



A CALL TO ACTION

THE GLOBAL RESPONSE TO DEMENTIA THROUGH POLICY INNOVATION

Report of the WISH Dementia Forum 2015

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مؤتمر القمة العالمي للابتكار في الرعاية الصحية
World Innovation Summit for Health

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CONTENTS

03	Foreword
04	Executive summary
08	Dementia: The challenge today and the path ahead
12	The response: Effective approaches and innovative solutions
12	Mobilize society to increase awareness, education and participation
16	Prevention and risk reduction to decrease prevalence of dementia
19	Diagnosis and care innovations to improve quality of life
22	Health and social care systems optimized for dementia care
24	Cure or disease-modifying treatments to minimize disease burden
25	Research, trials and regulatory pathways to accelerate drug development
28	Innovative finance mechanisms to increase funding across the arc of disease management
33	Policy recommendations
35	Acknowledgments
37	References

FOREWORD

The social and economic burden of dementia is clear enough today. Yet the future costs to societies and economies will be enormous without significant intervention now to change care practices and the course of disease.

World leaders and heads of state, including World Health Organization (WHO) Director-General Dr Margaret Chan and UK Prime Minister David Cameron, are joining international organizations in calling for a global effort to address dementia. In 2012, WHO released the report *Dementia: A public health priority*,¹ and in 2013 the UK led a Dementia Summit that brought together G8 health and science ministers, researchers, pharmaceutical companies and charities from around the world to address the need for improved care, better treatments and discovery of a cure for the diseases that cause dementia.

The momentum generated by the G8 Summit has been carried forward by many Legacy Events, the formation of the World Dementia Council and appointment of a World Dementia Envoy. Now WHO and the Organisation for Economic Co-operation and Development (OECD) are devoting more resources to dementia and sustaining the G8 commitments. This new activity adds to the valuable work already underway by organizations such as Alzheimer's Disease International, the Alzheimer's Association, the 10/66 Dementia Research Group and many others.

It is critical to ensure that those at the forefront of policy, research, drug development and care co-ordinate efforts toward identifying disease-modifying interventions, educating the public and implementing better care practices, all supported through aligned regulatory strategies and sustainable funding mechanisms. It is the aim of the World Innovation Summit for Health (WISH) to offer concise, actionable recommendations to health ministers and high-level policymakers globally. This report is intended to provide an overview of the global dementia landscape and to propose a way forward to an improved future, where accessible care and treatment will contribute to reducing the global burden of dementia.



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EXECUTIVE SUMMARY

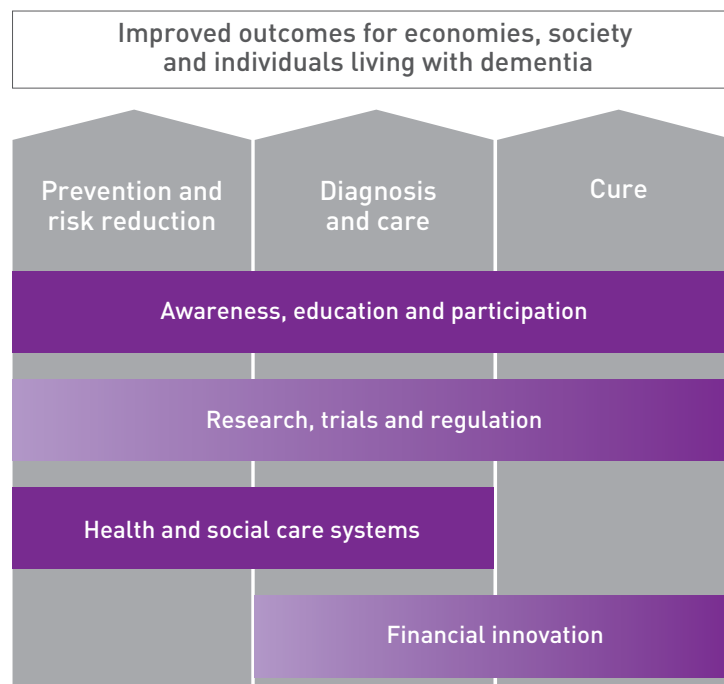
Dementia is the umbrella term for a number of symptoms relating to decline in memory and other cognitive functions severe enough to interfere with an individual's daily living activities. Types of dementia include Alzheimer's disease (AD), which accounts for 50–70 percent of all cases, vascular dementia, and less common forms such as frontotemporal dementia and Parkinson's disease dementia.²

Worldwide 44 million people live with dementia, and this figure is expected to reach 135 million by 2050.³ Meanwhile, the cost of care reached an estimated \$604 billion worldwide in 2010, equivalent to one percent of global gross domestic product (GDP), and costs are expected to exceed \$1 trillion annually in the US alone by 2050.⁴ Dementia has severe effects on the quality of life of individuals and causes tremendous strain on caregivers and healthcare systems.

This report outlines key issues in understanding dementia and the need to tackle the burden globally. It looks at solutions that are currently available and makes recommendations to policymakers to accelerate prevention, improve care and treatments, and potentially cure the diseases that lead to dementia.

To address dementia in a comprehensive way there are three primary themes to consider: prevention and risk reduction, diagnosis and care, and cure, as illustrated in Figure 1.

Figure 1: The WISH Dementia Forum framework



The shading gradation of the four cross-cutting bars in the figure reflects the applicability for each area.

Prevention and risk reduction

There is growing evidence that preventative measures for dementia risk factors such as hypertension and diabetes may reduce the prevalence of disease or delay the onset of impairment to some extent.⁵ Many of the strategies to improve cardiovascular health and non-communicable disease outcomes are also likely to have a positive influence on dementia prevalence. Meanwhile, clinical researchers are aiming to develop a drug to delay the onset or progression of AD, and five prevention trials are now underway.

Diagnosis and care

There is no cure or highly effective treatment for dementia, so care is the primary option available to manage this condition. However, care cost estimates are increasing, and caregivers, who are often the children or family of the individual, are facing a significant burden. While innovations in care are emerging through advances in technology, supported by the development of 'dementia-friendly' environments and infrastructure, there is more to be done. We must continue to develop well-evidenced and cost-effective best care practices that improve the quality of life for individuals with dementia and reduce the burden on caregivers and society.

Cure

No cure exists to restore cognitive function for people already diagnosed with dementia. The scientific pathway toward a cure is uncertain, and the research and development required will take considerable time and financial resources. The World Dementia Council and other organizations have called for the development of a cure or disease-modifying therapy by the year 2025, and efforts are being undertaken globally to lower the barriers to progress.

This report also describes four main mechanisms to improve outcomes for individuals with dementia, as represented by the cross-cutting bars in Figure 1.

Awareness, education and participation

Global awareness and understanding of dementia lags behind other diseases. It is often mistakenly considered a normal part of aging and, in many cultures around the world, people with dementia experience significant stigma. It is essential to increase awareness about dementia diagnosis, prognosis and treatment options to individuals with dementia, their families, healthcare providers, politicians, policymakers and to the general public. Increased participation is needed in all sectors, from patient enrollment in clinical trials to public participation in Dementia Friends campaigns.

Research, trials and regulation

Advances in research across prevention, care and cure are essential to tackle dementia comprehensively. To accelerate these advances, however, there is a need for increased clinical trial investment and innovation, and improved infrastructure to decrease the time and cost to execute trials. Commensurate with the burden of

dementia and unmet medical need, some risk in regulatory strategies may accelerate the timelines for drugs to move from the lab to marketplace.

Health and social care systems

Comprehensive care for people living with dementia will require co-ordinated health and social care systems with a well-trained workforce. Case managers and care co-ordinators are necessary to help direct individuals to services best suited to changing needs as diseases such as AD progress. While ensuring an optimal quality of life for individuals with dementia, healthcare systems must also offer programs to support caregivers.

Financial innovation

Government funding needs to increase, but alone it will not be sufficient to raise the resources required to address the challenge of dementia. Innovative financial mechanisms to attract private capital could increase investment in drug development assets and pay-for-success models of care. Examples discussed in this report include crowd equity, hybrid venture funds and social impact bonds.

The WISH Dementia Forum has developed 10 key policy recommendations for governments to consider. These recommendations aim to achieve improved outcomes for individuals living with dementia, for economies struggling to pay for the costs of care, and for societies facing the increasing prevalence and burden of dementia. The recommendations are directed at policymakers and outline what can be done now to reduce the burden caused by dementia today and in the future.

Recommendations

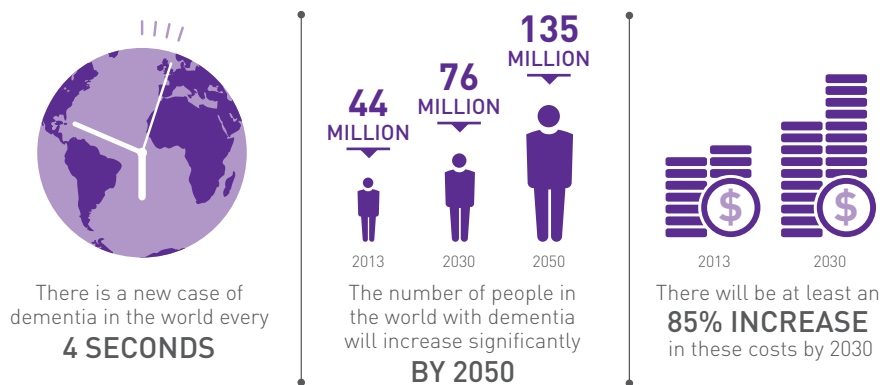
- 1. Develop a plan to address dementia nationally:** Create a national plan to address dementia in every country and/or include dementia as a priority in country-specific and United Nations (UN) plans for prevention and control of non-communicable diseases.
- 2. Increase awareness of dementia:** Engage the public, patients and caregivers by carrying out awareness campaigns (such as Dementia Friends), developing dementia-friendly environments and supporting the creation of Alzheimer's Associations in every country.
- 3. Expand healthy living to include brain health:** Embed brain health in public health strategies, taking a life course approach to healthy aging.
- 4. Improve the evidence base for prevention:** Fund studies and prevention trials that help to understand the effectiveness of risk reduction strategies and advance efforts to find a therapeutic intervention to delay or prevent the onset of dementia.
- 5. Improve dementia care:** Implement well-evidenced and cost effective best practices in dementia care, as appropriate to regional healthcare systems' available resources.

- 6. Strengthen integrated and co-ordinated health and social care systems:** Put in place financial incentives to create a well-trained workforce that will improve the quality of life for people living with dementia and reduce the burden on informal caregivers.
- 7. Institute and fund longitudinal studies:** Improve surveillance of people with, or at risk of developing, dementia to understand disease progression better and provide characterized cohorts for participation in clinical trials.
- 8. Reduce barriers to drug development:** Optimize the path of medicines from research to market. For example, offer accelerated approval and market protection, and support the Integrated Development Plan to increase dialogue between regulatory agencies, payers, scientists and policymakers.
- 9. Commit government investment of at least one percent of a country's cost of care:** Invest in basic, clinical and applied dementia-related research and technologies to ensure financially sustainable healthcare systems in the future via:
 - Budget increases to encourage capacity building to recruit more scientists and clinicians.
 - More resources to diversify therapeutic approaches.
 - International strategic research plans to provide finance co-ordination to minimize duplication and encourage funding of gaps and opportunities in research.
- 10. Facilitate innovative finance mechanisms:** Attract private investment among a wider range of investors and increase financial resources across the arc of disease management.

