

Supplementary Online Content

Gomm W, von Holt K, Thomé F, et al. Association of proton pump inhibitors with risk of dementia: a pharmacoepidemiological claims data analysis. *JAMA Neurol*. Published February 15, 2016. doi:10.1001/jamaneurol.2015.4791.

eTable 1. Regular and additional PPI use

eTable 2. Risk of incident any dementia, occasional PPI use

eTable 3. Risk of incident any dementia by omeprazole, pantoprazole, and esomeprazole use

eTable 4. Sample characteristics of omeprazole users and nonusers for Cox regression with time dependent covariates

eTable 5. Sample characteristics of pantoprazole users and nonusers for Cox regression with time dependent covariates

eTable 6. Sample characteristics of esomeprazole users and nonusers for Cox regression with time dependent covariates

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1: Regular and additional PPI use

PPI	Exposed (number)	Additional PPI	Additional PPI, exposed (number)	Additional PPI use, average no of quarters/person
all	2950			
Omeprazole	1340	Pantoprazole	69	1.2
		Esomeprazole	47	1.2
		Lansoprazole	3	2.0
		Rabeprazole	1	1.0
Pantoprazole	659	Omeprazole	46	1.2
		Esomeprazole	19	1.1
		Lansoprazole	4	1.0
		Rabeprazole	3	1.0
Esomeprazole	308	Omeprazole	15	1.5
		Pantoprazole	13	1.3
		Lansoprazole	2	1.0
		Rabeprazole	3	1.0
Lansoprazole	63	Omeprazole	3	2.0
		Pantoprazole	2	1.0
		Esomeprazole	1	1.0
		Rabeprazole	1	1.0
Rabeprazole	16	Omeprazole	1	1.0
		Pantoprazole	1	1.0
Mixed PPI use only	564			

eTable 2: Risk of incident any dementia, occasional PPI use

	Incident any dementia Hazard ratio (95% CI)	p value
PPI use ^{a,b}	1.16 (1.13,1.19)	<0.001
Age ^c	1.095 (1.093,1.097)	<0.001
Sex ^d	1.10 (1.08,1.13)	<0.001
Depression	1.31 (1.27,1.34)	<0.001
Diabetes	1.10 (1.07,1.12)	<0.001
Stroke	1.47 (1.40,1.55)	<0.001
Ischemic heart disease	0.94 (0.92,0.96)	<0.001
Polypharmacy ^e	1.14 (1.12,1.17)	<0.001
PPI use ^{a,f}	1.20 (1.17,1.23)	<0.001

^a Use of PPI before the diagnosis of dementia, occasional use: PPI prescription in less than six quarters within an interval

^b Calculation with potential confounding factors

^c In years at study begin 2004

^d Male (reference)

^e Defined as ≥ 5 drugs

^f Calculation without potential confounding factors

eTable 3: Risk of incident any dementia by Omeprazole, Pantoprazole, and Esomeprazole use

	Incident any dementia					
	Omeprazole		Pantoprazole		Esomeprazole	
	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
PPI use ^{a,b}	1.51 (1.40,1.64)	<0.001	1.58 (1.40,1.79)	<0.001	2.12 (1.82,2.47)	<0.001
Age ^c	1.084 (1.081,1.086)	<0.001	1.084 (1.081,1.086)	<0.001	1.084 (1.082,1.086)	<0.001
Sex ^d	1.15 (1.12,1.18)	<0.001	1.15 (1.11,1.18)	<0.001	1.15 (1.12,1.18)	<0.001
Depression	1.28 (1.24,1.33)	<0.001	1.29 (1.25,1.34)	<0.001	1.28 (1.24,1.33)	<0.001
Diabetes	1.05 (1.02,1.08)	<0.001	1.05 (1.02,1.08)	<0.001	1.05 (1.02,1.08)	<0.001
Stroke	1.38 (1.29,1.47)	<0.001	1.39 (1.30,1.48)	<0.001	1.38 (1.30,1.47)	<0.001
Ischemic heart disease	0.93 (0.91,0.96)	<0.001	0.93 (0.91,0.95)	<0.001	0.93 (0.91,0.95)	<0.001
Polypharmacy ^e	1.16 (1.13,1.19)	<0.001	1.16 (1.14,1.19)	<0.001	1.17 (1.14,1.20)	<0.001
PPI use ^{a,f}	1.81 (1.67,1.96)	<0.001	1.88 (1.66,2.12)	<0.001	2.40 (2.06,2.79)	<0.001

