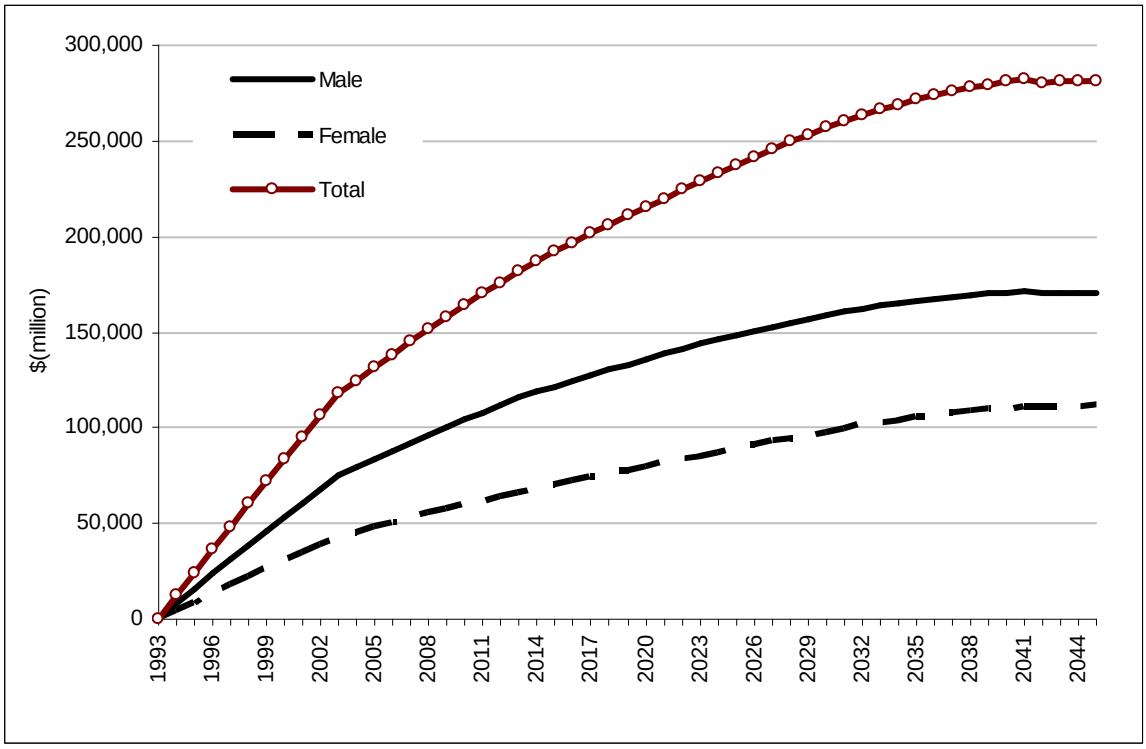
Based on an extensive review of international literature, Access Economics (2008) recommends a VSL of $6.0 million (with $8.1 million as an upper bound and $3.7 million as a lower bound due to the great variability across studies). Using a real discount rate of 3% (which aligns generally with discount rates used in Australian and international studies discounting healthy life and the current AIHW practices) over an estimated 40 years remaining life expectancy, this equates to an average VSLY in 2006 dollars of $252,014. Inflating the 2006 VSLY value to 2008 dollars by multiplying it by two years of inflation (2.9% in each year, from the Access Economics Macroeconomic model) results in a base case of $266,843 with lower and upper bounds of $164,553 and $360,238.

Applying the VSLY to the total number of DALYs averted per year and discounting the values back to 2008 levels (using 3%) results in the total value of gains in wellbeing in Australia between 1993 and 2045. The values of gains in wellbeing by gender are shown in Figure 2-8. They are the annual value of gains in wellbeing expected to result from all impacts on health, not just Australian R&D.

Figure 2-8 shows that the annual value of gains in wellbeing are expected to be larger for males than for females. This is primarily due to the expected larger decrease in the burden of disease for cardiovascular disease, malignant neoplasms, chronic respiratory disease, and injuries for males when compared to females. The larger increase in DALYs results from a larger rate of decrease for males from a larger DALY base for these causes.

For both males and females the annual value of discounted gains in wellbeing increase at a decreasing rate. This is because total gains in wellbeing increase close to a linear rate (especially after 2023 where a linear growth was used to project DALYs out to 2045) while the discount rate means the increase in the VSLY is non linear.

FIGURE 2-8: ANNUAL VALUE OF DISCOUNTED GAINS IN WELLBEING, BY GENDER, 1993-2045



Source: Access Economics.

3. EXPENDITURE ON HEALTH R&D

The expenditure on health R&D used within this study is based on Australian Bureau of Statistics (ABS) estimates derived from public and private (profit and non-profit) institutions. Expenditure is classified by the type of research (basic, applied, and experimental development) and by source of funds (Federal Government, state and local governments, business, other Australia and overseas). The R&D expenditure data cover all areas relating to health, including prevention, screening, diagnosis, treatment and epidemiological research, although much of the R&D is at a more basic level.

ABS data at the level of detail required for this study were available for the years 1992-93, 1994-95, 1996-97, 1998-99, 2000-01, 2002-03 and 2004-05. Estimates of R&D expenditure for the years that have not been collected between these years were derived from a linear extrapolation.

3.1 METHODOLOGY USED TO ESTIMATE EXPENDITURE ON HEALTH R&D IN AUSTRALIA

R&D activity is defined in Australia (ABS, 2006a:25) as:

> *'Systematic investigation or experimentation involving innovation or technical risk, the outcome of which is new knowledge, with or without a specific practical application, or new and improved products, processes, materials, devices or services. R&D activity extends to modifications to existing products/processes. R&D activity ceases and pre-production begins when work is no longer experimental'.*

The definition used by the ABS concords with the Organization for Economic Cooperation and Development (OECD) standard definition of R&D, which is 'creative work undertaken on a systematic basis in order to increase the stock of knowledge, including knowledge of man, culture and society, and the use of this stock of knowledge to devise new applications' (OECD, 1994).

Classification of research in this study is based on the Australian Standard Research Classification (ASRC) for 1998 (ABS, 1998), which in turn is based on OECD guidelines for member nations for both R&D measurement and survey data collection. R&D expenditure refers to gross expenditure on R&D (GERD).

3.1.1 DATA COLLECTION

The ABS data-gathering process uses a bottom-up approach. Data are collected through a survey of businesses, Government, private non-profit (PNP) organisations and higher education organisations, which are reported primarily in four publications:

- Cat No 8104.0: *Research and Experimental Development Australia 2004-05: Businesses* (ABS, 2006b);
- Cat No 8109.0: *Research and Experimental Development Australia 2004-05: Government and Private Non-Profit Organisations* (ABS, 2006c);
- Cat No 8111.0: *Research and Experimental Development Australia 2004-05: Higher Education Organisations* (ABS, 2006d); and

- Cat No 8112.0: *Research and Experimental Development Australia 2004-05: All Sector Summary* (ABS, 2006a).

The data presented in these reports are at a highly aggregated level. In order to investigate R&D expenditure on individual causes, more detailed data were collected from the ABS consultancy services at the division, subdivision, group, and class level. However, the ABS notes that these statistics should be used with caution for the following reasons (2006a:24).

- Many organisations provided best estimates due to a lack of separately recorded data on R&D activity.
- Data are subjectively classified by organisation to research field, socioeconomic objective and type of activity at the time of reporting. Some organisations may experience difficulty in classifying their R&D projects. The ABS makes every effort to ensure correct and consistent interpretation and reporting of these data by applying consistent processing methodologies.
- Estimation of overhead R&D expenditure varies across organisations.

More details on classification issues, data collection in Australia and other data sources can be found in Access Economics (2003).

3.1.2 CLASSIFICATION AND CATEGORISATION OF DATA

The ASRC (ABS, 1998) has two related classifications that can be used to identify health and cancer R&D. These include the research fields, courses and disciplines (RFCD) classification, which identifies all R&D undertaken using health disciplines, and the socioeconomic objective (SEO) classification, which identifies R&D with the objective or purpose of health. In evaluating the net benefits of health R&D, the SEO classification is more relevant as it includes R&D to improve health, not just health-related disciplines. This permits health benefits to be matched up with the costs associated with improving health. [4]In this study, the following SEO subdivisions were used.

- **Subdivision 730000** '**Health**' (130000 pre 2000-01) – directed to human health including the understanding and treatment of clinical diseases and conditions and the provision of public health and associated support services. This includes:
  - Group 730100 (130100 pre 2000-01) 'Clinical (Organs, diseases and abnormal conditions)';
  - Group 730200 (130200 pre 2000-01) Public health; and
  - Group 730300 (130300 pre 2000-01) Health and support services.
- **Group 670400** '**Human pharmaceutical products**' (070400 pre 2000-01) – which includes prevention, diagnostics, treatments and other pharmaceutical product uses.

In addition to the classification of research, expenditure data is categorised by the type of institution that undertakes the research. Four sectors are recognised as sources of R&D activity by the ABS.

[4] In Australia, data are available for both classifications and there is some debate about which method is superior. For RFCD, there is the risk of understatement due to possible exclusion of some pure basic research. For these reasons, health R&D tends to be lower when measured by RFCD than by SEO. The likely result is probably somewhere between the two estimates, although the authors of this paper take the view that SEO is likely to be a closer estimate. There is also the theoretical issue of whether an approach using the discipline in which the research (RFCD) is undertaken is conceptually superior to that of the ultimate purpose of the research (SEO). Again the authors would lean to the superiority of the SEO approach on this basis as well.

1 **Business** – includes all businesses whose primary activity is the production of goods and services for profitable sale to the general public and the PNP institutions mainly serving them. It excludes businesses mainly engaged in agriculture, forestry and fishing (Division A, Australia New Zealand Standard Industrial Classification) because of difficulties of collection and because their R&D activity is estimated to be minimal.

2 **Government** – includes all Commonwealth, State/Territory and local government departments and authorities. Local government organisations are excluded because their R&D activity is estimated to be minimal. Public sector organisations mainly engaged in higher education are included in 'higher education', while those mainly engaged in trading or financial activities are included in 'business'.

3 **Higher Education** – includes all universities and other institutions of post-secondary education whatever their source of finance or legal status, except non-university post-secondary institutions (for example, technical and further education colleges) because their R&D activity is estimated to be minimal.

4 **Private Non Profit (PNP)** – includes private or semi-public incorporated organisations established with the intention of not making a profit.[5]

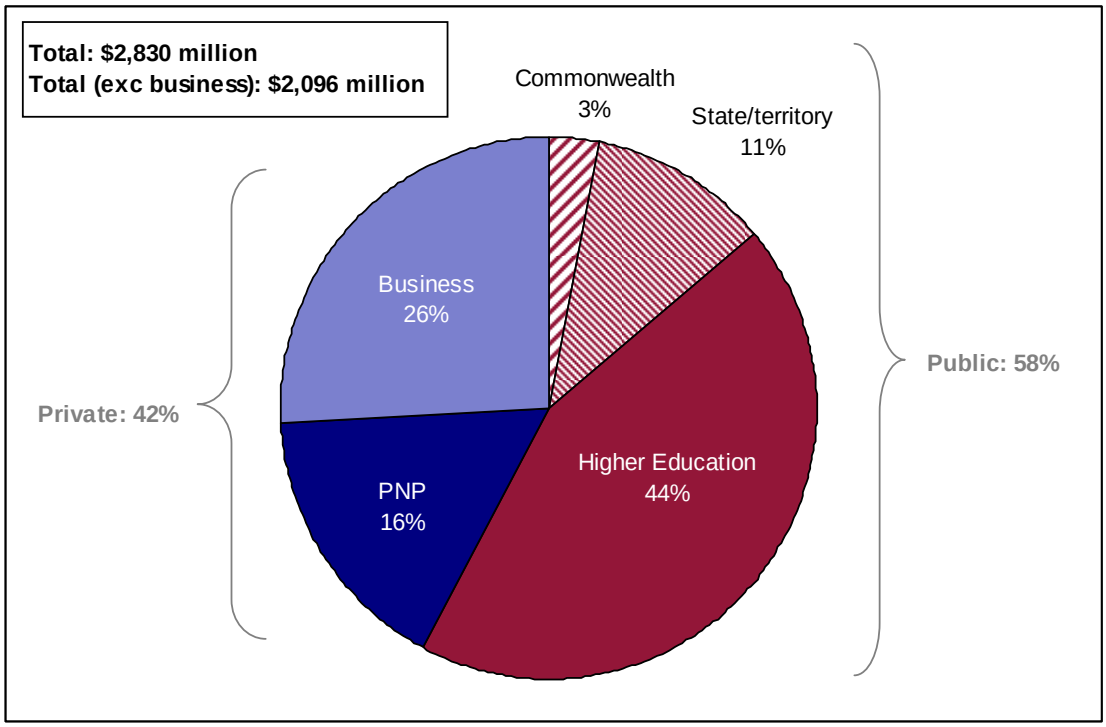
3.2 EXPENDITURE ON HEALTH R&D IN AUSTRALIA

3.2.1 HEALTH R&D EXPENDITURE PERFORMED BY SECTOR

In 2004-05, $2.8 billion was spent undertaking health R&D (SEO) in Australia by business, government, higher education facilities and private non-profit organisations. Figure 3-1 shows that higher education organisations performed the highest portion of health R&D with around $1.2 billion (44%). Private business and PNP organisations performed around $0.7 billion (26%) and $0.4 billion (16%) respectively, while State/Territory and Commonwealth performed around $0.3 billion (11%) and $0.08 (3%) billion respectively. Consequently, 58% of health R&D was performed by the public sector and 42% by the private sector. Non-business R&D amounted to $2.1 billion.

[5] It should be noted that in many cases attributing research performance between sectors is complex. For example, the Walter & Eliza Hall Institute and the Baker Heart Research Institute are both distinct entities classified to the PNP sector. However, they are both associated with universities. Funding and control of projects determine whether the research is reported by the universities or by the Institutes themselves. The majority of the research at each Institute is reported by the Institute and hence is included in the PNP sector.

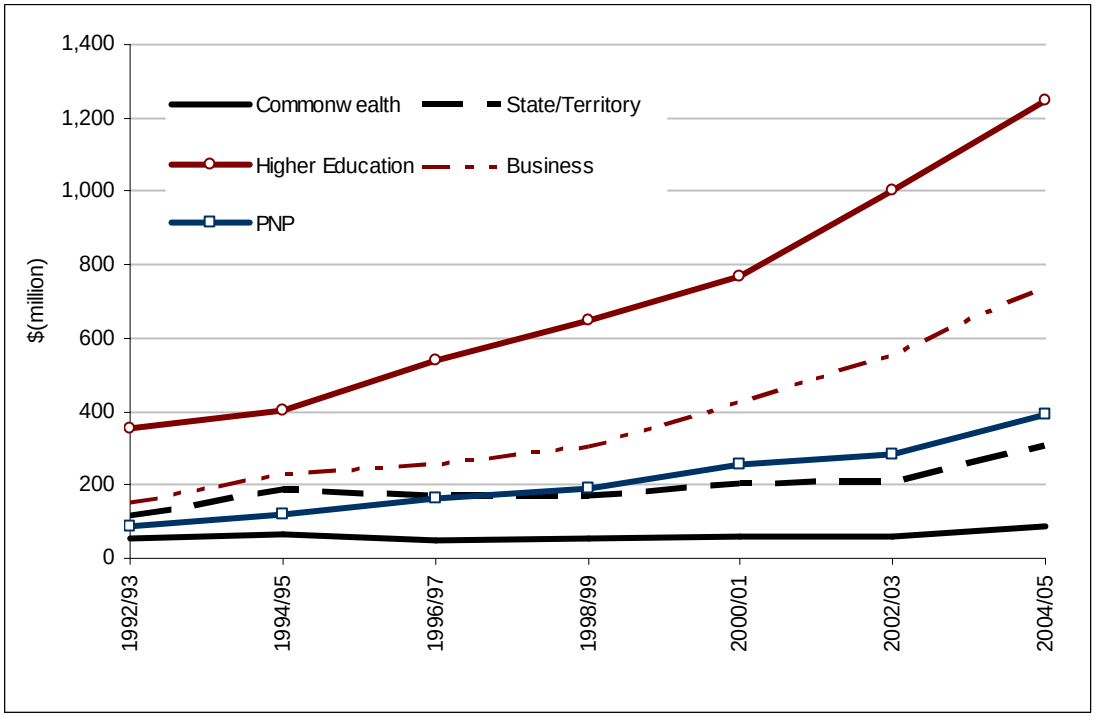
FIGURE 3-1: HEALTH R&D (SEO) PERFORMED BY SECTOR, 2004-05



Source: Access Economics, based on ABS data.

Since 1992-93, expenditure on health R&D has grown from around $800 million to $2.8 billion, representing an average annual growth rate of 12%. Figure 3-2 shows the trend in R&D performed by sector.

FIGURE 3-2: TREND IN HEALTH R&D (SEO) PERFORMED BY SECTOR, 1992-93 TO 2004-05



Source: Access Economics, based on ABS data.

The average growth rate of health R&D performed by Business has been the highest at around 15% per year. This is closely followed by PNP (15%), Higher Education (12%), State/Territory (10%) and the Commonwealth (4%). Table 3-1 shows the breakdown of health R&D by sector between 1992-93 and 2004-05, as a percentage of GDP, and per capita. In 2004-05, Australian non-business health R&D accounted for 0.23% of GDP and amounted to $103.10 per capita. In comparison, non-commercial health R&D was only 0.14% of GDP and $34.60 per capita in 1992-93.

TABLE 3-1: AUSTRALIAN HEALTH R&D (SEO), BY SECTOR, 1992-93 TO 2004-05

Sector ($'000)	1992-93	1994-95	1996-97	1998-99	2000-01	2002-03	2004-05
Commonwealth	57,179	66,232	51,630	57,008	53,339	62,133	84,809
State/territory	115,925	186,749	168,993	165,501	204,392	206,254	307,353
Higher Education	352,267	404,019	537,127	539,704	774,354	1,001,973	1,245,042
Subtotal Public	**525,370**	**657,000**	**757,749**	**762,212**	**1,032,085**	**1,270,361**	**1,637,205**
Business	151,911	226,497	257,246	304,641	432,263	553,202	733,569
PNP	85,856	132,728	169,290	202,776	263,747	323,956	458,738
Subtotal Private	**237,767**	**359,225**	**426,536**	**507,418**	**696,010**	**877,158**	**1,192,307**
Total	**763,137**	**1,016,225**	**1,184,285**	**1,269,630**	**1,728,095**	**2,147,519**	**2,829,512**
Total exc business	**611,226**	**789,728**	**927,039**	**964,989**	**1,295,832**	**1,594,317**	**2,095,943**

% of GDP	1992-93	1994-95	1996-97	1998-99	2000-01	2002-03	2004-05
Commonwealth	0.013%	0.014%	0.009%	0.009%	0.008%	0.008%	0.009%
State/territory	0.026%	0.038%	0.031%	0.027%	0.030%	0.026%	0.034%
Higher Education	0.080%	0.083%	0.098%	0.089%	0.112%	0.128%	0.139%
Subtotal Public	0.120%	0.135%	0.139%	0.125%	0.150%	0.163%	0.183%
Business	0.035%	0.047%	0.047%	0.050%	0.063%	0.071%	0.082%
PNP	0.020%	0.027%	0.031%	0.033%	0.038%	0.041%	0.051%
Subtotal Private	**0.054%**	**0.074%**	**0.078%**	**0.083%**	**0.101%**	**0.112%**	**0.133%**
Total	**0.174%**	**0.209%**	**0.217%**	**0.209%**	**0.251%**	**0.275%**	**0.316%**
Total exc business	**0.140%**	**0.162%**	**0.170%**	**0.159%**	**0.188%**	**0.204%**	**0.234%**

$ per capita	1992-93	1994-95	1996-97	1998-99	2000-01	2002-03	2004-05
Commonwealth	$3.24	$3.66	$2.79	$3.01	$2.75	$3.13	$4.17
State/territory	$6.56	$10.33	$9.13	$8.74	$10.53	$10.38	$15.12
Higher Education	$19.94	$22.36	$29.01	$28.52	$39.89	$50.42	$61.25
Subtotal Public	**$29.74**	**$36.36**	**$40.92**	**$40.27**	**$53.16**	**$63.93**	**$80.54**
Business	$8.60	$12.53	$13.89	$16.10	$22.27	$27.84	$36.09
PNP	$4.86	$7.34	$9.14	$10.71	$13.59	$16.30	$22.57
Subtotal Private	**$13.46**	**$19.88**	**$23.03**	**$26.81**	**$35.85**	**$44.14**	**$58.65**
Total	**$43.20**	**$56.23**	**$63.95**	**$67.08**	**$89.02**	**$108.06**	**$139.19**
Total exc business	**$34.60**	**$43.70**	**$50.06**	**$50.99**	**$66.75**	**$80.23**	**$103.10**

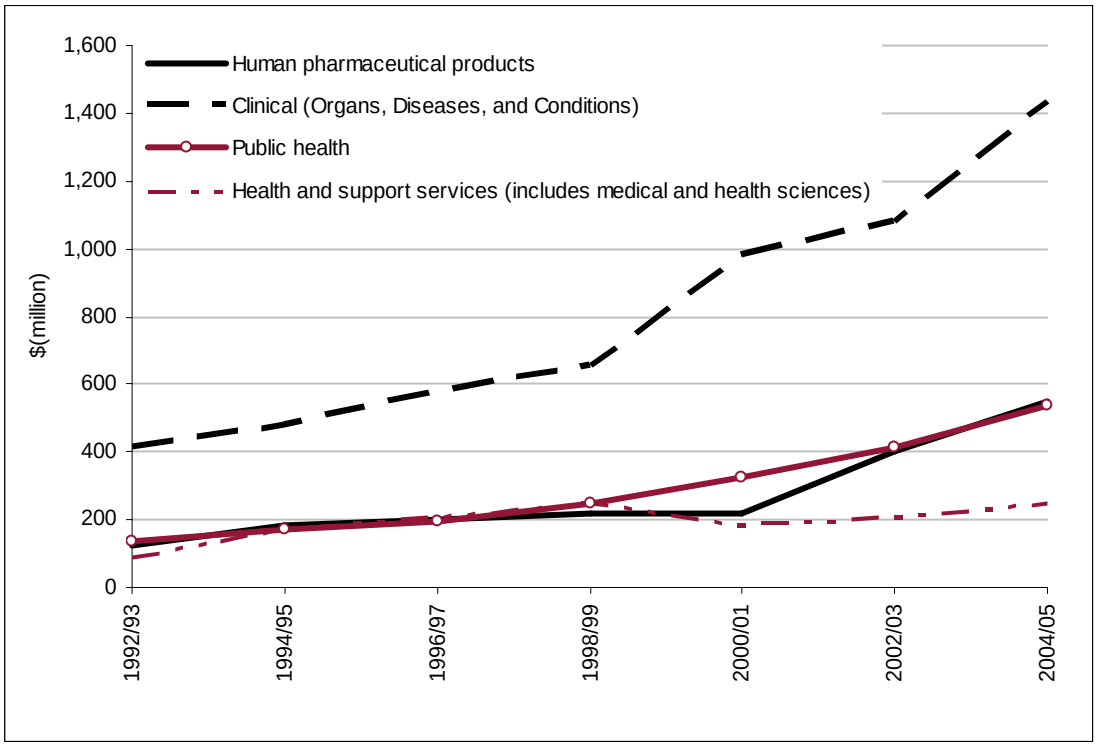
Source: Access Economics, based on ABS data.