DEMENTIA: THE CHALLENGE TODAY AND THE PATH AHEAD

In 2013, approximately 44 million people around the globe were living with some form of dementia. This number is projected to almost double every 20 years, to 76 million in 2030 and to 135 million by 2050, according to Alzheimer’s Disease International’s (ADI) 2013 World Alzheimer’s Report.⁶ The cost of care for dementia worldwide reached an estimated one percent of global GDP (\$604 billion) in 2010. If dementia care was a country, it would be the world’s 18th largest economy.⁷

Figure 2: Growing global burden of dementia



Source: ADI World Alzheimer’s Reports and 2013 G8 Policy Brief

Human life expectancy has doubled in the last 200 years due to improvements in medicine, diet and the environment.⁸ Fewer individuals are dying young, and across the globe people are living longer. According to the UN, by 2050 there will be 83 countries where 20 percent or more of their population is aged 65 and over.⁹ As the prevalence of AD and other dementias increases with age, the number of people with these conditions is also likely to grow very rapidly.¹⁰ These data should prompt a call to action for governments to address the alarming levels of dementia with urgency.

Dementia is not a single disease, but rather many distinct disorders unified by a common symptom of cognitive impairment. They include: AD; vascular dementia; dementia with Lewy bodies; mixed dementia; Parkinson’s dementia; frontotemporal dementia (Pick’s disease or frontal lobe dementia); and Creutzfeldt–Jakob disease. WHO and ADI emphasize that dementia is not a normal part of aging.

AD is a neurodegenerative condition characterized by protein deposits in the brain, and is the most common underlying cause of dementia. It accounts for an estimated 50–70 percent of dementia cases, either alone or in combination.^{11, 12} AD is most common in older people and initially manifests as memory and learning challenges. As it progresses AD compromises the ability for self-care and impairs recognition, sensory processing, sense of direction, communication and reasoning. The average duration of AD from diagnosis to death is 7–10 years,^{13, 14} though researchers agree it should be considered a disease that begins well before the onset of cognitive impairment.¹⁵ Ultimately AD leads to death, often by pneumonia or sepsis.

It should also be noted that dementia rarely presents alone. Rather, it is usually present among a number of age-related diseases (co-morbidities), raising vulnerability and complicating treatment for patients.¹⁶ Moreover, the underlying pathology leading to neuronal loss is often mixed.

While experts believe that early diagnosis can lead to better disease management for patients, there are only symptomatic treatment options. The limited treatments available are often further complicated by care systems that are not well organized or robust enough to meet the needs of people living with dementia, particularly in low- and middle-income countries.

A call to action

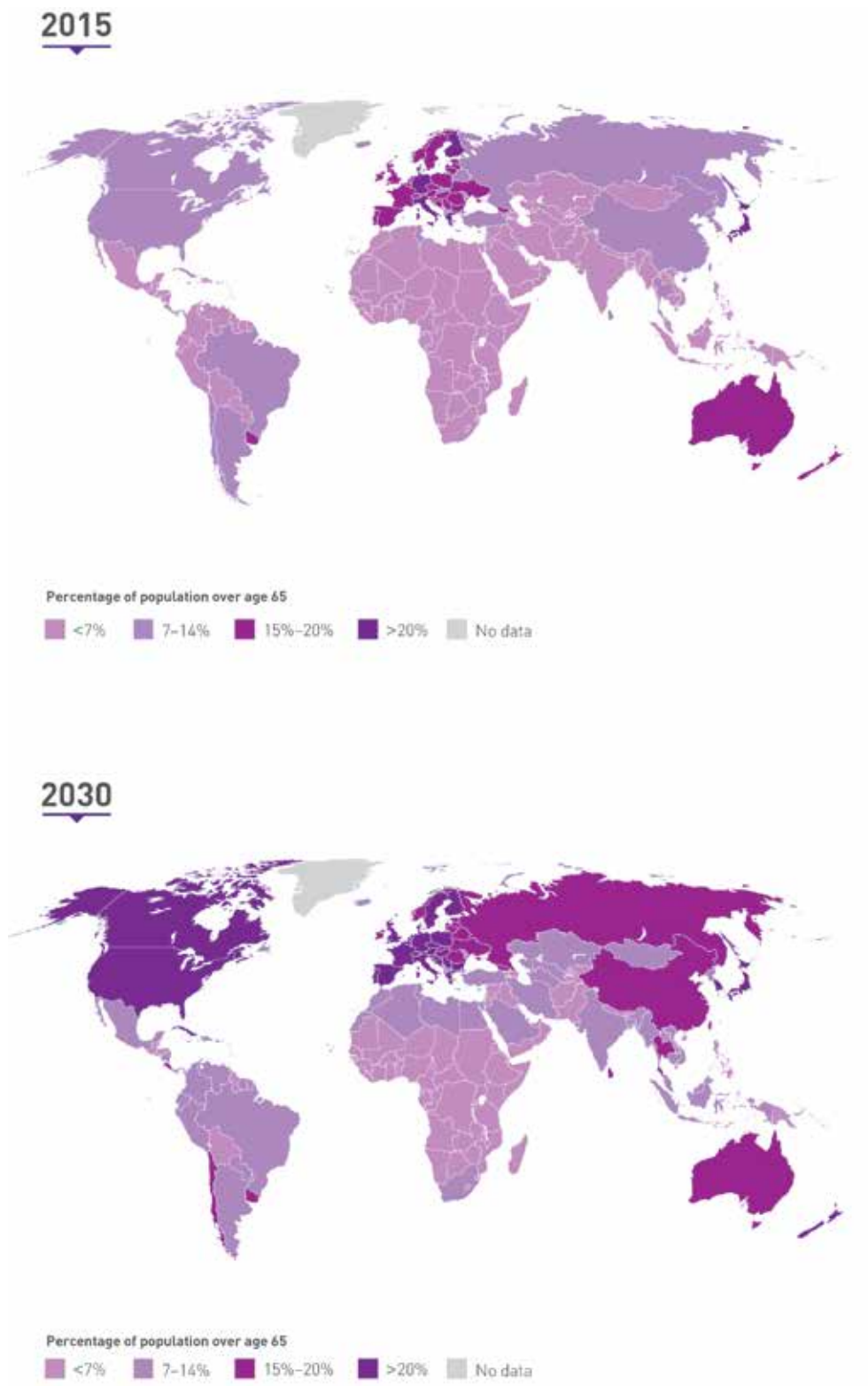
In recent years, increased international activity has brought much needed attention and resources to addressing dementia. In 2008, the WHO Mental Health Gap Action Programme¹⁷ identified dementia as a priority, the French Presidency held a conference on 'The fight against AD and related disorders', and Germany and Spain established new research centers. Two years later, the European Union Joint Programme on Neurodegenerative Disease Research (JPND) was announced.¹⁸ 2011 was then declared The Year of Alzheimer's Research in Spain, and further meetings in the European Parliament were held.

In 2012, WHO and ADI published *Dementia: A Public Health Priority*. The report calls for action at national and global levels to tackle the rising costs and prevalence of dementia.¹⁹ The UK then took advantage of holding the G8 presidency in 2013 to host a summit on dementia,^{20, 21, 22} which gathered G8 ministers, researchers, pharmaceutical companies and charities from around the world. The summit had many important outcomes that have sustained momentum, including: a signed declaration and communiqué;²³ the formation of the World Dementia Council; naming a World Dementia Envoy; three global dementia Legacy Events; and the launch of the Integrated Development Plan. The World Innovation Summit for Health, an initiative of Qatar Foundation, declared dementia one of its 2015 forums. This report aims to build on the momentum of the above-listed events to facilitate lasting and effective policy change.

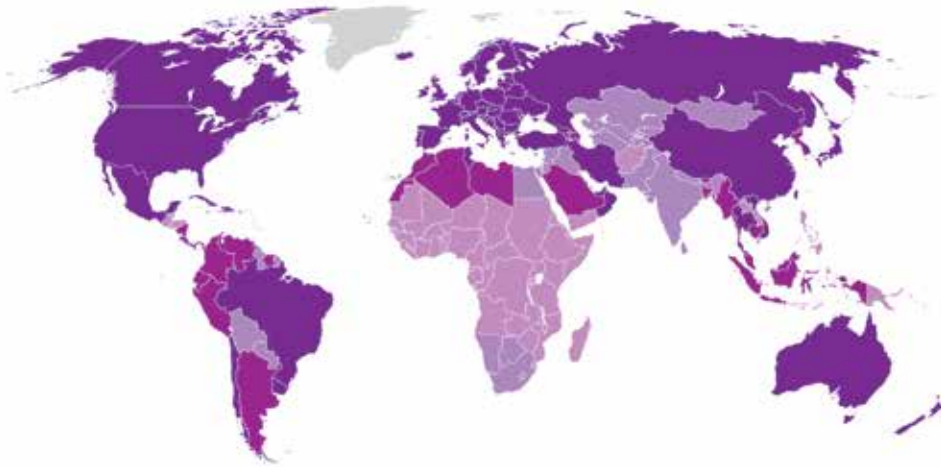
The roadmap

The goal of this report is to outline policy recommendations and innovative solutions that will lead to improved outcomes for individuals living with dementia, economies struggling to pay for the costs of care, and societies facing the increasing prevalence and burden of dementia. It is our hope that this report provides a summary view to complement the in-depth work of other initiatives. It is aimed at policymakers, outlining what can be done today. Priorities include public awareness, prevention and risk reduction, better diagnosis and care practices, and identifying effective therapeutics supported by thorough research, aligned regulatory strategies, robust healthcare systems, and sustainable funding mechanisms (see Figure 1).

Figure 3: Projected percentage of the global population over the age of 65



2050



Percentage of population over age 65

<7% 7-14% 15-20% >20% No data

COUNTRIES WITH A NATIONAL DEMENTIA PLAN



Australia, Belgium, Costa Rica, Cuba, Denmark, Finland, France, Israel, Italy, Japan, Mexico, Republic of Korea, Luxembourg, Netherlands, Norway, Switzerland, Taiwan, UK (England, Wales, Scotland, and Northern Ireland have individual plans), US.

Source: United Nations, World Population Prospects: The 2012 Revision (<http://esa.un.org/unpd/wpp/Excel-Data/population.htm>)

THE RESPONSE: EFFECTIVE APPROACHES AND INNOVATIVE SOLUTIONS

The following sections explore three current areas of focus for global dementia experts, including: prevention and risk reduction, diagnosis and care, and cure. Each section will describe current challenges and highlight possible solutions and best practices through innovative case studies.

Mobilize society to increase awareness, education and participation

Challenges

There are numerous challenges to educating the public, healthcare professionals and politicians about healthy aging, dementia and the value of participating in observational studies and clinical trials. Despite considerable costs and predictable increases in worldwide disease burden, many countries have demonstrated little urgency and political engagement in this problem. Notable exceptions include Australia, France, Japan and the UK.

Patient advocacy efforts face the challenge that dementia, in contrast to other diseases such as cancer, is considered a problem of later life, and once an individual is diagnosed his voice and 'will to fight' may be lost. Caregivers may be too burdened to engage in awareness outreach campaigns while they try to balance their own lives and provide constant care for a loved one.

Also, researchers conducting clinical trials on AD face obstacles in enrolling qualified patients. This may be due to high rates of misdiagnosis and apprehension of facing potential stigma. In fact, a 2012 poll by the Marist Institute for Public Opinion found that regardless of age, AD was the most feared disease, outranking cancer, stroke, heart disease and diabetes.²⁴ Many individuals who do seek medical advice often wait until they have exhibited advanced symptoms, long after irreversible damage has occurred. Moreover, it is frequently assumed that dementia is a normal part of aging, though each type of dementia is in fact a specific disease process.

