Les complications cardiovasculaires VII

- Les controverses
  - Théorie du cholestérol
- Les nouveaux facteurs de risque (non pris en considération dans les scores)
  - Tabagisme passif
  - Pollution atmosphérique
  - Stress
  - Horaires de travail long
  - IMC à l'adolescence
  - Origine développementale
  - Médicaments
  - Syndrome d'apnées obstructives du sommeil (SAS)
  - Covid

Les controverses

L'athéromatose n'est pas une maladie propre à notre civilisation

Atherosclerosis across 4000 years of human history: the Horus study of four ancient populations

Randall C Thompson, Adel H Allam, Guido P Lombardi, L Samuel Wann, M Linda Sutherland, James D Sutherland, Muhammad Al-Tohamy Soliman, Bruno Frohlich, David T Mininberg, Janet M Monge, Clide M Vallodolid, Samantha L Cox, Gomaa Abd el-Maksoud, Ibrahim Badr, Michael I Miyamoto, Abd el-Halim Nur el-din, Jagat Narula, Caleb E Finch, Gregory S Thomas

Summary

Background Atherosclerosis is thought to be a disease of modern human beings and related to contemporary lifestyles. However, its prevalence before the modern era is unknown. We aimed to evaluate preindustrial populations for atherosclerosis.

Methods We obtained whole body CT scans of 137 mummies from four different geographical regions or populations spanning more than 4000 years. Individuals from ancient Egypt, ancient Peru, the Ancestral Puebloans of southwest America, and the Unangan of the Aleutian Islands were imaged. Atherosclerosis was regarded as definite if a calcified plaque was seen in the wall of an artery and probable if calcifications were seen along the expected course of an artery.

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http://dx.doi.org/10.1016/S0140-6736(13)60639-X

Saint Luke's Mid America Heart Institute, and University of Missouri–Kansas City School of Medicine, Kansas City, MO

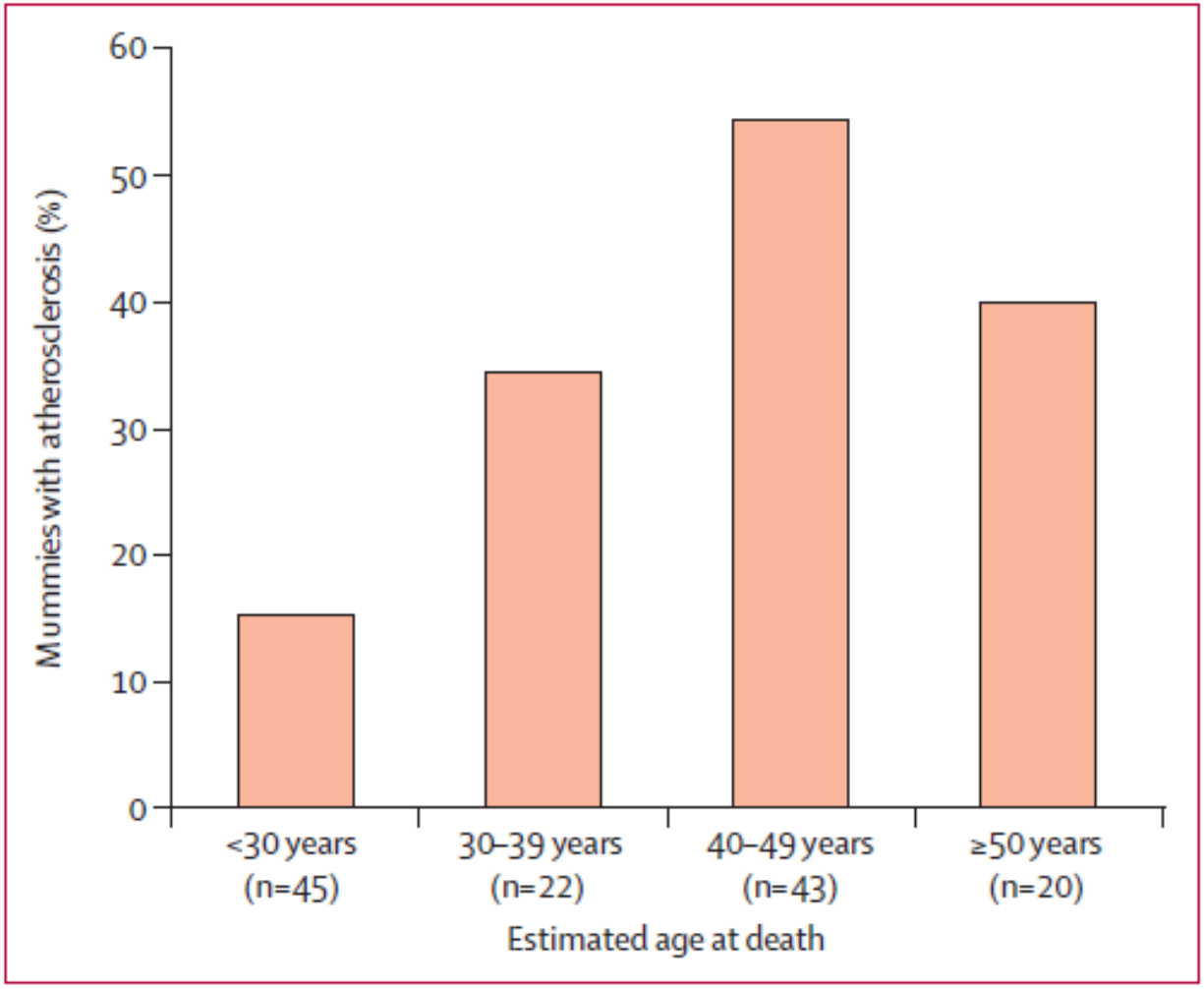

Figure 2: Frequency of atherosclerosis by age group

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La théorie du cholestérol

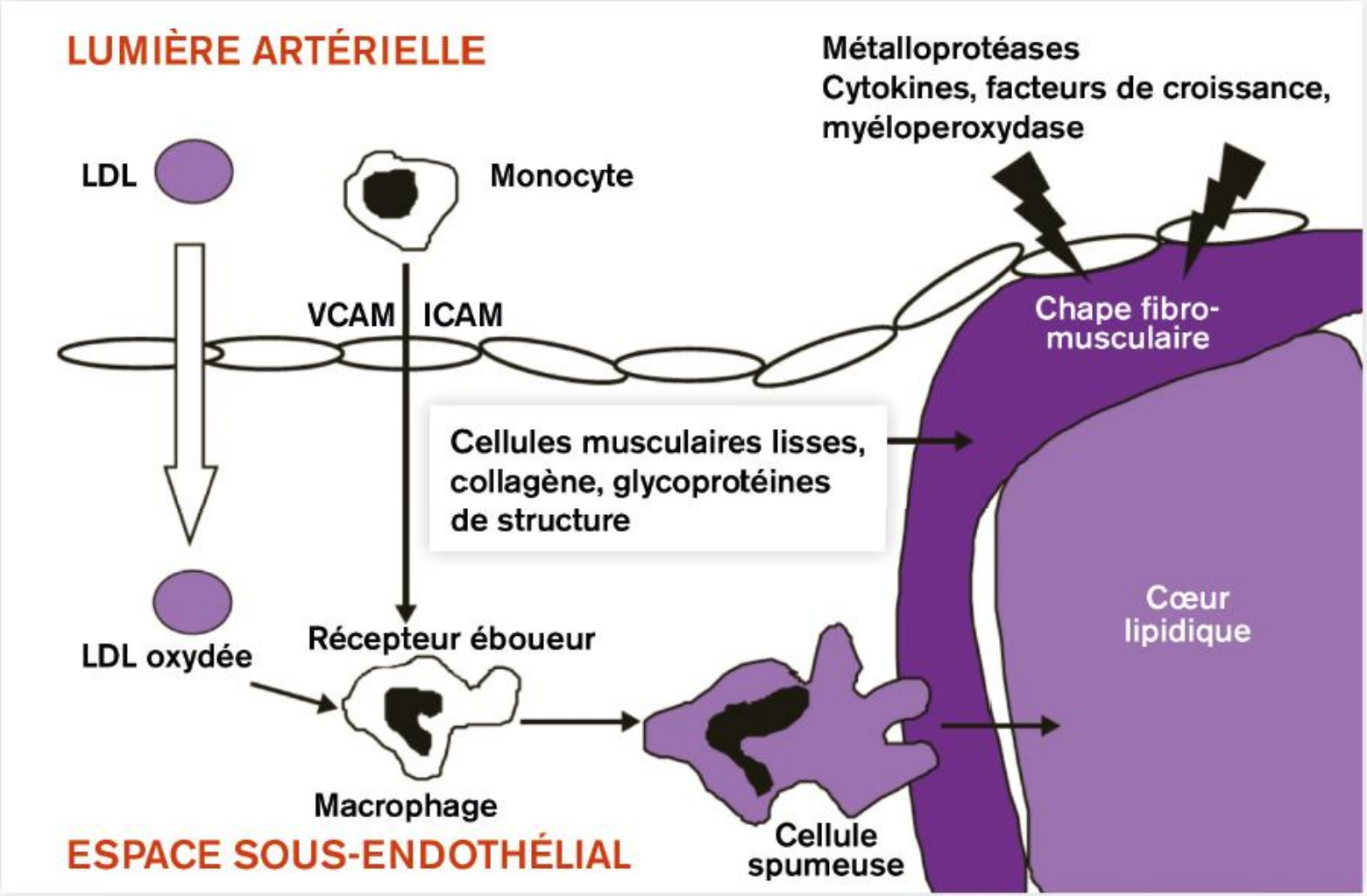

FIGURE Représentation simplifiée de l'athérogenèse.

La théorie du cholestérol : de plus en plus controversée

Articles

Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55 000 vascular deaths

*Prospective Studies Collaboration**

Summary

Background Age, sex, and blood pressure could modify the associations of total cholesterol (and its main two fractions, HDL and LDL cholesterol) with vascular mortality. This meta-analysis combined prospective studies of vascular mortality that recorded both blood pressure and total cholesterol at baseline, to determine the joint relevance of these two risk factors.

Lancet 2007; 370: 1829–39

See Comment page 1803

*Collaborators listed in full at end of paper

	Person-years (thousands)	IHD	Ischaemic stroke	Haemorrhagic stroke	Total stroke*	Other vascular
40–49 years	3442	1309	47	154	412	388
50–59 years	4140	5561	178	466	1370	1387
60–69 years	2751	10 419	540	743	2938	2590
70–79 years	1056	10 829	850	915	4311	3234
80–89 years	222	5626	519	422	2632	2256
Total (40–89 years)	11 611	33744	2134	2700	11 663	9855
Subtotal with HDL cholesterol	1496	3020	145	231	914	1032
MRFIT (40–89 years)	8058	21 243	480	945	3596	9403

*Includes 869 deaths from subarachnoid haemorrhage (not included with haemorrhagic stroke) and 5960 deaths in which the type of stroke was unknown or not reported.

Table 1: **Person-years and numbers of deaths attributed to IHD, stroke, and other vascular causes, by age at risk**

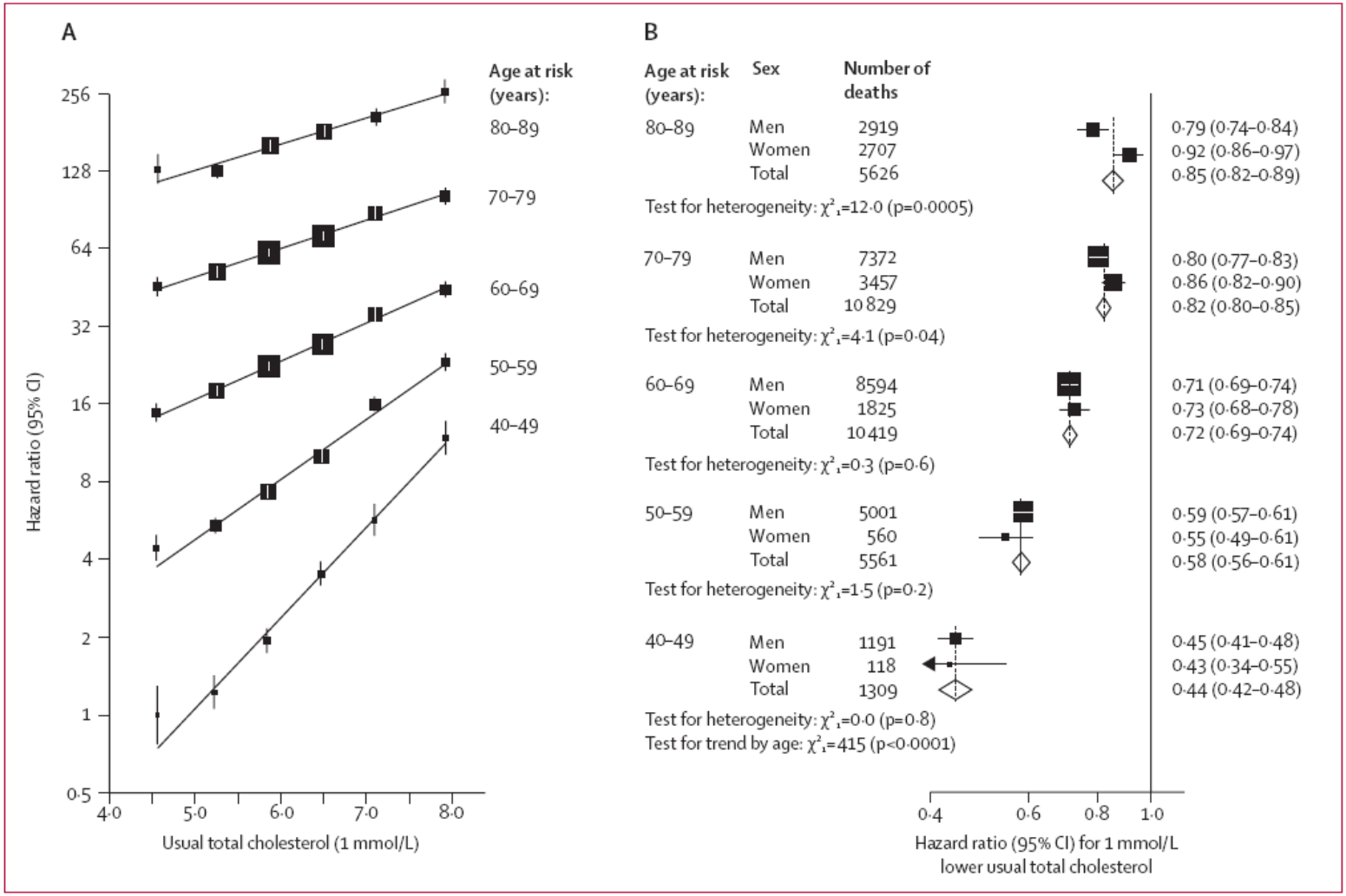

Figure 1: **IHD mortality (33744 deaths) versus usual total cholesterol**

(A) Age-specific associations. (B) Age-specific and sex-specific hazard ratios for 1 mmol/L lower usual total cholesterol. Hazard ratios on the left are plotted on a floating absolute scale of risk (so each log hazard ratio has an appropriate variance assigned to it). The slopes of the age-specific lines on the left are given on the right, subdivided by sex. Each square (left or right) has an area inversely proportional to the variance of the log of the hazard ratio that it represents.

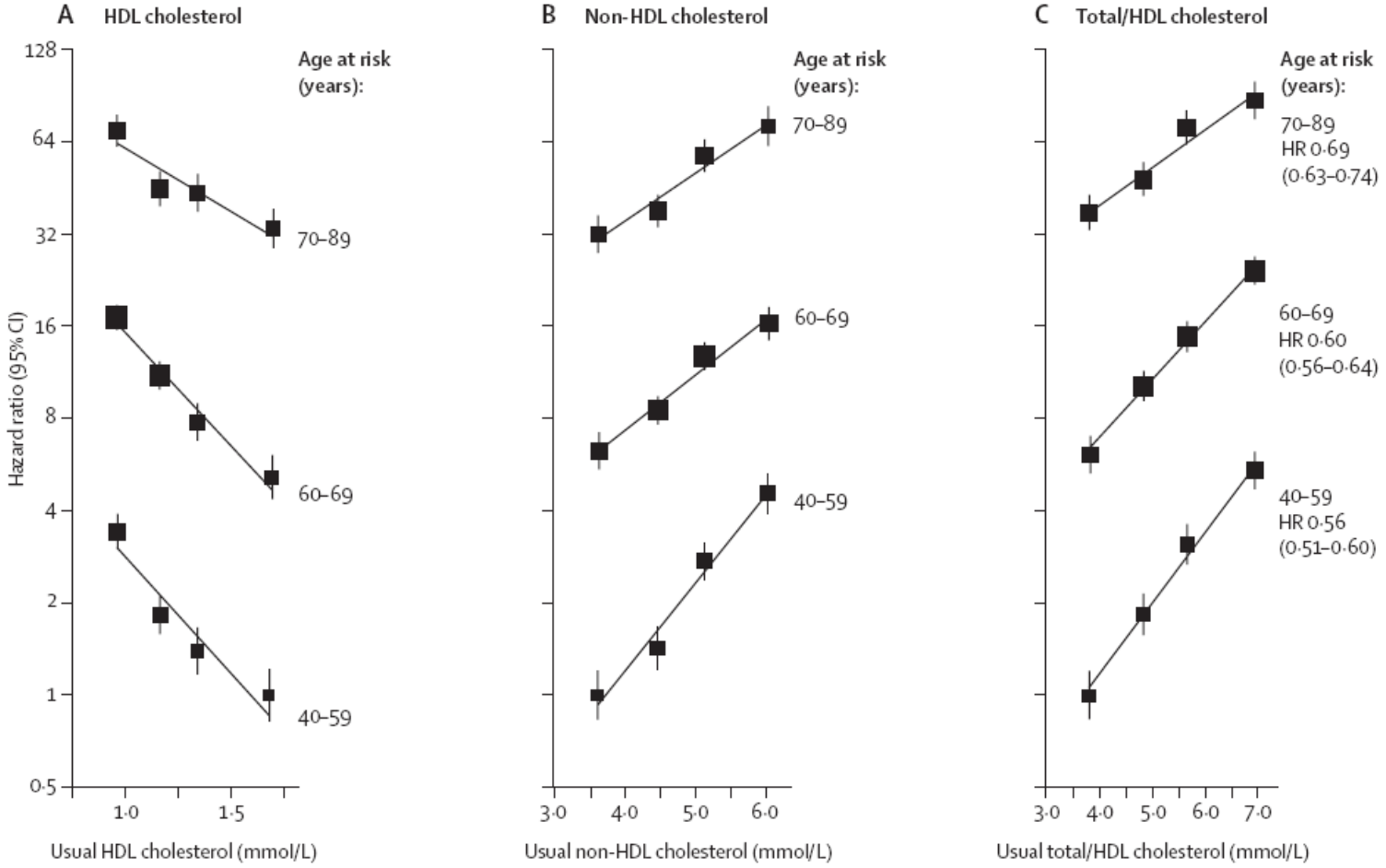

***Figure 3*: IHD mortality (3020 deaths) versus usual (A) HDL cholesterol; (B) non-HDL cholesterol; and (C) total/HDL cholesterol**

Age-specific associations. Conventions as in figure 1. HR denotes the hazard ratio (95% CI) per 1·33 lower total/HDL cholesterol (see also webfigure 5).

