Quoi de neuf en gériatrie …
… sur les maladies neurocognitives

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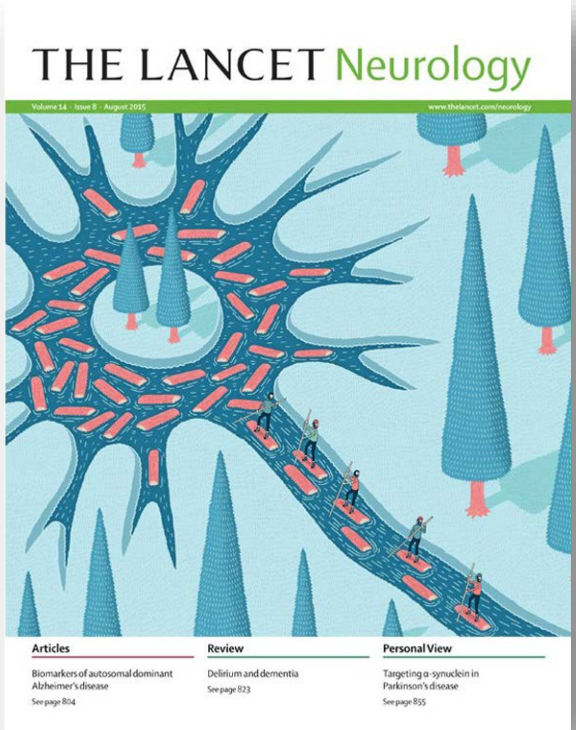
Epidémiologie de la maladie de Parkinson



Review

The epidemiology of Parkinson's disease: risk factors and prevention

Alberto Ascherio, Michael A Schwarzschild

Since 2006, several longitudinal studies have assessed environmental or behavioural factors that seem to modify the risk of developing Parkinson's disease. Increased risk of Parkinson's disease has been associated with exposure to pesticides, consumption of dairy products, history of melanoma, and traumatic brain injury, whereas a reduced risk has been reported in association with smoking, caffeine consumption, higher serum urate concentrations, physical activity, and use of ibuprofen and other common medications. Randomised trials are investigating the possibility that some of the negative risk factors might be neuroprotective and thus beneficial in individuals with early Parkinson's disease, particularly with respect to smoking (nicotine), caffeine, and urate. In the future, it might be possible to identify Parkinson's disease in its prodromal phase and to promote neuroprotective interventions before the onset of motor symptoms. At this time, however, the only intervention that seems justifiable for the primary prevention of Parkinson's disease is the promotion of physical activity, which is likely to be beneficial for the prevention of several chronic diseases.

Lancet Neurol 2016; 15: 1257–72

Departments of Epidemiology and Nutrition, Harvard T H Chan School of Public Health, Boston, MA, USA (Prof A Ascherio MD); Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA, USA (Prof A Ascherio); and Department of Neurology, Massachusetts General

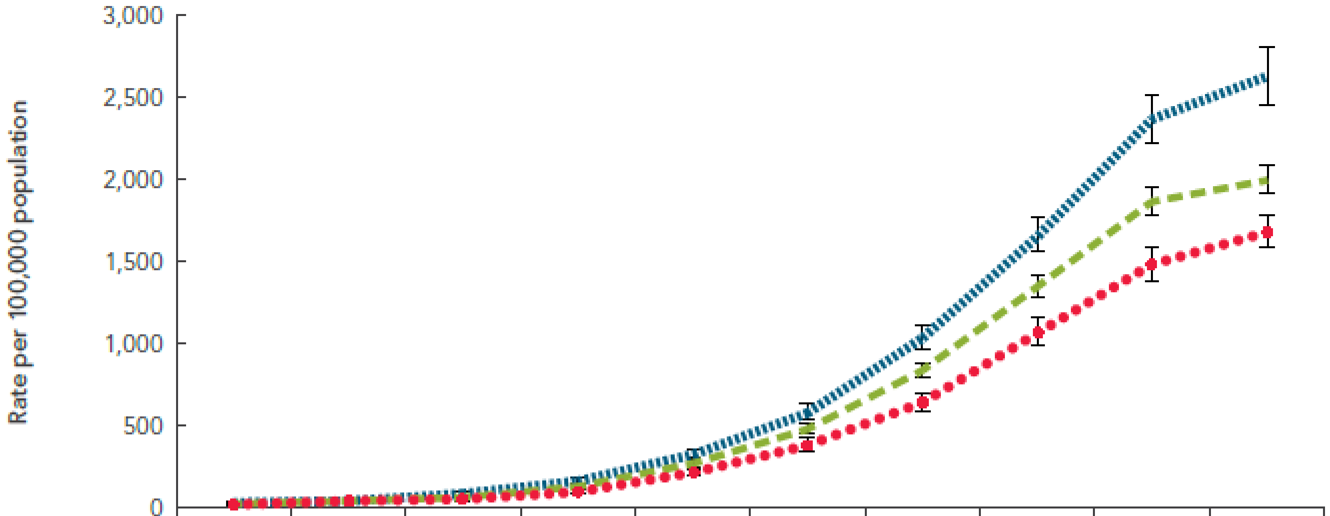
Ascherio A, Lancet Neurol 2016

Une revue systématique : MP idiopathique

- Etudes longitudinales depuis 2006
- Incidence annuelle : 160 cas pour 100 000 personnes > 65 ans
- Risque vie entière = 2% chez les hommes, 1,3% chez les femmes

Parkinson = $\frac{\text{Alzheimer}}{10}$

Europe = Amériques = Asie >> Afrique



	40 to 44	45 to 49	50 to 54	55 to 59	60 to 64	65 to 69	70 to 74	75 to 79	80 to 84	85+
Women	18	36	49	94	212	383	641	1,067	1,484	1,679
Men	27	46	83	161	327	575	1,036	1,653	2,365	2,623
Both	23	41	66	127	269	478	834	1,346	1,863	1,996

