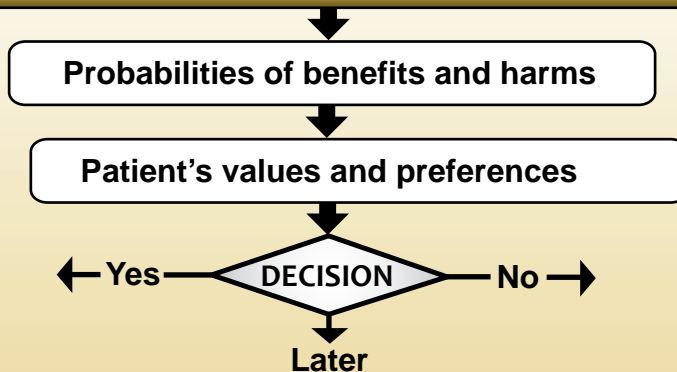


Cholinesterase inhibitors to reduce the symptoms of Alzheimer's disease



This document prepares the clinician to discuss scientific data with the patient so they can make an informed decision together.

Presenting cholinesterase inhibitors to patients

What are cholinesterase inhibitors for?

Cholinesterase inhibitors (ChEIs) are **medications taken daily** to modify the symptoms of Alzheimer's disease. These medications (donepezil, rivastigmine and galantamine) inhibit the breakdown of acetylcholine, an important neurotransmitter associated with memory, by blocking the enzyme acetylcholinesterase.

Who might consider taking this medication?

Individuals diagnosed with mild to moderate Alzheimer's disease.

Why do patient and carer preferences matter when making this decision?

▶ There are pros and cons to taking this medication:



PROS: 7% of individuals experience an improvement in global clinical state.¹

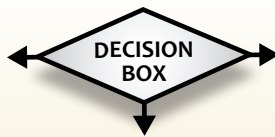
CONS: 10% of individuals discontinue treatment because of reversible side effects, such as **nausea and diarrhea**.¹

▶ Both taking and not taking the medication are acceptable options, so we propose that:

- ① The decision takes into account the **patient's and carer's values and preferences**
- ② The clinician **shares this decision with the patient and carer**

👉 Questions to identify the patient's decision making needs:

- ▶ Do you have any questions about the benefits and harms of each option?
- ▶ Which benefits and harms matter most to you?
- ▶ Do you feel sure about the best choice for you?
- ▶ Who will support and advise you in making a choice?



State of knowledge - November 2011

Selection of the best available studies

Benefits of medication

① Improves cognitive functioning

Individuals with Alzheimer's disease treated with cholinesterase inhibitors (ChEIs) improve on average:

- ▶ **2.7 points** on the Alzheimer's Disease and Associated Disorders Scale (ADAS-cog, range 0-70) compared to individuals receiving placebo.¹
- ▶ **1.4 points** on the Mini Mental State Examination score (range 0-30) compared to individuals receiving placebo.¹

② Improves global clinical state

For each 100 individuals with Alzheimer's disease who are treated with ChEIs, **7 more (7%)** experience improvements in their **global clinical state** (Clinician's Interview-Based Impression of Change scale, CIBIC-Plus) compared to 100 individuals receiving placebo.¹

③ Institutionalization

Institutionalization was not delayed in individuals with Alzheimer's disease after 3 years of treatment with ChEIs when compared to individuals receiving placebo.²

Harms of medication

① Side effects

For each 100 individuals with Alzheimer's disease who are treated with ChEIs, **15 more (15%)** experience an **adverse event** compared to 100 individuals receiving placebo.¹ The most common adverse events experienced are:

- ▶ nausea
- ▶ vomiting
- ▶ diarrhea
- ▶ anorexia
- ▶ headache
- ▶ syncope

② Intolerable side effects

For each 100 individuals with Alzheimer's disease who are treated with ChEIs, **10 more (10%)** experience **adverse events** that cause them to **discontinue treatment** compared to 100 individuals receiving placebo.¹

👉 How much confidence can we have in these results?

Cognitive functioning and global clinical state: **High** Results are founded on a systematic review of randomized controlled trials and are consistent across trials. Almost all included studies were industry sponsored and we cannot rule out an overestimation of beneficial effects.

Side effects: **Moderate** Results are founded on the same systematic review of randomized controlled trials and are slightly inconsistent across trials. Almost all included studies were industry sponsored and we cannot rule out an underestimation of adverse effects.

Institutionalization: **Low** Results are based on a single randomized controlled trial that was limited by a small sample size and a high attrition rate (40%). This study was not industry sponsored.

Study description and references:

1. **Birks.** Cochrane Database Syst Rev 2006, CD 005593(1).
Study design: systematic review of 13, multi-centre, randomized, double-blind parallel group trials comparing individuals treated with ChEIs (donepezil, galantamine and rivastigmine) versus placebo. **Participants:** 7,298 individuals from Europe, North America and Australia (mean age 73; range 49-94) with mild to severe dementia due to Alzheimer's disease. **Length of treatment:** Minimum of 6 months.
2. **AD 2000 Collaborative Group.** Lancet 2004, 363, 2105-152.
Study design: randomized controlled trial in the UK comparing the effects of ChEI treatment (donepezil) with a placebo on institutionalization and progression of Alzheimer's disease. **Participants:** 565 community-residents in the UK (median age 75) with mild to moderate Alzheimer's disease. **Length of treatment:** Minimum of 14 months.