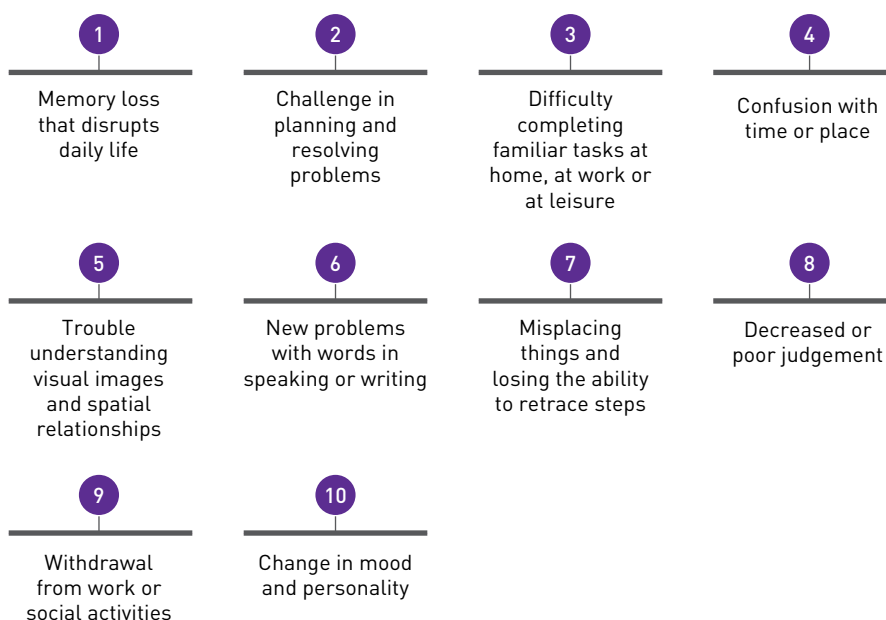
Solutions

There are a number of organizations and initiatives committed to mobilizing the public to increase awareness and education. The Global Alzheimer's and Dementia Action Alliance (GADAA) is a new umbrella organization designed to foster global collaboration among international non-governmental organizations (NGOs), professional associations, governments and international statutory bodies in an effort to co-ordinate

actions and raise awareness.²⁵ Specifically, GADAA aims to fulfill commitments 10 and 11 of the G8 Declaration:²⁶ “All sectors to treat people affected by dementia with dignity and respect, and to enhance their contribution to dementia prevention, care and treatment where they can” and “civil society to continue and to enhance global efforts to reduce stigma, exclusion and fear.”²⁷

To co-ordinate efforts and to raise awareness, September has been designated World Alzheimer’s Month.²⁸ This global campaign was first launched in 2011 by ADI. The goal is to offer a concentrated schedule on a local basis throughout the world of events, information sessions, Memory Walks, media appearances and free memory screenings, where possible. In conjunction with the first World Alzheimer’s Month, the Alzheimer’s Association launched a list of 10 common symptoms to assist individuals with identifying signs of AD. The list also highlights when it might be appropriate to seek further care for a loved one (see Figure 4).

Figure 4: 10 early signs of Alzheimer’s disease



Source: Alzheimer’s Association

Despite these efforts, awareness has been difficult to achieve through traditional channels. Stigma can also vary greatly from region to region, and these cultural differences make awareness campaigns difficult to carry out. Experts consulted for this project urged the use of varied communication strategies, using stories that appeal to a wide variety of audiences and age groups. Because caring for an individual with late stage disease is extremely demanding, communications strategies need to make obvious the burden on the caregiver – which is often a family member – in order to bring a personal connection to engage the average person in becoming educated about dementia.

Public awareness campaigns for other diseases have demonstrated effective strategies in promoting early diagnosis and treatment, and many lessons learned can be applied to dementia. For example, the Ice Bucket Challenge was launched in July 2014 as a public awareness campaign for amyotrophic lateral sclerosis (ALS), a debilitating neurodegenerative disease.²⁹ The challenge was simple: post a video on social media of someone pouring a bucket of ice water on another person and then challenge three friends to do the same to create a viral social media presence. Journalists have estimated that ALS challenge videos have been uploaded, commented on or liked by over 28 million Facebook users alone. Alternatively, the challenge could be declined and the social media user could donate to the ALS Association. The campaign's success led to over US\$115 million in donations in just three months.³⁰

Many new efforts are helping to map characteristics of disease progression and identify good candidates for clinical trial enrollment. Platforms like the Disconnected Mind, Alzheimer's Disease Neuroimaging Initiative, UK Biobank, MRC UK Dementias Research Platform, Guangzhou Biobank, and Australian Imaging, Biomarkers and Lifestyle Flagship Study of Aging are examples of longitudinal studies to help identify parameters that track with disease progression.^{31, 32, 33} The Global Alzheimer's Platform is a project under development by the Global CEO Initiative on Alzheimer's disease and the New York Academy of Sciences to decrease the time and cost of executing clinical trials via patient registries and characterized cohorts, activated trial sites and innovative clinical trial design. Altogether, these efforts should help increase the number of individuals engaged in observational and clinical trial studies.

National dementia plans can be an important tool for governments to increase resources and accountability for building dementia-capable programs.³⁴ While no systematic quantitative data have yet been compiled assessing their impact, for example on funding or number of programs, countries with a national plan typically develop more activity and infrastructure devoted to addressing dementia. For example, the French Alzheimer's plan led to the addition of more than 600 practitioners trained in clinical epidemiology, over 100 research projects launched, the addition of 65 new memory clinics and an effort to add more than 500 new diagnostic centers.³⁵ National plans are also capable of tailoring needs to the unique culture and demographics of each country. To date, 19 countries have developed national dementia plans. A report by ADI, *Improving Dementia Care Worldwide*, reviews existing plans and offers recommendations to governments for plan content, development and implementation.³⁶ Among key recommendations, ADI suggests a comprehensive government plan provide a mechanism to consider a range of issues including:

- Promoting broad public awareness of dementia and combating stigma.
- Quantifying the number of individuals with dementia.
- Identifying dementia-capable support services at all stages of the disease.
- Assessing and improving the quality of healthcare, social care and long-term care support and services for those living with dementia and for their caregivers.

- Committing funding.
- Effective monitoring, evaluation and update of the plan.
- Political and professional leadership at a national level.

Case study: Dementia Friends campaign (International)

Many people throughout the world have little, if any, contact with dementia and lack understanding of its cause, prognosis and treatment. Dementia Friends aims to help educate the public on how to help those living with dementia thrive in their local communities, and to develop patience and understanding among the wider public.

The first such initiative was the Nationwide Caravan to Train One Million Dementia Supporters, launched in 2004 by Japan's Ministry of Health, Labor and Welfare (MHLW).³⁷ The program's goal was to train one million 'dementia supporters,' who understand the symptoms and characteristics of the disease and support persons with dementia and their families in the community. This was accomplished through 90-minute seminars, available to the public and held throughout all areas of the country. Once trained, dementia supporters were expected to perform simple yet vital actions, such as helping someone find the correct bus, that allow those with dementia to live longer in the home setting and also maintain their dignity. Because of strong support by government, the private sector, and NGOs, nearly four million dementia supporters completed the training by 2012. The MHLW then adjusted its goal to six million people trained by 2017.³⁸

Following Japan's model, Alzheimer's Society has launched the Dementia Friends campaign, aimed at enrolling one million UK citizens by 2015. The campaign includes a variety of resources for individuals to educate themselves, such as books, fact sheets, videos and complementary actions that they can take to support someone living with dementia.

Since the UK program's inception in 2012, the campaign has enrolled almost 500,000 Friends through an online portal and local events across the country.³⁹ Alzheimer's Society has promoted the program through numerous articles in the media, celebrity participation and outreach, and partnerships with the UK government.

The Alzheimer Society of Canada and the Canadian Government are also in the process of launching Dementia Friends, though this remains in the planning stages at the time of writing.⁴⁰

Prevention and risk reduction to decrease prevalence of dementia

Challenges

Prevention of dementia is the single most effective way to diminish the burden on societies and economies. Current research suggests that most forms of dementia have genetic and environmental components, leading to risk factors that are both non-modifiable (for example, genetics, age, sex) and modifiable.⁴¹ Modifiable risk factors include: diabetes; hypertension; smoking; and lifestyle choices such as diet, physical activity levels, cognitive stimulation and social interactions. Edinburgh University's Disconnected Mind investigation showed that cognitive aging was due 24 percent to genetics and 76 percent to environmental factors.⁴²

There is no known intervention that can prevent dementia. Prevention is often illustrated in the following categories:

- Primary prevention – reducing the prevalence of disease by eliminating or treating specific risk factors that may decrease or delay dementia onset.
- Secondary prevention – reducing the prevalence of disease by shortening its duration.
- Tertiary prevention – reducing the impact of complications of long-term disease and disability.

To date, there are few clear interventions at any stage, and it is likely they would need to occur in mid-life before irreversible neuronal loss has occurred.

Solutions

With no effective strategy to completely prevent the onset of dementia, there is considerable effort placed on identifying strategies to minimize modifiable risk factors. Despite conflicts in the literature, there are numerous recent studies that suggest risk reduction is possible.^{43, 44, 45}

Public Health England published the *Blackfriars Consensus* on promoting brain health. It takes the position that scientific evidence is sufficient to justify considered action, both by reducing the modifiable risk factors and improving the recognized protective factors.⁴⁶ Current interventions (see Figure 5) include everything from challenging the brain by learning new material to increasing physical and social activities to maintaining healthy habits that are also good for the heart.⁴⁷

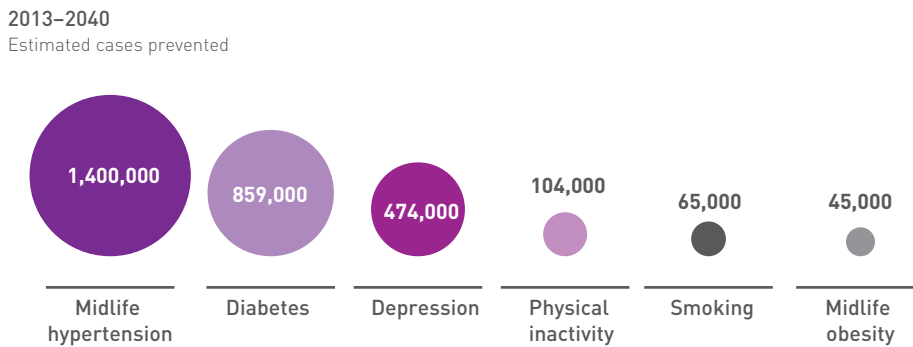
Figure 5: Risk reduction strategies



Figure adapted from ADI World Alzheimer Report 2014

When these interventions are translated into numerical outcomes they show significant promise for reducing dementia prevalence. Figure 6 shows best-case scenario estimates calculated by the International Longevity Centre – UK (ILC-UK).⁴⁸ They have predicted that current interventions could prevent up to 80,294 cases of dementia per year, and could prevent almost three million people from being diagnosed with the disease by 2040 in the UK alone. Further, these studies are predictions based on the current effectiveness of prevention interventions, which are expected to show improvement over time.

Figure 6: Preventing dementia through risk factor reduction



Source: ILC-UK Report on Prevention

However, the links between modifiable risk factors and prevention are not well evidenced, and significant additional research is required. While risk factors may play an important role in decreasing prevalence at the population level, they have less impact than genetic predisposition for a single individual. For example, while untreated midlife hypertension may put an individual 1.6 times more at risk of dementia, the presence of genetic APOE4 homozygosity increases the likelihood twelve-fold.⁴⁹ Identifying the benefits of both behavior-changing interventions and other forms of prevention is therefore important.

To date, the non-pharmacological interventions described above have shown only modest effects on risk reduction. However, a number of academic centers and pharmaceutical companies are pursuing strategies to significantly delay or prevent disease onset using a range of drug treatments. Five prevention trials (Anti Amyloid in Asymptomatic Alzheimer's Disease, Dominantly Inherited Alzheimer Network, TOMMORROW and two from the Alzheimer's Prevention Initiative) are directed at different patient populations and will provide unique insight.^{50, 51, 52, 53, 54}

Case study: FINGER study (Finland)

In 2009, researchers in Finland launched the largest prevention trial to date to study effective interventions to prevent or delay the onset of dementia. The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) study is a randomized controlled trial that tracks participants across several study sites to understand the effect on cognitive performance of nutrition, cognitive training and social activity, and management of metabolic and vascular risk factors.⁵⁵

Over 1,200 individuals from 60 to 77 years-of-age were identified for the FINGER study, all of whom had previously participated in monitoring studies for other chronic diseases. Individuals were shown to have average or slightly below average cognitive abilities for their age, but no major decline in abilities, and were split into a treatment group and control group.