Age group (years)

Les facteurs de risque et de protection

RISQUE

- Pesticides
- Laitages
- Mélanome
- Trauma cranien

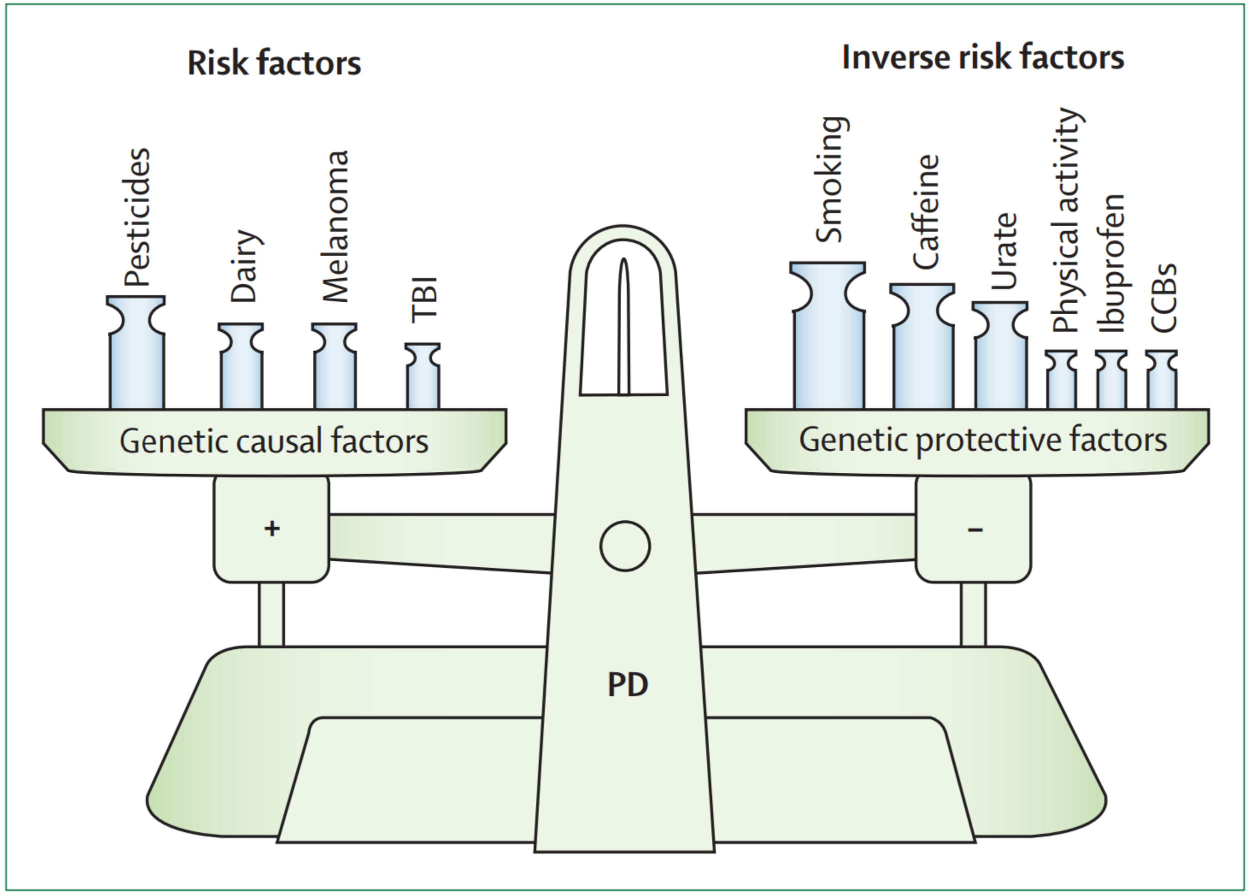


Figure 4: The balance of genetic and environmental factors that underlie Parkinson's disease occurrence

PROTECTION

- Tabagisme
- Café
- Uricémie
- Activité physique
- Ibuprofène
- Antagonistes calciques

Chen et al. BMC Complementary and Alternative Medicine (2017) 17:178
DOI 10.1186/s12906-017-1677-4

BMC Complementary and Alternative Medicine

RESEARCH ARTICLE Open Access

Association of traditional Chinese medicine therapy and the risk of dementia in patients with hypertension: a nationwide population-based cohort study

Kuen-Hau Chen[1], Ming-Hsien Yeh[1,2,3], Hanoch Livneh[4], Bor-Chyuan Chen[1], I-Hsin Lin[2], Ming-Chi Lu[5,6], Tzung-Yi Tsai[7,8,9*] and Chia-Chou Yeh[1,2,3*]

Une étude de population à Taiwan

- 143 383 personnes de 20-90 ans avec diagnostic récent d'HTA
- Suivi moyen de 15 ans ➔ incidence de la démence
- Etude de cette incidence en fonction de l'utilisation ou non de médecines traditionnelles chinoises à l'entrée dans l'étude

Table 1 Demographic data and selected comorbidities of the study subjects

Variables	Non-TCM users *n* = 91,017 (%)	TCM users *n* = 52,365 (%)	*P*-value
Age (yr)			<0.001
≤50	22,971 (25.2)	16,461(31.4)	
>50	68,046 (74.8)	35,904 (68.6)	
Mean (SD)	59.74 (13.6)	57.19 (12.4)	<0.001
Gender			<0.001
Female	40,794 (44.8)	29,597(56.5)	
Male	50,223(55.2)	22,768 (43.5)	
Monthly income			<0.001
Low	39,976(43.9)	21,506 (41.1)	
Median	46,352 (50.9)	28,123 (53.7)	
High	4689 (5.2)	2736 (5.2)	
Residential area			<0.001
Urban	49,720(54.6)	29,629 (56.6)	
Suburban	14,209(15.6)	8426 (16.1)	
Rural	27,088(29.8)	14,310 (27.3)	
Tobacco use			0.002
Yes	352 (0.4)	150 (0.3)	
No	90,665 (99.6)	52,215 (99.7)	
CCI			<0.001
Mean (SD)	3.50 (4.42)	4.23 (7.03)	

