

## Online Quiz

# Test Your Knowledge: Ten Questions about Dementia

This quiz is related to the Best Practice article in the January issue of *PLoS Medicine* (DOI: 10.1371/journal.pmed.0020007).

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## Question 1. What is the median life expectancy after diagnosis of Alzheimer disease?

- 1–2 years
- 5–6 years
- 8–9 years
- 10–11 years

## Question 2. Roughly what proportion of people in Europe aged over 65 years has some form of dementia?

- 1%
- 3%
- 6%
- 10%
- 15%

## Question 3. Which of the following best reflects the evidence on the effects of estrogen on cognition in postmenopausal women with Alzheimer disease?

- Randomized, controlled trials found no effects of the drug on Mini Mental State Examination (MMSE)
- Randomized, controlled trials found an improvement in the MMSE that is sustained for at least one year
- Randomized, controlled trials found clear evidence of clinical benefit as measured by clinical rating scales (these assess attributes such as self care, memory, and orientation)
- Randomized, controlled trials found some short-term improvements in the MMSE, but the effects were small and did not translate into any clinical benefit

## Question 4. Which of the following best reflects the evidence on the side effects in the first year of giving donepezil to patients with Alzheimer disease?

- In randomized, controlled trials with up to one year of follow-up, donepezil caused severe nausea, vomiting, and diarrhea, and a large proportion of patients withdrew from the drug because of these side effects
- The side effects in randomized, controlled trials were severe and persistent, but only a small proportion of patients withdrew from the drug
- The side effects in randomized, controlled trials were generally mild and transient, and a systematic review found no difference between donepezil and placebo in the proportion of people who withdrew for any cause

## Question 5. Which of the following best reflects the evidence on cognitive training for preventing and treating Alzheimer disease?

- There is good evidence from randomized, controlled trials with long follow-up that such training can prevent Alzheimer disease
- There is no good evidence that it can prevent Alzheimer disease, but there is good evidence that it is very effective at improving cognitive functioning in people with early-stage Alzheimer disease
- There is no good evidence from trials with long follow-up of a beneficial effect in preventing or treating the disease

## Question 6. Which of the following treatments has been proven conclusively to improve the cognitive symptoms of Alzheimer disease?

- Vitamin E
- Non-steroidal anti-inflammatory drugs
- Nicotine
- None of the above

## Question 7. Which of the following drug treatments for the agitated behavior often associated with dementia is best supported by evidence?

- Trazodone
- Sodium valproate
- Carbamazepine
- Donepezil

## Question 8. A 75-year-old man presents with the gradual onset of cognitive impairment, which is fluctuating, together with falls, visual hallucinations, and Parkinsonism. What is the most likely diagnosis?

- Multi-infarct dementia
- Alzheimer disease
- Lewy body dementia

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**Question 9. What is the average life expectancy of people with Lewy body dementia?**

- 2 years
- 6 years
- 10 years

**Question 10. Which of the following best reflects the evidence on routine screening for dementia for all patients in primary care settings?**

- There is clear evidence that the benefits of screening outweigh the harms
- There is clear evidence that the harms of screening outweigh the benefits
- There is insufficient evidence to state whether screening is beneficial or harmful

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**Answer 1: 5–6 years**

Median life expectancy after diagnosis is 5–6 years [1,2].

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1. Warner JP, Butler R, Prabhakaran P (2003) Dementia. *Clin Evid* 9: 1010–1033.
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**Answer 2: 6%**

About 6% of people aged over 65 years and 30% of people aged over 90 years have some form of dementia [1]. The prevalence of dementia increases with age: it's only 0.8% in the age group 65–69 years but 28.5% among individuals 90 years and older.

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**Answer 3: Randomized, controlled trials found some short-term improvements in the MMSE, but the effects were small and did not translate into any clinical benefit**

A Cochrane systematic review identified five randomized, controlled trials that included 210 postmenopausal women with Alzheimer disease [1]. The reviewers looked at various outcomes (such as MMSE, memory, concentration, and cognitive function) after treatment with different types of estrogen, at different doses, delivered by different routes and for different durations. Meta-analyses showed that there was a limited positive effect from low-dose conjugated equine estrogens (0.625 mg once a day) but not from a higher dose (1.25 mg of conjugated equine estrogens once a day) on the MMSE after two months, but the effect disappeared after three, six, and 12 months of treatment. This effect was small and not clinically relevant. The reviewers concluded that estrogen therapy (with or without a progestagen) is not indicated as a treatment for improving or maintaining cognitive function in women with Alzheimer disease.

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1. Hogervorst E, Yaffe K, Richards M, Huppert F (2004) Hormone replacement therapy to maintain cognitive function in women with dementia. *Cochrane Database Syst Rev* 2004: CD003799.

**Answer 4: The side effects in randomized, controlled trials were generally mild and transient, and a systematic review**

**found no difference between donepezil and placebo in the proportion of people who withdrew for any cause**

A Cochrane systematic review identified sixteen trials, involving 4,365 participants, of donepezil for Alzheimer disease [1]. The trials were of 12, 24, or 52 weeks' duration, and they found that donepezil was associated with nausea, vomiting, and diarrhea, which tended to be mild and transient [2]. The review found no difference between donepezil and placebo in the proportion of people who withdrew for any cause [2]. In a long-term, open-label study of the efficacy and safety of donepezil for Alzheimer disease (conducted over almost five years), 86% of people taking donepezil ( $\leq 10$  mg) experienced at least one adverse effect, often occurring later in the study. Common adverse events included agitation (24%), pain (20%), insomnia (11%), and diarrhea (9%) [3].

