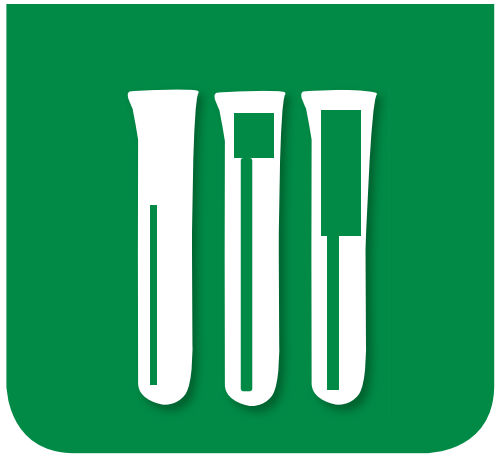
OECD Health Policy Studies

Addressing Dementia

THE OECD RESPONSE



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OECD
BETTER POLICIES FOR BETTER LIVES

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Foreword

Dementia is a debilitating condition for which there is currently no cure. As the condition progresses, those affected can be left dependent on others for support in their daily lives. The human and financial costs of dementia are of a worrying magnitude. Globally, it is the second largest cause of disability among those over the age of 70, with an estimated 44 million people living with dementia worldwide. In terms of financial burden, the global cost of dementia is well over half a trillion US dollars each year – roughly equal to the GDP of Switzerland. Nevertheless, health systems and social services are still failing to provide adequate support to people with dementia and their families. Given our ageing populations, these costs will only continue to escalate. Dementia is set to become 50% more common in high-income countries and 80% more common in low- and middle-income countries by 2030. It is high time that we provide a more effective policy response to dementia.

Our current model of innovation has failed to deliver the effective treatments that we urgently need. Progress has stalled, investment is low and it is becoming clearer that the existing regulatory framework and incentive structures are not working. Many people living with dementia face an unacceptably poor quality of life, while their family members are also under a major strain, left with health problems and the inability to work. Shortages in skilled professional caregivers force people with dementia to use unregulated, low-quality care, putting them at risk of abuse and neglect. More generally, fragmented, uncoordinated health care and social systems routinely fail people with complex needs, such as those with dementia. Tackling dementia will, thus, also help us to rethink our approach to supporting people with other complex health and social needs, and to transform innovation and drug development for other complex health conditions.

Dementia has been the focus of increased international collaboration and discussion, starting with the G8 Dementia Summit in London in December 2013, which formed the World Dementia Council, and continuing with subsequent legacy events hosted by other G7 countries. Throughout this process, the OECD has been at the forefront of the debate. The first Ministerial Conference on Global Action Against Dementia in March 2015, organised by the WHO and supported by the OECD, marks another stepping stone in our collective action to tackle dementia.

This report brings together for the first time our vision of how countries should address dementia, including how better policies could improve the lives of people living with the condition and of their families, how we can rethink our approach to innovation so as to deliver much-needed advances in dementia research, and the crucial role that big data and collaborative research can play in achieving these goals. By implementing the lessons highlighted in this report and by continuing to develop our knowledge through better research, evaluation and measurement, it should be possible to address dementia more effectively and to improve the lives of millions.

Angel Gurría, Secretary-General of the OECD

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The report draws on a range of recent OECD work and events. Chapters 1 and 2 are based on a draft paper presented by the OECD at the G7 dementia legacy event in Japan in November 2014 and funded by Japan. They also benefited from information provided by policy experts from Canada, France, Germany, Ireland, Japan, the Netherlands, the United Kingdom and the United States; and input from the OECD's Health Committee.

Chapter 3 presents a summary of work delivered under the OECD Working Party on Biotechnology. It draws on conclusions from the OECD workshop on "Enhancing translational research and clinical development for Alzheimer's disease and other dementias: The way forward", 11-12 November 2014, Lausanne, Switzerland. The workshop was hosted by the Government of Switzerland and supported by the Global CEO Initiative on Alzheimer's Disease and Alzheimer's Disease International. Key findings from an ongoing assessment of government funding of R&D on dementia are shown in Box 3.2. We would thank the designated correspondents from the G7 countries for providing information on government funding of dementia R&D.

Chapter 4 draws on key conclusions from two recent OECD meetings. The first, "Unlocking global collaboration to accelerate innovation for Alzheimer's disease and dementia", was held in Oxford in 2013 jointly with the Global Coalition on Ageing. The second, "Dementia research and care: Can big data help?", was held in Toronto in 2014 in collaboration with the Ontario Brain Institute (OBI) and the Institute for Health Policy, Management and Evaluation (IHPME) of the University of Toronto. The chapter also reports on work by the Oxford Internet Institute (UK) and the OECD on four data sharing initiatives related to dementia research.

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Acronyms and abbreviations

AD	Alzheimer's disease
ADNI	Alzheimer's Disease Neuroimaging Initiative
AUD	Australia dollar
BPSD	Behavioural and psychological symptoms of dementia
BRAIN	Brain Research through Advancing Innovative Neurotechnologies
CAD	Canadian dollar
CCNA	Canadian Consortium on Neurodegeneration in Aging
CDISC	Clinical Data Interchange Standards Consortium
CLSA	Canadian Longitudinal Study on Ageing
CNS	Central nervous system
CRO	Contract Research Organisation
DDI	Data-driven innovation
DNA	Deoxyribonucleic acid
DPUK	Dementias Platform UK
EHR	Electronic health record
EMA	European Medicines Agency
EMIF	European Medical Information Framework
FDA	US Food and Drug Authority
FTD	Frontotemporal dementia
GAAIN	Global Alzheimer's Association Interactive Network
GBAORD	Government budget appropriations or outlays for R&D
GDP	Gross domestic product
HERG	UK Health Economics Research Group
HGP	Human Genome Project
IADRP	Alzheimer's Disease Research Portfolio
IHPME	Institute for Health Policy, Management and Evaluation
JPND	Joint Programme – Neurodegenerative Disease Research
MRI/PET	Magnetic resonance imaging/Positron emission tomography

MS	Multiple sclerosis
NACC	US National Alzheimer's Coordinating Center
NDD	Neurodegenerative disease
NESTI	OECD Working Party of National Experts on Science and Technology Indicators
NIH	National Institutes of Health (United States)
NME	New Medical Entity
OBI	Ontario Brain Institute
PPP	Purchasing power parity
RCDC	Research, Condition, and Disease Categorization
USD	United States dollar

Executive summary

The large and growing human and financial costs of dementia make policy action an urgent priority. Dementia is already the second largest cause of disability for the over-70s and costs societies more than half a trillion US dollars every year globally, while ageing populations mean these costs are rising. Despite the urgency of addressing dementia, current policies are failing to deliver much-needed progress in finding a cure, while communities, health systems and social services are struggling to meet the needs of people with dementia and their families and carers. This report argues that urgent policy action is required to accelerate innovation and rethink how countries support those living with dementia now and in the future.

Developing a cure must be the long-term goal of dementia policy, but this can only happen if we fundamentally rethink our approach to innovation. This must involve the modernisation and international alignment of regulatory frameworks; greater investment and public-private risk-sharing mechanisms; more effective sharing and use of data; and more effective collaboration between the public and not-for profit sector, industry and academia. But even with these reforms, the development of disease-modifying therapies will realistically take several years.

In the meantime, an estimated 44 million people are living with dementia worldwide and health systems and social services are failing to provide adequate support. Many people living with dementia do not receive a timely diagnosis and face poor quality of life and loss of independence, while the families and carers who support them are under huge strain, suffer ill-health and are unable to work. Better policies are urgently needed to improve the lives of people living with dementia today.

This report brings together work carried out across the OECD to present a comprehensive vision for how dementia can be addressed now and in the future. With the issue having been brought to the forefront of the global policy debate by the G8 summit in London in December 2013, the subsequent legacy events, the work of the World Dementia Council and the First Ministerial Conference on Global Action Against Dementia in March 2015, this is a crucial time for global dementia policy. As world leaders come together to begin a new phase in their efforts to address the challenges posed by dementia, this report sets out the fundamental changes that are needed to make this phase dramatically more successful than the last.

Key recommendations

Communities and health and care systems must do more to support people with dementia and their families

- Too many people with dementia do not receive a timely diagnosis, which could help them to plan for future needs and access relevant services. Many countries rightly prioritise improving diagnosis rates, but in the absence of a cure, there is currently no therapeutic case for pre-symptomatic screening.

- Many people at early stages of dementia live in the community and rely heavily on support from families and other carers. Providing unpaid care leaves families and friends 20% more likely to suffer from mental health problems and makes it difficult for them to work. Improved counselling and respite care services, more flexible work arrangements and well-designed cash benefits are needed to support carers.
- As dementia progresses, good quality formal care services become increasingly important. Comprehensive workforce development strategies are needed to improve working conditions and skills levels in the workforce, and so reduce staff turnover and improve the quality of care. More person-centred models of institutional care are required to ensure that those with the most complex needs do not face a loss of control and social interaction.
- Good care co-ordination is a notable failure of most health systems, but it is even more important for people with dementia, who have complex needs and are less able to navigate fragmented systems. Better data sharing along the care pathway and across different care settings can ensure that their needs are promptly recognised and met with appropriate, specialist care.
- Although most people with dementia prefer to die at home, many still end up in hospital at the end of their lives. Access to palliative care outside of hospital must improve and a dementia-specific approach is needed to address challenges around consent and pain relief.

Regulatory and incentive frameworks must be reformed to drive progress in dementia research and care

- The complexity of dementia means that much research ends in failure, making it unattractive to private investors, while public funding for research is also low. Shared funding mechanisms that de-risk private investment are urgently needed, while increased public investment, including a global research fund, could provide additional resources and security.
- Regulatory frameworks need to be reformed to speed up progress and limit financial losses by allowing treatments that do not work to be discarded more quickly. National regulatory processes should be aligned to allow for more efficient international co-operation. Important regulatory and societal questions around conducting early-phase clinical studies involving people with pre-symptomatic dementia must also be addressed.
- Dementia research and development faces difficulties in scaling up: from pre-clinical research to human trials, then on to large clinical development programmes. Industry, academia, regulatory agencies, payers and patient organisations each play important roles at these different stages and stronger collaboration between these groups is needed.
- Clear reimbursement policies are required to ensure that people with dementia have access to the latest technological and medical developments and to provide clarity to developers around returns on investment. The development of technology assessment processes can help to address these concerns.

More effective collection and use of data is essential to advancing our knowledge around dementia care and treatment

- The measurement and evaluation of dementia policies remains a challenge. Innovative policies exist in many countries and an increasing number have published dementia strategies, but a greater focus on consistent implementation and evaluation is needed. The development of internationally comparable indicators should be prioritised, but this will only be possible with better recording of diagnoses, consistent clinical coding and linking of data across care settings.
- Recent advances in technology mean that it is increasingly possible to collect, store share and process huge amounts of health data. The complexity of both the biological processes underlying the disease and its progression means that broad (covering wide populations) and deep (detailed clinical and biological) data will play a crucial role in advancing our knowledge of how to tackle this condition.
- This will only be possible if researchers share their data with the wider scientific community, but significant disincentives and barriers prevent this from happening. Financial incentives, greater professional recognition or mandatory rules are required to encourage timely dissemination of findings and data. New models of consent need to be established, and privacy concerns and legal barriers addressed, to reduce current uncertainty around whether consent obtained for medical research allows data to be shared beyond an institution, collaboration, or nation. A publication portal for negative results could also ensure that these data are not lost and so reduce duplication of effort.
- To unlock the potential of big data, the international community needs to come together to identify and agree good practices in data governance and the setting of regulations and incentive mechanisms. The establishment of an international advisory body or reference centre to discuss key policy issues and explore good practices would be an important first step.

Assessment and recommendations

The large and growing human and financial cost of dementia provides an imperative for policy action. Dementia is a debilitating condition for which there is currently no cure. It is the second largest cause of disability for the over-70s and the global cost in 2010 was estimated to be USD 604 billion – more than the total economic output of Switzerland. Since dementia is strongly linked to age, its cost and burden will grow as people around the world live longer. By 2030, prevalence within the whole population is set to rise by 50% in high-income countries and 80% in low and middle-income countries. Governments and other organisations around the world need to act now to minimise the human and financial costs of dementia.

Finding a cure and preventive treatment must be the long-term goal of global dementia policy. This would be by far the greatest single step forward in addressing dementia. It would transform the lives of millions of people by relieving them of the burden of disability and save the billions of dollars every year that are the cost of dependency. But under existing models of innovation, progress has stalled and investment is low compared with other diseases of similar importance and profile, such as cancer and cardiovascular disease. Research into dementia is complex, risky and likely to fail, and the incentives for innovation are not strong enough to overcome these barriers. New approaches to innovation are badly needed, because it is not acceptable to simply write off conditions such as dementia – and the millions of people who suffer from them – as "too difficult".

Better policy can also ensure that people who are living with dementia now live better lives. Globally, an estimated 44 million people were living with dementia in 2013 and, with any medical breakthrough likely to be years away, millions more will develop the condition without the prospect of effective treatment. Communities are not well adapted to the needs of people with dementia, meaning that it can be difficult for them to remain independent and safe. Families and friends who look after those with dementia are not adequately supported, leaving them 20% more likely to suffer from mental health problems and often unable to work. People with dementia may need significant health and care for an extended period, but these systems are fragmented, difficult to navigate, and do not effectively manage their needs and risks.

Tackling dementia means addressing some of the most important policy challenges facing ageing societies across the OECD and beyond. It is essential to reconsider how dependency is managed and how those with complex medical and social needs are supported; and there is an urgent need to rethink the current model for innovation and drug development to make it work for complex conditions like dementia, where progress has effectively stalled. The complexity of these challenges means that the only way to address crucial gaps in knowledge around the management and treatment of dementia is by harnessing the potential of "big data" – the collection, storage, processing and effective use of massive amounts of research, clinical, and transactional information. The broad applicability of these issues means that dementia presents an acid test of

societies' ability to rise to some of the biggest policy challenges of the future. If these problems can be adequately addressed for people with dementia and other neurodegenerative diseases, the lessons learnt can be applied in other clinical and research areas.

1. Immediate action to address dementia now

Acting early to anticipate and prevent future needs

- *Healthy and active ageing may reduce dementia risks.* Lifestyle factors and preventive treatments are important determinants of the risk of developing a range of health conditions, and the same may be true for dementia. However, while some evidence suggests that diet and physical exercise might affect the risk of developing dementia, more research is needed to generate robust evidence.
- *Timely diagnosis can reduce the stress people with unexplained symptoms experience and facilitate care planning.* More than half of all people with dementia in many OECD countries are undiagnosed, leaving them without appropriate support or the opportunity to plan for future needs. It is therefore not surprising that many OECD countries are now prioritising increasing diagnosis rates. Progress in diagnostic techniques and better understanding of the biological mechanisms of dementia have improved the ability to detect signs of the condition many years before symptoms appear. In the absence of effective treatment, however, no therapeutic case for pre-symptomatic diagnosis can be made, since it causes distress without any offsetting benefits.

Improving quality of life for people living with dementia and their carers

As the condition progresses, people with dementia can become more dependent on others for their safety and well-being. This raises questions around who provides this support and in what setting.

- *Family and friends are the most important support mechanism for people with dementia living in the community.* Many OECD countries prioritise helping people to live at home for longer and helping communities adjust to accommodate people with dementia. This can provide people with dementia with a better quality of life, but with some estimates placing the proportion of community dementia care provided informally as high as 80%, it can also put strain on families and carers. More must be done to support them, including better respite care, counselling and peer-to-peer support, information and training, help to remain in employment and financial benefits. With increasing geographical mobility and female labour force participation, an increasing reliance on families to provide unpaid care may not be sustainable in the future.
- *Where family and friends are not able to meet the needs of someone with dementia, high quality professional care services are essential.* Standards and guidelines can help to ensure the quality of care, but they can only be effectively applied if there is an adequate supply of appropriately skilled carers. Many countries struggle to recruit and retain enough qualified staff and the shortfall is often filled by untrained, low-cost caregivers, providing unregulated care. A comprehensive approach to developing the long-term care workforce which tackles low pay, poor working conditions and the poor image of long-term care work is needed. Inappropriate care is still far too common: more than a third of care home residents receive antipsychotic medication, while physical restraints are used on between one in eight and half of all people with

dementia. Dementia-specific training, including alternative strategies for managing challenging behaviour, is needed to bring these rates down.

- *Some people with advanced dementia are better cared for in an institutional setting*, where complex needs and multiple comorbidities can be managed and the risk of hospitalisation reduced. However, some care institutions are not optimal for people with dementia and there is a risk that in focusing on helping those that can to live independently in the community, countries neglect the needs of those who cannot. Alternative types of "small-scale" institution are increasingly available in OECD countries, such as group homes in Japan or dementia villages in the Netherlands, but models of care that promote greater control and social interaction for people with dementia may be more important than the structure or size of the institution.

Improving access to high quality, person-centred care

- *Providing person-centred, co-ordinated care is one of the most pressing challenges facing health systems today, but it is even more crucial for people with dementia,* who have complex needs but limited ability to navigate complex health and social care systems. Both top-down approaches, such as better data sharing, and bottom-up approaches, such as case management, show promise, but progress has been limited due to legal, technical and financial challenges. Data sharing across care settings can ensure that people with dementia are better recognised in health care facilities, but this will only be beneficial if trained staff or specialist wards can then provide appropriate care.
- *Clear reimbursement policies for new technological and pharmaceutical developments would facilitate access for people with dementia and returns on investment for developers, subject to guarantees of safety and cost-effectiveness.* While technology has the potential to transform long-term care and significantly improve the lives of people living with dementia, there are few products on the market and even these have not always been robustly evaluated. Development does not always reflect the needs and preferences of people with dementia and long-term care systems do not have clear reimbursement policies or efficacy thresholds. The development of care technology assessment processes could address these concerns and allow developers to invest more confidently in dementia technology. Coverage and payment decisions for any future disease-modifying therapy need to be based on available medical evidence and relative costs of existing therapies, but policies also need to consider the ethical, epidemiological, and economic opportunities and constraints of a possible future disease-modifying treatment for Alzheimer's disease and other dementias.
- *The specific challenges around palliative care for dementia must be addressed to ensure people can die with dignity in a place of their choosing.* Although most people with dementia wish to die at home, far too many still die in hospital. Difficulties in communication and the management of consent mean that pain can go under-recognised and undertreated. A palliative care approach that recognises the specific needs and challenges of dementia and similar conditions is required, along with increased availability of this care outside of the hospital setting.

2. Developing our knowledge to address dementia better in the future

Rebalancing risks and rewards to encourage earlier and broader dementia research

- *Current basic and clinical research regulatory frameworks do not work well for dementia.* Clinical trials are crucial to provide safe and effective therapies to patients and to improve our understanding of dementia pathologies, but the translation of pre-clinical evidence into human trials is a complex and lengthy process which often slows down drug development. Policies and regulatory frameworks need to enable earlier entry into clinical research to foster the collection of valuable pharmacokinetic and pharmacodynamic information from patients. Adaptive clinical trials would enable early failure, limit financial loss and increase the chance of success. Greater alignment of national regulations would help to accelerate multinational trials and providing more resources to regulatory agencies for scientifically sound decision making would speed up the process of reform without putting patients' health at risk.
- *Greater involvement of people with early dementia in research is crucial.* Since the biological processes related to dementia may start years before symptoms appear, treatment options should be evaluated at earlier stages in an attempt to change the course of the disease. This means including patients with early or even pre-symptomatic dementia in research and clinical trials. A paradigm shift in dementia research is needed, with reforms in the design of clinical trials, patient selection and the choice of outcome measures and biomarkers. Participation in trials can be increased by strengthening public trust, transparency, and oversight in diagnostic campaigns, global patient registries, and clinical trial platforms. Crucially, important ethical and regulatory questions linked to pre-symptomatic research must be addressed.
- *Greater collaboration between the public and private sectors can deliver more effective results in dementia research.* Collaboration between industry, academia, regulatory agencies, payers and patient organisations is particularly important in scaling up research: first, translating pre-clinical evidence into first-in-human trials; then entering large, resource-intensive clinical development programmes after successful proof-of-concept. Governments play a key role in encouraging collaboration; they can help implement mechanisms that respect the potential, needs, and constraints of all stakeholders. However, collaborative partnerships will require new systems and structures that create the incentives for active participation and allow the rewards of success to be shared.
- *Public funding and risk-sharing mechanisms can help to increase investment in dementia research.* Too little funding is being directed towards dementia research, which accounts for only 0.8% of public spending on research and development. Meanwhile, the high likelihood of failure and financial loss makes drug development for Alzheimer's disease and other dementias unattractive for private investment. Governments, in close collaboration with other stakeholders, should explore risk-sharing mechanisms, such as shared funding structures in translational and early clinical research. Better monitoring of public resources committed to dementia research and shared standards for reporting project funding can improve the basis for public research funding decisions. A global dementia research fund could provide the necessary resources and planning security to translate innovation into the clinical setting.

Better collection and use of data to drive forward research into risk reduction, care and treatment

- *The complexity of dementia means that big data will play a crucial role in advancing our understanding of risk reduction, care and treatment.* Research into the cause and progression of dementia increasingly seeks to understand numerous interactions between age and gender, genetics and epigenetics, environment and lifestyle across the various stages of the disease. Meanwhile, the complex needs of people with dementia make evaluating care models difficult, so that we often do not know which approaches are the most effective. There is an emerging consensus that the research and evaluations needed to tackle these complex issues will require massive and diverse data collection, storage and processing and new investments in research and infrastructure. Recent advances in information technology make this increasingly feasible. Governments can promote these efforts by setting an appropriate regulatory and legal framework around privacy, data access and data standardisation; and through their roles as the largest funders of health and social services, and the largest supporters of research.
- *Perverse incentives for researchers, restrictive consent models and inadequate infrastructure are barriers to data sharing.* While these barriers are not specific to dementia, it provides a compelling illustration of some of the most important issues faced by the research community. Some barriers are of a technical nature, such as interoperability and standards, storage and infrastructure, but the most significant challenges lie elsewhere. There is no open data culture and academic credit-sharing structures create disincentives to share data, especially in research at the pre-publication stage. Mandatory requirements in research grant agreements, financial incentives or the recognition of open science in career advancement could address these concerns. Tiered, step-by-step or dynamic consent models can address issues of privacy and consent, which mean that data collected in one study often cannot be used by the wider research community. A publication portal for negative results could ensure that results from all clinical trials are disseminated, reducing the amount of missing data and duplication of effort.
- *Highlighting good practices and agreeing common principles are the key next steps in advancing the use of big data in dementia research.* Multinational consortia that are already doing this well should be surveyed to identify best practice approaches in data collection and sharing; common principles for realigning incentive frameworks to promote data sharing should be agreed internationally; the possibility of establishing an international advisory body or reference centre to discuss key issues and support the development of big data projects should be explored; and demonstration cases should be promoted that show the benefits of big data in dementia research and serve as pilot sites for working through challenges.
- *Primary research must be coupled with a renewed focus on measurement, evaluation and international benchmarking of dementia policy.* In too many areas of dementia policy the best approach is not yet known. Policies are not always properly evaluated and there are few robust metrics around dementia – while fewer still are internationally collected. The development and collection of robust, comparable measures should be a priority for all countries. Crucially, this will only be possible if improvements are made to data systems, such as better recording of diagnoses, more consistent coding of dementia in health care facilities and the linking of data across care settings.

Chapter 1

The growing human and financial cost of dementia: The case for policy action[1]

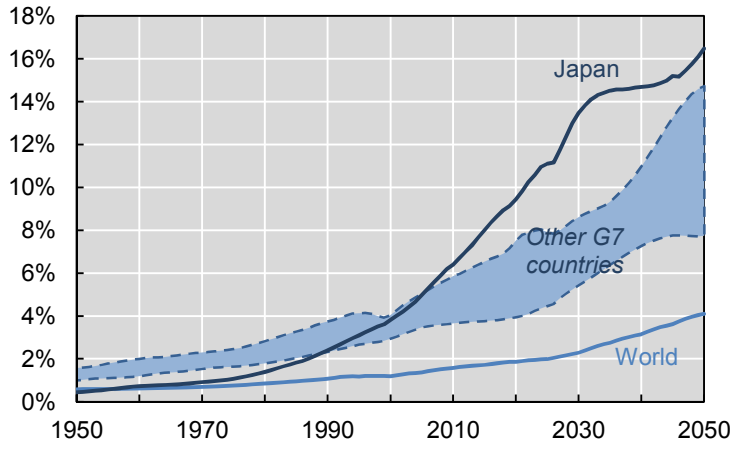
The global cost of dementia – both in terms of the financial cost and the burden of disease – is large and rising. Since dementia is strongly associated with old age, increasing life expectancies across the world will mean more people living with the condition. As a result, dementia is the fastest growing major cause of disability globally, and the cost to society – already estimated at USD 645 billion – is set to rise further. This is why dementia has rightly become a key policy priority for countries across the world. In the long-term, policy must aim to find a cure and preventive treatment – but this will take some time to deliver results. In the meantime, millions of people are living with dementia and policy must focus on what can be done to improve their lives.

Dementia is strongly associated with age, so will become more common as societies get older

Advances in medical care and improved living conditions mean that across the world people are living longer than ever. This is one of the great success stories of the last century and a cause for celebration. However, it also means that older people account for a greater share of the population. This is true globally, but more extreme for G7 countries, where life expectancies tend to be longer. The speed of ageing in Japan makes it an outlier even among the G7. In the middle of last century, Japan had a younger population than any other G7 country and even in 1990 it was young by G7 standards, with just 2.4% of the population over 80. However, rapid increases in life expectancy have seen Japan go from being the youngest G7 country to the oldest in just 20 years, and by 2050 around 16.5% of the population will be over 80 (Figure 1.1).

Figure 1.1. G7 countries are old by global standards and set to age further

Proportion of the total population over 80, Japan, other G7 countries and the world



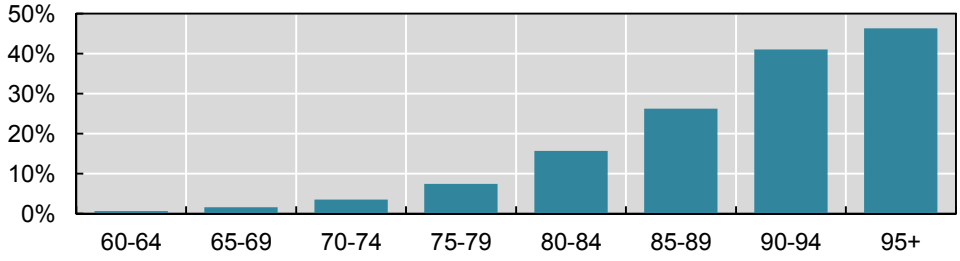
Source: OECD population projections.

Ageing societies present new challenges, such as the rising prevalence of age-related conditions like dementia. The likelihood of having dementia is strongly correlated with age (Figure 1.2). Dementia remains relatively rare in working age adults, with between 2% and 10% of cases starting before the age of 65 (World Health Organization, 2012a). However, after the age of 80, prevalence increases steeply and nearly half of all Europeans over the age of 95 have dementia.

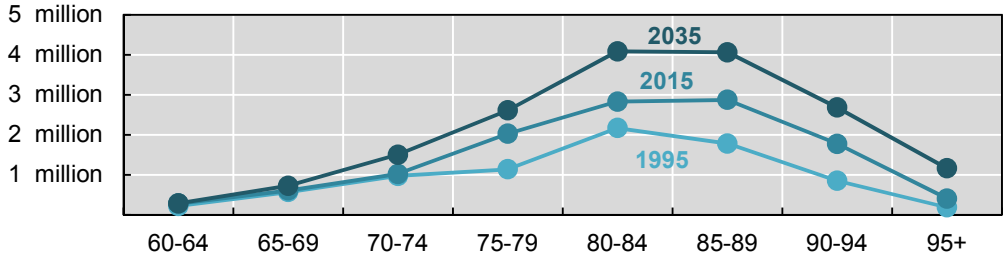
Ageing populations therefore mean more cases of dementia. If age-specific prevalence rates are assumed to remain constant, demographic change has led to a 50% increase in overall prevalence in Europe over the last 20 years and we should expect a similar increase in the next 20 years. There will be a particularly rapid increase in the number of people over 95 with dementia.

Figure 1.2. Dementia prevalence will continue to grow over the next 20 years, with the oldest groups becoming increasingly important

Panel A. Dementia prevalence in Europe by age band



Panel B. The number of people with dementia in Europe by age band in different years (millions)



Source: OECD analysis of data from Alzheimer's Europe and the United Nations; assumes age-specific prevalence rates are constant over time.

But it is not just in Europe, G7 countries and the developed world that dementia is on the rise. As developing countries catch up economically, they are also ageing at a faster rate than the developed world. While dementia prevalence is expected to rise by around 50% in high income countries by 2030, it is expected to rise by nearly 80% in low and middle income countries. These increases will take the total number of people living with dementia worldwide from 44 million in 2013 to 76 million in 2030 and 135 million in 2050 (Alzheimer's Disease International, 2013).

Although there is no consensus on how age-specific prevalence rates will change over time, some recent research has suggested that they may be falling in some countries (Matthews et al., 2013; Larson et al., 2013). This would offset some of the projected increases in overall prevalence, but would not be enough to cancel out the effect of population ageing and the number of people living with dementia would still continue to rise significantly.

Box 1.1. What is dementia?

Dementia is a syndrome – usually of a chronic or progressive nature – in which there is deterioration in cognitive function (i.e. the ability to process thought) beyond what might be expected from normal ageing. It affects memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgement. Consciousness is not affected. The impairment in cognitive function is commonly accompanied, and occasionally preceded, by deterioration in emotional control, social behaviour, or motivation. Dementia is caused by a variety of diseases and injuries that primarily or secondarily affect the brain, such as Alzheimer's disease or stroke.