TCM Traditional Chinese Medicine, *SD*, standard deviation; *CCI* Charlson-Deyo comorbidity index

L'usage de médecine traditionnelle chinoise est associé à une diminution de 27% du risque de démence

Table 2 Risk of dementia for HTN subjects with and without TCM

Patient group	Event	PYs	Incidence	Crude HR (95% CI)
Non-TCM users	10,316	892,960.27	11.55	1
TCM users	3933	467,500.55	8.41	0.73(0.71–0.76)
TCM use within 30–180 days	2706	289,829.43	9.34	0.82 (0.78–0.85)
TCM use for more than 180 days	1277	177,671.13	6.91	0.60 (0.57–0.64)

TCM Traditional Chinese Medicine, *PYs* per 1000 person-years, *HR* hazard ratio, *CI* confidence interval
[a]Model adjusted for age, gender, urbanization level, monthly income, and CCI scores

Risque de démence en fonction du type de médecine traditionnelle chinoise

Table 5 Risk of dementia in relation to the top 15 commonly used TCMs

TCM name	Crude HR (95% CI)	Adjusted HR[j] (95% CI)	
Tian-Ma-Gou-Teng-Yin [a,c,d,e,f,g,h,i]	0.77 (0.68–0.86)	0.82 (0.76–0.95)[k]	*
Dan-Shen [a,d,e,f,g,h,i]	0.71 (0.61–0.83)	0.80 (0.69–0.92)[k]	*
Gou-Teng-San	0.78 (0.65–0.92)	0.90 (0.74–1.07)	
Gou-Teng	0.75 (0.61–0.90)	0.89 (0.75–1.08)	
Xia-Ku-Cao	0.70 (0.56–0.86)	0.79 (0.60–1.02)	
Zhi-Bai-Di-Huang-Wan	0.88 (0.68–1.10)	0.97 (0.76–1.23)	
Da-Huang	0.89 (0.67–1.15)	0.92 (0.70–1.20)	
Xue-Fu-Zhu-Yu-Tang	0.82 (0.67–0.99)	0.91 (0.75–1.21)	
Chuan-Niu-Xi [e,f,i]	0.73 (0.58–0.92)	0.79 (0.62–0.98)[k]	*
Ge-Gen [a,b,f,g,h,i]	0.62 (0.43–0.79)	0.65 (0.52–0.83)[k]	*
Qi-Ju-Di-Huang-Wan	0.87 (0.68–1.12)	0.85 (0.66–1.09)	
San-Qi	0.85 (0.66–1.10)	0.89 (0.69–1.19)	
Tian-Ma	0.98 (0.79–1.22)	0.96 (0.77–1.19)	
Jia-Wei-Xiao-Yao-San [a,b,i]	0.70 (0.54–0.91)	0.79 (0.64–0.98)[k]	*
Jue-Ming-Zi [a,e,h,i]	0.57 (0.41–0.80)	0.68 (0.49–0.96)[k]	*

Un effet gradient associé à la durée

Table 2 Risk of dementia for HTN subjects with and without TCM

Patient group	Event	PYs	Incidence	Crude HR (95% CI)	Adjusted HR[a] (95% CI)
Non-TCM users	10,316	892,960.27	11.55	1	1
TCM users	3933	467,500.55	8.41	0.73(0.71–0.76)	0.76 (0.74–0.81)
TCM use within 30–180 days	2706	289,829.43	9.34	0.82 (0.78–0.85)	0.86 (0.82–0.90)
TCM use for more than 180 days	1277	177,671.13	6.91	0.60 (0.57–0.64)	0.65 (0.62–0.69)

TCM Traditional Chinese Medicine, *PYs* per 1000 person-years, *HR* hazard ratio, *CI* confidence interval
[a]Model adjusted for age, gender, urbanization level, monthly income, and CCI scores

Les plus fortement associées à la réduction du risque

-35%

Ge-gen

-33%

Jue-Ming-Zi

-31%

Xia-Ku-Cao

Effect of long-term omega 3 polyunsaturated fatty acid supplementation with or without multidomain intervention on cognitive function in elderly adults with memory complaints (MAPT): a randomised, placebo-controlled trial

*Sandrine Andrieu, Sophie Guyonnet, Nicola Coley, Christelle Cantet, Marc Bonnefoy, Serge Bordes, Lawrence Bories, Marie-Noëlle Cufi, Thierry Dantoine, Jean-François Dartigues, Françoise Desclaux, Audrey Gabelle, Yannick Gasnier, Alain Pesce, Kristel Sudres, Jacques Touchon, Philippe Robert, Olivier Rouaud, Philippe Legrand, Pierre Payoux, Jean-Paul Caubere, Michael Weiner, Isabelle Carrié, Pierre-Jean Ousset, Bruno Vellas, for the MAPT Study Group**

Summary

Background No large trials have been done to investigate the efficacy of an intervention combining a specific compound and several lifestyle interventions compared with placebo for the prevention of cognitive decline. We tested the effect of omega 3 polyunsaturated fatty acid supplementation and a multidomain intervention (physical activity, cognitive training, and nutritional advice), alone or in combination, compared with placebo, on cognitive decline

Lancet Neurol 2017; 16: 377–89

Published **Online**
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http://dx.doi.org/10.1016/S1474-4422(17)30040-6