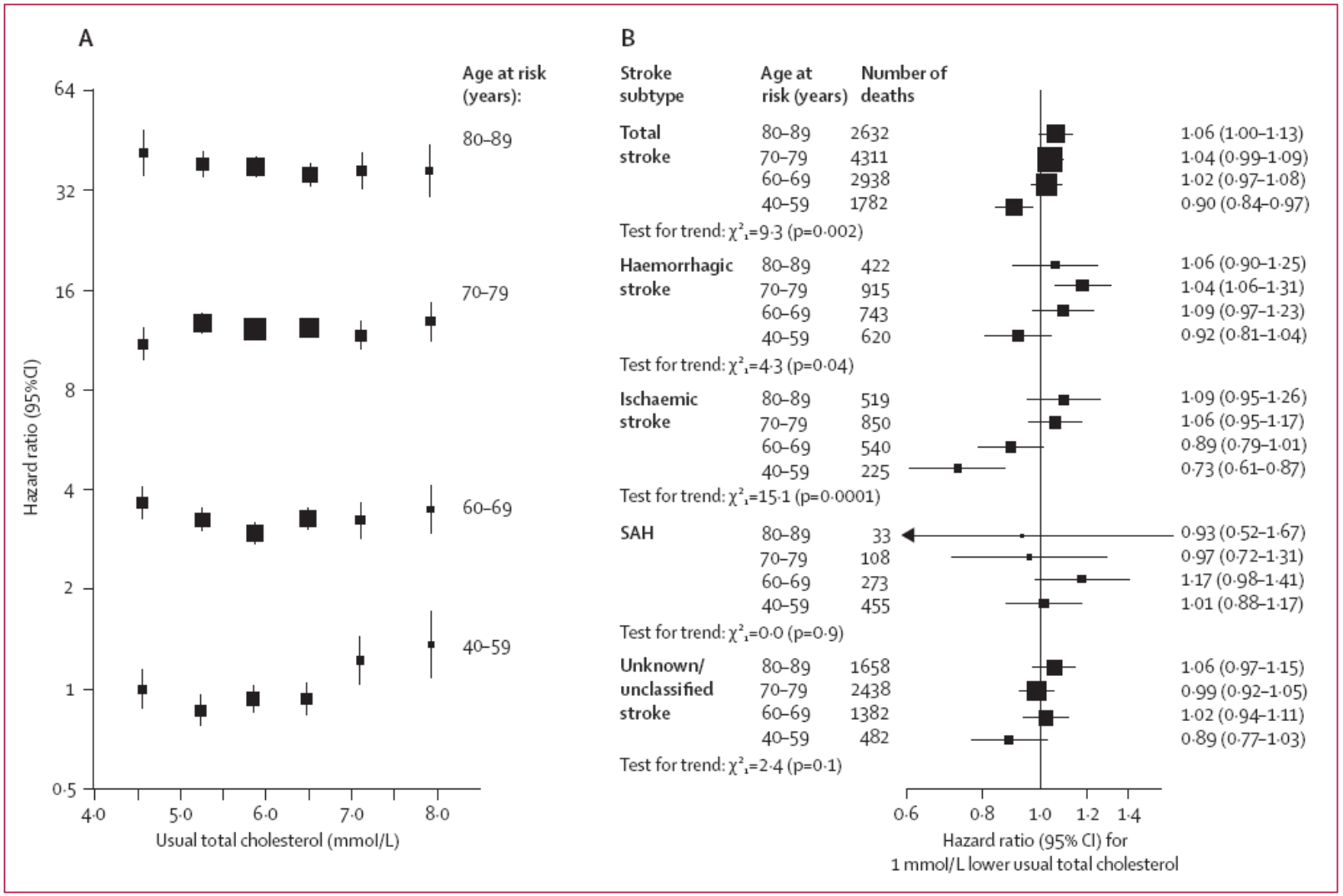

Figure 4: **Stroke mortality (11 663 deaths) versus usual total cholesterol**

(A) age-specific associations for total stroke; and (B) subtype-specific and age-specific hazard ratios for 1 mmol/L lower usual total cholesterol. Conventions as in figure 1. SAH=subarachnoid haemorrhage.

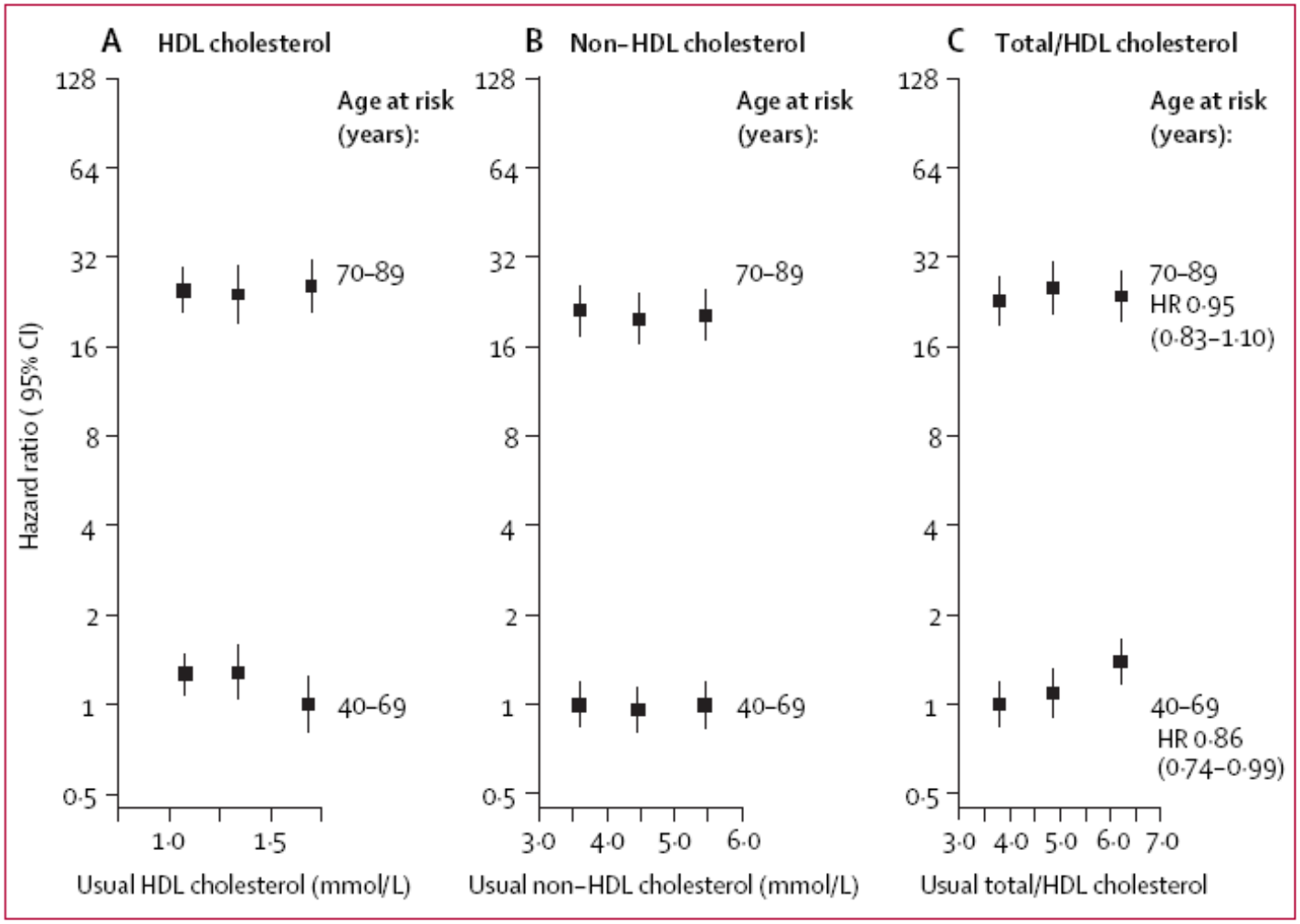

Figure 6: **Stroke mortality (914 deaths) versus usual (A) HDL cholesterol; (B) non-HDL cholesterol; and (C) total/HDL cholesterol**

Age-specific associations. Conventions as in figures 1 and 3. HR denotes the hazard ratio per 1·33 lower total/HDL cholesterol.

Lancet 2007; 370: 1829–39

Interprétation

- Le cholestérol total a été associé positivement à la mortalité par IDM chez les patients d'âge moyen et avancé et à tous les niveaux de pression artérielle.
- L'absence d'association positive indépendante du cholestérol avec la mortalité par accident vasculaire cérébral, en particulier chez les personnes âgées ou à pression artérielle élevée, est inexpliquée et appelle de nouvelles recherches.
- Néanmoins, des essais randomisés ont montré de manière concluante que les statines réduisent considérablement non seulement le taux d'événements coronariens, mais également le taux d'accidents vasculaires cérébraux totaux chez les patients de tous âges et de toute pression artérielle.

Open Access Research

BMJ Open

Lack of an association or an inverse association between low-density-lipoprotein cholesterol and mortality in the elderly: a systematic review

Uffe Ravnskov,[1] David M Diamond,[2] Rokura Hama,[3] Tomohito Hamazaki,[4] Björn Hammarskjöld,[5] Niamh Hynes,[6] Malcolm Kendrick,[7] Peter H Langsjoen,[8] Aseem Malhotra,[9] Luca Mascitelli,[10] Kilmer S McCully,[11] Yoichi Ogushi,[12] Harumi Okuyama,[13] Paul J Rosch,[14] Tore Schersten,[15] Sherif Sultan,[6] Ralf Sundberg[16]

Ravnskov U, *et al. BMJ Open* 2016;**6**:e010401. doi:10.1136/bmjopen-2015-010401

Un taux accru de cholestérol transporté par les LDL n'est pas associé à une mortalité globale et cardiovasculaire accrue chez le sujet âgé de 60 ans ou plus

Cette synthèse méthodique n'a pas établi de lien entre un taux élevé de LDL-C et la mortalité cardiovasculaire ou globale chez des sujets âgés de 60 ans ou plus. Au contraire plusieurs études épidémiologiques vont dans le sens d'une relation inverse. Comme les auteurs l'argumentent très bien, la théorie du cholestérol s'avère en conflit avec beaucoup de critères de Bradford Hill. De nouvelles recherches sont nécessaires pour élucider les causes de l'athéromatose et surtout les recommandations de pratique clinique sur la gestion du risque cardiovasculaire doivent être revues à la lumière de toutes les données suggérant que le rôle de l'hypercholestérolémie a été exagéré ainsi que le bénéfice des traitements hypocholestérolémiants en tant qu'agissant sur le taux de cholestérol. Les effets positifs de certains de ces médicaments rapportés relèvent probablement d'autres mécanismes d'action.

Critères de Bradford et Hill

Une simple corrélation n'est pas synonyme de causalité.

1. Force de l'association (plus l'ampleur des effets liés à l'association sont larges, plus un lien causal est probable, même si un faible effet n'implique pas une absence de lien de causalité)
2. Stabilité de l'association (sa répétition dans le temps et l'espace)
3. Cohérence (les mêmes observations sont réalisées dans différentes populations)
4. Spécificité (une cause produit un effet particulier dans une population particulière en l'absence d'autres explications)
5. Relation temporelle (temporalité). Les causes doivent précéder les conséquences.
6. Relation dose-effet (une plus large dose mène à un plus large effet).
7. Plausibilité (plausibilité biologique, possibilité d'expliquer les mécanismes impliqués).
8. Preuve expérimentale (chez l'animal ou chez l'homme).
9. Analogie (possibilité d'explications alternatives).

Les nouveaux facteurs non pris en considération

Le tabagisme passif : un risque sous-estimé

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Declines in Acute Myocardial Infarction After Smoke-Free Laws and Individual Risk Attributable to Secondhand Smoke

James M. Lightwood and Stanton A. Glantz

Circulation 2009;120;1373-1379; originally published online Sep 21, 2009;
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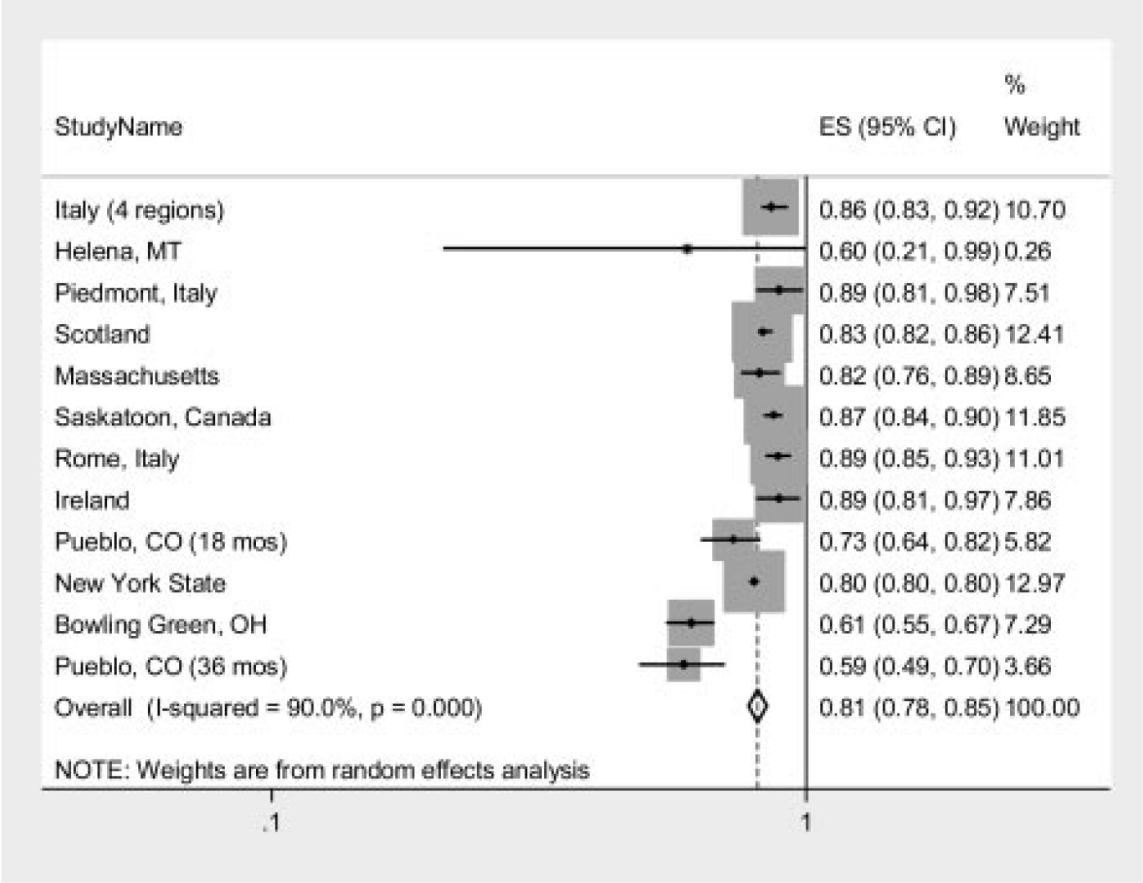


Figure 1. Random-effects meta-analysis of reduced community risks associated with 100% smoke-free policies. Boxes indicate weights in random-effects meta-analysis. Studies are listed in order of duration of follow-up after implementation of the smoke-free law. ES indicates the effect size for the relative reduction in community AMI risk.

(*Circulation*. 2009;120:1373-1379.)