3.2.2 HEALTH R&D EXPENDITURE BY GROUP

Figure 3-3 shows the trend in health R&D expenditure by group between 1992-93 and 2004-05. The majority of R&D since 1992-93 has been undertaken in clinical research, which has increased from around $413 million to $1.43 billion at an average annual growth rate of 12%. R&D expenditure on human pharmaceutical products and public health had similar expenditures in 2004-05 with $548 million and $536 million spent respectively, although the average annual growth rate for the former was larger at 15% compared to 12%. Health and support services (which includes medical and health sciences prior to 2000-01) had the

lowest expenditure in 2004-05 at $250 million and the lowest average annual growth rate at 12%.

FIGURE 3-3: TREND IN HEALTH R&D (SEO) EXPENDITURE BY GROUP, 1992-93 – 2004-05



Source: Access Economics, based on ABS data.

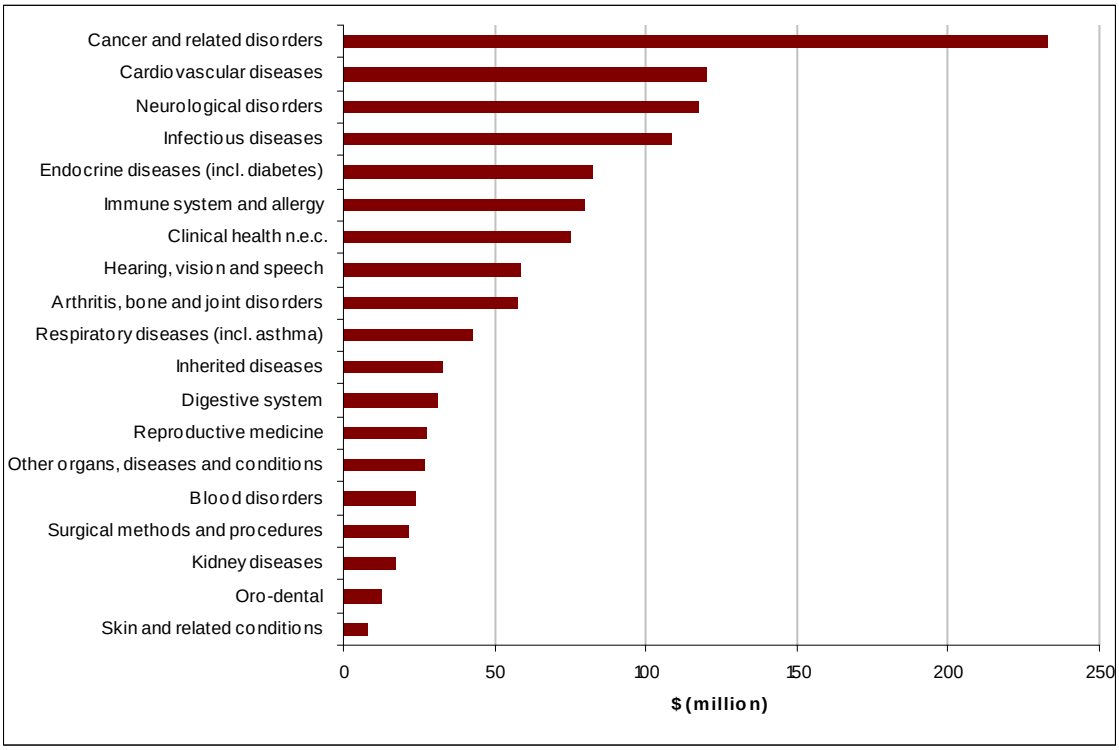
3.2.2.1 CLINICAL NON-BUSINESS HEALTH R&D EXPENDITURE BY CLASS

Focusing on clinical R&D and disaggregating expenditure by class shows that cancer and related disorders had the greatest expenditure in 2004-05 within the non-business sector[6]. Figure 3-4 shows that around $233 million was spent on cancer, which was nearly double the expenditure for cardiovascular disease at $120 million. The smallest class of expenditure in 2004-05 was for skin and related conditions, at around $8 million.

It is a different story when looking at growth in R&D performed since 1992-93. Figure 3-5 shows the average annual growth rate of non-business clinical R&D performed by class between 1992-93 and 2004-05. Growth was highest for arthritis, bone and joint disorders at around 17%, while infectious diseases had the second highest growth rate of around 13%. Growth in R&D expenditure for cardiovascular diseases and cancer and related disorders were ranked in the middle with both at around 11%. The lowest growth rate was for reproductive medicine at around 5%.

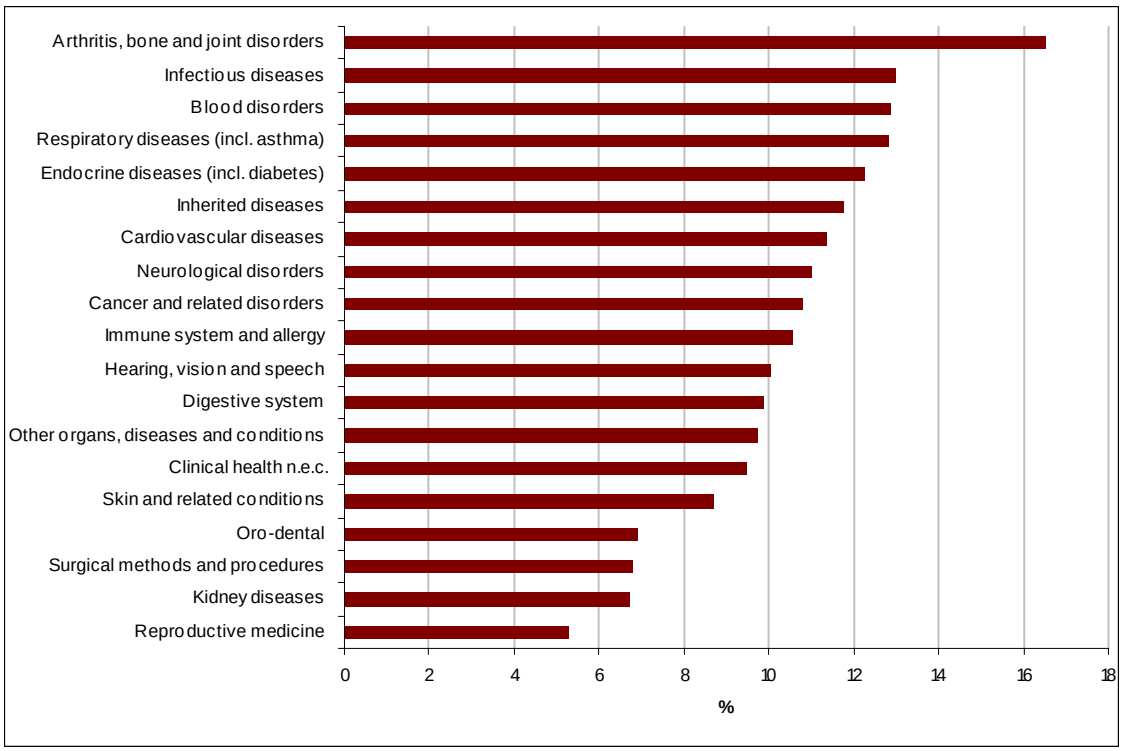
[6] As data for the business sector at class level may be commercially sensitive it was not provided by the ABS.

FIGURE 3-4: TOTAL NON-BUSINESS CLINICAL R&D (SEO) EXPENDITURE, BY CLASS, 2004-05



Source: Access Economics, based on ABS data.

FIGURE 3-5: AVERAGE ANNUAL GROWTH RATE OF NON-BUSINESS CLINICAL R&D (SEO) EXPENDITURE, BY CLASS, 1992-93 – 2004-05



Source: Access Economics, based on ABS data.

3.2.3 HEALTH EXPENDITURE BY SOURCE OF FUNDS

Table 3-2 shows the cross tabulation of health R&D performed by sector and source of funds. Although the Commonwealth sector performs the least amount of health R&D, most of the funding comes from the Commonwealth government. In 2004-05, the Commonwealth contributed around $1.4 billion of funds across all five sectors. The majority of this spending went to Higher Education facilities (79%) while Business received the lowest amount of funding (2%). The business sector spends the second highest amount of funds on health R&D and, not surprisingly, most of these funds are spent on R&D undertaken by business. Overseas funding accounts for around $121 million (4%) of Australian health R&D spending, of which the majority is performed by the PNP sector.

TABLE 3-2: AUSTRALIAN HEALTH R&D (SEO) BY SECTOR AND SOURCE OF FUNDS, 2004-05

Source of funds	Business	Commonwealth Govt	State/Territory Govt	Other Australian	Overseas
Commonwealth	4,262	71,908	2,340	4,308	1,990
State/territory	20,196	49,213	179,459	50,075	8,411
Higher Education	70,691	1,066,703	43,061	27,269	37,318
Subtotal Public	**95,150**	**1,187,824**	**224,860**	**81,653**	**47,718**
Business	681,470	28,452	2,597	4,291	16,760
PNP	38,315	138,692	45,760	178,784	57,187
Subtotal Private	**719,784**	**167,144**	**48,357**	**183,075**	**73,947**
Total	**814,935**	**1,354,968**	**273,217**	**264,727**	**121,665**
Total exc business	**133,465**	**1,326,516**	**270,620**	**260,436**	**104,905**

Source: Access Economics, based on ABS data.

4. NET BENEFITS FROM AUSTRALIAN HEALTH R&D

4.1 METHODOLOGY

Investment in health R&D to develop new technologies and methods has one primary goal in mind - to improve the health and wellbeing of individuals. However determining the impact of health R&D on the wellbeing of individuals over time is a difficult task due to the many confounding factors that impact health. To ensure these confounding factors are removed and only the impacts of Australian health R&D are included in the analysis, the following five steps were undertaken.

1 **Health scenarios were established 'with R&D' and 'without R&D'**. The 'with R&D' scenario is the current wellbeing scenario faced by Australia, as described in Chapter 2. The 'without R&D scenario' is the wellbeing scenario that would have occurred if Australian health R&D was not undertaken. For the purposes of this study it was assumed that DALYs per capita were those of 1993 – the year that the first R&D expenditure data were available.

2 **The impact of Australian R&D was estimated**. The impact that Australian R&D has had on the wellbeing of Australians was calculated by multiplying the proportion of health gains attributable to world R&D by the proportion of world R&D that is contributed by Australia. More information on these key parameters used in the modelling can be found in Section 4.2

3 **The net benefit stream was modelled**. This was done by applying the VSLY to the gains in Australia's wellbeing to derive a monetary value for the benefits of Australia's R&D (recall Section 2.3.1) and then subtracting Australia's expenditure on R&D.

4 **The economic evaluation measures were calculated.** These included the net benefits, return on investment (ROI) and B/C ratio.

5 **A sensitivity analysis was undertaken**. This was important to test the sensitivity of the economic evaluation measures to variation in key parameters.

As noted in Chapter 3, expenditure data were available biennially for the years 1992-93 to 2004-05 so estimates of net benefits from Australian health R&D cover this period only.

A major issue in calculating the net benefits of health R&D is the treatment of time lags between health R&D expenditure and gains in wellbeing. The very nature of scientific investigation is that its results and timeframes are uncertain, and successes are cumulative. In pharmacological research, timeframes are somewhat more predictable, but such developmental research tends to build on public sector basic research that involves greater risks and externalities.

How can such lags be captured? In Access Economics (2003), we retrospectively compared the estimated gains in any year with the research spend in that same year. This provided an estimate that did not capture the lag between R&D and its benefits, but was a conservative proxy. For this study, it was decided that in order to provide more realistic estimates of the return from R&D, the lag between expenditure and gains in wellbeing should be captured.

However, the lag before returns begin, and the period over which benefits last, are both uncertain. In any year, benefits reflect many different previous R&D investments from earlier years, and it is extremely difficult to allocate benefits over a stream of years to investments over a corresponding earlier stream of years. Therefore, in order to calculate the net benefits for health R&D in Australia we made some simplifying assumptions.

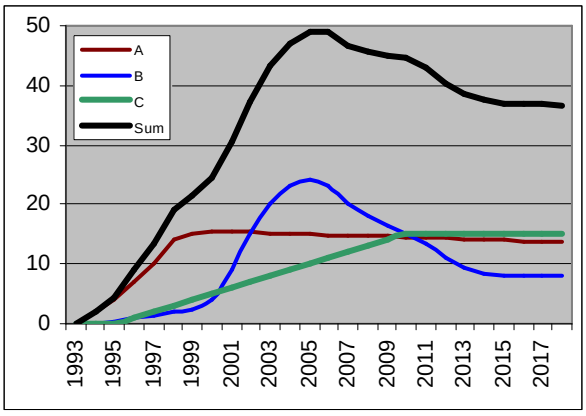
Figure 4-1 shows a stylised approached to capturing the lags. Panel A depicts the hypothetical wellbeing gains from R&D projects. The vertical scale is a hypothetical index scale. The gains are shown as streams associated with R&D in each year. Thus, the 'A' stream shows gains from R&D projects completed[7] in 1993, the 'B' stream from projects in 1994 and the 'C' stream for projects in 1995. The sum of the three streams to 2018 and beyond reflects the different pattern of benefits – some projects may build up to maximum returns (quickly or slowly) and then stay at that level, others may become more obsolescent over time, although newer technologies may build on their findings.

In Panel B, the black line represents the sum of all the projects over time (simply replicating A, B and C to the end of the period), while the blue line above it shows the sum of projects prior to 1993. The bars show the actual and projected R&D expenditure, and the burgundy bars are ABS-measured expenditure years.

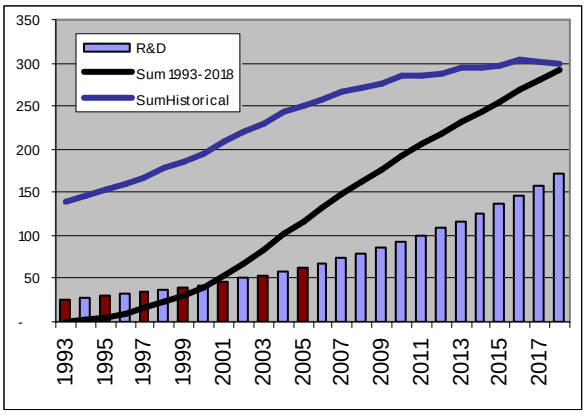
The assumption used within the net benefits calculation was that the total benefit from R&D undertaken in one year is lagged 40 years. That is, the benefits that are projected to be experienced in 40 years are used as a proxy for the benefits expected from R&D undertaken 40 years prior. The R&D expenditure in 1993 was therefore compared with the projected wellbeing gains in 2033. Similarly, the expenditure in 1994 was compared with the projected wellbeing gains in 2034 and so on. This was continued up to 2005 where the expenditure data finishes. The economic evaluation measures were calculated by comparing the total projected wellbeing gains associated with total expenditure between 1992-1993 and 2004-2005, which were both adjusted to 2008 prices using a discount rate of 3%.

FIGURE 4-1: CONCEPTUAL ROI METHODOLOGY FOR CALCULATING ROI (HYPOTHETICAL)

Panel A: Wellbeing gains



Panel B: Summed wellbeing gains and R&D



In order to determine the impact of different assumptions regarding the delay, a sensitivity analysis was undertaken that changed the delay between 20 and 60 years (Section 5.5) using ten year increments.

4.2 KEY PARAMETERS USED IN THE MODELLING

Only a proportion of gains in wellbeing in Australia can be attributed to Australian R&D. This is because there will be other factors that impact health which are not related to R&D, such as improved income, education programs, better food and improved environment. Furthermore, health R&D undertaken outside Australia has had a significant impact on the

[7] This recognises that projects can take many years to complete.

health of Australians; this impact must be removed if a true representation of the benefits from Australian health R&D is to be made. Consequently, modelling the net benefits and ROI for Australian health R&D critically depends on the following parameters:

- the proportion of health gains attributed to world health R&D rather than other factors that impact health; and
- the contribution of Australian health R&D to the total health gains attributable to world health R&D

These parameters are discussed below.

4.2.1 PROPORTION OF HEALTH GAINS ATTRIBUTABLE TO TOTAL R&D

In its 2003 report, Access Economics (2003) used the base case assumption that R&D is responsible for 50% of the improvements in healthy lifespan. This was based on research quoted in Hatfield et al (2000), who estimated that 33% of total health gain related to a reduction in mortality and morbidity from cardiovascular disease that is the result of medical research, while a share of the remaining 67% can be linked to research since gains attributed to changes in public policy and individual behaviour depend on research-derived information. However, benefits from research in some areas are less immediately apparent, particularly if research and higher medical expenditure may have little impact on mortality or morbidity such as in the case of musculoskeletal conditions (Hanney et al, 2004).

In the meantime, several papers have been written about the issue of how to attribute health gains to R&D. Buxton et al (2004), for instance, reviewed key studies related to the impact of health research – including the Access Economics (2003) study – concluding that estimating the economic value to societies of health research is complex as it involves multiple issues such as identifying and valuing the relevant research inputs, accurately ascribing the impact of the research and appropriately valuing the attributed economic impact. Weiss (2007) argued that in order to calculate the clinical return on an investment in medical research, three outcomes need to be measured: awareness, implementation and patient benefit, but the ability to provide that information is limited at present. However, no better estimate of the actual percentage of health gains attributable to total R&D has been made.

Consequently the base case assumption of 50% (with sensitivity analysis at 30% and 70%) can still be seen as appropriate given the complexity of the issue and the lack of alternative estimates.

4.2.2 PROPORTION OF WORLD R&D ATTRIBUTABLE TO AUSTRALIAN R&D

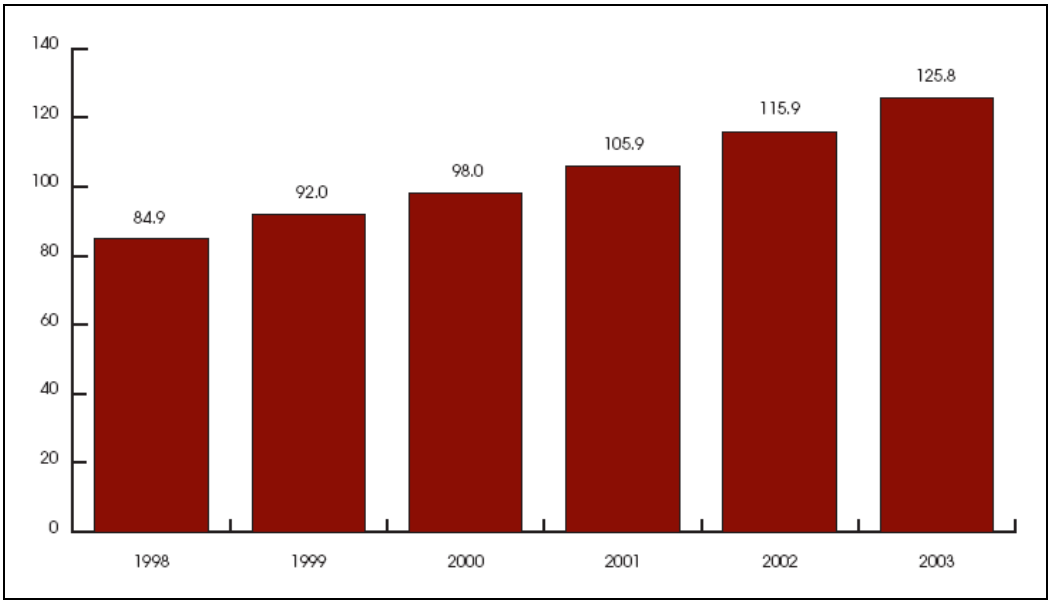
Although Europe and North America are major contributors to Australia's health gains, as evidenced by the amount of resources used to undertake health R&D in these regions and the number of journal articles created from the research, Australia has also made considerable achievements in health R&D. Wills (1998) concluded that, with 0.3% of the world's population, Australia produces about 2.5% of the world's health R&D output. Australian scientists have received four Nobel prizes for Medicine or Physiology while the impact of our health R&D ranks consistently in the top eight countries across a range of fields.

There are two methods that have been investigated within this study to determine Australia's contribution to world R&D. The first examines the share of inputs into R&D by looking at the expenditure of Australia R&D compared to the rest of the world. The second examines the share of R&D outputs by looking at the share of Australian publications compared to the rest of the world. Both methods are discussed below.

4.2.2.1 INPUTS INTO R&D: AUSTRALIA'S SHARE OF R&D EXPENDITURE

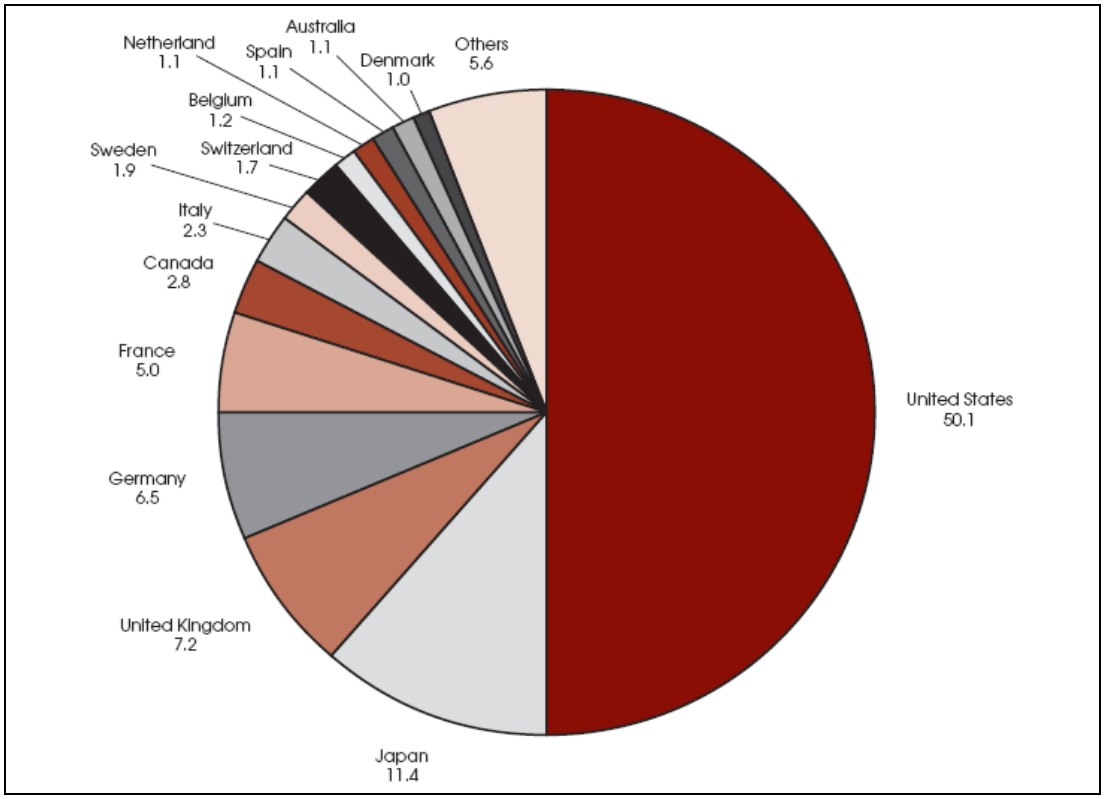
Burke and Monot (2006) estimated global health research spending to be US$125.8 billion in 2003 (Figure 4-2). This estimate is based on various data sources including OECD data. The OECD, for instance, estimates global overall R&D spending in 2003 to have been in the order of US$645 billion. Approximately 20% of the total global R&D expenditure is estimated to have been for health research which would amount to US$129 billion. Looking at country shares, Burke and Monot (2006) estimate Australia's health R&D expenditure to be 1.1% of global health R&D expenditure.

