



## Guideline Summary NGC-9576

### Guideline Title

**World Alzheimer report 2011: the benefits of early diagnosis and intervention.**

### Bibliographic Source(s)

Prince M, Bryce R, Ferri C. World Alzheimer report 2011: the benefits of early diagnosis and intervention. London (UK): Alzheimer's Disease International (ADI); 2011 Sep. 68 p. [302 references]

### Guideline Status

This is the current release of the guideline.

### Scope

#### Disease/Condition(s)

Alzheimer's disease

#### Guideline Category

Diagnosis

Evaluation

Management

Risk Assessment

Screening

#### Clinical Specialty

Family Practice

Geriatrics

Internal Medicine

Neurology

Preventive Medicine

#### Intended Users

Advanced Practice Nurses

Health Care Providers

Health Plans

Hospitals

Physician Assistants

Physicians

Utilization Management

#### Guideline Objective(s)

- To provide evidence-based guidance for policy and practice on early diagnosis and interventions for Alzheimer's disease
- To increase awareness of the burden of Alzheimer's disease and dementia to society and show how earlier diagnosis and early intervention are important mechanisms

#### Target Population

Persons aged 65 years and over with complaints of memory impairment

### Interventions and Practices Considered

1. Promoting earlier diagnosis
  - Primary care screening for dementia
  - Audit of diagnostic activity
  - Promoting shared care with specialist services
  - National networks of specialist diagnostic centres
  - Explicit recommendations for care
2. Conducting more observational research on dementia
3. Providing early interventions
  - Acetylcholinesterase inhibitors and cognitive stimulation
  - Gingko biloba, if indicated
  - Peer support groups and individual behavioural therapy
  - Physical activity programs
  - High quality caregiver education, training and support
4. Publicising effective interventions to health and social care professionals

### Major Outcomes Considered

- Patient outcomes
  - Cognitive function
  - Functional status
  - Mortality
  - Admission to institutional care
  - Quality of life
  - Psychological wellbeing
  - Challenging behaviour (e.g., aggression, agitation, wandering)
  - Social participation (social, employment, education, leisure, etc.)
  - Dignity and rights
- Carer outcomes
  - Quality of life
  - Psychological wellbeing
  - Strain
- Other outcomes: healthcare and/or societal costs

## Methodology

### Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Searches of Unpublished Data

### Description of Methods Used to Collect/Select the Evidence

#### Early Diagnosis

#### Strategy for the Systematic Review

For studies of clinical populations, the guideline authors sought any longitudinal studies that included information on disease stage at time of diagnosis (defined broadly as duration of symptoms before diagnosis, or any appropriate indicator of dementia severity, e.g., Mini Mental Status Examination [MMSE] score or other indicator of cognitive impairment, or Clinical Dementia Rating [CDR] or any other indicator of disease staging) and the subsequent course and outcome of dementia (see Box 1 in the original guideline document for list of outcomes considered relevant). The authors used the same approach in the search for informative population-based studies, bearing in mind that such studies would also identify people with dementia who have not yet sought help or received a diagnosis, as well as those who have received a diagnosis at varying stages in the disease process; this information could also therefore be correlated with future outcomes.

The guideline authors used three search strategies to identify relevant studies. First they sought to identify any longitudinal studies of course and outcome conducted in memory clinic settings (search 1). Memory clinics usually have a standardised approach to recording clinical information at diagnosis, which usually includes information regarding dementia severity or stage. Often, outcome data is also collected systematically for clinical and research purposes. Second, they conducted a search based upon keywords for 'disease stage' limited to studies of dementia (search 2). Finally, they conducted a series of searches focussing upon key relevant outcomes – institutionalisation (search 3).

Finally, they conducted a series of searches focusing upon key relevant outcomes: institutionalisation (search 3), disease progression (search 4), and mortality (search 5) – again all limited to studies of dementia. Details of the search terms used can be found in Annex 1 of the original guideline document.

In the search for relevant evidence, the guideline authors sought to identify:

1. Primarily, quantitative findings from observational epidemiological or clinical research (as described above)
2. Expert consensus statements and guidelines
3. Non-evidence based narratives asserting the benefits of early diagnosis and their attendant justifications. Many such narratives were found in the background or introductory sections of papers that were scrutinised for possible relevance, while not being informative with respect to 1 or 2 above.

See Chapter 3 of the original guideline document for more information.