Treatment participants took part in training, physical activity and check-ups with doctors over the two-year study period. Control group participants were given general health advice but did not participate in the specific interventions. Participants were then tracked for cognitive performance using standardized tests such as the modified Neuropsychological Test Battery. They were also tracked against secondary outcomes that included: diagnoses of dementia; cardiovascular and cerebrovascular morbidity and mortality; dietary intake; dietary markers; and disability.

Initial results from the study were presented in July 2014.⁵⁶ They showed that the group treated with interventions showed better overall health, as well as significantly better results on "specific tests of memory, executive function (complex aspects of thought such as planning, judgment and problem-solving), and speed of cognitive processing." This marks a significant breakthrough in the evidence base for using prevention interventions to help curb the effects of dementia.

Further studies are expected in the future, including a seven-year study. This study will combine the interventions with more advanced methodologies such as biomarker levels and MRI (magnetic resonance imaging) and PET (positron emission tomography) techniques.

Case study: Collaboration for Alzheimer's Prevention (International)

The Collaboration for Alzheimer's Prevention (CAP) is a consortium developed to maximize learning and co-ordinate synergies among prevention trials.^{57, 58} Three academic-led trials (A4, API-ADAD and DIAN) were founding members in 2011, and membership is expected to grow as more groups initiate pre-symptomatic AD treatment trials. Regular meetings include discussion of shared concerns such as clinical trial design, clinical outcome measures, biomarkers and regulatory approval mechanisms. This agenda is critical because prevention trials aim to prevent, delay or slow onset of cognitive decline in individuals not yet exhibiting signs of cognitive impairment.

Demonstrating the effectiveness of the prevention trials will require sensitive cognitive tests or surrogate markers together with lengthy surveillance times. This is particularly important if drug treatments are successful in delaying cognitive impairment. In addition, there are ethical considerations about treating asymptomatic individuals as well as questions about the disclosure of disease risk that some participants may or may not want to know. One criterion for joining CAP is the requirement to make trial data freely available on completion for additional analysis in the research community. This innovative condition will facilitate dissemination more broadly of lessons learned from these trials.

Diagnosis and care innovations to improve quality of life

Challenges

While efforts to find better treatments for neurodegenerative diseases are underway, tens of millions of individuals and their families will continue to be affected. Identifying best practices and measurements of performance for care is a priority, and support for caregivers is essential. Low- and lower-middle-income countries have a disproportionately high reliance on informal structures for care, compared with other nations.⁵⁹ High- and upper-middle-income countries have the ability to rely on formal care structures, reducing stress on caregivers but increasing costs. Rates of diagnosis also vary in different regions. According to examples from the 2011 World Alzheimer report, only 20–50 percent of AD cases are diagnosed in high-income countries, while 90 percent are undocumented in India.⁶⁰

Many care practices are unique to health systems or cultural practices, but it is important to generate a strong evidence base that identifies the most successful, cost-effective practices that are also scalable to meet growing demand. Importantly, health systems will save money if care innovations can reduce costs in other areas, for example hospital readmissions or requirements for extended institutionalized care.

Solutions

Visiting a physician upon experiencing the early signs of memory impairment can have many benefits. Almost one in ten individuals who report to a memory clinic with cognitive problems are diagnosed with reversible cognitive impairment because of depression or vitamin B12 deficiency.⁶¹ Dementia diagnosis may also enable access to, and information about, care services and symptomatic treatments. Planning for the future is important before cognitive decline inhibits the ability to make informed choices. Finally, individuals with a definitive AD diagnosis may choose to participate in clinical trials.

The Alzheimer's Association's *Value of Knowing* guide⁶² suggests public health officials undertake the following:

- Design campaigns to educate the public and the medical community about the warning signs of dementia and the benefits of early detection.
- Develop best practices aimed at early detection and risk reduction of co-morbid conditions in individuals with AD.
- Educate physicians on the importance of discussing memory issues with adult patients, particularly those over age 65.

Best care practices are being examined in a number of arenas, including a focus on care at the 2014 Japan-led G7 Global Dementia Legacy Event.⁶³ One primary recommendation is to enable individuals with dementia to live as independently and productively at home for as long as possible.⁶⁴ The goals are to improve cognitive ability and daily function of patients, and to reduce the burden on caregivers in a cost-effective way. There is also a pressing need to support caregivers, and this help can come from top-down approaches through policy changes, and from bottom-up interactions in the caregiver community.

People with dementia have been shown to feel isolated from their communities as disease progresses. Activities they once enjoyed may become off limits without support. In response, the Alzheimer's Society in the UK has created dementia-friendly communities, where aspects of local communities are altered to allow individuals with dementia to continue to contribute to society and participate in everyday activities.⁶⁵

A dementia-friendly community takes a broad approach to ensure that the community is as hospitable to individuals with dementia as possible, whether it is through accessible transport or having businesses and services that meet patient-specific needs.

One such innovation has been the launch of dementia cafés.⁶⁶ The cafés are social gatherings, held periodically, that allow individuals to come together and meet other people with dementia to share experiences and build a sense of community. Families and caregivers often attend the gatherings for moral support, to discuss tips and strategies on care, and to seek advice from other caregivers, experts and guest speakers.

Another innovative program is the House of Memories, run by National Museums Liverpool in the UK.⁶⁷ It provides training to raise awareness and understanding of people's experiences of living with dementia. The program is based on the premise that historical items can help unlock memories. It teaches caregivers how to engage people living with dementia using the exhibits and memorabilia from their personal histories. The museum also has resources that allow caregivers to tailor their learning. They include a memory suitcase, which provides objects on loan to caregivers, and a memory toolkit that is a how-to guide for creating a personalized reminiscence project with an individual.

In many parts of the world, especially the Middle East, the stigma associated with dementia requires a different outreach strategy. Experts consulted for this report agree that online resources will be increasingly important, as they provide a readily accessible way to learn about dementia and how to care for the people living with it. The US Alzheimer's Association created ALZConnected®, which provides message boards for individuals with dementia and their caregivers to discuss topics ranging from care strategies, to clinical trials, to losing someone.⁶⁸ It was also noted that internet-based resources should be translated into many different languages, including Arabic.

Technological aids take advantage of design features that maximize independent living and quality of life. For example, the PDShoe offers vibratory feedback for improving the gait of Parkinson's patients.⁶⁹ A new monitoring device offered by an Intel and Michael J. Fox Foundation collaboration measures gait, tremors and sleep patterns to understand trends that emerge from factors such as medicine or food intake. The data collected will also provide a more comprehensive view of disease progression compared to sporadic doctor visits.

Other helpful technologies include eating utensils like the Stanford Center on Longevity Design Challenge winner Eatwell⁷⁰, Lift Labs⁷¹ and Smartphone apps such as GE MIND, Memory Maps and Lumosity.⁷² There is increasing availability of therapeutic robots that provide: music and movement for entertainment; services such as household chores; telepresence video such as Giraff and VGo; and companionship (see case study below). Evidence suggests that these robots can help improve mood and quality of life.⁷³ The role of the medical device and IT industries was discussed at the 2014 Canada–France G7 Global Dementia Legacy Event, which promoted the idea that this type of care innovation will be increasingly important.⁷⁴

Case study: Dementia care robots (Japan)

Animal therapy has long been used to help relieve the stress caused by medical conditions, and it is now commonplace in many hospitals and care centers around the world.

There are some challenges using live animals, which have led to a new innovation in animal therapy in the form of robotic animals. These therapeutic stuffed animals

(Case study continued)

are made by the Japanese company Paro, and are being used in Japan and the UK to care for individuals with dementia.⁷⁵

Paro robots are designed to look like seals, chosen because they are generally liked, and are used as companions for individuals with dementia. The robots contain artificial intelligence software that allows them to react to light, touch and even words. The robots learn their name and can remember actions that please the individual and will recreate those actions more often. The robots also have the ability to show emotion including happiness, anger and surprise.

A randomized trial published in 2013 showed positive outcomes for people with dementia who had Paro robots.⁷⁶ The trial showed decreased anxiety levels in this group and marked improvements in recognized dementia quality-of-life indicators. The introduction of robots into care settings also increased social interaction among individuals with dementia and with their caregivers.

Ethical concerns have been voiced about using the robots. Critics have expressed unease that real care is replaced with robotic surrogates.⁷⁷ The robots also cost \$5,000 each, which requires significant funding for implementation.

Health and social care systems optimized for dementia care

Challenges

Many healthcare systems offer services through fragmented departments, leading to challenges for individuals with dementia and their caregivers. The median duration of AD is 10 years, with fairly predictable changes in symptoms as the disease progresses.⁷⁸ Each stage offers unique challenges for health and social care systems.

Dementia is rarely the only contributor to poor health, and people frequently suffer simultaneously from other long-term conditions. Up to 25 percent of all older patients in hospitals have dementia, and traditional care frameworks may neglect the complexity of treating individuals with multiple chronic conditions.⁷⁹ This results in longer hospital stays, more readmissions and more costly care.

Solutions

The 2012 WHO report and the 2009 World Alzheimer Report describe the successful health and social care systems and workforce training needed to address dementia.^{80,81} A key factor is integration of care services by case managers, who provide a centralized point of contact to co-ordinate comprehensive care plans. Many countries are already implementing these ideas, including France, Australia, the UK and Japan.

The Integrated Care Program organized by Age UK brings together health and care services with community and volunteer organizations at the local level to provide

a combination of medical and non-medical services for older people with multiple long-term conditions such as dementia. These partnerships develop co-ordinated care models that guide participants on the appropriate care pathway, and include offering benefits advice, social activities and home help. Services in this program range across the spectrum, from handyman assistance around the home to transport options and exercise programs. The program was piloted in the county of Cornwall with an initial sample size of 100 individuals. Evaluations demonstrated a 23 percent improvement in mental wellbeing and a 30 percent reduction in non-elective hospital admissions.⁸² Future goals for the program are to enroll over 2,200 people and study the program's effects on health outcomes.

Workforce training is also essential to build capacity and minimize the burden on informal care structures. This includes professionals interacting with individuals throughout the spectrum of care and disease management including: pre-diagnosis; diagnosis; post-diagnostic support; co-ordination and care management; community services; continuing care; and end-of-life palliative care. Training programs must also be tailored to regional health and social care systems. One solution to training formal and informal caregivers is the Dementia Quality Care Online Training Program in China, described in the case study below.

A RAND report recently summarized policy options into five objectives for dementia long-term services and supports (LTSS).⁸³

1. Increase public awareness of dementia to reduce stigma and promote earlier detection.
2. Improve access to and use of LTSS.
3. Promote high-quality, person- and carer-centered care.
4. Provide better support for family caregivers.
5. Reduce the burden of dementia LTSS costs on individuals and families.

Case study: Dementia Quality Care Online Training Program (China)

To address the shortage of trained carers for China's growing number of people living with dementia, the China Alzheimer's Project worked in collaboration with Alzheimer's Disease Chinese (ADC) and the Peking University Institute of Mental Health to design the Dementia Quality Care Online Training Program.^{84, 85}

The program, which recently won the MetLife-ADI Award for Dementia Care Education, promotes person-centered dementia care and provides students – who range from nurses to social workers to family caregivers – with the tools to better understand the behavior of those with dementia and provide them with more effective and compassionate care.⁸⁶

The initial 10 online training modules combine mixed media, slides, and interactive questions to engage participants actively, and also include online exams. The

(Case study continued)

program has a simple user-friendly format with practical content, easy access and relatively low cost. It makes the material accessible to a wide audience, which will ultimately make the biggest difference in improving the quality of life for people living with dementia.