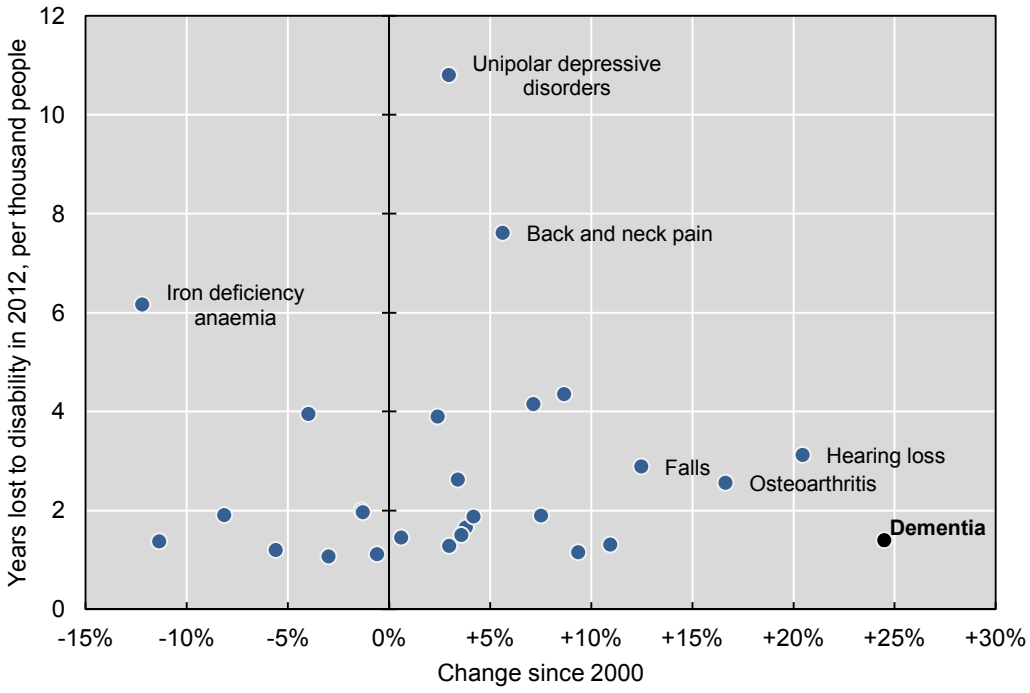
Source: World Health Organization (2012), "Fact Sheet Number 362. Dementia", www.who.int/mediacentre/factsheets/fs362/en/.

Dementia is a significant contributor to the global burden of disease and the fastest growing major cause of disability

Burden of disease, according to the WHO definition, is a combination of the burden of premature mortality and the burden of living with a disability. While dementia can reduce life expectancy (Dodge et al., 2003) it is often not recorded as a cause of death making mortality estimates unreliable. However, dementia is a significant contributor to the burden of disability. The WHO quantifies this in terms of the number of years of life "lost" due to disability and in 2012 dementia was responsible for 1.3% of the global total – or 1.4 years lost per thousand people. Dementia is the second largest cause of disability for people over 70, and the fastest growing major[2] cause of disability for all age groups, with its burden increasing by 24% between 2000 and 2012 (Figure 1.3).

Figure 1.3. The burden of disability associated with dementia is rising faster than any other major cause

Global years lost due to disability in 2012 (vertical axis) and how this has changed since 2000 (horizontal axis), for all major causes of disability, where major means those contributing at least 1% of the total global burden of disability



Source: WHO Global Burden of Disease estimates.

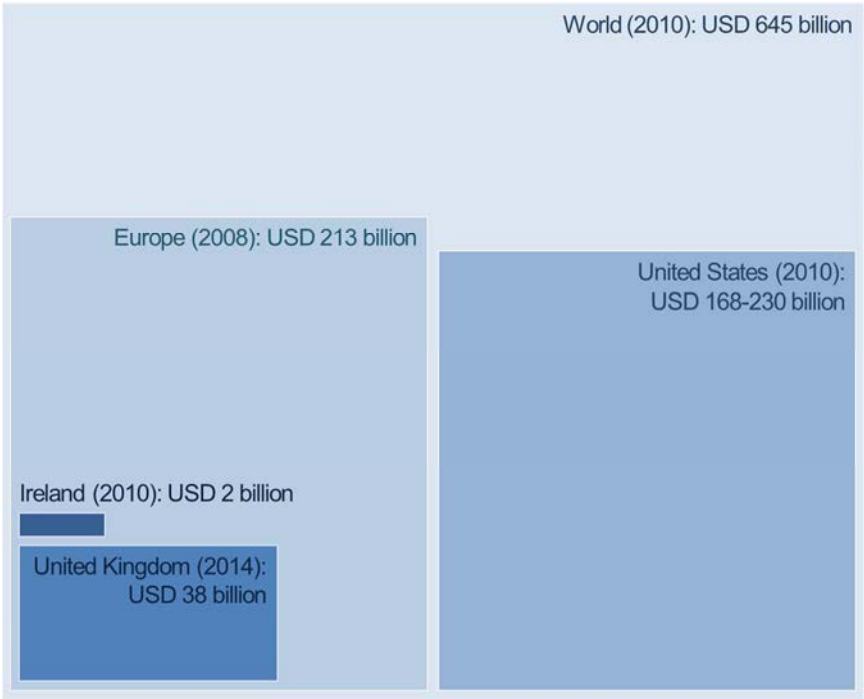
The financial cost of dementia is large and growing, although quantifying it remains a challenge

The direct costs of dementia account for a significant proportion of health spending (including long-term care) in OECD countries, although there is cross-country variation. For example, in the Netherlands (2011), dementia accounts for 5.5% of total health spending; while in Germany (2008) it accounts for 3.7%; and in Korea (2009) it accounts for 3%. The majority of the costs relate to nursing home care, except in Korea where hospital costs dominate.[3]

However, the direct costs of dementia are only part of the story since indirect costs arise from the impact on families, carers and the wider community. Studies in a number of countries have tried to capture the full cost of dementia, including both direct and indirect costs, and the results of some of these studies are summarised in Figure 1.4. These estimates indicate that the global cost of dementia is very large – around USD 645 billion per year globally, equivalent to the GDP of Switzerland. Most of this cost currently falls in high-income countries, with Europe and the United States accounting for about a third each. However, with prevalence rising more quickly in low and middle-income countries, they may account for a greater share of the cost in the future.

Measuring and estimating indirect costs presents methodological challenges and the cost of informal care is particularly hard to quantify, since it is not always clear how much is being provided or how to assign a monetary value. As a result, different studies take different approaches and there is significant uncertainty around the resulting numbers, so Figure 1.4 should be taken as a rough illustration of scale of global costs, rather than a robust set of estimates.

Figure 1.4. An overview of existing estimates of the financial cost of dementia



Note: There are considerable methodological differences between the studies summarised here, so this figure should be treated as illustrative only. In general, estimates include indirect costs, such as the opportunity cost of informal care, but methodologies for estimating these costs vary. All costs are in US dollars, inflated to 2013 in line with consumer prices, and so may not match the numerical values stated in the source papers.

Source: Wimo, A. et al. (2011), "The Economic Impact of Dementia in Europe in 2008 – Cost Estimates from the Eurocode Project", *International Journal of Geriatric Psychiatry*, Vol. 26, No. 8, pp. 825-832; Wimo, A. et al. (2013), "The Worldwide Economic Impact of Dementia 2010", *Alzheimer's & Dementia,* Vol. 9, No. 1, pp. 1-11, http://dx.doi.org/10.1016/j.jalz.2012.11.006; Connolly, S. et al. (2014), "Estimating the Economic and Social Costs of Dementia in Ireland", *Dementia*, Vol. 13, No. 1, pp. 5-22; Prince, M. et al. (2014), *Dementia UK*, Second edition, Alzheimer's Society; Hurd, M.D. et al. (2013), "Monetary Costs of Dementia in the United States", *New England Journal of Medicine*, Vol. 368, pp. 1326-1334.

While much of the cost of dementia is borne by families and other carers, the majority of the cost of formal services is met from public budgets (Colombo et al., 2011). Long-term care is a labour-intensive service with limited opportunities for efficiency gains, so caring for people with dementia is likely to cost increasing amounts of public money and place increasing strain on families and carers. It is therefore essential that spending on formal care achieves the best possible outcomes and value for money, and that the burden on families and carers is minimised through an appropriate mix of policies.

The long-term aim of dementia policy must be to find a cure and effective preventive treatment, but in the short term it should focus on improving the lives of people living with dementia

There is currently no cure for dementia and the few drugs that are available only temporarily help in modifying the symptoms. Finding a cure and an effective preventive treatment would be the single greatest step forward that could happen in the field of dementia and would alleviate huge amounts of disability and suffering across the world. However, progress in dementia research has been slow and investment is a fraction of what it is for other diseases such as cancer. We urgently need to reinvigorate this field so that effective therapeutic options (i.e. disease-modifying treatments) are found as soon as possible. Chapter 3 discusses how this can be achieved.

But even a reinvigorated programme of research will take time – perhaps decades – to deliver results. In the meantime, millions of people are living with dementia and millions more will develop the condition. Policy must therefore focus on what can be done to improve the lives of these people, whether that is by improving long-term care services, making adjustments so that people with dementia can remain part of the community, reducing social stigma or proving safer and more appropriate health. Chapter 2 discusses the objectives, policy options and evidence of what works.

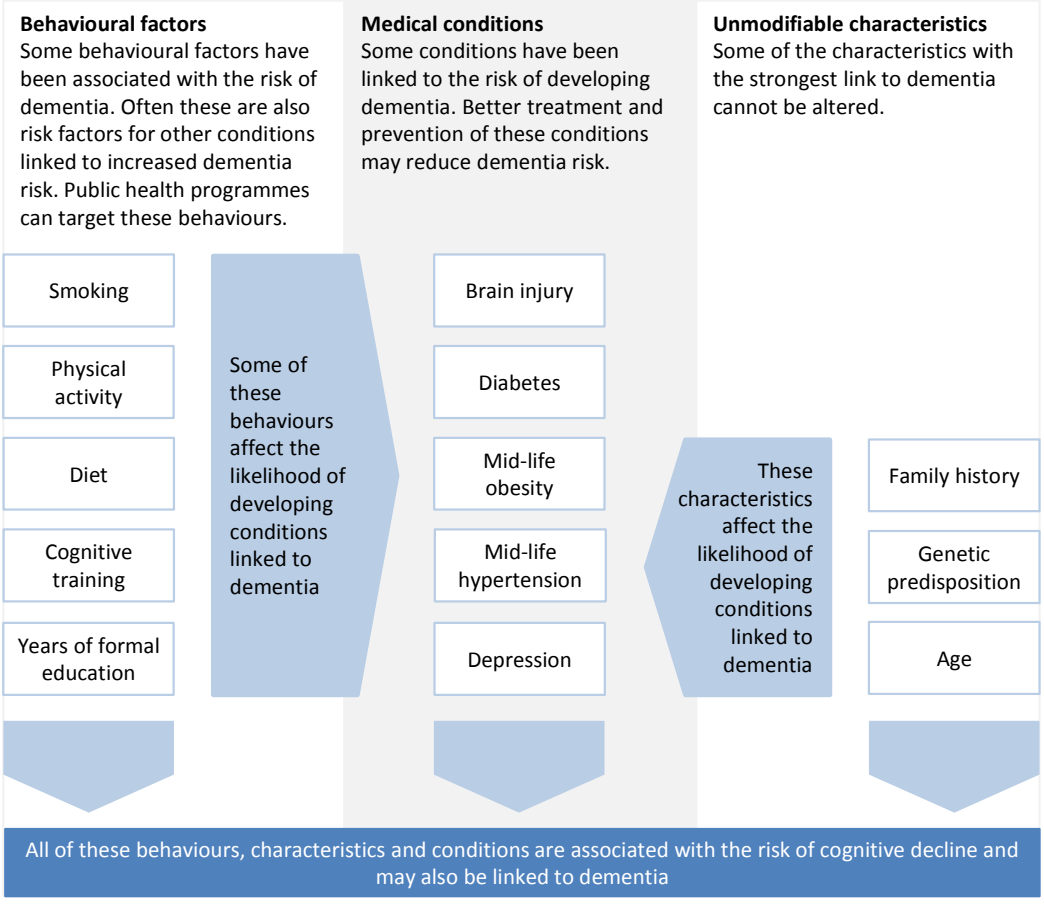
These objectives – both in the short and in the long term – will not be easy to achieve. This is in part because of a lack of knowledge: we simply do not understand dementia well enough to know how to cure it; and there are many gaps in our knowledge around what may be the best care approaches. Because of the clinical and biological complexity of dementia an emerging consensus is that the crucial studies needed to underpin drug discovery, validate alternative models of risk reduction and care and develop new therapeutic strategies aimed at slowing disease progression will require massive and diverse data collection, storage and processing and new investments in research and infrastructure. Harnessing the power of this data has numerous methodological, ethical and economic advantages "as no one nation has all the assets to pursue this type of research independently". The potential of big data, and how it can be used to drive improvements in care and medical research, is discussed in Chapter 4.

Box 1.2. Reducing the risk of people developing dementia

A recent review conducted by the Alzheimer's Association for the World Dementia Council looked at the academic literature around risk factors for dementia. Although the evidence is often inconclusive, due in part to a lack of systematic data and a limited number of clinical studies of specific interventions, the review concluded that there is sufficient evidence to support the association of some modifiable risk factors with cognitive decline and to suggest that they may also be linked to dementia. This is in line with the conclusions of other recent reviews of the evidence in this area (Alzheimer's Association, 2014).

The diagram below summarises the risk factors identified. Modifiable factors fall into two broad categories: behavioural factors and medical conditions. The behavioural factors identified include a number of cardiovascular risk factors, which can be targeted by healthy ageing campaigns; while better treatments of certain medical conditions may also reduce risk. In both cases, the approach will not be specific to dementia, so the Alzheimer's Association recommends that "governments around the world should incorporate brain health promotion messages into their public health campaigns" – rather than developing dementia-specific strategies. The OECD and others have published research on what works in promoting healthy behaviours and lifestyles, but since this is a large topic and not specific to dementia, it will not be covered in detail here.

Overview of possible risk factors for cognitive decline and dementia



Notes

1. This chapter was authored by Tim Muir, Klara Lorenz and Yuki Murakami from OECD Directorate for Employment, Labour and Social Affairs.
2. Where "major" causes are those contributing at least 1% of the total global burden of disability.
3. These costs are likely to be underestimates, due to under-diagnosis, under-recording and the difficulty of capturing information about home care services.

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Chapter 2

Improving the lives of people living with dementia[1]

Until a cure or preventive treatment for dementia is developed, policy must focus on improving the lives of people living with the condition and their families. This means keeping them as safe and healthy as possible, but also ensuring they live dignified lives, retain control and independence and maintain social relationships. All countries need to consider the key policy objectives identified in this chapter – covering all stages of dementia, from risk reduction and detection through to the end of life – and use the best available evidence to design appropriate policies. Some countries have published dementia strategies reflecting many of these priorities, but implementation remains a challenge. A better understanding of what works in improving the lives of people living with dementia is also needed. Countries should focus on evaluating their policies and sharing the results, and the development of an internationally comparable set of indicators around dementia should be explored.

Introduction: The aims and objectives of dementia policy

Although there is no cure or effective treatment for dementia, better policy can improve the lives of people living with dementia

There is currently no cure for dementia and the few drugs that are available to slow the progress of the condition have only limited effectiveness for a short period. However, better policy can still improve the quality of life that people with dementia and their families experience, by promoting a more accommodating society and ensuring access to high quality health and care services. Quality of life is an inherently difficult thing to define and measure and there is no single definition of the concept. A range of subjective (focusing on self-reported well-being) and objective (identifying objective factors that influence well-being) definitions exist. Various outcome measures are used in the studies on which this chapter is based, so it is not possible to assess all the policies discussed against a single definition of quality of life. However, it is important to have in mind what people with dementia see as the key determinants of their quality of life (Box 2.1) and these themes will be picked up throughout this chapter.

Box 2.1. What people with dementia see as the key determinants of their quality of life

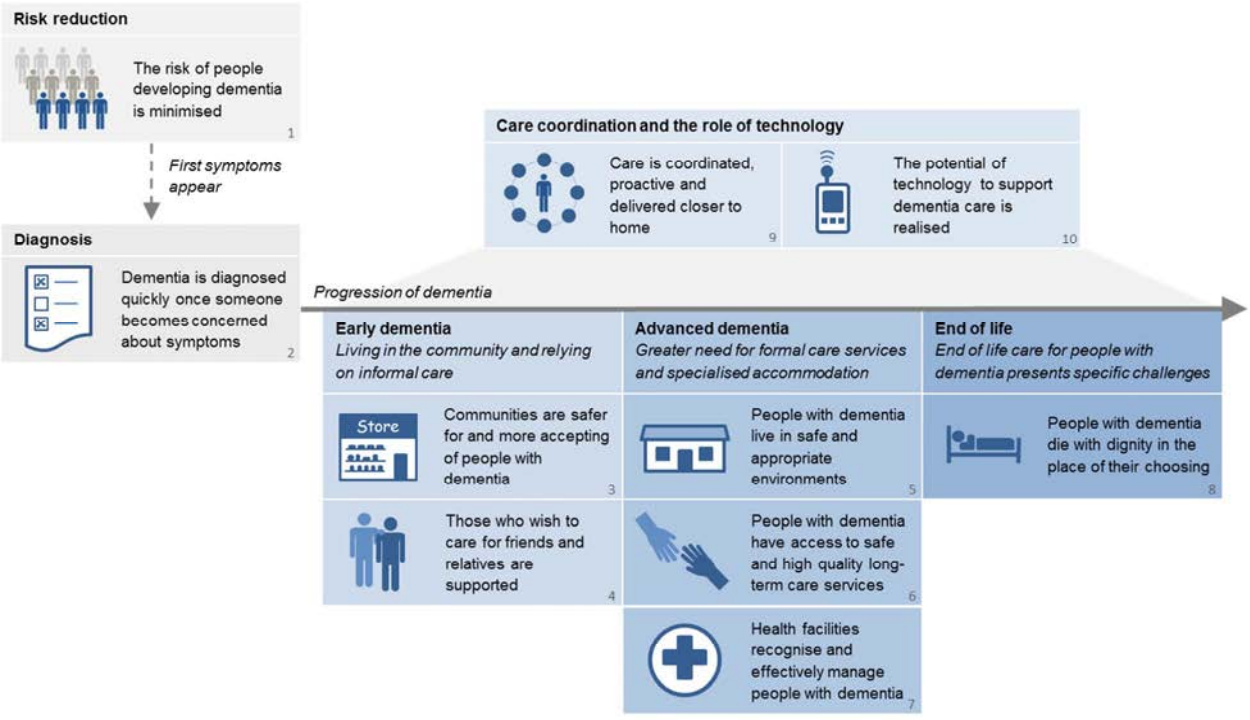
- *Social interaction:* Maintaining relationships with others; having someone to talk to; being able to communicate and share humour with others; being able to engage in social and leisure activities.
- *Comfort and security:* Living in an environment that feels comfortable and safe; financial security.
- *Health:* Remaining as physically healthy as possible.
- *Dignity, independence and sense of self:* Having independence, choice and control; retaining a sense of personal identity such as being able to practice faith or religion; not experiencing stigma around dementia.

Source: Adapted from: Dröes, R. et al. (2006), "Quality of Life in Dementia in Perspective: An Explorative Study of Variations in Opinions Among People with Dementia and their Professional Caregivers, and in Literatures", *Dementia,* Vol. 5 No.4, pp. 533-558, http://dx.doi.org/10.1177/1471301206069929; Alzheimer's Society (2010), *My Name Is Not Dementia – People with Dementia Discuss Quality of Life Indicators,* Alzheimer's Society, London, www.alzheimers.org.uk/site/scripts/download_info.php?fileID=876.

Better policy can make a difference at all stages of dementia

Dementia is usually a progressive condition and people at different stages typically have different needs and require different services. This chapter looks at how better policy can make a difference to the quality of life that people with dementia experience, focusing on diagnosis and access to care; the needs and issues primarily associated with early and advanced dementia,[2] care co-ordination and the role of technology; and how progress in dementia policy can be measured. Based on a review of the literature and current practice, and an OECD questionnaire sent to selected countries, this chapter identifies the key objectives that policy should be seeking to achieve at each stage of dementia (Figure 2.1) and possible policy approaches to address these objectives (Figure 2.2).

Figure 2.1. Key objectives of dementia policy



A number of countries (Belgium, Denmark, France, Germany, Netherlands, Norway, Sweden, England, Scotland) have already published dementia strategies that reflect many of these key objectives and set out policy approaches to achieving them. However, ensuring that these policies are effectively implemented remains a challenge. Another challenge is that we do not have enough evidence of what works in improving the lives of people with dementia. As countries implement their strategies and policies for dementia, the benefits of different approaches should be rigorously evaluated to provide a robust evidence base that can help countries to refine and improve their approaches to dementia. Pilot schemes (such as the *Leuchtturmprojekt Demenz* – Dementia Beacon Project – in Germany) can be a valuable way to test new policy ideas before wider implementation, but there is also a need for more primary research focusing on improving the lives of people living with dementia. The development of internationally comparable indicators of the effectiveness of dementia policies, linked to the objectives set out in Figure 2.1, should also be prioritised.

Figure 2.2. Examples of possible approaches to key objectives of dementia policy

A summary of policies that countries have implemented to tackle the key objectives identified in this chapter, or policies that have been found to be effective in the academic literature

1	The risk of developing dementia is minimised	Healthy ageing strategies targeting generic risk factors
2	Dementia is diagnosed quickly once someone becomes concerned about symptoms	Increase the availability and accessibility of diagnostic services; provide training to primary care staff in identifying dementia (and what to do next); incentivise primary care staff to identify and manage dementia; post-diagnostic support to link people to appropriate health and long-term care services
3	Communities are safer for and more accepting of people with dementia	Public awareness campaigns to reduce stigma; dementia education in schools; targeted education of those who come into contact with people with dementia (e.g. shopkeepers, bus drivers)
4	Those who care for friends and relatives with dementia are supported	Increase the availability and uptake of respite care services; provide training to carers; peer-to-peer support networks
5	People with dementia live in safe and appropriate environments	Provide guidance and financial support to help people to make their homes suitable for living with dementia; accelerate the introduction of alternative models of institutional care that promote dignity
6	People with dementia have access to safe and high quality long-term care services	Implement guidelines and standards of practice for dementia care; develop a comprehensive approach to recruiting and training a dementia care workforce; systematically monitor the management of behavioural symptoms, including the use of antipsychotics and physical restraints; promote independence and self-determination through user-directed support
7	Health services recognise and effectively manage people with dementia	Establish dementia registries or electronic health records to ensure that diagnoses are always shared; train staff in recognising and responding to people with dementia; specialist staff and dedicated wards in hospitals
8	People with dementia die with dignity in the place of their choosing	Increase access to end-of-life care outside of hospitals; train care home staff in palliative care
9	Care is co-ordinated, proactive and delivered closer to home	Provide more proactive primary care for people with dementia; encourage establishment of multidisciplinary and co-ordinated services; provide acute services outside of hospital where possible; better management of comorbidities; primary care physicians available on-site or on call in care institutions; better recording and sharing of patient data
10	The potential of technology to support dementia care is realised	Support an increased focus on user requirements in the development of new technologies; promote robust, independent evaluations; develop care technology assessment processes; integrate effective technologies into health and care systems

Diagnosis and access to care

Dementia is often diagnosed too late, so a continued focus on timely diagnosis is needed, but screening people who are not concerned about symptoms may do more harm than good

Diagnostic testing should be available to anyone who is concerned about dementia, but there is currently no rationale for screening

There is currently no cure for dementia and treatments to slow its progress have limited efficacy. Nonetheless, timely diagnosis of dementia can have several benefits. If people are more aware of their condition and its likely trajectory, they can make advance preparations for the care that they will need and take decisions about their end-of-life care, they may choose to undergo medical or psychological therapies to slow cognitive decline as far as possible, and behavioural and psychological symptoms of dementia can be more effectively managed. Timely diagnosis can also help carers to understand difficult behavioural changes. These benefits need to be weighed against the disbenefits of diagnostic testing, including the unnecessary distress caused by over-diagnosis – mild cognitive impairment does not always lead to dementia and all diagnostic tests can result in false positive results – while even a correct diagnosis can lead to distress and social stigma (Milne, 2010).

There is evidence that where people are concerned about symptoms, even a positive diagnosis can lead to reduced anxiety (Carpenter, 2008), suggesting that this is the optimal time for dementia to be diagnosed. Diagnosis at an earlier stage, such as pre-symptomatic screening, may cause unnecessary distress; while diagnosis at a later stage may lead to missed opportunities for treatment and planning. Policy in OECD countries generally reflects these trade-offs: most OECD countries aim to make diagnosis available, but some do not actively promote it and none have implemented pre-symptomatic screening. For example, people in France are provided with the opportunity of diagnostic testing, but have the right to refuse (Haute Autorité de Santé, 2011); people in the Netherlands are entitled to testing, but early dementia detection is not actively promoted.

Early detection of dementia is a priority for many OECD countries, but increasing timely diagnosis rates remains a challenge

Improving early detection rates is a priority for many OECD countries and is included in a number of dementia strategies (Australia, France, England, Germany, Switzerland and the United States). But even where diagnostic services are available, people may not be aware of them or may be reluctant to take them up. Some OECD countries have addressed this by pro-actively offering testing to high-risk groups. In Australia, primary care doctors are encouraged to assess people who are exhibiting symptoms or have certain risk factors, including a "family history of dementia, repeated head trauma, increased cardiovascular risk, depression [or] Down syndrome" (Royal Australian College of General Practitioners, 2012). Other countries provide financial incentives for primary care doctors to offer testing to high-risk groups, such as those learning disabilities or other neurological conditions, or those who have had a stroke (England); or to assess people in their own homes (France).

However, diagnosis rates are still low. Fewer than half of the people living with dementia in England have been diagnosed (Department of Health, 2013) and in Germany, 44.5% of care home residents with dementia have no record of diagnosis (Schäufele, 2013). An increased focus on detection can improve these diagnosis rates. In 2008,

Scotland set a target to increase its dementia diagnosis rate and support was provided to local health and care systems to make the necessary improvements. As a result, the diagnosis rate has risen from around 40% in 2008 to its current level of 67% (Scottish Government, 2014).

Box 2.2. Principles of timely diagnosis from the ALCOVE project

The ALCOVE project, which sought to develop evidence-based recommendations around dementia for policy makers in Europe, looked at the issue of timely diagnosis. Based on the idea that the best time for a person to receive a diagnosis is that point at which that diagnosis is most beneficial to them, and least harmful, four principles were developed to guide policy. In common with other research, these principles indicate that diagnosis should be available when people first become concerned about symptoms. However, they also stress the importance of minimising social stigma to reduce the negative impacts of diagnosis; prioritising the rights and wishes of the individual; and recognising that how a diagnosis is delivered can have a major impact on how well people adjust to living with dementia.

Principle 1. Timely diagnosis of dementia should be available to all citizens who require it and accessible to all sections of the community at a stage when people first notice changes in cognitive function

Principle 2. Decreasing fear and stigma about dementia is a necessary precursor for increasing the numbers of people coming forward for diagnosis

Principle 3. The rights and wishes of the person with suspected dementia should be paramount in engaging with the assessment process used to achieve a diagnosis

Principle 4. Giving and receiving a diagnosis of dementia is a key intervention in the complex adjustment process to living with dementia

Source: Brooker, D. et al. (2014) "Public Health Guidance to Facilitate Timely Diagnosis of Dementia: Alzheimer's Cooperative Valuation in Europe Recommendations", *International Journal of Geriatric Psychiatry*, Vol. 29, No. 7, pp. 1099-1166, http://dx.doi.org/10.1002/gps.4066.

Standardised, comprehensive needs assessment can improve diagnosis and access to care

Most OECD countries use some form of standardised needs assessment to measure a person's level of disability and determine whether they are eligible for public support. Many needs assessment tools also assess cognitive and behavioural issues, which are relevant dementia. For example, assessment processes in France and Ireland include a Mental State Examination; InterRAI (an assessment tool used in a number of countries) includes a section to screen for cognitive impairment; and the Aged Care Funding Instrument used in Australia includes a domain on behaviour. The inclusion of cognitive tests in assessment tools can promote the timely diagnosis of dementia by either providing a diagnosis directly or indicating the need for further testing (OECD/European Commission, 2013).

Once someone is diagnosed with dementia, they need access to follow-up support and services if the benefits of diagnosis are to be realised

Once someone has been diagnosed with dementia, they may want to access health or long-term care services; take decisions about their future care; apply for disability-related benefits; or arrange their financial and legal affairs, such as by making a will. The range of options can be daunting and the services that people need are often spread across health and

care systems and beyond. A single point of access for information on dementia can help, and advocacy groups and governments in some OECD countries provide websites (such as the "e-seniors" internet portal in France) and phone lines (such as Alzheimer's Australia's National Dementia Helpline). Primary care doctors often play an important role in diagnosis and access to care, so many OECD countries including Australia, England, Germany, the Netherlands, Ontario (Canada) and Japan provide them with training on identifying the symptoms of dementia and directing people to appropriate care and treatment.

But even with access to all the relevant information, arranging care services can be confusing and distressing, so more active support can be beneficial, especially in the early stages after diagnosis. Initial phase intensive support, provided by multi-disciplinary teams of nurses, physical therapists and care co-ordinators, is being trialled in 14 regions of Japan. These teams conduct home visits, carry out assessments and help to build capacity so that people can manage their own affairs when the intensive support finishes (Nakanishi and Nakanishi, 2013). The Dementia Behaviour Management Advisory Service in Australia also offers short-term case management, including assessment, clinical advice, care planning, and education and training (Curry et al., 2013). The Scottish Government has committed to providing one year's post-diagnostic support from a named link worker to all people with a new diagnosis of dementia. Progress towards this target is being measured, with the aim of achieving full coverage by March 2016 (Care Information Scotland, 2014).

Early dementia: Living in the community and relying on informal care

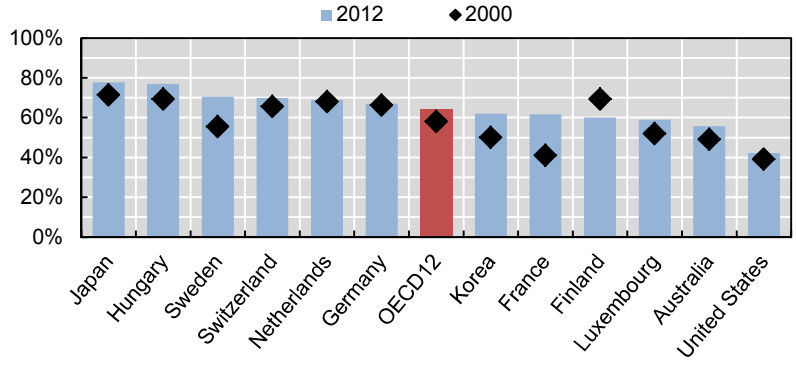
People with dementia are living in the community for longer, so their homes and communities need to adapt to their needs

Most OECD countries aim to support people with dementia to live in the community for as long as possible because it can be cheaper and lead to a better quality of life

Many people with dementia would prefer to stay in their own home for as long as possible. Familiar surroundings can be reassuring and remaining at home can promote a greater sense of independence, control and identity. Providing care in the community rather than institutions can reduce formal care costs, because of the greater role played by families and informal carers. Many countries consider helping people with dementia to remain at home among their top priorities for dementia policy (including France, Germany, Ireland, Japan and the Netherlands). As shown in Figure 2.3, there has been a wider move in recent years towards providing long-term care in the community. Although dementia-specific data is not systematically collected, a 2010 survey by Alzheimer's Disease International found that, on average, high income countries have around two-thirds of people with dementia living in the community (Wimo and Prince, 2010).

