Research Priorities: Dementia.

A submission to the National Research Priorities Taskforce.

By Jerome Maller, Centre for Mental Health Research, ANU

and

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August 2002.

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Dear Sir,

I have pleasure in enclosing a submission from Alzheimer’s Australia (and Alzheimer’s Australia Research).

Jerome Maller, at the Australian National University Centre for Mental Health Research, and Glenn Rees, National Executive Director of Alzheimer’s Australia, have prepared this submission. In doing so they have had the opportunity of talking with Professor Henry Brodaty, Professor Tony Broe, Professor Tony Jorm and Dr Mike Bird.

While those discussions have helped inform and shape this submission, the views expressed are of course those of Alzheimer’s Australia (and Alzheimer’s Australia Research).

I should like to thank Jerome Maller and Glenn Rees for the work they have done in putting this submission together.
I should also like to thank Janssen-Cilag for funding this project.

I very much hope that this submission is helpful to you in your important task of determining criteria for setting research priorities and that you will agree dementia should rate a high priority.

Thank you for this opportunity of making a submission.

Yours sincerely,

Dr Robert Yeoh
President
Alzheimer’s Australia

23rd August 2002
Table of Contents

Executive Summary 1

1. Background 3

2. Criteria for National Health Research Priorities 4
   Prevalence 4
   Disease Burden and Health System Cost 6
   Cost to Carers 7
   Cost to Employers 7

3. Dementia as a Research Priority within Mental Health 7
   Publications and Competitive Funding 8

4. Breakdown of Current Dementia Research 9
   Comparison of Dementia Research Goal Grant Funding to Other Mental Health Disorders 10
   Research Settings 11

5. What Should Be the Priorities for Dementia Research? 13

References 16

List of Figures

Figure 1 Projected increase in dementia cases, elderly population and total population for Australia, 1995-2041. 4
Figure 2 Disease burden and health system cost as a function of type of disorder. 6
Figure 3 Publications and grant funding as a function of type of disorder. 8
Figure 4 Research topics of dementia publications and grants. 9
Figure 5 Percentage of cumulative research grant funding for dementia as a function of research goal. 10
Figure 6 Distribution of competitive grant funding for each mental health disorder across total settings. 11
Figure 7 Distribution of grant funding across research settings for dementia and other disorders. 12
Figure 8 Distribution of grant funding for dementia only according to research setting. 12

List of Tables

Table 1 Scheme for classifying content on current research. 7
Table 2 Standards to compare with. 8
Table 3 Distribution of competitive research grant funding according to some of the types of mental disorders and research goals. 10
Table 4 Priority rating for research settings. 11
Executive Summary

Criteria for National Health Research Priorities

Research is fundamental to the vision of Alzheimer’s Australia of a society committed to the prevention of dementia, while valuing and supporting people living with dementia. The absence of easily accessible information about what research dollars are going where makes it difficult for community organizations to assess what research priorities are or what is happening within their own particular fields of interest.

In contrast to Alzheimer’s Associations in the U.S.A. and the United Kingdom, the Association has very limited resources to promote research through Alzheimer’s Australia Research – small grants totaling annually some $30,000. In 2000, dementia related research grants in Australia totaled around $2.5million.

The Association believes that by any benchmark dementia should be a high health research priority. This is so because:
- Dementia already represents a significant cost to the health care system.
- These costs are likely to grow dramatically as the numbers of people with dementia increase rapidly by the middle of this century.
- There are significant costs to families and carers of people with dementia.
- Dementia is a major cause of disability burden – dementia is currently the third leading cause of disease burden among women and by 2016 it will be number one.
- Overseas work has started to identify significant costs for employers as a result of dementia care.

Equally, the criteria should take into account the evidence that while morbidity related to chronic systemic diseases (particularly cardiovascular diseases, lung diseases, and cancer) appears to be declining, or being compressed to the end of life, the morbidity related to neurodegenerative disease, particularly the dementias, is increasing with advanced old age.

Even within the mental health area, recent work done by the Centre for Mental Health Research at the ANU suggests that dementia has not been given a high priority. Of published articles on mental health disorders, a relatively low percentage dealt with dementia at the time of the ANU study and only a small percentage of those dealt with dementia treatment, service research, epidemiology, prevention and promotion. By contrast rather more was directed towards biological research.