Un essai randomisé sur 1525 personnes > 70 ans

- Plainte mnésique ou vitesse de marche diminuée ou bien limitation d'une activité de la vie quotidienne
- Randomisation en 4 groupes :
  - Supplémentation en oméga3 sans intervention multidomaine
  - Supplémentation en oméga3 avec intervention multidomaine
  - Placebo sans intervention multidomaine
  - Placebo avec intervention multidomaine
- Suivi de 3 ans avec test cognitifs

Intervention multidomaine = stimulation cognitive, conseils diététiques, consultations de prévention, conseils sur l'activité physique

Population de l'étude

	Multidomain plus polyunsaturated fatty acids (n=374)	Multidomain plus placebo (n=390)	Polyunsaturated fatty acids (n=381)	Placebo (n=380)	Overall (n=1525)
Age, years	75·4 (4·4)	75·0 (4·1)	75·6 (4·7)	75·1 (4·3)	75·3 (4·4)
Female sex	229 (61%)	252 (65%)	245 (64%)	252 (66%)	978 (64%)
Education					
No diploma or primary school certificate	75 (20%)	81 (21%)	96 (26%)	82 (22%)	334 (22%)
Secondary education	145 (39%)	129 (33%)	120 (33%)	117 (31%)	511 (34%)
High school diploma	52 (14%)	56 (15%)	43 (12%)	67 (18%)	218 (15%)
University level	100 (27%)	120 (31%)	108 (29%)	110 (29%)	438 (29%)
APOE ε4	71 (23%)	76 (24%)	64 (21%)	76 (24%)	287 (23%)
Composite score (mean Z score)	−0·04 (0·68)	0·00 (0·71)	0·03 (0·63)	0·02 (0·66)	0·00 (0·67)
Mini Mental State Examination	28·15 (1·57)	28·05 (1·62)	28·14 (1·60)	28·10 (1·53)	28·11 (1·58)
Clinical dementia rating					
0	223 (60%)	224 (57%)	220 (58%)	220 (58%)	887 (58%)
0·5	151 (40%)	166 (43%)	160 (42%)	160 (42%)	637 (42%)

Conclusion

- Pas d’effet significatif pour prévenir le déclin cognitif
  - Ni avec oméga3
  - Ni avec l’intervention multidomaine

“Interpretation The multidomain intervention and polyunsaturated fatty acids, either alone or in combination, had no significant effects on cognitive decline over 3 years in elderly people with memory complaints.

THE LANCET

Pollution atmosphérique et risque de maladies neurologiques

2 cohortes de population vivant en Ontario en 2001 depuis plus de 5 ans et suivies pour étudier l'incidence de la SEP, de la maladie de Parkinson et de la démence.

Living near major roads and the incidence of dementia, Parkinson's disease, and multiple sclerosis: a population-based cohort study

Hong Chen, Jeffrey C Kwong, Ray Copes, Karen Tu, Paul J Villeneuve, Aaron van Donkelaar, Perry Hystad, Randall V Martin, Brian J Murray, Barry Jessiman, Andrew S Wilton, Alexander Kopp, Richard T Burnett

Lancet 2017; 389: 718–26

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See Comment page 675

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Summary

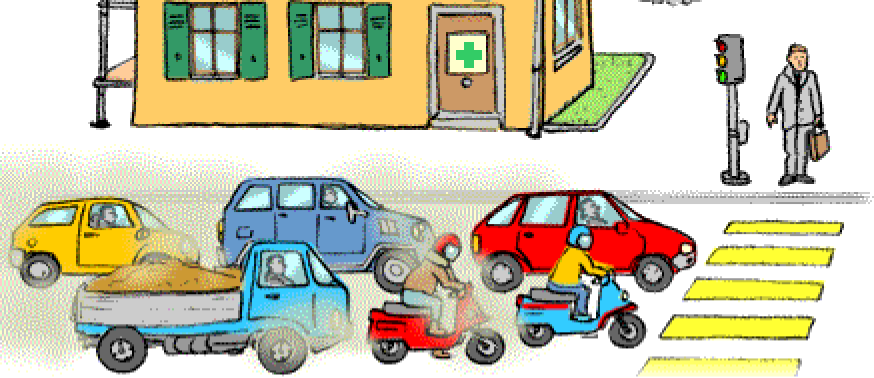
Background Emerging evidence suggests that living near major roads might adversely affect cognition. However, little is known about its relationship with the incidence of dementia, Parkinson's disease, and multiple sclerosis. We aimed to investigate the association between residential proximity to major roadways and the incidence of these three neurological diseases in Ontario, Canada.

Methods In this population-based cohort study, we assembled two population-based cohorts including all adults aged 20–50 years (about 4·4 million; multiple sclerosis cohort) and all adults aged 55–85 years (about 2·2 million; dementia or Parkinson's disease cohort) who resided in Ontario, Canada on April 1, 2001. Eligible patients were free of these neurological diseases, Ontario residents for 5 years or longer, and Canadian-born. We ascertained the individual's proximity to major roadways based on their residential postal-code address in 1996, 5 years before cohort inception. Incident diagnoses of dementia, Parkinson's disease, and multiple sclerosis were ascertained from provincial health administrative databases with validated algorithms. We assessed the associations between traffic proximity and incident dementia, Parkinson's disease, and multiple sclerosis using Cox proportional hazards models, adjusting for individual and contextual factors such as diabetes, brain injury, and neighbourhood income. We did various sensitivity analyses, such as adjusting for access to neurologists and exposure to selected air pollutants, and restricting to never movers and urban dwellers.