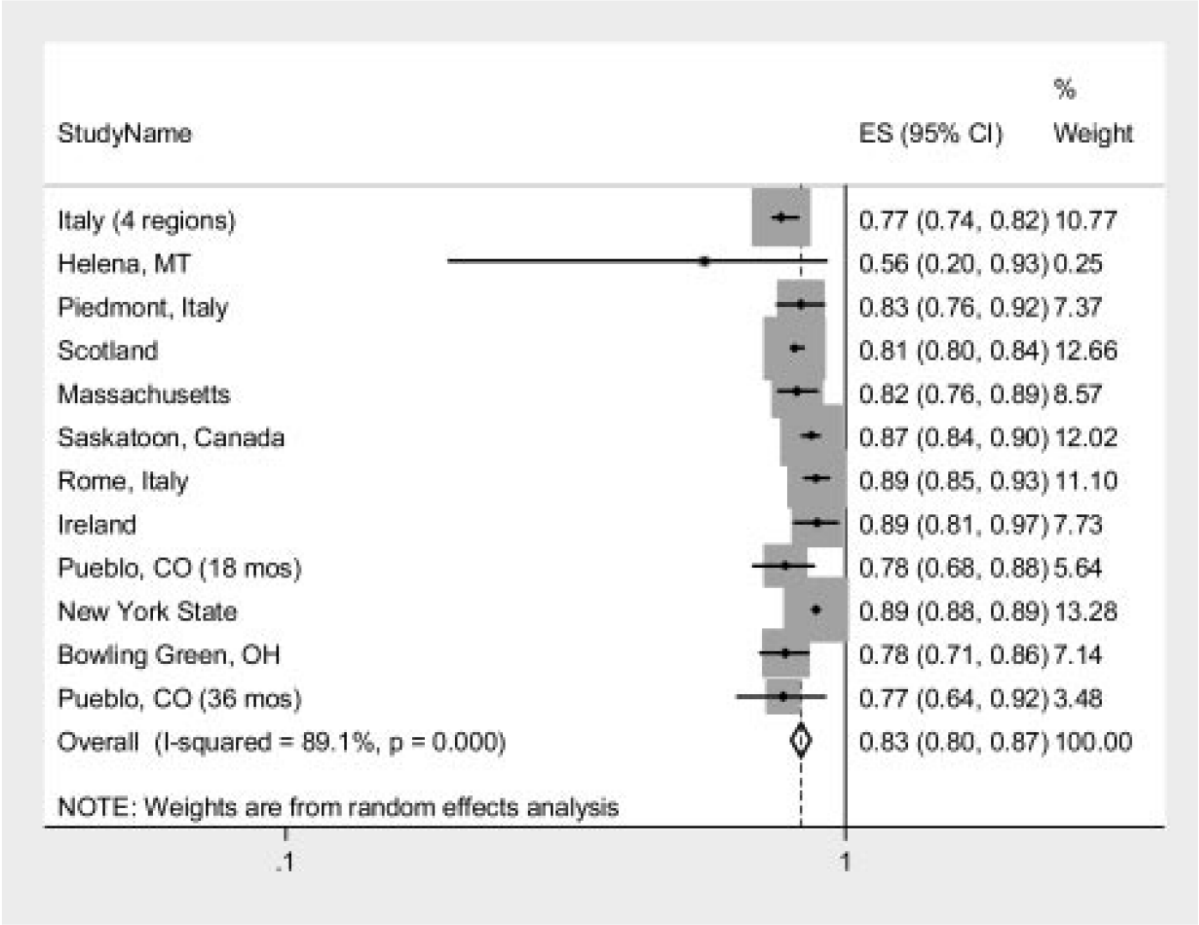


Figure 4. Random-effects meta-analysis of reduced community risks, with all studies adjusted to 12 months after implementation of 100% smoke-free workplace laws. ES indicates the effect size for the adjusted (to 12 months) relative reduction in community AMI risk.

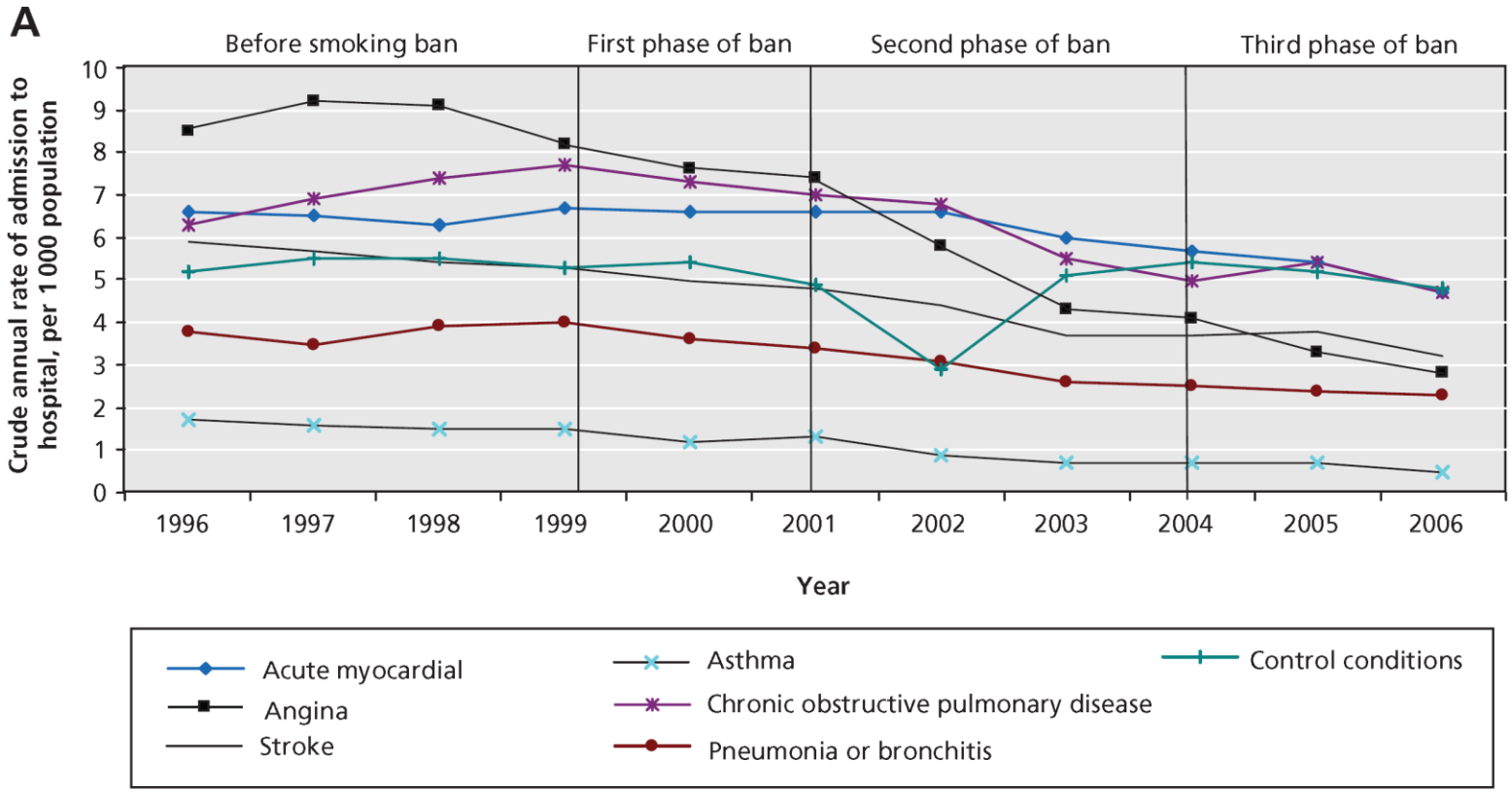
(*Circulation*. 2009;120:1373-1379.)

CMAJ RESEARCH

Association of anti-smoking legislation with rates of hospital admission for cardiovascular and respiratory conditions

Alisa Naiman MHSc MD. Richard H. Glazier MD MPH. Rahim Moineddin PhD

CMAJ 2010. DOI:10.1503/cmaj.091130



CMAJ 2010. DOI:10.1503/cmaj.091130

A
Before smoking ban
First phase of ban
Crude annual rate of admission to hospital, per 10 000 population
Observed rate
Predicted rate
Period
B
First phase of ban
Second phase of ban
Crude annual rate of admission to hospital, per 10 000 population
Observed rate
Predicted rate
Period
C
Second phase of ban
Third phase of ban
Crude annual rate of admission to hospital, per 10 000 population
Observed rate
Predicted rate
Period

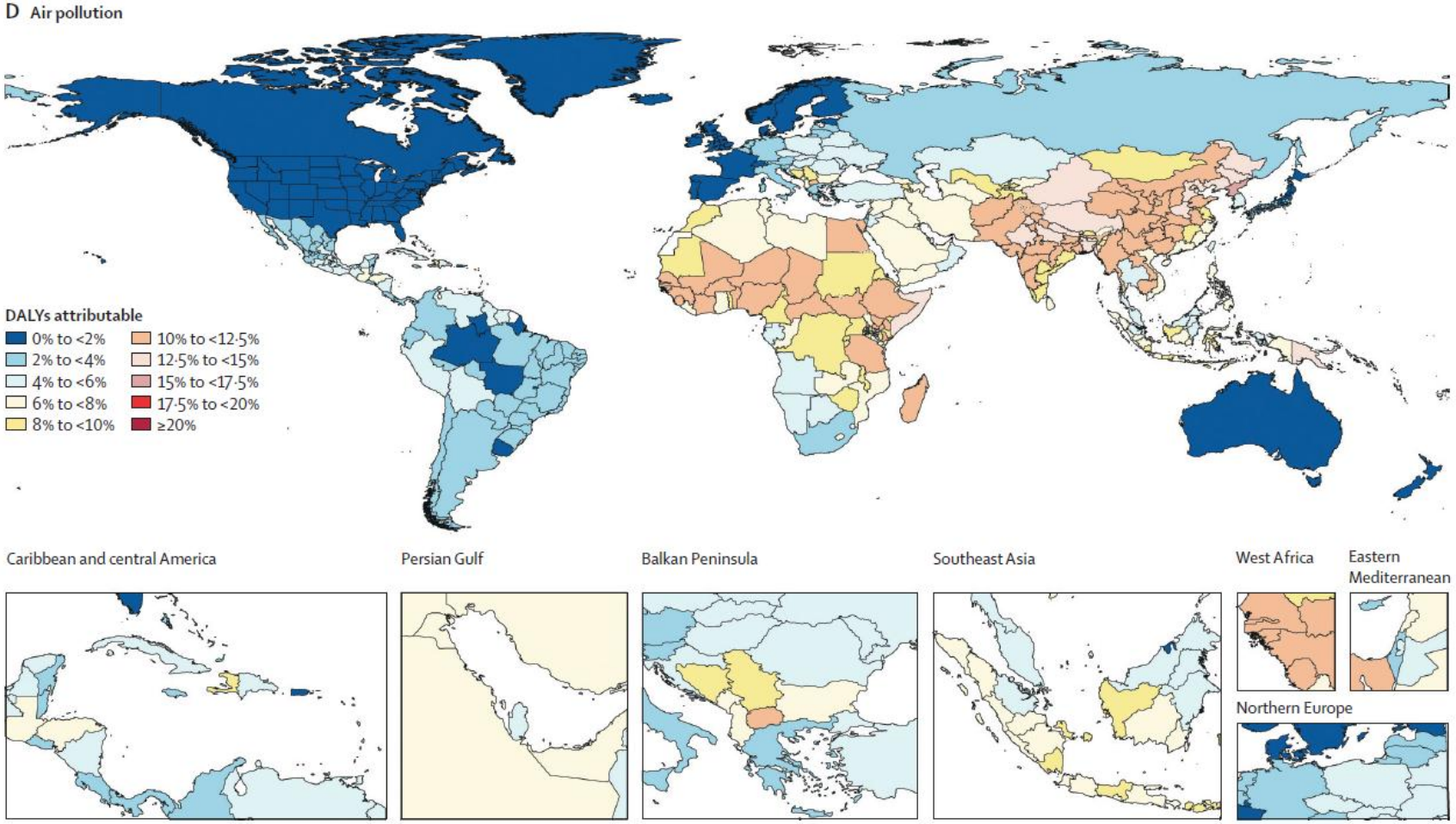
angor

Table 2: Reduction in annual rates of admission to hospital for cardiovascular, respiratory and control conditions, per 10 000 population

Condition	Smoking ban in public places and workplaces v. no ban			Smoking ban in restaurants v. in public places and workplaces			Smoking ban in bars v. in restaurants		
	Reduction in rate of admission (95% CI)		*p* value	Reduction in rate of admission (95% CI)		*p* value	Reduction in rate of admission (95% CI)		*p* value
AMI	0.171	(–0.59 to 0.40)	0.150	–0.477	(–0.95 to –0.003)	0.040	–0.611	(–1.03 to –0.19)	0.004
Angina	–0.913	(–1.24 to –0.59)	< 0.001	–0.166	(–0.21 to –0.12)	< 0.001	0.021	(–0.11 to 0.15)	0.750
Ischemic stroke	0.143	(–0.28 to 0.57)	0.510	–0.454	(–0.91 to –0.001)	0.040	–0.296	(–0.80 to 0.21)	0.250
Asthma	–0.201	(–0.42 to 0.02)	0.070	–0.354	(–0.53 to –0.018)	< 0.001	–0.161	(–0.33 to 0.008)	0.060
COPD	0.433	(–0.33 to 1.19)	0.260	–1.040	(–1.81 to –0.27)	0.008	–0.748	(–1.56 to 0.07)	0.070
Lung infection*	–0.152	(–0.44 to 0.14)	0.300	–0.598	(–0.98 to –0.21)	0.002	–0.408	(–0.90 to 0.08)	0.100
Control	–0.003	(–0.03 to 0.012)	0.750	–0.004	(–0.03 to 0.02)	0.680	–0.030	(–0.03 to 0.02)	0.830

Note: AMI = acute myocardial infarction, CI = confidence interval, COPD = chronic obstructive pulmonary disease, Control = acute cholecystitis, bowel obstruction and appendicitis.
*Lung infection refers to pneumonia or bronchitis.

Pollution atmosphérique



Lancet 2020; 396: 1223–49

DALYs : disability-adjusted life-years

Main Air Pollutants and Myocardial Infarction

A Systematic Review and Meta-analysis

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Mohammad H. Murad, MD, MPH
Sylvie Escolano, PhD
Muriel Tafflet, MSc
Marie-Cécile Périer, MSc
Eloi Marijon, MD
Dewi Vernerey, MSc
Jean-Philippe Empana, MD, PhD
Xavier Jouven, MD, PhD

Context Short-term exposure to high levels of air pollution may trigger myocardial infarction (MI), but this association remains unclear.

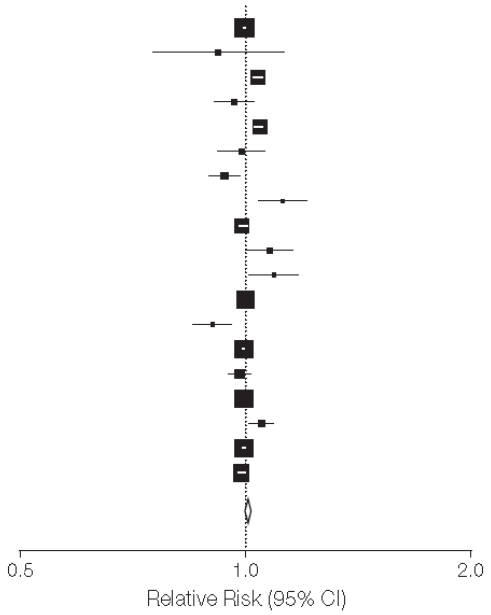
Objective To assess and quantify the association between short-term exposure to major air pollutants (ozone, carbon monoxide, nitrogen dioxide, sulfur dioxide, and particulate matter ≤10 μm [PM_{10}] and ≤2.5 μm [$PM_{2.5}$] in diameter) on MI risk.

Data Sources EMBASE, Ovid MEDLINE in-process and other nonindexed citations, and Ovid MEDLINE (between 1948 and November 28, 2011), and EBM Reviews–Cochrane Central Register of Controlled Trials and EBM Reviews–Cochrane Database of Systematic Reviews (between 2005 and November 28, 2011) were searched for a combination of keywords related to the type of exposure (air pollution, ozone, carbon monoxide, nitrogen dioxide, sulfur dioxide, PM_{10}, and $PM_{2.5}$) and to the type of outcome (MI, heart attack, acute coronary syndrome).