Figure 2.3. An increasing proportion of older people with care needs remain in their own homes

Proportion of older LTC recipients receiving care at home in selected OECD countries in 2000 and 2012 (or nearest available years)



Source: OECD Health Statistics, www.oecd-ilibrary.org/social-issues-migration-health/data/oecd-health-statistics_health-data-en.

Adapted living environments can reduce the risks faced by people with dementia who remain in their own homes

The trend towards community care brings new challenges as well as benefits. When someone develops dementia, tasks that were previously part of their daily routine can become difficult and even dangerous. Dementia advocacy groups in a number of countries (including England, the United States and Australia) provide guidelines to support carers to create a dementia-friendly environment at home, focusing on: mitigating risks to the person's safety (e.g. by securing dangerous kitchen appliances or installing handrails in the bathroom); aiding memory (e.g. by including colours and cues around the home to help the person remember how to carry out their daily routine); preventing wandering (e.g. by keeping keys out of sight or camouflaging doors and door knobs); and increasing comfort and well-being (e.g. by adding personal touches such as family pictures). Home adaptations are provided by long-term care services in some countries. For example, people diagnosed with dementia in France can have their home assessed to see if adaptations could be beneficial (Alzheimer Plan 2008>2012, 2013); while community services in Sweden have an increasing focus on home adaptations (Henning et al., 2009).

There is a strong focus in many OECD countries on making communities safer and more accessible for people with dementia

People living with dementia in the community are at risk of becoming socially isolated. In England, Wales and Northern Ireland, a third of people with dementia only leave their homes once a week, while one in ten only go out once a month (Alzheimer's Society, 2014a). If people with dementia are to be cared for in the community – rather than confined to their houses – communities need to adjust to help them to remain engaged and involved. A number of OECD countries are therefore promoting dementia-friendly communities. For example, the Alzheimer's Society in the United Kingdom runs a process for communities to be recognised as dementia friendly, with 69 signed up as of August 2014; while in Ireland, there are 11 fully operational Age-Friendly Counties programmes and a further ten due to start soon.

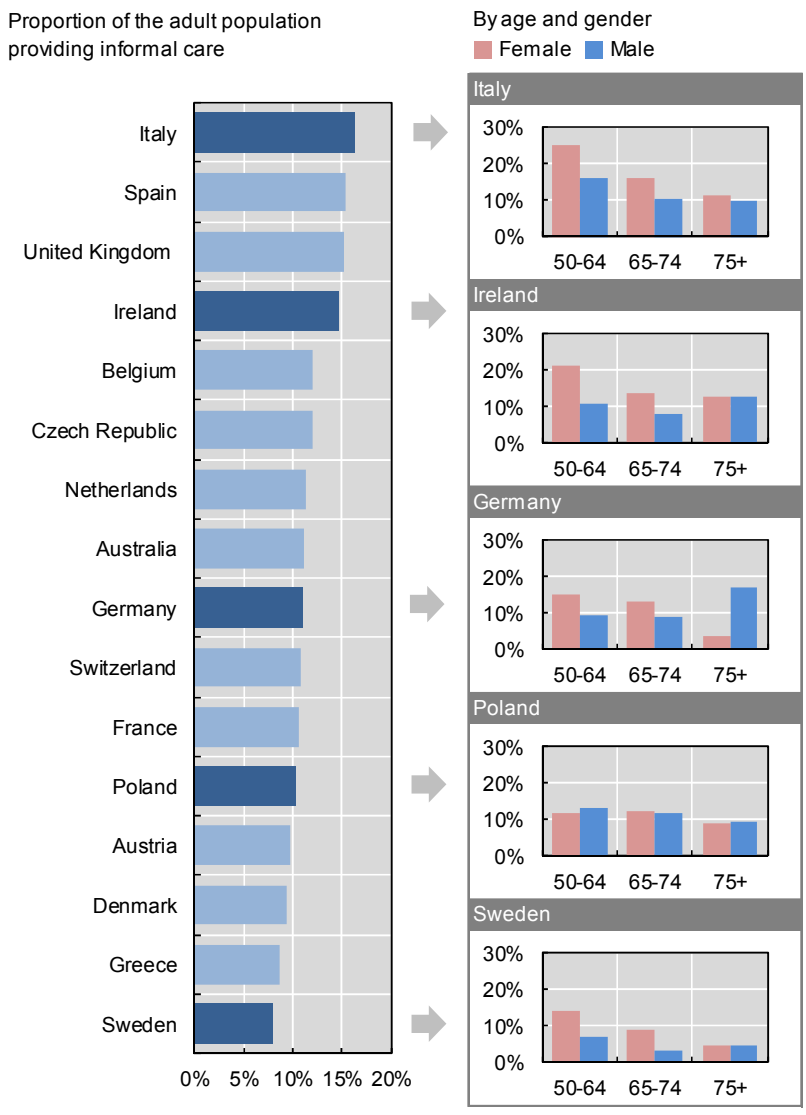
Dementia-friendly communities are first and foremost about people and some countries provide training on how to interact with and support those with dementia. As of March 2014, there were 4.8 million people in Japan trained as "dementia supporters", who wear an orange bracelet to identify themselves and act as advocates within the community (Community-Care Policy Network, 2014). Similar programmes exist in other countries, such as Dementia Friends in the United Kingdom and *Demenzpaten* (dementia champions) in Bavaria (Germany). The Intergenerational Schools Project worked with 10 primary and 12 secondary schools in England, teaching children about dementia and introducing them to people with dementia and their carers, and an evaluation of the project found that it had been effective in increasing awareness and reducing stigma and fear (Atkinson and Bray, 2013). Similar approaches are being developed in Germany and the Netherlands. Awareness campaigns through national television (Netherlands) or regional conferences (France) also aim to alter the perception of dementia and reduce social stigma; and in Germany, *Lokale Allianzen für Menschen mit Demenz* (Local Alliances for People with Dementia) aim to raise awareness about the needs of people with dementia and provide support to them and their families.

People with dementia may find it hard to navigate towns and cities and use shops and amenities. Ramps, raised platforms and low-floor buses can allow people with dementia to continue to use public transport. Barrier-free access to buildings, well maintained pavements, accessible and safe green spaces, places to sit down, public toilets and proper lighting can make town centres more accessible (WHO, 2007). In Bavaria (Germany), shops that meet certain standards of service, accessibility, interior layout and behaviour can display a "generation friendly shopping" (Generationenfreundliches Einkaufen) sign, allowing people with dementia to identify places where they will be welcomed and accommodated (Bayerisches Staatsministerium für Arbeit und Sozialordnung, 2012). In the United Kingdom, the Alzheimer's Society and Lloyds Banking Group have jointly developed a charter to provide dementia-friendly financial services. Measures include appointing a senior-level dementia champion within the bank, staff training and co-operation with the police and other agencies to protect people from financial abuse (Alzheimer's Society, 2013). Not everyone with dementia lives in or around towns and cities, so Canada has produced a guide aimed at helping remote communities become dementia friendly.

Promoting community care means an increasing role for informal care, which has costs and benefits

One in ten adults in OECD countries is providing informal care to a friend or relative, although there is significant cross-country variation – from 8% in Sweden to 16% in Italy (Figure 2.4). Rates of caring are highest among the older working age population (ages 50-64), many of whom are caring for a parent or other older relative, and carers in this age group are predominantly women. In Italy and Ireland, over 20% of all women aged 50-64 are providing informal care and across studies from 25 different countries, a woman was identified as the main caregiver for between five and nine every ten people with dementia (Wimo et al., 2013). There are also a significant number of older carers (aged over 75), who are just as likely to be men as women, are often caring for a spouse and generally provide a greater number of hours of care (Dahlberg et al., 2007). Most care in the community is provided informally: estimates from the United States have put the proportion of community dementia care provided informally as high as 80% (Alzheimer's Association, 2013) and estimates from England are shown in Figure 2.5. As a result, policies to keep people with dementia in their own homes will increase the role of informal care.

Figure 2.4. The proportion of the population providing informal care varies between countries and by age and gender



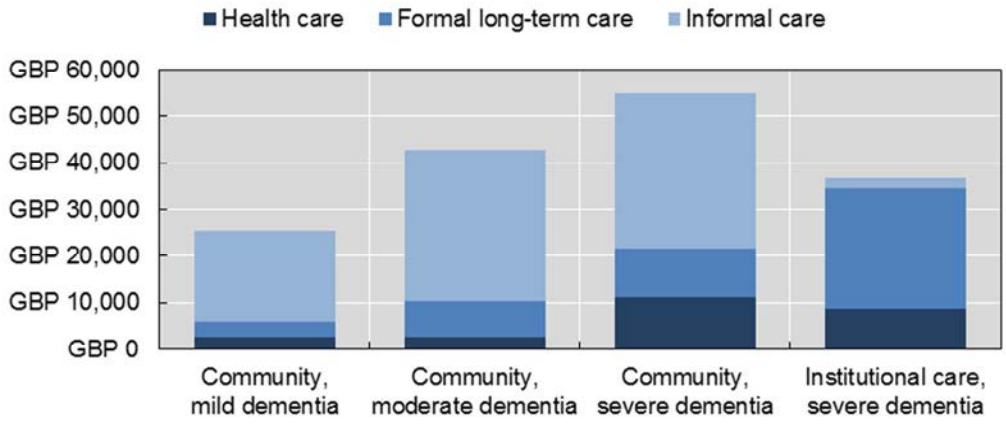
Source: Colombo, F. et al. (2011), *Help Wanted? Providing and Paying for Long-Term Care*, OECD Publishing, Paris, http://dx.doi.org/10.1787/9789264097759-en.

Informal care can benefit people with dementia by allowing them to remain more independent, living in their own homes and receiving care from someone they know and trust. It can also have benefits for the carer, with many reporting that the experience is rewarding (Vugt and Verhey, 2013). However, it can be challenging for the carer and have a negative impact on their well-being. Mental health problems are 20% more common in carers than non-carers (Figure 2.6) and increase with the intensity of care. These effects are more acute for dementia carers, with a greater proportion finding caring highly stressful (a quarter compared to 15% of other carers) and as many as one in five suffering from depression (Schulz et al., 1995; Baumgarten et al., 1992; Fisher et al., 2011; Alzheimer's Association, 2013; Cuijpers, 2005).

People caring intensively are more likely to work part-time or not at all (Colombo et al., 2011) and those that do retain their jobs often have to make major changes to their work schedules (Alzheimer's Association, 2013), miss work more often than their peers (Tilly, 2007) and earn less than non-carers (Knapp et al., 2007). This has an economic cost if carers would otherwise be in higher productivity jobs and the reductions in tax revenue from people exiting the formal workforce may partially offset savings to government budgets from reduced spending on formal care. Since most working age carers are women, a greater role for informal care may have a negative effect on gender equality in the labour force.

Figure 2.5. Caring for people with dementia in the community increases the role of informal carers

Estimated value of formal and informal service for people with dementia in England in 2015 (2012 prices)

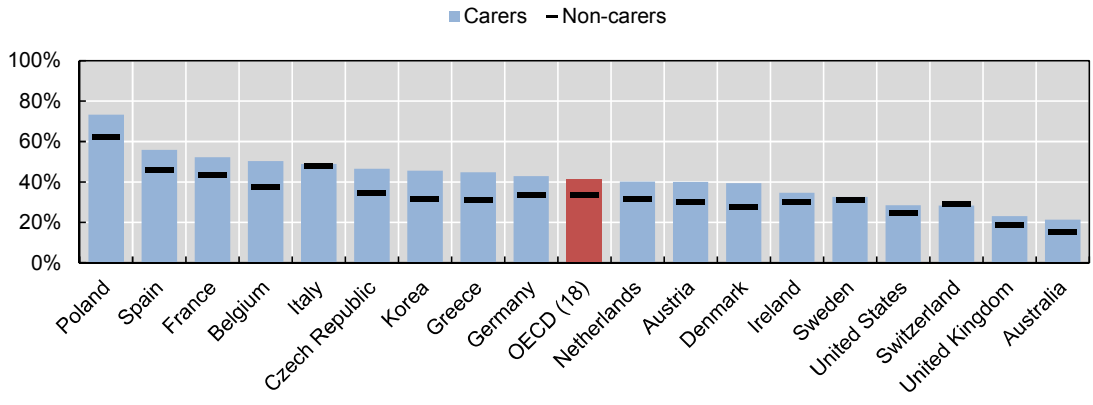


Note on methodology: Patterns of care are derived from data from a number of UK trials and other studies; standard unit costs are applied for formal services, usually from publicly available sources; informal care is valued as the cost of replacing it with formal services, or the opportunity cost, depending on the type of care activities undertaken.

Source: Prince, M. et al. (2014), *Dementia UK*, Second edition, Alzheimer's Society.

Figure 2.6. Carers are more likely to have mental health problems than non-carers

Percentage of carers and non-carers with mental health problems in OECD countries



Source: Colombo, F. et al. (2011), *Help Wanted? Providing and Paying for Long-Term Care,* OECD Publishing, Paris, http://dx.doi.org/10.1787/9789264097759-en.

Box 2.3. Examples of policies to support the well-being of informal carers for people with dementia

Psychological interventions for informal carers in Thessaloniki, Greece

Informal carers in Thessaloniki, Greece, receive a range of support services from memory clinics, hospitals and day centres, including psychological support and education on effective care and coping strategies. Support groups and web-based seminars allow people to communicate and exchange experiences with other carers; family therapy helps families to deal with the challenges of supporting someone with behavioural and psychological symptoms of dementia; and relaxation programmes reduce carer stress levels (ALCOVE, 2013).

Annual assessment of dementia carers' well-being in France

In 2010, the *Haute Autorité de Santé* issued a reference guide for monitoring the health of dementia carers. Under these guidelines, primary care doctors provide an annual consultation to monitor carers' mental and physical health and review whether appropriate support is in place, such as individual or group counselling, support groups, telephone or internet consultations, training courses or psychotherapy (Haute Autorité de Santé, 2010).

Respite care on Green Care Farms in the Netherlands

Since 2000, farms in the Netherlands have been offering day care to people with long-term care needs and around 10% of them offer places to people with dementia. Activities include feeding animals, cultivating fruit and vegetables, preparing dinner, dish washing and gardening. An evaluation of the impact of Green Care Farms on people with dementia found that they had more physical activity, spent more time outside, had fewer behavioural symptoms and consumed fewer psychotropic drugs than those in regular day care (De Bruin et al., 2009).

Appropriate support services should be available to all people caring for family or friends with dementia

Choice and control is an important aspect of quality of life for people with dementia and their families and they should be supported to make an informed choice about care arrangements, considering the costs and benefits of different options. Where families choose to provide informal care, there are a range of policies that can minimise the associated costs. *Respite care* can give carers a break from their caring duties, in their own home or elsewhere; *counselling services* can relieve stress; *peer-to-peer support* can link people with dementia and their carers to others in the same situation (e.g. Dementia Cafés in Japan) or former carers who can provide support and advice (e.g. the NHS Dementia Carers' Support Service in England); *information and training* can provide knowledge and skills to help carers carry out their role effectively and minimise negative impacts (e.g. the new "Dementia Link" telephone information service in Canada); *policies to support employment* of informal carers exist in a number of countries – for example, the *Pflegezeitgesetz* (Act on Long-term Carer's Leave) and Familienpflegezeitgesetz (Family Caregiver Leave Act) in Germany give carers the entitlement to take time off work or temporarily reduce their hours, with interest-free loans available from the state to compensate for the reduction in income; and *financial benefits* can be provided as a direct cash payment (e.g. England), a benefit via the person receiving care (e.g. Germany) or a tax break (e.g. Canada).

Knowledge about the effectiveness of these different strategies remains limited. Some longitudinal studies have found that flexible working arrangements can help working age women to remain in work when they take on caring roles, although the effect on overall employment is uncertain. Good respite care services should aim to deliver benefits for

both the carer and the person with dementia (Alzheimer's Australia, 2013), but while these services highly valued by many carers, there is limited evidence of positive outcomes. Informal counselling is often provided through community support groups, but evidence on the impact of this approach on mental health outcomes is inconclusive (Colombo et al., 2011).

Box 2.4. *In voor Mantelzorg* – Improving the interface between informal and formal care in the Netherlands

The ongoing reforms in the Netherlands aim to move care out of institutions and into the community – a direction of travel shared by most OECD countries. Dutch policy makers have recognised the increased impact that this will have on informal carers and families, raising the question of what can be done to support them more effectively. Their response to this challenge – the *In voor Mantelzorg* programme – takes a different approach to many policies to support carers in other OECD countries, in that it focuses on the relationship between informal and formal care.

Many people with dementia or other long-term care needs who are living in the community receive both formal and informal care, but the two do not always work well together or communicate effectively. Sometimes there may be duplication of effort, while a lack of communication can lead to gaps in care and unmet needs. *In voor Mantelzorg* aims to support care organisations to communicate better with informal carers. Participating organisations must submit a plan for improving their practices. If the plan is accepted, the organisation will be provided with a coach who has expertise in long-term care, communication and training, to help implement the plan. EUR 4 million of public funding has been allocated to fund this programme, which is enough to provide coaching to 80 organisations.

Risks to the supply of informal care might make current care models unsustainable

If current care models are to be sustained, the rising number of people with dementia and other care needs will have to be matched by a rise in the number of informal carers. If the trend towards providing more care in the community continues, the number of informal carers will need to rise faster. However, there are reasons to believe that fewer people may be willing and able to care for their parents in the future. A reduction in intergenerational households (Sinha, 2012) and increasing geographical mobility may mean that fewer children are in a position to care for their parents (OECD, 2004). Changing social attitudes and expectations may mean that fewer are willing to do so. Most working age carers are currently women, but as gender equality increases, future generations of women will have greater career opportunities and may be less willing to give up work to care for their parents. The net effect on the future supply of informal care is not well understood, but the risk that the supply of informal care may be insufficient to sustain current care models must be taken seriously.

Advanced dementia: A greater need for formal care services and specialised accommodation

A dementia-specific and person-centred approach to long-term care is needed, supported by an effective workforce strategy and standards

People with advanced dementia may require significant professional care, especially if they are living in an institution or do not have family members who can care for them in the community, and they can often have different needs and face different risks to other care users. They may have behavioural symptoms, find it difficult to maintain social relationships or be unable to make choices about their care. While all dependent people

are at risk of violence, abuse and neglect, these risks are greater for people with dementia, as a result of the difficulties in managing symptoms and the effect that this has on caregivers (Tilly, 2007). As a result, half of all people with dementia may have experienced verbal, physical, or psychological abuse or neglect at some point (Shih et al., 2014). This suggests that a dementia-specific approach to improving care is needed.

*General standard*s for long-term care institutions exist in a number of countries, covering the number and skill level of care workers, aspects of the living environment, governance and care provision. Some countries (including England, Ireland, the Netherlands and the United States) have also included criteria around the quality of life and dignity of residents, individualised care planning and the reporting of adverse incidents (OECD/European Commission, 2013). These general standards can be effective in ensuring a minimum level of quality and safety in long-term care services, but the unique challenges of caring for people with dementia mean that more specific guidelines can be beneficial. Some countries, including Canada, the United Kingdom and Sweden, have already developed *dementia-specific guidelines* and others should consider doing so. However, even where guidelines exist, care workers are often not aware of them and they are not widely applied. Guidelines therefore need to be accompanied by implementation programmes to ensure that improvements in dementia care are delivered in practice.

High quality long-term care requires a *workforce* with the knowledge and skills to deal with the challenges of caring for people with dementia. However, the care workforce is often under-prepared for the task and inadequate training on dementia is a significant contributor to poor quality of life, poor quality care, abuse and neglect in nursing homes (Hawes, 2003). Some countries provide dementia training for long-term care staff. For example, Australia has five Dementia Training Study Centres; while in Ireland, the National Dementia Education Project 2012 focused on raising standards by providing training and information resources to care professionals (Health Service Executive, 2012). But low pay, poor working conditions and a lack of professional prestige mean that it is difficult to attract and retain qualified long-term care workers. This shortfall is often filled by untrained, low-cost caregivers, leaving older adults vulnerable to poor or unregulated care (Shih et al., 2014). Countries need a more comprehensive approach to developing the workforce, which may need to consider increased recognition of long-term care as a profession; improving the image of careers in long-term care; more opportunities for training and development (including dementia-specific training); improving working conditions; and raising wages.

There is increasing recognition in OECD countries that the needs of care users are best met through person-centered care services that put users and their families at the centre of all decisions and gives them independence and control. More than two-thirds of OECD countries have introduced *user-directed support* into their long-term care systems, usually by offering benefits in the form of cash payments, vouchers or personal care budgets, instead of services. This allows people with dementia to choose the types of service they prefer, which may go well beyond traditional care. Social interaction is seen by many people with dementia as the most important aspect of their quality of life (Alzheimer's Society, 2010) but it can be difficult for them to maintain relationships. The ability to choose social activities, such as attending day centres, going on group walks or attending cultural events, as part of a care package could significantly improve their well-being and several studies have shown that cash-for-care and voucher schemes can lead to higher satisfaction among care users. However, there are risks with this approach. Unregulated use of care budgets risks encouraging the purchasing of non-professional, unregulated care services, undermining efforts to improve quality (OECD/European

Commission, 2013). Where people with advanced dementia can no longer make decisions about their care independently, families and carers can often make decisions on their behalf. However, the needs of carers are not always the same as the needs of the person with dementia, and safeguards are required to prevent financial abuse.

Better monitoring of how the symptoms of dementia are managed is needed to reduce the harm done by inappropriate care

Behavioural and psychological symptoms of dementia (BPSD) arise primarily from the degeneration of the brain caused by the condition itself, but can also be linked to depression, psychosis, pain, frustration, loneliness or worry (ALCOVE, 2013). As many as 90% of people with dementia experience BPSD at some point during the course of the condition (EYENET Sweden, 2009; BPSD, 2014), often becoming aggressive or refusing care, so caregivers need strategies for preventing and managing these symptoms.

Antipsychotic drugs can reduce the symptoms of BPSD, but at the expense of an increased risk of stroke, pneumonia, venous thrombosis and falls, as well as accelerating cognitive decline. As a result, they are not approved for this purpose by medical regulators and their use has declined in recent years. Nonetheless, significant numbers of people with dementia still receive antipsychotics for BPSD. A study of care homes in Europe found that 35.6% of residents had been given antipsychotics, with rates as high as 60% in Italy (ALCOVE, 2013). A report by the US Government found that 39.4% of people with BPSD in nursing homes have received antipsychotic drugs without a documented diagnosis of psychosis (Watson-Wolfe et al., 2014). Alternative strategies – such as the Grip on Challenging Behaviour care programme in the Netherlands, which shows care staff how the latest guidelines can be incorporated into their daily practice – have been shown to be effective at reducing the use of antipsychotics (Zwijsen et al., 2014) and countries should consider applying these approaches more widely.

Physical restraints (such as chairs with deep seats; bed rails; the removal of mobility aids; or in extreme cases, leg, wrist or ankle restraints) are sometimes used to manage the risk that people with BPSD can pose to themselves and others (Retsas, 1998). The proportion of people with dementia on whom these measures are used varies between and within countries, with studies from various countries reporting rates from 12% to 49% in residential care (Peisah and Skladzien, 2014). Physical restraints can increase the risk of injury, such as bruises or skin tears (Alzheimer's Association, 2009); cause decubitus ulcers, reduced muscle strength and increased dependence; and lead to increased agitation, depression, fear and anxiety (Castle, 2006). As a result, many countries have taken steps to reduce their use. For example, clinical guidelines in Australia indicate that physical restraints should be an intervention of last resort (Burns et al., 2012); in Germany, physical restraints require judicial approval, except in an emergency (dejure.org, 2014); and educational materials on alternative approaches to managing BPSD are available to care professionals in the United States and Germany (Minnesota Department of Health, 2010; Bundesministerium für Familie, Senioren, Frauen und Jugend, Bundesministerium für Gesundheit, 2014).

Alternative strategies are needed to reduce the harm done by antipyschotics and physical restraints. There is evidence that training care home staff to provide person-centred care and psychological support to people with dementia can be effective at preventing and manging BPSD and reduce the use of medication (Fossey et al., 2006) although the evidence base on non-pharmacological approaches to BPSD is in general weak and further research is needed (ALCOVE, 2013). The introduction of systematic collection of data on BPSD, for example through registries such as Sweden's National

BPSD Registry, would allow policies to be evaluated more effectively and support quality improvement. However, while some countries collect data on the use of physical restraints (United States, Canada, Netherlands, Korea) and antipsychotic medication (Netherlands, Canada) the majority do not and there is no international standardisation (OECD/European Commission, 2013).

Living arrangements that promote dignity and independence should be more widely available to people with dementia who are unable to continue living in their own home

When dementia is advanced, people become highly dependent and need constant supervision, so it may not be safe or practical for them to remain in their own home. Institutions may have expertise in managing complex conditions with multiple comorbidities and experience of treating people with advanced dementia, which is difficult to find in a community setting (Feng et al., 2014) and may be better at managing risks – dementia increases the risk of hospitalisation for people living in the community, but not for nursing home residents (US Department of Health and Human Services, 2013b). This is reflected in the make-up of the care home population. Around half of all care home residents in the United States and Australia (US Department of Health and Human Services, 2013a; Australian Government – Deparment of Health, 2013), more than a third in France (Dossiers solidarité et santé, 2011) and two thirds in Germany (Alzheimer Europe, 2013), have dementia; while 90% of the care home population in Scotland have dementia or exhibit signs of cognitive decline (Lithgow et al., 2011).

However, some care homes may not be optimal for people with dementia and can mean a loss of choice, control, privacy and dignity. Living arrangements need to combine the best features of institutional care (safety and access to health and care services) with the best features of community care (dignity and independence). New models of care that address these needs are being developed and implemented, often focusing on providing small, home-like environments (see Box 2.5).

Box 2.5. Homes, not institutions – Alternatives to institutional care for people with dementia

- In Germany, **flat living communities** (*Wohngemeinschaften für Menschen mit Demenz*) offers an alternative to traditional care homes. Up to 12 people with dementia live as a community in a house or apartment, with their own private bedrooms which they can furnish with their belongings. Care is provided by a constant group of caregivers who are familiar to the residents (Bundesministerium für Familie Senioren, Frauen und Jugend, 2013). This model of care is often subsidised by long-term care insurance.
- **Group homes** in Japan are a similar concept. Between five and nine people with dementia live in each home, each with their own bedroom but sharing communal bathrooms and living areas. Residents are encouraged to participate in meal preparation and housework to encourage a sense of independence and ownership over the house (Japanese Ministry of Health, Labour and Welfare, 2013).
- **Dementia villages**, such as De Hogeweyk in the Netherlands, provide a living environment modelled on a small village. Shops and amenities are staffed by care workers, while residents can participate in a range of activities. While dementia villages can provide a comfortable and familiar environment, allowing people with dementia to lead "normal" lives, they also raise ethical questions about whether it is right to deceive people with dementia about the nature of their surroundings.

However, evaluations comparing well-being of people with dementia, their families and care workers in these small-scale institutions with those in larger, more traditional care homes have shown mixed results. This may be because the benefits of "small-scale"

care – such as the control that residents have over their lives and the opportunities they have to form relationships with others – can be found in all types of care setting, including large, traditional care homes (Pot, 2013). Ultimately, the care model applied by an institution and its staff is more important than the size or configuration of that institution, and there is evidence that dementia-specific approaches to care, such as the Enriched Opportunities Programme in the United Kingdom, can be effective at improving quality of life (Brooker et al., 2011).Specialist teams and wards can help to manage the risks faced by people with dementia in hospitals

People with dementia are admitted to hospital 2-3 times more frequently than other people of the same age (US Department of Health and Human Services, 2013a; Tilly et al., 2011), stay on average twice as long (Australian Institute of Health and Welfare, 2013) and have a greater risk of readmission (Care Quality Commission, 2012). They are also more expensive: in Australia, people with dementia admitted to hospital cost 2.7 times as much as other people (Australian Institute of Health and Welfare, 2013); while in the United States, annual Medicare costs for people with dementia are three times as high as for those without dementia (Tilly et al., 2011). But despite these high costs, outcomes are poor. Around 15-30% of people with dementia develop delirium while in hospital and one in five still have symptoms six months later (Hermann et al., 2014); a Canadian study found that a third of elderly people discharged from hospital have less functional ability than when they went in and half of these people never recover (Sinha, 2012). There is an urgent need for hospitals to improve their management of people with dementia.

The first step to improving hospital care for people with dementia is ensuring that they are identified through better sharing of data across the health system. Hospitals can then take steps to ensure that their risks and needs are effectively managed. *Consultation and liaison services*, which support people with symptoms of dementia or in high risk groups when they are admitted to hospital, can reduce the risk of depression following a long stay in hospital. *Specialist geriatric wards*, staffed by multidisciplinary teams, can lead to shorter hospital stays, reduced risk of illness or injury and improved cognitive function. *Dedicated dementia wards*, headed by a dementia specialist, can give people with dementia and their carers a better experience of hospital care and may reduce the risk of care home admission (Hermann et al., 2014).