### **Intervention**

For the purpose of this review, the guideline authors used the following scoping question: *For which pharmacological, psychological, or psychosocial interventions, when compared with placebo/usual care, is there evidence of clinical benefit/harm for people with dementia and their carers, specifically when applied in the early stages of dementia?*

### **General Search Strategies**

The guideline authors first identified relevant systematic reviews conducted through the Cochrane Collaboration using the Cochrane Reviews website (Dementia and cognitive improvement review group) and Cochrane Library. They also consulted UK National Institute for Health and Clinical Excellence (NICE) guidelines for dementia management, together with specific evidence-based guidance for individual therapies. They also accessed the US Alzheimer's Association's systematic reviews on non-pharmacological interventions specifically for early stage Alzheimer's disease, conducted in 2007. They supplemented these systematic reviews with a new search in PubMed looking for more recent randomised controlled trials focusing on early stage dementia. They used the following terms: "Randomized Controlled Trial"[Publication Type] AND "Dementia"[Mesh] AND ("early stage"[All Fields] OR "mild"[All Fields]) and restricted the time from June 2005 to June 2011. Finally, they contacted specialists in the area enquiring about more recent data on interventions for early stage dementia and cross checked their responses to the evidence gathered so far.

The guideline authors were principally interested in trials that recruited only people with mild or early stage dementia. However, mindful that in many cases trials might include people with mild/early stage disease as well as those with more advanced dementia (moderate or severe) they also included such trials in the narrative review. For these trials they sought to ascertain the proportion of participants that had mild/early stage dementia, and the mean MMSE score as a further indicator of the distribution of severity. They also clarified if the trial results had been analysed by severity either a) a stratified analysis with results presented separately for those with mild dementia or b) a test for interaction, testing formally whether the effect of the intervention varied by dementia severity.

See Chapter 4 of the original guideline document for additional details on the selection of evidence.

## **Number of Source Documents**

### **Early Diagnosis**

Of 8039 papers (abstracts and titles) only three papers provided relevant quantitative evidence. Five consensus statements or practice guidelines were also identified.

### **Intervention**

Not stated

## **Methods Used to Assess the Quality and Strength of the Evidence**

Not stated

## **Rating Scheme for the Strength of the Evidence**

Not applicable

## **Methods Used to Analyze the Evidence**

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

## **Description of the Methods Used to Analyze the Evidence**

### **Early Diagnosis**

Several of the papers that the guideline authors reviewed in the course of their systematic review contained statements regarding the benefits of early diagnosis. Many were unreferenced, and where references were provided these were generally to other papers making similar, non-evidence-based assertions. These statements should therefore be considered, at best, to represent expert opinion. The importance of early dementia diagnosis has also been highlighted and supported by many stakeholders including, importantly, Alzheimer's associations representing and advocating for the interests of people with dementia and their carers.

The guideline authors have subjected all of this material to narrative analysis, and have attempted to categorise the perceived benefits of earlier diagnosis under nine broad themes:

1. Optimising current medical management
2. Relief gained from better understanding of symptoms
3. Maximising decision-making autonomy
4. Access to services

5. Risk reduction
6. Planning for the future
7. Improving clinical outcomes
8. Avoiding or reducing future costs
9. Diagnosis as a human right

### **Intervention**

The guideline authors were principally interested in trials that recruited only people with mild or early stage dementia. However, mindful that in many cases trials might include people with mild/early stage disease as well as those with more advanced dementia (moderate or severe) they also included such trials in our narrative review. For these trials they sought to ascertain the proportion of participants that had mild/early stage dementia, and the mean MMSE score as a further indicator of the distribution of severity. We also clarified if the trial results had been analysed by severity either a) a stratified analysis with results presented separately for those with mild dementia or b) a test for interaction, testing formally whether the effect of the intervention varied by dementia severity.

### **Methods Used to Formulate the Recommendations**

Expert Consensus

### **Description of Methods Used to Formulate the Recommendations**

Alzheimer's Disease International (ADI) commissioned an independent research group to collate and review, for the first time, all of the available evidence relating to early diagnosis and early intervention for the World Alzheimer Report 2011. This is the third World Alzheimer Report that ADI has commissioned. People with dementia actively participated in the 2011 Alzheimer's Disease International meeting in Canada.