Findings Between 2001, and 2012, we identified 243 611 incident cases of dementia, 31 577 cases of Parkinson's disease, and 9247 cases of multiple sclerosis. The adjusted hazard ratio (HR) of incident dementia was 1·07 for people living less than 50 m from a major traffic road (95% CI 1·06–1·08), 1·04 (1·02–1·05) for 50–100 m, 1·02 (1·01–1·03) for 101–200 m, and 1·00 (0·99–1·01) for 201–300 m versus further than 300 m (*p* for trend=0·0349). The associations were robust to sensitivity analyses and seemed stronger among urban residents, especially those who lived in major cities (HR 1·12, 95% CI 1·10–1·14 for people living <50 m from a major traffic road), and who never moved (1·12, 1·10–1·14 for people living <50 m from a major traffic road). No association was found with Parkinson's disease or multiple sclerosis.

Population étudiée

	Multiple sclerosis cohort* (n=4 372 720)		Dementia/Parkinson's disease cohort* (n=2 165 268)	
	Subject count	%	Subject count	%
Age at entry (years); mean (SD)	35·9 (8·7)	··	66·8 (8·2)	··
20–29	1 198 499	27·4	··	··
30–39	1 475 303	33·7	··	··
40–50	1 698 918	38·9	··	··
55–64	··	··	978 235	45·2
65–74	··	··	731 685	33·8
75–85	··	··	455 348	21·0
Sex				
Male	2 178 448	49·8	1 013 010	46·8
Female	2 194 272	50·2	1 152 258	53·2



Incidence de la démence

	Main model ‡		Indirectly adjusted for smoking		Further indirectly adjusted for BMI, physical activity		Further indirectly adjusted for education	
	Hazard ratio	95% CI	Hazard ratio	95% CI	Hazard ratio	95% CI	Hazard ratio	95% CI
Distance† by category								
<50 m	1·07	1·06–1·08	1·06	1·05–1·08	1·06	1·05–1·08	1·06	1·05–1·08
50–100 m	1·04	1·02–1·05	1·03	1·02–1·05	1·03	1·02–1·05	1·04	1·02–1·06
101–200 m	1·02	1·01–1·03	1·01	1·00–1·02	1·01	1·00–1·03	1·02	1·01–1·04
201–300 m	1·00	0·99–1·01	1·00	0·98–1·01	1·00	0·99–1·02	1·01	0·99–1·03
>300 m	Reference	..	Reference	..	Reference	..	Reference	..
Log (distance)§	0·91	0·89–0·92	0·92	0·90–0·93	0·92	0·90–0·93	0·92	0·90–0·93

Indirect adjustment for smoking, body-mass index (BMI), physical activity, and attained education. Data of smoking, BMI, physical activity, and educational attainment were obtained from Ontario respondents to the 1996 cycle of National Population Health Survey and the 2000–01, 2003 cycles of Canadian Community Health Survey, and who were 50 to 85 years old at the time of the surveys (n=16 441). †Major traffic roads include primary urban roads and arterial roads whereas highways include expressways and primary and secondary highways, as defined by Ontario Government Road Network Data Standards. ‡Cox proportional hazards model with age as time axis, stratified by an indicator for living in the Greater Toronto Area or not, adjusted for sex, history of diabetes, hypertension, coronary heart disease, stroke, congestive heart failure, arrhythmia, and traumatic brain injury, income quintile, urban/rural indicator, census division-level unemployment, education, and recent immigrants, as well as the subtraction of these variables at the census dissemination level from their census division. §Distance was fitted as a continuous variable, using natural logarithm of distance. The hazard ratios were expressed per interquartile-range increase in distance (310 m).

***Table 3*: Hazard ratios and 95% CI for associations between residential proximity to major roadways in 1996 and the risk of incident dementia in Ontario during the follow-up period 2001–12**

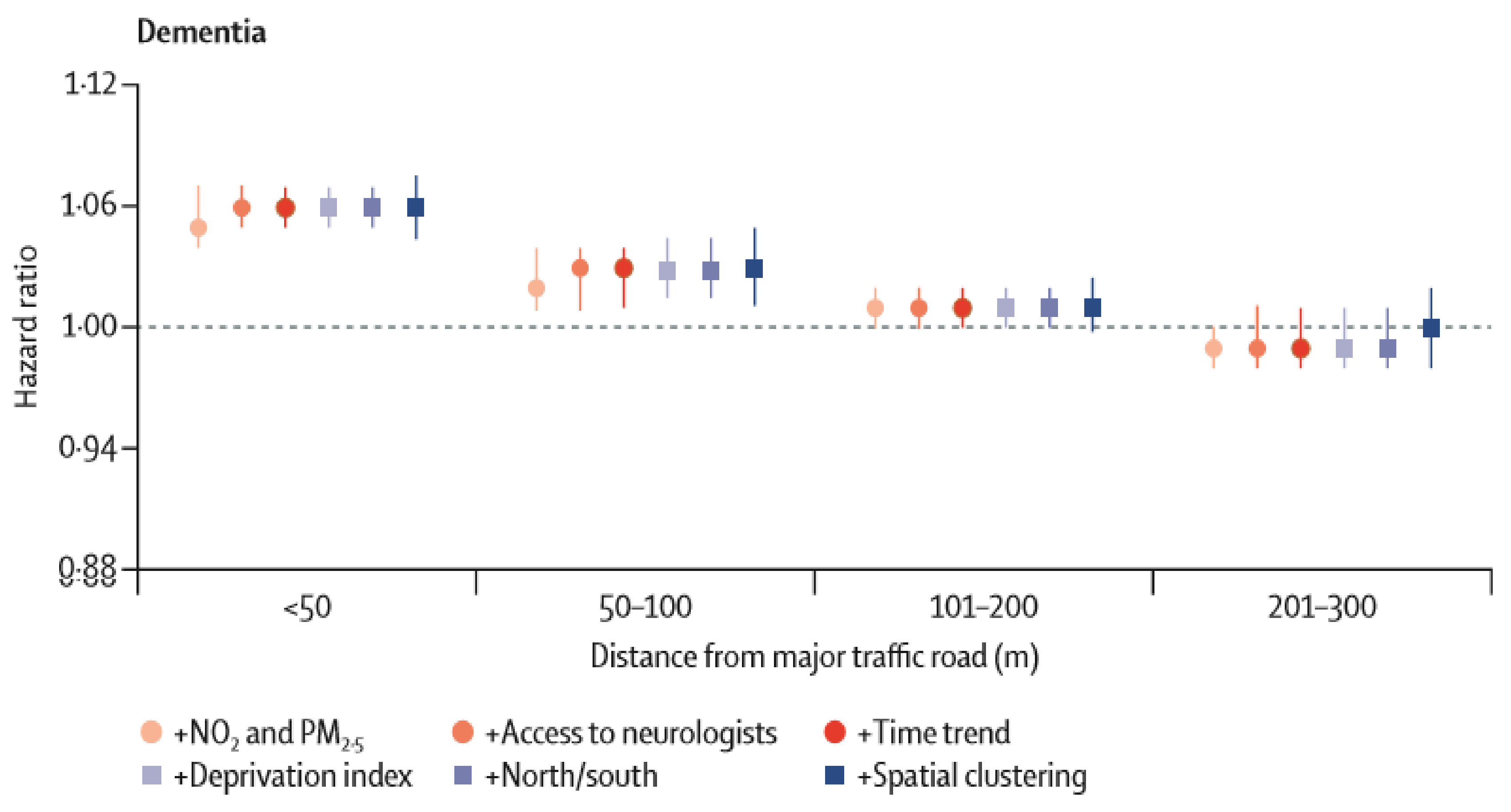
Incidences de la maladie de Parkinson et de la SEP