FIGURE 4-2: ESTIMATES OF TOTAL EXPENDITURES ON HEALTH RESEARCH (US$ BILLION)



Source: Burke and Monot (2006).

FIGURE 4-3: GLOBAL DISTRIBUTION OF R&D FOR HEALTH EXPENDITURES, 2003



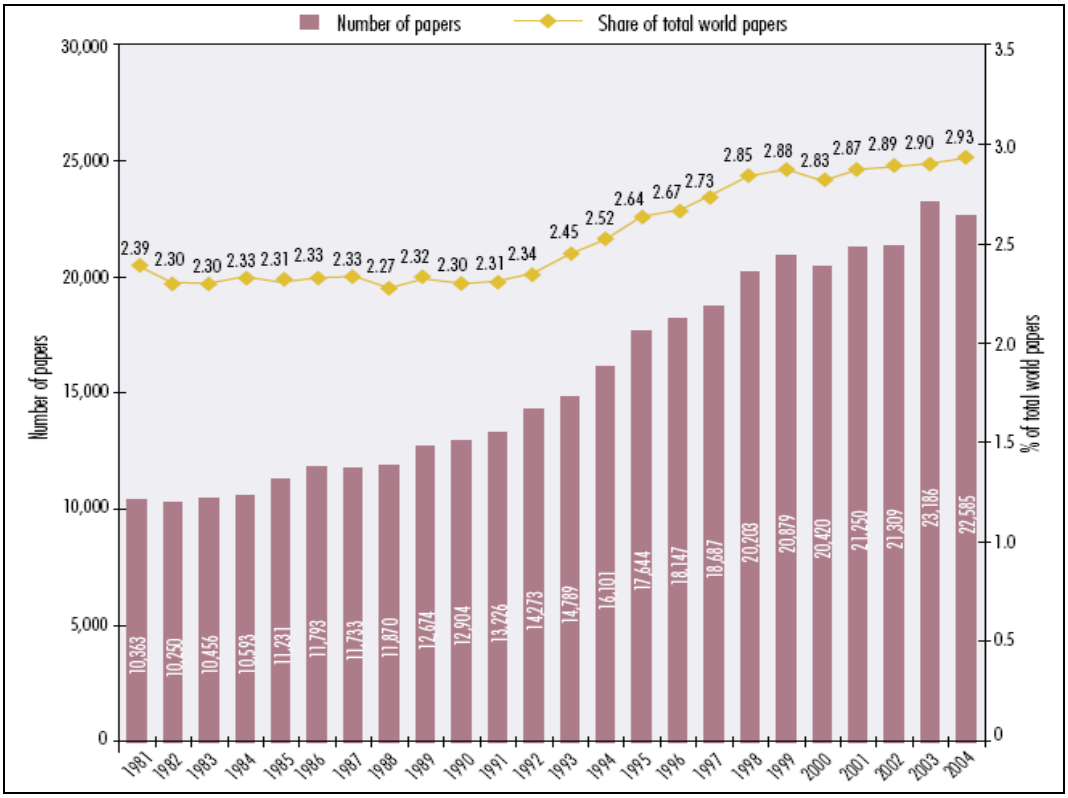
Source: Burke and Monot (2006).

However, expenditure data provide information on the inputs into health R&D. As such, it is not particularly useful in measuring the extent to which a country might contribute in terms of R&D outputs. Consequently, it is problematic to use expenditure data to measure the contribution of Australia's R&D to wellbeing because it is the quantity and quality of R&D that matters. For this task, bibliographic (reference and citation) evidence is superior, as it is output-focused.

4.2.2.2 OUTPUT FROM R&D: AUSTRALIA'S SHARE OF PUBLICATIONS

The total number of Australian research publications rose fairly steadily from 10,363 in 1981 to 22,585 in 2004. Australia's share of total world research publications stayed steady around 2.3% until the early 1990s when it experienced an upward trend, rising to 2.93% in 2004 (Figure 4-4). With this share, Australia ranked 11th in the world and ninth among OECD countries. In 2004, Australia's citation impact was 1.14 times the worldwide average. From 1981 to 2004, Australian citation impact was generally above the world average, but dipped below that average on eight occasions between 1987 and 1997 (DEST, 2005).

FIGURE 4-4: AUSTRALIA'S NUMBER AND SHARE IN RESEARCH PUBLICATIONS, 1981 TO 2004



Source: DEST (2005)

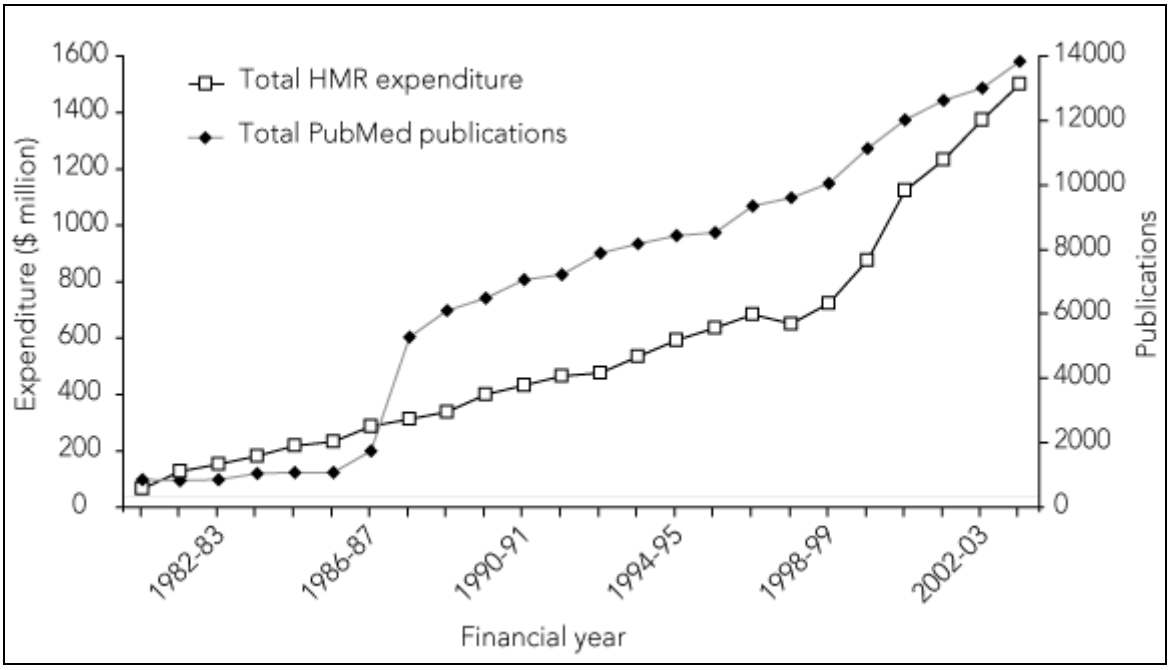
Mendis and McLean (2006) estimate that Australian PubMed publications increased from 844 in 1980/81 to 13,836 in 2003/04 during a time when Australian health and medical research funding increased from $66 million to $1,503 million. This is shown in Figure 4-5.

Australian research publications on clinical medicine accounted for 3.04% of the world total between 2000 and 2004. Shares in other health related fields varied: psychiatry accounted for 4.53%, immunology for 3.79%, neuroscience for 2.71% and pharmacology for 2.38%. The citation impact for Australian clinical medicine publications was 1.12 times the world average between 2000 and 2004 (DEST, 2005).

For cancer research, Australia's share of total world research publications between 1999 and 2006 was somewhat lower than the 3.0% for clinical medicine publications stated in DEST (2005) and varied between 2.2% based on Science Citation Index / Social Science Citation Index (SCI-SSCI) and 1.5% based on Medline (Access Economics, 2008). Shares increased steadily from 2.0% in 1999 to 2.4% in 2006 based on SCI-SSCI and from 1.4% to 1.6% based on Medline.

The citation impact for research in immunology (1.07%) and pharmacology (1.03%) was around the world average, while the impact for psychiatry (0.90%) and neuroscience (0.86%) was below world average (DEST, 2005).

FIGURE 4-5: AUSTRALIAN PUBMED PUBLICATIONS AND HEALTH AND MEDICAL RESEARCH EXPENDITURE, 1980/81 TO 2003/04



Source: Mendis and McLean (2006).

Given that the majority of health R&D undertaken in Australia is clinical and that recent health R&D funding has increased in Australia (which is expected to translate into more outputs), the proportion of world R&D attributable to Australian R&D has been estimated at 3.04% in line with DEST (2005).

4.3 NET BENEFITS FROM AUSTRALIAN HEALTH R&D

There are several evaluation measures that can be used in the analysis of the value of Australian health R&D. The two most commonly used discounted measures of benefits derived from R&D are the net present value (NPV) and the return on investment (ROI). This study used both these measures along with the B/C ratio.

The NPV of R&D is also known as the discounted value of the net benefit stream. It is obtained by discounting the stream of net benefits produced by the R&D back to its value in the chosen base period, in this case 2008. The general NPV formula can be represented by:

$$\text{NPV} = \sum_{t=0}^{n} \frac{B_t - C_t}{(1+r)^t}$$

where:

B_t is the benefits from R&D in period t. In this study, benefits projected 20 years out from period t are used

C_t is the expenditure on R&D in period t

r is the economic discount rate, in this case 3%

n is the number of years the benefits from R&D are accrued. In this study, benefits beyond 2035 were not included.

Within this study, costs that were incurred before 2008 were increased to 2008 levels.

The ROI was calculated as the ratio of the discounted net benefits of Australian health R&D expenditure relative to the cost of Australian health R&D. It can be represented by:

$$\text{ROI} = \sum_{t=0}^{n} \frac{B_t - C_t}{C_t}$$

The B/C ratio was calculated as the ratio of the sum of the discounted benefits of Australian health R&D relative to the cost of Australian health R&D. It can be represented by:

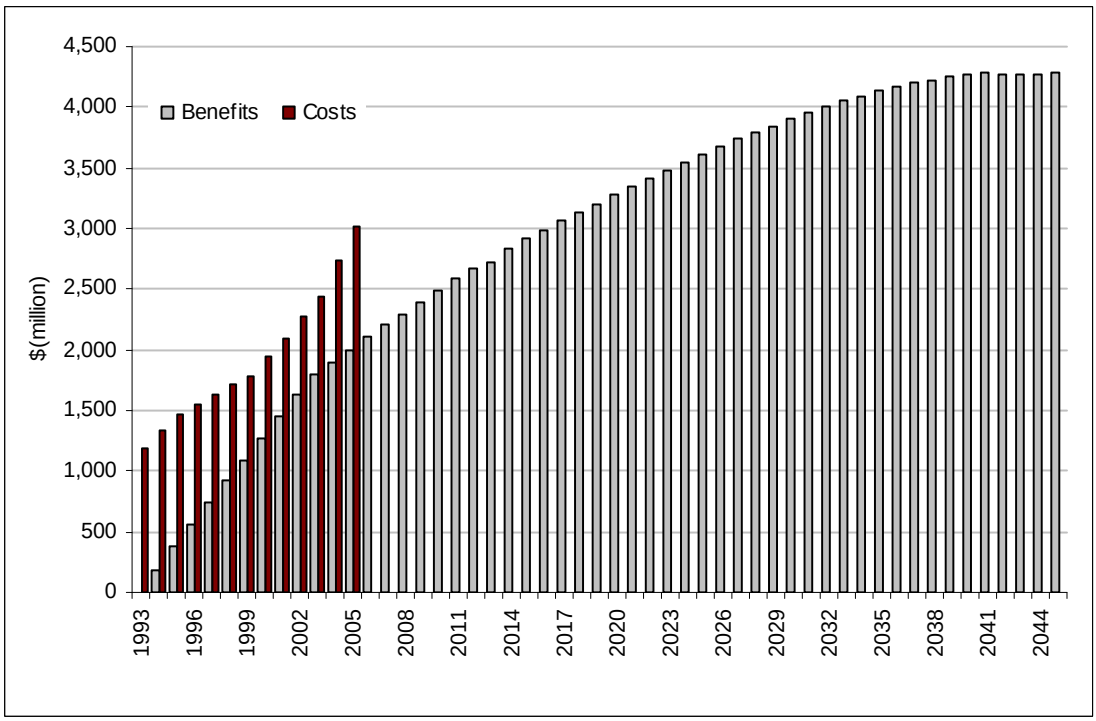
$$\text{Benefit/Cost ratio} = \sum_{t=0}^{n} \frac{B_t}{C_t}$$

Although the B/C ratio will provide the same decisions outcomes as the ROI, the major advantage of the B/C ratio is that it is readily understood by non-economists.

4.3.1 NET BENEFITS, ROI AND BENEFIT/COST RATIO

The annual benefit stream from gains in wellbeing and the cost stream associated with Australian health R&D are shown in Figure 4-6. It shows that expenditure has increased substantially since 1993, reaching just over $3.0 billion (in 2008 prices). Similarly, benefits have also been increasing since 1993 but at a decreasing rate. For example, annual benefits tend to flatten out at around 2040. Although gains in wellbeing are expected to continue beyond 2040, discounting the values from these gains tends to reduce the rate of increase.

FIGURE 4-6: BENEFIT AND COST STREAMS FROM AUSTRALIAN HEALTH R&D, 1993 TO 2045



Source: Access Economics.

The net benefits, ROI, and B/C ratio for Australian health R&D performed between 1992-93 and 2004-05 are shown in Table 4-1.

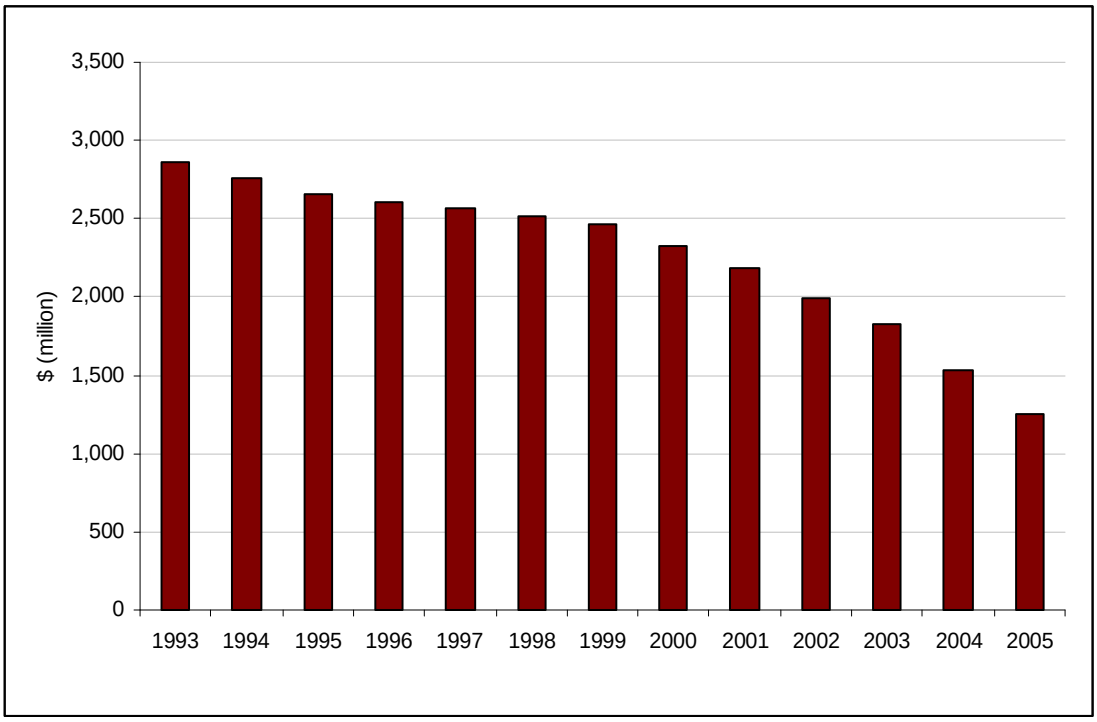
TABLE 4-1: NET BENEFITS, ROI, AND BENEFIT/COST RATIO FOR R&D EXPENDITURE FOR THE PERIOD 1992-93 TO 2004-05

Net benefit	$29,527,169,294
ROI	117.1%
Benefit/Cost ratio	2.17

Table 4-1 shows that Australian health R&D returned a net benefit of approximately $29.5 billion between 1992-93 and 2004-05, which gives an average net benefit of around $2.3 billion per year. The annual net benefits for each year are shown in Figure 4-7. The decrease in net benefits since 1993 is the result of increased real R&D expenditure over the period without similar growth in the expected wellbeing gains – that is, the marginal benefits from Australian health R&D are modelled as decreasing. However, this may be an artefact of the AIHW projections in DALY growth rates not capturing the true impact of recent R&D on the health of Australians. If this is the case, then the projections of annual net benefits are a conservative estimate. Regardless, net benefits are still significant.

The exceptional return on investment in Australian health R&D is also shown in the ROI and B/C ratio. The ROI is around 117%, which means that a dollar invested in Australian health R&D has returned an average net health benefit valued at $1.17. To put it another way, the B/C ratio is 2.17, which means that a dollar invested in Australian health R&D has returned $2.17 in health benefits.

FIGURE 4-7: NET BENEFITS FROM HEALTH R&D PERFORMED BETWEEN 1992-93 AND 2004-05



Source: Access Economics.

It is problematic to determine the net benefits of health R&D for individual causes. R&D expenditure data supplied by the ABS for Human pharmaceutical products, Public health, and Health and support services does not provide enough detail for an adequate cost allocation to causes from these subdivisions to occur. Consequently, to gauge the impact Australian R&D has had on the health of Australians for individual causes, the discounted benefits from Australian R&D conducted between 1992-93 and 2004-05 have been investigated. These are shown in Table 4-2.

TABLE 4-2: BENEFITS FROM AUSTRALIAN HEALTH R&D, BY CAUSE

Cause	$ million
Infectious and parasitic diseases	165.3
Acute respiratory infections, chronic respiratory disease	2,778.5
Maternal conditions, neonatal causes	662.2
Malignant neoplasms and other neoplasms	15,739.3
Diabetes mellitus, endocrine and metabolic disorders	-4,491.4
Mental disorders, nervous system and sense organ disorders	-1,369.3
Cardiovascular disease	35,927.0
Diseases of the digestive system	1,197.6
Genitourinary diseases	140.3
Skin diseases	20.6
Musculoskeletal diseases	-299.6
Congenital anomalies	588.4
Other	3,691.7
All causes	**54,750.5**

It is important to note that the benefits presented in Table 4-2 do not take into consideration the expenditure on R&D for each cause so the table does not provide any indication of which type of R&D (by cause) provides the most welfare gains to Australia. Indeed, those areas where there are large projected gains are also expected to have the largest costs.

Cardiovascular disease is expected to provide the greatest wellbeing gain to Australia, with a total benefit of around $35.9 billion. This is followed by R&D relating to malignant neoplasms and other neoplasms, which is expected to provide a benefit of around $15.7 billion. R&D into skin diseases is expected to provide the lowest positive benefits for a class, at around $20.6 million.

An interesting insight from Table 4-2 is that the benefits from R&D relating to three classes are negative: diabetes mellitus, endocrine and metabolic disorders; mental disorders, nervous system, and sense organ disorders; and musculoskeletal diseases. This does not mean that R&D undertaken between 1992-93 and 2004-05 was not effective. It indicates that current Australian R&D spending in these areas is not sufficient to outweigh the expected increase in these disorders and as such, the burden of disease will be greater in the future than in 1993. Even though these disorders and diseases do not have a large burden due to mortality, they do have a large burden due to morbidity, and it is expected that this burden will apply to a larger proportion of the Australian population in the future. This highlights the need to also direct health R&D to areas where morbidity is a dominant burden.

4.4 SENSITIVITY ANALYSIS ON THE VALUE OF HEALTH GAINS FROM AUSTRALIAN HEALTH R&D

The results reported in Section 4.3 are estimates of the net benefits, ROI and B/C ratios generated from health R&D in Australia over the period 1992-93 to 2004-05. As they are point estimates based on uncertain inputs into the model, the accuracy of the estimates cannot be determined from these results alone. In order to incorporate the uncertainty of inputs into the model, and thus ascertain the accuracy of the estimates, a sensitivity analysis was undertaken.

A sensitivity analysis investigates how the net benefits, ROI and B/C ratio change with different assumptions regarding inputs used within the model. This provides an indication of

how confident we are in the results presented in Section 4.3. The inputs that were investigated included:

- the VSLY;
- the delay in benefits from R&D;
- the proportion of Australia health gains attributed to world R&D; and
- the proportion of world R&D gains attributed to Australian R&D.

For each of the inputs, a probability distribution was placed around the mean. The probability distributions account for uncertainty by describing the probability of the input taking on a certain value. For example, the VSLY estimate used within the model was $266,843, which represents the most likely value. As this is only an estimate, the true value may be some other number, either higher or lower than the estimate used in the model. The probability distribution attaches a probability to these other numbers.