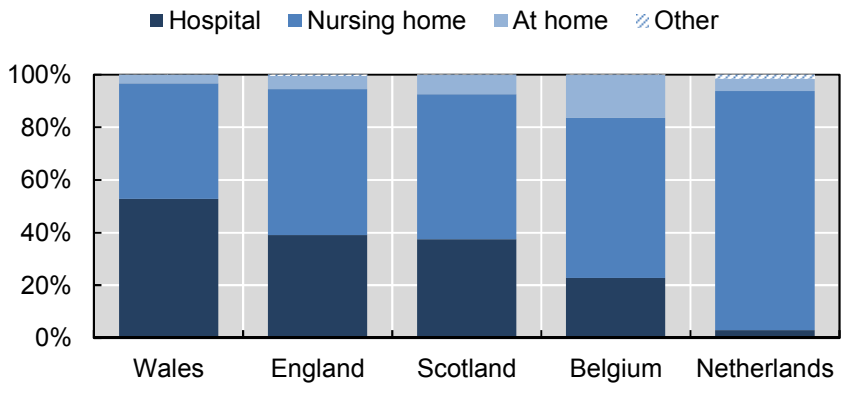
These approaches are being implemented in some OECD countries. For example, in Ontario (Canada), geriatric emergency management (GEM) nurses are stationed in hospital emergency departments to identify, assess and work with frail elderly people who are at risk of losing their independence, and to establish connections to community services after discharge (Sinha, 2012). In the United Kingdom, just over a third of all hospitals have a care pathway in place for people with dementia; around half have a care pathway in development; and more than three quarters have appointed dementia champions (Royal College of Psychiatrists, 2013). In France, some *filières de soins gériatriques* (geriatric care networks) manage care pathways for frail older people with multiple co-morbidities during their time in hospital, but also before admission and after discharge. Examples of good practice such as these exist in some countries, but the human and financial cost of failing to treat people with dementia appropriately suggests that a much greater scale and pace of change is required.

Better access to dementia-specific palliative care outside of hospital can ensure that more people with dementia die with dignity in a place of their choosing

In the advanced stages of conditions such as cancer and dementia, a palliative approach to care, focusing on quality of life can empower the patient by controlling symptoms, but there are specific challenges around dementia. People with dementia are not always able to express when they are in pain, meaning that pain can go under-recognised and undertreated – in one study, hip fracture patients with dementia received only a third of the pain relief given to those without dementia (Hughes et al., 2007). Untreated pain can manifest itself in behavioural symptoms, leading to the unnecessary use of psychotropic medicines (Alzheimer's Association, 2009). Those with advanced dementia may be unable to take decisions about their own care, so a number of OECD countries (e.g. England, Australia) offer advance care planning. These challenges suggest that a dementia-specific approach to palliative end-of-life care is needed. Some countries have started to develop policies – for example, the *Building the Future of Palliative Care Together* initiative in Canada will include a specialised training module on palliative care for dementia – but more progress is needed.

Dementia policy in some OECD countries recognises the importance of the place of death: for example, in the United Kingdom, NICE guidelines on dementia care state that a palliative approach should enable people "to die with dignity and in the place of their choosing" (NICE, 2014). However, although most people with dementia would prefer to die in their own homes (Harris, 2007), a significant proportion still die in hospital (Figure 2.7). The availability of medical and palliative care outside of hospital may be a significant factor in determining place of death. In the Netherlands, on-site geriatricians are stationed in care homes (Hoek et al., 2003) and only 3% of people with dementia in the Netherlands die in hospital – compared to between 20% and over 50% in the some other countries – while a significantly higher proportion die in nursing homes. Some OECD countries are therefore taking steps to increase the availability of palliative care outside of hospital (e.g. *The Way Forward* project in Canada).

Figure 2.7. The proportion of people with dementia dying in different settings



Source: Houttekier, D. et al. (2010), "Place of death of Older Persons with Dmentia: A Study in Five European Countries", *Journal of the American Geriatrics Society*, Vol. 58, No. 4, pp. 751-756.

Care co-ordination and the role of technology

A more proactive and co-ordinated approach to community health care can improve outcomes and reduce the risk of hospitalisation

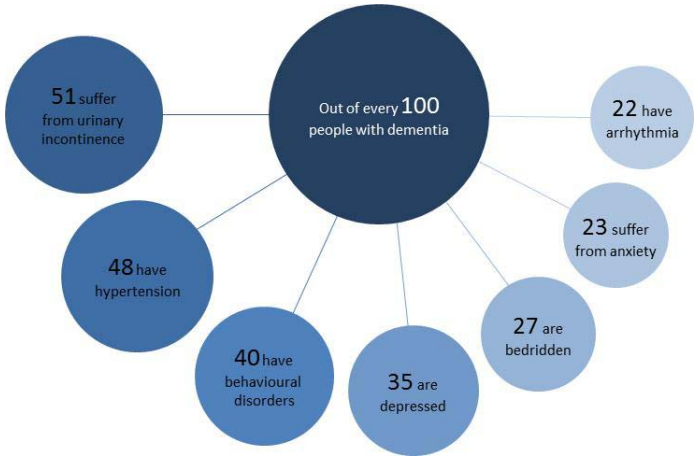
People with dementia often have complex needs and a limited ability to manage their own affairs, so there is a case for targeted care co-ordination

People with dementia often have multiple comorbidities and complex health and long-term care needs (Box 2.6). The services that they require may be provided by multiple organisations and professions, in separate parts of the health and care system, with separate eligibility and funding rules – while cognitive decline can mean that they are less able to deal with these complexities. Although better care co-ordination is a priority for many OECD countries, there is an even stronger rationale for action in the case of people with dementia.

Box 2.6. People with dementia often suffer from multiple comorbidities

People with dementia rarely just have dementia. The diagram below illustrates the most common comorbidities in care homes in France. More than half have urinary incontinence, just under half have hypertension and 40% have behavioural disorders. The fact that the rates of these three diagnoses alone sum to more than 100% shows that many people have a number of these conditions at the same time. This does not mean that these conditions are causally linked to dementia, since they are also present in many other older people, but it does mean that people with dementia tend to have complex needs and require a wide range of health and long-term care services.

Common comorbidities for people with dementia in care homes in France



Source: Dossiers solidarité et santé (2011), *Les personnes âgées en institutions,* Ministère des Affaires sociales et de la Santé, Paris.

Some countries have responded to this by offering targeted case management for people with dementia. In Japan every person living with dementia in the community is appointed a case manager (Curry et al., 2013). Case management is also provided in some regions of Canada (Alberta Health Services, 2014) and the Netherlands (Minkman et al., 2009). The *Maisons pour l'Autonomie et l'Integration des Malades Alzheimer* in France (Box 2.7) aim to provide co-ordinated dementia services and use case managers in the most complex cases; and in England, proactive case management is provided for the most vulnerable 2% of older people, many of whom will have dementia (Gov.uk, 2014a).

Box 2.7. The MAIA (Maisons pour l'Autonomie et l'Intégration des Malades Alzheimer) in France

In recognition of the importance of co-ordinated care for people with dementia, 252 MAIA have been established across France and a further 100 are expected to be established by 2016. Each of these centres provides a single access point, linking people with dementia and their carers to appropriate services. Inter-disciplinary teams provide integrated health and long-term care services; training and support is available for carers; and person-centred case management is provided to those with the most complex needs. The MAIA also have a role in evaluating service quality and developing practice guidelines.

However, evaluations of case management programmes have shown mixed results. Some studies suggest it can lead to more appropriate care and a lower risk of hospitalisation (Vickrey et al., 2006; Clark et al., 2004); reduced stress levels in carers (Callahan et al., 2006); or the ability to remain living in the community for longer (Parsons et al., 2012). But some studies have been unable to detect any positive effects (Fortinsky et al., 2009) and a recent systematic review concluded that case management does not reduce unplanned admissions in older people (Huntley et al., 2013) – although this finding is not specific to dementia. This highlights the need for careful design and evaluation of case management programmes to ensure that they deliver the maximum benefits. More proactive community care, provided closer to home by multi-disciplinary teams, can reduce the risk of hospitalisation for people with dementia.

Box 2.8. Joining up dementia care in Ireland

Local initiatives in Ireland are working to improve the co-ordination of care for people with dementia. However, as in many OECD countries, these are isolated examples of good practice that are still in the early stages of implementation. Schemes such as these need to be evaluated, refined and scaled up or replicated, so that all people with dementia can expect the best possible care.

Connolly Hospital Integrated Care Pathways for People with Dementia

This project will aim to reduce the negative impact of hospitalisation on people with dementia, by reducing admissions, improving hospital care and supporting people after discharge. Support nurses in the hospital and community will build links with community services; a specific area within the hospital will provide complex ambulatory care for people with dementia; a defined "dementia care bundle" will ensure that key interventions are always provided; and a person-centred communication tool will help staff to communicate effectively with people with dementia.

Cork Integrated Dementia Care Across Settings (Cork-IDEAS)

Mercy University Hospital is working with community services to provide alternatives to hospital admission and support families to care for people with dementia at home. When hospital admission is unavoidable, families will be supported to continue to care for the person within the hospital setting and to plan and prepare for discharge. Hospital staff will receive additional training to communicate better with people with dementia, get to know them and their families and work more effectively with community services and care institutions.

Better management of comorbidities by community care services can reduce the risk of complications and hospital admission. However, the limited ability of people with dementia to articulate their needs and travel to appointments mean that they may not always get the care that they need unless community care is more proactive and provided closer to home. The House Calls Programme in Toronto (Canada) shows the potential of this approach. A multi-disciplinary team including primary care doctors, nurses, social

workers, occupational therapists, physiotherapists and geriatricians provides medical and social care to around 400 frail elderly people and their carers in their own homes. This has resulted in a 29% reduction in unscheduled hospital admission and enabled more than two thirds of these people to die at home (Sinha, 2012). Proactive care services can be provided to people in institutional care with similar results: in the United States, the presence of on-site nurse practitioners has reduced hospitalisations due to acute infections by 71% (Carter et al., 2005); and in Australia, specialist care units (SCUs) for people with dementia, including on-site specialist nurses, have decreased the risk of hospitalisation by 10% (Australian Institute of Health and Welfare, 2013). Although there is increasing recognition in OECD countries that this type of care model is beneficial, a range of organisational, systemic and resource issues mean that it is not yet widely applied in many countries.

Hospital-type services are starting to be provided to people in their own homes in some OECD countries (including the United States, Australia, the United Kingdom and Italy) although the availability of these services is often limited. Evaluations suggest that these services can lead to shorter "length of stay", fewer complications and lower stress levels for carers (Australian Institute of Health and Welfare, 2013; Tibaldi et al., 2004; Leff et al., 2005). There are also indications that these services could be cost effective. An evaluation of the Australian scheme concluded that without Hospital at Home, hospitals in Victoria would have needed 500 extra beds (Sinha, 2012; Monalto, 2010); and when similar services closed in Jerusalem, hospital costs increased by USD 6.2 million (Jacobs et al., 2007). Further research is needed to validate these findings.

Better recording and sharing of patient data across health and care systems can improve the co-ordination of care

Better information sharing can ensure that the needs of people with dementia are always recognised in all care settings

Health and care systems in OECD countries are often fragmented and information is not always shared between different parts of the system. Better systems for recording and linking data can support a better understanding of the needs of people with dementia and a more co-ordinated approach to care. Given the risks faced by people with dementia in hospital, it is particularly important that they are identified in this setting. However, the evidence suggests that this is not always the case: a study of people with dementia admitted to hospital in Australia found that 47% did not have a diagnosis recorded (Australian Institute of Health and Welfare, 2013). And even when dementia is recognised, this information is not always shared within the hospital: a UK study found that 59% of hospitals had no system in place for informing different medical specialities about the presence of dementia (Royal College of Psychiatrists, 2013). Better information sharing within hospitals and across the health and care system has the potential to change this by ensuring that people diagnosed with dementia are always recognised in all care settings.

OECD countries are beginning to implement data sharing systems, but face significant challenges around data protection and consistent recording

The development of electronic health records in many OECD countries can unlock the potential of coherent, linked health and care data, but legal, technical and financial challenges have hampered progress to date. Leading countries (including Canada, Denmark, Finland, Israel, Korea, New Zealand, Singapore, Sweden and the United

Kingdom) are able to use personal identifiers to link data from across the health and care system to evaluate quality and cost-effectiveness, monitor adverse events, improve guidelines and support research – although few examples currently focus on dementia. However, careful design of these systems is important to avoid problems: for example, in Japan the identifier is created from names and dates of birth, so may not always be unique (OECD, 2013a). Bespoke data sharing systems for dementia are rarer. Sweden is the only country that currently operates a dementia registry (Box 2.9), although the *Banque nationale Alzheimer* in France collates information on people with dementia from some health care services, and the Netherlands and Germany are working towards the creation of national dementia registries.

Box 2.9. SveDem: The Swedish dementia registry

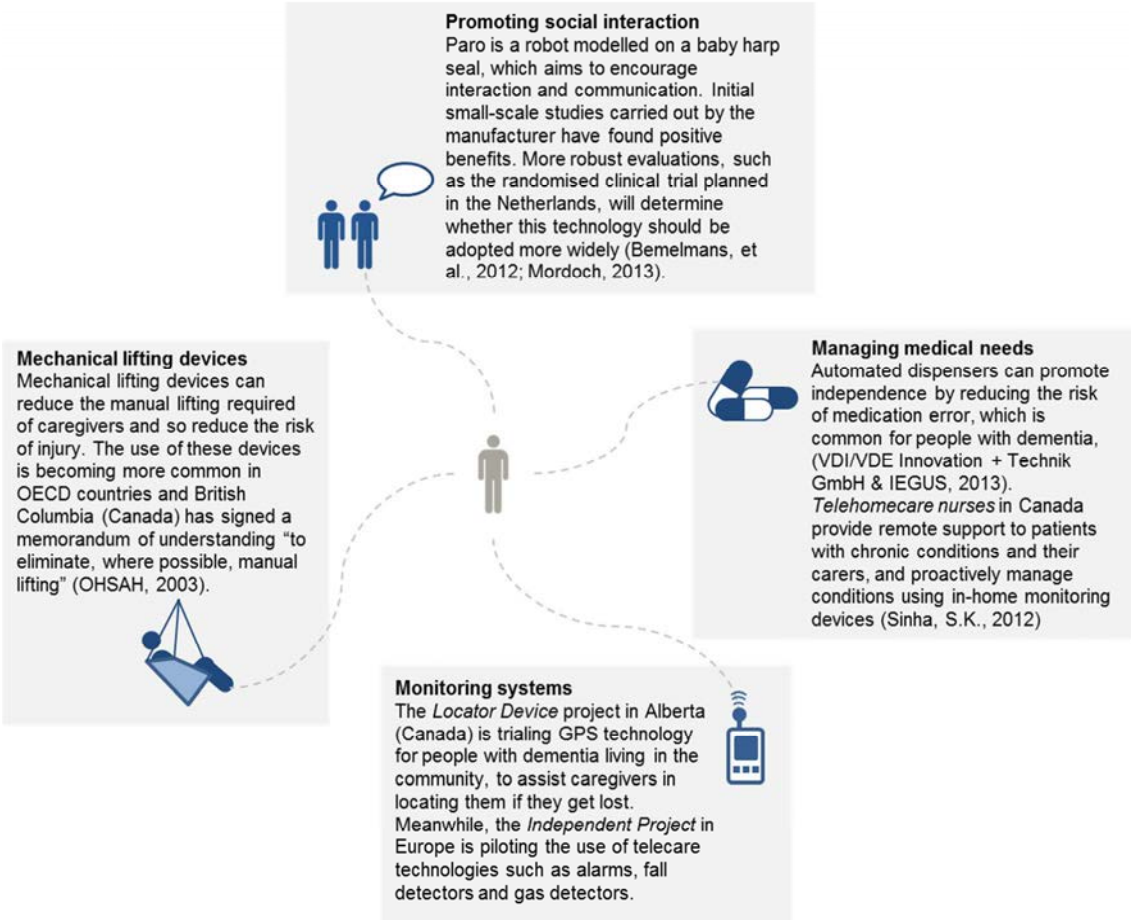
The Swedish dementia registry, SveDem, was set up in 2007 to improve the quality of dementia diagnostics, treatment and care. SveDem aims to register every person diagnosed with dementia and follow up with them annually. It records key information such as age, gender, heredity, mini-mental state examination (MMSE) scores, comorbidities, medical treatment and community support. Each person registered can access their personal statistics online and results from participating units can be benchmarked against national and regional data. As of June 2014, 41 934 people with dementia were registered, 25 565 had been followed-up and 95% of memory clinics were co-operating with the registry (SveDem, 2014; OECD, 2013b).

In promoting the wider sharing and use of patient-level data, a robust data governance framework is required to protect patients' right to privacy. This will require effective collaboration between health ministries, justice ministries and data privacy regulators; public consultation and information; enabling legislation with suitable safeguards; data processors that are held to high standards for data governance; fair and transparent data-use approval processes; and use of best practices in data de-identification and secure data access. Standards and guidelines for the content and quality of health data are also needed to address concerns about under-coverage of patients and missing or improperly coded data. Clinical terminology standards have not been adequately implemented in some OECD countries and international standards are not widely available or applied. National standards, laws or incentives; certification of software vendors; and data quality auditing can help to address these concerns (OECD, 2013a).

If the potential of technology to transform care is to be realised, a greater focus on user requirements and robust, independent evaluation is needed

Technology has the potential to transform dementia care, improve the lives of people with dementia and reduce strain on carers. Governments and other organisations involved in the care of people with dementia in OECD countries are exploring these possibilities – for example, projects such as ENABLE and ISISMED in Europe have sought to develop and evaluate technologies that promote independence for people with mild dementia; while the Japanese Government has set out a five-year plan to develop and introduce robots to support nursing care. Some types of technology are already used in dementia care in OECD countries and examples of these technologies are shown in Figure 2.8, while Box 2.10 looks in more detail at how some countries are using technology to address the issue of wandering. However, the use of technology is not widespread and a recent review of home care technologies for the German Government concluded that, while there were many research and development projects, few were ready for implementation (VDI/VDE Innovation + Technik GmbH & IEGUS, 2013).

Figure 2.8. Examples of current care technologies



If technology is to form a central part of the solution to meeting our future long-term care needs, three key barriers need to be addressed.

- *Identifying user needs:* Some current technologies do not address the needs that are most important to care users and their families (Compagna and Kohlbacher, 2014). By working more closely with users and their families, product developers will increase their chances of developing an effective, marketable product.
- *Robust, independent evaluation:* Care technologies should be subject to the same level of rigour as medical technologies, but many of those currently available have not been evaluated properly and in many cases the only available studies were carried out by the manufacturer (Bemelmans et al., 2012). For care systems to have the confidence to adopt new technologies, robust, independent and credible evaluation needs to be built into the development process. Real-world assessments, taking advantage of the opportunities presented by big data, are needed to evaluate the comparative-effectiveness of technologies in real populations.
- *Clarifying the criteria for reimbursement:* Most long-term care systems do not currently have an established system for assessing care technologies and deciding which should be provided or reimbursed. To help manufacturers to understand what they should be aiming to achieve, care systems need to be clear about the evaluation criteria which they will apply when making reimbursement decisions.

One important step that countries could take, which would address the last two barriers, is to establish care technology assessment processes, mirroring the health technology assessment processes that already exist in many countries. Given the international nature of the development of and market for care technologies, international collaboration could play an important role in establishing a common framework for assessing care technologies and sharing learning.

Box 2.10. Tracking devices can reduce risks around wandering, but do not replace other approaches

People with dementia wandering from their home and getting lost is a significant and growing problem in OECD countries, affecting between 12.6% and 63% of people with dementia (Faucounau et al., 2009; Klein et al., 1999). As well as putting the person at risk of physical harm or death, this can also lead to stress for carers and efforts to find missing people can place significant costs on public services, including police forces. There were 9 607 cases of people with dementia going missing in Japan in 2012 and 12 322 in 2013 – amounting to 11% and 12% of all missing people in those years. Although most of these people were later found and returned home, others were confirmed dead or remain missing (National Policy Agency, 2014).

A number of OECD countries are looking to technology to manage this risk, by providing people with dementia with tracking devices so that they can be easily located. This has proved controversial. On the one hand, these devices can reduce the risk of a person coming to harm, save money and time spent locating missing people, reduce stress for carers and lead to the person with dementia being allowed more freedom and independence. But there are also concerns that while tracking devices may have benefits for carers, this comes at the cost of disempowering the person with dementia and taking away their privacy and dignity (Bantry White et al., 2010; Pot et al., 2012).

Where tracking devices are used, they generally complement, rather than replace, other methods of managing risks. Making adjustments to the person's living environment and daily routine, such as establishing a consistent routine, keeping keys out of sight or camouflaging doors and door knobs, can make it less likely that a person who is affected by wandering will leave the house. Supportive community networks can help to find and return a person who does wander from their home: neighbours can be informed that a person is at risk of wandering, while wider communities can learn to recognise the signs of wandering and alert the authorities or return the person to their home (Alz.org, 2014).

High-tech and low-tech solutions to wandering in the United States

MedicAlert® + Alzheimer's Association Safe Return®

This scheme, run by the Alzheimer's Association and the MedicAlert Foundation, provides people with dementia with a bracelet or pendant engraved with a 24-hour emergency response telephone number, a unique membership number and any critical medical information. If this person wanders and gets lost, anyone who meets them can call the number to contact MedicAlert. MedicAlert will then notify the local Alzheimer's Association and the police, who can help the person to return home.

ComfortZone®

People participating in this scheme are provided with wearable tracking devices. Families can monitor the whereabouts of the person with dementia through a web-based interface and set up alerts to notify them if the person leaves a designated safe zone. As no location system is 100% reliable, this is not seen as a replacement for the low-tech approach and ComfortZone® is usually combined with MedicAlert® + Alzheimer's Association Safe Return® (Alz.org, 2014).

The most effective technologies are likely to be a complement to, rather than a replacement for, human carers, limiting their ability to reduce costs

Long-term care is a labour-intensive service so there are limited opportunities to improve productivity, but it is hoped that technology could change this. However, users of formal care services often value the human interaction that they get from these services and see the cheerfulness and demeanour of staff, or their having time to stop for a chat, as important aspects of quality (Henderson, 2006).

As a result, care users may not be keen to adopt technologies that reduce human contact (Mordoch, 2013) and research in Germany found some users resistant to the idea of automated medicine dispensers which would reduce contact time with their doctor (VDI/VDE Innovation + Technik GmbH & IEGUS, 2013). Technology may instead work best as a complement to labour, allowing care workers to spend more time on delivering a higher quality service.

Some types of technology seek to replicate the experience of human contact, providing social interaction and companionship. While there is initial evidence that this type of "social assistive robot" can have a therapeutic benefit, there are also concerns that these technologies risk infantilising and deceiving people with dementia, or that they may lead to overly reduced human contact (Alaiad and Zhou, 2014; Bemelmans et al., 2012; Mordoch, 2013).

Social and cultural context may drive choices about the role of social robots, which may vary between OECD countries. For example, Japanese culture takes a more positive view of therapeutic robots, while North America has been slower to accept the concept (Mordoch, 2013).

Measuring progress in dementia policy

Measurement of dementia is essential to improving policy, but only few robust measures currently exist and these are not collected in many countries. The OECD has begun to explore issues around data and measurement for dementia, and recently published the proceedings of an event on "Dementia research and care: Can big data help?", held in Toronto in 2014 in collaboration with the Ontario Brain Institute (OBI) and the Institute for Health Policy, Management and Evaluation (IHPME) of the University of Toronto (OECD, 2015). However, much more work is needed to move towards robust, internationally comparable measures around dementia policy.

Figure 2.9 suggests some initial ideas of current and possible future indicators for measuring progress against the key policy objectives identified in this chapter. Further work is needed to refine this list and build consensus around the best indicators for monitoring progress in dementia care.

Figure 2.9. Possible indicators for benchmarking performance

The indicators described in this table are initial suggestions. Many of them do not exist, or are not collected in many countries, and some may be infeasible. This list is intended to be a starting point for discussions about indicators and further work is needed in this area.

1	The risk of developing dementia is minimised	Basket of healthy ageing measures (e.g. obesity, alcohol, smoking, stroke)
2	Dementia is diagnosed quickly once someone becomes concerned about symptoms	Stage of dementia at diagnosis (mild, moderate, severe) Proportion of primary care doctors with specific dementia training Inclusion of cognitive testing in long-term care needs assessment Access to appropriate services is ensured once diagnosed
3	Communities are safer for and more accepting of people with dementia	Survey data on public attitudes to dementia Proportion of communities taking steps to become dementia friendly
4	Those who care for friends and relatives with dementia are supported	Take-up rates for respite care and/or training among informal carers Quality of life or rates of mental illness for informal carers
5	People with dementia live in safe and appropriate environments	Take-up rates for home adaptations Information to create safe and appropriate environments for people with dementia are widely available Availability of alternatives to traditional residential care
6	People with dementia have access to safe and high quality long-term care services	Comprehensive and standardised needs assessment are used to develop individualised care plans Existence and implementation of standards of practice / training Rates of inappropriate care (use of antipsychotics, physical restraints) and adverse events (pressure ulcers, falls) Rates of certified / accredited long-term care workers
7	Health services recognise and effectively manage people with dementia	Proportion of people with dementia on a registry or with an EHR Proportion of hospitals that have dementia training or specialist staff Proportion of hospitals that have dedicated wards and space for people with dementia Readmission rates for people with dementia (and reasons for readmission)
8	People with dementia die with dignity in the place of their choosing	Proportion of people with dementia dying at home Proportion of people with dementia with advance directives about their end-of-life care
9	Care is co-ordinated, proactive and delivered closer to home	Availability / reimbursement of community medical care services Hospital admission rates for people with dementia
10	The potential of technology to support dementia care is realised	Assistive technologies with proven benefits and cost-effectiveness come to market Existence of clear criteria for reimbursement decisions

Measuring and benchmarking practice and performance is essential, but there is a lack of robust measures of the impact of dementia policy

This chapter has identified what policy should be aiming to do for people with dementia at different stages of the condition and in different settings; the latest evidence of how these aims can be best achieved; examples of how countries are seeking to achieve these aims; and areas where a greater focus is needed going forward. This can serve as an information resource for countries, but the ability to measure progress is also

essential to improving the lives of people with dementia. Progress in dementia policy can be measured by looking at performance (the outcomes that systems are achieving for people with dementia) or practice (whether systems are implementing the processes that we believe will deliver the best outcomes).

The ultimate outcome that dementia policy should aim to achieve is the well-being, or quality of life, of people with dementia and their carers and families, but there is no single definition of the concept and range of definitions and measurement tools exist, which may give conflicting results. Measuring quality of life for people with dementia presents further challenges, since they may not be able to communicate their well-being effectively. Benchmarking practice and identifying proxy outcome measures may be more realistic, but in the case of dementia policy there are significant barriers to measurement, meaning that few meaningful indicators are currently available. A concerted international effort is needed to support the development of meaningful and comparable indicators and to help countries develop the systems and processes to enable the collection of these measures.

Improving information architecture across health and care systems can be a key enabler of measurement for dementia care

Most of the measures set out in Figure 2.9 are not currently available in most OECD countries, or not available for people with dementia specifically. Moving towards collecting these or other measures systematically will require significant improvements in the collection and use of data from across health and care systems. The following aspects are particularly important.

Improving diagnosis rates and recording

Understanding how well policy is working for people with dementia requires an understanding of the target population. However, many people with dementia do not receive a diagnosis, or are not diagnosed until an advanced stage, and there is often no systematic recording of diagnoses. Countries should move towards systematically recording all dementia diagnoses, including the stage of dementia at diagnosis, assessed using a standard test of cognitive function.

Consistent identification and coding of dementia in hospitals

People with dementia suffer from multiple comorbidities, so are often admitted to hospital for a reason not directly related to dementia. Hospitals do not always recognise the person's dementia, and even where they do the diagnosis is not routinely coded. This makes it impossible to replicate common measures such as admission and readmission rates for people with dementia. Countries can address this issue by improving the detection of dementia in hospitals (e.g. by better data sharing) and ensuring that when identified it is always coded, even if it is not the primary diagnosis.

Linking data across health and care systems using dementia registries or electronic health records

In many countries, data from different parts of the health and care systems exists in silos. Data systems are incapable of matching up, for example, a diagnosis of dementia that a person received in primary care with the type of long-term care that they are receiving in their own home and the number of times they have been admitted to hospital

in the past year. This severely limits the scope to measure the impact of dementia-specific policies.

Many countries are working towards the implementation of electronic health records (EHRs), which will link patient data across all care settings and create new possibilities for performance and practice measurement. If these systems are successfully implemented, they will be a hugely important step towards international benchmarking of dementia care. However, EHRs are wide-ranging and complex, meaning that they are costly and time-consuming to implement. Some countries may still be a long way away from full implementation, meaning that EHRs will not be the answer to measuring progress in dementia care in the foreseeable future.

Where EHRs are not imminent, countries should explore whether there is a case for dementia-specific data sharing solutions, such as dementia registries. In their simplest form, these systems could allow the recording and sharing of dementia diagnoses across the health and care system. This would improve data on prevalence and allow the benchmarking of diagnostic services; and ensure that dementia is recognised by all health and long-term care professionals who work with the person. More ambitious registries could also include other information that is useful operationally or for benchmarking.

Conclusions

Improving the lives of people living with dementia has rightly risen to the top of the policy agenda in many OECD countries. To support countries in addressing this challenge, this chapter has identified, based on the best available evidence and current practice in OECD countries, ten key policy objectives that reflect the main areas that governments should focus on when developing policies to improve the lives of people living with dementia (Figure 2.1); and a number of policy approaches that are supported by the evidence or are being implemented in OECD countries (Figure 2.2).

Many of these policies are reflected in the dementia strategies that an increasing number of countries have published. However, ensuring that these policies are consistently implemented remains a challenge and there is still too much uncertainty around which policy approaches are the most effective. More comprehensive and robust evaluation of the implementation and effectiveness of policies is essential if the knowledge base on dementia policy is to improve. This must be supported by the development of comparable international metrics, improvements in data systems to enable more effective measurement and an increased focus on primary research for dementia. This chapter has provided some initial suggestions of indicators (Figure 2.9) – such as the stage of dementia at diagnosis, rates of use of antipsychotics and physical restraints, and hospital readmission rates for people with dementia – and identified some of the key enablers – such as improving diagnosis rates, better coding of dementia in health care facilities and linking data across care settings. This remains an important area for further work.

There is an important role for the international community, supported by organisations such as the OECD and WHO, to play in continuing to highlight key policy objectives; collate and disseminate the best available evidence on the effectiveness of policy options; develop internationally comparable metrics to monitor progress; and understand the key enablers that are necessary to support better measurement. This report is a first step in this process, but further work if countries are to effectively address dementia now and in the future.