Study Selection Two independent reviewers selected studies of any study design and in any language, using original data and investigating the association between

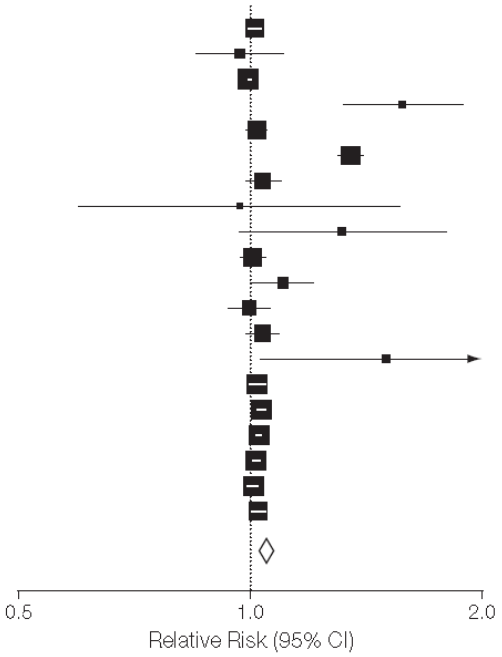
A Ozone analysis

Source	Study Design	Relative Study Weight, %	Relative Risk (95% CI)	*P* Value
Bhaskaran et al,[46] 2011	Case-crossover	11.44	0.999 (0.993-1.005)	.74
Berglind et al,[10] 2010	Case-crossover	0.10	0.920 (0.750-1.129)	.42
Cheng et al,[33] 2009	Case-crossover	6.84	1.042 (1.025-1.060)	<.001
Henrotin et al,[37] 2010	Case-crossover	0.97	0.967 (0.908-1.030)	.30
Hsieh et al,[34] 2010	Case-crossover	7.41	1.044 (1.028-1.060)	<.001
Peters et al,[20] 2001	Case-crossover	0.69	0.989 (0.917-1.067)	.78
Peters et al,[43] 2005	Case-crossover	1.54	0.940 (0.895-0.987)	.01
Ruidavets et al,[44] 2005	Case-crossover	0.66	1.123 (1.039-1.214)	.003
Zanobetti and Schwartz,[45] 2006	Case-crossover	7.50	0.993 (0.978-1.008)	.36
Eilstein et al,[23] 2001	Time-series	0.74	1.078 (1.002-1.159)	.04
Cendon et al,[11] 2006	Time-series	0.70	1.093 (1.014-1.178)	.02
Hoek et al,[32] 2000	Time-series	12.54	1.001 (0.999-1.003)	.33
Koken et al,[8] 2003	Time-series	1.06	0.904 (0.851-0.960)	.001
Lanki et al,[24] 2006	Time-series	10.61	0.994 (0.986-1.002)	.14
Linn et al,[12] 2000	Time-series	2.68	0.982 (0.948-1.017)	.31
Mann et al,[39] 2002	Time-series	12.35	0.996 (0.993-0.999)	.009
Medina et al,[26] 1997	Time-series	2.17	1.050 (1.009-1.093)	.02
Poloniecki et al,[27] 1997	Time-series	11.43	0.996 (0.990-1.002)	.19
Stieb et al,[28] 2009	Time-series	8.56	0.990 (0.978-1.003)	.12
Combined (I^2 = 83%, Egger regression test, *P* = .56)			1.003 (0.997-1.010)	.36



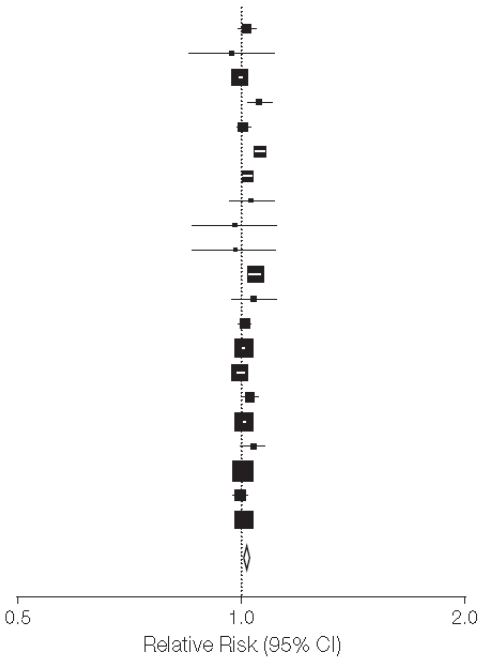
B Carbon monoxide analysis

Source	Study Design	Relative Study Weight, %	Relative Risk (95% CI)	*P* Value
Barnett et al,[9] 2006	Case-crossover	7.10	1.016 (0.992-1.040)	.19
Berglind et al,[10] 2010	Case-crossover	1.91	0.970 (0.849-1.108)	.65
Bhaskaran et al,[46] 2011	Case-crossover	7.74	0.998 (0.993-1.004)	.48
Cheng et al,[33] 2009	Case-crossover	1.20	1.581 (1.323-1.890)	<.001
D'Ippoliti et al,[36] 2003	Case-crossover	6.59	1.021 (0.989-1.055)	.21
Hsieh et al,[34] 2010	Case-crossover	6.15	1.352 (1.300-1.406)	<.001
Nuvolone et al,[42] 2011	Case-crossover	5.15	1.040 (0.985-1.098)	.16
Peters et al,[20] 2001	Case-crossover	0.19	0.971 (0.600-1.571)	.91
Peters et al,[43] 2005	Case-crossover	0.44	1.320 (0.968-1.800)	.08
Sullivan et al,[22] 2005	Case-crossover	6.16	1.012 (0.973-1.052)	.55
Zanobetti and Schwartz,[45] 2006	Case-crossover	3.06	1.105 (1.005-1.214)	.04
Cendon et al,[11] 2006	Time-series	4.40	0.998 (0.934-1.067)	.95
Eilstein et al,[23] 2001	Time-series	5.43	1.039 (0.998-1.092)	.13
Hoek et al,[32] 2000	Time-series	0.31	1.501 (1.033-2.181)	.03
Lanki et al,[24] 2006	Time-series	7.03	1.025 (1.000-1.051)	.05
Linn et al,[12] 2000	Time-series	7.49	1.035 (1.020-1.051)	<.001
Mann et al,[39] 2002	Time-series	7.68	1.030 (1.021-1.039)	<.001
Poloniecki et al,[27] 1997	Time-series	7.54	1.020 (1.006-1.034)	.005
Sharovsky et al,[40] 2004	Time-series	7.42	1.012 (0.995-1.029)	.16
Stieb et al,[28] 2009	Time-series	7.00	1.026 (1.000-1.052)	.05
Combined (I^2 = 93%, Egger regression test, *P* = .03)			1.048 (1.026-1.070)	<.001



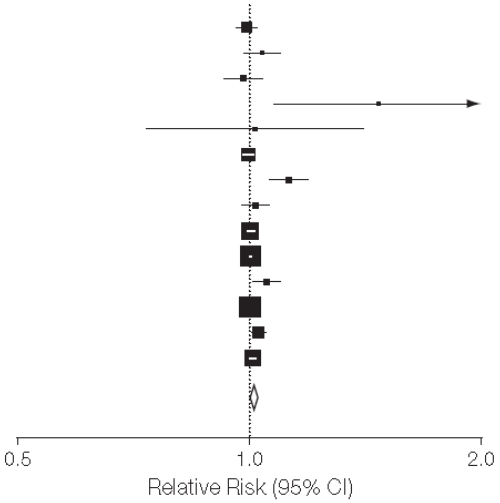
A Nitrogen dioxide analysis

Source	Study Design	Relative Study Weight, %	Relative Risk (95% CI)	*P* Value
Barnett et al,[9] 2006	Case-crossover	2.54	1.017 (0.998-1.046)	.25
Berglind et al,[10] 2010	Case-crossover	0.14	0.970 (0.849-1.108)	.65
Bhaskaran et al,[46] 2011	Case-crossover	9.78	0.995 (0.987-1.003)	.22
Cheng et al,[33] 2009	Case-crossover	1.39	1.057 (1.015-1.101)	.008
D'Ippoliti et al,[36] 2003	Case-crossover	3.45	1.006 (0.983-1.030)	.62
Hsieh et al,[34] 2010	Case-crossover	4.63	1.059 (1.039-1.079)	<.001
Nuvolone et al,[42] 2011	Case-crossover	4.71	1.020 (1.001-1.039)	.04
Peters et al,[20] 2001	Case-crossover	0.51	1.031 (0.962-1.105)	.39
Peters et al,[43] 2005	Case-crossover	0.15	0.980 (0.860-1.117)	.76
Ruidavets et al,[44] 2005	Case-crossover	0.15	0.980 (0.860-1.117)	.76
Zanobetti and Schwartz,[45] 2006	Case-crossover	4.51	1.038 (1.018-1.058)	<.001
Cendon et al,[11] 2006	Time-series	0.46	1.038 (0.965-1.117)	.32
Eilstein et al,[23] 2001	Time-series	3.95	1.011 (0.990-1.033)	.31
Hoek et al,[32] 2000	Time-series	11.00	1.005 (0.999-1.011)	.10
Lanki et al,[24] 2006	Time-series	8.31	0.995 (0.985-1.006)	.35
Linn et al,[12] 2000	Time-series	2.90	1.029 (1.002-1.056)	.03
Mann et al,[39] 2002	Time-series	11.55	1.010 (1.005-1.015)	<.001
Medina et al,[26] 1997	Time-series	1.40	1.037 (0.996-1.080)	.08
Poloniecki et al,[27] 1997	Time-series	12.42	1.004 (1.001-1.007)	.009
Stieb et al,[28] 2009	Time-series	3.63	0.997 (0.975-1.020)	.79
Ye et al,[19] 2001	Time-series	12.42	1.006 (1.003-1.009)	<.001
Combined (I^2 = 71%, Egger regression test, *P* = .08)			1.011 (1.006-1.016)	<.001



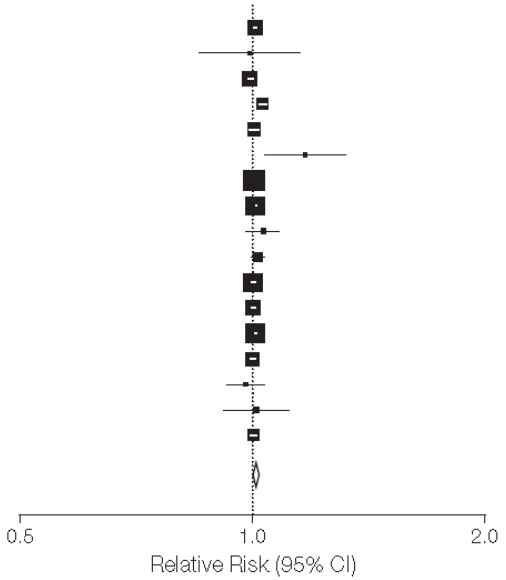
B Sulfur dioxide analysis

Source	Study Design	Relative Study Weight, %	Relative Risk (95% CI)	*P* Value
Bhaskaran et al,[46] 2011	Case-crossover	4.53	0.992 (0.962-1.022)	.60
Hsieh et al,[34] 2010	Case-crossover	1.57	1.042 (0.986-1.101)	.14
Peters et al,[20] 2001	Case-crossover	1.43	0.982 (0.927-1.041)	.54
Peters et al,[43] 2005	Case-crossover	0.05	1.475 (1.077-2.020)	.02
Ruidavetset al,[44] 2005	Case-crossover	0.05	1.020 (0.735-1.416)	.91
Sullivan et al,[22] 2005	Case-crossover	7.77	1.000 (0.979-1.021)	>.99
Cendon et al,[11] 2006	Time-series	1.45	1.129 (1.066-1.196)	<.001
Cheng et al,[33] 2009	Time-series	2.38	1.022 (0.978-1.068)	.33
Eilstein et al,[23] 2001	Time-series	15.17	1.007 (0.996-1.018)	.21
Hoek et al,[32] 2000	Time-series	21.85	1.002 (0.998-1.006)	.33
Medina et al,[26] 1997	Time-series	2.38	1.056 (1.011-1.104)	.02
Poloniecki et al,[27] 1997	Time-series	22.52	1.005 (1.002-1.008)	.001
Sharovsky et al,[40] 2004	Time-series	6.35	1.030 (1.005-1.055)	.02
Stieb et al,[28] 2009	Time-series	12.50	1.012 (0.998-1.026)	.09
Combined (I^2 = 65%, Egger regression test, *P* = .03)			1.010 (1.003-1.017)	.007



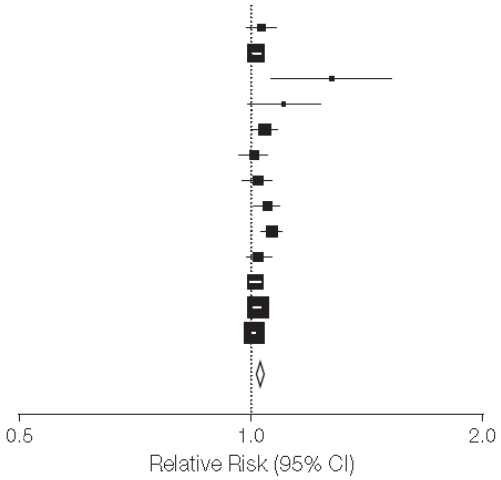
A PM_{10} analysis

Source	Study Design	Relative Study Weight, %	Relative Risk (95% CI)	*P* Value
Belleudi et al,[41] 2010	Case-crossover	8.80	1.007 (0.999-1.015)	.09
Berglind et al,[10] 2010	Case-crossover	0.06	0.990 (0.851-1.152)	.90
Bhaskaran et al,[46] 2011	Case-crossover	6.95	0.992 (0.982-1.002)	.12
Hsieh et al,[34] 2010	Case-crossover	4.78	1.031 (1.017-1.045)	<.001
Nuvolone et al,[42] 2011	Case-crossover	5.10	1.004 (0.991-1.017)	.55
Peters et al,[20] 2001	Case-crossover	0.08	1.169 (1.034-1.322)	.01
Zanobetti and Schwartz,[45] 2006	Case-crossover	14.10	1.006 (1.003-1.009)	<.001
Braga et al,[7] 2001	Time-series	13.10	1.007 (1.003-1.011)	.001
Cendon et al,[11] 2006	Time-series	0.45	1.032 (0.979-1.087)	.24
Cheng et al,[33] 2009	Time-series	2.82	1.015 (0.996-1.035)	.13
Hoek et al,[32] 2000	Time-series	11.97	1.001 (0.996-1.006)	.70
Lanki et al,[24] 2006	Time-series	8.77	1.003 (0.995-1.011)	.46
Linn et al,[12] 2000	Time-series	12.02	1.010 (1.005-1.015)	<.001
Mann et al,[39] 2002	Time-series	5.63	0.999 (0.987-1.011)	.87
Medina et al,[26] 1997	Time-series	0.41	0.979 (0.927-1.034)	.45
Sharovsky et al,[40] 2004	Time-series	0.13	1.010 (0.914-1.116)	.84
Stieb et al,[28] 2009	Time-series	4.84	1.002 (0.989-1.016)	.77
Combined (I^2 = 57%, Egger regression test, *P* = .61)			1.006 (1.002-1.009)	.002



B $PM_{2.5}$ analysis

Source	Study Design	Relative Study Weight, %	Relative Risk (95% CI)	*P* Value
Barnett et al,[9] 2006	Case-crossover	3.93	1.031 (0.983-1.082)	.21
Belleudi et al,[41] 2010	Case-crossover	13.82	1.018 (1.001-1.036)	.04
Peters et al,[20] 2001	Case-crossover	0.33	1.272 (1.061-1.525)	.009
Peters et al,[43] 2005	Case-crossover	0.89	1.105 (0.991-1.232)	.07
Pope et al,[35] 2006	Case-crossover	5.58	1.042 (1.003-1.083)	.04
Rich et al,[21] 2010	Case-crossover	4.43	1.010 (0.966-1.056)	.66
Sullivan et al,[22] 2005	Case-crossover	4.50	1.020 (0.976-1.066)	.38
Zanobetti and Schwartz,[45] 2006	Case-crossover	5.25	1.051 (1.010-1.094)	.02
Maté et al,[25] 2010	Time-series	7.26	1.066 (1.033-1.101)	<.001
Stieb et al,[28] 2009	Time-series	5.14	1.024 (0.983-1.066)	.25
Ueda et al,[38] 2009	Time-series	11.31	1.013 (0.991-1.035)	.24
Zanobetti et al,[30] 2009	Time-series	17.53	1.022 (1.011-1.034)	<.001
Zanobetti and Schwartz,[31] 2009	Time-series	20.03	1.011 (1.004-1.018)	.002
Combined (I^2 = 51%, Egger regression test, *P* = .004)			1.025 (1.015-1.036)	<.001



Conclusions

Tous les principaux polluants atmosphériques, à l'exception de l'ozone, ont été associés de manière significative à une **augmentation du risque d'IDM** :

- monoxyde de carbone: 1,048; IC à 95%, 1,026 à 1,070
- dioxyde d'azote: 1,011; IC à 95%, 1,006 à 1,016
- dioxyde de soufre : 1,010; IC à 95%, 1,003 à 1,017
- PM10: 1,006; IC à 95%, 1,002 à 1,009
- PM2,5: 1,025; IC à 95%, 1,015 à 1,036)
- Ozone: 1,003 (IC à 95%, 0,997-1,010; p = 0,36).

Les analyses de sous-groupes ont fourni des résultats comparables à ceux de l'ensemble des analyses.

Les fractions attribuables à la population variaient entre 0,6% et 4,5%, selon le polluant.

Le changement climatique

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Pollution and the Heart

Sanjay Rajagopalan, M.D., and Philip J. Landrigan, M.D.