	Parkinson's disease				Multiple sclerosis			
	Main model‡		Indirectly adjusted for smoking and physical activity‖		Main model‡		Indirectly adjusted for smoking‖	
	Hazard ratio	95% CI	Hazard ratio	95% CI	Hazard ratio	95% CI	Hazard ratio	95% CI
Distance† by category								
<50 m	1·01	0·98–1·04	1·01	0·98–1·05	1·02	0·95–1·09	1·00	0·93–1·07
50–100 m	1·01	0·97–1·05	1·02	0·98–1·06	0·93	0·86–1·01	0·93	0·86–1·01
101–200 m	0·99	0·96–1·03	0·99	0·96–1·03	1·01	0·95–1·08	1·00	0·93–1·06
201–300 m	0·99	0·96–1·02	1·00	0·97–1·03	1·01	0·94–1·08	1·00	0·93–1·07
>300 m	Reference	..	Reference	..	Reference	..	Reference	..
Log (distance)§	0·99	0·97–1·01	1·00	0·98–1·02	1·00	0·98–1·02	0·99	0·97–1·02

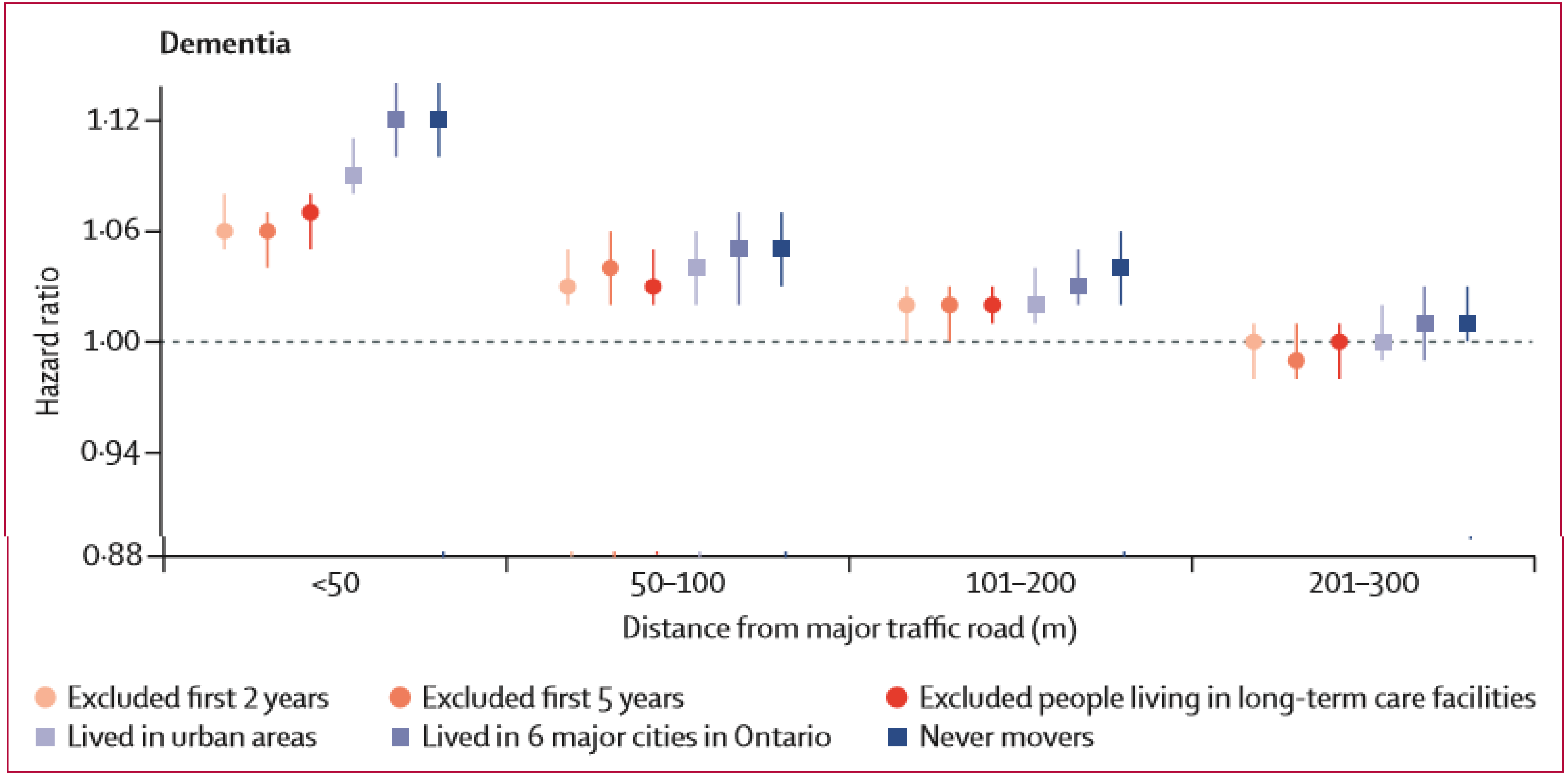
Indirect adjustment for smoking and physical activity for Parkinson's disease, and for smoking for multiple sclerosis. Data of smoking and physical activity were obtained from Ontario respondents to the 1996 cycle of National Population Health Survey and the 2000–01 and 2003 cycles of Canadian Community Health Survey. For Parkinson's disease, respondents aged 50–85 years at the time of the surveys were included (n=16 441) and for multiple sclerosis, those who were 20–55 years old were included (n=31 635). †Major traffic roads include primary urban roads and arterial roads whereas highways include expressways and primary and secondary highways, as defined by Ontario Government Road Network Data Standards. ‡Cox proportional hazards model with age as time axis, stratified by an indicator for living in the Greater Toronto Area or not, adjusted for sex, history of diabetes, hypertension, coronary heart disease, stroke, congestive heart failure, arrhythmia, and traumatic brain injury, income quintile, urban/rural indicator, census division-level unemployment, education, and recent immigrants, as well as the subtraction of these variables at the census dissemination level from their census division. For multiple sclerosis, the model was also adjusted for latitude. §Distance was fitted as a continuous variable, using natural logarithm of distance. HRs expressed per interquartile-range increase in distance (dementia/Parkinson's disease cohort: 310 m and multiple sclerosis cohort: 320 m). ‖For Parkinson's disease, p_{trend}=0·38 and for multiple sclerosis, p_{trend}=0·53.