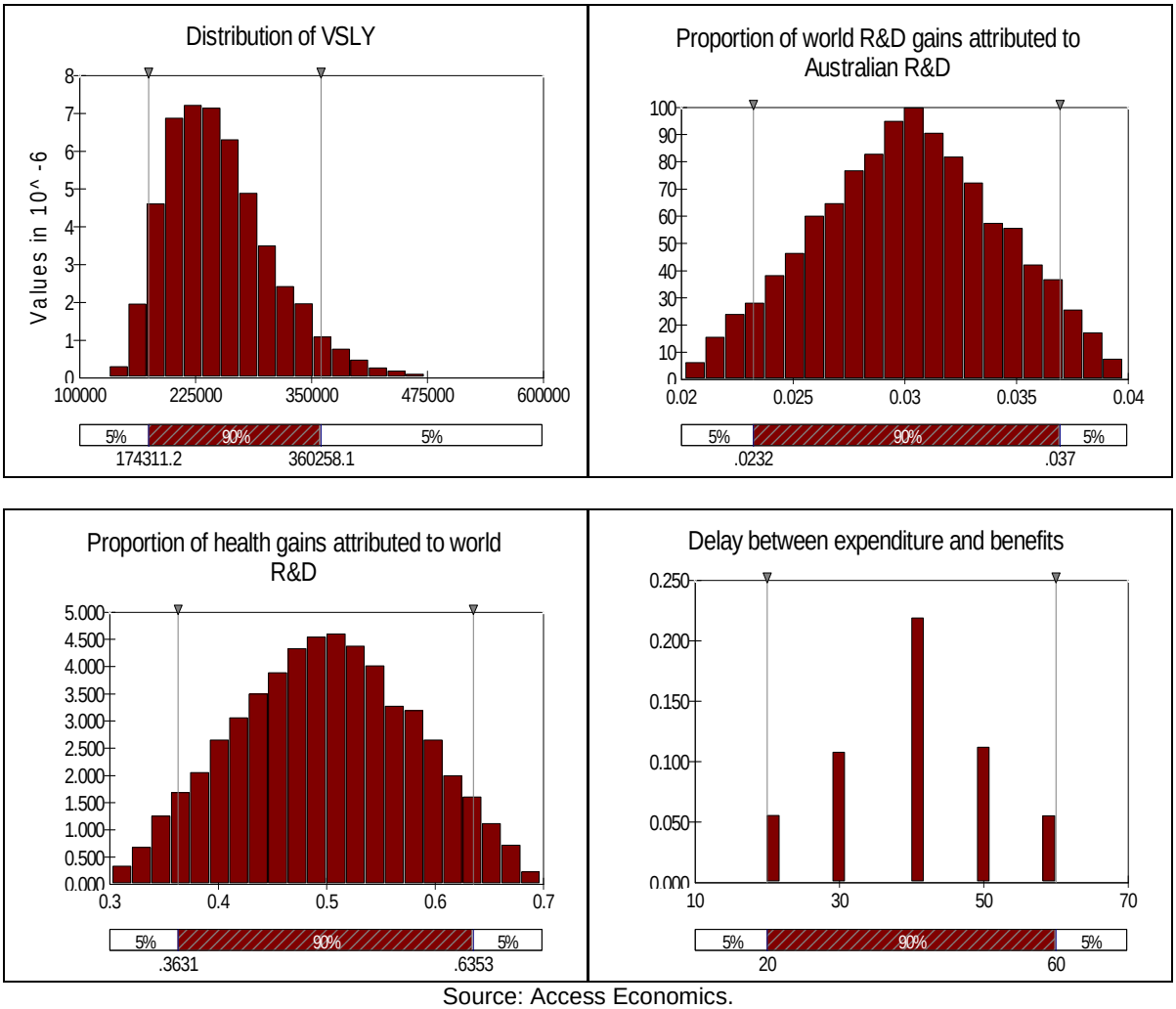
The probability distributions used within the sensitivity analysis were constructed based on the most likely lower and upper bounds for each of the inputs and the most likely type of probability distribution for that input. For VSLY, a gamma distribution was used to account for the asymmetry of the probability distribution of VSLY estimates[8]. For the delay in benefits from R&D, a discrete distribution was used, while for the remaining inputs a triangular distribution was used. The distributions for each input are shown in Figure 4-8.

The sensitivity analysis was undertaken using a Monte Carlo simulation[9]. The simulation simultaneously drew a random number for each input from their distribution and recalculated the ROI and B/C ratio. This process was done 10,000 times to provide 10,000 different estimates. From these estimates, worst case and best case scenarios were developed, along with the most likely scenario.

[8] Although the lower and upper bounds prescribed by Access Economics (2008) for the VSLY were $164,553 and $360,238, the sensitivity analysis has used a Gamma distribution skewed to the right. The lower and upper bounds from Access Economics (2008) were therefore used to establish a 90% confidence interval, although the combination of the scale and shape parameters did not allow for an exact match.

[9] Monte Carlo simulation is a well known technique used to determine the sensitivity of model outputs from key model inputs. It iteratively replaces numbers attached to key parameters (inputs) with random numbers drawn from a specified distribution, where the type of distribution, the upper and lower bounds on the distribution, and the number of iterations are chosen by the analyst. The Monte Carlo simulation provides a distribution around chosen outputs (such as the return on investment) from which sensitivity of outputs to inputs can be determined. The program used to undertake the Monte Carlo simulation was @Risk.

FIGURE 4-8: DISTRIBUTION OF INPUT PARAMETERS IN THE SENSITIVITY ANALYSIS



Source: Access Economics.

4.4.1 RESULTS OF THE SENSITIVITY ANALYSIS

The results from the simulation are presented in Table 4-3 and their distributions are shown in Figure 4-9. The table shows the minimum, most likely, and maximum ROI and B/C ratio generated from the simulation. It also shows the 90% confidence intervals for each estimate, which is represented by the last two columns. The charts show the shape of the distributions around the simulation mean, between the lower and upper bounds.

TABLE 4-3: RESULTS OF THE SENSITIVITY ANALYSIS

Output	min	mean	max	5%	95%
Net benefits ($m)	-10,776.4	29,527.2	126,344.8	3,930.0	59,117.5
ROI (%)	-42.72	117.1	500.91	15.58	234.38
Benefit/Cost ratio	0.57	2.17	6.01	1.16	3.34

FIGURE 4-9: DISTRIBUTION OF NET BENEFIT, BENEFIT/COST RATIO, AND ROI FROM SENSITIVITY ANALYSIS

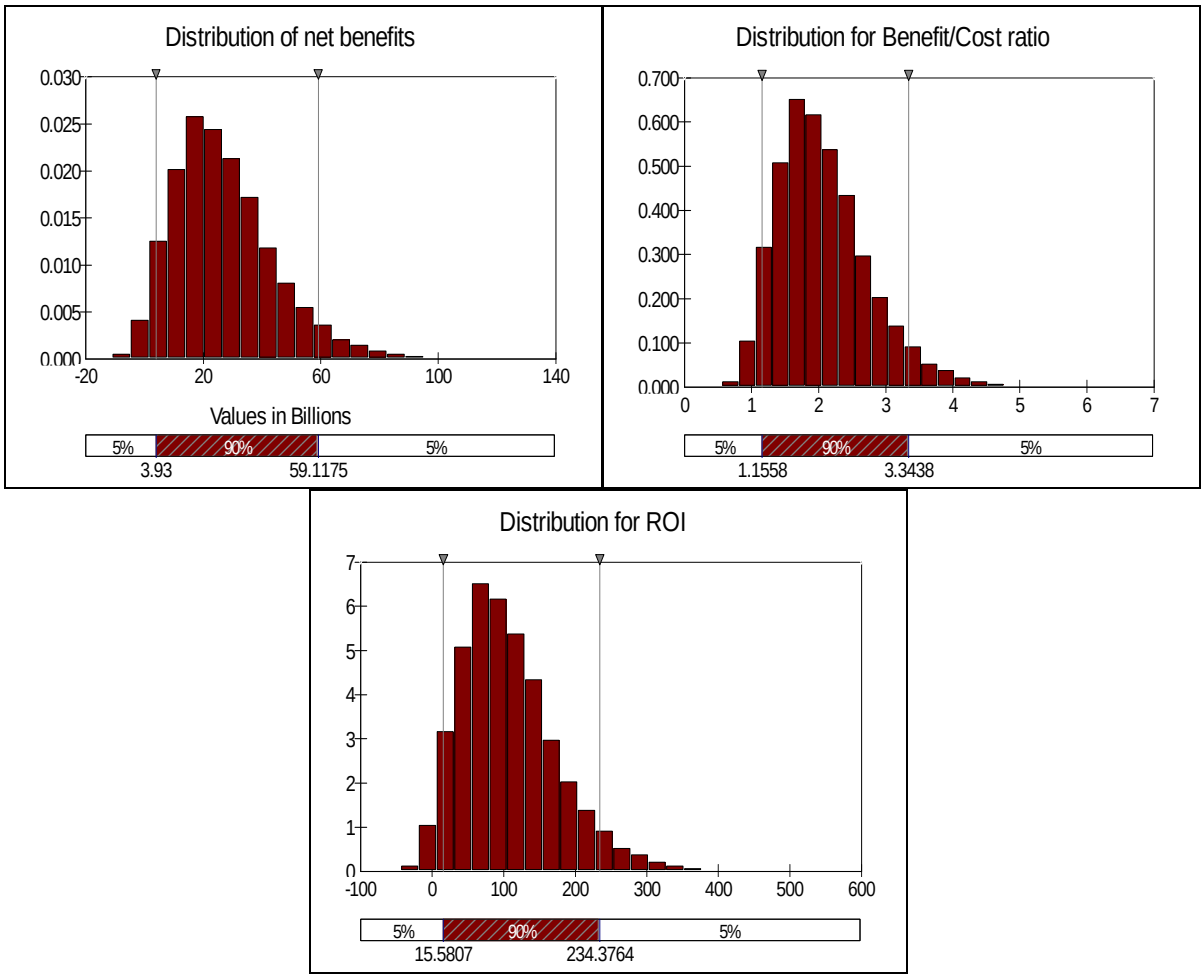


Table 4-3 shows that given the uncertainty around each input, the benefits from R&D under the best case scenario would be:

- Net benefits of $126.3 billion;
- a ROI of 501%; and
- a B/C ratio of 6.01.

Table 4-3 shows that given the uncertainty around each input, the benefits from R&D under the worst case scenario would be:

- Net loss of -$10.8 billion;
- a ROI of -42%; and
- a B/C ratio of 0.57.

The probability of actually realising the best and worst case scenarios is extremely small and should therefore be viewed with caution. Instead it is best to look at the confidence intervals to determine where the true estimates are likely to lie.

The confidence intervals reveal the probability that the real net benefits, ROI and B/C ratio lie between their confidence interval bounds. For example, Table 4-3 shows that even though there is large uncertainty surrounding the inputs, there is a 90% chance that the interval for

the net benefits from Australian R&D ($3.9 billion, $59.1 billion) contains the true net benefits from Australian R&D. Similarly there is a 90% chance that the interval for:

- the ROI from Australian R&D (15.6%, 234.4%) contains the true ROI; and
- the B/C ratio for Australian R&D (1.16, 3.34) contains the true B/C ratio.

The simulation results presented in Table 4-3 are the product of each input changing simultaneously within the simulation. However, changes in inputs do have the same effect on the results due to the alternative distributions placed around the inputs. For example, changing the VSLY by 10% will have a different impact on the results compared to changing some other input by 10%.

To determine which inputs are driving the simulation results, the sensitivity of the results to each input was determined using a rank order correlation. This measures the strength of the relationship between the benefits from R&D and the inputs under investigation. It provides an indication of the change in the benefits from a change in an input while holding all other inputs constant.

FIGURE 4-10: SENSITIVITY OF RESULTS TO KEY INPUTS

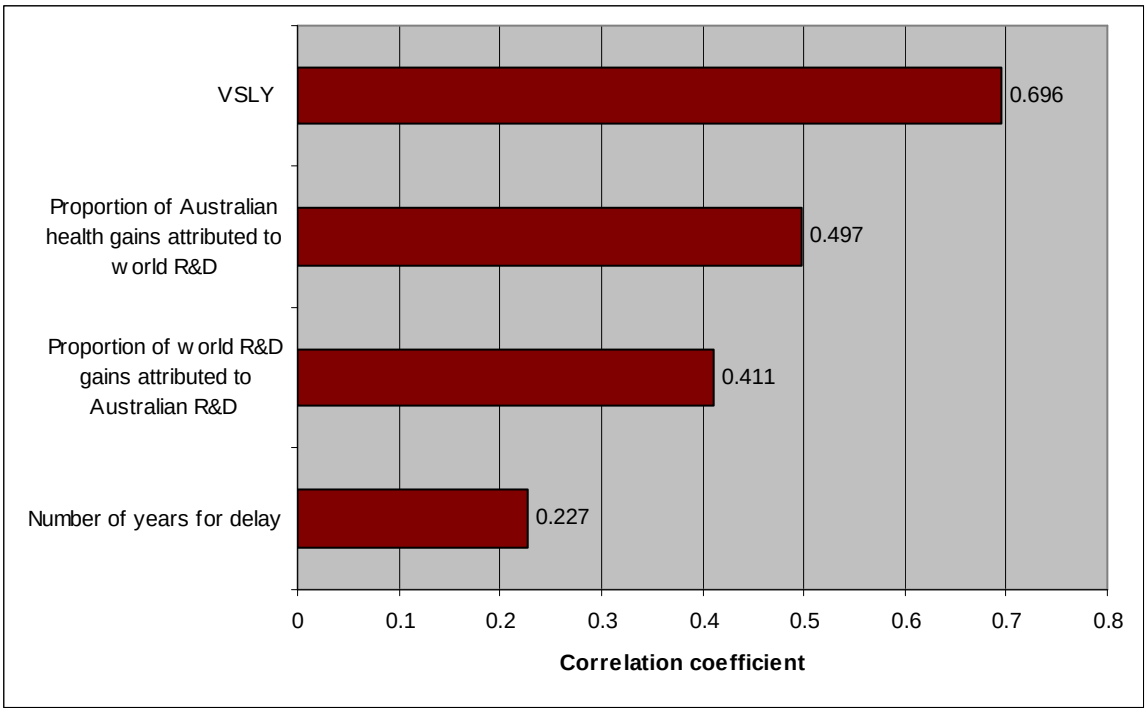


Figure 4-10 shows the correlation of the simulation results to each input for Australian R&D, given the ranges adopted in the sensitivity analysis. The higher the correlation, the greater the impact of changes in the input on benefits. Estimates are most sensitive to the VSLY, followed by the proportion of Australian health gains attributed to world R&D. Changes in the proportion of world R&D gains attributed to Australian R&D had the third highest impact, while the number of years for delay between expenditure and benefits had the lowest impact on results.

4.5 OTHER IMPACTS FROM AUSTRALIAN HEALTH R&D THAT HAVE NOT BEEN QUANTIFIED

In addition to gains in wellbeing, there are many other potential benefits to the economy that could be generated from Australian health R&D. These can be broadly grouped into the following two categories.

- Direct benefits – derived from a reduction in resources used in diagnosis, treatment, care, and rehabilitation of individuals due to less demand for health care services. An example includes a reduction in hospitalisation required as a result of improved wellbeing. The savings in resources can be released into the economy for other welfare improving purposes.
- Indirect benefits - all other avoided costs such as enhanced productivity outcomes, reduced burden on informal carers, lower payments for health aids and home modifications, reduced emotional and psychological impacts on family and friends, taxation revenue and welfare payment savings, commercialisation spinoffs, and other significant benefits.

Measuring direct benefits is a complex task. Allocating health system costs to a specific disease is complicated by the relative lack of recent data available on the contribution of a specific disease to health system costs, the existence of comorbidities (eg, determining whether comorbidities are independent or interdependent when it comes to cost in the health care system) and the reality that curing one disease (eg, cancer) may mean that the person may live to contract another disease later on in life (eg, dementia). Measuring indirect costs is even more difficult, primarily due to the lack of comprehensive, comparable data available on indirect impacts of disease and injury in Australia. Although the direct and indirect benefits may be realised for some causes (eg, Access Economics has measured the direct and indirect costs of many but not all diseases), they have not been quantified in this report.

There will also be some costs from Australian health R&D that are in addition to R&D expenditure. These costs are typically flow-on effects into the economy such the cost of adopting and implementing new discoveries and demand and supply side impacts on prices. For example, the use of labour to undertake health R&D means there will be less resources in the health care system, which has implications for the supply of labour and consequently the price of labour.

Furthermore there will be an opportunity cost associated with health R&D. The opportunity cost is the loss in welfare from the next best alternative use of resources that would have been undertaken given resources were not used to undertake health R&D. An opportunity cost arises because there are many demands that compete for government and private budgets. Using resources for health R&D means these resources cannot be used elsewhere in the economy.

It is unclear whether quantifying these benefits and costs in the analysis would under estimate or over estimate the net benefits from Australian health R&D presented in this study. For example, although Australia has experienced an increase in wellbeing, this has come at an increased per capita cost to the health care system.

Regardless of whether there is a net benefit or cost from the non-quantified impacts, the number is likely to be very small relative to the benefits generated from improvements in wellbeing. Consequently the decision rule gained from the economic evaluation measures in this study is likely to be the same.

5. BENCHMARKING ANALYSIS

5.1 RECENT INCREASES IN PUBLICLY FUNDED HEALTH R&D

To focus on the future role of health and medical research up to the year 2010, a Health and Medical Research Strategic Review was commissioned in March 1998 by the then Minister for Health, Dr Michael Wooldridge. The Review was conducted by an eminent committee under the chairmanship of Mr Peter J Wills (AM). The report of the committee, entitled '*The Virtuous Cycle: Working together for health and medical research*' provided some key findings and recommendations for policy action in Australia, many of which have been implemented (Wills, 1998).

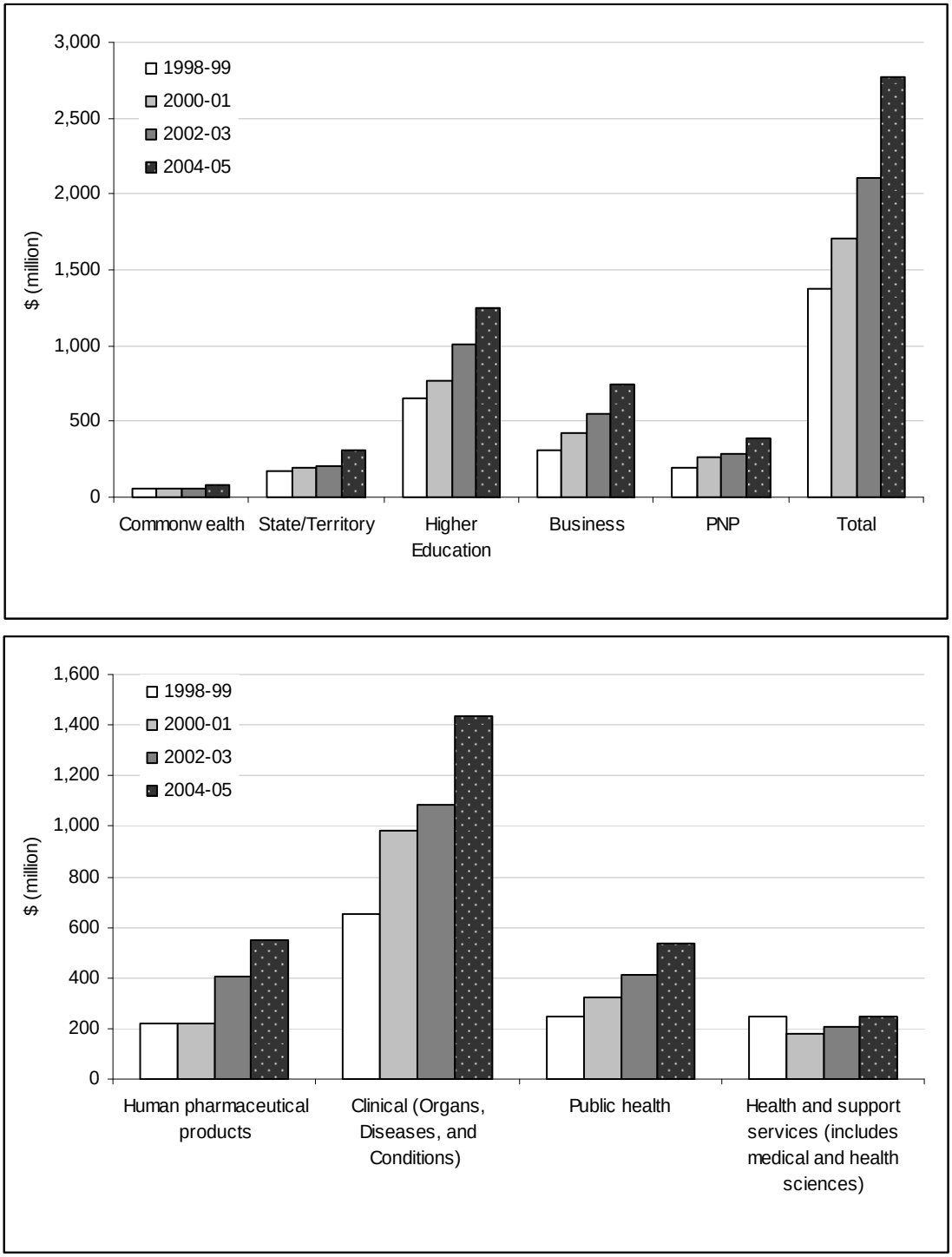
The final report contained 120 strategic recommendations for improving Australia's health and medical research workforce. Those recommendations, and the arguments in support of them, formed a compelling blueprint for change including the immediate injection of an additional $614 million for health and medical research by the Federal Government. This cash injection doubled the Commonwealth's contribution to health and medical research channelled through the National Health and Medical Research Council.

One of the most significant key findings of the 'Wills review' was that the outlook for health and medical research lies not only in greater government investment, but also in establishing the links between public funding, research and the commercialisation of findings through industry. The Government's Implementation Committee Report focused on the strategic issues required to build the collaborations and partnerships needed to engage the States and industry in a coordinated, whole of government approach to health and medical research.

Since the Wills review, expenditure on health R&D has increased significantly, from around $1.7 billion to $2.8 billion and averaged a growth rate of around 12% per year. Figure 5-1 shows health R&D undertaken since the Wills report, by sector and by subdivision. The increase in health R&D has been across all sectors, although the business sector has experienced the highest growth rate at around 17% per annum on average. PNP, Higher education, and State/Territory health R&D has grown at similar rates of 14%, 12% and 12% respectively, while health R&D undertaken by government has grown the least at around 8% per annum. The majority of this growth was in 2004-05.

Figure 5-1 also shows that the Wills report primarily led to increases in R&D performed across all areas other than Human pharmaceutical products. Health and support services experienced a 76% increase in R&D undertaken between 1998-99 and 2000-01, whereas Clinical experienced a 50% increase and Public health experienced a 31% for the same period. Since then, there has been a steady increase in R&D performed across all subdivisions.

FIGURE 5-1: HEALTH R&D (SEO) UNDERTAKEN SINCE THE WILLS REPORT, BY SECTOR AND SUBDIVISION



Source: Access Economics, based on ABS data.

5.2 INTERNATIONAL COMPARISONS OF EXPENDITURE ON HEALTH R&D

There is not currently a consistent and comparable set of figures that allows a robust international comparison of country specific expenditures on health R&D. The closest available are those collected by the OECD. OECD (2001) discusses many of the issues in collecting this type of information and highlights some of the inconsistencies that exist in the

country-specific data, notably due to differences between health systems and data collection processes between countries. It also provides a framework for the collection and classification of expenditures on health R&D and, to this end, attempts to overcome some of the data inconsistencies for ten participating countries, including Australia.[10] Thus, while good comparative data are still elusive, the data provided by each country can be assessed individually taking into consideration some of these limitations. For more detail see Access Economics (2003), which also discusses other data sources such as the Wills report (Wills, 1998).

The OECD health database for 2007 (OECD, 2007) provides the latest health data for 30 countries. For R&D expenditure, three categories of information within the database are relevant:

- expenditure on pharmaceutical industry R&D (pharmaceutical industry activity);
- public expenditures on health R&D (expenditure on health-related functions); and
- total expenditures on health R&D (expenditure on health-related functions).

Total non-pharmaceutical expenditure on health-related R&D category is somewhat of a catch-all, generally including all residual items that are non-Federal and non-pharmaceutical. Country results for each of these categories are presented in Table 5-1, Table 5-2, and Table 5-3, noting that the grand total cannot strictly be summed due to different collection years and content anomalies.

