

Is proton pump inhibitor use associated with risk of Alzheimer's disease?

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CONFLICT OF INTEREST DISCLOSURE

I have the following potential conflicts of interest to report

- Lecture fee from MSD
- Lecture fee form Professio

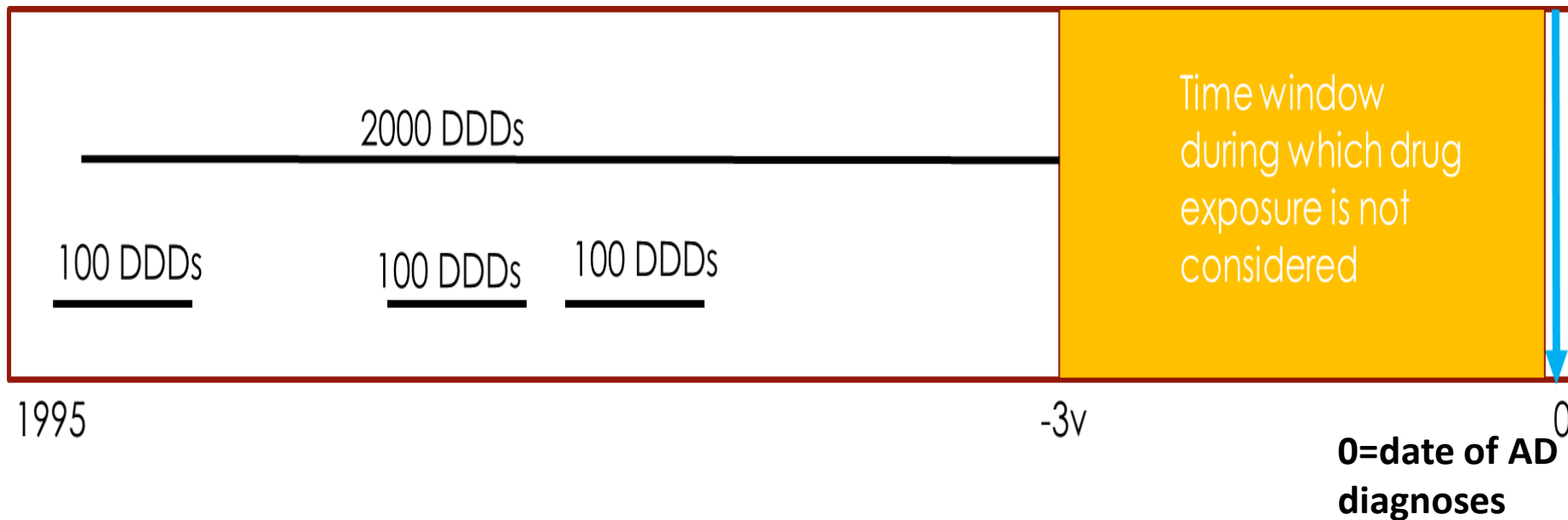
Objective

- To investigate whether PPI use is associated with an increased risk of incident, clinically verified Alzheimer's disease
 - Is there dose-response relationship and differences between specific PPIs

MEDALZ study

- Includes all community-dwelling persons diagnosed with Alzheimer's Disease (AD) during 2005-2011 in Finland N=70,718
 - Identified from Special Reimbursement register
- For a nested case-control design, up to four matched comparison persons without AD were identified for each case, N=282,858
 - Matched for age, gender and region of residence
 - Identified by Social Insurance Institution, from register including all residents

Study design – nested case-control study



Exposure and analyses

- Proton pump inhibitor (PPI) use
 - any use (ATC-code A02BC),
 - cumulative duration of use, cumulative amount per duration =dose
- Lag window for exposure: observation period for exposure ended 3 years before AD diagnosis in the main analyses
 - Sensitivity analysis with 5 year lag and without any lag window
- Conditional logistic regression analyses (matched design taken into account)

Results

- Persons with and without AD
 - 65% were female
 - Median age of persons with AD 80.8
- Use of PPIs was frequent among both groups, with no lag window
 - 44.1% of persons with AD used PPIs
 - 42.3% of comparison persons used PPIs

Results

Exposure	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Any use of PPIs before Alzheimer's Disease diagnoses		
No lag	1.08 (1.06-1.09)	1.02 (1.00-1.04)
3 year lag	1.06 (1.04-1.07)	1.03 (1.00-1.05)
5 year lag	1.07 (1.05-1.09)	1.05 (1.03-1.07)

Analyses adjusted for: cardiovascular diseases, diabetes, history of depression, history of stroke and number of drugs (0, 1-4, 5-9, ≥ 10), measured at the beginning of lag window

Results

– cumulative duration of use

Exposure	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
3 year lag window		
<1 year	1.06 (1.04-1.08)	1.03 (1.01-1.05)
1-3 years	1.05 (1.01-1.10)	1.01 (0.97-1.06)
≥3 years	1.02 (0.97-1.08)	0.99 (0.94-1.04)

Analyses adjusted for: cardiovascular diseases, diabetes, history of depression, history of stroke and number of drugs (0, 1-4, 5-9, ≥10), measured at the beginning of lag window

Results – dose

(in Defined Daily Doses DDDs/day)

Exposure	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
3 year lag window (cumulative purchased amount divided by duration of use), DDDs per day		
0.0001-0.4999	1.04 (0.98-1.10)	1.01 (0.96-1.07)
0.5-0.49999	1.05 (1.03-1.07)	1.02 (1.00-1.04)
1.0-1.49999	1.09 (0.95-1.18)	1.06 (1.02-1.10)
≥1.5	1.06 (0.95-1.18)	1.03 (0.92-1.14)

Analyses adjusted for: cardiovascular diseases, diabetes, history of depression, history of stroke and number of drugs (0, 1-4, 5-9, ≥10), measured at the beginning of lag window

Results – specific PPIs

Exposure	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
3 year lag window		
Omeprazole	1.06 (1.02-1.10)	1.03 (0.99-1.07)
Pantoprazole	1.03 (1.00-1.07)	1.01 (0.97-1.05)
Lansoprazole	1.07 (1.04-1.11)	1.05 (1.01-1.09)
Rabeprazole	1.08 (0.84-1.40)	1.06 (0.82-1.37)
Esomeprazole	1.00 (0.95-1.04)	0.98 (0.93-1.02)
Combination	1.07 (1.04-1.10)	1.04 (1.01-1.07)

Combination:
 use of two or
 more PPI
 drugs during
 the
 observation
 period

Analyses adjusted for: cardiovascular diseases, diabetes, history of depression, history of stroke and number of drugs (0, 1-4, 5-9, ≥10), measured at the beginning of lag window

Lack of dose response in both dose and duration of use underline the lack of medically meaningful association between proton pump inhibitor use Alzheimer's Disease.

When studying medication as a risk for Alzheimer's Disease, it is important use lag window and to do sensitivity analyses

CONCLUSION

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No Association Between Proton Pump Inhibitor Use and Risk of Alzheimer's Disease

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Thank you for your attention!



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MEDICATION USE &
ALZHEIMER'S DISEASE