Table 4**: Hazard ratios and 95% CI for associations between residential proximity to major roadways in 1996 and risk of incident Parkinson's disease and multiple sclerosis in Ontario, during the follow-up period 2001–12**

Relation robuste / facteurs confondants



Risque accru pour ceux qui ont résidé plus longtemps

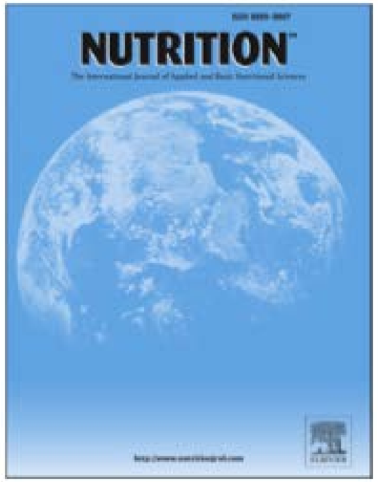


Conclusion

- Vivre près de routes à fort trafic est associé à une augmentation du risque de démence
- Notamment si < 50 m, centres urbains, et si pas de déménagements
- Pas d'association avec le risque … nson ou de

Mécanismes d'action et hypothèses ➔

- Exposition au gaz d'échappement
- Particules fines, oxides nitriques, particules / friction des pneus
- Bruit
- Inflammation + stress oxydant liés à l'exposition à ces polluants



Nutrition 32 (2016) 628–636

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Meta-analysis

Habitual coffee consumption and risk of cognitive decline/dementia: A systematic review and meta-analysis of prospective cohort studies

Qing-Ping Liu M.D. [a,b], Yan-Feng Wu M.D. [a,b], Hong-Yu Cheng M.D. [a], Tao Xia M.D. [c], Hong Ding M.D. [b], Hui Wang M.D. [b], Ze-Mu Wang M.D. [d], Yun Xu M.D., Ph.D. [a,*]

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Liu QP, Nutrition 2016

Revue systématique de littérature

- Liens entre consommation de café et santé cognitive
- 11 études retenues dans l'étude < == > 29 155 personnes