TABLE 5-1: HEALTH-RELATED R&D EXPENDITURE (IN US$ MILLION), OECD 12-COUNTRY SECTORAL COMPARISON

	Pharmaceutical expenditure on R&D		Public expenditure on R&D		Total non-pharmaceutical expenditure on R&D		Grand total	
Country	**Year**	**US$M**	**Year**	**US$M**	**Year**	**US$M**	**Year**	**US$M**
Korea	n.a.	n.a.	2005	$767	2005	$767	n.a.	n.a.
Switzerland	n.a.	n.a.	1999	$441	2000	$1,220	n.a.	n.a.
New Zealand	1996	$13	2005	$113	2005	$127	comb	$253
Japan	1998	$3,940	1999	$665	1997	$5,347	comb	$9,952
Czech Republic	2003	$598	2005	$15	2005	$63	comb	$676
Australia	**2004**	**$197**	**2004**	**$1,023**	**2004**	**$1,282**	**2004**	**$2,502**
Germany	2004	$3,634	2005	$3,094	2005	$3,094	comb	$9,822
France	2003	$2,993	2005	$1,007	2005	$3,696	comb	$7,696
Canada	2003	$1,088	2005	$2,491	2005	$2,376	comb	$5,955
US	2003	$15,962	2000	$22,459	2000	$25,388	comb	$63,810
UK	2004	$5,243	1999	$1,533	1997	$5,639	comb	$12,415
Denmark	2004	$721	1999	$260	1999	$779	comb	$1,760

Source: OECD (2007).

[10] The other nine countries were Austria, Canada, Denmark, France, Israel, Norway, Spain, the United Kingdom and the United States.

TABLE 5-2: HEALTH-RELATED R&D EXPENDITURE (IN US$ PER CAPITA), OECD 12-COUNTRY SECTORAL COMPARISON

	Pharmaceutical expenditure on R&D		Public expenditure on R&D		Total non-pharmaceutical expenditure on R&D		Grand total	
Country	**Year**	**US$ pc**	**Year**	**US$ pc**	**Year**	**US$ pc**	**Year**	**US$pc**
Korea	n.a.	n.a.	2005	$15.88	2005	$15.88	n.a.	n.a.
Switzerland	n.a.	n.a.	1999	$61.73	2000	$169.82	n.a.	n.a.
New Zealand	1996	$3.57	2005	$27.57	2005	$30.98	comb	$62.12
Japan	1998	$31.15	1999	$5.25	1997	$42.38	comb	$78.78
Czech Republic	2003	$58.62	2005	$1.47	2005	$6.16	comb	$66.25
Australia	**2004**	**$9.80**	**2004**	**$50.92**	**2004**	**$63.81**	**2004**	**$124.53**
Germany	2004	$44.05	2005	$37.52	2005	$37.52	comb	$119.09
France	2003	$49.75	2005	$16.54	2005	$60.72	comb	$127.01
Canada	2003	$34.36	2005	$77.19	2005	$73.63	comb	$185.17
US	2003	$54.88	2000	$79.59	2000	$89.97	comb	$224.44
UK	2004	$87.63	1999	$26.12	1997	$96.70	comb	$210.45
Denmark	2004	$133.49	1999	$48.80	1999	$146.41	comb	$328.70

Source: OECD (2007).

TABLE 5-3: HEALTH-RELATED R&D EXPENDITURE (AS % OF GDP), OECD 12-COUNTRY

	Pharmaceutical expenditure on R&D		Public expenditure on R&D		Total non-pharmaceutical expenditure on R&D		Grand total	
Country	**Year**	**% GDP**	**Year**	**% GDP**	**Year**	**% GDP**	**Year**	**% GDP**
Korea	n.a.	n.a.	2005	0.072%	2005	0.072%	n.a	n.a.
Switzerland	n.a.	n.a.	1999	0.214%	2000	0.557%	n.a	n.a.
New Zealand	1996	0.020%	2005	0.106%	2005	0.119%	comb	0.245%
Japan	1998	0.130%	1999	0.022%	1997	0.175%	comb	0.327%
Czech Republic	2003	0.322%	2005	0.007%	2005	0.030%	comb	0.359%
Australia	**2004**	**0.030%**	**2004**	**0.155%**	**2004**	**0.194%**	**2004**	**0.379%**
Germany	2004	0.147%	2005	0.122%	2005	0.122%	comb	0.391%
France	2003	0.174%	2005	0.053%	2005	0.194%	comb	0.421%
Canada	2003	0.112%	2005	0.209%	2005	0.194%	comb	0.515%
US	2003	0.146%	2000	0.230%	2000	0.260%	comb	0.636%
UK	2004	0.276%	1999	0.110%	1997	0.433%	comb	0.819%
Denmark	2004	0.415%	1999	0.180%	1999	0.540%	comb	1.135%

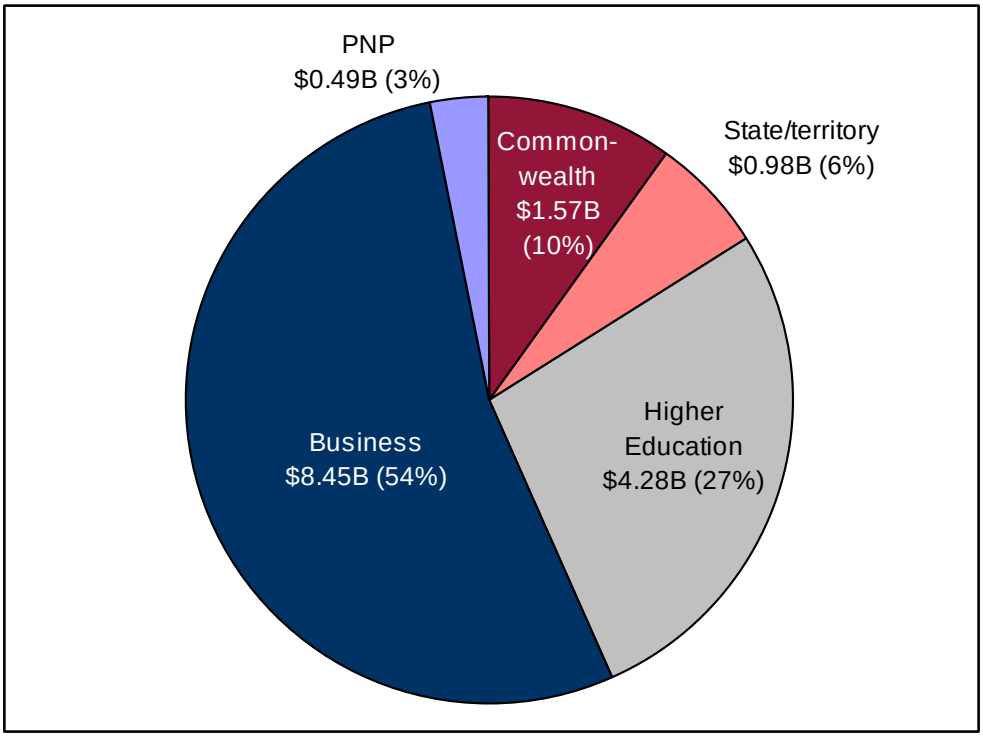
Source: OECD (2007).

The OECD data for Australia is slightly higher than our estimates. Based on ABS data and depending on classification and whether commercial R&D expenditure is included, Australian health R&D expenditure was between 0.2% and 0.3% of GDP in 2004-05. Based on OECD data, health R&D expenditure is 0.38% of GDP. Comparing different OECD countries shows that Denmark and the UK are leaders in terms of health R&D expenditure, the US, Canada and France rank in the middle, while Australia ranks between Germany and the Czech Republic. However, there is need for caution due to inconsistencies in the data. For example, in Australia around 25% of the manufacturing of pharmaceutical products is performed outside the pharmaceutical industry (OECD, 2001). Furthermore, more than 20% of the R&D performed by the pharmaceutical industry in Australia is not for health reasons (OECD, 2001).

5.3 EXPENDITURE ON HEALTH R&D COMPARED TO OTHER SECTORS OF THE AUSTRALIAN ECONOMY

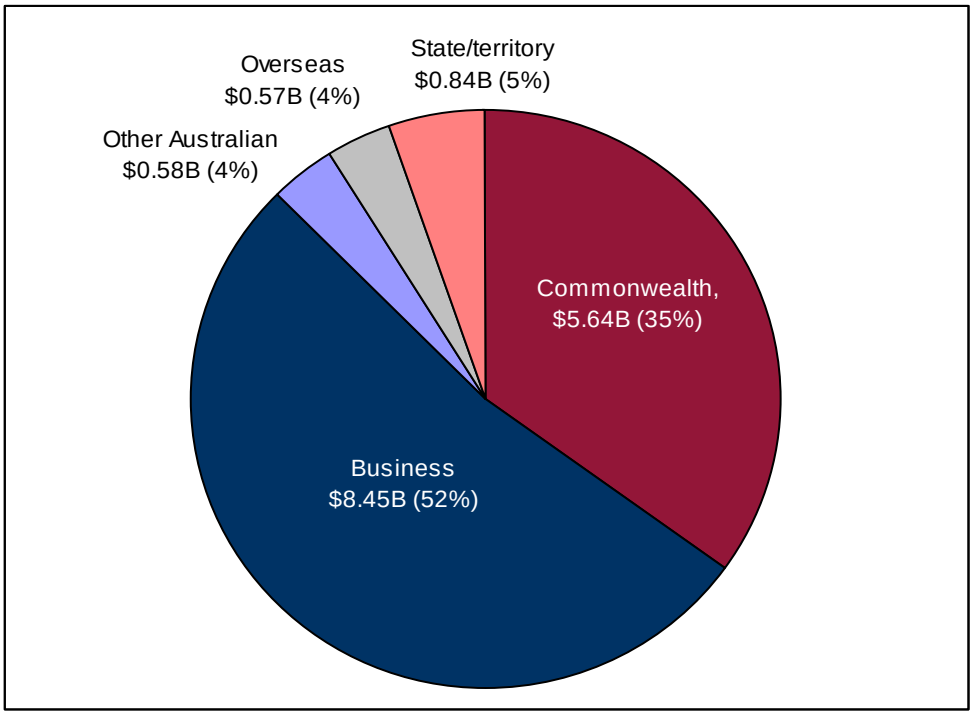
In 2004-05, GERD was $15.8 billion, an increase of 19.4% over 2002-03 ($13.2 billion). At 1.8% of GDP, Australia's GERD/GDP ratio remained below the OECD average of 2.3%. The major sectors for overall R&D in 2004-05 were business (54%), higher education (27%) and the Commonwealth government (10%) (Figure 5-2). The major sources of funds were business (52%) and the Commonwealth government (35%) (Figure 5-3).

FIGURE 5-2: R&D EXPENDITURE BY SECTOR UNDERTAKING R&D, 2004-05



Source: ABS (2006a). Note: B=billion.

FIGURE 5-3: R&D EXPENDITURE BY SOURCE OF FUNDS, 2004-05

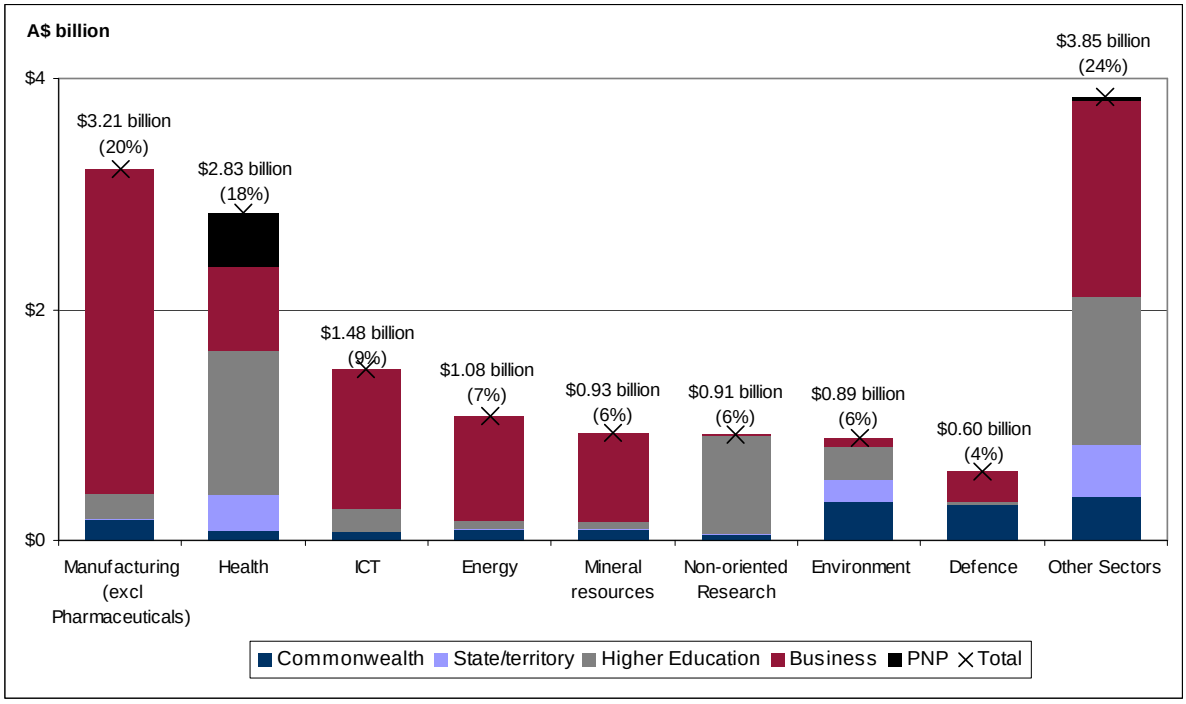


Source: ABS (2006a). Note: B=billion.

Figure 5-4 illustrates R&D expenditure by sector. Manufacturing ($3.2 billion) dominated the field, while health ($2.8 billion) was second and Information and Communications Technology (ICT) third ($1.5 billion).

According to Thomson Scientific's index (cited in Invest Australia, 2006[11]), engineering and ICT also feature highly in international citations: Australian ICT has been cited above the worldwide average for each field of ICT research (eg, physics citations accounted for 6.8% of Australian publications and 1.07 times the world average for physics, while engineering publications account for 6.6% of Australian publications and 1.07 times the world average for engineering). However, Australia's impact in health research has been even larger: clinical medicine, for instance, accounts for 26% of Australian scientific publications and is cited at 1.12 times the world average.

FIGURE 5-4: AUSTRALIAN R&D EXPENDITURE BY SECTOR (BY SEO), 2004-05



Source: ABS (2006a).

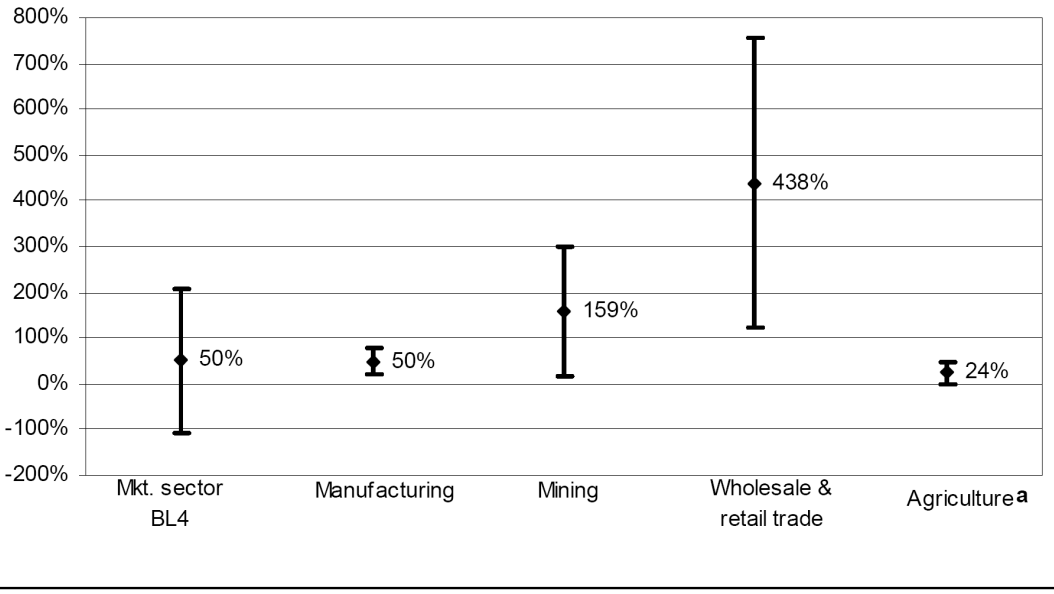
Returns on research investments are generally difficult to establish due to a number of measurement and methodological issues. Hence, studies generally provide broad estimates rather than specifics when it comes to returns on research investments. Nevertheless, benefits from research spending are often shown to exceed costs in broad industry terms.

Dowrick's (2003) international literature survey on returns to R&D (2003) found that based on microeconomic studies, gross returns to firms' own investment in R&D is typically in the range of 20% to 30% (though rising to up to 40% when including industry-wide spillovers). Macroeconomic studies show that economy-wide returns range from 50% to 100%, indicating that returns provided to society (those returns that are not captured by the organisation undertaking the R&D, such as spillover effects) are significantly greater than private returns.

Shanks and Zheng (2006) estimate the gross returns to Australian business R&D undertaken between 1974-75 and 2002-03 to be in the order of 50% at the general industry level (see Figure 5-5). In the case of manufacturing, the estimated return is 50%, while the estimated return for R&D in agriculture is only 25%. For mining and wholesale and retail trade, the model indicated exceptionally high returns of 159% and 438% respectively.

[11] The citation referred to the previous branding of Thomson ISI (Institute of Scientific Information).

FIGURE 5-5: INDUSTRY-SPECIFIC RATES OF RETURN TO R&D



a The return for Agriculture is the return to public R&D.

Note: Point estimate and confidence interval based on plus or minus two standard errors. Mkt. sector BL4 refers to the market sector using the BL4 model as defined by Shanks and Zheng (2006).

Source: Shanks and Zheng (2006).

In 2007, the Productivity Commission (2007) released a review into the economic, social and environmental returns on public support for science and innovation in Australia, concluding that there are widespread and important benefits to Australia from its public support for science and innovation. Case studies within the review showed that B/C ratios for non-agricultural cost-benefit studies ranged between 0.1 to 1 and 76.5 to 1, with a mean of 13.3 to 1 and a median of 2.3 to 1. Panel data evidence that encompassed R&D across Australian jurisdictions suggests Australia-wide average gross rate of return is about 165% to 185% for business R&D (with significant variation between jurisdictions). The Australian rate of return for GERD was estimated to be 140% to 240% (depending on model specification). Note that these rates are comparable to the health R&D B/C estimated in this report of 2.17 (or a gross return of 217%).

Comparing the results presented in Shanks and Zheng (2006) and the Productivity Commission (2007) review with results presented in this report show that the B/C ratio and the ROI for health R&D are similar. For example, the B/C ratio and the ROI has been calculated at 2.17 and 117% respectively within this study, which is larger than results presented for the market sector, manufacturing and agriculture in Figure 5-5. However it is lower than mining and wholesale and retail trade, although higher than the average gross rate of return presented within the Productivity Commission review.

However, caution must be taken when comparing estimates. This is because there is a wide variation in methodologies and assumptions associated with the evaluation of R&D projects across industries and jurisdictions within Shanks and Zheng (2006) and the Productivity Commission (2007) report. Furthermore, comparing average returns should also consider the underlying risks associated with any particular R&D project, so the average cannot be considered in isolation to the broad range of potential returns.

6. CASE STUDIES

While the preceding analysis is based on modelled outcomes from overall wellbeing gains, the purpose of this final chapter is to provide some 'real world' case study examples of the value of health R&D in Australia, specifically in cancer, diabetes, dementia and indigenous health. This is achieved by reviewing evidence where specific R&D activities have led to (or could possibly lead to) mortality reductions and enhancements in quality of life.

In many cases, Australian researchers have collaborated with other researchers internationally, particularly for multi-site trials where one of the sites was Australian. For example, the Herceptin Adjuvant (HERA) trial included 127 Australian women as well as over 5,000 other women from around the world. Collaborative multi-site research is particularly important in the health sector to determine whether there may be environmental, ethnic or cultural impacts on efficacy of the trialled interventions.

There are many other examples of research that is predominantly home grown. For example, an important Australian R&D project in the cardiovascular area relates to injections of granulocyte-colony stimulating factor, which is about to enter Phase II trial testing – a join initiative of the Victor Chang Cardiac Research Institute and St Vincent's Hospital involving 40 patients with refractory angina. Granulocyte-colony stimulating factor is currently used by haematologists to treat people with malignancies such as leukaemia to try to stimulate their bone marrow to produce more cells. However, there appear to be unexpected beneficial impacts on heart cells and this is being investigated in the Sydney trials.

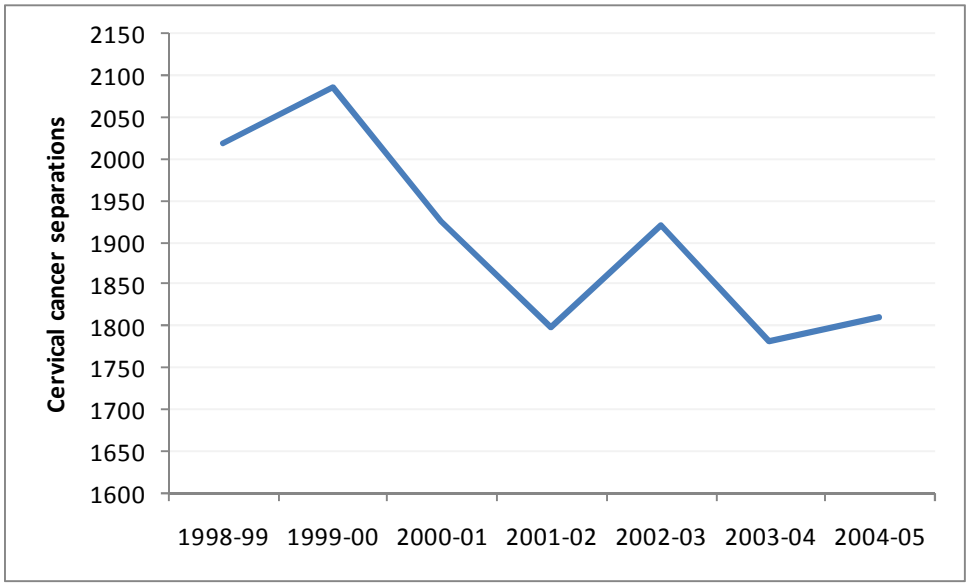
Another local example is the Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) study, where researchers have found that patients who have suffered a heart attack or unstable angina can live longer by taking a cholesterol lowering drug - pravastatin. The LIPID study is the largest of its kind in the world, involving 9,000 men and women from 87 hospitals around Australia and New Zealand. Those treated with pravastatin had a 23% reduced mortality rate, 29% fewer heart attacks, 20% less stroke, and 24% less need for heart surgery and angioplasty. The LIPID study was conducted by an independent group of researchers and coordinated by the National Health and Medical Research Council's Clinical Trial Centre at the University of Sydney. The study was conducted under the auspices of the National Heart Foundation of Australia and funded by a grant from the manufacturers of the drug pravastatin, Bristol-Myers Squibb.

6.1 VIRUS-BASED VACCINES AND GARDASIL

Gardasil is a vaccine against certain types of human papillomavirus (HPV) which is founded on research breakthroughs initiating from Australia. Specifically, Gardasil protects against HPV types 6, 11, 16 and 18, which cause around 70% of cervical cancer, essentially by causing self-replicating mutations in the cells lining the cervix. Gardasil is provided free of charge by the Commonwealth Government for 12 and 13 year old girls under the National Immunisation Program[12]. Despite an increasing and ageing population, cervical cancer incidence numbers are already falling due to an effective cervical screening program (Figure 6-1) and now there is a vaccine too.