Program costs range from CNY 360 (approximately \$60) for a 30-day individual course to CNY 3,600 (approximately \$600) for one-year access for groups/institutions. There is an additional CNY 360 charge to take the online certification exam. Successful completion of the exam awards participants with an ADC-issued dementia care quality certificate that can be accessed and verified using the site. Since launching in July 2014, over 700 individuals have completed the training.⁸⁷

Cure or disease-modifying treatments to minimize disease burden

Challenges

A cure implies that a person no longer suffers from the disease initially diagnosed, but as yet there is no cure for any dementia due to neurodegeneration. Treatments may delay the progression of symptoms for a short time but do not address the underlying cause of the disease. Finding a cure is a major challenge because it is believed that by the time symptoms appear, significant neuronal loss has already occurred, highlighting the importance of early diagnosis.⁸⁸

Current understanding of the causal molecular mechanisms of the diseases that cause dementia is limited. One of the challenges in identifying targets is that most pre-clinical testing uses animal models that may not accurately mimic human disease. Also, dementia often presents with other co-morbidities such as heart disease, and clinical symptoms may represent multiple underlying pathologies.

Solutions

Finding a cure for dementia will require basic research, translational drug development and a regulatory environment prepared to accept risk commensurate with the significant unmet medical need. All of these strategies will require a highly trained workforce and significant financial resources.

One of the most important solutions is to increase basic research efforts to better understand disease mechanisms and risk factors. Much work is directed toward a limited set of targets, and some experts are calling for diversified therapeutic targets for drug development.⁸⁹ With a better understanding of the basic biology of aging, insights will emerge about why dementia most often occurs later in life. The study of co-morbid conditions, in conjunction with bridging research communities focused on individual disease pathologies of different types of dementia, could facilitate identifying common features and mechanisms. By better understanding the risk factors,

it will be possible to classify the population according to risk. This would then allow health systems to focus resources such as expensive diagnostic brain imaging on the most at-risk individuals. It may even be possible to reverse some cognitive impairment, even when neurons are already lost, if techniques are developed to promote neurogenesis (the creation of new neurons) or replenish neurons with stem cell therapies.⁹⁰ Growth factors may encourage improved health and communication among neurons that remain.

While efforts to create new disease-modifying therapies are important, we must also continue to develop better symptomatic treatments to improve the quality of life of people living with dementia.

The World Dementia Council has highlighted that it will require an adjustment to the risk/reward ratio to incentivize the acceleration of drug development of a cure or disease-modifying treatments.⁹¹ Budget neutral ideas include regulatory changes to increase market protection or accelerated approval of new drugs. Governments may also participate in innovative financial models that include: offering guarantees and social impact bonds; participating as limited partners in funds; and accepting first loss or capped returns to draw more risk-averse private investment. These ideas are discussed further below.

Research, trials and regulatory pathways to accelerate drug development

Challenges

Drug development for diseases such as AD faces a number of challenges: a history of failures; long development times; and costly clinical trials. Between 1998 and 2012, 101 unsuccessful attempts were made to develop AD drugs, and only three new medicines gained approval to treat symptoms.⁹² Indeed, the last new drug for AD (memantine) received regulatory approval more than 10 years ago. In the last 10 years, many promising disease-modifying compounds have been identified, although none have succeeded in Phase III trials.⁹³ Moreover, some trials have been terminated due to significant negative side effects.

Lengthy clinical trials pose another challenge, adding cost and burden to patients and companies. Although a clinically meaningful outcome can be measured in three to six months for symptomatic AD treatments, the gradual nature of disease progression means that Phase III trials for disease-modifying agents in early stages of disease must last at least 18 to 24 months.^{94,95} Importantly, prevention trials are performed in populations that are not yet demonstrating cognitive impairment, so there is a need to demonstrate the effectiveness of a drug in a time frame that still enables a label with significant patent life protection for the drug developer to make it worth the investment.

If the 10 years of drug development starting from first testing in humans is not daunting enough, it is estimated that the cost of developing a new drug can range from

\$0.5 to \$5.7 billion.⁹⁶ The net effect of these challenges is a decrease in the number of pharmaceutical companies maintaining active drug development programs for neurodegenerative diseases.

Solutions

Increasing basic, applied and clinical research will be essential for decreasing the global burden of dementia. Infrastructure and clinical trial innovations will also be needed to decrease the time and cost required to execute clinical trials. To address this issue the Innovative Medicines Initiative is launching the European Prevention of Alzheimer's Disease consortium (IMI EPAD) to accelerate adaptive Phase II proof-of-concept studies.⁹⁷ The Global Alzheimer's Platform is also being developed to offer the same capabilities outside of Europe, but also to offer trial-ready sites and patient cohorts for large-scale trials.

In addition to advances in research and clinical science, regulatory science innovations can help shift the risk-reward balance in favor of attracting new investments in AD and dementia drug development. Many specific regulatory approaches could help decrease development time and cost.⁹⁸ They include accelerated or conditional approval assuming that there are: qualified surrogate biomarkers and/or sensitive cognitive endpoints; special designation such as breakthrough therapy in the US or Sakigake in Japan; extension of data exclusivity, for example orphan drug framework; adaptive licensing; priority review; fee waivers; incentives for data sharing; and guidance from multiple regulatory agencies that is synchronized in content and timing where possible.

Regulatory agencies have begun to think specifically about the challenges posed by drug development for dementia and offer guidance and consultations. The US Food and Drug Administration (FDA) issued draft guidance looking at trials in early stage AD,⁹⁹ while the European Medicines Agency issued a discussion paper in 2014.¹⁰⁰ While progress and openness in individual regulatory bodies is helpful, the UK Government Integrated Development Plan aims to increase communication and progress among many regulatory agencies simultaneously (see case study).

Case study: Integrated Development Plan (International)

The UK Government and the World Dementia Council recognize regulatory strategies as an important part of changing the risk-reward ratio to incentivize drug development.

In the UK Prime Minister's 2014 letter to Heads of State, he proposed: "To give patients earlier access to new drugs, ensure new dementia medicines are affordable across the globe and encourage a move for greater innovation and collaboration between government, industry, regulators and the scientific community."¹⁰¹

(Case study continued)

The Council's Regulatory Lead, Raj Long, and colleagues from the UK Dementia Innovation Unit are developing an Integrated Development Plan to optimize the path of medicines for dementia, from research to market, by reducing barriers and encouraging regulatory innovation.¹⁰²

The Plan aims to address the many challenges that must be overcome to realize this vision. First steps include working with global experts to establish a common understanding of gaps in current research science, then working with leading regulatory agencies to collectively evaluate how to align the current research baseline and regulatory science to help address these gaps and thus accelerate drug development efforts in dementia.

Case study: Adaptive Licensing (European Union)

Timely access to innovative medications requires co-ordination among many different parties, including pharmaceutical and biotech companies, regulatory agencies and payers. Current approaches can prohibit new medications from reaching the marketplace, while patients with unmet needs must await treatment.

A new program from the European Medicines Agency (EMA) addresses wait times and allows staggered access to medications based on a pre-planned, flexible timeline. This process allows early access to a limited number of patients who need medicines urgently and are willing to accept the risk before studies have been fully executed. Then, evidence on the effectiveness and safety of the medication is used to gradually increase the number of patients using the drug. In the initial phase, the program received 29 applications from drug makers, and as of November 2014, nine had been chosen for further discussion.¹⁰³

While the program shows significant promise in helping to treat patients with no other alternatives, there remains work to be done on the business model for these drugs. Current payer requirements include extensive testing and understanding of drugs before they become eligible for reimbursement and payment. The EMA aims to continue to work with stakeholders to outline how this process will work in the future as more applicants are accepted into the program.

The use of adaptive licensing and other accelerated approval pathways may balance the risk of testing less proven drugs with the benefit of finding a treatment or cure for devastating diseases.

Innovative finance mechanisms to increase funding across the arc of disease management

Challenges

There is underinvestment in dementia research and development, relative to its social and economic burden. There will be an estimated 85 percent increase in costs globally by 2030, based only on the predicted increases in the number of people with dementia.¹⁰⁴ Dementia research receives significantly less funding than other major diseases, which does not reflect the disease burden and rising cost that dementia will impose on international economies. For example, in the US the National Institutes of Health funding for HIV/AIDS research is more than five times the level of that for AD research, despite the fact that there are five times as many Americans with AD than with HIV.¹⁰⁵

Some experts speculate that the lack of funding has created an environment of competition in academia and that repeated and costly failures in drug development have created funding fatigue in donors and pharmaceutical companies. They believe that this has caused the field to become more conservative, and limited unconventional strategies and parallel drug discovery opportunities. Between 2009 and 2014, large pharmaceutical companies cut their number of active central nervous system programs in half, which also negatively impacted small start-ups and biotechnology companies.¹⁰⁶

In the absence of major breakthroughs, dementia will move from a major health challenge to a global economic crisis. We must define a new, robust approach to innovative public-private mechanisms, combining the mix of investor segments needed to finance advances in dementia research and development as well as care delivery.

Solutions

In 2013, leaders of the G8 countries united to increase financial resources for AD research significantly. The UK has named a World Dementia Envoy and established the World Dementia Council, with one of their three stated priorities being to increase financial resources for dementia research and drug development.¹⁰⁷

Many recent meetings have begun to identify routes to mobilize substantial new funding for basic and translational research, drug development and care delivery. Specific ideas from the 2013 Path to 2025 Alzheimer's Disease Summit include:¹⁰⁸ crowd-funding and crowd equity accessing funds from the traditional middle class; venture capital models with government or philanthropy taking first loss (and thus allowing a competitive return on investment (ROI) to attract limited partners from capital markets); and social impact investing. Accessing sovereign wealth funds, bond structures and pay-for-success programs are also being investigated. These ideas rely on a two-pronged approach of increasing contributions from existing investor populations, and creating new funding vehicles to attract a broader pool of investors.

Similar ideas were discussed at the UK-led Global Action Against Dementia G7 Global Dementia Legacy Event. JP Morgan has been tasked with the creation of a \$110 million pre-clinical fund by the World Dementia Council, and various other groups – such as the World Economic Forum, Institute of Medicine, *FasterCures*, New York Academy of Sciences and the Global CEO Initiative on Alzheimer’s Disease – are working on additional ideas.¹⁰⁹ While individual groups can advance these mechanisms, ultimately there is a need to engage finance ministers and treasury departments in the dementia funding discussion.

Investor groups and innovative funding vehicles are described below.¹¹⁰

Disease foundations

Dedicated research funding groups like the Alzheimer’s Association, Bright Focus Foundation, Alzheimer’s Drug Discovery Foundation, Cure Alzheimer’s Fund and Alzheimer’s Research UK provide philanthropic funding to high-risk projects without the typical restrictions associated with government or financially-oriented funding.

High net worth individuals and philanthropy

Individuals or groups can fund basic research and help build research institutes. The opportunities and infrastructure these institutes provide attract well-respected researchers and clinicians.

Crowdfunding

Organizations like Benefunder are creating crowdfunding platforms to fund basic and clinical research. Patient advocacy organizations such as the Alzheimer’s Association, Michael J. Fox Foundation, Alzheimer’s Society and others are increasingly using funds collected from large and small donations to fund basic and translational research.

Accelerators

Other companies are concentrating on the funding gap to ensure sufficient assets move from academically interesting to pharmaceutically attractive leads. The idea is to generate promising research leads in which pharmaceutical companies can invest. Examples of companies in this ‘accelerators-to-optimized-leads’ space include BioMotiv, Accelerator Corp, Cydan and AmorChem, among others.

Venture capital and venture philanthropy

These funds support projects that entail higher risks than government and industry are willing to accept. The venture capital divisions of major pharmaceutical companies are also a strategic source of capital potentially available for higher-risk projects, which purely financial investors traditionally avoid.

Sovereign funds

Countries are beginning to recognize the drag on global economic growth being created by the costs of AD care, making a sovereign fund investment for reduction in dementia a potential opportunity. Greater private investments could be gained through the guarantee or credit enhancement of private investments in cost-reducing dementia research.