Notes

1. This chapter was authored by Tim Muir, Klara Lorenz and Yuki Murakami from OECD Directorate for Employment, Labour and Social Affairs.
2. This chapter identifies the issues *primarily* associated with early and advanced dementia. However, reality is not as simple as this stylised presentation, and all of these issues could apply in an early or advanced stage of dementia, depending on the needs and circumstances of each individual person.

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Chapter 3

Towards a cure for dementia[1]

Finding a cure and a preventive treatment for Alzheimer's disease and other dementias must be the long-term goal of global dementia research policy. This would transform the lives of millions of people by relieving them of the burden of disability and save the billions of dollars every year that dependency costs. But working towards an effective therapy requires that we rethink the systems and incentives that drive biomedical research and health innovation. Under our current model, progress in dementia research and drug development has stalled and investment is just a fraction of what it is for other diseases of similar importance and profile. Areas where progress should be made include: greater patient and public engagement in the innovation process; increased collaboration and stronger public-private partnerships; a more convergent and synchronised regulatory environment; flexible and adaptive clinical trial designs; greater use of open science and data; enhanced public research funding and increased risk sharing as well as respect for access to medicines and payers' perspectives. While finding a cure is paramount, policy makers should also strengthen the focus on risk reduction and foster the development of better symptomatic treatments. Finally, better data on the public resources devoted to research and health innovation on dementia are required.

Introduction

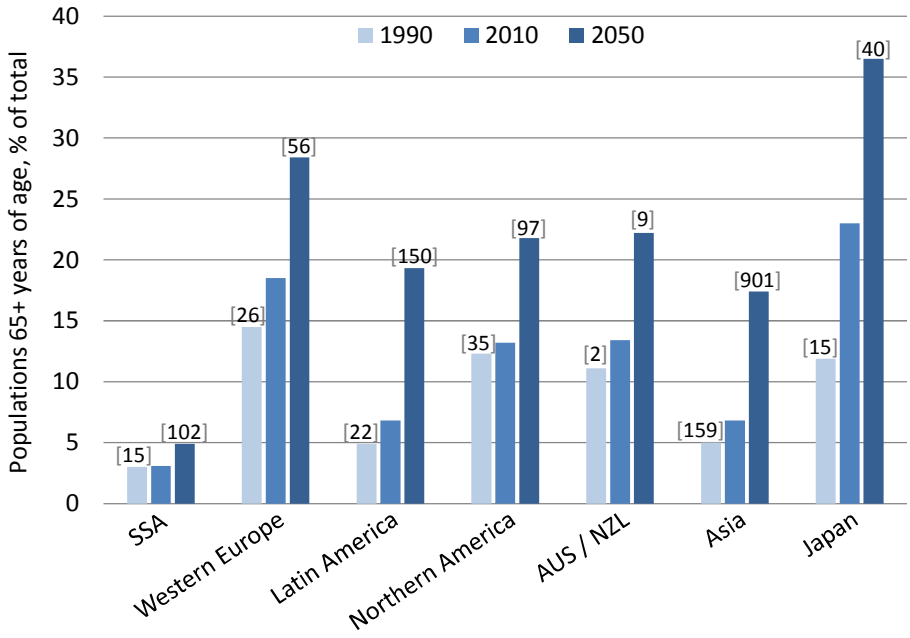
Alzheimer's disease is the most common form of dementia and accounts for 50-70% of dementia cases in the elderly (Feldman et al., 2014). Although young-onset is increasingly recognised, partly due to the importance of this age group for diagnostic/therapeutic research and drug development, dementia is a syndrome that predominantly affects people 65 years and older. As shown in Figure 3.1, the proportion of people over the age of 65 is expected to increase significantly during the next 35 years, coupled with a rise in dementia prevalence in all regions of the world. Due to a pronounced maturing of populations, inadequate public-health systems, and financial constraints, some emerging economies will be impacted more strongly by the rising dementia epidemic.

For these reasons, there is an urgent need for disease-modifying therapies that can prevent, delay the onset, slow the progression, or improve the symptoms of Alzheimer's disease and other dementias. However, biomedical research and health innovation has proven to be challenging in the area of neurodegenerative diseases (PhRMA, 2012; Riordan and Cutler, 2011). There is, as yet, no effective treatment for Alzheimer's disease and the five drugs that are currently on the market focus on symptoms and only offer a partial improvement in the quality of life through a temporary and relative enhancement of cognitive functions. According to Cummings et al. (2014) no new treatments have been approved for Alzheimer's disease since 2003 and clinical trials conducted from 2002 to 2012 (413 clinical trials, 244 compounds) showed an extremely low success of 0.4% (i.e. 99.6% of compounds failed).

The reasons for these failures and for the comparatively low number of clinical trials conducted for Alzheimer's disease are manifold. They include, persistent knowledge gaps in the disease pathology, lack of qualified biomarkers (i.e. measurable indicators of disease status and therapeutic effect), limited evidence base for therapies under investigation, great heterogeneity in patients, inadequate clinical trial protocols and processes, and insufficient funding for research and innovation (Becker et al., 2008; Berk and Sabbagh, 2013). There are at present several encouraging experimental therapeutic options in clinical development that have the potential to deliver a first disease-modifying therapy for Alzheimer's disease by the end of this decade. At the same time, available estimates suggest that research spending on Alzheimer's disease and other dementias remains low compared with the cost burden (see Box 3.2).

The development of disease-modifying therapies that alter disease progression or provide a cure is the main goal of Alzheimer's therapeutic research. However, preventive measures and therapeutic routes to improve the living conditions of symptomatic patients should not be neglected. Treatments with a sustained symptomatic effect can have a significant impact on people living with neurodegenerative diseases and can facilitate care, and should therefore be developed in parallel. There is also an urgent need for better understanding the impact of lifestyle, food and nutrition on healthy ageing and the development of Alzheimer's and other neurodegenerative diseases (Barak and Aizenberg, 2010; Morris et al., 2014). A growing body of evidence suggests that key metabolic indicators (e.g. cholesterol levels, high blood pressure, high blood sugar levels etc.) are associated with the risk of developing chronic diseases. Healthy diet and active living are the pillars of well-being at any stage of life and may help to combat the growing burden of chronic diseases, including Alzheimer's and other dementias.

Figure 3.1. Populations 65 years of age and above in some countries and regions



Note: Sub-Saharan Africa (SSA), Australia/New Zealand (AUS/NZL). Figures in brackets are the absolute numbers of people 65+, millions.

Source: OECD, based on www.unpopulation.org (accessed January 2015).

The development of new therapies for dementia relies on biomedical research, the translation of research into therapies, and the development of new biomedical technologies. Translational neuroscience focuses on the linkages between basic neuroscience and the development of new diagnostic and therapeutic products that will improve the lives of patients or prevent the occurrence of brain disorders (Cummings et al., 2013). Emerging biomedical technologies, such as synthetic biology, nanotechnology, pharmacogenomics, and stem cell technology offer the tools and techniques to shift the conventional drug development model to one that allows for more disruptive innovation. However, in order to realise opportunities in health most of the emerging biomedical technologies still need to transition from the academic research environment to an industrial scale and to clinical use (Berger et al., 2014; Ruder et al., 2011).

Over the past decades, the main driver of most drug discovery and development were large pharmaceutical companies. Partly due to more resource-intensive research approaches, shrinking returns-on-investment, and persistent knowledge gaps in the biomedical underpinnings of diseases, traditional drug discovery and development processes have become unsustainable (Bennani, 2011; Liu et al., 2014). To accelerate the development of new therapies for Alzheimer's disease and other dementias and to manage high financial risks, stakeholders are increasingly following cross-sectoral, collaborative strategies. Public-private partnerships, in particular, have the potential to facilitate a reform of traditional research and health innovation models towards more efficient innovation strategies (Galea and McKee, 2014). In providing a neutral environment, public-private partnerships can help to accelerate the development of effective therapies for Alzheimer's disease by supporting the mission of each stakeholder and bridging the innovation gap in

neuroscience – ultimately, by reducing the attrition rate during clinical research and by reducing financial risks.

As the many failures in clinical research have shown, drug development for Alzheimer's disease remains a high risk endeavour. Governments, in close collaboration with other stakeholders, are exploring new funding and risk-sharing mechanisms to support resource-intensive research (Feldman et al., 2014; Scott et al., 2014). To translate therapeutic efficacy into effective public-health systems, cost-benefit measures are gaining importance for the regulatory assessment and marketing approval of therapies. However, when a new therapy is introduced into the market, there often remains uncertainty about its performance within the public-health system – outside the strict controls of a clinical trial. Therefore, besides the assessment of efficacy and safety parameters, the successful development of innovative medicines should include the early consideration of future treatment costs (Foster et al., 2014). Striking an appropriate balance in the respective financial risks of producers (researchers, manufacturers) and purchasers (insurers, patients) could help to support innovative research, enhance access to medicines, and foster rational use and cost containment. Policies to support price transparency and the measurement of therapeutic effectiveness can help to assure value for money and the responsible use of limited resources.

At present, the probability of success for the development of central nervous system (CNS) drugs, Alzheimer's disease and other dementias in particular, is lower than in many other disease areas (Tufts, 2014; Box 3.1). In general, CNS drugs are more challenging to develop than other medicines because the nervous system disorders that the drugs aim to treat are often chronic and complex, and outcomes of clinical trials are difficult to measure. In addition, the brain is inaccessible to study and to treat – making it difficult to develop accurate models and to reach therapeutic targets. The low success rate of clinical trials coupled with high investment costs has been a significant factor in the withdrawal of some pharmaceutical companies and funding organisations from neuroscience research. However, recent government-led initiatives, for example the commitments made by G7 governments following the 2013 Dementia Summit in London and the development of National Dementia Plans, have contributed to a range of actions by public and private stakeholders to increase investment.

A recent OECD workshop "Enhancing Translational Research and Clinical Development in Alzheimer's Disease and other Dementias: The Way Forward"[2] in Lausanne, Switzerland, provided an international forum for all stakeholders to drive forward a change in the global paradigm in biomedical research and health innovation for Alzheimer's disease and other dementias (OECD, 2015c). It demonstrated that therapeutic research needs to shift from established dementia to pre-clinical stages, which will require adequate diagnostic tools, new trial designs, and more flexible regulatory processes. It will be important to incorporate the learnings from clinical trials (positive and negative results) into regulatory science and agency qualification processes as rapidly as possible in order to enable policy development and regulatory decision making based on the best available science. This chapter highlights the need for a joint engagement amongst all stakeholders in order to strengthen innovative therapeutic research and to accelerate its translation into clinical practice.

Neurodegenerative diseases: Challenges and opportunities in therapeutic development

The pharmaceutical industry faces important challenges in research and drug development of innovative drugs. During the past decade declining productivity in terms of new drug approvals has been paralleled by escalating investment costs along the value chain of health innovation. The cost of developing a new drug is approximately USD 1 billion and even higher estimates apply for Alzheimer's disease (Bunnage, 2011; DiMasi, 2003; Sternitzke, 2010). According to Scott (2014), the total costs for the development of a disease-modifying therapy for Alzheimer's disease could be USD 5.7 billion. Over the past 40 years the pharmaceutical industry has experienced a ten-fold increase in drug development costs (USD 138 million to develop a new drug in 1975),[3] which reflects the various technical, regulatory and economic issues affecting private research and health innovation. The main contributors to inefficiency and declining return of investment in therapeutics research are rising drug development costs, the current economic downturn, reimbursement pressures, increasing regulatory demands, intense market competition, and the challenge to implement new research strategies into operational and regulatory frameworks (Bennani, 2011; Earm and Earm, 2014). Some of the responses of the pharmaceutical industry to these pressures, such as the growing externalisation of research activities and an increased focus on mergers, have been questioned as being effective. In essence, a portfolio focus on large and profitable market segments coupled with a trend towards decreasing internal research budgets are unlikely to spur the necessary therapeutic innovation in Alzheimer's disease and other forms of dementia.

In recent years, there have been some encouraging signs for pharmaceutical innovation, however, judging from data on the submission and approval rate of new drugs at the US Food and Drug Authority (FDA). With an all-time low of 18 New Medical Entities (NMEs) approved in 2007, the yearly average number of NME approvals was 21 over the past decade. However, approvals in recent years look more promising: 30 NMEs approved in 2011, 39 in 2012, 27 in 2013, and 41 in 2014.[4] The number of NMEs approved by the FDA is often referred to as a measure of the innovation output of the pharmaceutical industry and the effectiveness of government policies and regulatory frameworks. The recent increase in the number of NME approval applications (New Drug Application) could be a positive sign towards higher scientific productivity in the pharmaceutical industry. Novel therapeutic avenues might be emerging, resulting from a rethinking of translational research approaches, a better implementation and efficient use of biomedical technologies in research and production, a repositioning of established drugs, and more collaborative approaches to research (Earm and Earm, 2014; Mei et al., 2012).

According to Cesar et al. (2013), another factor contributing to this improvement could be the shortened processing time for new drug applications at the FDA and the related shift to just-in-time inventory management. Both the FDA and the European Medicines Agency (EMA) strive to facilitate the management of clinical trials while maintaining the highest standards for patient safety and for the robustness and reliability of trial data. FDA's "Breakthrough Therapy Designation" is only one regulatory novelty that is poised to change health innovation. It is intended to expedite the development and review of drugs for serious or life-threatening conditions, thereby shortening approval timelines and reducing costs. It allows for market approval when early clinical data demonstrate substantial improvements over available therapies for serious or life-threatening diseases. The programme provides an accelerated review process for drugs that demonstrate

remarkable activity early on in their development. For example, in neuroscience the Breakthrough Therapy Designation has already been applied to a new drug for Parkinson's disease that may also be useful for other mental illnesses, including Alzheimer's disease and schizophrenia.

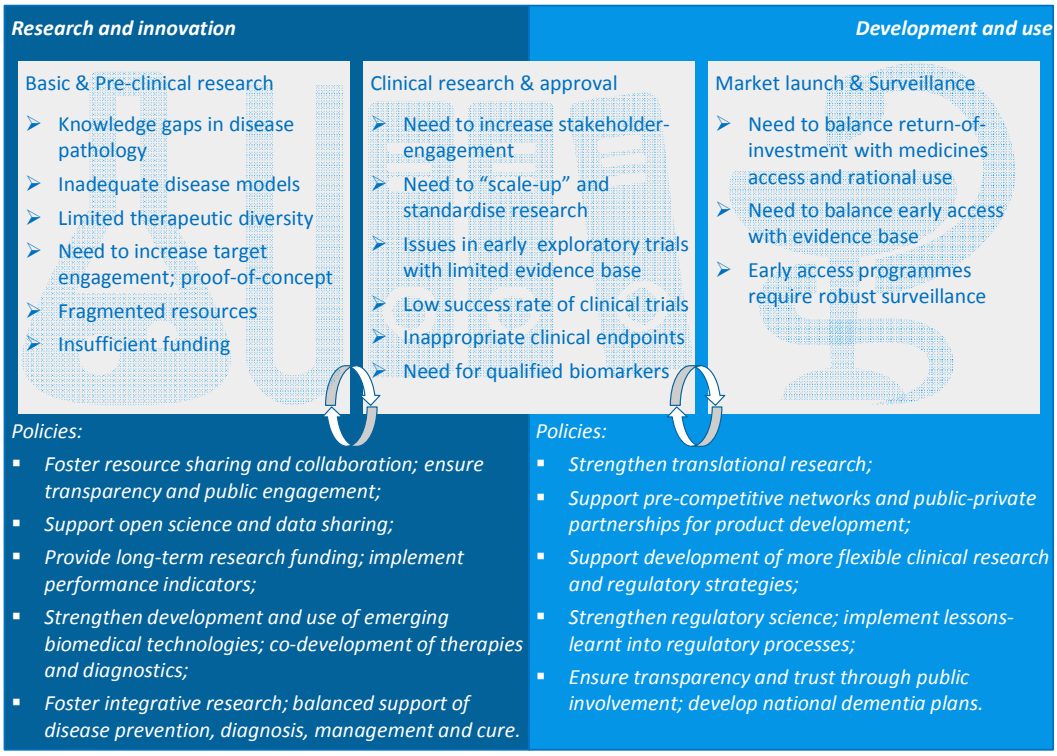
The question remains if the positive trend in submissions and approvals can be sustained in the future and, in particular, if this will have an impact on the development of drugs for neurodegenerative diseases. Notably, in 2014 only one innovative drug with a new mode of action was approved in the nervous system therapeutic area – compared to four in oncology. This is worrying because the need for (better) treatments for neurological and psychiatric disorders is vast. However, as noted before, drug development for the central nervous system is riskier than in other disease areas (Box 3.1). Preclinical research, clinical trials, and diagnostic procedures are more complex and resource-intensive – higher investments are often needed and drugs take longer to reach market approval. In addition, trials fail more often and show about half the average success rate compared to all therapeutic areas. Moreover, many CNS drugs fail in late-stage clinical development – when resource demands and costs are the highest and after a significant investment has already been made. As shown in Figure 3.2, the reasons for these failures are manifold and comprise complex pathological mechanisms in neurobiology, inadequate animal models of disease, difficulties in reaching targets in the brain, inadequate and subjective outcome measures of clinical trials, high placebo response rates, and the paucity of reliable biomarkers that can help assess disease progression and therapeutic efficacy (Johnson, 2014).

Box 3.1. Central nervous system research and drug development

A recent report of the Tufts Center for the Study of Drug Development (2014) states that CNS drugs take longer to develop, and have lower success rates than other drugs:

- Mean clinical development time for CNS drugs approved for marketing in the United States from 1999 through 2013 was 12.8 months, or 18% longer than that for non-CNS compounds;
- The overall clinical approval success rate for CNS compounds first tested in human subjects from 1995 to 2007 was 6.2%, or less than half the 13.3% rate for non-CNS drugs;
- The overall approval success rate for CNS compounds first tested in human subjects during 1995-07 varied from a low of 3.7% for 1997-00, to a peak of 11.3% for 2001-04, and then 4.7% for 2004-07;
- During 1999-2013, mean approval phase time for CNS compounds approved for marketing in the United States was 19.3 months, or 31% longer than the 14.7 months for non-CNS approvals;
- From 1999 to 2013, about one in six CNS compounds received a priority review rating from the FDA, compared to nearly half of all non-CNS compounds;
- Despite longer clinical and approval phase times, and lower clinical success rates, CNS approvals have held steady, accounting for about one in ten of all US approvals since the 1980s.The overall clinical approval success rate for CNS compounds first tested in human subjects from 1995 to 2007 was 6.2%, or less than half the 13.3% rate for non-CNS drugs.

Figure 3.2. Challenges and policy options along the trajectory of research and health innovation in Alzheimer's disease and other dementias



Possible options to address persistent challenges in central nervous system disorder research and drug development also apply to Alzheimer's disease and other dementias. This includes a strengthening of resource-intensive pre-clinical and translational research in order to identify potential targets for novel innovative therapeutic options. There are also options for policy makers and researchers to further leverage the potential of emerging biomedical technologies and innovative systems, for example synthetic biology and nanotechnology, through a closer communication, standardisation and policy development. A greater use of therapeutics and diagnostics co-development between academia and pharmaceutical companies would increase efficiency through a sharing of resources and could help to manage risks (Mei et al., 2012; Riordan and Cutler, 2011). Greater co-operation in Alzheimer's and other neurodegenerative diseases could catalyse innovative thinking, close knowledge gaps, and increase the efficient use of limited resources (Figure 3.2). In essence, a de-risking of drug development programmes would help to re-attract public and private research funding for this large and currently unmet medical need.

Accelerating research and drug development for Alzheimer's disease and other dementias

The prevalence and cost of mental disorders clearly demonstrates that there is a strong and growing demand for better treatments from the perspective of patient need and the high social and economic cost of failure to intervene effectively and promptly. Experience in Alzheimer's research and health innovation has shown that alternative approaches are needed to accelerate the delivery of effective therapies and diagnostics. Major bottlenecks have been identified, for example 1) animal and *in vivo* models of Alzheimer's do not sufficiently mirror the full picture of the disease in humans, implying that such models need

to be further developed in order to replicate and test disease-specific biochemical and molecular processes in the laboratory; 2) there is a lack of disease-specific and accessible biomarkers that would allow a reliable, non-invasive, and inexpensive diagnosis and disease assessment in clinical trials; 3) the relevant research community is complex, with the involvement of multiple stakeholders who are often not well-connected; 4) investment costs and (financial) risks are high; and 5) regulatory frameworks are not well-adapted to current needs. At the same time, an increased understanding of the biochemical and molecular underpinnings of Alzheimer's disease is a prerequisite for modern drug development as this can provide the necessary targets that can be addressed by drugs.

Governments, regulators, businesses and the research community are increasingly working together to develop and implement adequate policy and regulatory frameworks that can help translate the significant progress made in the understanding of neurodegenerative diseases into therapeutic options. Research strategies in Alzheimer's disease are evolving around the finding that the earliest pathological changes in the brain of patients can take place several years before the first clinical symptoms appear – offering an opportunity for early therapeutic intervention. This has led to the paradigm shift of research in patients with established dementia to people with the earliest signs of memory impairment (more than can be explained by ageing alone) and with mild-stage Alzheimer's disease. The resulting shift in research to treating very early stages of Alzheimer's disease and even healthy people with a genetic predisposition, is leading to both regulatory and ethical challenges.

Randomised clinical trials are the most reliable process to account for the variety of Alzheimer's pathologies within populations and to deliver the required data quality for eventual drug approvals. However, the translation of pre-clinical evidence into human trials remains a barrier to drug development. The likelihood of successfully developing new, effective treatments increases with the research community's fundamental understanding of Alzheimer's pathologies. It also increases with the successful application of this knowledge to, for example: the development of disease models, investigations into the clinical validity of drug targets, analysis of the performance characteristics of biomarkers for the enrichment of clinical trials, including the prediction of treatment effects, and improvements in the design of drug development programmes. Clinical trials can contribute much to the creation of this knowledge, and many insights can come only from such trials. Novel approaches to encourage greater dissemination of knowledge from both successful and unsuccessful clinical trials are therefore important. All stakeholders, including patient organisations, are currently discussing options for an earlier testing of potential new drugs into human trials to collect valuable pharmacokinetic and pharmacodynamic information from patients. This would help refine and improve clinical trials and enable the early failure of clinical trials, which is important for both ethical and economic reasons. Efforts are currently underway to build a Global Clinical Trials Platform, which combined with a future Central Clinical Database in Alzheimer's disease would offer the required international outreach.

There is also consensus that a more convergent and synchronised regulatory environment would increase the efficiency of translational and clinical research programmes (Kozauer and Katz, 2013). There are opportunities to accelerate and streamline the operational conduct of multinational clinical trials through more efficient and harmonised national regulations. The OECD's Lausanne workshop illustrated the increasing convergence of regulatory approaches towards Alzheimer's disease and other dementias among major regulatory agencies. It will be important to incorporate the learning from currently ongoing risk reduction trials into regulatory science and approval processes in order to change the regulatory paradigm based on the best available science. Providing

more resources to regulatory agencies for scientifically sound decision making would help to speed-up the process without putting patients' health at risk (Becker and Greig, 2014).

At the OECD workshop "Enhancing Translational Research and Clinical Development in Alzheimer's Disease and other Dementias: The Way Forward" speakers summarised the opportunities for more flexible and continuous global clinical trial systems with a close collaboration of stakeholders. Doing this will result in significantly faster cycle times, more efficient resource use, higher quality data and higher probability of success. Opportunities include:

- Strengthening of early, small, parallel-design trials supported by biomarkers in order to gain valuable insights into the performance of a potential new drug in patients before entering into full development programmes.
- Development of master protocols (experimental plan to test several candidate drugs) for "adaptive, seamless-design" trials, which allow for a continuous trial conduct and adaption of intervention supported by multiple stakeholders.
- Global clinical research networks which allow for multiple stakeholder engagement and testing of biomarkers and combination treatments.
- Central Institutional Review Board(s) as independent bodies to enhance the quality of human research protection in multi-site human research projects by performing appropriate ethical and medical scientific review.
- Fast-response regulatory access and advice for clinical trial set-up and conduct.
- Globally convergent and synchronised regulatory environments on, for example, definition of clinical meaningfulness, diagnostic standards, adaptive regulatory and clinical trial mechanisms, combination therapies.

Harnessing the potential of emerging biomedical technologies

A key policy question is how to balance governance, oversight and regulation with the flexibility required to enable disruptive innovation in biomedical research and drug development. Innovation in biomedical research and drug development often happens through stepwise, continuous changes along the technology trajectory and across therapeutic areas (Nutt and Attridge, 2014). However, more radical, disruptive innovation is linked to a technology novelty with a significant customer benefit – a breakthrough with a direct impact on existing therapeutic processes, patients' health, and markets (Sternitzke, 2010). How to accelerate such more radical technical change and how to implement new medical scientific and therapeutic paradigms into existing policy and regulatory frameworks are important questions in the arena of policy making. The complex dysfunctions seen in Alzheimer's disease are not adequately addressed by existing therapeutic approaches, but may be understood through research incorporating multiple approaches, technologies and disciplines, such as genomics, synthetic biology and/or systems biology. Strategies are required that deliver a deeper understanding of the complex interplay between genetic and environmental factors in the development of chronic diseases to enable evidence based decision making in research, medicines regulation, and policy development. Emerging biomedical technologies, open science, risk-sharing models, and a deepening of patients' involvement are some of the factors that can drive more disruptive health innovation.

Synthetic biology is considered a disruptive technology with a broad range of application areas in biomedical research and health innovation (Bugaj and Schaffer, 2012; OECD, 2014). It mirrors the gradual development of biological sciences from descriptive disciplines to rational engineering of complex cellular functions. Synthetic biology has greatly developed due to parallel advances and inspiration by, for example, molecular biology, genome sequencing and electrical engineering. As an example of a converging technology, synthetic biology offers the tools for a better understanding of the complex relationship between genetic principles and the environment in Alzheimer's disease. It is expected to provide more tailored, patient-specific diagnostics and future therapies. In particular, synthetic biology allows the exploitation of the natural diversity of bioactive molecules and also offers new routes to the creation of novel compounds and modular synthetic pathways. However, despite promising opportunities the impact of, for example, advanced DNA-sequencing technologies, nanotechnology, omics tools, and synthetic biology, on the health of patients remains limited (Collins, 2010). Significant barriers to the broad uptake and use of these technologies in a regulated research environment are insufficient standardisation, ongoing public dispute and the timing and appropriateness of their use in relation to the prevailing evidence base (Vamvakas et al., 2011).

The recent advancement in nanotechnologies for biomedical research and health innovation has highlighted nanoscience as another key enabling technology to close the translational gaps between pre-clinical research, drug development and patient use (Ajetunmobi et al., 2014). The development of neuroimaging tools in the diagnosis of Alzheimer's disease and other CNS disorders has led to new insights in our understanding of pathologies and helped the development of novel diagnostic modalities for therapeutic intervention. The use of synthetic nanoparticles with diverse surface chemistries and superb optical features represent a versatile diagnostic tool for combating the challenges of *in vivo* neuroimaging techniques. Over the next decade, nanotechnology will continue to play a vital role in neuroscience, not just in the development of highly specific and sensitive imaging probes and biosensor interfaces but also for potential treatment strategies.

However, despite their large future potential clinical nanotechnology applications to the CNS are further behind applications to other areas of medicine and biology, such as, for example, orthopaedic applications, DNA/genomic sensors, and novel drug and gene delivery approaches (Silva, 2010). In part this is due to the unique challenges imposed by the CNS itself – restricted and difficult anatomical access, as well as an extremely heterogeneous cellular and molecular environment. Nanoparticles are of particular importance for the treatment of both peripheral and CNS disorders, and may eventually offer the patient and clinician novel therapeutic choices and better target engagement through the blood-brain barrier. This is a highly selective permeability barrier that separates the circulating blood from the brain, representing the most important factor limiting the development of new drugs and biologics for central nervous system disorders (Brambilla et al., 2011; Re et al., 2012).

Progress in genomics research is another source of potential radical innovation, which has already significantly supported the understanding of the molecular mechanisms associated with ageing and dementia. In particular, genomics technologies could enable patient profiling in the development of diagnostic tools, clinical research and in the development of personalised medicines. The study of Alzheimer's disease has already benefitted from metabolomics[5] to enable a better understanding of the biochemical risk factors and molecular abnormalities in people at risk of developing the disease. However, metabolomics technologies require careful standardisation and are not yet mature enough to be implemented in large-scale studies. Personalised medicine aims to provide care tailored

to address specific patient characteristics such as the susceptibility of an individual to a disease or response to a drug. It is based on new methods of molecular analysis that can lead to more accurate and targeted diagnosis and treatment. A holistic, systems biology and patient-focused approach is expected to permit a more comprehensive understanding of Alzheimer's disease variability and should further increase the predictability of disease development.

The rise of emerging technologies and the stronger personalisation of medicines are generating new questions for policy makers (OECD, 2011). A number of ethical and regulatory issues could impede the translation of promising research findings into clinical development and hamper regulatory decision-making processes. In addition, the use of patient-specific information, such as bio-samples, and genetic or metabolic profiles may require governments to adapt existing policy and regulatory frameworks. There is uncertainty about the ethical, legal and regulatory implications of research in personalised medicines, especially with regard to the involvement in clinical trials of healthy volunteers or of patients at the very early stages of disease. There is a general understanding that regulators must serve as a gateway not as a barrier to swift translation of new ideas into innovation and products which are safe and effective for the people who most need them. Therefore regulatory science and governance frameworks must co-evolve creating conditions for early dialogue with main actors and new ways for sharing and managing knowledge on a global scale to achieve successful translation of biomedical research into clinical practice (OECD, 2013a). Improving regulatory science for the development, approval, and use of innovative biomedical therapies and diagnostics which are based on emerging biomedical technologies is therefore imperative. A strong science capacity is a prerequisite to ensure the regulators' ability to efficiently review products incorporating the latest technology (Anatol et al., 2013).