[12] The Program also provides Gardasil free of charge to females aged between 13 and 26 years for a two year 'catch-up' period. In June 2008, there are around 139,000 girls turning 13 according to the Access Economics Demographic Model based on ABS 2006 Census data.

FIGURE 6-1: ANNUAL CERVICAL CANCER SEPARATIONS, AUSTRALIA 1998-99 TO 2004-05



Source: AIHW Online Hospital Morbidity Database (aihw.gov.au)

In 2003, there were 298 deaths from cervical cancer in Australia – 1.8% of total female cancer fatalities (Begg et al, 2007).

6.1.1 THE BENEFITS OF VIRUS-BASED VACCINE BASIC RESEARCH

The key breakthrough in developing a vaccine for HPV – or potentially any virus – came from research at the University of Queensland by Professor Ian Frazer (2006 Australian of the Year) and his fellow researcher, the late Dr Jian Zhou. They realised that if they could manufacture a non-infectious synthetic virus with the same outside shell as a real virus, this virus-like particle (VLP) could trigger the human immune system into developing antibodies that would be effective against a real virus.

The National Health and Medical Research Council provided funding for Professor Frazer's early work in this area and continued support over two decades. Commonwealth Serum Laboratories (CSL) Australia and other institutions, including the US National Cancer Institute, also provided funding for Professor Frazer's work, in conjunction with the discovery of HPV as a potential vaccine target. CSL patented the vaccine in 1991 and in 1995, Merck acquired exclusive rights to the technology and began a vaccine development program. By 1997, vaccine preparations suitable for clinical trial were available and Phases I and II clinical trials were commenced globally, first establishing the safety, biochemical and physiological effects of the vaccine on health volunteers and then focussing on efficacy and dosing regimens with small patient groups. Merck Sharp & Dohme Australia managed the Australian phase III clinical trial sites in Melbourne, Sydney and Perth. By 2006, the US Food and Drug Administration and Australia's Therapeutic Goods Administration approved Gardasil®, followed by 60 other countries.[13]

Gardasil is a valuable commercial success for CSL. In 2007, when Gardasil was introduced, CSL's earnings reportedly increased by 36%; of this $257 million increase, $81 million came from Gardasil international royalties, and $143 million from Australian sales.[14]

[13] http://www.investaustralia.gov.au/media/FinalBiotechIndustryReportMay12007.pdf

[14] http://www.news.com.au/heraldsun/story/0,21985,23245243-664,00.html

6.1.2 CONTRIBUTION OF VLP VACCINE R&D

This ballpark analysis treats the knowledge of how to develop VLP vaccines as a public good and the production of Gardasil as a private good. As the former was necessary but not sufficient for the latter, R&D into VLP vaccines and the public Gardasil vaccination program each are accorded 50% of the benefits, in line with our modelling in Section 4.2.1.

Gardasil reportedly cost $1.3 billion to develop.[15] As CSL receives 7% of the royalties, and the University of Queensland reportedly 6%, this 13% might be held to be a proxy for Australia's share of the research effort[16] – ie, around $169 million in total. Over 20 years, say, this averages $8.5 million per annum in Australian R&D costs for Gardasil.

The potential returns from VLP vaccines across a range of diseases in Australia are substantial. As a proxy, the gross benefits from eliminating 70% of cervical cancers could be used as a potential maximum benefit. The AIHW (Begg et al, 2007) estimated that there are around 760 incident cases of cervical cancer per year in Australia. Access Economics (2006) showed that the ratio of cervical cancer active prevalence to incidence is around 1.24:1, indicating that in addition to current incidence, there would be another 941 women still requiring treatment for previously incurred cervical cancer. Out of this total prevalence of 1,701, Gardasil should be able to prevent 70%, or 1,191 cases, if everyone were immunised.

Access Economics (2006) also estimated that the total lifetime cost to society of a person contracting cervical cancer was $1.00 million based on 2003 estimates. Since then, Access Economics (2008) has revised up the value of a statistical life year for 2008 (from $162,561 to $266,843), which increases this cost to $1.63 million.

Multiplying the maximum number of prevalent cases potentially prevented by Gardasil with the total value of savings to society from each such prevented case, indicates a total potential benefit of $1.9 billion. Assigning 50% of this to R&D and 50% to the public vaccination program, and assuming 60% coverage by the vaccination program and 13% of the R&D component due to Australian (as opposed to overseas) research, yields an attributable benefit of $63 million per annum, which (compared to $8.5 million per annum in costs) yields a B/C ratio of 7.5:1.

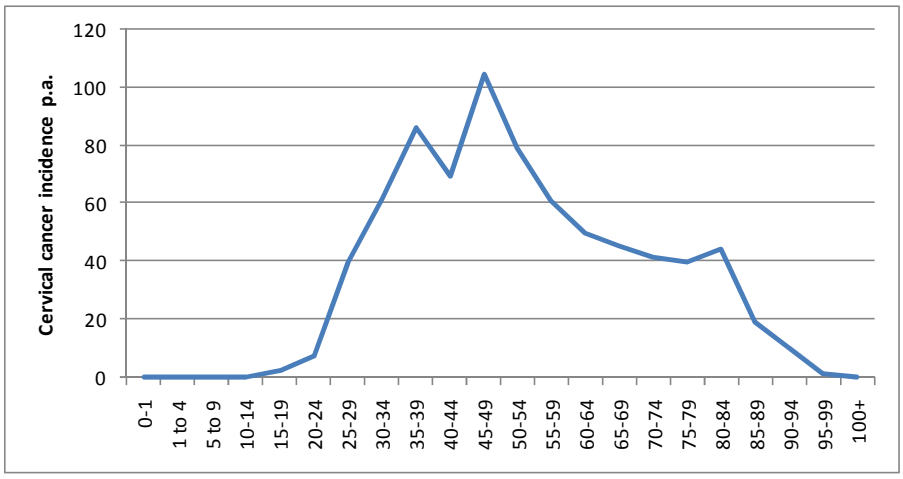
There are naturally some cautions in relation to these calculations. First, the costs are incurred today whereas the benefits are gained largely in the future, and this ballpark estimate has not discounted future streams. Most Australian women are not eligible for the vaccination program and many are already exposed to HPV virus so there is a substantial time lag before the benefits start to kick in of eradicating HPV-caused cervical cancer in Australia. If the average age of receiving Gardasil is 13 years and the average age of contracting cervical cancer is around 50 years (Figure 6-2), given society has a positive time preference, a discount rate is usually applied where money is spent now, but the benefits

[15] www.theaustralian.news.com.au/story/0,20867,20736508-5001641,00.html

[16] While the development of virus-based vaccines was an astounding Australian breakthrough with substantial worldwide benefits, Gardasil's development also has a significant American development content. Although CSL was granted a patient in 1991 for the generic development of vaccines based on VLPs, the intellectual property behind Gardasil per se is quite complex. Frazer and Zhou developed a VLP from HPV 16; however, it did not quite have the same structure as the HPV itself. Three quarters of the patents that Merck used to develop Gardasil come from American institutions: the University of Rochester in New York (which developed immunologically correct VLPs from HPV); the US National Cancer Institute (which developed VLPs from papilloma viruses in cows); and Georgetown University in Washington DC (which did not make any VLPs). These are in addition to patents from the University of Queensland. The US Patent Office granted the dominant patent to the Georgetown University (ironically, given it is the only one of the four claimants not to have developed a VLP). The Australian Patent Office found that Rochester was the first to make fully-functional VLPs from HPV.

only occur in the future. Access Economics uses a standard discount rate of 3% to discount wellbeing gains (Section 2.3.1)[17] At this rate, an event that is likely to occur 37 years in the future is valued at less than a third of the value of an event occurring now. So in NPV terms, the B/C ratio may be closer to 2.5:1 than 7.5:1.

FIGURE 6-2: CERVICAL CANCER INCIDENCE BY AGE



Source: AIHW (Begg et al, 2007).

Second, the calculation does not take account of the cost of the immunisation program, since this should be measured against the other 'half' of benefits (from implementing the public program, rather than from making the discovery – both are required for wellbeing gains to be realised).[18] The sale price of Gardasil is quite high at around $441[19] per treatment, making it one of the most expensive vaccines on the market. The British Columbia Cancer Agency (2006) found that HPV vaccination would only become cost effective at around $60 Canadian (about $70 Australian). GlaxoSmithKline produces an almost identical VLP based HPV vaccine, called Cervarix. By targeting additional HPV types, Cervarix prevents 80% of cancers compared to Gardasil's 70% and is approved in Australia for use by women up to age 45 years, although with no public funding (rejected by the Pharmaceutical Benefits Advisory Committee).

Third, neither cervical cancer vaccine has been demonstrated yet to have long term efficacy: Cervarix has been shown to be effective for 6.4 years[20], while Gardasil has only been followed up for four years so far. As such, long term effectiveness and potential side effects are not yet fully known.

[17] From the long-term bond rate of 5.8% and inflation of 2.8% (Access Economics, 2008).

[18] This report is not designed to analyse the cost effectiveness of the public vaccination program: the Pharmaceutical Benefits Advisory Committee rejected Gardasil for PBS benefits on the basis of lack of cost effectiveness, although former Prime Minister Howard decided to supply it free of charge for the target group under the National Immunisation Program, at an estimated program cost over the first four years of $436.8 million.

[19] http://www.pharmacydirect.com.au/PD_ProductOrderingInformation.asp?PID=21274, accessed 15 May 2008

[20] http://www.medscape.com/viewarticle/571208

Bearing in mind these cautions, a final positive point is that the HPV vaccine represents a significant advance in the prevention of cervical cancer *globally*. The four strains of the virus against which the vaccine affords protection have the potential to save 225,000 lives worldwide every year, and prevent almost half a million women from developing cervical cancer. As such, the HPV vaccine is an example of the outstanding potential benefits of Australian research and collaboration.

6.2 DIABETES

Diabetes mellitus (referred to below as 'diabetes' or DM) is characterised by persistently high blood glucose levels (hyperglycaemia), and disturbances of carbohydrate, fat and protein metabolism (AusDiab 2001:7). Diabetes is associated with long term damage, dysfunction and failure of various organs and tissues, including eye problems, kidney damage, foot ulcers, heart attack, stroke and amputation. As a result of these complications, diabetes is associated with higher mortality rates. An epidemiological study conducted in Australia in 1999 (the AusDiab study) found that close to 1,000,000 people aged 25 or more in Australia had diabetes.

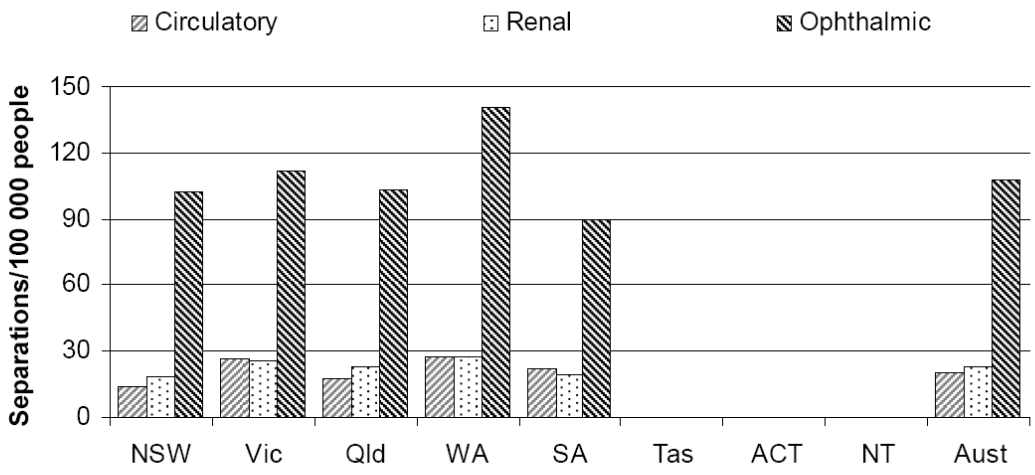
The focus of this case study is on diabetic eye diseases. The most common type of diabetes is type 2 (accounting for 80% of those with the disease). Of 10,652 people with type 2 diabetes aged 40 years or over and who responded to the Australian DiabCost survey in 2001, eye problems were the most common complication (Colagiuri et al, 2003). Further, ophthalmic complications are a major determinant of hospitalisations for the complications of type 2 diabetes (Figure 6-3).

The major eye diseases associated with diabetes are diabetic retinopathy (DR), cataract and neovascular glaucoma. Primary open angle glaucoma has also been associated with diabetes, but evidence of the link is equivocal.

Australian population studies of visual impairment suggest diabetic eye disease is a significant cause of visual impairment and blindness. Data from the Melbourne Visual Impairment Project revealed the following:

- Causes of visual impairment (defined as visual acuity of 6/12 or worse) were:
  - uncorrected refractive error (population weighted prevalence 24.68/1000);
  - age-related macular degeneration (AMD) (3.86/1000);
  - other retinal diseases (2.91/1000);
  - other disorders (2.8/1000);
  - cataract (2.57/1000);
  - glaucoma (2.32/1000);
  - neuro-ophthalmic disorders (1.8/1000); and
  - diabetic retinopathy (1.53/1000) (Van Newkirk et al, 2001).
- Dimitrov et al (2003) found that the main causes of new cases of visual impairment over a five year period were:
  - under-corrected refractive error (59%);
  - AMD, cataract and neuro-ophthalmic disorders (7% each);
  - glaucoma (3%); and
  - diabetic retinopathy (DR) (1%).

FIGURE 6-3: PROPORTION OF SEPARATIONS FOR PRINCIPAL DIAGNOSIS OF TYPE 2 DIABETES MELLITUS BY SELECTED COMPLICATIONS, ALL HOSPITALS, 2005-06



[a] Results for individual complications may be affected by small numbers, and need to be interpreted with care. [b] Differences across jurisdictions in policy and practice relating to the admission of patients, the availability of outpatient services and the incentives to admit patients rather than treat them as outpatients will affect estimates of hospital separations. [c] Morbidity data are coded under coding standards that may differ over time and across jurisdictions. [d] Data for Tasmania, the ACT and the NT are not published separately (due to private hospital confidentiality arrangements) but are included in the total for Australia.

Source: AIHW (unpublished); table 11A.43.

Source: Steering Committee for the Review of Government Service Provision (2008:Figure 11.34), reproduced.

While its prevalence rate among the general population is not as high as that of uncorrected refractive error, AMD, cataract or glaucoma, DR causing visual impairment occurred at a younger age than the other eye diseases. According to Weih et al (2000) around 1,200 Australians aged 50 to 59 years had visual impairment due to DR and around 3,600 Australians aged 60 to 69 years also had visual impairment due to DR.

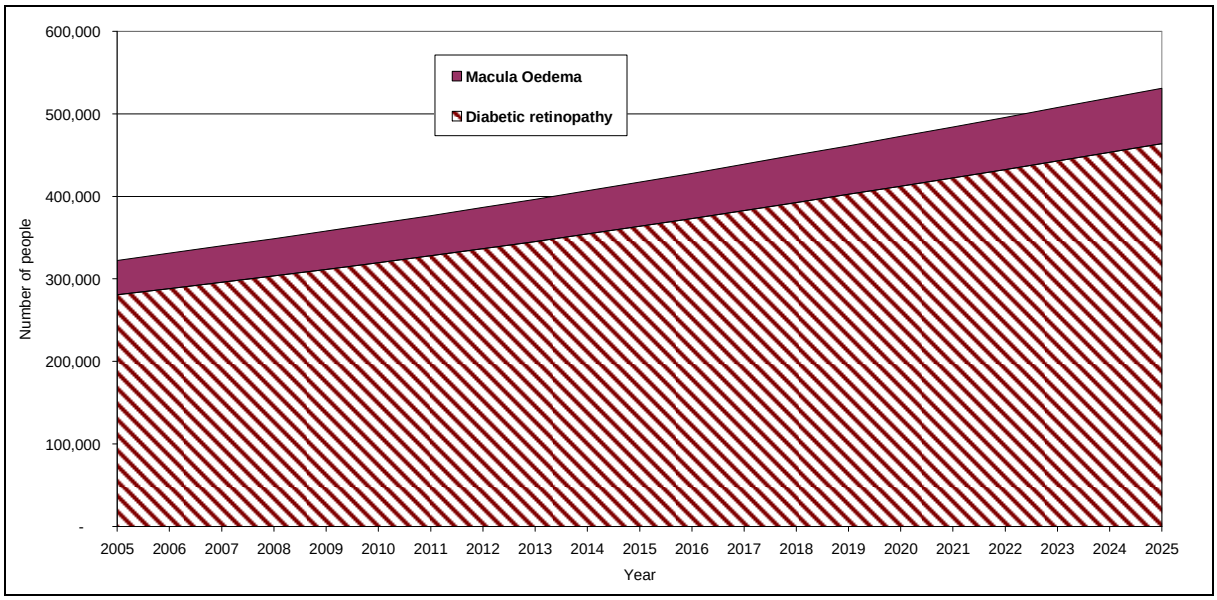
The purpose of this case study is to demonstrate the benefits that can be generated in Australia from health R&D that prevents or delays vision loss associated with diabetes, or that results in vision gain. This was done using a dynamic model of diabetic eye diseases developed by Access Economics that encompassed prevalence, incidence, risk factors, treatment options and measures of wellbeing associated with changes in prevalence of diabetic retinopathy (proliferative retinopathy, and macular oedema), cataract and glaucoma.

6.2.1 THE BASE CASE

In the base case, the results reflect current standard treatment as assessed from a literature review and advice from clinicians.

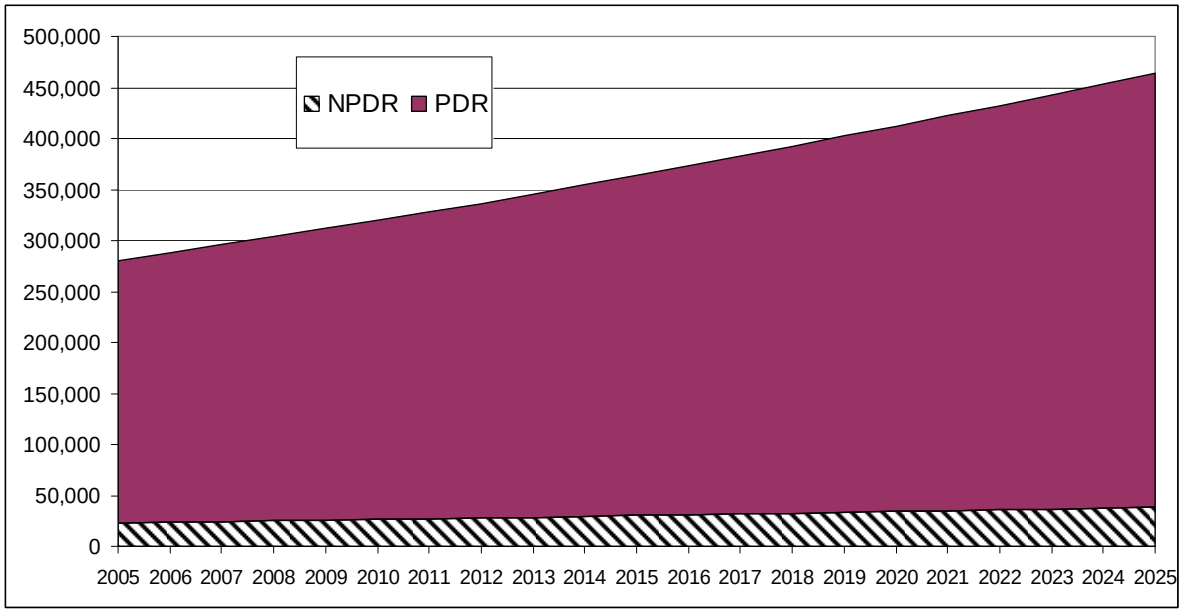
The modelled projections of the prevalence of DR and clinically significant macular oedema (CSMO) are shown in Figure 6-4. Prevalence rises from 280,609 people with DR and 41,768 with CSMO in 2005, to 463,737 with DR and 67,382 with CSMO in 2025. Prevalence projections for non-proliferative DR and proliferative DR are shown in Figure 6-5. The prevalence of non-proliferative and proliferative DR in 2005 is 257,410 and 23,199 respectively. In 2025, prevalence is projected to be 425,398 and 38,338 for non-proliferative and proliferative DR respectively.

FIGURE 6-4: PREVALENCE OF DIABETIC RETINOPATHY AND MACULAR OEDEMA, 2005 TO 2025



Source: Access Economics modelling based on Blue Mountains Eye Study, Melbourne Visual Impairment Project and Wisconsin Epidemiologic Study of Diabetic Retinopathy data

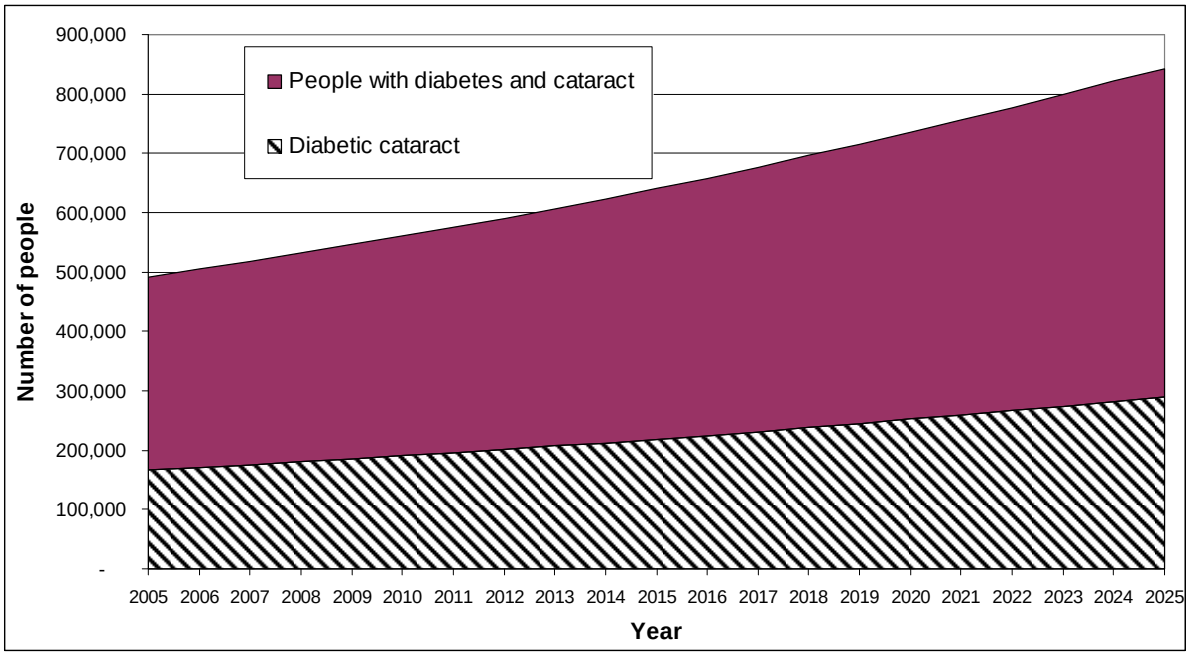
FIGURE 6-5: PREVALENCE OF NON-PROLIFERATIVE AND PROLIFERATIVE DR, 2005 TO 2025



Source: Access Economics modelling based on Blue Mountains Eye Study, Melbourne Visual Impairment Project and Wisconsin Epidemiologic Study of Diabetic Retinopathy data.
Note: NPDR=non-proliferative DR; PDR = proliferative DR.