Industry investment

Industry invests over \$5 billion annually in research on the central nervous system.¹¹¹ Strategic investments from industry in the pipeline of early stage companies can add further investment capital, particularly if coupled with the other venture financing models discussed above. However, a strong signal from the regulatory and policy arena might be required to generate interest.

Governments

In advance of the G8 Summit on Dementia, some scientists called on countries to invest at least one percent of the cost of care into basic research.¹¹² Governments may also offer guarantees for social impact bonds, support pay-for-success programs or participate as a limited partner in funds (see case study below).¹¹³

Crowd equity

Companies like Poliwoog Healthcare Investments collect relatively small funds from a larger pool of investors to finance young companies. They bridge the gap between compound screening and new drug development.

Social impact funds

There is growing demand to provide investment options that reflect investors' personal values and generate a measurable benefit to society as well as a financial return. A recent poll (non-representative) by one of the largest US banks indicated that 45 percent of high net worth investors said that they would like an investment option in their portfolios that reflects their values.¹¹⁴

One idea from *FasterCures* Ventures proposes a structure in which government or philanthropy takes first loss and capped returns to attract traditional ROI-focused investors with higher rates of return.

Social impact bonds

Social impact bonds or pay-for-success models rely on governments paying a portion of savings that result from an improved social outcome to investors that initially funded the social intervention. For example, governments would save money if an intervention successfully minimizes hospital readmissions or extended long term care and could refund investors who initially paid for the intervention.

See the case study, 'Green and purple bonds' for a more detailed description of social impact bonds.

Figure 7: Innovative structure or application of new and existing funding vehicles

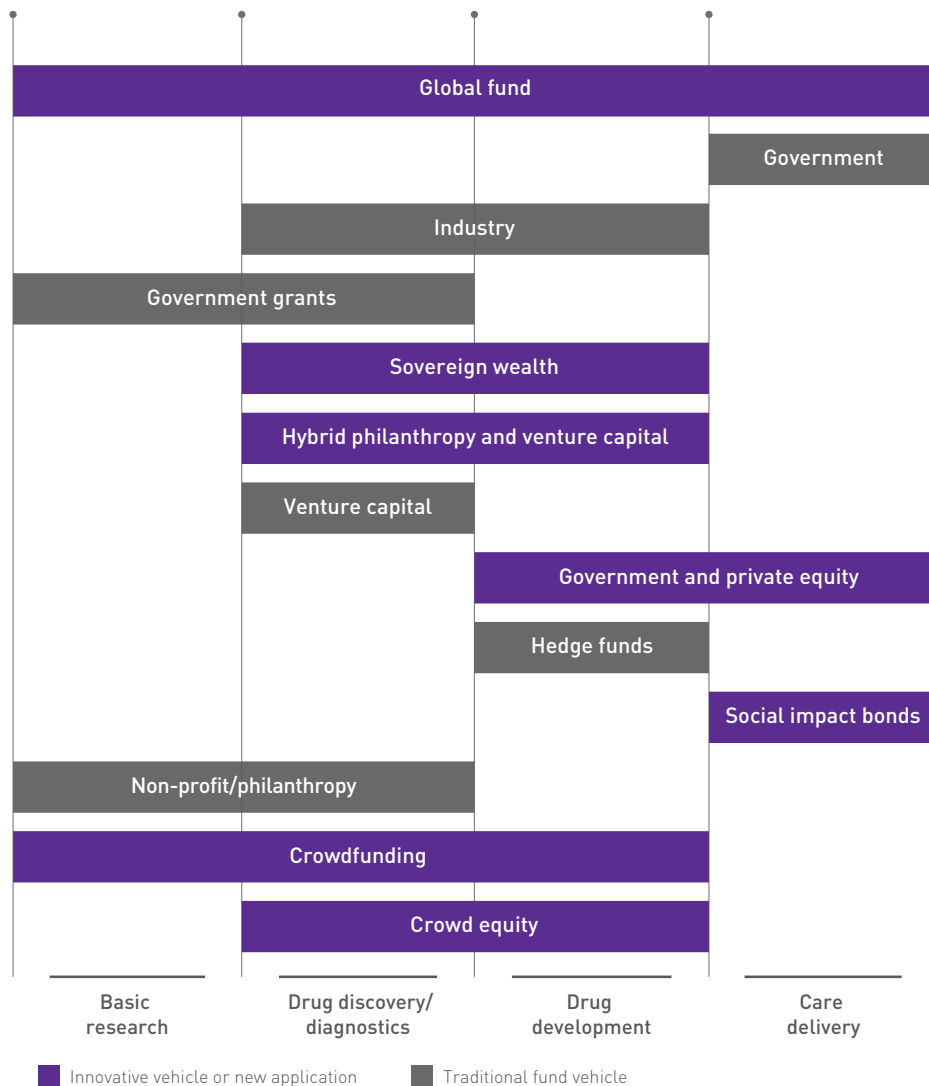


Figure modified from Stenull, Duggan and Vradenburg, UK G7 Global Dementia Legacy Event 2014.

While new funding is sought, it is also important to question where new resources would have the most impact. For example, what percentage should be spent on cure versus care? The first need is therefore to assess the current funding landscape and identify gaps. The International Alzheimer’s Disease Research Portfolio (IADRP) and WHO/OECD-led projects aim to do this. There have also been many efforts to prioritize a strategic agenda around the most promising opportunities. This includes, for example, the European Dementia Research Agenda, JPND Strategic Research Agenda and the UK Alzheimer’s Society Dementia Priority Setting Partnership with the Lind Alliance.^{115, 116, 117, 118} As part of the G8 Dementia Summit Declaration commitment, WHO is spearheading a dementia research prioritization exercise to be presented at the March 2015 Global Dementia Legacy Event.

Further important outcomes of increased financial resources include the ability to attract intellectual capital in the form of well-trained researchers and clinicians, to fund more diverse studies examining new pathways and targets, and to translate those opportunities into viable therapeutics.

Case study: Israel Life Sciences Investment Fund (Israel)

In an effort to bring intellectual property to the marketplace and to address a lack of investment in the life sciences, in 2006 the Israeli Government created the Israel Life Sciences Investment Fund.

The Israeli Government provided OrbiMed Israel Partners Limited Partnership with a \$50.8 million investment, and OrbiMed raised an additional \$171.2 million. The fund targets biotechnology, pharmaceutical, medical device and diagnostics companies at varying stages of maturity, from seed stage to growth equity.¹¹⁹

The fund is unique. It differs from traditional venture capital finance in that the Israeli government has agreed to take first loss on the investments to shield private investors from a level of risk. This has attracted capital that might otherwise be unfit for venture capital investing, and allowed returns to go to private investors first.

Case study: Green and purple bonds (International)

Solutions to combat climate change, such as the advancement of clean energy technology and reduction strategies for greenhouse gas emissions, are often capital-intensive and high-risk. This has made it difficult for the average investor to contribute actively to these solutions.

In response, financial institutions across the globe have created green bonds, which are debt instruments that are used to raise capital to support green projects that have beneficial outcomes to the climate and the environment. Green bonds reduce the cost of capital for climate-related projects and also spread risk across a number of projects, which allows conservative organizations, such as pension funds and endowments, to invest in causes that will have societal benefit.

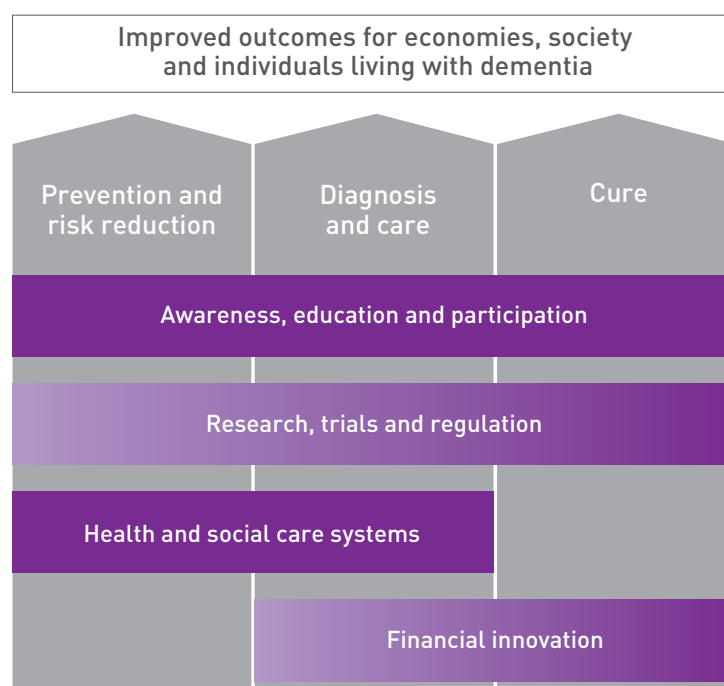
Green bonds were first launched by the World Bank in 2008 and have since developed into a full subset of the bond market. Financial institutions, corporations, governments and development banks had over \$500 billion dollars outstanding in 2014.¹²⁰

With the increasing success of the green bond market, dementia experts have begun to explore the adoption of this model to create purple bonds to address the research and development gap in AD treatment and the advancement of a cure.

POLICY RECOMMENDATIONS

The policy recommendations described in this report aim to achieve improved outcomes for individuals living with dementia, for economies struggling to pay for the costs of care and for society at large, facing the increasing prevalence and burden of dementia. The following recommendations are directed at policymakers, outlining what can be done today to decrease the present and future burden caused by dementia.

Figure 8: The WISH Dementia Forum framework



The shading gradation of the four cross-cutting bars in the figure reflects the applicability for each area.

Policy recommendations in each area are detailed below.

- 1. Develop a plan to address dementia nationally:** Create a national plan to address dementia in every country and/or include dementia as a priority in country-specific and United Nations (UN) plans for prevention and control of non-communicable diseases.
- 2. Increase awareness of dementia:** Engage the public, patients and caregivers by carrying out awareness campaigns (such as Dementia Friends), developing dementia-friendly environments and supporting the creation of Alzheimer's Associations in every country.
- 3. Expand healthy living to include brain health:** Embed brain health in public health strategies, taking a life course approach to healthy aging.

- 4. Improve the evidence base for prevention:** Fund studies and prevention trials that help to understand the effectiveness of risk reduction strategies and advance efforts to find a therapeutic intervention to delay or prevent the onset of dementia.
- 5. Improve dementia care:** Implement well-evidenced and cost-effective best practices in dementia care, as appropriate to regional healthcare systems' available resources.
- 6. Strengthen integrated and co-ordinated health and social care systems:** Put in place financial incentives to create a well-trained workforce that will improve the quality of life for people living with dementia and reduce the burden on informal caregivers.
- 7. Institute and fund longitudinal studies:** Improve surveillance of people with, or at risk of developing, dementia to understand disease progression better and provide characterized cohorts for participation in clinical trials.
- 8. Reduce barriers to drug development:** Optimize the path of medicines from research to market. For example, offer accelerated approval and market protection, and support the Integrated Development Plan to increase dialogue between regulatory agencies, payers, scientists and policymakers.
- 9. Commit government investment of at least one percent of a country's cost of care:** Invest in basic, clinical and applied dementia-related research and technologies to ensure financially sustainable healthcare systems in the future via:
 - Budget increases to encourage capacity building to recruit more scientists and clinicians.
 - More resources to diversify therapeutic approaches.
 - International strategic research plans to provide finance co-ordination to minimize duplication and encourage funding of gaps and opportunities in research.
- 10. Facilitate innovative finance mechanisms:** Attract private investment among a wider range of investors and increase financial resources across the arc of disease management.

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Any errors or omissions remain the responsibility of the authors.