### **Rating Scheme for the Strength of the Recommendations**

Not applicable

### **Cost Analysis**

#### **Significant Savings**

In high income countries, according to the World Alzheimer Report 2010, the average annual societal costs are US\$32,865 per person with dementia. Set against this, the one off costs of a high quality dementia diagnosis are around US\$5,000 per person. Even taking this and the additional costs of early intervention into account, we find that these costs are more than likely offset by projected future savings from delayed institutionalisation, with net savings of around US\$10,000 per person with dementia across the disease course. Improved health and quality of life of carers and people with dementia would make this an even more cost-effective investment. Though the evidence comes from a limited number of studies, there are indications that a significant amount could be saved at a time where governments are rightly concerned about increasing health and social care costs.

#### **Economic Analyses Identified**

The guideline authors identified three economic analyses that had attempted to model the impact of implementing earlier diagnosis on future costs health and social care system and/or societal costs:

1. Researchers from the University of Wisconsin conducted a Monte Carlo cost-benefit analysis, based on estimates of parameters available in the medical literature, which suggests that the early identification and treatment of Alzheimer's disease have the potential to result in large, positive net social benefits as well as positive net savings for states and the federal government.
2. The second economic analysis was carried out by researchers from the United BioSource Corporation, a consulting research firm, commissioned by Eisai Ltd, the manufacturers of donepezil.
3. The third economic analysis assessed the possible cost-effectiveness of nationwide introduction, in England, of the Croydon Memory Service model for early diagnosis and intervention in dementia.

#### *Conclusion*

The economic arguments in favour of early diagnosis and early intervention are strong, but not yet completely unassailable. The evidence, partly of necessity, is somewhat indirect and circumstantial, and several untested assumptions are quite critical to the case for there being a net benefit. On the other hand, the failure of most trials to include adequate assessment of the impact of the intervention on quality of life of people with dementia and their carers may have led to a substantial underestimate of the net benefits, were these to have been measured and weighed in the balance with the fiscal costs and benefits. These direct costs tend to be given more weight than wider societal benefits by governments and other health and social care purchasers.

See Chapter 6 of the original guideline document for more information on the economic analyses identified.

### **Method of Guideline Validation**

Not stated

### **Description of Method of Guideline Validation**

Not applicable

### **Recommendations**

## Major Recommendations

1. There is evidence that earlier diagnosis can be achieved through a) practice-based educational programs in primary care, b) the introduction of accessible diagnostic and early stage dementia care services (memory clinics) and c) promoting effective interaction between different components of the health system.

### Recommendations

- All primary care services should have basic competency in indicated screening for dementia, making and imparting a provisional dementia diagnosis (including exclusion of reversible causes), initial management (providing information and support, optimising medical care) and referral.
- Practice based registers should be maintained in order to audit diagnostic activity, and to promote shared care with specialist services.
- In resource-poor settings with limited or no access to specialist dementia diagnostic and care services, the World Health Organization (WHO) Mental Health Gap Action Plan (mhGAP) evidence-based intervention guide should be scaled up across primary care services.
- Where feasible, national networks of specialist diagnostic centres should be established, to which primary care centres could then refer all those identified with probable dementia for diagnostic confirmation.
- In complex health systems, explicit recommendations should be made regarding the roles of primary care, memory clinics and community care services in dementia diagnosis, early stage and continuing care.

2. There is, as yet, no unequivocal evidence that earlier diagnosis is associated with better outcomes for people with dementia and their carers, but there is a marked lack of observational research data from population studies and clinical cohorts from which to draw conclusions.

### Recommendations

- More observational research should urgently be commissioned and conducted, in particular making use of data routinely collected by clinical services at the time of diagnosis and in subsequent follow-ups.
- Population-based surveys of dementia prevalence should routinely ascertain where and when a formal diagnosis has been made, and what dementia-specific services have been received.

3. It is a myth that there is no point in early diagnosis, since 'nothing can be done'. In fact, there are a range of evidence-based early interventions that are effective in improving cognitive function, treating depression, improving caregiver mood, and delaying institutionalisation.

- Acetylcholinesterase inhibitors and cognitive stimulation may enhance cognitive function in people with mild Alzheimer's disease, and these interventions should therefore be routinely offered.
- Gingko biloba cannot be recommended as a first line treatment for Alzheimer's disease, but could be considered for non-responders to acetylcholinesterase inhibitors, and for those with other subtypes of dementia. Cognitive stimulation may also be effective across dementia subtypes.
- People with early stage dementia may benefit from participation in peer support groups, and individual behavioural therapy programs should be considered to treat depression.
- Consideration should be given to developing physical activity programs although the benefits for people with mild dementia are uncertain.
- High quality caregiver education, training and support interventions should be offered to carers in a timely fashion as care demands increase; their use is associated with improved carer mood, and delayed institutionalisation of the person with dementia.