Prevalence projections for cataract among people with diabetes are in Figure 6-6. In all, there are 492,026 diabetics with cataract in 2005, 165,500 of whom have diabetic cataract. By 2025, the model predicts that there will be 843,000 people with both diabetes and cataract, of which 289,600 will have diabetic cataract.

FIGURE 6-6: PREVALENCE OF CATARACT AMONG PEOPLE WITH DIABETES, 2005 TO 2025



Source: Access Economics modelling based on Blue Mountains Eye Study, Melbourne Visual Impairment Project and Wisconsin Epidemiologic Study of Diabetic Retinopathy data.

The prevalence of visual impairment due to diabetes is shown in Table 6-1. Net visual impairment is expected to increase from 31,343 people to 53,888 between 2005 and 2025 due to an increase in diabetes. Total visual impairment is expected to increase by 69% for DR, 61% for CSMO, 76% for cataract, and 65% for neovascular glaucoma (NVG).

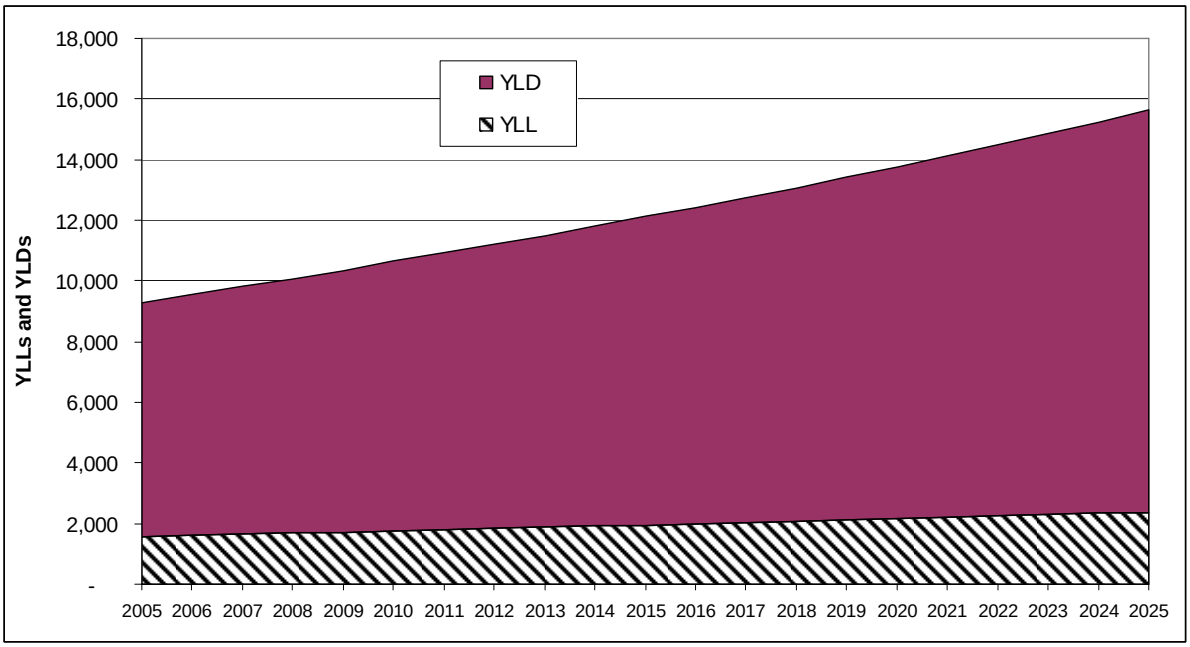
TABLE 6-1: PREVALENCE OF VISUAL IMPAIRMENT DUE TO DIABETES

	2005	2025
Net visual impairment		
Mild	11,564	19,883
Moderate	10,900	18,374
Severe	8,878	15,631
Total net visual impairment(a)	**31,343**	**53,888**
Total visual impairment and DR	17,535	29,647
Total visual impairment and CSMO	41,768	67,382
Total visual impairment and cataract	51,139	89,781
Total visual impairment and NVG	1,159	1,916

(a) These prevalence estimates include visual impairment from DR, CSMO, cataract and NVG — noting that people with more than one eye disease are not counted twice.

Projections of the burden of disease (DALYs) associated with diabetic eye disease are in Figure 6-7, showing the separate components of years of life lost due to disability (YLD) and years of life lost due to premature death (YLL). The 2005 estimates (1,576 YLLs and 7,694 YLDs) are consistent with Centre for Eye Research Australia (2004) who estimated 4,094 YLDs due to DR in 2004, not including diabetic cataract or CSMO.

FIGURE 6-7: DALYS DUE TO DIABETIC EYE DISEASE, 2005 TO 2025



6.2.2 BENEFITS FROM R&D INTO DIABETIC EYE DISEASE

The benefits from R&D will be the avoided cost and increase in wellbeing from reducing the prevalence and incidence of eye diseases that result from diabetes. Within this case study, the impacts of intensive blood glucose control on diabetic related eye diseases have been evaluated by looking at the impact of introducing intensive blood glucose control as per the Diabetes Control and Complications Trial and UK Prospective Diabetes Study clinical trials (see Box 6-1). There is strong evidence that compared with conventional treatment, tight glycaemic control reduces the incidence and progression of DR in both types 1 and 2 diabetes (Mohamed et al, 2007).

Box 6-1 Clinical trials of diabetes treatment

The **Diabetes Control and Complications Trial (DCCT)** investigated the effect of hyperglycemia in type 1 diabetic patients, as well as the incidence of diabetic retinopathy, nephropathy, and neuropathy. A total of 1,441 patients who had either no retinopathy at baseline (primary prevention cohort) or minimal-to-moderate non-proliferative DR (secondary progression cohort) were treated by either conventional treatment (one or two daily injections of insulin) or intensive diabetes management with three or more daily insulin injections or a continuous subcutaneous insulin infusion.

The **UK Prospective Diabetes Study** was a 20-year trial which enrolled 5,102 patients with type 2 diabetes in 23 clinical centres based in England, Northern Ireland and Scotland. It tested whether a policy of intensive blood glucose control and/or blood pressure control, with a variety of agents, reduced the risk of diabetes-related endpoints, diabetes-related deaths and all-cause mortality.

6.2.2.1 MODELLING APPROACH

Given the results from the clinical trials have now been available for some time, it was assumed that many people with diabetes are already receiving intensive glycaemic

treatment. Consequently this scenario examines the impact of extending treatment to the proportion of Australians whose diabetes remains uncontrolled (defined as HbA1c >7. Using data from the AusDiab study, around 28% of Australians with diabetes have poorly controlled blood glucose concentrations.

Treatment efficacy results were applied to 28% of the population with diabetes. For type 1 diabetes, after a delay of six years, intensive treatment results in an incidence rate in the intensive group which is 76% lower than in the conventional group, and a progression rate that is 54% lower in the intensive group. For type 2 diabetes, there is no delay in treatment efficacy. After ten years, the cumulative difference in incidence and progression rates is 25% (with the intensive group being lower). For cataract, the results for type 2 have been applied to type 1 as well. A summary of the parameters used in modelling intensive glycaemic control are shown in Table 6-2.

TABLE 6-2: SUMMARY OF MODEL PARAMETERS FOR INTENSIVE GLYCAEMIC CONTROL

	Proportion of patients with uncontrolled diabetes	Incidence of DR	Clinical progression of DR	Incidence of cataract surgery
Type 1	28%	↓76% after 6 years	↓72% after 6 years	↓24%
Type 2	28%	↓25% over 10 years	↓25% over 10 years	↓24%

Sources: Diabetes Control and Complications Trial Research Group (1993); Epidemiology of Diabetes Interventions and Complications Research Group (2000).

6.2.2.2 RESULTS

Extending intensive blood glucose treatment to those whose diabetes is currently not controlled (around 28% of people with treated diabetes) will result in a significant reduction in diabetic eye disease. Table 6-3 shows that the prevalence in 2025 will be lower for diabetic retinopathy, diabetic macula oedema, and diabetic neovascular glaucoma. For diabetic cataract, the prevalence is expected to be higher, which reflects the fact that as progression is slowed, people stay in the earlier stages longer where mortality rates are lower, and hence there are fewer deaths associated with visual impairment (eg, falls, accidents).

TABLE 6-3: RESULTS OF EXTENDING INTENSIVE BLOOD GLUCOSE CONTROL

	Baseline	Intensive blood glucose control
Prevalence 2025		
Diabetic retinopathy	463,737	449,011
Diabetic macula oedema	67,382	66,883
Diabetic cataract	289,620	291,237
Diabetic neovascular glaucoma	1,916	1,846
Visual impairment (VI) 2025		
VI and diabetic retinopathy	29,647	29,414
VI and MO	67,382	66,883
VI and cataract	89,781	75,415
VI and neovascular glaucoma	1,916	1,846
NET VI	53,888	49,776

For all diabetic related eye diseases, visual impairment is expected to be lower. By 2025, it is projected that there would be 4,111 fewer people with visual impairment than in the base case. Consequently, the burden of disease is 18,850 DALYs lower under this scenario. This means there is a NPV increase in wellbeing of around $7.6 billion (in 2008 prices).

There are additional benefits from treating blood glucose that flow from reducing other (non ophthalmic) complications of diabetes, which result from less glycaemic variability, lower HbA1c, and less incidence of severe hypoglycaemia. This can lead to a reduction in risks associated with diabetes beyond eye disease, including reduced risks to kidney, and heart disease, and reduced risk of amputation, nerve damage, and stroke. Although these have not been quantified in the modelling, they represent a significant benefit from intensive glucose control.

Although significant benefits are expected from intensive blood glucose control, there will also be additional costs. These have not been quantified in the modelling but need to be considered when evaluating the net impact of health R&D. They are likely to be significant and will include:

- Health system costs, which are expected to increase significantly due to the more intensive treatment, such as:
  - inpatient supervision immediately after initiation of therapy (multiple daily injections and with continuous subcutaneous insulin infusion);
  - frequent outpatient supervision immediately after initiation of therapy;
  - changes between multiple daily injections and with continuous subcutaneous insulin infusion (and vice versa);
  - ongoing intensive therapy; and
  - treatment of side effects of intensive therapy (for example, weight gain).
- Indirect costs associated with intensive treatment, such as increased caring costs and additional deadweight loss.

6.3 DEMENTIA

Alzheimer's disease (AD) is not a natural part of ageing. Recent developments in neuroscience, genetic and medical technology suggest that prevention in terms of slowing the progression of dementia is possible. Delaying dementia onset lessens the average number of years spent living with the disease. Median life span is around seven to ten years for people diagnosed in their 60s and 70s, but three years or less for patients diagnosed in their 90s. Those living with AD for longer periods tend to require considerably more health services per annum than newly diagnosed individuals. If delays in the onset of the condition through prevention were achievable through health R&D, it would produce substantial reductions in the future number of cases (prevalence) and in real costs of dementia.

Access Economics has modelled the effects of any successful intervention that would delay the onset of AD as a result of R&D, and its impacts on the number of new cases and on the prevalence of AD in the future, based on a methodology developed by Professor Ron Brookmeyer from John Hopkins University, Baltimore, and his colleagues (Brookmeyer et al, 1998). In particular, the methodology includes:

- calculating Australian AD age-specific incidence rates (ASIRs) based on Brookmeyer's estimated natural logarithm formula;
- projecting incidence and prevalence using the Brookmeyer et al (1998) methodology, age-specific incidence rates, and ABS population data; and
- modelling prevention programs that reduce ASIRs by 5%, 10%, 25% and 50%, corresponding to relative risks of 0.95, 0.90, 0.75 and 0.5 and delay in onset of 0.5, 1.0, 2.0 and 5.0 years respectively, for the years 2020, 2040 and 2050 (assuming the falls in incidence begin in 2005).

6.3.1 MODELLING THE DELAYS IN ONSET OF AD

By applying the age-specific incidence and prevalence derived from Brookmeyer et al (1998) to ABS Series II population forecasts, the incidence and prevalence for AD was projected forward to 2050. This was then compared to the 'base case' with four different scenarios based on 'shocks' to the model in the form of reducing each ASIR from 2005 onwards by a factor of 5%, 10%, 20% and 50%. These shocks correspond to delays of 0.4, 0.8, 1.6 and 4.8 years respectively in the onset of AD, in the absence of competing causes of death. Results are summarised in Table 6-4 and illustrated in Figure 6-8 and Figure 6-9.

If interventions due to R&D could reduce the ASIR of AD by 50% from 2005, delaying the onset of AD by around five years, then relative to current projections in Australia:

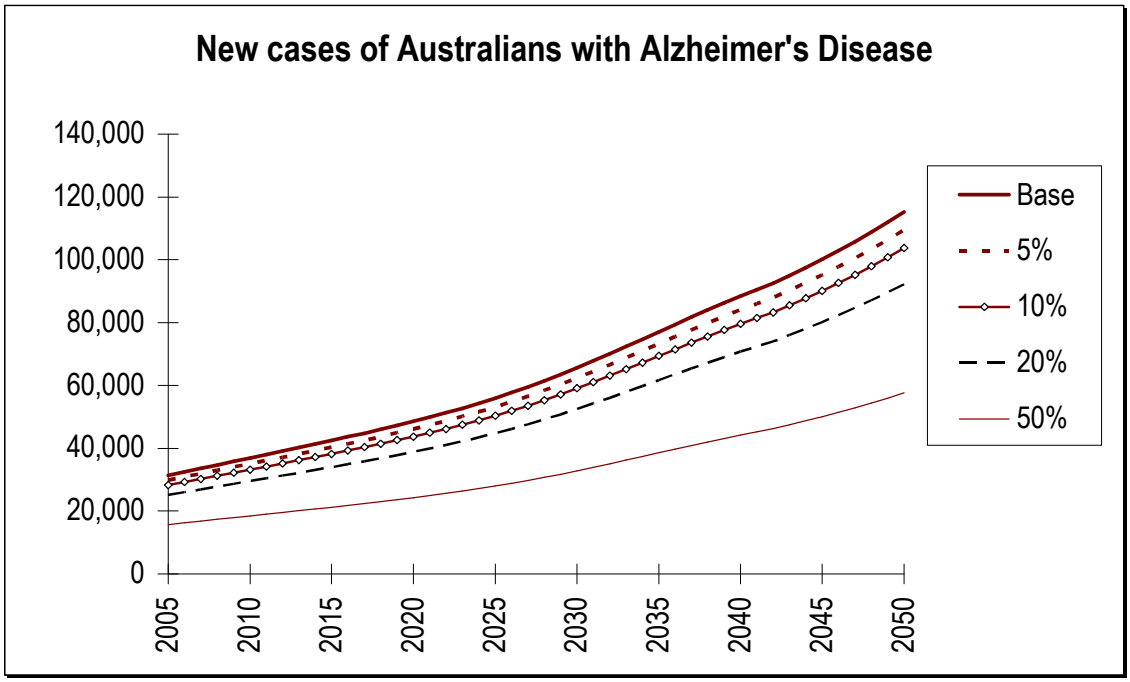
- by 2020 there would be 46,568 (35.2%) fewer cases of AD;
- by 2040 there would be 96,690 (48.5%) fewer cases of AD; and
- by 2050 there would be 113,611 (48.7%) fewer cases of AD.

TABLE 6-4: MODELLING RESULTS – IMPACTS OF DELAYS IN AD ONSET, 2020, 2040, 2050

Fall in ASR	Delay (years)	New Cases			Prevalence		
		2020	2040	2050	2020	2040	2050
Base Case	-	48,595	88,444	115,288	132,298	199,160	233,350
5%	0.4	46,165	84,022	109,524	127,714	189,698	222,249
10%	0.8	43,735	79,600	103,759	123,115	180,191	211,092
20%	1.6	38,876	70,755	92,230	113,867	161,040	188,607
50%	4.8	24,297	44,222	57,644	85,729	102,470	119,739
Fall in ASR	**Delay (years)**	**Change from base case (number of people)**					
		New Cases			**Prevalence**		
		2020	**2040**	**2050**	**2020**	**2040**	**2050**
Base Case		0	0	0	0	0	0
5%	0.4	-2,430	-4,422	-5,764	-4,583	-9,462	-11,100
10%	0.8	-4,859	-8,844	-11,529	-9,183	-18,970	-22,257
20%	1.6	-9,719	-17,689	-23,058	-18,430	-38,121	-44,743
50%	4.8	-24,297	-44,222	-57,644	-46,568	-96,690	-113,611
Fall in ASR	**Delay (years)**	**Change from base case (percent)**					
		New Cases			**Prevalence**		
		2020	**2040**	**2050**	**2020**	**2040**	**2050**
Base Case		0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
5%	0.4	-5.0%	-5.0%	-5.0%	-3.5%	-4.8%	-4.8%
10%	0.8	-10.0%	-10.0%	-10.0%	-6.9%	-9.5%	-9.5%
20%	1.6	-20.0%	-20.0%	-20.0%	-13.9%	-19.1%	-19.2%
50%	4.8	-50.0%	-50.0%	-50.0%	-35.2%	-48.5%	-48.7%

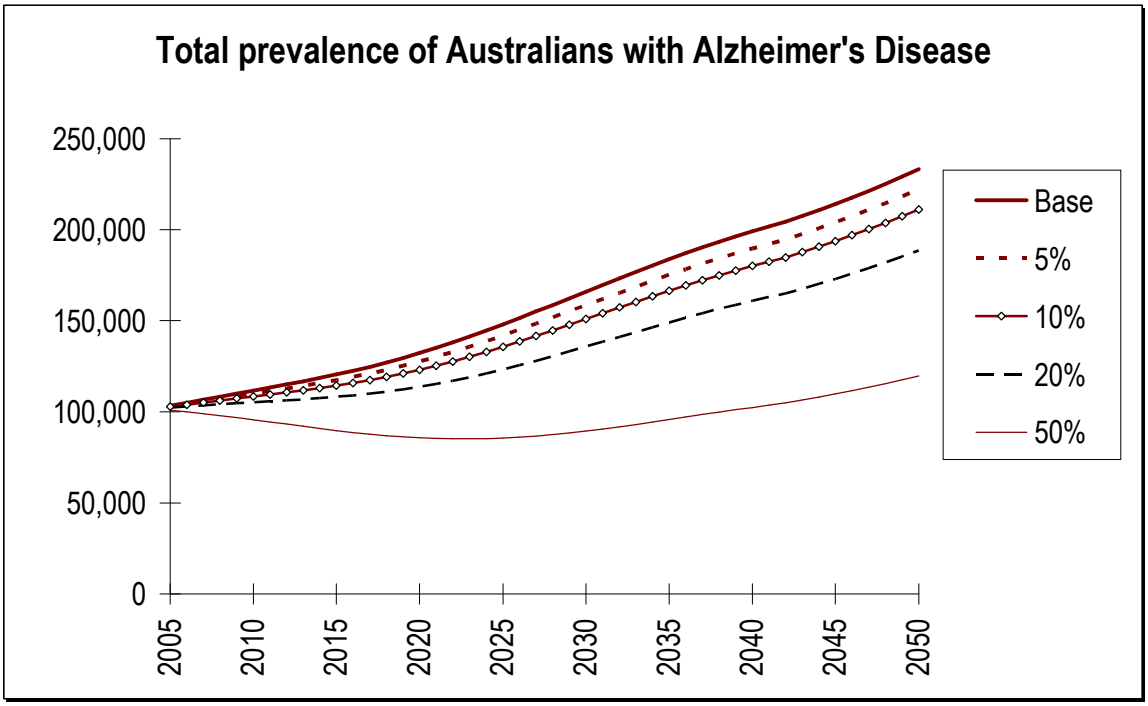
NB: ASIR is age-specific incidence rate for AD.

FIGURE 6-8: IMPACTS OF FALLS IN ASIR ON NEW CASES OF AD, AUSTRALIA, 2005-2050



Source: Access Economics estimates.

FIGURE 6-9: IMPACTS OF FALLS IN ASIR ON NEW CASES OF AD, AUSTRALIA, 2005-2050



Source: Access Economics estimates.

By 2040, when demographic ageing is projected to taper off, Australia would save almost entirely what it currently costs to care for people with AD per annum. If interventions could reduce the ASIR of AD by even 5% from 2005, delaying the onset of AD by around five months, then relative to current projections in Australia:

- by 2020 there would be 4,583 (3.5%) fewer cases of AD;
- by 2040 there would be 9,462 (4.8%) fewer cases of AD; and

- by 2050 there would be 11,100 (4.8%) fewer cases of AD.

By 2040, when demographic ageing is projected to taper off, Australia would save around 10% of what it currently costs to care for people with AD per annum.

The impacts in percentage terms begin to stabilise between 2040 and 2050. We thus provide results for the year 2030 as a further comparator in Table 6-5.

TABLE 6-5: MODELLING RESULTS – IMPACTS OF DELAYS IN AD ONSET, 2030

	New Cases	Prevalence
Base Case	65,622	166,107
5% fall in ASIR	62,341	158,581
10% fall in ASIR	59,060	151,023
20% fall in ASIR	52,498	135,811
50% fall in ASIR	32,811	89,390
	Change from base case (number of people)	
	New Cases	Prevalence
Base Case	0	0
5% fall in ASIR	-3,281	-7,526
10% fall in ASIR	-6,562	-15,084
20% fall in ASIR	-13,124	-30,296
50% fall in ASIR	-32,811	-76,718
	Change from base case (percent)	
	New Cases	Prevalence
Base Case	0.0%	0.0%
5% fall in ASIR	-5.0%	-4.5%
10% fall in ASIR	-10.0%	-9.1%
20% fall in ASIR	-20.0%	-18.2%
50% fall in ASIR	-50.0%	-46.2%

Source: Access Economics estimates.

To summarise these results we compare the smallest and largest shocks. By 2030:

- a 5% fall in ASIR would reduce AD prevalence by 7,526 cases (4.5%); and
- a 50% fall in ASIR would reduce AD prevalence by 76,718 cases (46.2%).

A final point is that these estimates may all be quite conservative. Compared to the projections from Access Economics (2003), total cases of dementia may reach 500,000 by around 2040 and 580,000 by 2050. If AD were to remain at 59% of these total cases, then overall prevalence would be higher than that estimated using the Brookmeyer formulae which gives lower overall prevalence estimates primarily due to the lower age-prevalence predicted in the highest age groups. If realised prevalence is closer to the Access Economics (2003) projections (around 300,000 by 2040 in contrast to the projected 200,000), then savings from early delays could potentially be up to 50% higher.

6.3.2 POSSIBLE BENEFITS FROM REDUCING THE ONSET OF AD

This statistical analysis supports the conclusion that AD will become an enormous public health problem in the coming decades and that modest delays in onset can have a significant impact in terms of reducing the burdens and costs associated with this debilitating disease. The possible benefits from reducing the onset of AD due to Australian R&D are presented in Table 6-6 and summarised for the smallest and largest impact scenarios as follows.