Déclin cognitif

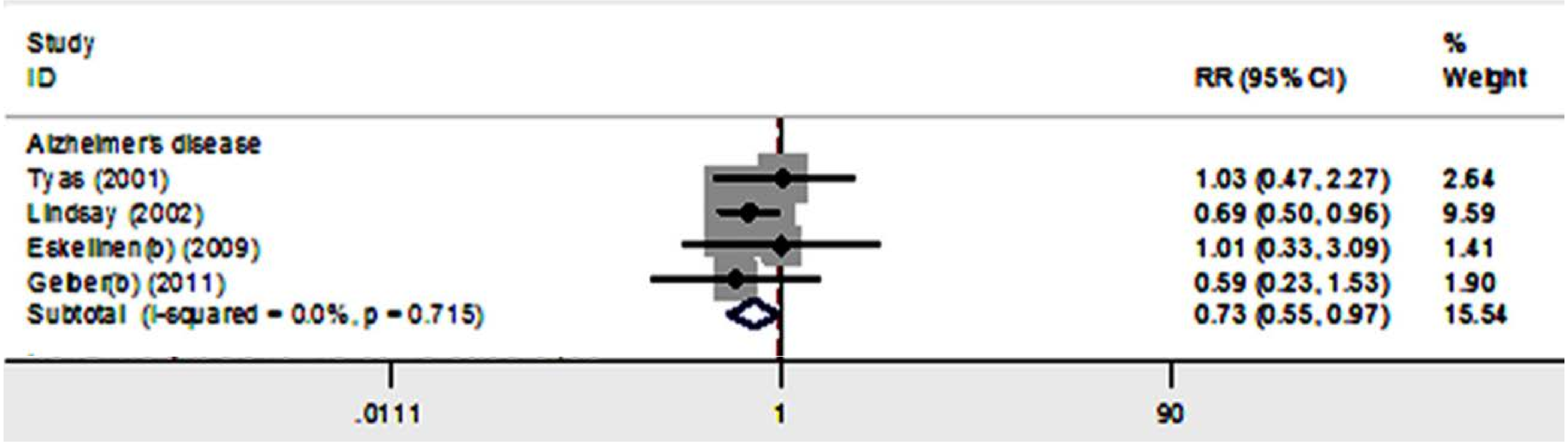
Démence

Mild cognitive impairment

Alzheimer

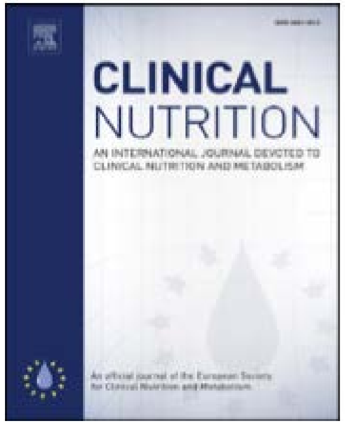
Démence vasculaire

Une consommation forte de café est associée à un risque diminué de maladie d'Alzheimer



Pas de relation avec démence vasculaire, MCI, déclin cognitif

Café = -27% Alzheimer



Clinical Nutrition 36 (2017) 730–736

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Meta-analyses

Coffee intake and the incident risk of cognitive disorders: A dose–response meta-analysis of nine prospective cohort studies

Lei Wu [a, b], Dali Sun [c], Yao He [a, b, d, *]

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[b] Beijing Key Laboratory of Aging and Geriatrics, Chinese PLA General Hospital, China
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[d] State Key Laboratory of Kidney Disease, Chinese PLA General Hospital, China

Wu L, Clin Nutrition 2017

Une ou deux tasses

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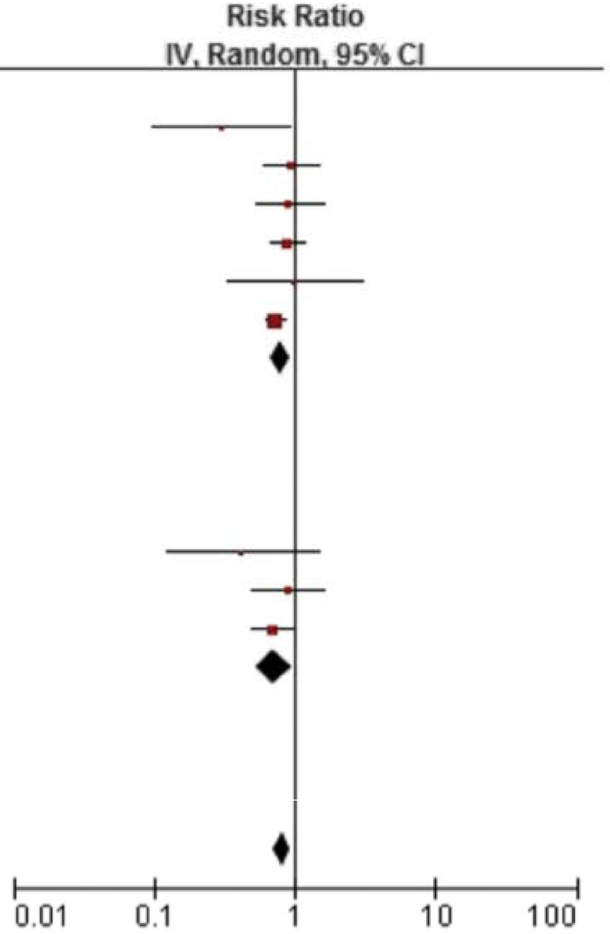
Diminution du risque de 22% par rapport aux non consommateurs

Study or Subgroup	Weight	Risk Ratio IV, Random, 95% CI
Dementia		
Eskelinen, 2009	1.4%	0.30 [0.10, 0.93]
Gelber, 2011	7.2%	0.93 [0.59, 1.46]
Laitala, 2009	5.2%	0.91 [0.52, 1.58]
Mirza, 2014	14.3%	0.88 [0.67, 1.16]
Noguchi-Shinohara, 2014	1.5%	1.00 [0.33, 2.99]
Sugiyama, 2016	22.8%	0.72 [0.61, 0.84]
Subtotal (95% CI)	**52.5%**	**0.78 [0.67, 0.91]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.53$, df = 5 (P = 0.35); $I^2 = 10\%$		
Test for overall effect: Z = 3.23 (P = 0.001)		
Alzheimer's disease		
Eskelinen, 2009	1.2%	0.42 [0.12, 1.46]
Gelber, 2011	4.8%	0.89 [0.50, 1.59]
Lindsay, 2002	11.4%	0.69 [0.50, 0.96]
Subtotal (95% CI)	**17.3%**	**0.71 [0.54, 0.94]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.29$, df = 2 (P = 0.52); $I^2 = 0\%$		
Test for overall effect: Z = 2.37 (P = 0.02)		
Total (95% CI)	**100.0%**	**0.82 [0.71, 0.94]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 17.34$, df = 13 (P = 0.18); $I^2 = 25\%$		
Test for overall effect: Z = 2.91 (P = 0.004)		
Test for subgroup differences: $Chi^2 = 2.31$, df = 3 (P = 0.51), $I^2 = 0\%$		



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