From a consumer perspective research priorities could be thought of in three ways:
1. Research directed towards identifying the causes of dementia.
2. Research directed towards finding a cure or delaying the disease.

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1 Research priorities in mental health.
Available evidence suggests that within the limited funding available for research on dementia in Australia, biological work has received a relatively high priority.

As regards to cure it is evident both overseas and within Australia that the large pharmaceutical companies are spending very significant resources on medications and vaccine research.

A particular gap both in Australia and overseas seems to be in the area of research into clinical practice and care. This is an area that could well be designated a priority in Australia, not least because of the high standard of its aged care system and dementia care relative to that elsewhere.

It is recommended that:
- The criteria set for determining research priorities in the area of health should include numbers of people affected, costs (including health system, carer and employer costs), trends in morbidity and degree of disability burden.
- On the basis of those criteria dementia should without question be regarded as a high priority for research in this millennium.
- Priorities can be established in terms of cause, cure and care, but a continuing priority in Australia should be given to biological research directed at causes and prevention and a higher priority established with respect to care – Suggested priorities for care related research are identified in this submission.

It is further recommended that if there is to be confidence in the wider community in the allocation of current research dollars in relation to the criteria there is an urgent need for publicly available information that shows the allocation of the health research dollar between health areas and, within those, on chronic diseases such as dementia.

Investing in dementia research is investing in what is important in ageing, and therefore, it is investing in the future and the quality of life of people with dementia, their families and carers. But dementia is not a disease in isolation and a multi-disciplinary and collaborative approach is required to address the complex inter-relationships of issues in this area.
1. **Background**

There is a limited information base on which to base the assessment of the extent to which the priority accorded to research on dementia in Australia and elsewhere is consistent with criteria for setting research priorities.

There is no doubt about dementia as a global epidemic, with an estimated 37 million people worldwide currently diagnosed with the illness, and Alzheimer’s Disease (AD) being responsible for causing the majority of the cases. With the ageing of populations, this figure is projected to rapidly increase in the next 20 years².

In Australia, health system cost of dementia for 1993-1994 was in the order of $714million per year. In 2000, the dementia-related competitive research grants (mainly project grants) from main funding sources totaled nearly $2.5million – three quarters of this was from the NH&MRC, representing less than 1.5% their total funding pool of around $172million (Jorm et al., 2001). In 2002, Alzheimer’s Australia Research Ltd has about $40,000 to extend towards research grants.

In 2002, the US federal government estimates spending at approximately $1.12billion (US$598.9million) for AD research³. The direct and total costs of AD in the US have been estimated at $1billion (US$536million) and $3.28billion (US$1.75billion), respectively, for the year 2000⁴. The Alzheimer’s Association (US) has granted nearly $225million (US$120million) in research funding since 1982.

A UK document demonstrates the information base that is desperately needed in Australia to have an informed view about research priorities. Commissioned by the Alzheimer’s Research Trust (UK), the report “Cost of Alzheimer’s Disease and Level of Research Funding” (Lowin, McCrone, & Knapp, 2000) summarises evidence on the costs of AD in the UK, and levels of research funding on this illness and its treatment. Furthermore, comparisons are made with three other major causes of mortality in the UK (heart disease, cancer, and stroke). It is estimated that the cost of AD to the UK in 2000 was between $20.23billion and $42.77billion (£7.06billion and £14.93billion), and that their Department of Health spent around $1.43billion (£500million) on all research⁵.

In 1998/9, 46% of R&D support money in the UK was attributed to five disease areas (cancer, CVD/stroke, mental health, primary care), with $5.93million (£2.07million) (0.6%) of that support money nationally for AD. In terms of research funding, support has been estimated at less than 1/30 of the support funding for cancer research and less than 1/20 of that received by CVD and stroke research combined⁶. In 2001, the UK government spent only $23.49 million (£8.2million) on dementia research – a drop in the ocean compared to the $544.32 (£190million) invested in cancer research. The point

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³ [www.alz.org/ResourceCenter/FactSheets/FSAlzheimerStats.pdf](http://www.alz.org/ResourceCenter/FactSheets/FSAlzheimerStats.pdf)
⁵ UK Department of Health, 2000
⁶ [http://secure.ebizz.co.uk/alzheimers/site/costofalzreport.htm](http://secure.ebizz.co.uk/alzheimers/site/costofalzreport.htm)
about these figures is that it is possible in the UK to have data on the relative health priorities in relation to health costs.