Enabling a global paradigm shift through stakeholder engagement

Concerns have been raised that the pharmaceutical industry and investors are withdrawing from research and drug development in neurodegenerative diseases. In a situation of high risk for the pharmaceutical industry, government-funded public research institutions have played a leading role in efforts to close the translational research gap and accelerate the development of innovative therapeutic options. It is evident that large investments in biomedical research and innovative conceptual frameworks are needed to address Alzheimer's disease. The following examples exemplify the significance of government funding in the area of Alzheimer's and other neurodegenerative diseases:

- In addition to other substantial funding mechanisms in dementia, the UK "Global Clinical Trials Fund" recently launched a new scheme to support clinical trials that have potential to be of benefit to dementia patients. The fund aims to make GBP 20 million available for early-stage trials over the next five years, supporting clinical research into new treatments for diseases like Alzheimer's. A focus will be put on: 1) clinical trials that aim to demonstrate target engagement, Phase I or Phase II clinical trials undertaken to ascertain the potential safety and efficacy of (novel or re-purposed) drug-based interventions in human subjects; 2) clinical trials of non-drug based, complex interventions; 3) opportunities for research "add ons" to ongoing clinical trials (e.g. biomarker add-ons).
- Canada has invested CAD 236 million over the past ten years in dementia-related research through the Canadian Institutes of Health Research.[6] More specifically, the Canadian Consortium on Neurodegeneration in Aging (CCNA) has received funding

of CAD 31.5 million over five years from the Government of Canada, through the Canadian Institutes of Health Research, and a group of 13 partners from the public and private sectors, including the Alzheimer Society of Canada and Fonds de Recherche du Québec – Santé. The CCNA researchers will also benefit from an additional CAD 24 million investment by a subset of the partners in Ontario and Quebec.[7]

- The Australian Federal Government decided in 2013 to invest AUD 559 million to support Australian health and medical researchers generating new health discoveries.[8] The sustained funding of biomedical research in Australia follows the government's position that research investment can retain scientific talent, generate health discoveries and help to reap the benefits of health and medical research. In a recent press release the Australian Government committed AUD 18 million of new funds to support innovative dementia research.[9] The grants cover a range of innovative research projects, from genetic studies of twins, to studying the effects of an intergenerational activity programme.
- In the United States the NIH expects to spend USD 566 million on Alzheimer's disease in the fiscal year 2015. Among others, translational research, genetics, neuroimaging, and biomarkers research will play an important role in ongoing and future research projects. In particular, the "Brain Research through Advancing Innovative Neurotechnologies" (BRAIN) initiative supports research collaborations in neurodegenerative diseases between academic institutions, the pharmaceutical industry, and other public agencies. The NIH committed USD 40 million to the BRAIN initiative in the fiscal year 2014 and plans to spend at least USD 65 million on research collaborations with academic institutions, the private sector, and other government agencies on the BRAIN initiative in the fiscal year 2015. A first wave of investments totalling USD 46 million to support the goals of the BRAIN initiative has been announced in September 2014. Additional funding should accelerate progress in, amongst others, Alzheimer's disease research – to provide further insights into the disease pathology and to establish new approaches to the development of next generation treatments. The NIH is committed to sustain the implementation of the individual research components of the National Plan to Address Alzheimer's Disease in order to provide an effective Alzheimer's treatment by 2025.

There is consensus that a joint engagement amongst all stakeholders is needed in order to strengthen integrative research strategies and to accelerate its translation into innovative therapies. Collaborations among public- and private-sector stakeholders in large and resource-intensive proof-of-concept trials are now beginning and offer a rich source of information – both, success and failure – for the larger field of neurodegenerative disease research. However, several challenges remain to open sharing between stakeholders. These include: the protection of intellectual assets (trade secrets, and intellectual property), strategic long-term portfolio decisions, and marketing strategies. Stakeholders frequently address these through an early definition of their expectations and roles in collaborative models.

Alzheimer's disease is a good example of how close collaboration between stakeholders can advance product development and help to modernise policy and regulatory frameworks (Carillo, 2013). The design and implementation of more efficient innovation strategies in Alzheimer's disease and other dementias includes the need to balance between traditional research and business models and more disruptive strategies with some uncertainties. Therefore, the opinions and needs of patients and the public (especially of caregivers and payers) should be a corner stone while bridging the gap between the development push

from pharmaceutical research and the demand-pull by dementia patients. Government policies can help to deepen the involvement of patients and the wider public through a strengthening of public trust, transparency and oversight in broad diagnostic campaigns, and by encouraging participation in global patient registries, and clinical trial platforms.

Public-private partnerships for product development mirror best the multidimensional nature of Alzheimer's disease and combine the strengths of scientific disciplines and policy areas. The lead in forming these new partnerships is often taken by philanthropic organisations, governments and regulatory agencies, but can also emerge from the business sector. Key drivers for stakeholders to join collaborative partnerships in Alzheimer's disease and other dementias are: 1) the increasing burden of the disease and related medical, social and economic consequences; 2) the complexity of unresolved biomedical questions; 3) the need to share knowledge and infrastructure, in order to manage high investment costs and risks; 4) the need to reform regulatory frameworks through the strengthening of regulatory science and increased flexibility in clinical trials; and 5) the importance of respecting patients' needs (OECD, 2015a). In essence, stakeholders join public-private partnerships to take advantage of the benefits from working together, for example in realising economic advantages, fostering upstream research through open science approaches, gaining access to innovation and accelerating its translation into clinical applications, or in strengthening the bonds with patients and the public.

There is a tendency between stakeholders in neurodegenerative disease research to jointly develop non-competitive research strategies through a sharing of resources, opportunities and risks (Norris et al., 2014). The definition of common ground is closely linked with the description of "pre-competitive space". Delineating the boundaries of "pre-competitive space" is of particular importance in Alzheimer's disease, where public-private partnerships often contain both pharmaceutical competitors [hence Mullard's (2011) use of the term "pharma-pharma-public" alliances] and, as noted by Mattes (2014), many non-profit organisations and public research institutes that also typically compete with each over scarce resources. In order to avoid potential disagreement over issues such as intellectual property or competing marketing strategies, public-private partnerships therefore evolve predominantly in a pre-competitive space that is limited to activities such as target validation and safety, pharmacological and proof-of-concept studies (Goldman et al., 2013).

Most existing public-private partnerships in Alzheimer's disease have emerged over the last 15 years and focus on discovery research and sharing of resources (infrastructure, data, knowledge, and funds). In parallel the complexity and scope of partnerships in biomedical research and health innovation has been changing – from industry-academia task-based collaborations to long-term, more inclusive collaborative networks for know-how exchange. Public-private partnerships in Alzheimer's disease often have additional foci, which may include the design and facilitation of clinical trials, strengthening of operational excellence, the modernisation of policy and regulatory frameworks, and the sharing of investment risks and benefits. The broad spectrum of areas addressed and the high number of otherwise economically competing pharmaceutical industries joining public-private partnerships reflect the magnitude of the challenges in Alzheimer's disease. The horizontally-structured public-private partnerships in Alzheimer's disease and their focus on both research issues (basic, discovery and translational research) and governance issues (operational excellence, policy and regulatory frameworks) exhibit unique characteristics:

- a focus on unresolved biomedical questions upstream of research and health innovation,
- clearly defined terms of reference for the partnerships,

- mutual responsibility, and shared benefits and risks for stakeholders as appropriate,
- involvement of many, otherwise competing public and private entities in cross-sectoral collaborations (pharma-pharma-public alliances),
- direct involvement of non-profit/ patient organisations in goal setting to align strategies with patients' needs,
- broadening of the common ground through more inclusive partnerships and widening of the precompetitive space,
- the aim of reforming policy and regulatory frameworks to accelerate product development through new, non-linear drug development models.

Public-private partnerships offer significant advantages for stakeholders but, given their heterogeneity, diverging and competing interests, may require new forms of co-ordination, which are increasingly offered by centres of excellence or research enablers. There is now considerable experience with issues related to the establishment of public-private partnerships in biomedical research and health innovation, and efficiency and effectiveness lessons can be learned from existing partnerships concerned with Alzheimer's disease. Professional management of partnerships is a prerequisite for the efficient use of limited resources and the generation of value out of collaborative efforts.

Public and private research entities, funding organisations and policy makers fulfil complementary roles in biomedical innovation and in the development of new therapies. In particular, researchers from both academia and the pharmaceutical industry share the same interest in providing treatments for unmet medical needs and require access to specialised talent and infrastructure. In order to leverage the full spectrum of advantages of public-private partnerships in Alzheimer's disease, the issues and needs, ideologies, and objectives of each individual stakeholder need to be addressed upfront. Policy frameworks that define the legal, economic and ethical implications of topics at the boundary between the precompetitive and competitive space (for example, topics such as intellectual property and defining mechanisms for joint proof-of-concept and late stage trials) can facilitate collaboration and help to manage financial and non-financial risks.

Stakeholders can work together to develop flexible and context-specific policies on risk governance. These can help to manage uncertainties over the life-cycle of medicinal products, thereby leveraging the inherent society gains of collaborative biomedical research and the development and use of emerging and converging technologies. Questions remain to be answered, including: What are the options to develop risk-regulation frameworks in a proportionate and balanced way to provide society with the gains and benefits of innovation? How to involve non-government actors in the development and implementation of risk-governance systems supporting the translation of scientific research into innovation and application?

Stakeholders have realised that more can be achieved by combining strengths and sharing rewards between academic and private research partners in health science and policy. A key success factor of partnerships is the value gained to each individual stakeholder relative to alternative investments. Policy options to harness and integrate the strengths of public-private partnerships for research and health innovation in Alzheimer's disease and other dementias include:

- developing national governance frameworks for public-private partnerships with transnational outreach;

- ensuring that public-private partnerships are affordable, respect value for money, are transparently treated in budget processes, and are monitored for quality and efficient use of resources;
- empowering academia and small and medium-sized biotech companies as a key source of innovation and partner of the pharmaceutical industry and providing the frameworks which support scientists at academia in field-testing innovative ideas and translating innovations ideas into products;
- developing terms of reference for multiple industry-industry collaborations in public-private partnerships;
- enabling information sharing and a systems approach in research and health innovation through the development of infrastructure, norms, standards, and policies across research areas and between stakeholders; supporting open innovation models through the right frameworks at the interface between the precompetitive and the competitive space;
- encouraging investment, joint thinking, and innovation through the development of novel funding structures, incentive models, risk-sharing and risk-managing schemes; and
- developing tailored research and drug development approaches for Alzheimer's disease and other dementias by adapting existing policy and regulatory frameworks to evolving, non-linear drug development models.

In essence, two major trends in research and health innovation partnerships for Alzheimer's disease: a rethinking of the traditional, linear drug development model, and an expanding of vertical to horizontal, multi-stakeholder partnerships.

De-risking drug development for dementia

The ageing of populations and current lack of effective preventive options leads to substantial and ever growing medical need in Alzheimer's disease. The potential size of the untreated dementia and CNS market is so great that the future growth of this market could outpace the growth in all other sectors of the pharmaceutical industry. However, despite significant medical scientific progress and increased testing of potential therapeutic solutions, Alzheimer's disease still represents an area of limited resources and high investment risks (Mattke et al., 2013; Pritchard, 2008). This is partly due to failure of major development programmes in CNS disorders and to larger, cross-sectoral issues and developments in the pharmaceutical sector: Between 2000 and 2011, the number of large pharmaceutical and biotech companies fell by 50% (a change from 20 to 10 core companies) through mergers and acquisitions (Bartfai and Lees, 2013). The percentage of companies involved in antibiotics discovery fell from 90 to 30% (a change from 18 to 3 core companies) of all active companies, and in CNS from 100 to 40% (a change from 20 to 4 core companies). According to Choi et al. (2014), the number of CNS programmes of key pharmaceutical companies has been cut by half from 2009 to 2014. Additional innovation risks arise from a pronounced outsourcing of research activities to Contract Research Organisations (CROs), which can result in the fragmentation of innovation processes. In essence, with each merger, acquisition, and increased outsourcing, capabilities for research and development are often lost.

Increased public investment and shared funding structures in translational and clinical research offer market push incentives that could help to de-risk processes and foster

research into an area which has been traditionally characterised by high attrition rates and financial loss. Market pull incentives aim to increase the benefits of success in order to keep the research community and funders in business. A policy change that regulates therapeutic market returns can provide an economic rationale for CNS research and drug development (Choi et al., 2014). Governments and the pharmaceutical industry are implementing risk-reduction techniques, permitting stakeholders to remain successfully in drug development. Broad partnerships, adequate policies and innovative drug development models can help to overcome barriers to financial investment and reduce strategic risks in Alzheimer's disease and other dementias through, for example:

- *Purchaser agreements*: Agreements between purchasers (insurers, patients) and providers (innovators, manufacturers) in the form of risk-sharing schemes are one way to control potential financial losses resulting from failure in research and development and can support investment in uncertain, high-risk disease areas. Performance-based risk-sharing arrangements (risk-sharing schemes) involve a plan by which the performance of the medicine is tracked in a defined patient population over a specified period of time and the amount or level of reimbursement is based on the health and cost outcome achieved.
- *Patent extensions*: The patent system aims to offer the inventor a monopoly to recover research and development costs with a premium as reward. However, long drug development timelines can diminish the potential return-on-investment after entering a market, as a firm may have only a limited number of years remaining on a patent when the drug is approved. There are options to adapt the current patent system to the changing environment of therapeutic development. It has been suggested to allow for an extension of patent monopolies, depending of the need for the respective treatment, investments made, and resource needs. Alternatively, the patent clock could start only after a drug has gone through Phase I clinical trials.
- *Enabling early failure*: This involves the conduct of small clinical trials in well-defined patient population early during development. Such trials may provide significant insights into the properties of the potential drug, its behaviour in humans, and its side effects at an early stage. Results either lead to early failure (which reduces costs) and can significantly increase the likelihood of success of a larger trial in a larger indication when successful.
- *Policy changes*: Governments can take the lead in driving the development and implementation of adequate policies which foster shared responsibilities and enable sufficient benefits for investors. A strong involvement of patient organisations, insurers and pharmaceutical companies (investors) should ensure a joint discussion of shared benefits and risks, and payers' perspectives regarding possible higher downstream expenses. Ultimately, policy adjustments will affect existing regulatory frameworks and could require the public and private research community to further embrace a system of open innovation.

Risk-sharing schemes and other incentives, which may attract the pharmaceutical industry back into the market, reflect a paradigm shift from the traditional, linear business model towards value-based agreements between stakeholders for the development and population-wide use of innovative medicines (Adamski, 2010). In order to measure the effectiveness and applicability of the various approaches, an in-depth understanding of the issues, opportunities and trade-offs of each is required. Pilot risk-sharing projects and surveys may provide the evidence needed to create generic implementation models and policies (Espín, 2011; Garrison, 2013).

Governments, in partnership with other stakeholders, can help to explore new funding vehicles and risk-sharing mechanisms to support resource-intensive research in neurodegenerative diseases and to mitigate financial risks. At the G8 Dementia Summit in London[10] participants agreed on a new international approach to encourage research and co-operation on Alzheimer's disease and other dementias. The G8 Dementia Summit Declaration sets the goal to support the identification of a disease-modifying therapy for dementia by 2025 and to increase collectively and significantly the amount of funding through a pooling of international expertise and the attraction of new sources of finance, including exploring the possibility of developing a private and philanthropic fund to support global dementia innovation. In fact, a global Alzheimer's research fund could provide the necessary resources and planning security to translate innovation into the clinical setting.

Economic growth and public health are dependent on technological and scientific discoveries, which are provided through the interplay of innovation, development, manufacturing and commercialisation. Here scientific contributions of public research institutions and the pharmaceutical industry are crucial. Available studies show that government funding of basic research is relatively more important in the development of innovative, priority-review drugs, than for standard-review drugs (Sampat, 2011; Stevens, 2011). Given the long-term nature and inherent uncertainties of basic science the pharmaceutical industry still depends on federally-funded research to create a strong foundation for drug development. However, the roles of the public and private sectors in research funding are less clearly defined than they were before the biotechnology area and governments and their agencies now have a much more direct role in applied medical scientific research (Stevens et al., 2011). Recent studies have looked into the relevance and impact of public and private research investment (Families USA, 2008; Malinowski, 2012; Zycher, 2010) and concluded that in general terms both public and private stakeholders play a significant, complementary role in the delivery of innovative therapies.

The ultimate outcomes and benefits of government funded research are generally considered a public good and contribute to business profits, the stimulation of further investment, economic growth, a healthier population, and longer and healthier lives. These rewards materialize from innovations which are largely generated through fundamental research projects at universities and other public research institutions. The UK Health Economics Research Group (HERG, 2008) concluded that: 1) in addition to health gains, the United Kingdom publicly and charitably funded medical research generates additional national economic gains, including higher incomes for residents; 2) public medical research leads to additional private research and development spending which contributes to increases in gross domestic product (GDP); 3) there are indications that the total social rate of return to public and charitable medical research is in the range 20 to 67%, with a core estimate of 30%.

Pre-competitive, open-source, open-access, and crowdsourcing efforts have been tested to contribute to a more efficient use of resources, better information sharing, and de-risking of health innovation (Moors et al., 2014; Schuhmacher et al., 2013). One of the major challenges of open-source models is how to ensure the rewards and recognition for innovative ideas, investment costs and failure. Intellectual property rights represent the foundation of economic growth within the pharmaceutical industry and concerns have been raised about the future status of intellectual property rights (Munos, 2010; Saha and Bhattacharya, 2011). Sharing intellectual property rights in the competitive space of pharmaceutical development could run the risk of dis-incentivising private partners and, thus, reduce their interest in collaboration (FitzGerald, 2010; Judd, 2013; Taubman, 2010).

Optimisation of patient access, respect for stakeholder needs, and ensuring an adequate return of investment along the life cycle of a future disease-modifying therapy for Alzheimer's disease requires a broad stakeholder discussion early during development. Coverage and payment decisions are based primarily on available medical evidence and the relative costs of existing therapies. To date and in the case of Alzheimer's disease there is a paucity of discussion about the future use and pricing of a potential disease-modifying therapy. Special attention should be paid to the implementation of payer considerations, affordability, and access into regulatory decision making. In anticipation of a disease-modifying and possibly expensive treatment for Alzheimer's disease becoming available and in order to adequately plan for access and rational use, governments, pharmaceutical industry, payers, patient organisations, and regulators should discuss access arrangements, pricing and reimbursement structures. In some situations, additional studies designed to demonstrate value and comparative effectiveness might be needed. Such studies could examine outcomes of representative populations in community settings. There is growing awareness that to assure scientific advances in diagnosis and treatment benefit in patients, developing evidence to support reimbursement will become as important as obtaining regulatory approval. In this regard, much can be learnt from the multitude of existing data and experiences in related medical fields that can offer evidence-based policy support and help accelerate clinical trials in Alzheimer's disease.

In summary, approaches to improve and facilitate the decision-making process for market approval of innovative therapies appear to be spreading rapidly. They mark a paradigm shift towards more value-based agreements and offering potential benefits to all main stakeholders: purchasers and providers, manufacturers and patients. For the manufacturer, an agreement may open up market access for a product that may otherwise have been denied coverage on the grounds of uncertainty about its relative cost-effectiveness. For purchasers, there is the opportunity to reduce costs and to increase the number of potential useful treatments reaching patients. Finally, for patients, the benefit is in faster access to potentially life-saving products. The sustainability of these schemes – as well as the many related methodological, economic, and infrastructure issues – needs to be further explored through international exchange on good practices.

Measuring and evaluating health innovation

The concept of value has moved to the forefront of health care decision making. Measurements of economic impacts, health benefits and returns on investment in research are important components in evidence based decision making by governments. The direct link between research investment and quantified output has been questioned by some economists (Macilwain, 2010) and society often does not benefit from the immediate impact of governmentally supported projects alone – spillovers feed into research performed by public institutes and private firms and can stimulate additional investments, leading to innovation (RAND, 2010; Stribley et al., 2012). Not at least because of the substantial funding of basic research by governments, and the use of results as public goods and for commercial purposes, public and private stakeholders are exploring possible measures to quantify and maximise the return of investment (Sampat, 2011; Schacht, 2011).

However, a conclusive assessment of the relevance, extent and efficiency of funding/investment in dementia research and drug development is currently limited by the lack of actual and disease-area specific data. Often, the collection and analysis of research expenditure does not differentiate sufficiently between the types of research (for example: basic research, applied research, experimental development, clinical research) and sectors

(for example: technical science, physics, diagnostics, biomedical science, infectious diseases, chronic non-communicable diseases, public-health and health care). There is a need for a global, co-ordinated approach across countries to collect data about public (and private) investment into biomedical research and health innovation for dementia, and Alzheimer's disease in particular, to support evidence-based decision making (Box 3.2).

There is also a need for indicative baseline figures about public and private investment into Alzheimer's and dementia research and drug development. In addition, performance indicators may be required to evaluate the efficiency of research and health innovation processes and investment systems, and to assess the quality of results delivered. In Alzheimer's disease, evidence-based decision making requires a broad knowledge base consisting of reliable, valid and clinically meaningful medical, scientific and economic data. Shrinking market returns of innovative medicines and financially constrained health systems put additional pressure on stakeholders and have led governments, agencies and the pharmaceutical industry to search for more efficient approaches to the delivery of innovative therapies. Monitoring and evaluation processes should form an integral part of research and health innovation for the delivery of quality results. Three themes address both the performance of research and health innovation, and the quality and value of results:

- *Efficiency of research and health innovation*: The efficiency of discovery research and drug development processes affects the delivery of results and the downstream impacts on patients and public health systems. Parameters for measuring process efficiency include input measures, process efficiency indicators and measureable outputs, for example: expenditure on education, infrastructure, research and product development – including opportunity costs; number and quality of identified targets, lead compounds entering clinical development, the attrition rate of the different phases of clinical research, the times from compound selection in discovery research to regulatory approval, and the time-lag between filing a patent and commercialisation; number of NME applications filed and approved, the number of revenue-generating medicines; the number of scientific publications and citations, the number of patents issued, the revenues generated from patents, the revenues generated from the sale of medicines as a percentage of investment, and the indirect benefits of the use of medicines from a reduction in days lost through sickness.
- *Therapeutic efficacy and effectiveness*: Medicines safety, efficacy and rational use[11] parameters are being assessed throughout the whole product life cycle. There is a tendency to initiate the evaluation of the cost-effectiveness of a potential new drug early during development. The term "therapeutic efficacy" refers to evidence derived from pre-clinical and clinical safety and efficacy information. The evaluation of "therapeutic effectiveness" considers the selection of the product (based on its clinical efficacy and safety) and its actual use in the health system. This encompasses selecting the appropriate medicine and determining how it should be used for maximum benefit.
- *Therapeutic cost-effectiveness*: Effective therapies can generate direct and indirect cost savings through, for example, shortening of treatment times, lowering of care costs and avoidance of productivity loss. In an environment of economic uncertainty, the analysis of cost-effectiveness[12] offers an important tool for decision making about therapeutic interventions. Given the potential increase in overall health expenditure (for example from costs associated with technologically complex therapies), treatment costs should be considered upstream of product development and not only during the review of the application for marketing approval. According to Hill (2012), the two key questions, which should be answered are: i) how much does the new intervention cost compared

with current practice? and ii) is it more effective? (and if so, how much more?). In measuring these, the following are important to consider: the parameters and methods used in cost-effectiveness studies, possible approaches to integrating economic evidence into regulatory decision making, and ways of differentiating between the value of a new medicine for populations and for individual patients.

Box 3.2. Measuring government funding of R&D on dementia

A better understanding of how public research budgets are allocated can help inform whether efforts directed towards dementia are commensurate to the gravity of the health, social and economic challenges posed by this disease, supporting future research policy decisions. As part of its role in collecting and publishing data on research and innovation and defining global measurement standards, the OECD has recently been asked to contribute to raising awareness of the global level of resources dedicated to fighting dementia and related neurodegenerative diseases by assisting G7 countries as part of their Health Ministers' December 2013 Dementia Summit Declaration commitment to "report on expenditure on publicly funded national dementia research". The OECD has been compiling for decades estimates of government R&D budgets dedicated to "*protecting and improving human health*", one of the socioeconomic objectives attributed to R&D budgets, alongside others such as energy and the environment, defence or the general advancement of knowledge. These health R&D budget estimates are a timely but only first approximation to stated research policy priorities, and depend on how the government presents its priorities. As a result, they reflect differences in national mechanisms of R&D resource allocation and are therefore not such a good indicator of the ultimate content and health relevance of the R&D that is being funded.

This measurement challenge is particularly important for comparing internationally the level of funds that governments devote to R&D on specific health areas or diseases such as dementia. In contrast with data on disease incidence and burden, relatively little is known about the size of efforts to identify solutions through R&D or other types of investments. These data are not systematically collected for statistical purposes by OECD countries, owing to a lack of underlying data sources and the absence of a tested methodology for allocating R&D resources to diseases. Different conditions and diseases can be highly intertwined in terms of their aetiology, symptoms, and treatment. Advances in the understanding of a given disease can be driven not only by targeted research but also by research in neighbouring areas or more general subjects. Separating between dementia R&D and R&D on other diseases can thus be arbitrary and potentially misleading, especially in areas that require major advances in fundamental understanding of some of the underlying neurological processes.

The recent G7 compilation of data on public funding of R&D on dementia has drawn on a number of national efforts to report information at the level of specific health research areas, conditions and diseases. The initial aim was to take stock of available estimates within each country, in order to better understand their coverage and main gaps. In light of the several challenges, it was not the intention that this initial pilot would be able to gather comprehensive and internationally comparable data on dementia R&D. A simple questionnaire, supported by a short background note, was designed to assist G7 countries in describing the boundary between support for dementia, other related neurodegenerative diseases (NDDs), and other related research; the extent of under-coverage of research funds ultimately used for health research in this area; the landscape of agency support; the type of dementia research funded, from research on the disease's foundations, through to clinical and health care R&D; and recent and expected funding trends. As of 23 January, all G7 countries bar Italy had responded to the OECD, though all returns were only partially completed returns and some relevant auxiliary information was missing. The interim results are summed up in the table below, with the highly experimental estimates of dementia and NDD R&D funding alongside available estimates of health R&D and overall R&D budgets.

The data returns indicate that the United States dedicate nearly four times as much as the combined rest of G7 countries to NDD R&D, just slightly below the 3.4 times for estimated health R&D funding, and 1.25 times for general R&D budgets. These differences may be partly due to the inherent biases in collecting health R&D data, in particular the need to rely on data at the programme and project level, as shown by this collection.

Box 3.2. Measuring government funding of R&D on dementia *(cont.)*

Public funding of research and development on neurodegenerative diseases (NDD) in G7 countries

Million USD in purchasing power parity (PPP) terms

	Reference year	Funding for dementia R&D	Funding for NDD R&D	Health R&D budget (GBAORD)	R&D budget (GBAORD total)
Canada	2012/13	31	38	1,356	7,743
France	2012	55	170	1,338	17,997
Germany	2012	n/a	115	1,634	30,956
Japan	2012	21	40	1,657	35,273
United Kingdom	2011	49	75	2,736	12,982
United States	2012	625	1,671	33,924	143,737
Italy*	2011	n/a	6	1,209	11,708
G7 area		781	2,115	43,854	260,396

Source: OECD (2015), "Government Funding of R&D on Dementia: Key Findings of Data Collection for the G7 Countries", *OECD Science, Technology and Industry Working Papers*, forthcoming. These are experimental, source-driven indicators, based on non-fully comprehensive NDD and dementia R&D funding data submitted by Canada, Germany, France, United Kingdom, Japan and United States. (*) Data for Italy collected from JPND report, and OECD GBAORD data, Research and Development Statistics Database (www.oecd.org/sti/rds).

For the combined G7 group of countries, the equivalent of 0.8% of public R&D budgets is reported as being dedicated to research on NDD. In the United States, this figure is as large as almost 1.2%. An important feature of the data collected so far is the relatively high weight of public funding for NDD R&D that is dedicated to understanding the foundations of disease, relative to the categories of clinical or health care related research. This may well be adequately reflect the current gaps in scientific knowledge about the disease, but the low share of health care R&D raises a question on whether enough research is being undertaken with the view to improving the living conditions of NDD patients. The data collected so far appear to indicate a stable to increasing trend in funding levels for NDD research among the countries submitting data, in particular in reference to other areas. However, it cannot be excluded that this may be partly due to some degree of reclassification of existing funding lines.

These highly experimental results need to be taken with great caution. These are after all only indicative figures that will likely be significantly revised as they become more thoroughly inspected and some gaps can be better addressed. Based on this data gathering experience and other previous related initiatives (e.g. JPND), the most promising approaches for collecting future data on dementia R&D work appear to point to the use of searchable and open project-based information which can be analysed semantically in order to identify the relevance of the project to any given disease. Examples can be found in the NIH's use of the Research, Condition, and Disease Categorization (RCDC) in its reporting system. The NIH also maintains a dedicated classification system for Alzheimer's (CADRO) and uses it to develop an International Alzheimer's Disease Research Portfolio (IADRP). Other databases available for individual or multiple institutions in other countries can be used for similar purposes, such as KAKEN in Japan. Most countries are characterised by having agencies with very different reporting systems and not entirely consistent with each other (the Gateway to Research in the United Kingdom is a recent exception).

This situation hampers efforts to report across agencies on a detailed level, rendering these systems as far from being suitable tools for international comparisons or tracking developments over time within a given country. This challenge does not apply solely to G7 countries. Improving the coverage of this type of mapping exercises would likely require access to databases on researcher profiles, and may require the use of ancillary information such as data on scientific publications (e.g. Vanderelest and Speybroeck, 2013) or ad hoc surveys to infer whether their research work is relevant to the study of dementia. Further progress requires significant within-and between-country institutional co-ordination on the collection and management of research funding records and applying consistent classification criteria and ontologies that support a wide range of uses. Notwithstanding the potential initial burdens of ensuring system convergence, this would be of benefit not only to those with an interest in dementia or health R&D, but also to the wider research policy community across a wide range of policy objectives. The openness of large public databases on support for R&D can also be a major source of improved governance of S&T systems, supporting an improved public understanding of how tax money is being used to address social challenges.

Box 3.2. Measuring government funding of R&D on dementia *(cont.)*

In order work towards realising the ambition of the G7 ministerial declaration, it is important that those in charge of collecting and reporting data on R&D at the national level can discuss with their peers in other countries how best to advance the measurement of how R&D budgets are targeted to specific social challenges. The OECD provides, through its Working Party of National Experts on Science and Technology Indicators (NESTI), such a forum for discussion and decision on relevant statistical standards. NESTI could also work in the near future in partnership with its parent policy committee to assist countries who wish to move towards improved and more open administrative systems to keep track of their R&D funding. The OECD can also potentially build on a number of ongoing initiatives, such as its work on bibliometric indicators and the activities of researchers, to develop new evidence on research on dementia.

Source: OECD (2015), "Government Funding of R&D on Dementia: Key Findings of Data Collection for the G7 Countries", *OECD Science, Technology and Industry Working Papers*, forthcoming.