^a Use of PPI before the diagnosis of dementia

^b Calculation with potential confounding factors

^c In years at study begin 2004

^d Male (reference)

^e Defined as ≥ 5 drugs

^f Calculation without potential confounding factors

eTable 4: Sample characteristics of Omeprazole users and nonusers for Cox regression with time dependent covariates

	Incident any dementia ^a		p value ^b
	No use	use	
Omeprazole use ^c	70,729 (98.1%)	1,340 (1.9%)	
Age ^d	83.0 (5.6)	84.4 (5.5)	<0.001
Sex ^e	52,041 (73.6%)	1,038 (77.5%)	0.001
Depression	9,849 (13.9%)	266 (19.9%)	<0.001
Diabetes	23,063 (32.6%)	425 (31.7%)	0.49
Stroke	2,661 (3.8%)	59 (4.4%)	0.22
Ischemic heart disease	26,739 (37.8%)	535 (39.9%)	0.11
Polypharmacy ^f	37,564 (53.1%)	1,023 (76.3%)	<0.001

^a Sample characteristics include demented and non-demented patients

^b Results of *t*-test or Chi-square test for group comparison

^c Omeprazole use in at least one interval

^d In years (SD) at study begin 2004

^e Female

^f Defined as ≥ 5 drugs

eTable 5: Sample characteristics of Pantoprazole users and nonusers for Cox regression with time dependent covariates

	Incident any dementia ^a		p value ^b
	No use	use	
Pantoprazole use ^c	70,729 (99.1%)	659 (0.9%)	
Age ^d	83.0 (5.6)	83.8 (5.4)	<0.001
Sex ^e	52,041 (73.6%)	518 (78.6%)	0.004
Depression	9,849 (13.9%)	117 (17.8%)	0.005
Diabetes	23,063 (32.6%)	229 (34.8%)	0.24
Stroke	2,661 (3.8%)	31 (4.7%)	0.21
Ischemic heart disease	26,739 (37.8%)	295 (44.8%)	<0.001
Polypharmacy ^f	37,564 (53.1%)	523 (79.4%)	<0.001

^a Sample characteristics include demented and non-demented patients

^b Results of *t*-test or Chi-square test for group comparison

^c Pantoprazole use in at least one interval

^d In years (SD) at study begin 2004

^e Female

^f Defined as ≥ 5 drugs

eTable 6: Sample characteristics of Esomeprazole users and nonusers for Cox regression with time dependent covariates

	Incident any dementia ^a		p value ^b
	No use	use	
Esomeprazole use ^c	70,729 (99.6%)	308 (0.4%)	
Age ^d	83.0 (5.6)	83.9 (5.2)	0.005
Sex ^e	52,042 (73.6%)	236 (76.6%)	0.23
Depression	9,849 (13.9%)	45 (14.6%)	0.73
Diabetes	23,063 (32.6%)	83 (27.0%)	0.035
Stroke	2,661 (3.8%)	17 (5.5%)	0.11
Ischemic heart disease	26,739 (37.8%)	116 (37.7%)	0.96
Polypharmacy ^f	37,565 (53.1%)	225 (73.1%)	<0.001

^a Sample characteristics include demented and non-demented patients

^b Results of *t*-test or Chi-square test for group comparison

^c Esomeprazole use in at least one interval

^d In years (SD) at study begin 2004

^e Female

^f Defined as ≥ 5 drugs