The UK Alzheimer’s Research Trust is currently funding four major five-year programme grants totaling more than $6.3million (£2.2million)\(^7\), and the Alzheimer’s Society has invested more than $12.89 (£4.5million) in research through voluntary donations.

2. Criteria for national health research priorities

**Rising Prevalence**

Over 160,000 Australians currently have dementia\(^8\). With the ageing population, we can expect a proportionate increase in the number of people affected by dementia including carers (who are ageing as well), within the next few decades. As a result, it is estimated that in 2006 there will be a rise to 183,000 people affected by dementia, and in 2011 to 210,000 people (Figure 1) (Henderson & Jorm, 1998). Put another way, between 1995 and 2041 the number of people with dementia in Australia is expected to increase by 254% to over 450,000 people because the old old (who are the most likely to suffer from dementia) are expected to increase at a faster rate than either the total population or the young old (Henderson & Jorm, 1998). In other words, while our total population will increase by only 40%, our population with dementia will increase by three and a half times. In addition, dementia affects many more than those represented by these figures as there are a large number of people with early symptoms.

Figure 1. Projected increase in dementia cases, elderly population and total population for Australia, 1995-2041\(^9\).
While morbidity related to chronic systemic diseases (particularly cardiovascular diseases, lung diseases, and cancer) appears to be declining, or being compressed to the end of life, the morbidity related to neurodegenerative disease, particularly the dementias, is increasing with advanced old age. This ongoing decline in mortality has been attributed to new public health measures, including changes in major risk factors for systemic degenerative diseases such as smoking, diet and exercise, as well as advances in medical technology and drugs. However, these measures have not been demonstrated to be protective against the chronic neurodegenerative diseases. Other protective factors for these diseases may be found however, particularly those related to early brain growth and development, and to intellectual ability and education in early life.\footnote{Population Ageing, Human Lifespan and Neurodegenerative Disorders: A Fifth Epidemiologic Transition (Broe, G.A., In Press). Swets & Zeitlinger Publishers, USA.}

The Sydney Older Persons Study (1991 to 2002) showed that disability due to the chronic systemic diseases is being reduced or delayed, however systemic disease related disability is being replaced by a new wave of disability due to neurodegenerative disorders, specifically dementia, which are increasing exponentially in the most rapidly growing sector of the population, the “old-old”, forming a new disease transition.

Lilienfeld and Perl (1993) used US Census Bureau population estimates to project the annual death rate from 3 neurodegenerative diseases (dementia, PD and MND) and from 6 comparison systemic diseases (liver cirrhosis, colon cancer, lung cancer, cancer of the female breast, multiple sclerosis, and malignant melanoma) over the period between 1990 and 2040. Assuming that the US disease-age-gender-race-specific death rates for these years remained constant over the period between 1990 and 2040, they found that neurodegenerative disease mortality increased by 119-231%, depending on the population model used. For the “middle” population growth model the increase was 166%, with the major component being deaths due to dementia. The increases in mortality for the 6 comparison diseases ranged from 52% (multiple sclerosis) to 130% (colon cancer). A number of factors make it likely that these projections for neurodegenerative disease mortality are underestimates including under-ascertainment on death certificates and the conservative nature of the US Census Bureau estimates of population ageing. Furthermore the comparison with cancer deaths is with a category of systemic disease in which mortality is either still rising or static or showing the slowest falls, in comparison with other common systemic diseases, such as cardiovascular and lung disease, in which mortality is declining rapidly.
Disease Burden and Health System Cost.

It could be argued that diseases which contribute the greatest burden nationally should receive the most research attention. Dementia is currently the third leading cause of disease burden among women, and by 2016 it will be number one\(^1\). With men, dementia is currently the fifth leading cause of disease burden and is estimated to remain there by 2016. It is ahead of respiratory diseases, breast cancer, colorectal cancer, cancer, diabetes and arthritis. When disease burden is examined (Figure 2), dementia contributed a hefty percentage of the total mental health system (18.6\%)\(^2\).