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REFERENCES

01. World Health Organization (WHO) and Alzheimer's Disease International (ADI). Dementia: A public health priority. Available at: www.who.int/mental_health/publications/dementia_report_2012/en/
02. Fratiglioni L, De Ronchi D, Aguero-Torres H. Worldwide prevalence and incidence of dementia. *Drugs & Aging*. 1999;15:365–75. Available at: www.ncbi.nlm.nih.gov/pubmed/10600044
03. Alzheimer's Disease International (ADI). The global impact of dementia 2013–2050. Available at: www.alz.co.uk/research/GlobalImpactDementia2013.pdf
04. Alzheimer's Association (AA). 2014 Alzheimer's disease facts and figures. Available at: www.alz.org/downloads/Facts_Figures_2014.pdf
05. Andrieu S et al. IAGG Workshop: Health promotion program on prevention of late onset dementia. *Journal of Nutrition, Health & Aging*. 2011 Aug;15(7):562–75. [See also references 43, 44, 45.]
06. Alzheimer's Disease International (ADI). World Alzheimer Report 2013: Journey of caring. Available at: www.alz.co.uk/research/WorldAlzheimerReport2013.pdf
07. Alzheimer's Disease International (ADI). World Alzheimer's Report 2010: The global economic impact of dementia. Available at: www.alz.co.uk/research/files/WorldAlzheimerReport2010.pdf
08. Finch C. Evolution of the human lifespan and diseases of aging: Roles of infection, inflammation and nutrition. *Proceedings of the National Academy of Sciences of the United States of America* (PNAS). 2010;107(1):1718–1724. Available at: www.ncbi.nlm.nih.gov/pmc/articles/PMC2868286/
09. United Nations Department of Economic Affairs. World population prospects: The 2012 revision. Available at: <http://esa.un.org/unpd/wpp/Excel-Data/population.htm>
10. Hebert LE et al. Alzheimer disease in the United States (2010–2050) estimated using the 2010 Census. *Neurology*. 2013;80(19):1778–83. Available at: www.ncbi.nlm.nih.gov/pubmed/23390181
11. Fratiglioni L, De Ronchi D, Aguero-Torres H. Worldwide prevalence and incidence of dementia. *Drugs & Aging*. 1999;15:365–75. Available at: www.ncbi.nlm.nih.gov/pubmed/10600044
12. Alzheimer's Association (AA). 2014 Alzheimer's disease facts and figures. Available at: www.alz.org/downloads/Facts_Figures_2014.pdf
13. Brookmeyer R, Corrada MM, Curriero FC et al. Survival following a diagnosis of Alzheimer disease. *Archives of Neurology*. 2002;59:1764–7. Available at: www.ncbi.nlm.nih.gov/pubmed/12433264

14. Cummings JL, Cole G. Alzheimer disease. *Journal of American Medical Association (JAMA)*. 2002;287:2335–8. Available at: www.ncbi.nlm.nih.gov/pubmed/11988038
15. Albert MS et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Ageing-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia*. 2011;7(3):270–79. Available at: www.alz.org/documents_custom/Diagnostic_Recommendations_Alz_proof.pdf
16. Schubert et al. Comorbidity profile of dementia patients in primary care: Are they sicker? *Journal of the American Geriatrics Society*. 2006;54(1):104–9. Available at: <http://onlinelibrary.wiley.com/doi/10.1111/j.1532-5415.2005.00543.x/abstract>
17. World Health Organization (WHO). mhGAP Mental health gap action programme: Scaling up care for mental, neurological, and substance use disorders, 2008. Available at: www.who.int/mental_health/evidence/mhGAP/en/
18. EU Joint Programme – Neurodegenerative Disease Research (JPND research). About JPND. Available at: www.neurodegenerationresearch.eu/about/
19. World Health Organization (WHO) and Alzheimer's Disease International (ADI). Dementia: A public health priority. 2012. Available at: www.who.int/mental_health/publications/dementia_report_2012/en/
20. UK Department of Health. Global action on dementia. Available at: <http://dementiachallenge.dh.gov.uk/category/g8-dementia-summit/>
21. Fox NC, Petersen RC. The G8 dementia research summit – a starter for eight? *The Lancet*. 2013 December 14;382(9909):1968–9. Available at: [www.thelancet.com/journals/lancet/article/PIIS0140-6736\(13\)62426-5/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)62426-5/fulltext)
22. G8 dementia summit: a chance for united action. *The Lancet Neurology*. 2014 January;13(1):1. Available at: [www.thelancet.com/journals/laneur/article/PIIS1474-4422\(13\)70275-8/fulltext](http://www.thelancet.com/journals/laneur/article/PIIS1474-4422(13)70275-8/fulltext).
23. UK Government. G8 Dementia Summit Declaration 2013. Available at: www.gov.uk/government/uploads/system/uploads/attachment_data/file/265869/2901668_G8_DementiaSummitDeclaration_acc.pdf
24. Marist Poll. Alzheimer's most feared disease. Available at: www.maristpoll.marist.edu/1114-alzheimers-most-feared-disease
25. Alzheimer's Disease International (ADI). Global Alzheimer's and Dementia Alliance launches at World Health Assembly in Geneva. Available at: www.alz.co.uk/news/global-alzheimer-s-and-dementia-alliance-launches-at-world-health-assembly-in-geneva

26. UK Government. G8 Dementia Summit Declaration 2013. Available at: www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=2363&pageNumber=4
www.gov.uk/government/uploads/system/uploads/attachment_data/file/265869/2901668_G8_DementiaSummitDeclaration_acc.pdf
27. Ibid.
28. Alzheimer's Disease International (ADI). About World Alzheimer's Month. Available at: www.alz.co.uk/world-alzheimers-month/about
29. ALS Association. The ALS ice bucket challenge. Available at: www.alsa.org/fight-als/ice-bucket-challenge.html
30. Ibid.
31. Weiner MW et al. The Alzheimer's disease neuroimaging initiative: A review of papers published since its inception. *Alzheimer's & Dementia*. 2013 September;9(5):e111–94. Available at: www.ncbi.nlm.nih.gov/pubmed/23932184
32. Gui H, Jiang CQ et al. Influence of Alzheimer's disease genes on cognitive decline: the Guangzhou Biobank Cohort Study. *Neurobiol Aging*. 2014 October;35(10):2422.e3–8. Available at: www.ncbi.nlm.nih.gov/pubmed/24863667
33. Ellis KA et al. Enabling a multidisciplinary approach to the study of ageing and Alzheimer's disease: An update from the Australian imaging biomarkers and lifestyle (AIBL) study. *International Review of Psychiatry*. 2013 December;25(6):699–710. Available at: www.mdlinx.com/psychiatry/news-article.cfm/5060896/alzheimer-disease
34. Wortmann M. Importance of national plans for Alzheimer's disease and dementia. *Alzheimer's Research & Therapy*. 2013;5:40. Available at: <http://alzres.com/content/5/5/40>
35. Alzheimer Europe. France – National plans for Alzheimer and related diseases. Available at: www.alzheimer-europe.org/Policy-in-Practice2/National-Dementia-Plans/France?#fragment-1
36. Bupa/Alzheimer's Disease International (ADI). Improving dementia care worldwide: Ideas and advice on developing and implementing a national dementia plan. 2013. Available at: www.alz.co.uk/sites/default/files/pdfs/global-dementia-plan-report-ENGLISH.pdf
37. Miyamoto M et al. Government, professional, and public efforts in Japan to change the designation of dementia (chiho). *Dementia*. 2011;0(0):1–12. Available at: <http://dem.sagepub.com/content/early/2011/08/27/1471301211416616>

38. Hayashi M. The lessons Japan has for the UK on dementia. *Guardian*. 2013 June 11. Available at: www.theguardian.com/society/2013/jun/11/dementia-lessons-from-japan-hunt
39. Dementia Friends. *Become a friend*. Available at: www.dementiafriends.org.uk/
40. Alzheimer Society Canada. About dementia friends. Available at: www.alzheimer.ca/en/News-and-Events/feature-stories/dementia-friends
41. Small GW, Rabins PV, Barry PP et al. Diagnosis and treatment of Alzheimer disease and related disorders. Consensus statement of the American Association for Geriatric Psychiatry, the Alzheimer's Association and the American Geriatrics Society. *Journal of the American Medical Association (JAMA)*. 1997;278:1363–71. Available at: www.ncbi.nlm.nih.gov/pubmed/9343469
42. Deary IJ et al. Genetic contributions to stability and change in intelligence from childhood to old age. *Nature*. 2010;482:212–215. Available at: www.nature.com/nature/journal/v482/n7384/full/nature10781.html
43. The International Longevity Centre – UK. The European dementia research agenda. 2011. Available at: http://ilcuk.org.uk/files/pdf_pdf_165.pdf
44. Alzheimer's Disease International (ADI). Nutrition and Dementia report 2014. Available at: www.alz.co.uk/sites/default/files/pdfs/nutrition-and-dementia.pdf
45. Mayeux R, Stern Y. Epidemiology of Alzheimer Disease. *Cold Spring Harbor Perspectives in Medicine*. 2012;2(8):a006239. Available at: www.ncbi.nlm.nih.gov/pubmed/22908189
46. UK Prevention First Forum/Public Health England. Blackfriars Consensus on promoting brain health: Reducing dementia risks in the population. 2014. Available at: www.ukhealthforum.org.uk/prevention/pie/newsresults/?entryid43=35395
47. Alzheimer's Disease International (ADI). World Alzheimer Report 2014: Dementia and risk reduction an analysis of protective and modifiable factors. Available at: www.alz.co.uk/research/WorldAlzheimerReport2014.pdf
48. The International Longevity Centre – UK . Preventing dementia: A provocation. 2011. Available at: www.ilcuk.org.uk/index.php/publications/publication_details/preventing_dementia_a_provocation
49. Rubinsztein DC, Easton DF. Apolipoprotein E genetic variation and Alzheimer's disease: A meta-analysis. *Dementia and Geriatric Cognitive Disorders*. 1999;11(4):238. Available at: www.ncbi.nlm.nih.gov/pubmed/10325447
50. Sperling RA et al. The A4 study: Stopping AD before symptoms begin? *Science Translational Medicine*. 2014 March 19;6(228):228fs13. Available at: <http://stm.sciencemag.org/content/6/228/228fs13.abstract>

51. Moulder KL et al. Dominantly Inherited Alzheimer Network: Facilitating research and clinical trials. *Alzheimer's Research and Therapy*. 2013 October 17;5(5):48. Available at: www.ncbi.nlm.nih.gov/pubmed/2413156
52. Reiman EM et al. Alzheimer's Prevention Initiative: a plan to accelerate the evaluation of presymptomatic treatments. *Journal of Alzheimers Disease*. 2011;26 Suppl 3:321-9.
53. Roses AD et al. New applications of disease genetics and pharmacogenetics to drug development. *Current Opinion in Pharmacology*. 2014;(14):1-102.
54. Riedel WJ. Preventing cognitive decline in preclinical Alzheimer's disease. *Current Opinion in Pharmacology*. 2014 February;14:18-22. Available at: www.ncbi.nlm.nih.gov/pubmed/24565007
55. Ngandu T et al. Recruitment and baseline characteristics of participants in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) – a randomized controlled lifestyle trial. *International Journal of Environmental Research and Public Health*. 2014 September 10;11(9):9345-60. Available at: www.mdpi.com/1660-4601/11/9/9345
56. Alzheimer's Association (AA). Research advances from 2014 Alzheimer's Association International Conference. Available at: www.alz.org/aaic/releases_2014/mon-730pm-finger.asp
57. ALZFORUM. Collaborative umbrella CAPS three prevention trial initiatives. Available at: www.alzforum.org/news/conference-coverage/collaborative-umbrella-caps-three-prevention-trial-initiatives
58. Worley S. After disappointments, Alzheimer's researchers seek out new paths: Biomarkers and combination therapies may lead to disease-modifying treatments, experts say. *Pharmacy and Therapeutics*. 2014;39(5):365-369, 374. Available at: www.ncbi.nlm.nih.gov/pmc/articles/PMC4029120/
59. World Health Organization (WHO) and Alzheimer's Disease International (ADI). Dementia: A public health priority. 2012. Available at: www.who.int/mental_health/publications/dementia_report_2012/en/
60. Alzheimer's Disease International (ADI). World Alzheimer Report 2011: The benefits of early diagnosis and intervention. Available at: www.alz.co.uk/research/WorldAlzheimerReport2011.pdf
61. Alzheimer's Association. Alzheimer's disease facts and figures 2014. Available at: www.alz.org/downloads/Facts_Figures_2014.pdf
62. Alzheimer's Association. Early diagnosis: The value of knowing. 2013. Available at: http://act.alz.org/site/DocServer/Value_of_Knowing_Fact_Sheet__Public_Health_.pdf?docID=1781
63. Alzheimer's Disease International (ADI). Global dementia legacy event highlights care as a main priority. Available at: www.alz.co.uk/news/global-dementia-legacy-event-highlights-care-as-main-priority