Health innovation increasingly draws on new, investment-intensive tools and processes offered by biotechnological innovations. Recent approval data from the FDA indicates a move to high quality therapeutics that are based on cell technologies, gene editing, synthetic biology, biochips, bioprinting, and tissue engineering. These have the potential to accelerate the development of treatments for entire therapeutic areas and may help to close the gap between biomedical research and unmet medical needs in rare and complex diseases. The maturing of biologics research and production, for example, monoclonal antibodies, vaccines, hormones, gene, and cell therapies clearly opens innovative therapeutic strategies in Alzheimer's and other dementias. The example of biologics' success in the CNS market is highlighted by the success of recent therapies that target multiple sclerosis (MS) and, generally, the smaller number of side effects and higher success rates of clinical trials (DiMasi et al., 2010; Hay et al., 2014). This success has encouraged researchers to increase their engagement in this area and seek future opportunities for biologics in other CNS diseases. Recent data show that 25% (USD 81 billion) of the US spending on brand-name drugs in 2012 was accounted for by biologics (Hoffman and Furcht 2014). However, while a wave of biologics innovation is helping restore the industry fortunes in complex diseases like Alzheimer's, it may also bring some measure of rationality to therapeutic pricing and cost-effectiveness (*The Economist*, 2014). The higher price of biologics-based therapies is mainly due to the more complex production and delivery (formulate, store and apply) systems compared to conventional small-molecule drugs.

Conclusions

A number of conclusions emerge from OECD work, demonstrating the complex and multifaceted nature of the challenge in biomedical research and health innovation for Alzheimer's disease and other dementias. However, discussions at the OECD's Lausanne workshop have shown that progress on these issues is being made, thanks to a willingness of stakeholders to join forces and work together towards a future cure. The main areas for policy action are:

- *Increase patient and public engagement*: To utilise the full potential of both innovative therapeutic research and patient engagement in clinical trials, policy makers, regulators and the research commun
- ity need to balance between traditional, low-risk approaches and new drug development strategies that involve some uncertainties. Policies and draft guidance which reflect the

opinions and needs of patients and the public (especially caregivers and payers) would help regulators bridge the gap between the development push from pharmaceutical research and the demand-pull by patients. Government policies can help to deepen the involvement of patients and the wider public through a strengthening of public trust, transparency, and oversight in broad diagnostic campaigns, global patient registries, and clinical trial platforms.

- *Foster collaborative research*: Public-private partnerships are innovation vehicles that can deliver results more effectively than one individual partner or traditional model could achieve on their own. Policies need to allow for collaboration between stakeholders at the interface between the pre-competitive space (common ground) and late stage clinical development (after proof-of-concept in Phase 2). Governments play a key role at the interface between public and private research partners; they can help implement mechanisms to respect the potential, needs, and constrains of all stakeholders. However, given their heterogeneity, diverging and competing interests, collaborative partnerships in Alzheimer's disease require new forms of co-ordination. Ultimately, more inclusiveness, higher productivity and longer sustainability of public-private partnerships in Alzheimer's diseases and other dementias can be achieved through: 1) sharing of benefits and rewards; 2) development of incentives for active participation; 3) innovative funding structures for all stakeholders; 4) de-risking of translational research and clinical development.
- *Drive the paradigm shift*: Significant progress has been achieved in the diagnosis of Alzheimer's disease and other dementias, both on a genetic/molecular and biochemical basis. This has led to the paradigm shift of research focused on people with established dementia to people with pre-clinical and mild-stage disease. However, in these settings, the traditionally accepted regulatory frameworks may not be appropriate. Fostering research in this area and accelerating the discovery of medicines that can slow or stop disease, will require collaboration and openness to novel approaches involving industry, academia, regulatory agencies, payers and patient organisations.
- *Strengthen risk reduction and symptomatic treatment:* The development of disease-modifying therapies and diagnostic tools are the main goals of Alzheimer's disease clinical research. However, treatments with a sustained symptomatic effect can have a significant impact on people living with neurodegenerative diseases and should be developed in parallel. There is a need for better understanding the impact of lifestyle, food and nutrition on healthy ageing and the development of Alzheimer's and other neurodegenerative diseases. Public funding can help shape research priorities and should lead to a comprehensive, cross-disciplinary research agenda.
- *Adapt regulatory processes:* A more convergent and synchronised regulatory environment would help increase the efficiency of translational and clinical research programmes. There are opportunities to accelerate and streamline the operational conduct of multinational clinical trials through more harmonised national regulations. Treatment options should be evaluated at earlier stages of Alzheimer's disease in an attempt to change the course of the disease. Patients in an early stage of the disease and even pre-symptomatic need to be included in clinical development programmes. This paradigm shift has implications for clinical trials designs, patient selection, the choice of outcome measures and biomarkers, which will need to be considered in a revision of the current Alzheimer's disease guidance. Providing more resources to regulatory agencies for scientifically sound decision making would help speed-up the process without putting patients' health at risk. Governments must help incorporate the learnings from currently

ongoing research programmes into regulatory science and approval processes in order to change the regulatory paradigm based on the best available science.

- *Foster translational research and clinical trial conduct*: The translation of pre-clinical evidence into human trials remains a step that slows down drug development. Researchers and regulators aim to balance the incomplete pre-clinical knowledge base with the urgent need for more, high quality data from human testing. The likelihood of successfully developing new, more effective treatments increases with the research community's fundamental understanding of Alzheimer's pathologies. Clinical trials can contribute much to the creation of this knowledge, and many key insights can come only from clinical trials of potentially disease-modifying therapies. Policies and regulatory frameworks need to enable an earlier entry into trials to foster the collection of valuable pharmacokinetic and pharmacodynamic information from patients. Such adaptive clinical trials would enable early failure, limit financial loss and have a greater chance of success.
- *Promote open science and smart data:* There is an enormous potential of open science for the generation and sharing of smart data to accelerate Alzheimer's research and health innovation. Combining efforts of building a Global Clinical Trials Platform with a distributed and interoperable network of big data related to Alzheimer's disease (see Chapter 4) would offer the required international outreach and leverage synergies from a joint use of infrastructure, better aligned national regulatory and policy frameworks, and the implementation of incentives for all stakeholders. New funding mechanisms and incentive structures should be developed along the data life cycle, supporting data creation, management, analysis, storage, access and long-term use. Importantly, while policy should encourage a greater dissemination of knowledge, policies and processes in research and health innovation, it must safeguard the rights, aims, and interests of all stakeholders. Future work on open science and smart data in Alzheimer's research should be built around 1) information governance (the creation of the right frameworks for use and exchange of information, e.g. Bermuda principles for Alzheimer's disease and other dementias); 2) data management (e.g. global dementia research inventories); 3) patient and public engagement (e.g. enrichment of data by patient-centred outcome information).
- *Fund and de-risk:* Drug development for Alzheimer's disease remains a high-risk endeavour. Because of the limited (financial) resources being devoted to research, there is a growing need for governments, funders and the pharmaceutical industry to co-ordinate research investments in a systematic way. Governments, in close collaboration with other stakeholders, should help explore new funding vehicles and "risk-sharing" mechanisms to support resource-intensive research in neurodegenerative diseases and to mitigate financial risks. Increased investment and shared funding structures in translational and early clinical research could help to de-risk processes and attract researchers into an area which has been traditionally characterised by high attrition rates and financial loss. A global Alzheimer's research fund could provide the necessary resources and planning security to translate innovation into the clinical setting. Greater efforts are needed to drive the national and global collection and analysis of indicative baseline figures about public and private funding of Alzheimer's and dementia research and health innovation.
- *Improve the monitoring of public resources devoted to research on dementia*: In the context of broader government support for health and other social challenges, initial indicative findings from a pilot collection of data for G7 countries – carried out in the framework of the G7 declaration commitment to report on research and development funding – indicate that there is limited and highly disperse coverage of public agencies' support for research and development on dementia and other neurodegenerative

diseases (NDD). Available estimates indicate that funding for dementia and other NDDs accounts for less than 1% of research and development budgets in the G7, with most support dedicated to understanding the foundations of the disease and very little to health care. Increased record openness, co-ordination, shared standards for reporting public project funding and researcher activity can help inform public research funding decisions.

- *Respect medicines access and the payers' perspective:* Optimisation of patient access and respect for stakeholder needs (e.g. return of investment) along the life cycle of a future disease-modifying therapy for Alzheimer's disease requires a broad, cross-stakeholder discussion. Coverage and payment decisions are based primarily on available medical evidence and relative costs of existing therapies. Special attention should be paid to the implementation of payer considerations, affordability, and access into regulatory decision making. Policies need to consider the ethical, epidemiological, and economic opportunities and constraints of a possible future disease-modifying treatment for Alzheimer's disease.

Notes

1. This chapter was authored by Hermann Garden and Fernando Galindo-Rueda from the OECD Directorate for Science, Technology and Innovation.
2. www.oecd.org/sti/biotech/alzheimers-dementia-research-workshop.htm.
3. IFPMA, "The Pharmaceutical Industry and Global Health, Facts and Figures 2012", www.ifpma.org.
4. www.fda.gov.
5. Metabolomics is the systematic study of small-molecule and chemical process profiles in humans, tissues, organisms and other biological systems.
6. www.hc-sc.gc.ca/ahc-asc/minist/messages/_2014/2014_01_14-eng.php.
7. www.news.gc.ca/web/article-en.do?nid=883069.
8. www.pm.gov.au/media/2013-10-23/federal-government-delivers-funding-new-medical-research-discoveries.
9. www.nhmrc.gov.au/media/releases/2014/18-million-new-funds-support-innovative-dementia-research.
10. www.dementiachallenge.dh.gov.uk/category/g8-dementia-summit/.
11. World Health Organization, definition of rational use of medicines: "Patients receive medications appropriate to their clinical needs, in dose that meet their own individual requirements, for an adequate period of time and at the lowest cost to them and their community", www.who.int.
12. Costs of the treatment options in relation to health benefits.

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Chapter 4

The role of big data in driving global co-operation and innovation in dementia research[1]

The need to harness the large quantities of broad and deep data generated across laboratories worldwide, promote global collaboration and data sharing to accelerate research and development and the testing of new therapies and care models for Alzheimer's and other dementias is today undisputed. The complexity of the dementia challenge and its heterogeneity requires moving beyond the traditional hypothesis-predicated scientific approach to the simultaneous assessment of a multitude of factors within big data to discover the unexpected. Capitalising on big data will require, however, a strong effort at several levels. Big data for dementia is not just important for its size, but also for its scope that will go beyond the borders of the health system, requiring data sharing and collaboration among governments, researchers and industry, i.e. linking different communities together. Current research models are however, not well set up for this complexity. While big data networks are proliferating, and the volume and velocity of personal health and other data are rising, barriers still remain with respect to data sharing efforts. Some barriers are of a technical nature, as for issues related to interoperability and standards, storage, the technical infrastructure to allow data sharing. The most significant challenges are, however cultural, legal and ethical and are related to the lack of an open data culture or the disincentives that researchers and scientists face with respect to the disclosure of data. Public policy has a crucial role to play ensuring that framework conditions to promote data sharing are sound and supportive and in setting the conditions for trust and partnerships.

Introduction

Much evidence today suggests that dementia can arise from a number of neurodegenerative disorders that are characterised by a progressive decline in cognitive function. The most common diseases include Alzheimer's disease (AD), vascular cognitive impairment, frontotemporal dementia (FTD), dementia with Lewy bodies (DLB) and Huntington's disease, while some people with Parkinson's disease may also develop dementia. All such disorders share two important features in that they have long periods before the emergence of clinically defined symptoms, with varying disease progression trajectories, and their causation is driven by both genetic and environmental factors (Murray et al., 2011; Lam et al., 2013).

Research addressing the causes and progression of dementia is, therefore, increasingly directed towards understanding the result of numerous interactions between age and gender, genetics and epigenetics, environment and lifestyle across the various stages of the disease. Such studies also need to be informed by comparisons across neurodegenerative diseases and with the ageing process in non-affected individuals as there is growing consensus among researchers that the neurobiological underpinnings of dementia may start many years before the appearance of any clinical signs (Kozauer et al., 2013). Individual risk factors may precipitate the development of dementia and affect the trajectory of the disease. In addition, specific changes in gene expression, which can accumulate with age in some individuals, as well as the interplay with other comorbidities, may lead to an enhanced susceptibility to the disease.

Because of the clinical and biological complexity of dementia an emerging consensus is that the crucial studies needed to underpin drug discovery, validate alternative models of risk reduction and care and develop new therapeutic strategies aimed at slowing disease progression will require massive and diverse data collection, storage and processing and new investments in research and infrastructure. Advocates of this "data-driven" research paradigm argue that harnessing the large quantities of data generated across laboratories worldwide (behavioural, genetic, environmental, epigenetic, clinical, administrative, etc.) has numerous methodological, ethical and economic advantages "as no one nation has all the assets to pursue this type of research independently" (OECD, 2014a).

Calls for open science to make the growing consortia, databases, and analytic tools publicly and freely accessible have recently garnered increasing strength and visibility following the 2013 G8 Science Ministers statement[2] for publicly funded scientific research data to be open.

This chapter draws on key conclusions from two recent OECD meetings. The first, on "Unlocking Global Collaboration to Accelerate Innovation for Alzheimer's Disease and Dementia" (OECD, 2014a), was held in Oxford in 2013 jointly with the Global Coalition on Ageing. This meeting brought together experts from OECD member countries to scope and obtain perspectives on the challenges and opportunities of big data to accelerate innovation on AD and the variety of governance issues and policies that are facilitating or inhibiting collaboration across OECD countries. The second, on "Dementia research and care: can big data help?", held in Toronto in 2014 in collaboration with the Ontario Brain Institute (OBI) and the Institute for Health Policy, Management and Evaluation (IHPME) of the University of Toronto, further discussed the policy areas that require attention in promoting linkage of the massive amounts of

population-based health and health care data that are routinely collected (broad data) with detailed clinical and biological data (deep data) to create an international resource for dementia research.. The proceedings of this second event are published separately (OECD, 2015b).

During the past 12 months, the Oxford Internet Institute (United Kingdom) and the OECD have also been investigating best practices in four data sharing initiatives related to dementia research: the Alzheimer's Disease Neuroimaging Initiative (ADNI), the IMI AddNeuroMed programme, UK Biobank and the Swedish Brain Power studies (Deetjen et al., 2015). Highlights of this study are summarised in this chapter.

The next sections review the evidence in favour of data sharing and the barriers that will need to be overcome to enable data-driven dementia research to become more prevalent. It examines the key drivers towards early data access and greater use of large-scale (big) data to generate knowledge and yield new intelligence for dementia research, health care and policy making.

The chapter concludes with a discussion of success factors and the actions needed to progress towards data-driven dementia research to accelerate innovation and improve care. It highlights specific opportunities for stepping up international co-operation on dementia research in response to the direct mandate from the G8 Dementia Summit Declaration to the OECD to "take stock of our current national incentive structure for research […] and consider what changes could be made to promote and accelerate discovery and research and its transformation into innovative and efficient care and services".[3]

Towards high-power data-driven research and large-scale data sharing

Radical improvements in information technologies and the increasing gathering and sharing of electronic health data make it imperative to take stock of global capacity to undertake multidisciplinary research

The complexity and multifactorial nature of dementia demands increasingly large study numbers in order to find small-sized effects with a sufficient degree of certainty. While a few large studies such as the UK Biobank with 500 000 individuals already come with much broader data than smaller scale projects such as AddNeuroMed or ADNI, much greater effort is needed if data are to be combined beyond labs, consortia, and even national boundaries in order to realise the potential of being able to scale-up scientific research to find the really difficult to detect signals in the data.

Data sharing also allows the verification or scientific results and the re-analysis of data for different purposes from the ones originally conceived. This not only enhances the utilisation of data, but promotes competition of ideas and research (Gardner et al., 2003) and fosters collaboration (Piwowar and Chapman, 2008). Data sharing also reduces the duplication of efforts from different researchers attempting to collect the same datasets (Kowalczyk and Shankar, 2010).

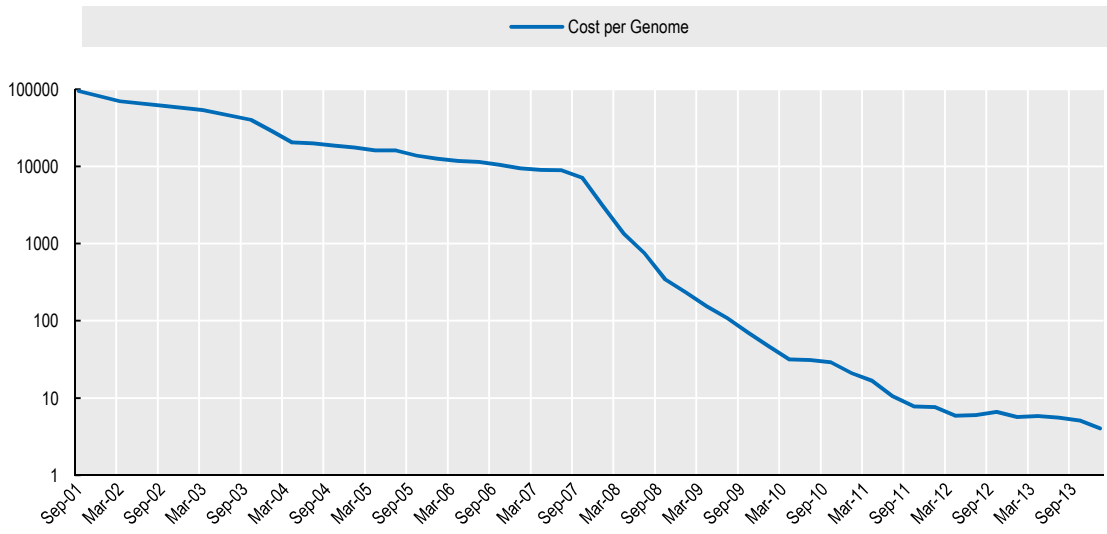
Large scale data gathering and sharing is now possible because health and biological data are increasingly collected in digital form. Health care professionals, biomedical researchers, and patients are producing on a daily basis huge amounts of data of great value to health care and research from an array of sources such as electronic health records (EHRs), genomic sequencing, metabolomics, high-resolution

medical imaging, ubiquitous sensing devices, and smart phone applications that monitor patient health. It is predicted that more medical information and health and wellness data will be generated in the next few years than ever before (OECD, 2013).

The remarkable expansion of digital health data is largely driven by the confluence of important technological developments, notably the increasing ubiquity of broadband access and the proliferation of electronic health records, smart mobile devices and smart ICT applications such as sensor networks and machine-to-machine (M2M) communication. The large decrease in sequencing cost per genome – from USD 100 million in 2001 to less than USD 6 000 in 2013 – has also been a significant driver. The sequencing cost per genome has dropped at higher rates than Moore's Law – which holds that processing power doubles about every 18 months, relative to cost or size of central processing units (CPUs) (Moore, 1965) – would predict (Figure 4.1). Improvements in data analytics have also played a significant role, as has the provision of super computing resources in a flexible, elastic, on-demand format through cloud computing.

Figure 4.1. Cost of genome sequencing, September 2001 to January 2014

Thousand dollars, logarithmic scale



Source: OECD (2014), *Measuring the Digital Economy: A New Perspective*, based on NHGRI Genome Sequencing Program (GSP), www.genome.gov/sequencingcosts/.

The many new sources of digital data can create a tremendous resource to accelerate innovation for research in neurodegenerative disease. Their potential uses extend today from genomic research to clinical care and environmental studies to derive better insights into these diseases. Comparative-effectiveness researchers are combing large administrative claims databases and clinical databases for proof of the best, most cost-effective treatments, information that could transform health care policy (Schneeweiss, 2005). Researchers now have access to human genetic data and genomic databases they can combine to study treatment outcomes.

There is growing evidence of the potential of how these multiple streams and large volumes of health data can be leveraged to transform research and care in dementia.

This vision rests on four basic categories of data that bring value to citizens, care providers and the system itself to facilitate health research, improve patient care, for health system management, for risk reduction and public health research (Canadian Institute for Health information, 2013):

- *Primary research and technical regulatory data to facilitate research:* This involves basic research data; i.e. biomedical, cognitive, behavioural and epidemiological data, biomarkers and clinical trial data, drug safety surveillance, and other data generated to support product and service development and market authorisation). Such research spans multiple fields. For example, multiple sources of data can be integrated to find early (bio)markers of disease (i.e., measurable indicators of disease status and therapeutic effect), the cost-effectiveness of different interventions can be evaluated, and historical data can be used to simulate and model trends in long-term care needs and evaluate different policy options to meet those needs.

- *Personal health care/clinical data to improve patient care:* This involves basic medical and clinical patient records and the ancillary data linked to them, such as family history, laboratory, pathology, prescription history, pharmacy, interview, and therapy data. Secondary use of personal health data can for example improve quality of care initiatives and the effectiveness of patient care in both clinical and home care settings.

- *Health care administrative data for health system management:* This refers to eligibility, admissions and discharge data; routine operational data; and insurance and financial transactional data. These health data can be used to manage and improve the effectiveness and efficiency of the health system by informing programme, policy and funding decisions. For example, costs can be reduced by identifying ineffective interventions, missed opportunities and duplication of services.

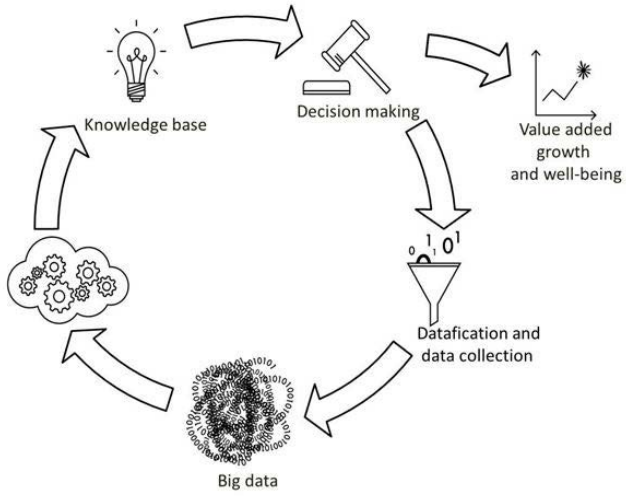
- *Population-based public health data for population and public health:* This includes birth, death and other demographic records; screening and disease-monitoring data; lifestyle, diet and nutrition, psycho-social, and environmental exposure data; health-services data and registries. These data can be used to understand the burden of illness and quality of life of dementia populations, and to manage and evaluate public health interventions including for health promotion and risk reduction.

Additionally, big data from outside the health system (such as loyalty card data, mobile phone data or banking data) may provide insights relevant to dementia, even though these data remains largely untouched in dementia research to date. Harnessing these data may be useful both for identifying early signs of dementia, but also for looking back into the lives of those individuals who have been diagnosed. As with all types of routine data, these data have already been collected as a by-product in various areas of daily life. These data categories reflect key phases of the data value cycle in health systems which, as in other sectors of the economy, is not a linear process but involves feed-back loops at several phases of the value creation and data-driven innovation (DDI) process (OECD, 2015a; Box 4.1).

Box 4.1. The big data value cycle: From datafication to data analytics and decision making

Data-driven innovation is best described through a process that takes into account the different phases through which data are transformed to finally lead to innovation. The figure below illustrates a stylised data value cycle, which is based on the recognition that data-driven innovation is not a linear process, and thus cannot be sufficiently represented through a simple value chain. In contrast, data-driven innovation involves feed-back loops at several phases of the value creation process.

The data value cycle



The following phases have been identified, whereby the phases which constitute an action are underlined, while those constituting a state are not:

- *Datafication (*Mayer-Schönberger, 2013) *and data generation* refer to the process of transforming the world into processable and quantifiable data and data generation, for example through the digitisation of media, monitoring of activities including real world (offline) activities and phenomenon through sensors.
- *Data storage /Big data* refers to the result of datafication and data collection which lead to a large pool of data that can be exploited through data analytics. Data in this phase is "raw" and, and often without any orderly structure or clear set of internal relationships.
- *Data processing /analytics*: Until processed and interpreted via data analytics, big data is typically resistant to human understanding since at first glance no patterns are obvious, and the data are often far too large to comprehend in raw form, with millions or billions of data points or lines of text. Data analytics refers to a set of techniques and software tools that are used to extract information from data. The value of data is highly context-dependent and relies upon how data are being linked to other data sets, which is what data analytics is also about. Finally, data analytics is increasingly undertaken via cloud computing or server clusters, partly because the data files are too large and frequently accumulating at too high a volume to be handled on stand-alone computers.
- *The knowledge base*: Refers to the knowledge that individuals or systems (incl. organisations) accumulate through data analytics over time. It is typically embodied in humans when gaining insights (though learning). However, it can also be embedded in tangible and intangible products, including publications, standard procedures and, last but not least, knowledge-based capital such as patents, design and software.
- *Data-driven decision making*: The social and economic value of data is mainly reaped when data are transformed into knowledge (gaining insights) and when they are used for decision making (taking action). Analysis of these data could for example, improve: the selection of eligible patients for clinical trials, refine care co-ordination, enable the selection of cost-effective treatments, support the evaluation of clinical care guidelines and more.

Cutting across these categories are the concepts of "deep" and "broad" data, which need to be effectively integrated if the opportunities for progress are to be realised. "Deep" data represents detailed biological and clinical data that might be acquired on individuals, for example extensive clinical, cognitive, biochemical, imaging, genetic and other omic data such as proteomic or metabolomic data (i.e., data on the products of chemical processes in tissues and organs) that might be obtainable in a longitudinal prospective study. "Broad" data typically encompasses more routinely collected data, for example that acquired on larger numbers of individuals from sources such as health care administrative data, medical records, social care data and, potentially, even commercial datasets such as retail histories and social media.

The potential benefits of big data approaches are undisputed although also largely as yet unrealised, and may be delivered through the ability to simultaneously acquire and analyse biological, clinical/medical and population-based data to investigate the interaction of numerous factors to illuminate and validate existing concepts, or identify entirely novel approaches for addressing the risk reduction, treatment and care of those affected by dementia. Such data may be acquired through research across the full range of health care structures, including general hospitals and primary and community care, as well as from non-medical data such as retail/credit card and mobile phone usage and performance on Internet-based gaming.

Through analysis of linked deep biological and broad population-based datasets it is anticipated that new insights will be provided on i) fundamental biological processes underlying conditions that lead to dementia, which may provide new therapeutic targets; ii) potential biomarkers of early stages of disease to aid diagnosis; and iii) factors that modify disease progression and/or symptoms (OECD, 2015b). In addition, big data approaches may allow the testing of a wide range of interactions on a scale that is not practical by existing hypothesis-driven approaches, which might for example uncover unanticipated interactions such as the influence of other clinical indications (comorbidities), the discovery of the unintended benefits from therapies prescribed for other diseases, or lifestyle influences.

Pilot examples of linking broad and deep data on a national/regional and international basis are, however, needed (OECD, 2015b). These initiatives could shed light on the framework – standards / guidelines / governance models etc. – that need to be in place to ensure that this research is done in a way to maximise outcomes while protecting the privacy and security of patients and their information.

Early data access: Looking to genomics

Big data is not just a quantitative change, it is a conceptual and methodological change. It will transform the way we do science and the way we deliver care (OECD, 2014a). It depends on the adoption of an international data sharing and open access agenda for co-operation that can sustain an effective response over the coming decades. This agenda could draw on the frequently invoked model of data access in genomics and is consistent with calls for publicly funded scientific research data to be open, while at the same time respecting concerns in relation to privacy, safety, security and commercial interests.

The informatics revolution and today's computational power is of central importance to the advancement of this agenda. The Internet has not only transformed expectations about global knowledge transfer and data sharing but also the timescales

on which they occur. Rapid access to shared resources has led to extraordinary growth and development in many fields from basic science to big business. However, with the exception of the accomplishments in genetics, medical research has largely failed to capitalise on these opportunities. Instead, the field has followed traditional models of research where unique data are the primary commodity available to generate funding and subsequently publications, and the ability to sustain this circular economy ultimately determines the success of most research groups. To move forward, it is vital to examine these cultural barriers and look for inspiration from other fields on how to begin to dismantle them.

At the outset of the Human Genome Project (HGP), realising the societal significance of the data that would be generated, the genetics community disrupted traditional models of scientific practice by agreeing on a ground-breaking set of principles (Bermuda Principles, 2003). The Bermuda Principles, as they became known, called for all human genomic sequence information to be freely available in the public domain and rapidly released, in some cases automatically and within 24 hours. These principles have subsequently been reaffirmed and extended to include data from other large scale "community resource projects" in genomics, and other omics research fields such as transcriptomics, proteomics and metabolomics (Wellcome Trust, 2003; Rodriguez et al., 2009; Toronto International Data Release Workshop Authors, 2009). Enabling such a radical change in practice required compliance from all stakeholders, establishing clear responsibilities for resource producers, resource users, funding agencies and publication streams. Omics research has recognised the profound value of making the vast amounts of data generated quickly and widely available to scientists, to achieve results beyond what the data producers themselves could produce within the same time period, and often beyond the scope of the original project.

Conversely, there is increasing awareness in dementia research that it is impossible to generate the wealth of data required to understand the complexities of neuro-degeneration without sharing resources (Anderson, 2014), at all levels of investigation, from genomics to clinical research.

To emulate the omics model, the dementia research community should identify data sources suitable for rapid release to best serve the community. A useful starting point may be a publication portal for negative results. Negative results are seldom disseminated despite having the potential to significantly reduce duplication of effort, make better use of valuable resources, and, as a result, accelerate scientific discovery (Matosin, 2014). The provision of a searchable database and a straightforward publication template could help to re-evaluate current models of scientific communication. Additional guidelines for use in terms of both data entry, and due diligence searching as part of a grant application process, could help ensure such a provision was used to its full potential.

More challenging models of early access are based on the pre-publication release of data. The benefits of this approach may be far reaching, not only increasing the rate of scientific discovery, but also helping to address one of the major problems in science; the failure to replicate results (Nature Editorial, 2014). Rapid publication of methods and data could allow results to be confirmed or refuted by other groups, preventing flawed methods being carried through to final publication, and producing greater confidence in those that are. Not only could this approach have a major impact on drug discovery, it would also provide a novel and more responsible publication

route, potentially relieving researchers from the current pressure to publish quickly by offering greater recognition for due diligence.