N Engl J Med 2021;385:1881-92.
DOI: 10.1056/NEJMra2030281

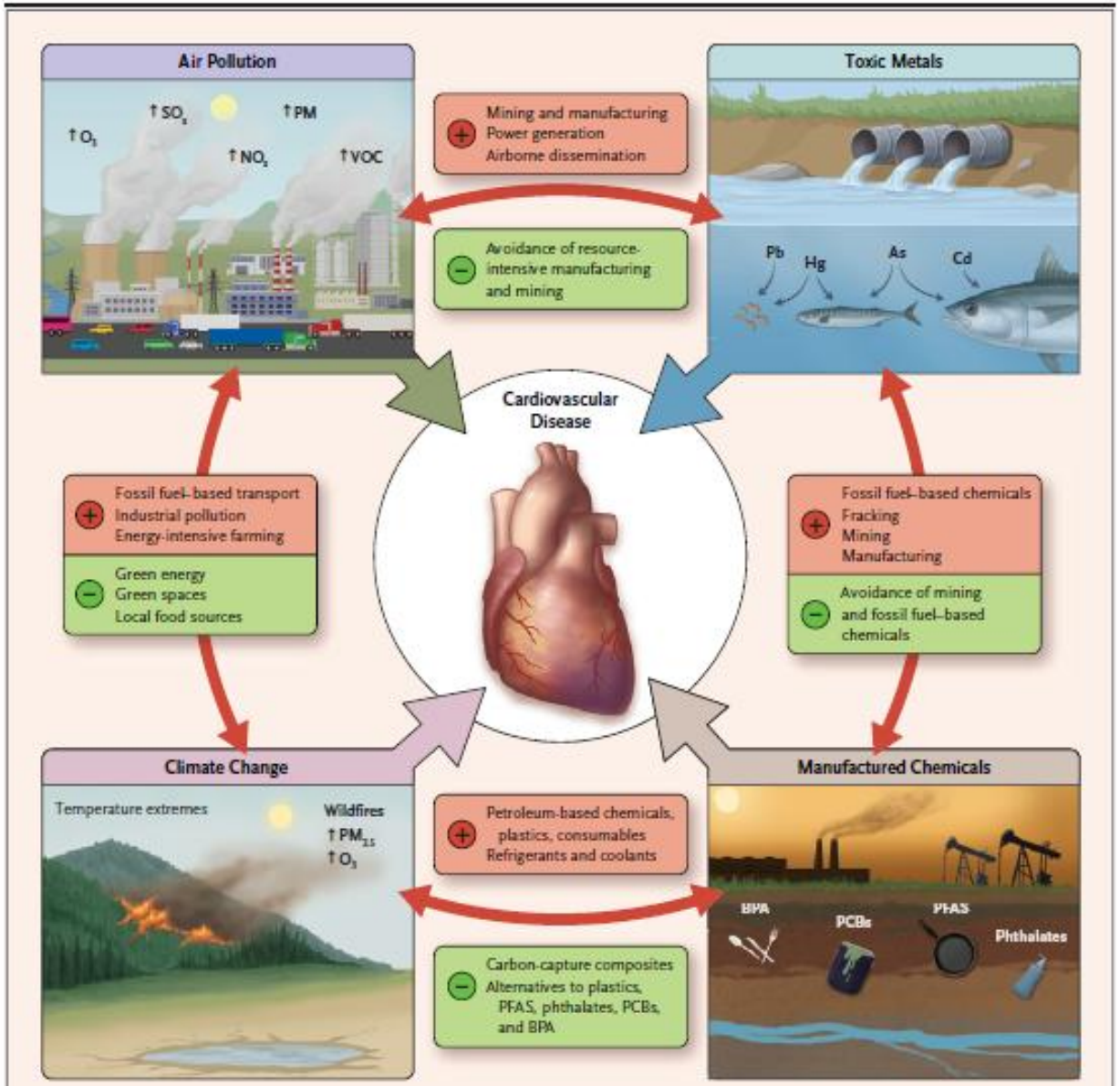
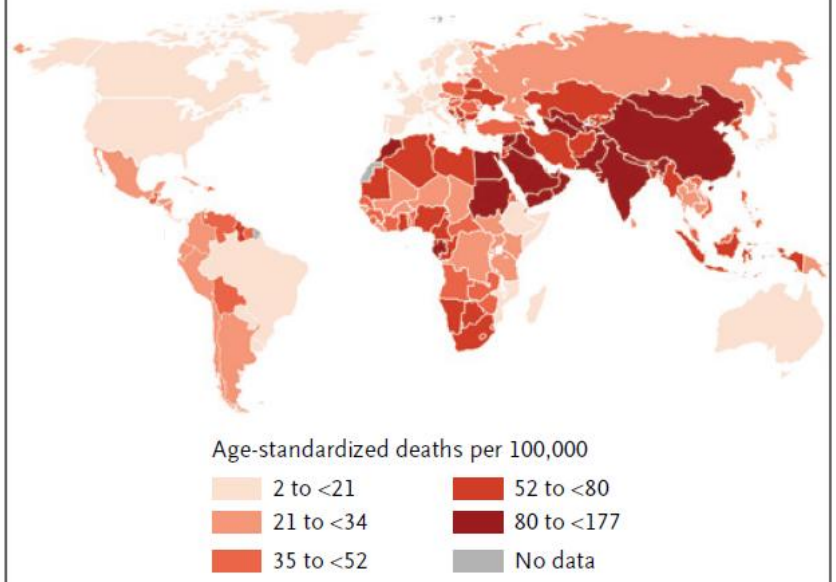


Figure 1. Pollution, Climate Change, and Cardiovascular Disease.

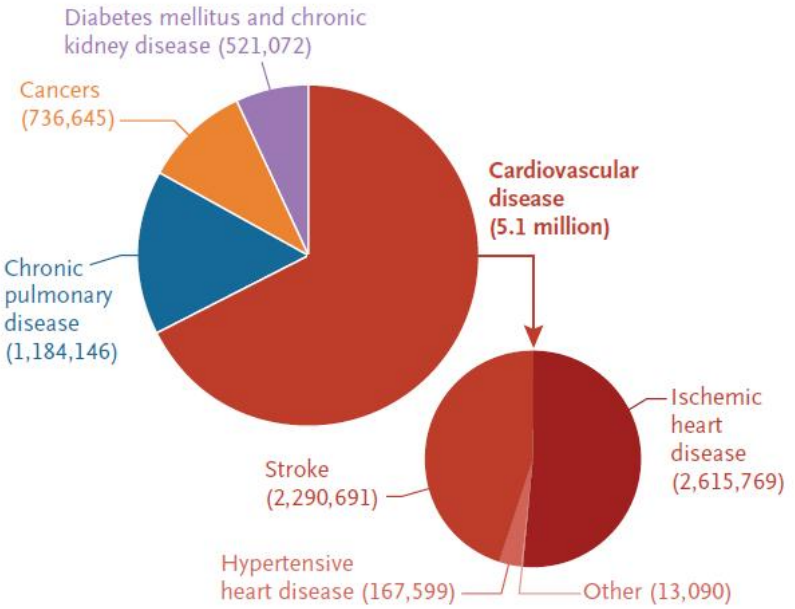
Plus and minus signs indicate potentiators and mitigators of pollution, respectively. The abbreviation As denotes arsenic, BPA bisphenol A, Cd cadmium, Hg mercury, NO_x oxides of nitrogen, O_3 ozone, Pb lead, PCBs polychlorinated biphenyls, PFAS perfluoroalkyl substances, PM particulate matter, $PM_{2.5}$ PM that is less than 2.5 μm in aerodynamic-mass median diameter, SO_x oxides of sulfur, and VOC volatile organic compounds.

N Engl J Med 2021;385:1881-92.
DOI: 10.1056/NEJMra2030281

A Global Cardiovascular Disease Mortality Attributable to Air Pollution



B Global Pollution-Related Deaths According to Disease



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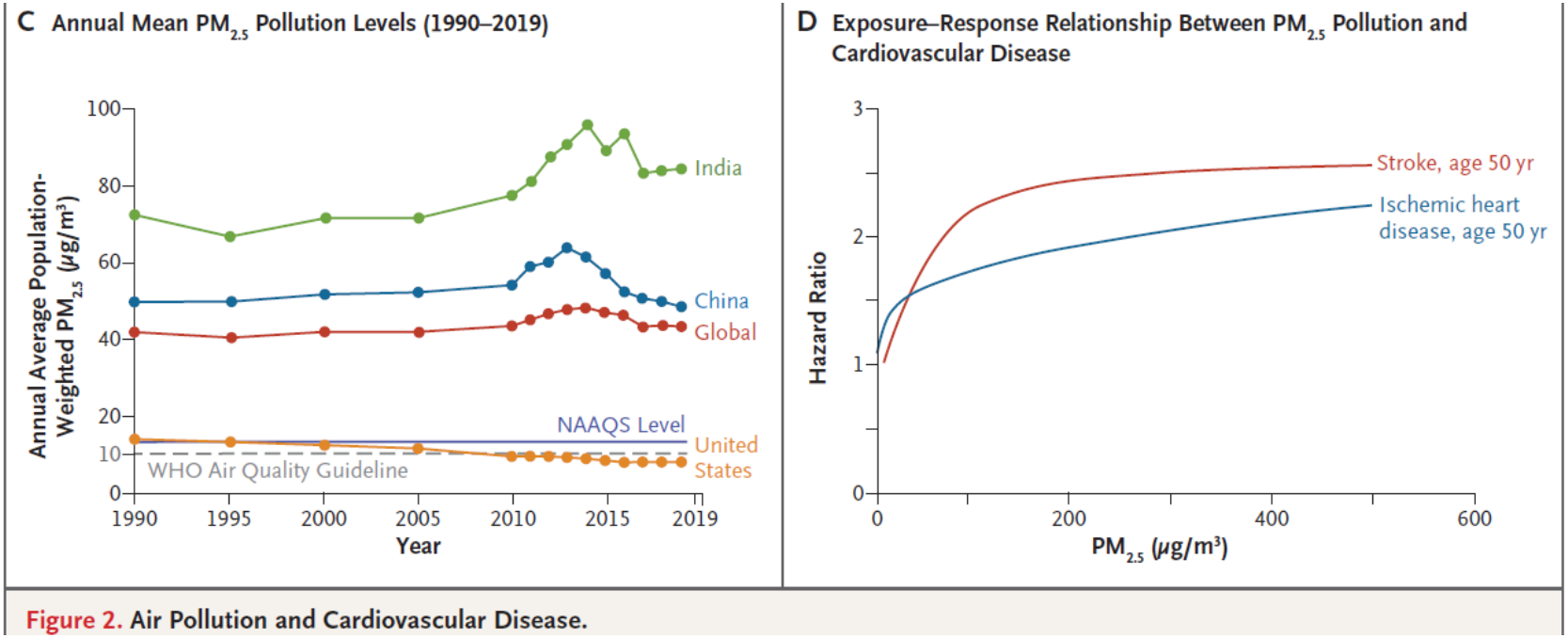

Figure 2. Air Pollution and Cardiovascular Disease.

U.S. National Ambient Air Quality Standard (NAAQS):12 μg / ml³
WHO annual mean air-quality guideline level : 10 μg / ml³

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DOI: 10.1056/NEJMra2030281

Pollution Exposure	Initiating Mechanisms	Effector Pathways	Development of Risk Factors	Cardiovascular Outcomes
• Nasal and pulmonary • Gastrointestinal • Cutaneous surfaces and mucous membranes	• Oxidative stress • Inflammation • Neural reflex arcs • Ligation of pattern-recognition receptors	• Biologic intermediates • Autonomic dysfunction • Endocrine disruption • Direct translocation	• Endothelial dysfunction • Thrombosis and hypercoagulation • Hypertension • Type 2 diabetes • Plaque instability	• Death • Acute coronary syndrome • Stroke • Heart failure • Atrial and ventricular arrhythmias

Progression of Cardiovascular Disease

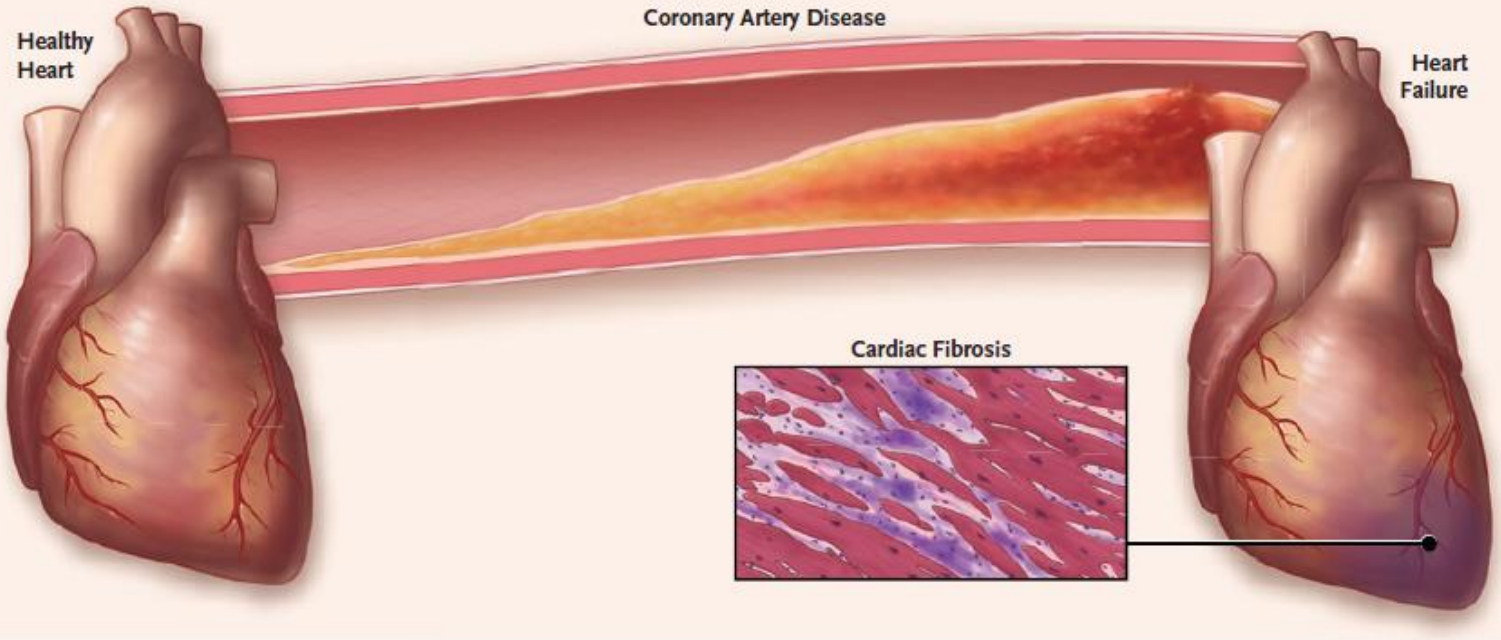
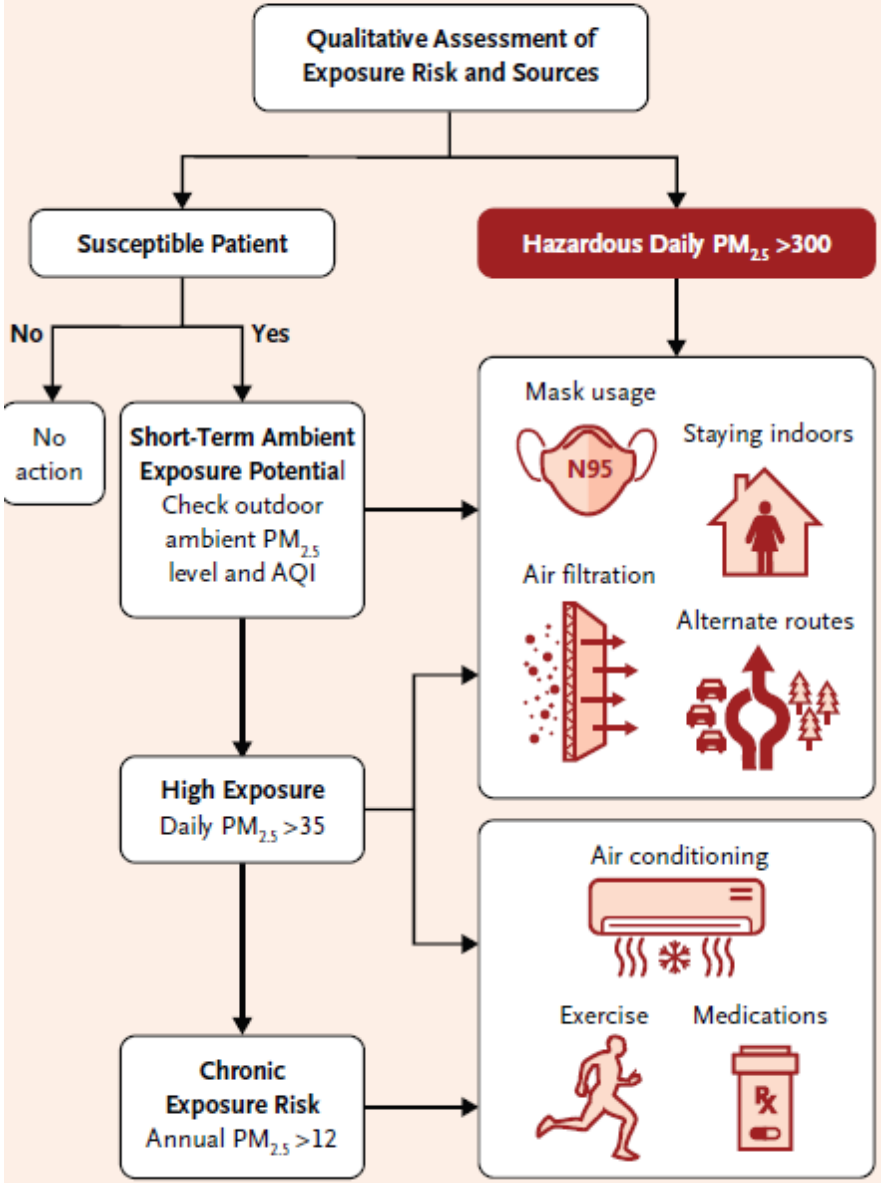


Figure 3. Mechanistic Framework Linking Pollution to Cardiovascular Risk Factors and Disease.