64. Zhu C W, Sano M. Economic considerations in the management of Alzheimer's disease. *Journal of Clinical Interventions in Aging*. 2006;1(2):143–154. Available at: www.ncbi.nlm.nih.gov/pmc/articles/PMC2695165/#b87-cia-0102-143
65. Alzheimer's Society. Dementia friendly communities. Available at: www.alzheimers.org.uk/dementiafriendlycommunities
66. Alzheimer's Society. Services supported by our partnership. Available at: www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=2019&pageNumber=3
67. National Museums Liverpool. House of memories. Available at: www.liverpoolmuseums.org.uk/learning/projects/house-of-memories/
68. Alzheimer's Association. ALZconnected. Available at: www.alz.org/dm/alz_connected/general.htm
69. Winfree KN et al. The effect of step-synchronized vibration on patients with Parkinson's disease: Case studies on subjects with freezing of gait or an implanted deep brain stimulator. *IEEE Transactions on Neural Science and Rehabilitation Engineering*. 2013;21(5):806–11.
70. Parker CB. Stanford Center on Longevity competition challenges students to design products for seniors. *Stanford News*. 2014 April. Available at: <http://news.stanford.edu/news/2014/april/longevity-design-challenge-041414.html>
71. Lift Labs. About us. Available at: www.liftlabsdesign.com/
72. Lumosity. About Lumosity. Available at: www.lumosity.com/about
73. Shibata T, Wada K. Robot therapy: a new approach for mental healthcare of the elderly – a mini-review. *Gerontology*. 2011;57(4):378–86. Available at: www.ncbi.nlm.nih.gov/pubmed/20639620
74. Canada Institutes of Health Research. Second global dementia legacy event Co-hosted by Canada-France. Harnessing the power of discoveries: Maximizing academia–industry synergies. Available at: www.cihr-irsc.gc.ca/e/47902.html
75. Sabanovic S et al. PARO robot affects diverse interaction modalities in group sensory therapy for older adults with dementia. International Conference on Rehabilitation Robotics. 2013. Available at: www.ncbi.nlm.nih.gov/pubmed/24187245. www.researchgate.net/publication/258255139_PARO_robot_affects_diverse_interaction_modalities_in_group_sensory_therapy_for_older_adults_with_dementia
76. Moyle W et al. The effect of PARO on social engagement, communication, and quality of life in people living with dementia in residential care. *Journal of Gerontological Nursing*. 39(5):46–53. Available at: www.dementiaresearch.org.au/index.php?option=com_dcrc&view=dcrc&layout=project&Itemid=101&pid=93

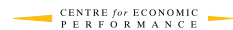
77. Calo CJ et al. Ethical implications of using the paro robot with a focus on dementia patient care. Human-robot interaction in elder care. Available at: www.aaai.org/ocs/index.php/WS/AAAIW11/paper/view/3808
78. Alzheimer's Association. Facts and figures 2014. Available at: www.alz.org/downloads/Facts_Figures_2014.pdf
79. Counting the cost: Caring for people with dementia on hospital wards. Alzheimer's Society. 2009.
80. World Health Organisation (WHO) and Alzheimer's Disease International (ADI). Dementia: a public health priority. 2012. Available at: www.who.int/mental_health/publications/dementia_report_2012/en/
81. Alzheimer's Disease International (ADI). World Alzheimer Report 2009. Available at: www.alz.co.uk/research/files/WorldAlzheimerReport.pdf
82. Age UK, Cornwall & Isles of Scilly. People, place, purpose: Shaping services around people and communities through the Newquay Pathfinder. 2013. Available at: www.cornwall.gov.uk/media/6162062/Newquay-pathfinder-Evaluation-proof3.pdf
83. Shih RA et al. Improving dementia long-term care: A policy blueprint. RAND Corporation. 2014. Available at: www.rand.org/pubs/research_reports/RR597.html
84. See www.memory360.org/
85. See www.921abc.com/
86. Alzheimer's Disease International (ADI). MetLife-ADI awards for dementia care education. Available at: www.alz.co.uk/metlife-adi-awards
87. Hong L. Executive Director, China Alzheimer's Project. Personal communication. 2014 October 31.
88. Cheng et al. Clinical Progression in Parkinson's disease and the neurobiology of axons. *Annals of Neurology*. 2010;67(6):715–725. Available at: www.ncbi.nlm.nih.gov/pubmed/20517933
89. Burke M. Renewed focus on dementia checked by drug challenges. *Chemistry World*. 2014. Available at: www.rsc.org/chemistryworld/2014/07/asd
90. Brinton RD, Wang JM. Therapeutic potential of neurogenesis for prevention and recovery from Alzheimer's disease: allopregnanolone as a proof of concept neurogenic agent. *Current Alzheimer Research*. 2006;3(3):185–90. Available from: www.ncbi.nlm.nih.gov/pubmed/16842093
91. World Dementia Council (WDC). World Dementia Council publishes Statement of Purpose. Available at: <http://dementiachallenge.dh.gov.uk/2014/05/30/world-dementia-council-publishes-statement-of-purpose/>

92. Pharmaceutical Research and Manufacturers of America (PhRMA). Researching Alzheimer's medicines: Setbacks and stepping stones. 2012. Available at: www.phrma.org/sites/default/files/pdf/alzheimersetbacksreportfinal912.pdf
93. Ghezzi L et al. Disease modifying drugs in Alzheimer's Disease. *Drug Design, Development and Therapy*. 2013;7:1471–9.
94. Wilkinson DG et al. Randomized 12-week comparative study of donepezil and rivastigmine in patients with mild to moderate Alzheimer disease. *International Journal of Clinical Practice*. 2002;56(6):441–6.
95. Rogers SL et al. Randomized, double-blind, placebo-controlled, 24-week study in 473 patients with mild to moderate Alzheimer disease donepezil. *American Academy of Neurology*. 1998;50:136–145. Available at: www.stvincents.ie/dynamic/File/Donepezil%20study.pdf
96. Scott TJ et al. Economic analysis of opportunities to accelerate Alzheimer's disease research and development. *Annals of the New York Academy of Sciences*. 2014;1313:17–34. Available at: <http://onlinelibrary.wiley.com/doi/10.1111/nyas.12417/pdf>
97. ALZFORUM. European project mixes adaptive design with trial-ready cohort. Available at: www.alzforum.org/news/conference-coverage/european-project-mixes-adaptive-design-trial-ready-cohort
98. Canady M. Is regulatory transformation for Alzheimer's therapies needed?. *BiotechNow*. Available at: www.biotech-now.org/health/2014/07/is-regulatory-transformation-for-alzheimers-therapies-needed#
99. US Food and Drug Administration (FDA). Guidance for Industry. Alzheimer's disease: Developing drugs for the treatment of early stage disease. Available at: www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm338287.pdf
100. European Medicines Agency. Discussion paper on the clinical investigation of medicines for the treatment of Alzheimer's disease and other dementias. Available at: www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/10/WC500176827.pdf
101. UK Government. UK commits to new action to find breakthrough on dementia. Available at: www.gov.uk/government/news/uk-commits-to-new-action-to-find-breakthrough-on-dementia
102. Alzheimer's Disease International (ADI). World Dementia Council announces next steps. Available at: www.alz.co.uk/news/world-dementia-council-announces-next-steps
103. European Medicines Agency. Adaptive Licensing. Available at: www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000601.jsp
104. Alzheimer's Disease International (ADI). World Alzheimer's Report 2013: An analysis of long-term care for dementia. Available at: www.alz.co.uk/research/world-report-2013

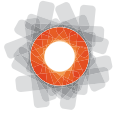
105. Golde T et al. Right sizing funding for Alzheimer's disease. *Alzheimer's Research and Therapy*. 2011;3(3):17. Available at: <http://alzres.com/content/pdf/alzrt76.pdf>
106. Choi D. Medicines for the mind: Policy-based 'pull' Incentives for creating breakthrough CNS drugs. *Neuron*. 2013;84(3):554–563. Available at: [www.cell.com/neuron/abstract/S0896-6273\(14\)00947-7](http://www.cell.com/neuron/abstract/S0896-6273(14)00947-7)
107. Alzheimer's Disease International (ADI). World Dementia Council announces next steps. Available at: www.alz.co.uk/news/world-dementia-council-announces-next-steps
108. New York Academy of Sciences (NYAS). Path to 2025: Alzheimer's Disease Summit. Reforms urgently needed to streamline road to Alzheimer's prevention and treatment as global prevalence is set to triple. Available at: www.nyas.org/AboutUs/MediaRelations/Detail.aspx?cid=7f193251-433b-4d4f-8a75-b61f68bf3b87
www.nyas.org/Publications/EBriefings/Detail.aspx?cid=e7aa2db6-e559-44c9-b50e-18f31055ca26
109. Milken Institute. Fixes in financing. Available at: www.fastercures.org/programs/fixes-in-financing/
110. New York Academy of Sciences (NYAS). Innovative funding models for Alzheimer's Disease and dementia research. Available at: www.nyas.org/AboutUs/AcademyNews.aspx?cid=1ac62356-31c1-4ff1-ad4e-b2c2ef44784d
111. Choi D. Medicines for the mind: Policy-based 'pull' Incentives for creating breakthrough CNS drugs. *Neuron*. 2013;84(3):554–563. Available at: [www.cell.com/neuron/abstract/S0896-6273\(14\)00947-7](http://www.cell.com/neuron/abstract/S0896-6273(14)00947-7)
112. Cheng M. International push for dementia drug or cure by 2025. *Huffington Post*. 2013. Available at: www.huffingtonpost.com/2013/12/11/dementia-cure_n_4427225.html
113. Lo AW, Ho C, Cummings J, Kosik KS. Parallel discovery of Alzheimer's therapeutics. *Science Journals*. 2014;18(6):241. Available at: <http://stm.sciencemag.org/content/6/241/241cm5>
114. Bank of America Private Wealth Management. 2013 US Trust Insights on wealth and worth. Bank of America Corporation. Available at: www.ustrust.com/publish/content/application/pdf/GWMOL/UST-Highlights-Brochure-Insights-on-Wealth-and-Worth-2013.pdf
115. Feldman HH, Haas M, Gandy S, Schoepp DD, Cross AJ, Mayeux R, Sperling RA, Fillit H, van de Hoef DL, Dougal S, Nye JS. Alzheimer's disease research and development: a call for a new research roadmap. New York Academy of Sciences. 2014 April;1313(1):1–16. Available at: www.nyas.org/WhatWeDo/Alzheimers/Publications.aspx
116. International Longevity Centre Global Alliance. The European research agenda. Available at: www.ilc-alliance.org/index.php/reports/report_details/the_european_dementia_research_agenda

- 117.** EU Joint Programme – Neurodegenerative Disease Research (JPND). Available at: www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/
- 118.** Alzheimer’s Society. Dementia Priority Setting Partnership. Available at: http://alzheimers.org.uk/site/scripts/documents_info.php?documentID=1804
- 119.** Orbimed. Our strategies. Available at: www.orbimed.com/en/about-us/our-strategies
- 120.** World Bank. Green bonds attract private sector climate finance. Available at: www.worldbank.org/en/topic/climatechange/brief/green-bonds-climate-finance

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