Another standard for judging which diseases should be receiving research attention is their health system cost. Figure 2 reveals that dementia accounted for the largest percentage of mental health system costs (24.8\%) and it has been argued that mental health is under-funded in the total health care system. It has been estimated that health system costs of dementia in Australia for 1993-1994 was in the order of $714million per year (Mathers et al., 1999). This is likely to be a considerable underestimate, because much health expenditure is not specifically attributed to dementia in hospital and other health service statistics. At least 30\% of residents in low care facilities and 60\% of residents in high care facilities have a diagnosis of dementia (Rosewarne et al., 1997), but fewer than 5\% of all people with dementia live in dementia specific settings (occupying less than 6\% of all residential aged care places; Rosewarne et al., 2000).

Figure 2. Disease burden and health system cost as a function of type of disorder\(^2\).

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\(^2\) Jorm et al., 2001.
Cost to Individuals and their Carers

The health system cost is only part of the total cost because it does not include the costs - both financial and emotional - to individuals and their families and carers. Information on the Carers Australia web site suggests that many carers experience financial and health disadvantage as a consequence of their caring role. Carers may incur higher costs, work less hours and earn less income. However, we have only a very incomplete picture of costs to individuals – this needs to be corrected with a concerted program of studies that systematically address these questions.

Cost to Employers

We know of no work in Australia which has investigated the cost of AD to employers. Recent work in the USA suggests that the total cost to businesses of workers who are caregivers of people with AD has been put at $68.3 billion (US$36.5 billion), and the total cost to businesses of health care for people with AD at $46 billion (US$24.6 billion).

3. Dementia as a research priority within mental health

In the absence of any more broad ranging analysis across major diseases, the work of the National Mental Health Working Group in 1999 on research priorities in mental health provides some evidential basis for examining what priority is given to research on dementia. They established a consultancy to provide information about current research projects and gaps in the research agenda. The first step was to find out what research is currently being done, and the second was to compare the current research against various standards suggesting what should be done. Dementia was included in the scope of this consultancy and the relevant data on this topic are presented here.

In order to respond to the first step, a search was conducted which yielded 685 published articles from 1998 with an Australian senior author, as well as 326 competitive grants in the year 2000 from NHMRC (source of 75.2% of funds), ARC (11.9%) and SPIN databases (12.9%). The data from these sources was classified into the type of mental disorder investigated, the goals of the research, and the setting (Table 1).

Table 1. Scheme for classifying content on current research.

| ♦ Type of mental disorder investigated |
| ♦ Goals of the research (e.g. genetics, risk factors, service evaluation) |
| ♦ Setting (community, primary care, specialist care) |

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14 [www.alz.org/Media/newsreleases/current/062602ADCosts.pdf](http://www.alz.org/Media/newsreleases/current/062602ADCosts.pdf)
The standards by which they were compared to (Table 2) were prevalence, disease burden, health system expenditure, and the rating priorities of stakeholders.

Table 2. Standards to compare with.

- Prevalence
- Disease burden
- Health system expenditure
- Rating priorities of stakeholders (researchers, committees that evaluate grants, clinical service providers, consumer and carer advocates, and mental health administrators)

Publications and Competitive Funding

Results revealed that mental health received $20.4 million (8.9%) of total competitive research funding. Substance abuse (Figure 3) was the most often published of all the mental health disorders included in the search (25%) and the most highly funded (23%). By contrast, only 8% of publications and 12% of grant funding was related to dementia, making dementia ranked fifth for publications and third in terms of funding. Contrasted against disease burden and health system cost (Figure 2), it is obvious from Figure 3 that dementia is severely underfunded.

Figure 3. Publications and grant funding as a function of type of disorder\(^\text{15}\).

\(^{15}\) Jorm et al., 2001
4. **Breakdown of Current Dementia Research**

In relation to research publications and grants on dementia (Figure 4), biological research was clearly the most represented (46% of publications and 71.2% of grants), while epidemiology and description and assessment were the next highest types. A relatively lower percentage of grants (3.6%) dealt with treatment for dementia (10.7% of publications), while prevention and promotion received the least amount of funding (0.1% of grants, no publications).