N Engl J Med 2021;385:1881-92.
DOI: 10.1056/NEJMra2030281

Patient-Centered Strategy for Reducing Air-Pollution Exposure and Pollution-Related CVD



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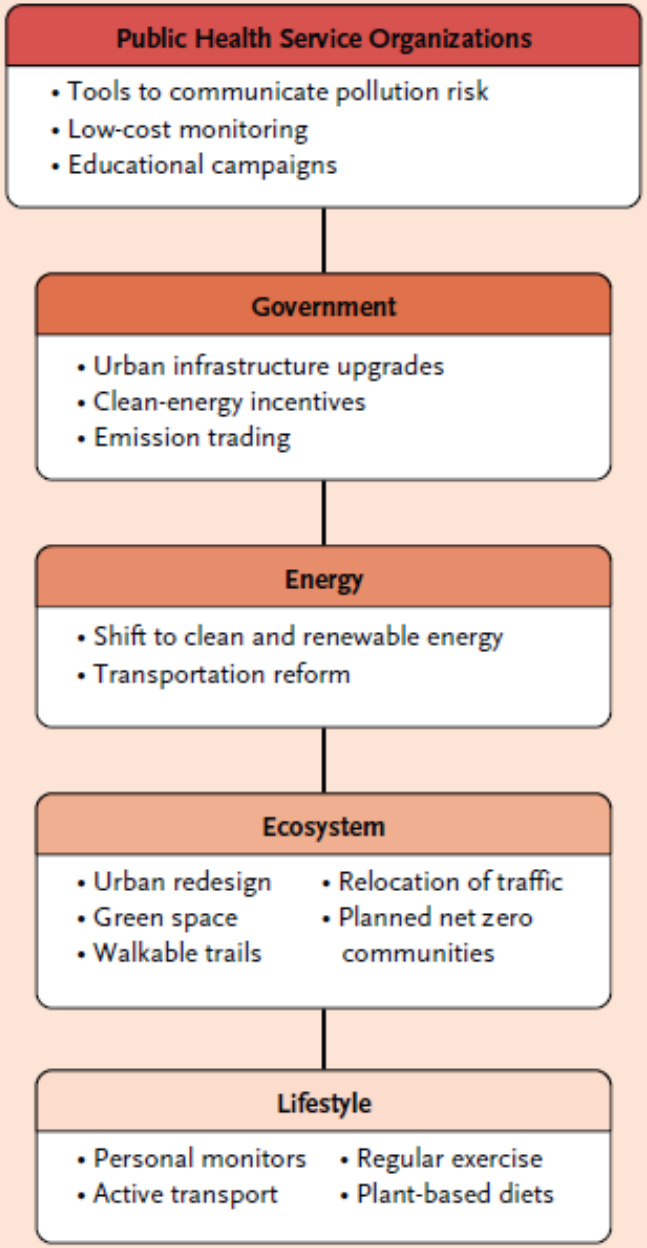
Societal and Governmental Strategies for Reducing Air-Pollution Exposure and Pollution-Related Disease



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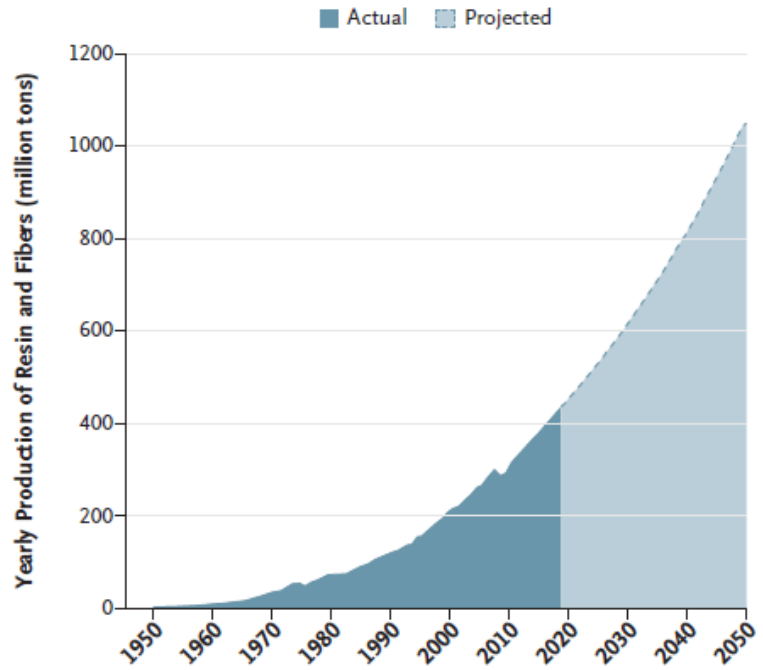
Les plastiques



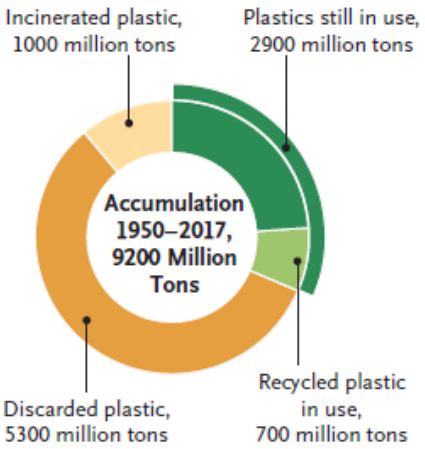


Figure 1. Global Plastic Production, Accumulation, and Trends.
Adapted with permission from GRID–Arendal.

ORIGINAL ARTICLE

Microplastics and Nanoplastics in Atheromas and Cardiovascular Events

R. Marfella, F. Prattichizzo, C. Sardu, G. Fulgenzi, L. Graciotti, T. Spadoni, N. D'Onofrio, L. Scisciola, R. La Grotta, C. Frigé, V. Pellegrini, M. Municinò, M. Siniscalchi, F. Spinetti, G. Vigliotti, C. Vecchione, A. Carrizzo, G. Accarino, A. Squillante, G. Spaziano, D. Mirra, R. Esposito, S. Altieri, G. Falco, A. Fenti, S. Galoppo, S. Canzano, F.C. Sasso, G. Matacchione, F. Olivieri, F. Ferraraccio, I. Panarese, P. Paolisso, E. Barbato, C. Lubritto, M.L. Balestrieri, C. Mauro, A.E. Caballero, S. Rajagopalan, A. Ceriello, B. D'Agostino, P. Iovino, and G. Paolisso

ABSTRACT

BACKGROUND

Microplastics and nanoplastics (MNPs) are emerging as a potential risk factor for cardiovascular disease in preclinical studies. Direct evidence that this risk extends to humans is lacking.

METHODS

We conducted a prospective, multicenter, observational study involving patients who were undergoing carotid endarterectomy for asymptomatic carotid artery disease. The excised carotid plaque specimens were analyzed for the presence of MNPs with the use of pyrolysis–gas chromatography–mass spectrometry, stable isotope analysis, and electron microscopy. Inflammatory biomarkers were assessed with enzyme-linked immunosorbent assay and immunohistochemical assay. The primary end point was a composite of myocardial infarction, stroke, or death from any cause among patients who had evidence of MNPs in plaque as compared with patients with plaque that showed no evidence of MNPs.

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Marfella can be contacted at raffaele.marfella@unicampania.it or at the Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli," Piazza Miraglia, 2, 80138, Naples, Italy.

Drs. Marfella, Prattichizzo, Iovino, and G. Paolisso contributed equally to this article.

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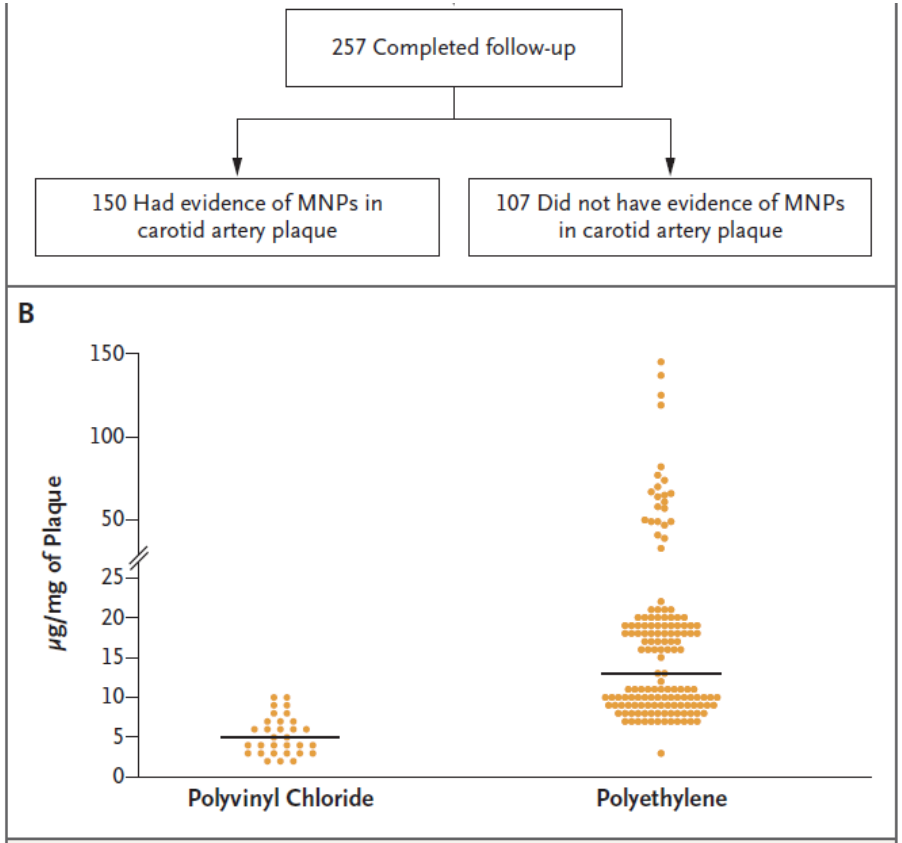

Figure 1. MNPs in Carotid Artery Plaque.

Enrolled patients were screened for the presence of microplastics and nanoplastics (MNPs) in carotid artery plaque excised during endarterectomy (Panel A). Median and individual levels of polyethylene and polyvinyl chloride in excised carotid artery plaque that contained evidence of these compounds are shown in micrograms per milligram of atherosclerotic plaque (Panel B).

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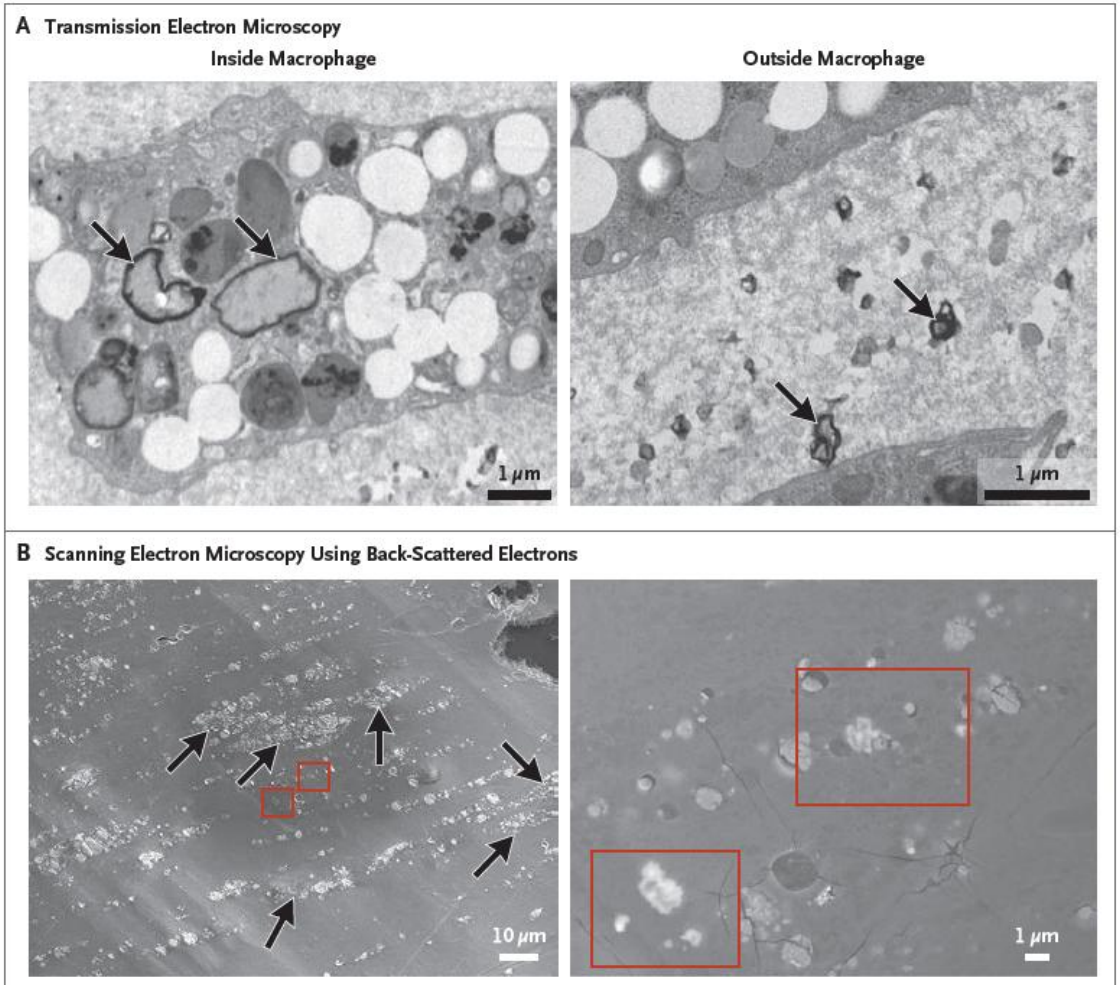

Figure 2. Electron Microscopy Analysis of Atheromatous Plaque.

Panel A shows transmission electron microscopy images of particles of high internal electron transparency contoured by a very thin electron opaque line. These particles do not resemble usual organic material owing to their particularly irregular shape. These particles (arrows) were detected inside living macrophages and outside in the amorphous material of the plaque (arrows). Panel B shows images of the same specimen obtained with scanning electron microscopy using back-scattered electrons, which showed macrophages dispersed in the amorphous plaque material (arrows) and small particles of low-reflecting material contoured by a thin line of high-reflecting material identified in the plaque (red boxes).

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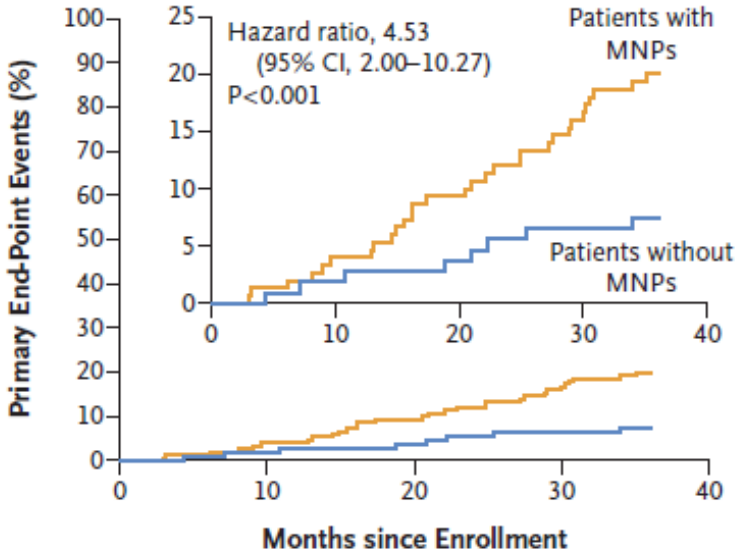

No. at Risk					
Patients with MNPs	150	144	136	126	120
Patients without MNPs	107	105	103	99	99

Figure 4. Associations between the Presence of MNPs and Cardiovascular Events.

Shown is the cumulative incidence curve of the composite outcome — nonfatal stroke, nonfatal myocardial infarction, or death from any cause. The results were estimated with the use of Cox regression analysis with adjustment for age, sex, body-mass index, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, creatinine, diabetes, hypertension, and previous cardiovascular events in the group of patients with evidence of MNPs in plaque and the group of patients with no evidence of MNPs in plaque. The inset shows the same data on an expanded y axis.

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Perturbateurs endocriniens dérivés des combustibles fossiles

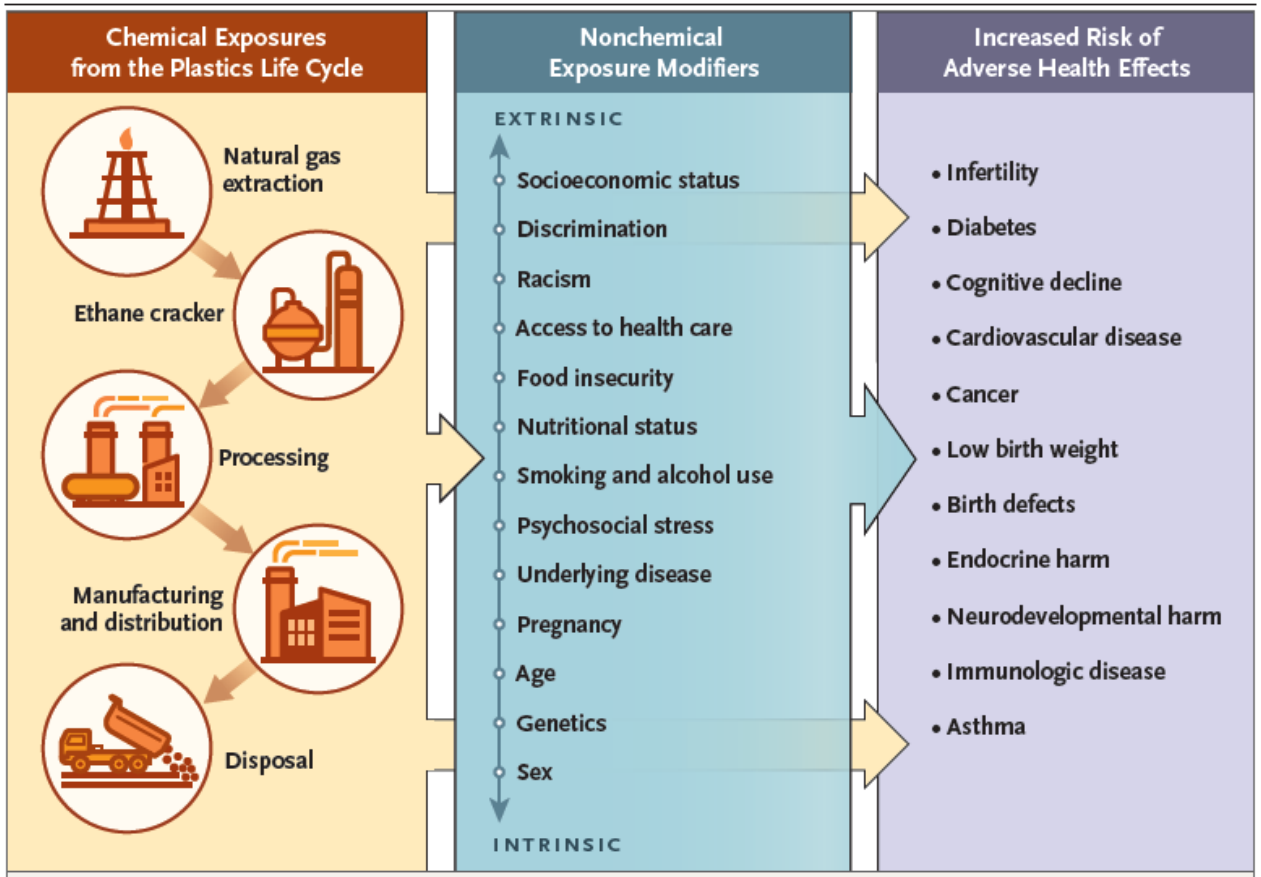

Figure 2. Adverse Effects of Chemical Exposures on Health Outcomes.