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2. Warner JP, Butler R, Prabhakaran P (2003) Dementia. *Clin Evid* 9: 1010–1033.
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**Answer 5: There is no good evidence from trials with long follow-up of a beneficial effect in preventing or treating the disease**

There is no good evidence from randomized, controlled trials with long follow-up to support cognitive training as a way to prevent Alzheimer disease [1]. When improvements in cognitive tests are found with cognitive training, they are often modest, may not be maintained over time, and do not generalize beyond the skill being trained. In one randomized, controlled trial of cognitive training for older adults, though improvements in cognitive tests with training were maintained over two years, the training had no significant effect on measures of everyday functioning [2]. A Cochrane systematic review of cognitive rehabilitation and cognitive training for early-stage Alzheimer disease and vascular dementia found six randomized, controlled trials: none of the trials found any statistically significant effects on cognitive functioning [3].

**References**

1. Gatz M (2005) Educating the brain to avoid dementia: Can mental exercise prevent Alzheimer disease? *PLoS Med* 2: e7.
2. Ball K, Berch DB, Helmers KF, Jobe JB, Leveck MD, et al. (2002) Effects of cognitive training interventions with older adults: A randomized controlled trial. *JAMA* 288: 2271–2281.
3. Clare L, Woods RT, Moniz Cook ED, Orrell M, Spector A (2003) Cognitive rehabilitation and cognitive training for early-stage Alzheimer's disease and vascular dementia. *Cochrane Database Syst Rev* 2003: CD003260.

**Answer 6: None of the above**

One randomized, controlled trial compared four treatments: vitamin E ( $\alpha$ -tocopherol; 2,000 IU/day), selegiline, vitamin E plus selegiline, or placebo [1]. The trial found no significant difference in cognitive function with high-dose vitamin E alone for two years compared with placebo.

One randomized, controlled trial in people with Alzheimer disease found no significant difference in cognitive function after 25 weeks' treatment with diclofenac plus misoprostol compared with placebo [2]. Another trial found insufficient evidence to compare indomethacin versus placebo in people

with Alzheimer disease [3]. Yet another trial found no significant difference between naproxen or rofecoxib and placebo in cognitive function at one year [4].

One systematic review found no high-quality randomized, controlled trials on the effects of nicotine in people with dementia [5].

#### References

1. Sano M, Ernesto C, Thomas RG, Klauber MR, Schafer K, et al. (1997) A controlled trial of selegiline,  $\alpha$ -tocopherol, or both as treatment for Alzheimer's disease. *N Engl J Med* 336: 1216–1222.
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5. López-Arrieta JM, Rodríguez JL, Sanz F (2001) Nicotine for Alzheimer's disease. *Cochrane Database Syst Rev* 2001: CD001749.

#### Answer 7: Carbamazepine

In their systematic review of relevant randomized, controlled trials, Warner et al. concluded that carbamazepine is “likely to be beneficial,” while trazodone, sodium valproate, and donepezil are of “unknown effectiveness,” in treating the agitation associated with dementia [1].

One randomized controlled trial found that carbamazepine reduced agitation and aggression over six weeks compared with placebo in people with various types of dementia and behavioral and psychological symptoms [2].

One small randomized, controlled trial in people with Alzheimer disease and agitated behavior found no significant difference in outcomes over 16 weeks between trazodone, haloperidol, behavior management techniques, and placebo [3]. Another small randomized, controlled trial in people with agitated behavior associated with dementia found no significant difference in agitation over nine weeks between trazodone and haloperidol [4]. Both trials may have been underpowered to detect a clinically important difference.

One randomized, controlled trial found limited evidence that sodium valproate reduced agitation over six weeks compared with placebo in people with dementia plus behavioral and psychological problems [5]. But a second randomized, controlled trial found no significant difference in aggressive behavior over eight weeks between sodium valproate and placebo [6].

One randomized, controlled trial found that donepezil improved functional and behavioral symptoms at 24 weeks compared with placebo [7], but two other randomized, controlled trials found no significant difference in psychiatric symptoms at six months to one year between donepezil and placebo [8,9].

#### References

1. Warner JP, Butler R, Prabhakaran P (2003) Dementia. *Clin Evid* 9: 1010–1033.
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#### Answer 8: Lewy body dementia

Lewy body dementia involves insidious impairment of executive function with Parkinsonism, visual hallucinations, fluctuating cognitive abilities, and increased risk of falls or autonomic failure [1].

Multi-infarct dementia involves a stepwise deterioration in executive function with or without language and motor dysfunction. Patients usually have risk factors for atherosclerosis (such as diabetes, hypertension, and smoking). It tends to have a more sudden onset and stepwise progression than Alzheimer disease.

Alzheimer disease is characterized by an insidious onset and slow deterioration.

#### References

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#### Answer 9: 6 years

People with Lewy body dementia have an average life expectancy of about six years after diagnosis [1].

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#### Answer 10: There is insufficient evidence to state whether screening is beneficial or harmful

The United States Preventive Services Task Force systematically reviewed the evidence and concluded that the evidence is insufficient to recommend for or against routine screening for dementia in older adults in primary care [1]. The task force found good evidence that some screening tests have good sensitivity but only fair specificity in detecting cognitive impairment and dementia. There is fair to good evidence that several drug therapies have a beneficial effect on cognitive function, but the evidence of their beneficial effects on activities of daily living is mixed, with the benefit being small at best. There is insufficient evidence to determine whether the benefits observed in drug trials are generalizable to patients whose disease would be detected by screening in primary care settings. The accuracy of diagnosis, the feasibility of screening and treatment in routine clinical practice, and the potential harms of screening (for example, labeling effects) are also unknown. The task force therefore could not determine whether the benefits of screening for dementia outweigh the harms.

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