### Recommendations

- The availability of effective interventions should be actively publicised to health and social care professionals through training, and to the public through population health promotion and primary and secondary healthcare and social care facilities.
- Purchasers and providers of dementia care services should ensure that these evidence-based interventions are made available, as indicated, to people in the early stage of dementia. This will involve commissioning early stage dementia services, securing appropriate financing, and providing training and support to staff.

- Implementation and uptake should be monitored through regular service audits.

• More randomised controlled trials are required to promote evidence-based intervention in early stage dementia. Priorities include:

- Testing drug interventions earlier in the course of dementia, over longer periods of time, and in larger and more diverse populations
- The efficacy, and optimal targeting, duration and type of psychological intervention or support for those who have recently received a diagnosis of dementia
- The efficacy of psychological interventions (cognitive behavioural therapy, behavioural therapy, supportive psychotherapy) for depression and anxiety in early stage dementia
- The efficacy, including longer-term benefits, of sustained physical activity programs for people with early stage dementia
- The efficacy, including longer-term benefits, of sustained comprehensive micronutrient and essential fatty acid supplementation for people with early stage dementia
- The optimal timing of effective caregiver intervention, including more nuanced stepped care models for introducing and escalating provision of information, education, training, and support from the time of diagnosis through early-to mid-stage dementia

4. There is evidence from economic modelling that the cost of an earlier dementia diagnosis and the downstream costs of providing evidence-based treatment may be more than offset by the cost savings accrued from the benefits of a) antidementia drugs and caregiver interventions, and b) delayed institutionalisation and enhanced quality of life for

people with dementia and their carers.

### Recommendations

- Current economic models are to some extent specific to the health system context (UK and US) for which they were generated. Policymakers need evidence of the real-world costs and benefits of scaling up earlier diagnosis and early-stage dementia care services, specific to the setting in which the economic evidence is to be applied.
- Commissioning of such studies, whether based on observational data or cluster-randomised controlled trials, should be prioritised by stakeholders committed to evidence-based advocacy, and by governments for evidence-based policymaking.

### Clinical Algorithm(s)

None provided

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

Three papers provided relevant quantitative evidence for early diagnosis: one large, well-conducted observational study and two longitudinal studies. Randomized controlled trials and systematic reviews were utilized to support the use of interventions.

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

- Earlier diagnosis and appropriate interventions for Alzheimer's disease and dementia
- Earlier diagnosis has the potential to change the way societies view and approach Alzheimer's disease and other dementias.

### Potential Harms

Not stated

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

### Implementation Tools

Foreign Language Translations

Patient Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Living with Illness

### IOM Domain

Effectiveness

Patient-centeredness

## Identifying Information and Availability

### Bibliographic Source(s)

Prince M, Bryce R, Ferri C. World Alzheimer report 2011: the benefits of early diagnosis and intervention. London (UK): Alzheimer's Disease International (ADI); 2011 Sep. 68 p. [302 references]

### Adaptation

Not applicable: The guideline was not adapted from another source.

### Date Released

2011 Sep

2011 Sep

### Guideline Developer(s)

Alzheimer's Disease International - Disease Specific Society

### Source(s) of Funding

This project was funded with an educational grant from Bayer HealthCare. Alzheimer's Disease International is fully responsible for the content.

### Guideline Committee

Not stated

### Composition of Group That Authored the Guideline

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### Financial Disclosures/Conflicts of Interest

Not stated

### Guideline Status

This is the current release of the guideline.

### Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the [Alzheimer's Disease International Web site](#).

### Availability of Companion Documents

The following is available:

- World Alzheimer report 2011: The benefits of early diagnosis and intervention. Executive summary. London (UK): Alzheimer's Disease International; 2011 Sep. 36 p. Electronic copies: Available in Portable Document Format (PDF) from the [Alzheimer's Disease International Web site](#). Translations of the executive summary (Chinese and Arabic) and a summary (French and German) are also available from the [Alzheimer's Disease International Web site](#).

### Patient Resources

The following are available:

- Know the faces of dementia: what you need to know about Alzheimer's disease and related dementias. London (UK): Electronic copies: Available in Portable Document Format (PDF) in English and Spanish from the [Alzheimer's Disease International Web site](#).

Additional booklets, factsheets, and publications are available in various languages from the [Alzheimer's Disease International Web site](#).

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