Chemical exposures from the plastics life cycle (from fossil-fuel extraction and processing to product manufacturing, distribution, and disposal) interact with social vulnerabilities and biologic susceptibilities, resulting in adverse health outcomes. These lists are not exhaustive.

Chemical Class and Examples	Major Exposure Sources	Health Effects		Specific Effects
		Known or Likely	Suspected	
PFASs: PFOA, PFOS, PFHxS, PFBS, PFBA†	Consumer products (e.g., nonstick cookware, stain-resistant clothing), building materials (e.g., stain-resistant carpeting), personal care products (e.g., cosmetics, menstrual products), food packaging materials, drinking water, industrial facility releases, legacy environmental exposures	Decreased infant and fetal growth, dyslipidemia, decreased antibody response to vaccines in children and adults[9]	Kidney cancer, testicular and breast cancer, gestational hypertension and preeclampsia, thyroid disease and dysfunction[9]	A meta-analysis of 24 studies showed a 10.5-g decrement in birth weight per 1-ng increase in PFOA/ml, and an analysis of 29 studies showed a 3-g decrement in birth weight per 1 ng PFOS/ml increase.[45] EPA's proposed new standard to reduce drinking water levels of PFOA and PFOS to 4.0 ppt is projected to result in savings of $175 million annually because of increased birth weight and reduced deaths attributed to low birth weight.
Ortho-phthalates: DEHP, DBP, BBP, DEP, DINP	Food, personal care products (e.g., fragrances), food packaging materials, building materials (e.g., PVC flooring), industrial facility releases	Male reproductive toxicity (e.g., sperm effects), decreased anogenital distance,[30,44] preterm birth,[44] metabolic disorders (e.g., insulin resistance, diabetes)[44]	Spontaneous abortion,[44] neurodevelopmental harms (e.g., ADHD)[46]	A meta-analysis of 5 studies showed that a log increase in gestational DEHP levels was associated with a 4% reduction in anogenital distance in human male offspring, reflecting reduced fetal testosterone production.[30]
Flame retardants: PBDEs, organophosphate ester flame retardants (OPFRs)	Consumer products (e.g., electronics, furniture, mattresses, children's products), personal care products (e.g., nail polish), plastics, industrial facility releases, legacy environmental exposures	Impaired neurodevelopment[47]	Altered thyroid function in newborns,[33] reproductive toxicity[4,23]	A meta-analysis of 4 U.S. and European studies showed that an increase by a factor of 10 in PBDE exposure during pregnancy was associated with a decrement of 3.7 IQ points in the offspring.[47]
Bisphenols: BPA, BPS	Polycarbonate plastic products (e.g., water bottles, food-storage containers and packaging, eyeglasses), epoxy resin liners of aluminum cans, and other consumer goods such as thermal paper receipts[36]	Adverse effects on ovarian development and function,[48] female reproductive toxicity, impaired neurodevelopment, metabolic abnormalities, immune system abnormalities[10]		A study of 700 couples from China showed that an increase of 1 ln unit in urinary concentrations of BPA in women was associated with a longer time to pregnancy (OR, 0.87; 95% CI, 0.78–0.98) and an increased risk of infertility (OR, 1.23; 95% CI, 1.00–1.50).[49]‡

Heavy metals: lead, cadmium, mercury, arsenic[2]	Consumer products (e.g., dishware, ceramics, jewelry, children's products), spices, personal care products (e.g., skin lighteners), tobacco smoke, industrial facility releases, legacy environmental exposures	Impaired neurodevelopment, male reproductive toxicity (e.g., impaired semen quality, fertility effects), female reproductive toxic effects, cancer, immunosuppression[36,50]		A pooled analysis with a total of 1333 children from 7 longitudinal cohort studies showed a 6.9-point reduction in IQ with an increase in blood lead levels by a factor of approximately 10.[51]
Pesticides: organophosphate pesticides, neonicotinoids, pyrethroids, DDT[2]	Food and drinking water, insecticides, rodenticides, herbicides, spray drift from use in agricultural fields	Impaired neurodevelopment (e.g., lowered IQ),[36] reduced sperm quality[52]	Increased susceptibility to childhood cancers (e.g., leukemia and brain tumors), increased susceptibility to testicular cancer, impaired fetal growth[3,4,23]	A birth cohort study of 329 children showed an average 7-point IQ deficit for children in the highest quintile of exposure to organophosphate pesticides during pregnancy, as compared with those in the lowest quintile of exposure.[53]
Volatile organic compounds: benzene, formaldehyde, toluene	Consumer products (furniture, textiles, glues, paints, detergents, disinfectants), personal care products (cosmetics, fragrances, nail polish), tobacco smoke, gas-stove emissions, fireplace emissions, industrial facility releases	Respiratory toxicity, lung cancer, nasopharyngeal cancer, leukemia, acute neurologic harm (e.g., dizziness, vomiting), female reproductive toxicity (e.g., increased time to pregnancy, spontaneous abortion risk), altered male reproductive system, reduced fetal growth[3,4,23,54]		A meta-analysis of 15 studies showed an elevated risk of leukemia (RR, 1.54; 95% CI, 1.18–2.00) among workers exposed to high levels of formaldehyde.[55]

Bisphénols

- groupe de composés aromatiques utilisés dans les produits en plastique polycarbonate (par exemple, les bouteilles d'eau, les contenants de conservation des aliments et emballages et lunettes), les revêtements en résine époxy des canettes en aluminium et d'autres biens de consommation tels que les reçus en papier thermique.
- l'exposition au BPA (Bisphénol A), le composé le plus connu de cette classe, a de multiples effets néfastes sur la santé : connu pour imiter les œstrogènes, susceptible d'augmenter les risques d'effets immunotoxiques (par exemple, asthme ou allergie), d'effets neurotoxiques sur le développement et d'effets toxiques sur le système reproducteur féminin (par exemple, développement ovarien anormal) plus tard dans la vie, même à des niveaux extrêmement faibles d'exposition.

PFAS (per- and polyfluoroalkyl substances)

- composés organofluorés synthétiques comportant un ou plusieurs groupes fonctionnels alkyle per- ou polyfluorés.
- largement utilisés dans les applications antiadhésives, notamment les ustensiles de cuisine et les emballages alimentaires, les vêtements et tapis résistants à l'eau et aux taches, ainsi que la production de plastiques pour recouvrir des articles tels que des bouteilles et des récipients pour aliments transformés
- risque accru d'effets néfastes sur la santé, notamment une croissance fœtale réduite, une dyslipidémie, une diminution de la réponse en anticorps aux vaccins et un risque accru de cancer du rein.

Phtalates

- comprennent des dizaines de produits chimiques de structure similaire, utilisés pour rendre les plastiques plus durables et plus souples, pour aider à dissoudre d'autres matériaux et pour servir de stabilisants de parfum dans les produits de consommation.
- Un certain nombre de ces produits chimiques sont antiandrogènes (par exemple, ils inhibent la production de testostérone chez le fœtus mâle en développement), effets néfastes sur la reproduction masculine et féminine (par exemple, infertilité, diminution du nombre de spermatozoïdes et diminution de la réserve ovarienne) et augmentation des risques de troubles métaboliques (par exemple, résistance à l'insuline et diabète).

Stress au travail

CMAJ RESEARCH

Associations of job strain and lifestyle risk factors with risk of coronary artery disease: a meta-analysis of individual participant data

Mika Kivimäki PhD, Solja T. Nyberg MSc, Eleonor I. Fransson PhD, Katriina Heikkilä PhD, Lars Alfredsson PhD, Annalisa Casini PhD, Els Clays PhD, Dirk De Bacquer PhD, Nico Dragano PhD, Jane E. Ferrie PhD, Marcel Goldberg MD, Mark Hamer PhD, Markus Jokela PhD, Robert Karasek PhD, France Kittel PhD, Anders Knutsson MD, Markku Koskenvuo MD, Maria Nordin PhD, Tuula Oksanen PhD, Jaana Pentti BSc, Reiner Rugulies PhD, Paula Salo PhD, Johannes Siegrist PhD, Sakari B. Suominen MD, Töres Theorell MD, Jussi Vahtera MD, Marianna Virtanen PhD, Peter J.M. Westerholm MD, Hugo Westerlund PhD, Marie Zins MD, Andrew Steptoe DSc, Archana Singh-Manoux PhD, G. David Batty PhD; for the IPD-Work Consortium

Table 1: Characteristics of 102 128 men and women free of coronary artery disease at baseline in 7 cohort studies

Characteristic	No. (%) of participants* n = 102 128
Age, yr, mean ± SD	44.3 ± 9.0
Sex	
Men	49 219 (48.2)
Women	52 909 (51.8)
Current smoking	
Yes	22 150 (21.7)
No	79 978 (78.3)
Heavy drinking†	
Yes	8 205 (8.0)
No	93 923 (92.0)
Physical inactivity	
Yes	15 655 (15.3)
No	86 473 (84.7)
Obesity‡	
Yes	10 796 (10.6)
No	91 332 (89.4)
Job strain§	
Yes	15 986 (15.7)
No	86 142 (84.3)

Note: SD = standard deviation.
*Unless specified otherwise.
†Consumption of ≥ 21 units (women) or ≥ 28 units (men) of alcohol per wk.
‡Body mass index ≥ 30.
§Defined as having a job with high demands (a job-demand mean score above the study-specific median) and low control (a job-control mean score below the study-specific median); "no job strain" was denoted by all other combinations of demands and control.

Table 2: Age-, sex- and cohort-adjusted 10-year incidence of coronary artery disease by job strain, lifestyle risk factors and their combinations at baseline

Variable	No. of participants	No. of events of coronary artery disease	10-yr incidence per 1000*	Difference in incidence
Job strain†				
No	86 142	921	14.7	0 (ref)
Yes	15 986	165	18.4	3.7
No. of lifestyle risk factors‡				
0	55 090	437	12.0	0 (ref)
1	33 347	382	17.8	5.8
2–4	13 691	267	30.6	18.6
No. of lifestyle risk factors‡ and job strain				
0 – No	47 154	375	11.6	0 (ref)
0 – Yes	7 936	62	14.7	3.1
1 – No	27 815	319	17.1	5.5
1 – Yes	5 532	63	21.7	10.1
≥ 2 – No	11 173	227	30.4	18.8
≥ 2 – Yes	2 518	40	31.2	19.6

Note: ref = reference group.
*Adjusted for age, sex and cohort.
†Defined as having a job with high demands (a job-demand mean score above the study-specific median) and low control (a job-control mean score below the study-specific median); "no job strain" was denoted by all other combinations of demands and control.
‡Smoking, heavy drinking, physical inactivity and obesity. 0 lifestyle risk factors = healthy lifestyle, 1 risk factor = moderately unhealthy lifestyle, 2–4 risk factors = unhealthy lifestyle.

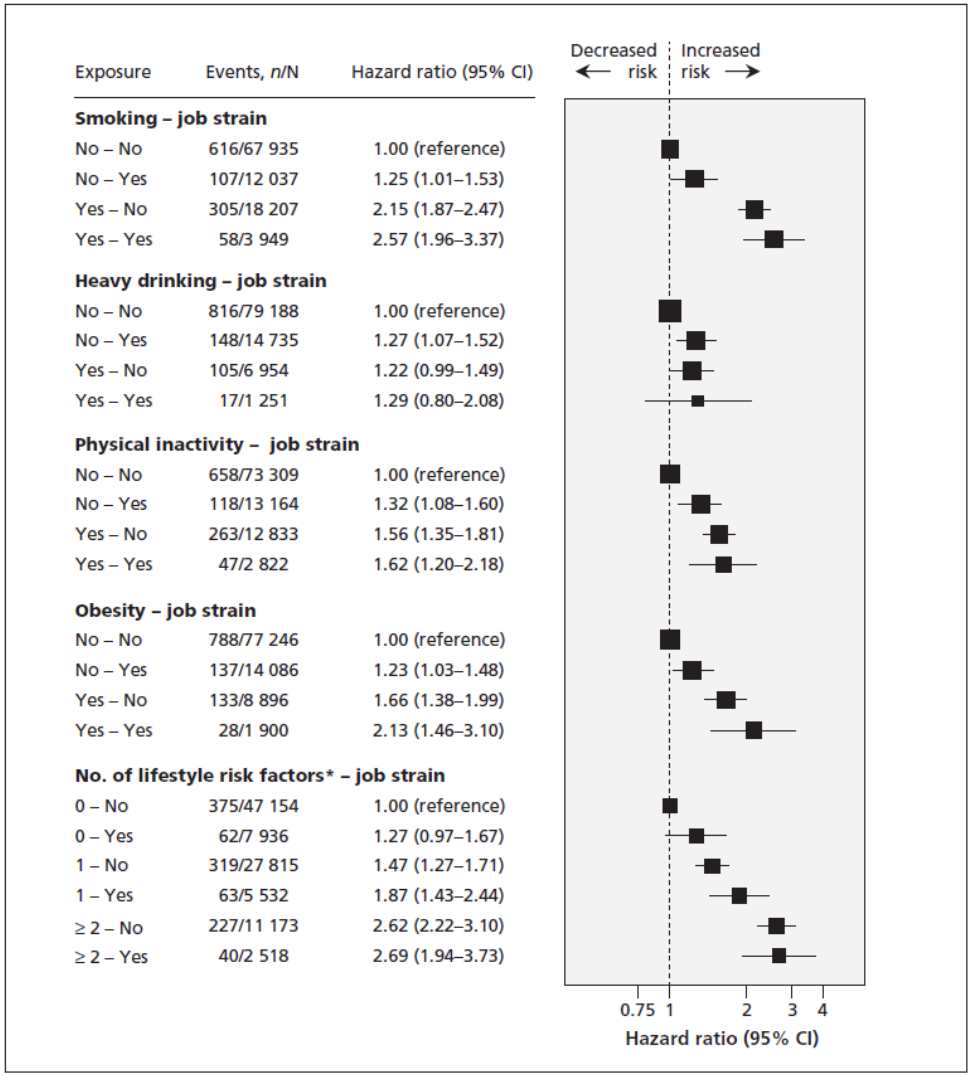

Figure 1: Associations of lifestyle risk factors and job strain with risk of coronary artery disease after adjustment for age, sex and cohort. Values greater than 1.0 indicate an increased risk of incident coronary artery disease. CI = confidence interval. *0 risk factors = healthy lifestyle, 1 risk factor = moderately unhealthy lifestyle and ≥ 2 risk factors = unhealthy lifestyle.

Conclusion

Dans cette méta-analyse des données regroupées provenant d'études de cohortes prospectives, **le risque de maladie coronarienne était le plus élevé parmi les participants ayant signalé des tensions professionnelles et un mode de vie malsain**; ceux qui éprouvaient des difficultés au travail et qui menaient un mode de vie sain avaient environ la moitié du taux de cette maladie.

Ces données d'observation suggèrent qu'un mode de vie sain pourrait réduire considérablement le risque de maladie coronarienne chez les personnes souffrant de contraintes professionnelles. En plus du counselling sur le stress, les cliniciens pourraient envisager de prêter une attention accrue aux facteurs de risque du mode de vie des patients signalant des tensions professionnelles.

Horaires de travail longs (≥55 h par semaine vs 35 – 40 h)

Long working hours and risk of coronary heart disease and stroke: a systematic review and meta-analysis of published and unpublished data for 603 838 individuals

Mika Kivimäki, Markus Jokela, Solja T Nyberg, Archana Singh-Manoux, Eleonor I Fransson, Lars Alfredsson, Jakob B Bjorner, Marianne Borritz, Hermann Burr, Annalisa Casini, Els Clays, Dirk De Bacquer, Nico Dragano, Raimund Erbel, Goedele A Geuskens, Mark Hamer, Wendela E Hooftman, Irene L Houtman, Karl-Heinz Jöckel, France Kittel, Anders Knutsson, Markku Koskenvuo, Thorsten Lunau, Ida E H Madsen, Martin L Nielsen, Maria Nordin, Tuula Oksanen, Jan H Pejtersen, Jaana Pentti, Reiner Rugulies, Paula Salo, Martin J Shipley, Johannes Siegrist, Andrew Steptoe, Sakari B Suominen, Töres Theorell, Jussi Vahtera, Peter J M Westerholm, Hugo Westerlund, Dermot O'Reilly, Meena Kumari, G David Batty, Jane E Ferrie, Marianna Virtanen, for the IPD-Work Consortium

Lancet 2015; 386: 1739–46

Published Online
August 20, 2015
http://dx.doi.org/10.1016/S0140-6736(15)60295-1

Summary

Background Long working hours might increase the risk of cardiovascular disease, but prospective evidence is scarce, imprecise, and mostly limited to coronary heart disease. We aimed to assess long working hours as a risk factor for incident coronary heart disease and stroke.