- If incidence of AD could be reduced by 5% through Australian R&D, then over the period 2005-2010, cumulative savings of $195 million would be realised - $10.3 billion over 2005-2050.
- If incidence of AD could be reduced by 50% through Australian R&D, then over the period 2005-2010, cumulative savings of $1.97 billion would be realised - $104.9 billion over 2005-2050.
- Over half of these savings (an estimated 57%) would be in the health and residential care sector.

TABLE 6-6: CUMULATIVE SAVINGS SCENARIOS, 2005-2050, $M (REAL CONSTANT 2008 PRICES)

	2005-2010	2005-2020	2005-2030	2005-2040	2005-2050
5% fall in ASIR	219	1498	3993	7458	11 569
10% fall in ASIR	439	3002	8000	14946	23 190
20% fall in ASIR	880	6024	16 060	30 014	46 584
50% fall in ASIR	2221	15 210	40 600	75 972	118 025

Source: Access Economics estimates.

Delays in the onset of AD even as short as five months to a year can have significant public health implications, in terms of planning the resources necessary to care for people with disability. By delaying onset, the years living with the disease are lessened, on average. If the condition is diagnosed when a person is in their 60s and 70s, median life span is seven to ten years, while for patients whose conditions are diagnosed in their 90s, median lifespan with AD is only three years or less (Brookmeyer et al, 2002). This is primarily due to the risk of dying from some other cause being relatively higher at older ages. Individuals living with AD for longer periods are likely to require considerably more health services than newly diagnosed individuals, so the costs savings may potentially be even greater than estimated here.

Numerous preventive strategies are currently being investigated, including anti-inflammatory drug therapy, hormone replacement therapy, reduction of cardiovascular risk factors (high blood pressure, high blood cholesterol, smoking, poor diet and physical inactivity, for example), antioxidant therapy, prevention or removal of beta-amyloid plaques, potential pharmacotherapies and other interventions. Promising research is showing linkages between AD and the presence of the ApoE gene, as well as improving understanding of neurogenesis, mitotic signalling and the relative contributions of multiple AD risk factors. Improved diagnosis is now possible through new neuroimaging technologies. However, there is a need for further research and, in particular, large randomised prevention trials, before the potential gains of reduced incidence rates can be fully quantified. Although the resources needed to conduct such trials may seem, the costs are small in comparison with the long term economic and social costs of delaying disability in our ageing population.

6.4 INDIGENOUS HEALTH – GROUP A STREPTOCOCCI

Group A streptococci (GAS) are bacteria that can be found on the skin and in the throat. GAS is spread by direct contact through nose or throat discharges of an infected individual or through fluid from infected skin lesions. On occasions, individuals can carry the bacteria without showing symptoms of infection. An infected person can also contaminate food, which can then be used by the bacteria as a host for transmission.

Most infections with GAS result in mild illnesses, such as streptococcal pharyngitis (strep throat), cellulitis and impetigo (inflammatory diseases of the skin). However, on occasions GAS infections can invade the tissue and pass the body's defences through breaks in the skin. People with chronic illnesses (such as diabetes, cancer, kidney and heart disease) or people who undertake activities that are known risk factors (cigarette smoking, use of non-steroidal anti-inflammatory agents, alcohol misuse and intravenous drug use) are at a greater risk of developing invasive GAS infections.

Invasive GAS infections can lead to much more serious illnesses. These include necrotising fascilitis (commonly described as 'flesh eating bacteria'), blood stream infections, pneumonia, scarlet fever and streptococcal toxic shock syndrome (STSS). STSS is a rapidly progressing infection that causes low blood pressure and injury to organs such as acute glomerulonephritis, a serious kidney disease. Repeated invasive GAS infections can also cause rheumatic fever and rheumatic heart disease leading to heart failure, which significantly reduces quality of life and life expectancy.

6.4.1 THE IMPACT OF GAS INFECTION IN AUSTRALIA

Invasive GAS infection is usually associated with poverty. It is an endemic disease in developing countries, with the WHO estimating there are currently more than 18 million cases that lead to around 500,000 deaths each year (WHO, 2008).

Australia's indigenous population suffers the highest incidence of invasive GAS infection in the world (WHO, 2008). Between 1991 and 1996 the crude incidence rate of invasive GAS infection in the Northern Territory was found to be 9.3 per 100,000 per year, which included 23.8 per 100,000 for indigenous people and 4.7 per 100,000 per year in non-indigenous people (Carapetis et al, 1999). In Northern Queensland, where the population structure, climate and environment is similar to the Northern Territory, the crude incidence rate was found to be much higher at 82.5 per 100,000 for the indigenous population and 10.13 per 100,000 per year for the non-indigenous population (between 1996 and 2001). The overall mortality rate was 7% (Norton et al, 2004). It is unclear whether the difference in incidence rates is due to differences in the environment, risk factors, GAS strains or study methodologies.

Invasive GAS infection is not limited to tropical Australia. A study conducted in Victoria between 2002 and 2004 found an incidence rate for invasive GAS infection of 2.7 per 100,000 per year. Of the cases examined, STSS was identified in around 14.4% of patients and necrotising fascilitis was identified in around 11%. The case fatality rate ranged from 7.8% for all type of disease resulting from an invasive GAS infection to 23% for STSS (O'Grady et al, 2007).

6.4.2 DEVELOPMENT OF A GAS VACCINE

Treatment of GAS infections, both mild and invasive, is undertaken through the use of antibiotics. The most common antibiotic used is penicillin, although other types are used depending on the seriousness of the infection and the patient's allergies to antibiotics. In some cases, individuals with invasive GAS infections may require intensive care treatment and surgery.

Although research into developing a GAS vaccine has been occurring since the mid 1970s, there is currently no vaccine that is proven to be effective and safe. In addition, primary prevention of life-threatening invasive GAS infection through prompt diagnosis and treatment is ineffective in controlling the disease in developing countries or remote areas where health infrastructure is not readily accessible. Although invasive GAS infections may respond well to

conventional antibiotic treatment, the large number of cases in rural and remote areas, the highly transmissible nature of the infection in hospital settings, and the risk of significant morbidity and fatal outcomes from an infection means the prevention of invasive GAS infections is a highly desirable outcome. It would not only reduce the burden on the health care system from invasive GAS infections but would lead to better expected health outcomes for those who are at risk of an infection.

The Cooperative Research Centre for Vaccine Technology (CRC-VT)[21] in collaboration with the Swedish company Active Biotech initially developed and undertook preclinical testing of a prototype peptide-based GAS vaccine. The major challenge in its development was the existence of a large number of bacterial variants with different M proteins[22], which made mediating immunity to GAS through antibodies attached to the surface M protein difficult. Another challenge was ensuring antibodies did not cross-react with human tissues, such as the heart.

Subsequent research by CRC-VT identified a peptide from one M protein which can induce antibodies that protect the body against multiple strains of GAS, including strains from Australia, Thailand, USA and India. Several other antigens and peptides have been evaluated for suitability as vaccine candidates, and the group has investigated multi-antigen component vaccines containing a variety of GAS-derived peptides to determine their immunogenicity and efficacy in vivo (CRC-VT, 2008). In addition, the CRC-VT has developed procedures for the identification of potentially novel additional vaccine candidates.

Along with undertaking R&D into a GAS vaccine, the CRC-VT has developed methods for nasal and parenteral[23] delivery of the vaccine candidate through lipid-based generic technology. This technology can also be used with non-streptococcal peptide-based vaccines. Negotiations are currently being undertaken to further develop the vaccine through Phase I clinical trials. Efficacy trials of the vaccine are expected to be long and the WHO is currently involved in developing standard protocols for the clinical evaluation of GAS vaccines (WHO, 2008).

6.4.3 POSSIBLE BENEFITS FROM A GAS VACCINE

Assuming a vaccine can be developed from R&D undertaken by CRC-VT, there is a question over whether the vaccine would be administered to those that are at risk or the population at large. At a minimum it is expected that the vaccine would be administered to the indigenous community. However, the relatively high incidence of GAS within the non-indigenous population (compared to other bacterial infections) and the possibility of serious consequences from an invasive infection are likely to drive a vaccination program that covers the entire population. For example, a routine childhood and adolescence vaccination program in Australia for type C meningococcal disease was introduced in 2003. The incidence in Australia for type C meningococcal is around 2.4 per 100,000 (DoHA, 2008) or approximately 11% lower than the incidence for GAS infections. Furthermore, in Australia the case mortality rate due to meningococcal disease is around 2.2% (DoHA, 2008), whereas for invasive GAS infections it is approximately 7.8% (O'Grady et al, 2007). This means that a

[21] The CRC-VT is a venture that brings together the Queensland Institute of Medical Research, the Walter and Eliza Hall Institute of Medical Research, Commonwealth Scientific and Industrial Research Organisation, University of Melbourne, and CSL Limited (Australia's largest vaccine manufacturer).

[22] M protein is a virulence factor of the bacterium Streptococcus pyogenes.

[23] Not through the alimentary canal but rather by injection through some other route, as subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, and so on.

GAS vaccination program has the potential to reduce a greater number of infections and deaths compared to the meningococcal vaccination program.

Table 6-7 shows the mortality gains that could be made each year assuming an immunisation program within Australia could reduce the incidence of GAS infection to zero. The incidence for indigenous people used within the table has been calculated as 53.15 per 100,000, which is the mid point between incidence found in Carapetis et al (1999) and Norton et al (2004). The incidence for non-indigenous people used within the table is 2.7 per 100,000, which is the incidence found in Victoria by O'Grady et al (2007). Mortality has been calculated by multiplying the incidence for indigenous and non-indigenous people by the proportion of GAS infections that result in death, which is 7.8%. In the Northern Territory, there is evidence to suggest the fatality rate is around 13%, so this figure has been used for calculating expected deaths in the Northern Territory (Carapetis et al, 1999).

TABLE 6-7: ESTIMATED ANNUAL INCIDENCE AND DEATH AVOIDED FROM A GAS VACCINE

	Population		Incidence		Mortality	
	Indigenous	Non-Indigenous	Indigenous	Non-Indigenous	Indigenous	Non-Indigenous
NSW	138,507	6,019,395	74	163	5	12
Victoria	30,143	4,636,251	16	125	1	9
Queensland	127,580	3,552,043	68	96	5	7
South Australia	25,556	1,419,464	14	38	1	3
Western Australia	58,710	1,773,047	31	48	2	4
Tasmania	16,768	436,810	9	12	1	1
Northern Territory	53,661	122,734	29	3	4	0
ACT	3,875	305,136	2	8	0	1
	454,800	**19,398,170**	**242**	**524**	**17**	**37**

Source: ABS 4705.0 (2006), Carapetis et al (1999), Norton et al (2004), O'Grady et al (2007).

The average age of mortality from invasive GAS infection found in the Northern Territory was 56.8 years for the indigenous population and 61.7 years for the non-indigenous population. Applying these averages across all states and territories and assuming a life expectancy of 87.7 years for the non-indigenous population and 70.7 for the indigenous population[24], it is estimated that an invasive GAS infection that leads to death will reduce years of expected life by 26 years for non-indigenous people and 13.9 years for indigenous people on average. Using the expected mortality figures from Table 6-7, a GAS vaccine could lead to the avoidance of 962 YLLs for non-indigenous people and 236 YLLs for indigenous people, or a total of 1,198 YLLs avoided per year. Multiplying this by the VSLY ($266,843 in 2008 prices), **the value of a GAS vaccine could provide health benefits valued at $319.7 million per year**, of which $78.4 million would be realised by indigenous Australians.

[24] These are the average life expectancy of an individual given they have already reached 50 years of age in 2006. The life expectancy for the non-indigenous population has been derived from ABS Publication 3302.0 (2006) while the life expectancy for the indigenous population has been derived from the non-indigenous population life expectancy minus 17 years, the average life expectancy gap at birth between non-indigenous and indigenous populations.

However, the value of reduced mortality from a GAS vaccine is a minimum benefit. This is because it does not take into consideration the many other health related benefits and savings to the health care system that could be averted by the implementation of a GAS vaccination program. For example, O'Grady et al (2007) notes that of the invasive GAS infections studied in Victoria, 97.8% were hospitalised, 48.7% were required to stay in hospital for 10 days or more, and 23.3% were admitted to an intensive care unit. Of those that entered hospital, 48.4% of cases required surgery as a result of their GAS infection and of these, 9.4% required amputation of a limb. It is likely that a major benefit to society would also come from a reduction in the number of antimicrobial prescriptions for sore throat symptoms.

Recently the government has renewed its efforts to reducing the health and wellbeing gap between indigenous and non-indigenous Australians. Due to low socioeconomic status, poor nutrition and hygiene, and limited access to health care infrastructure, one of the most effective ways of reducing the gap for the indigenous population is to undertake preventive measures such as vaccination programs. Universal vaccination programs that have been implemented within indigenous populations in Australia have reduced the disease burden gap between indigenous and non-indigenous population, including programs for measles, mumps, rubella, poliomyelitis, diphtheria and tetanus (McIntyre, 2005). It is likely that a vaccine for GAS currently being developed by CRC-VT would also achieve this task if administered appropriately.

Development of a vaccine for Group A streptococci bacteria, currently commencing Phase I trials, has potential wellbeing gains in terms of deaths averted worth around $319.7 million, of which $78.4 million would be realised by indigenous Australians. This may be conservative given the scale of other benefits, such as morbidity and hospitalisations averted. Such vaccination R&D aligns well with the Rudd Federal Government commitment to preventive health and to removing the mortality gap between indigenous and non-indigenous Australians.

7. CONCLUSIONS AND RECOMMENDATIONS

Section 7.1 summarises the findings of the previous chapters, while Section 7.2 draws together the key messages with recommendations for areas of application.

7.1 SUMMARY OF FINDINGS

Gains in wellbeing

- Nearly 1.34 million DALYs are estimated to be averted in Australia in 2023 relative to 1993 burden of disease levels (in terms of DALYs per 1,000 population).
- Of these, 839,000 DALYs are averted by males and 497,286 by females, primarily reflecting higher expected benefits to males in the future in relation to cardiovascular disease, cancer, chronic respiratory disease, injuries, and endocrine and metabolic disorders.
- Notably – there are wellbeing *losses* projected in the future for acute respiratory infections, diabetes mellitus, nervous system and sense disorders, musculoskeletal disease and oral conditions – as well as mental disorders for females and, for males, infectious and parasitic diseases. These conditions are those where disability is the main source of disease burden rather than premature mortality.
- Together with the increasing overall proportion of Australia's burden of disease that is due to YLD rather than YLL, this suggests that a prime emphasis of health R&D in the future should also be on reducing disability within the Australian population.
- Applying the VSLY to the total number of DALYs averted, **the annual value of gains in wellbeing from health R&D expected to result from all impacts on health** (not just Australian R&D) **are over $100 billion for females and over $270 billion for males by 2045**.

Expenditure on health R&D

In 2004-05, **$2.8 billion was spent on health R&D in Australia** – Australian Standard Research Classification (ASRC) SEO subdivision 730000 Health.

- Around 44% of health R&D was performed by higher education facilities, 26% by business, 16% by private non-profit (PNP) organisations and 14% by Government facilities.
- Although the Commonwealth sector performs the least amount of health R&D, most of the funding comes from the Commonwealth government. In 2004-05, the Commonwealth contributed around $1.4 billion of funds across all five sectors. The majority of this spending went to higher education facilities (79%) while business received the lowest amount of funding (2%). The business sector spends the second highest amount of funds on health R&D and, not surprisingly, most of these funds are spent on R&D undertaken by business. Overseas funding accounts for around $121 million (4%) of Australian health R&D spending, of which the majority is performed by the PNP sector.
- The majority of health R&D since 1992-93 has been undertaken in clinical research, which has increased from around $413 million to $1.43 billion at an average annual growth rate of 12%. R&D expenditure on human pharmaceutical products and public health had similar expenditures in 2004-05 with $548 million and $536 million spent respectively, although the average annual growth rate for the former was larger at 15% compared to 12%. Health and support services (which includes medical and health

sciences prior to 2000-01) had the lowest expenditure in 2004-05 at $250 million and the lowest average annual growth rate at 12%.

- Of non-business clinical R&D (business data were not available by class), around $233 million was spent on cancer, which was nearly double the expenditure for cardiovascular disease at $120 million. The smallest class of expenditure in 2004-05 was for skin and related conditions, at around $8 million.

Net benefits from Australian health R&D

- The projected net benefits from health R&D over the period 1992-93 to 2004-05 are estimated as $29.5 billion, representing an average net benefit of around $2.3 billion per year.
- The ROI is around 117%, which means that a dollar invested in Australian health R&D is estimated to return an average net health benefit valued at $1.17. To put it another way, the B/C ratio is 2.17, which means that a dollar invested in Australian health R&D returns $2.17 in health benefits on average.
- Expenditure has increased substantially since 1993, reaching just over $3.0 billion (in 2008 prices). Similarly, benefits have also been increasing since 1993.
- Even though there is large uncertainty surrounding the inputs, there is a 90% chance that the net benefits from Australian R&D lie in the range $3.9 billion to $59.1 billion that the ROI from Australian R&D is between 15.6% and 234.4% and the B/C ratio is in the range 1.16 to 3.34.
- The B/C ratio of 2.17 (90%CI 1.16 to 3.34, min 0.57, max 6.01) compares with 2.4 (min 1.0, max 5.0) in the 2003 analysis. The slight decline largely reflects the increased expenditures on health R&D in the interim together with lower expected future gains as the disability burden of the chronic diseases of ageing are projected to increase in coming decades, despite the contribution of R&D.

Benchmarking analysis

- **Historical**: **Australia's health R&D expenditure has increased substantially since the Wills review in 1998**. Compared to historical benchmark at that time of around $1.7 billion, R&D reached $2.8 billion in 2004-05, an average growth rate of around 12% per year. This real growth has occurred across all sectors (although highest in the business sector) and across all areas (health and support services, clinical R&D and public health R&D) except for human pharmaceutical products.
- **International**: **Australia ranks in the middle of comparable countries with health R&D** expenditure estimated as 0.38% of GDP[25] (Organization for Economic Cooperation and Development – OECD, 2007). New Zealand, The Czech Republic and Japan spend less relative to GDP, while the UK, US, Germany, France, Denmark and Canada all spend more, of the ten countries studied.
- **Sectoral**: **The ROI for health R&D is higher than the average ROIs for R&D in other sectors**. According to Shanks and Zheng (2006), the ROI for health R&D of 117% is higher than the market and manufacturing sectors (each around 50%) and agriculture (around 24%), but lower than the mining sector (159%) and the wholesale and retail trade sector (a very high 438%). The health R&D ROI is also higher than the average gross rate of return presented within the Productivity Commission (2007) review (65% to 85%).

[25] The OECD estimate is a little higher than the ABS estimate, which is closer to 0.3% of GDP.

Case studies

- To place the modelling in the context of real world examples, four studies were reviewed based on R&D activity translating into wellbeing gains.
  - The development of Gardasil to vaccinate against 70% of cervical cancer has potential returns in terms of wellbeing of around 2.5:1.
  - Prevention or delay of vision loss associated with diabetes, or vision gain through intensive hyperglycaemic control means 4,111 fewer people with visual impairment by 2025 representing savings of $7.6 billion (in 2008 prices).
  - Decreasing incidence of Alzheimer's disease by 5% through Australian R&D will result in savings of $10.3 billion by 2050. Over half of these savings would be in the residential care sector.
  - The value of a Group A Streptococci (GAS) vaccine could provide health benefits valued at $319.7 million per year, of which $78.4 million would be realised by indigenous Australians.

7.2 IMPLICATIONS AND RECOMMENDATIONS

This report has confirmed that the ROI in health R&D, measured in terms of the value of life and wellness gained, continue to be exceptional. What does this imply for Australian policy responses?

Federal government initiatives following the Wills Review stepped up Commonwealth investment in health R&D, with a view to reversing its previous decline. Many initiatives have been put in place that aim to make more sizeable and smarter health R&D investments primarily through collaboration and workforce improvements.

Ongoing issues are as follows.

- Australia appears to have some comparative advantage in health R&D given our levels of discovery, publications, citations and other evaluative criteria relative to our size in the global market.
  - Economic theory suggests we should specialise in areas of comparative advantage. Yet Australia has a deficit in the balance of trade in pharmaceuticals, medical equipment and other health and medical industries that, given our ageing population and increasing demand for medical treatments, is not likely to improve on its own.
  - There is potentially more that can still be done in relation to translating health R&D into Australian-owned products. Even for Gardasil, only 13% of royalties are to Australian entities.
  - The commercial benefits are not included in the benefits measured in this report, which just measures wellbeing benefits. Although commercial benefits are likely to be small relative to the value of wellbeing benefits, there is scope for them to become more substantial.
- As the investment in health R&D increases, the law of diminishing marginal returns suggests that average returns may decline a little, but they are currently still outstanding relative to many alternative investments.
- There remains a key role for the public sector in basic science and applied research, in reducing the social and economic burden of disease.
- Collaborative partnerships with the private sector should be carefully and strategically nurtured, particularly with a view to attracting ongoing high levels of funding growth

from overseas sources. The benefits of collaborative efforts should continue to be monitored by monitoring health R&D expenditure by source of funds.

- Priorities need to be balanced with risk in the R&D portfolio, so that promising lines of attack against minor sources of mortality and morbidity are included as well as higher risk investigations against major ones. It is vital that, due to 'critical mass' and serendipity, a broad coverage of research areas is maintained.
- Without 'picking winners', there is a need to invest in R&D areas where burden of disease is likely to grow in the future, to curb that growth – in particular in areas with high disability burden, such as mental health, neurodegenerative diseases and musculoskeletal conditions.
- In relation to indigenous health, the Rudd Federal Government's commitment to eradicating the mortality gap between indigenous and non-indigenous Australians is a worthy commitment. It will be important to deliver appropriate services and interventions to that end and this requires an evidence basis of what works best in a resource constrained world. Health R&D is required to supply that evidence.

Health R&D can be seen as an investment in wellness with exceptional returns. The corollary is that public finance should be strategically targeted to cost-effective high priority R&D areas. The ageing of the baby boomer population, who started turning 60 from 2005, will place unprecedented demands on the Australian health system in particular in relation to chronic conditions of ageing such as Alzheimer's disease, arthritis, cardiovascular disease and cancer. With dependency ratios (those over 65 years relative to the whole population) set to rise from 12% to 25% and Australian Government health spending set to rise from 3.8% to 7.3% of GDP over the next 40 years (Australian Government, 2007), the projected cost and impact of chronic illness is forecast to present a challenging burden whose greatest hope is new R&D breakthroughs.

> *'The new view of health economics should shape the way we think about health policy… Over the last half century, economic welfare from health care expenditures appears to have contributed as much to economic welfare as the rest of consumption expenditures. It is an intriguing thought to contemplate that the social productivity of health-care spending might be many times that of other spending.' (Nordhaus, 2002:42).*

The past 40 years have witnessed an amazing epidemiological transition, riding on the technological wave. Our generation has benefited from standards of living never before experienced. In this country we now face a future full of promise and challenge for preventing and treating disease for ourselves and our children, by virtue of applying recent dramatic advances in genetics, bioengineering, neuroscience and molecular and structural biology. The challenge is to ethically translate the promise into the reality of new understanding, communication, collaboration and improved clinical outcomes.

This report has shown that on average every dollar invested in this challenge in Australia is likely to be recouped as highly valued healthspan, and in most cases, many times over. Health R&D remains an exceptional investment, with exceptional returns.

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