Figure 4. Research topics of dementia publications and grants\(^{16}\).

\(^{16}\) Jorm et al., 2001
Comparison of Dementia research goal grant funding to other mental health disorders and their research goal grant funding

It is evident when comparing to other disorders and research goals (Table 3), that prevention and promotion for dementia received a low percentage of funding. The finding that a proportionally low amount of dementia research grant funding was spent on treatment (Figure 4) is made even more obvious when compared to the proportion that was spent on treatment for other disorders, or for disorders overall (Figure 5).

Table 3. Distribution of competitive research grant funding according to some of the types of mental disorders and research goals17.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Description</th>
<th>Biological Research</th>
<th>Treatments</th>
<th>Health Services</th>
<th>Epidemiology</th>
<th>Prevention &amp; Promotion</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance abuse</td>
<td>239 (5.1)</td>
<td>1,079 (23.1)</td>
<td>664 (14.2)</td>
<td>379 (8.1)</td>
<td>106 (2.3)</td>
<td>239 (5.1)</td>
<td>1,963 (8.5)</td>
</tr>
<tr>
<td>Childhood conditions</td>
<td>226 (8.1)</td>
<td>571 (20.4)</td>
<td>565 (20.2)</td>
<td>43 (1.6)</td>
<td>823 (29.4)</td>
<td>559 (20)</td>
<td>13 (0.5)</td>
</tr>
<tr>
<td>Affective disorders</td>
<td>249 (10.5)</td>
<td>848 (35.6)</td>
<td>316 (13.3)</td>
<td>121 (5.1)</td>
<td>440 (18.5)</td>
<td>206 (8.6)</td>
<td>203 (8.5)</td>
</tr>
<tr>
<td>DEMENTIA</td>
<td>262 (10.8)</td>
<td>1,731 (71.2)</td>
<td>88 (3.6)</td>
<td>58 (2.4)</td>
<td>176 (7.2)</td>
<td>3 (0.1)</td>
<td>114 (4.7)</td>
</tr>
<tr>
<td>Suicide</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>17 (5.6)</td>
<td>0 (0)</td>
<td>87 (28.7)</td>
<td>158 (51.9)</td>
<td>42 (13.8)</td>
</tr>
<tr>
<td>Mental retardation</td>
<td>15 (0.8)</td>
<td>1,577 (83.3)</td>
<td>139 (7.4)</td>
<td>122 (6.4)</td>
<td>40 (2.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Figure 5. Percentage of cumulative research grant funding for dementia as a function of research goal17.

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17 Jorm et al., 2001.
Research Settings

When the research settings were rated, dementia received the third highest funding within mental health from all competitive grants combined (Figure 6). Primary care and community research were seen by stakeholders as higher priorities than research in specialist settings. By contrast, most research is actually carried out in specialist settings (Table 4) than in primary care or the community (Figure 7). This is particularly true for dementia, whereby no grant funding at all was spent on research in primary care settings (Figure 8).

Table 4. Distribution of dementia research across settings.

<table>
<thead>
<tr>
<th>Research setting</th>
<th>% of research</th>
<th>% of funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>♦ People in the general community</td>
<td>30</td>
<td>21.2</td>
</tr>
<tr>
<td>♦ Patients in primary care</td>
<td>3.4</td>
<td>9.7</td>
</tr>
<tr>
<td>♦ Patients in hospital or other specialist settings</td>
<td>66.6</td>
<td>69.1</td>
</tr>
</tbody>
</table>

Figure 6. Distribution of competitive grant funding for each mental health disorder across total settings\(^\text{18}\).

\(^{18}\) Adapted from data from Jorm et al., 2001.
Figure 7. Distribution of grant funding across research settings for dementia and other disorders\textsuperscript{19}.

Figure 8. Distribution of grant funding for dementia only according to research setting\textsuperscript{19}.

\textsuperscript{19} Adapted from data from Jorm et al., 2001.
5. What should be the priorities for dementia research?