In addition, pre-publication could also extend to cohort data from longitudinal studies. Data release could be scheduled after every time-point or released in batches based on acquisition of an agreed number of participants. By encouraging multi-centre collaboration and harmonisation of data collection tools this model could be extended to include many more data points, contributing to a larger more useful pool of data and essentially creating new, larger cohorts than have previously been assembled. Moreover, as dementia research moves towards preclinical trials there is an opportunity to build on work already started in population based studies and encourage greater collaboration and integration with social sciences and epidemiological research groups who already have well-established protocols for data sharing (ESRC, 2010).

To move towards greater sharing of resources and faster paced development it would be prudent to also consider the benefits of sharing analysis tools, software and computing resources. In the case of wet biomarker data, such as spinal fluid or blood, where lab based analysis can have a major impact on the reported measure (Toombs, 2013), it may be useful to set up centres of excellence conforming to agreed lab standards, where locally acquired samples can be sent for analysis and the results subsequently made available to the wider community. In terms of computational analysis, state of the art algorithms and tools could be made more widely available by pooling valuable computational resources and harnessing the power of cloud computing.

As the omics community has demonstrated, successful and timely data sharing hinges on a system of shared responsibilities between resource producers, resource users, funding bodies and publishers

Incentives for change are needed, and as will be discussed in later sections, must primarily safeguard the interests of data generators whilst ensuring the economic benefits of shared resources and the increased pace of discovery are experienced by the entire research community and, more importantly, by society as a whole.

Patients and carers take time out of their heavily burdened lives to provide researchers with data in the hope and belief that they will use these data responsibly to help, if not them, then future generations. From blood samples, to questionnaires, to brain donations, it is vital to treat each donation with the respect it deserves and maximise the value that can be derived from it by accurately recording and sharing the data with the wider scientific community. Existing barriers to the timely release of data are largely cultural and, therefore, with enough leverage and support from within the scientific community, can be overcome, opening the way for essential progress in the pursuit of therapies.

Data sharing in dementia: Key structural challenges

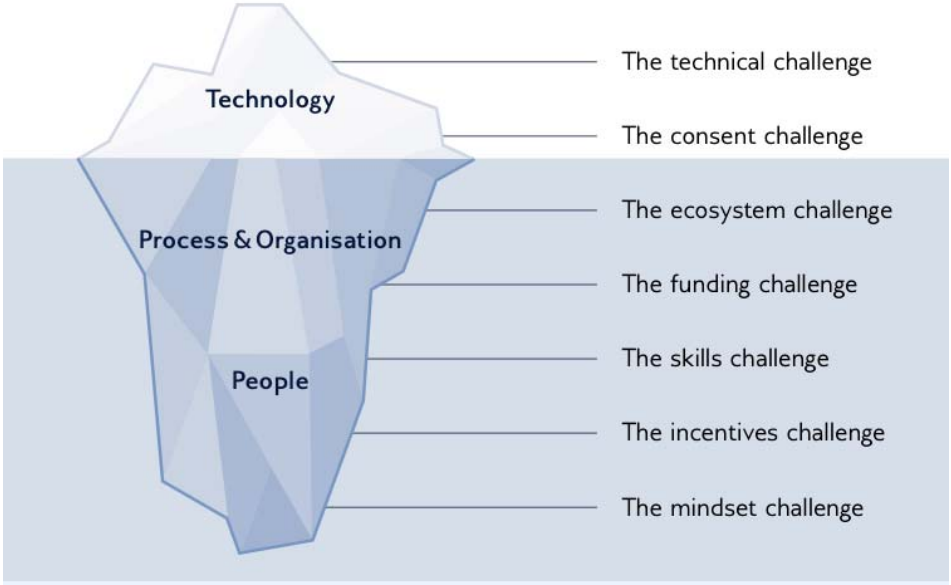
Without compatible data governance frameworks built into even the most advanced of data management systems, the ability of these systems to authenticate and properly move, use and share data is compromised

Today the sources and types of data are expanding continuously, with hundreds of new health and wellness data sources and data networks in existence. But each seems

to have its own governance structure. Reports from the Ontario Brain Institute (OBI) , the Alzheimer's Disease Neuroimaging Initiative (ADNI), the Joint Programme – Neurodegenerative Disease Research (JPND), and the US National Alzheimer's Coordinating Center (NACC) indicate that rigorous and compatible data governance frameworks are needed to catalyse the development of an integrated ecosystem of data that can be shared to accelerate innovation (OECD, 2014a).

Data governance refers to the overall management of the availability, accessibility, usability, integrity and security of the data collected and stored. In addition, there must be policies that conform to the governance of the data in order to form a consistent and effective framework. Recent work led by the OECD and the Oxford Internet Institute (OECD, 2014a; Deetjen et al., 2015) has identified three key categories of challenges that need to be addressed to harness the big data potential: technology, process and organisation, and finally people and culture. They can be depicted in the form of an iceberg (Figure 4.2) whereby the most visible and tractable issues relate to technological challenges. Below the surface are challenges that are often less recognised and more difficult to address, relating to process and organisation, and above all to people and cultural challenges. Examples of these challenges are further described below.

Figure 4.2. Structural challenges to data sharing



Source: Deetjen U., E.T. Meyer and R. Schroeder (2015), *Big Data for Advancing Dementia Research*, OECD Publishing, Paris, forthcoming.

The need for compatible standards and interoperability

Without compatible data collection standards and interoperable frameworks, the ability to authenticate, use, process and share data is compromised. A key barrier to dementia research is for example the variable nature of data collected across population cohorts. This variability arises from several factors; for deep data these may include differences in biological measurements, or differences in the quality or reliability of the data even when the same or similar measurement tools are used. These challenges are

mirrored by broad data challenges emerging from the inconsistent disease coding of dementia in routinely collected health care data, inconsistent diagnosis or case-finding protocols, and different definitions necessary to qualify for benefits. All of these variations reduce the within-dataset utility of information on dementia and the ability to link across data sets and data across countries.

Therefore, an important challenge that must be resolved by consortia involved in big data projects on dementia is to harmonise at least some of the data tools and/or to develop methods that allow highly similar datasets to be merged. This will be simpler for some data items (e.g. imputing genotypes from different forms of genetic information such as single nucleotide polymorphisms in genome-wide association studies, whole-exome sequencing, and whole-genome sequencing studies). Conversely it may be impossible to merge data for cognitive and behavioural measures if the tests that were used examined very different functions (e.g. episodic memory versus executive function). This challenge is already being faced by longitudinal clinical and population-based studies, where new follow-up data are often collected with tools or instruments that are either more sensitive or were not available during the earlier data collections (OECD, 2015).

Groups such as the US National Institute of Health and the Critical Path Institute have initiated considerable work around establishing common data elements, which others can use to ensure that data collection is standardised. The Critical Path Institute and the Clinical Data Interchange Standards Consortium (CDISC) announced recently the release of version 1.0 of the Alzheimer's disease Therapeutic Area Standard (SDTM AD/Mild Cognitive Impairment User Guide). This guide was developed for the clinical research community to facilitate analysis and learning from clinical studies for treatment or risk reduction. The User Guide outlines a standardised set of data elements so that pharmaceutical companies and other medical researchers can more easily, and consistently, collect data that can be reliably pooled and compared.

Co-ordinated government action could further promote the uptake of standards so that data and knowledge can be shared internationally.

Funding challenges

The costs of collecting, storing, linking, organising, and analysing data require considerable investment and collaboration (OECD, 2014a). A key foundation for success in big data research is the use of carefully curated databases, appropriate replication cohorts, development of effective systems biology approaches to integrate multiple types of data from different sources into biologically plausible models for dementia, and thoughtful use of validating biological experiments that may involve a range of carefully chosen model organisms. Appropriate funding needs to be set aside for all phases of this big data discovery paradigm.

Appropriate funding is also needed to sustain the big data infrastructures. For many big data projects, networks or federated research platforms, the most significant challenge once the initial funding runs out is the development of a sustainable business model, that as a bare minimum, would sustain the curation and maintenance of data in an accessible form. Long-term sustainability and financing appear to be the most challenging aspect of the many databases, networks and other big data initiatives in existence today.

The challenge of long-term sustainability often arises from the cyclical nature of project-or-programme-specific financing that has long been the tradition in the biomedical research and health sectors. Funding has typically been dependent on localised research strengths and capabilities aimed at serving a specific research need. As new research questions emerge, subsequent funding sources are made available, either through grants, nonprofit foundations, or in some instances, private sector. However, this "start and stop" style of incrementally funding of projects in short durations is inconsistent with the need for data over an extended period of time and particularly for longitudinal studies. This issue is exacerbated when multiple funders are involved, either nationally or across borders.

This problem is stimulating a renewed interest in the cost and economic viability of big data research infrastructures. These infrastructures are often multi-million dollar operations and the start-up investment and operating cost requirements for even a modest database represent a significant commitment.

Although data sharing initiatives rely on an assortment of funding models- from private capital, to government-funded, charitable not-for-profit, and public-private collaborations all must equally consider fundamental business principles to achieve economies of scale and understand the costs of doing business, as well as establish a compelling value proposition.

The lack of data on costs and agreed indicators/criteria to measure benefits/outcomes from large scale databases makes quantifying benefits in this sector extremely difficult. Yet, the need to demonstrate value to payers – e.g., the role of these resources in facilitating research and in providing a calculable return on public and private investments – is becoming increasingly important.

Owing to the difficult economic times, budget constraints are now leading to the termination of truly unique resources and projects. This problem is stimulating a renewed interest in public-private partnerships and shared global research data infrastructures.

Data linkages and privacy

The value of data is multiplied exponentially when it can be shared and linked with other data, thus data integration is a major creator of value. Most OECD countries have large national datasets that would support regular data linkage to monitor health care quality and system performance (OECD, 2013b). One important barrier to broad and deep data linkage is uncertainty over the actual risks of research results, either for individuals or groups. When data are linked, the combined dataset provides more information about the data subjects than the original unlinked datasets. Thus, the resulting linked data could cause more harm to data subjects if lost, stolen or otherwise misused (OECD, 2015b).

Much remains to be done towards assessing and quantifying risks to privacy that may result from data linkage and in determining the effectiveness of public policy protections already in place.

An OECD study on country practices (OECD, 2013b) indicates that differences in approaches to the protection of data subjects' privacy among OECD countries have resulted in some countries advancing the generation of health data and its use for research and statistical purposes and others restricting data collection, sharing and use. These cross-country differences are significant and can be attributed to differences in

risk-benefit evaluations. Many OECD countries report legislative barriers to the use of personal health data, including enabling data linkages and developing databases from electronic health records. This complexity extends to multi-country data sharing initiatives that remain rare, challenged by concerns regarding differences in data privacy protection laws and whether shared data will be adequately protected in the receiving country.

Informed consent

An important requirement prior to personal data collection for health research is the issue of obtaining patient consent. Explicit consent has become the pillar for protecting autonomy in research involving human subjects. The requirement for consent is underpinned by ethical principles of respect for persons and individual autonomy. Consent is also the basis for data protection and privacy law in most countries. Within the medical/scientific field, informed consent generally presumes the ability to indicate clearly to the participant the use and purpose of the particular research activity. While this is feasible for purpose-specific research, with the new and emerging forms of big data biomedical research, it is difficult to obtain explicit consent for all future research uses at the time of research recruitment, as is required in the original formulations of the Declaration of Helsinki (World Medical Association, 1964).[4] In respect of the Declaration, use for research purposes different from the original would require re-contacting large population groups to obtain a new consent, which is often impossible or impracticable. Re-consenting is costly and time-consuming, and difficulties in locating people can result in high drop-out rates and therefore significant loss of crucial data.

In the case of dementia the very nature of the disease renders the provision of this type of information particularly difficult (OECD, 2014a). New approaches are clearly needed to meet ethical and legal requirements for consent and to accommodate the changes in data use and research practices.

A tiered or step-by-step consent approach, has been recently adopted at Imperial College London in the Chariot Register (a recently established cohort of >20 000 healthy volunteers for reducing the risk of dementia and other age-related neurodegenerative diseases). Participants initially consented to be approached for individual observational or interventional studies, were then offered a menu of options pertaining to such research uses, request to re-consent, interest in returning results, etc. Another model has been adopted by the UK Biobank: research participants take part in the initial examination where deep biological, genetic and imaging data is collected, but consent to be followed up via routinely collected data from primary and secondary care. This broad consent is coupled with ethical oversight from the Ethics and Governance Council, thereby ensuring that patient rights are respected, while at the same time avoiding constraints due to the limits of consent. This may present an avenue to ensure that consent does not come in the way of what both researchers and participants want: to make the best use of the data, ideally without participants necessarily having to be re-contacted for follow-ups or re-consent (Deetjen et al., 2015). Other approaches recently proposed in the scientific literature include “adaptive” or “dynamic” models of consent forms, whereby (following the initial “general” consent) participants would be asked to re-consent for any “new” direction of travel/use of their data, potentially using web-based communication tools. This approach is “dynamic” because it allows interactions over time; it enables participants

to consent to new projects or to alter their consent choices in real time as their circumstances change and to have confidence that these changed choices will take effect (Kaye, 2014).

Timely sharing and dissemination of findings and data

Data that are accessible only to a limited number of investigators clearly represent a potential bottleneck in the discovery pathway. One example of potentially highly useful information that is known to exist, but is not widely available, is the large amounts of normative data obtained from the very well-characterised control cohorts within the numerous clinical trials being undertaken on neurodegenerative diseases. Between 25% and 50% of clinical trials remain unpublished even several years after completion (Chan et al., 2013; Decullier et al., 2005; Von Elm et al., 2008; Turner et al., 2008; Rising et al., 2008). These studies also suggest that half to two-thirds of all government-funded studies are published two or more years after completion of the clinical trial (Ross et al., 2012), that is, after completion of enrolment and observation. Much of the data from clinical trials in AD and dementia are currently not available to the scientific and clinical communities. A number of measures similar to those considered in the previous section may help reduce the existence and impact of data dissemination delays and bias, including changes to the policies on publication of publicly-funded research (open access policies), electronic publishing, as well as the prospective registration of interventional clinical trial studies.

Governments, as key funders of public research, play an important role in developing policies to foster more rapid and greater deposition, sharing and access to and use of scientific research data. For example, public policies and guidance from research funding agencies can facilitate the sharing of and access to data resulting from publicly funded research (OECD, 2007).

Skills and capacity building

Although there is a value in using big data, it requires large numbers of people who are very highly trained and in huge demand from other sectors. Data-related skills including, but not limited to, data specialist skills could become the most critical enabler for big data dementia research. Some evidence suggests that the demand for data specialists already exceeds the supply. The Economist Intelligence Unit 2012 survey, for example shows that "shortage of skilled people to analyse the data properly" is indicated at the second biggest impediment to make use of data analytics (Economist Intelligence Unit, 2012).

Incentives are needed to promote education and training of data analysts and bioinformatics experts to use big data effectively for health research. Governments have for example the opportunity to create dedicated funding streams to train, attract and retain data analysts, early career researchers, and public health and health administrators to learn strategies for collaboration and use of large datasets. They may also support methodological research to create the new tools necessary to use big (broad and deep) data studies to understand dementia, for example by comparing findings from genetics with brain imaging results (Scott et al., 2013). Similarly, governments can attract researchers by making available broad and deep data through research funding requirements or other mechanisms.

Overcoming barriers to data sharing and use: Examples of successful practices

Over the past ten years, the sharing of data for dementia research has gained momentum through a handful of international multi-site federated data networks and regional collaborative consortia. The latter use collective expertise and distributed management to create research tools that are designed and validated by scientific consensus. By temporarily putting aside their institutional differences, these collaborations aim to accelerate individual research efforts by building broadly accessible standardised resources.

Examples include the Ontario Brain Institute (OBI), the Alzheimer's Disease Neuroimaging Initiative (ADNI), the Joint Programme – Neurodegenerative Disease Research (JPND), the Dementias Platform UK (DPUK), the Canadian Consortium on Neurodegeneration in Aging (CCNA) and the US National Alzheimer's Coordinating Center (NACC).

ADNI in particular illustrates an area of dementia research (neuroimaging) that has demonstrated the benefits of data sharing. Since 2005, ADNI has been validating the use of biomarkers including blood tests, tests of cerebrospinal fluid, and MRI/PET imaging for AD clinical trials and diagnosis. In particular, ADNI has defined the gold standard in terms of both data availability and speed and ease of accessibility.

Access to data resources for dementia research varies in terms of what the access procedures are in terms of effort and detail required for application, and time between application and actual data access needed. Access generally requires approval from a responsible body (e.g., custodian, original data collectors, independent body, or data access committee). This mechanism, while primarily designed to protect study participants, is viewed also as a way to protect investigators, database hosting institutions, and funders from exposure to legal liability. It is, however, resource-intensive and may involve considerable wait times for researchers.

Open access remains the norm for health data that cannot be linked with other data to generate information that would uniquely identify an individual. Open access is becoming a well-established practice for large-scale, publicly funded, data-intensive community science projects, particularly in the field of genomics and neuroimaging.

A number of initiatives in the field, for example ADNI, AddNeuroMed and UK Biobank, promote data access through a simple managed procedure which utilises an application process to verify the bona fide status of the researcher and obtain a short description of the intended research.

Once access is granted there are currently two main main ways in whichresearchers can get hold of the actual datasets: the lending library (or exporting) model, which physically transfers the dataset to the researcher (as has been adopted by ADNI, AddNeuroMed and UK Biobank), and the reading library model, which means that data can be accessed through a remote access to the machine on which the data is stored, without the data leaving this secure environment (as envisioned by the Dementia Platform UK, incorporating UK Biobank data). The key advantage of the lending library model is that it provides the researcher with more flexibility in terms of what can be done with the data – e.g. in terms of combining data with other sources, while the reading library model offers greater data security and control (Deetjen et al., 2015).

To be useful, shared data that are intended to be federated with other data types and sources must be interoperable. Large-scale collaborations can be highly effective, especially if researchers agree in advance on standards and protocols so that data can be pooled and compared easily. As opposed to routine big data where researchers cannot directly influence data collection, information in these collaborations can be gathered consistently and thereby permits effective linkage and secondary analysis of data.

In a networked environment, interoperability means agreement on common protocols defining the basic mechanisms by which users and resources negotiate, establish, manage, and exploit sharing relationships. Also, interoperability means sharing not only data but anything that connects to the data production and processing including computing tools, applications, methods, software, metadata, workflows across different platforms and even communication. A standards-based open architecture facilitates extensibility, interoperability, portability, and code sharing; standard protocols make it easy to define standard services that provide enhanced capabilities.

For example, AddNeuroMed has adopted imaging standards for their MRI data, so that data from ADNI and AddNeuroMed can be combined. This has been exploited in the usage of ADNI as the main dataset for the recent SAGE Synapse AD Big Data DREAM challenge,[5] in which AddNeuroMed was used as the test dataset. At the same time, the UK Biobank is a good example for linkage to other routine datasets, as individuals have agreed to data from their electronic medical record being used for follow-up, as is also the case in other population-based cohort studies, such as in the Canadian Longitudinal Study on Ageing (CLSA). This allows tracking conditions these individuals develop at later stages in their lives without the need for follow up.

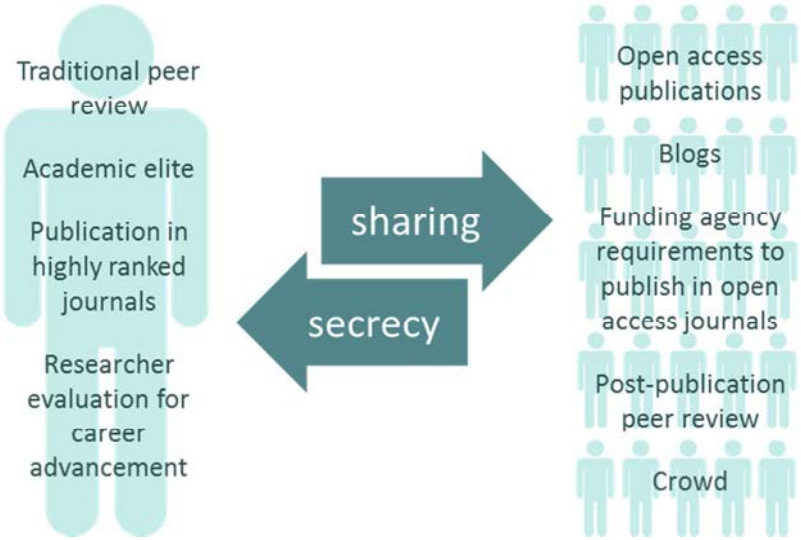
Unambiguous definitions of terms are also necessary for researchers in order to identify the relevant datasets and produce meaningful results when combining data from disparate sources. The question of "findability" is especially important in data catalogues such as the Global Alzheimer's Association Interactive Network (GAAIN), NeuGRID4U or the European Medical Information Framework (EMIF), where scientists or clinicians may look for datasets with specific features of individuals, or specific measures taken – which of course can only be found based on good and accurate metadata.

In addition to metadata, good documentation is important to allow use of the data, and is often challenging due to the additional efforts beyond the data collection. Using wikis, for example, may help to keep information up to date and allow users of the data to contribute to documentation as well.

Incentives to data sharing

Creating a culture of open science will require understanding and addressing the concerns of scientists and partnering with the institutions that employ and support researchers. There may be various reasons for an investigator delaying deposition and publication of data. These include pressure from commercial sponsors, protection of credit for the scientific lead, potential for patent application etc. Other reasons include policies and practices at universities that place a premium on patenting over publishing (particularly data publishing) and weak incentives for researchers to share data (Figure 4.3).

Figure 4.3. Conflicting incentives and channels for researchers to disclose results



As previously discussed, there are good scientific reasons to share data for dementia research, particularly as dementia shares with many other medical conditions being researched today the requirement for large samples in order to detect small effects. But the culture of scientific research has generally been slow to shift towards an open science paradigm and much relevant data still remains inaccessible.

A recent survey about data-sharing practices among scientists revealed considerable unwillingness to disclose whether or not they share data. Nearly half of the respondents said they do not share data, citing reasons of lack of time, underdeveloped standards, and inadequate infrastructure. A majority of these respondents indicated, however, an interest in having access to other researchers' datasets (Tenopir, 2011). It must also be recognised that sharing data is complex and expensive, and that these end-of-project expenses are only rarely included in project budgets set many years earlier.

The provision of high-quality data can indeed require significant time and up-front investments before it can be shared. These include the costs related to i) datafication, ii) data collection, iii) data cleaning and iv) data curation. Effective data sharing is, however, as indicated in the previous section not limited to data itself. In many cases data alone are not sufficient to share, but may require a number of complementary resources ranging from additional (meta-) data, to data models and algorithms for data storage and processing, and even access to secure IT infrastructures for (shared) data storage, processing, and access.

Given the significant burdens attached to the provision of data, creators and controllers of data do not necessarily have the incentives to share their data. The following reasons can be identified: i) the costs for data sharing are perceived as higher than the expected private benefits of data sharing; ii) as data are in principle non-exclusive goods for which the costs of exclusion can be high, it is often assumed that the possibility of "free riders" can provide an additional incentive problem. It is thereby often argued that if data are shared, free-riding users can "consume the resources without "paying" an adequate contribution to investors, who in turn are unable to recoup their investments" (Frischmann, 2012).

Gaining scientific recognition is generally perceived by academic researchers as an incentive to sharing, although professional recognition and credit towards one's career progression are often unclear for data creators. Some data creators, such as those in the Swedish Brain Power studies, often also become co-authors on papers written using data they created. Other initiatives, such as ADNI, ask for one of the authors of any papers to be the consortium itself, or require an acknowledgement in the paper, as with the UK Biobank. Acknowledgement may be given, for example, through providing a citation for the dataset that counts for academic metrics. Furthermore, a model of adding data and feeding it back to the main resource may help to establish a win-win situation for data collectors and users. Currently, there are few incentives to share data the way academia is set up, with recognition being mostly attributed to publishing papers. Being creative in finding new incentives and widening our understanding of what is deserving of recognition are a crucial underlying mechanism both for building resources of future value and for sharing data more generally (Deetjen et al., 2015).

Recognition of expertise is also important to increase incentives for new partners to participate in dementia research. These new partners may include informatics specialists with technical skills that can be applied in biomedical contexts. There is currently an undersupply of people with these skills, however, and often a lack of training opportunities to provide the paths into these careers. Creating incentives for students to train for these positions is needed as well as creating rewarding career paths within those professions. Additionally, just as important as training more bio-informaticians, it may also be important to increase collaboration across disciplines.

One of the conclusions of past open challenges was that the winners were often teams of statisticians with little to no medical knowledge. Of course, results from open challenges will have to be followed up with proper medical knowledge and by no means replace rigorous controlled experiments, but they may open up new threads to be followed up, all of which may be worthwhile exploring (Deetjen et al., 2015).

Advancing big data dementia research: Key findings and policy conclusions

Research addressing the causes and progression of dementia is increasingly directed towards understanding the result of numerous interactions between age and gender, genetics and epigenetics, environment and lifestyle across the various stages of the disease. Because of the clinical and biological complexity of dementia, an emerging consensus is that the crucial studies needed to underpin drug discovery, validate alternative models of risk reduction and care, and develop new therapeutic strategies aimed at slowing disease progression will require massive and diverse data collection, storage and processing and new investments in research and infrastructure. Advocates of this "data-driven" research paradigm argue that harnessing the large quantities of broad and deep data generated across laboratories worldwide (behavioural, genetic, environmental, epigenetic, clinical, administrative, etc.) has numerous methodological, ethical and economic advantages "as no one nation has all the assets to pursue this type of research independently". Capitalising on this promise will require, however, a strong effort at several levels. Big data for dementia is not just important for its size, but also for its scope that will go beyond the borders of the health system, requiring data sharing and collaboration among governments, researchers and industry, i.e. linking different communities together. Moreover, the complexity of the dementia challenge and its heterogeneity requires moving beyond the traditional hypothesis-predicated scientific approach to the simultaneous assessment of a

multitude of factors within big data to discover the unexpected. Current research models are not well set up for this complexity. Public policy has a crucial role to play ensuring that framework conditions to promote data sharing are sound and supportive and in setting the conditions for trust and partnerships. The main findings and policy conclusions of OECD work on these issues follow below.

First, the field of dementia research is at a critical juncture to benefit from information technology developments. Recent advances in information technology are radically changing the way in which health data are collected, stored and used. Governments need to promote efforts to create deep and broad data resources through their regulatory and legislative roles related to privacy, data access, and data standardisation; through their role as a provider and funder of health and social services; and as the largest supporters of research.

However several barriers to data sharing still remain. Although there is a clear potential to improve science and innovation systems through big data and open science, barriers still remain with respect to data sharing efforts. Some barriers are of a technical nature, as for issues related to interoperability and standards, storage, the technical infrastructure to allow data sharing. The most significant challenges to data sharing in this field are, however, cultural and ethical and are related to the lack of an open data culture or the disincentives that researchers and scientists face with respect to the disclosure of data, especially relative to research at the pre-publication stage and dilemmas around credit sharing in the academic economy. Publications by whole consortia or with numerous authors still present challenges for academics concerned about how these publications will be credited and recognised for career promotion by their institutions. This raises the question of the actions needed to promote data access and openness to boost research and innovation without discouraging data collection from individual researchers.

There is value in further exploring incentives structures and articulating a minimum set of principles and best practices through the OECD, addressed to funders and the associated government agencies. Although many of these issues are going to be generic, dementia provides a good demonstration area, and also one where the G7 governments have called for action. Measures may include different efforts and initiatives, such as mandatory rules, incentive mechanisms or enablers:

- *Mandatory rules* are often implemented in the form of requirements in research grant agreements or in some cases are defined in national strategies or institutional policy frameworks. By favouring open standards and taking interoperability as requirement into account in funding research, governments can for example, indirectly promote interoperability and standardisation.
- *Incentive mechanisms* may be in the form of financial incentives to cover the release of datasets. They may also be in the form of proper acknowledgment of open data efforts of researchers and academics, for instance in the form of data set citations or career advancement mechanisms partly based on metrics that take into account open science or data sharing initiatives.
- *Enablers* are for example the infrastructure developed to assemble and share data, initiatives undertaken to develop an open science and open data culture, amendments to the legal framework to make them increasingly open-science friendly or the development of the skills necessary for researchers to share and re-use the research outputs produced by others.

Researchers' willingness to share data can also be constrained by concerns for the privacy of the human research participants who are the data sources, and the data-sharing permissions they have granted in consenting to participate. Currently, most informed consent forms cover the consent for the use of the participant's data for the research questions related to the primary study focus and not for potentially unrelated investigations that could follow from open access to these data in the wider research community. New tiered step-by-step or dynamic consent models are needed to meet ethical and legal requirements and at the same time accommodate the changes in data use and research practices.

Advocates of *early data access* frequently invoke the success of research in genomics as a model for data sharing. To emulate the omics model, a useful starting point for the dementia research community may be a publication portal for negative results. Negative results are seldom disseminated despite having the potential to significantly reduce duplication of effort, make better use of valuable resources, and, as a result, accelerate scientific discovery. The provision of a searchable database and a straightforward publication template could help to re-evaluate current models of scientific communication.

There is an increasing need to develop analytical *skills and competencies* related to data curation, processing and preservation. A number of countries have begun to address the shortage of data management skills, by requiring researchers to develop data management plans in grant agreements or by developing training programmes or new academic curricula. There is a general need to understand the demand for those skills and the type of skills currently lacking in the research community and beyond to fully reap the benefits of data sharing.

Next steps for international action identified by OECD experts include four main approaches:

- Survey exemplary multinational data consortia to identify where comparable data exists to *promote best practice in data collection* for greater data interoperability, linkage studies and data sharing; and define the common data elements that might underpin future studies.
- *Identify and reach agreement on common principles and best practices* for the establishment of incentives to facilitate open access to research data generated with public funding.
- *Pursue the possibility to develop an international advisory group* to discuss issues and take stock of developments around good practice in data governance, privacy protection and data standards to support national development of broad and deep data and multi-country projects involving data sharing in dementia research.
- *Promote demonstration cases* involving the linkage of broad and deep data as a pilot or proof of concept study to demonstrate the benefits of this type of data to dementia research and care and as a test bed to work through challenges and develop solutions for future projects.

Notes

1. This chapter was authored by Elettra Ronchi from the OECD Directorate for Science, Technology and Innovation; Ulrike Deetjen, Eric T. Meyer and Ralph Schroeder of the Oxford Internet Institute, University of Oxford, UK; Lorna Harper and Martin Rossor of the University College London Institute of Neurology, UK; and Robin Buckle of the Medical Research Council.
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