Consumers, at least in the area of dementia care, have not had much involvement in priority setting in research. There is a need to survey Australian consumers on their priorities but broadly the priorities identified by the Alzheimer’s Society in the UK through consultation probably cover the ground well:

1. Research directed at the causes of dementia:
   - Basic science research into causes of dementia.
   - Epidemiological research on the risk factors for dementia (lifestyle, diet, personality, environment).
   - Genetics research on dementia.
   - Investigation of triggers for dementia and mechanisms of disease prevention.
   - Biochemical research on the brain.
   - Research on biochemical markers which could plot the course of the many dementias.
   - Research on symptoms similar ME in people with early onset dementia.

2. Research directed at a cure:
   - Development of new drug treatments.
   - Research on prevention.
   - Stem cell research into dementia.
   - The cure for Alzheimer’s disease.
   - Disease modifying therapy.
   - Vaccine research.
   - Alternative and complimentary therapy.
   - Availability of drugs for early onset patients.

3. Research directed at dementia care:
   - Research on diagnosis (early diagnosis, differential diagnosis, diagnostic test).
   - Research on effects of care standards (community care, long term care, terminal care, care needs and planning).
   - Improving dementia in primary care GPS.
   - Research on staff training (nurse, care workers, home car staff etc).
   - Research on carers support.
   - Alleviating distressing behavioural symptoms.
   - Detection and alleviation of pain for non-verbal patients.
   - Medication for nursing homes.
   - Research into true levels of awareness (insight) in dementia\(^{20}\).

The pharmaceutical industry is investing considerable sums in new drug treatments with most of these major companies researching and developing at least one dementia-related product. For this reason, notwithstanding its importance, research in this sort of direction will probably not be the highest priority for government and research agencies.

\(^{20}\) http://www.alzheimers.org.uk/
Biological research into the causes of dementia is currently given a high priority, and this should remain so if prevention is to become a reality. However, dementia is not a disease in isolation and the need is for an approach which:

- Is multidisciplinary and collaborative within and between disciplines, which will bring different research groups together while maintaining scientific rigor. Most funding is currently spent on heart, lung and kidney research, but the brain is intimately linked to these organs. Increasing collaboration will enable researchers to investigate and consider the role of other disorders in producing dementia. Furthermore, most people with dementia will have issues in addition to their dementia. Increased collaboration will enhance clinicians’ ability to deal with these issues.
- Examines the impact of other conditions upon dementia with a view to promoting prevention. For example, it has been shown that diabetes confers a relative risk of 1.5 of developing AD or 3.0 if you combine AD with cerebrovascular dementia (Peila et al., 2002), and that life style intervention can result in up to 58% reduction in risk of diabetes mellitus (Knowler et al., 2002). Extrapolating, this would reduce the prevalence of diabetes mellitus from 110 per 1000 to 48 per 1000 people and as a consequence dementia.
- Focuses on the healthy brain ageing and why some people’s brains develop neurodegenerative diseases and not others.
- Addresses the interconnections of the many different causes of dementia, of which AD is the most common.

Research into dementia care is very under-represented in Australia, yet Australia has an aged care system that is world class in many respects. Australia needs to demonstrate its expertise through rigorous analysis of service delivery if it is to succeed in exporting its expertise.

It is beyond the competence of the Association at this time to detail priorities within the biological and cure areas of research. However, in the area of dementia services the Association believes that research could focus on:

- The key factors that make staying at home more or less likely - including understanding better the role of psychosocial approaches to keeping people with dementia at home.
- The importance of new technology in the design and modification of homes.
- The importance of autonomy in user satisfaction with long-term care and the role of the consumer as budget holder.
- The evidence available for achieving better co-ordination of services - in the community and at discharge from hospital in particular.
- The meaning of domestic/homely in the context of residential care.
- The advantages and disadvantages of early diagnosis for a consumer and the role of memory clinics.
- The profile of the minority who will need dementia specific care.
Neuro-degenerative disease is the key to ageing research – and Alzheimer’s Disease is the most important single cause. As a result of us having become better and better at treating the major killers in infection, cancer and heart disease so degenerative diseases, and particularly degenerative diseases of the nervous system should become a pre-emptive target for research. Investing in dementia research is investing in what is important in ageing, and therefore, it is investing in the future.
References