Methods We identified published studies through a systematic review of PubMed and Embase from inception to

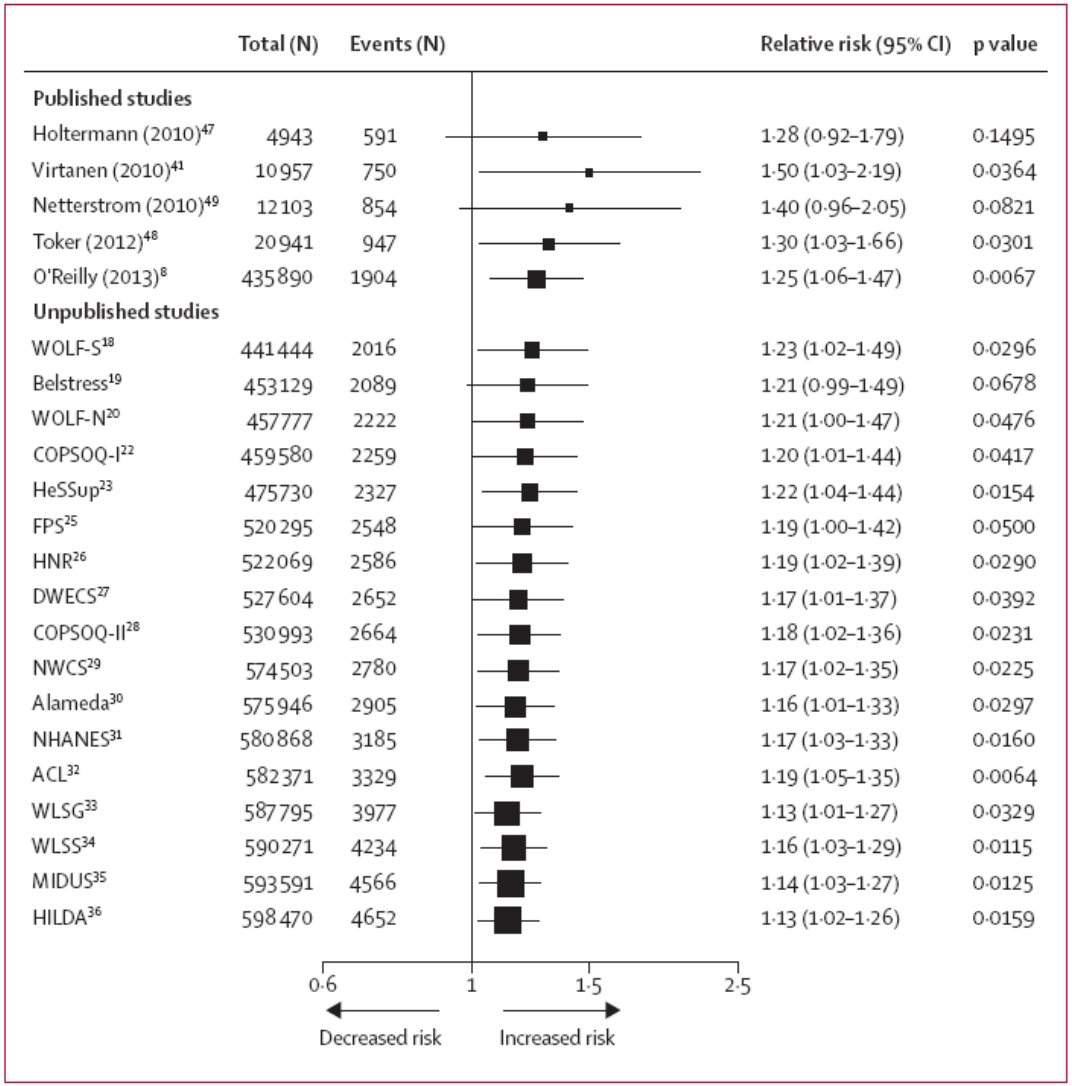

Figure 2: **Cumulative meta-analysis of published and unpublished data of the association between long working hours and incident coronary heart disease**
Estimates adjusted for age, sex, and socioeconomic status.

Lancet 2015; 386: 1739–46

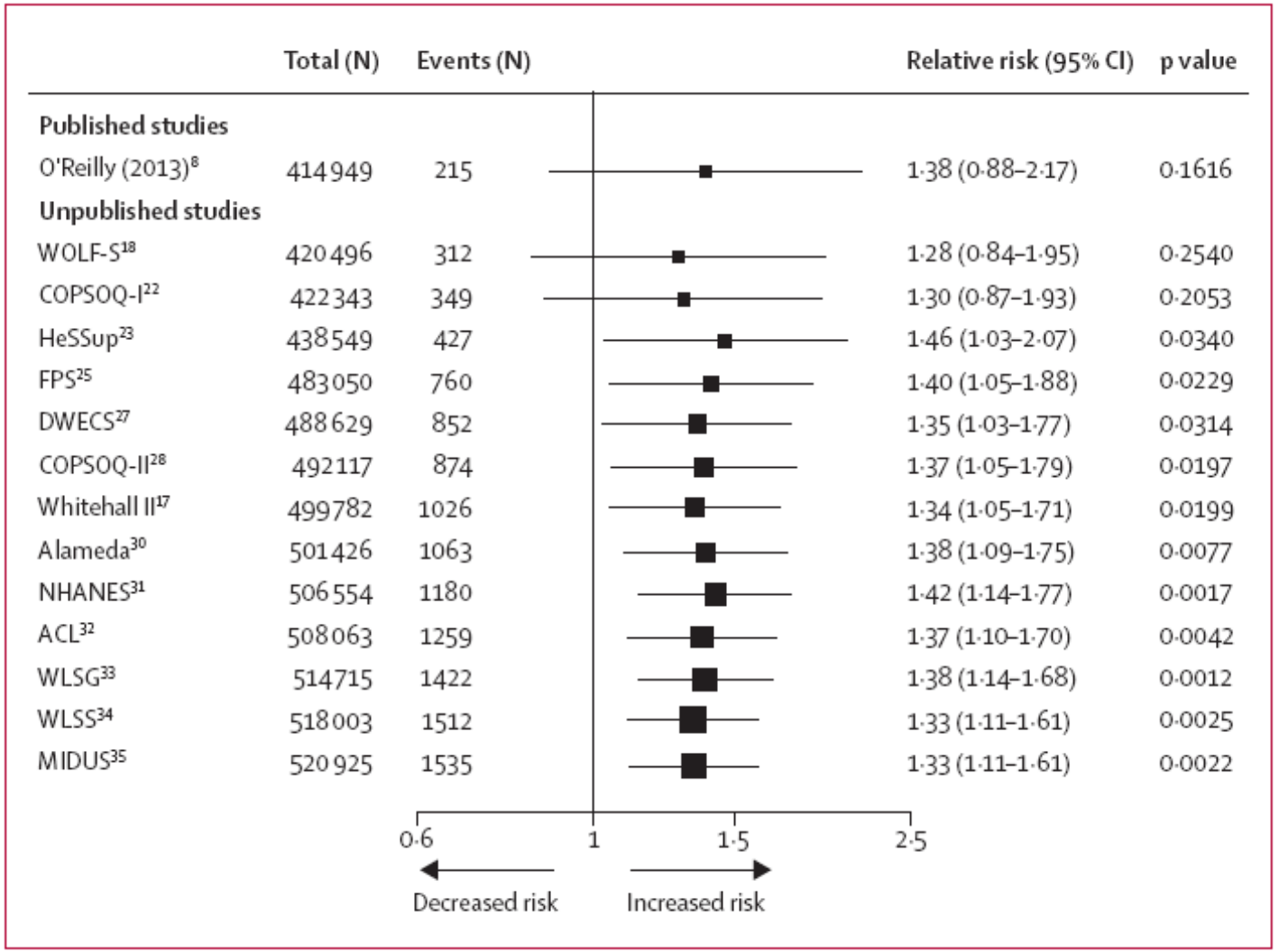

Figure 3: **Cumulative meta-analysis of published and unpublished data of the association between long working hours and incident stroke**

Estimates adjusted for age, sex, and socioeconomic status.

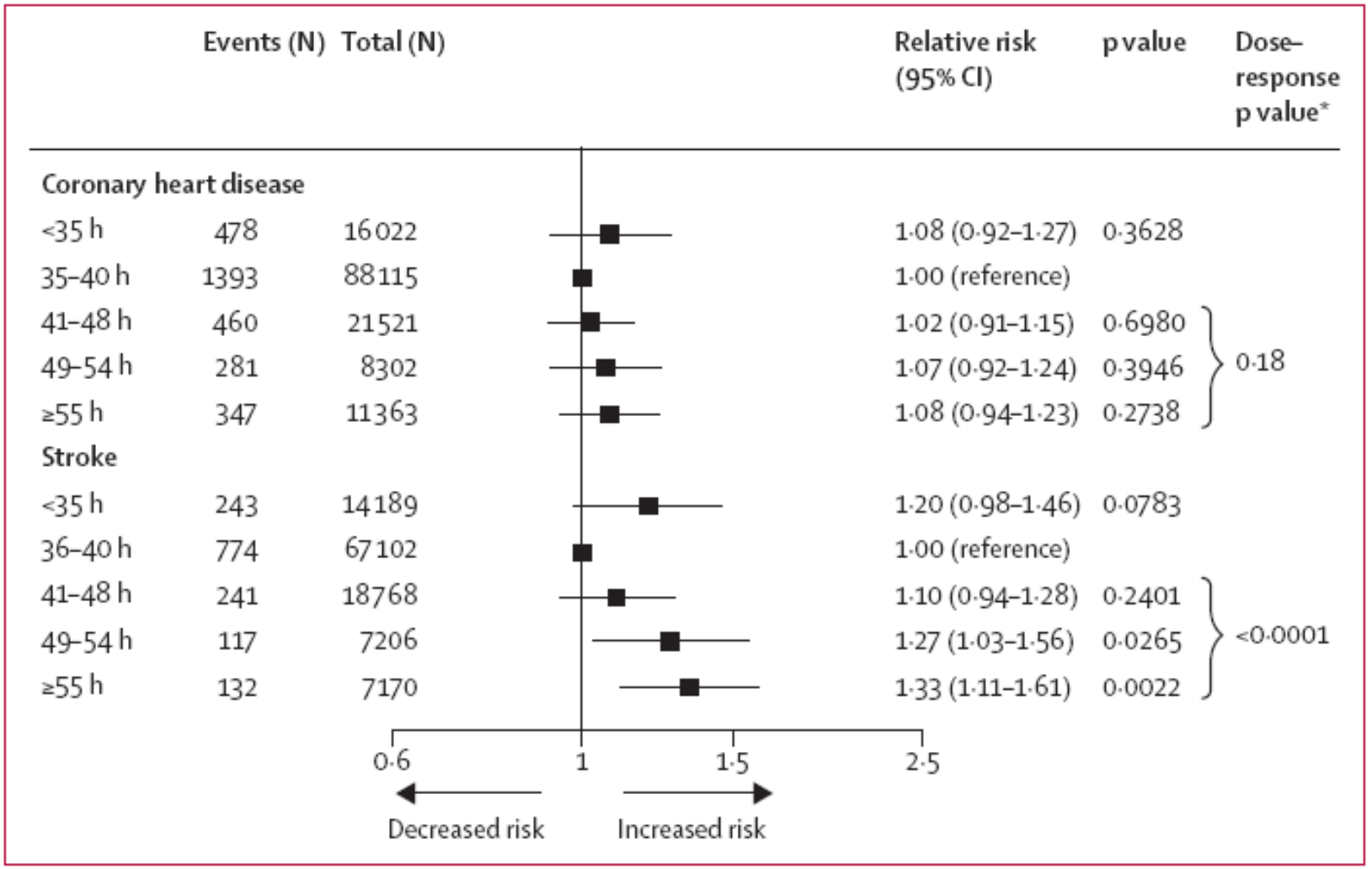

Figure 4: **Association of categories of weekly working hours with incident coronary heart disease and stroke**
Estimates adjusted for age, sex, and socioeconomic status. *For trend from standard to long working hours.

Origine développementale

médecine/sciences 2016 ; 32 : 9-10

Éditorial

Environnements précoces, origines précoces de la santé et des maladies

Marie-Noël Bruné Drisse

ÉDITORIAL

> Les enfants d'aujourd'hui habitent un monde en pleine évolution. La globalisation et l'industrialisation offrent aux populations des opportunités dans de nombreux domaines, mais elles nous exposent en parallèle à des risques nouveaux. Pendant ces dernières décennies, les connaissances scientifiques ont connu des avancées rapides. Ainsi, les recherches réalisées autour du concept de la DOHaD (origines développementales de la santé et des maladies) ont permis de mettre en évidence la vulnérabilité toute particulière des enfants, depuis leur conception et pendant les premières années de vie, aux facteurs de risque chimiques, biologiques et physiques présents dans leurs environnements, mais les pays à revenus faibles ou intermédiaires, le coût de l'exposition et de son impact représentait 1,20 % du produit intérieur brut (PIB) mondial en 2011 [2].

Les études mettent également en évidence un lien entre l'exposition prénatale à la pollution de l'air et le petit poids de naissance et le développement cognitif chez l'enfant. Les périodes de développement, et donc de vulnérabilité, pourraient ainsi représenter des périodes de prévention au cours desquelles l'impact de nos interventions serait le plus efficace. Un renforcement de nos politiques environnementales et une adaptation des

L'IMC à l'adolescence

ORIGINAL ARTICLE

Body-Mass Index in 2.3 Million Adolescents and Cardiovascular Death in Adulthood

Gilad Twig, M.D., Ph.D., Gal Yaniv, M.D., Ph.D., Hagai Levine, M.D., M.P.H., Adi Leiba, M.D., M.H.A., Nehama Goldberger, M.Sc., Estela Derazne, M.Sc., Dana Ben-Ami Shor, M.D., Dorit Tzur, M.B.A., Arnon Afek, M.D., M.H.A., Ari Shamiss, M.D., M.P.H., Ziona Haklai, M.A., and Jeremy D. Kark, M.D., Ph.D.

ABSTRACT

BACKGROUND

In light of the worldwide increase in childhood obesity, we examined the association between body-mass index (BMI) in late adolescence and death from cardiovascular causes in adulthood.

METHODS

We grouped data on BMI, as measured from 1967 through 2010 in 2.3 million Israeli adolescents (mean age, 17.3±0.4 years), according to age- and sex-specific percentiles from the U.S. Centers for Disease Control and Prevention. Primary outcomes were the number of deaths attributed to coronary heart disease, stroke, sudden death from an unknown cause, or a combination of all three categories (total cardiovascular causes) by mid-2011. Cox proportional-hazards models were used.

RESULTS

During 42,297,007 person-years of follow-up, 2918 of 32,127 deaths (9.1%) were from cardiovascular causes, including 1497 from coronary heart disease, 528 from stroke, and 893 from sudden death. On multivariable analysis, there was a graded increase in the risk of death from cardiovascular causes and all causes that started among participants in the group that was in the 50th to 74th percentiles of BMI (i.e., within the accepted normal range). Hazard ratios in the obese group (≥95th percentile for BMI), as compared with the reference group in the 5th to 24th percentiles, were 4.9 (95% confidence interval [CI], 3.9 to 6.1) for death from coronary

From the Department of Medicine (G.T., A.L., D.B.-A.S., A.S.) and the Dr. Pinchas Bornstein Talpiot Medical Leadership Program (G.T., G.Y.), Sheba Medical Center, Tel Hashomer, the Israel Defense Forces Medical Corps (G.T., G.Y., A.L., E.D., D.T.), Sackler School of Medicine, Tel Aviv University, Tel Aviv (G.T., A.L., E.D., D.B.-A.S., A.A., A.S.), and Hebrew University–Hadassah School of Public Health and Community Medicine (H.L., J.D.K.) and the Israel Ministry of Health (N.G., A.A., Z.H.), Jerusalem — all in Israel; and the Department of Medicine, Mount Auburn Hospital, Harvard Medical School, Cambridge, MA (A.L.). Address reprint requests to Dr. Twig at the Department of Medicine B, Sheba Medical Center, Tel Hashomer, Ramat Gan 52621, Israel, or at gilad.twig@gmail.com.

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DOI: 10.1056/NEJMoa1503840
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Conclusion

Un IMC compris entre le 50ème et le 74ème percentile, dans la fourchette normale acceptée, à l'adolescence est associé à une augmentation de la mortalité cardiovasculaire et de toutes causes confondues au cours des 40 années de suivi.

Le surpoids et l'obésité sont fortement associés à une mortalité cardiovasculaire accrue à l'âge adulte.

Les médicaments

OPEN ACCESS

Diclofenac use and cardiovascular risks: series of nationwide cohort studies

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Additional material is published online only. To view please visit the journal online.

Cite this as: *BMJ* 2018;362:k3426 http://dx.doi.org/10.1136/bmj.k3426

Accepted: 19 July 2018

ABSTRACT

OBJECTIVE

To examine the cardiovascular risks of diclofenac initiation compared with initiation of other traditional non-steroidal anti-inflammatory drugs, initiation of paracetamol, and no initiation.

DESIGN

Series of 252 nationwide cohort studies, each mimicking the strict design criteria of a clinical trial (emulated trial design).

SETTING

Danish, nationwide, population based health registries (1996-2016).

PARTICIPANTS

Individuals eligible for inclusion were all adults without malignancy; schizophrenia; dementia; or cardiovascular, kidney, liver, or ulcer diseases (that is, with low baseline risk). The study included 1 370 832

RESULTS

The adverse event rate among diclofenac initiators increased by 50% compared with non-initiators (incidence rate ratio 1.5, 95% confidence interval 1.4 to 1.7), 20% compared with paracetamol or ibuprofen initiators (both 1.2, 1.1 to 1.3), and 30% compared with naproxen initiators (1.3, 1.1 to 1.5). The event rate for diclofenac initiators increased for each component of the combined endpoint (1.2 (1.1 to 1.4) for atrial fibrillation/flutter, 1.6 (1.3 to 2.0) for ischaemic stroke, 1.7 (1.4 to 2.0) for heart failure, 1.9 (1.6 to 2.2) for myocardial infarction, and 1.7 (1.4 to 2.1) for cardiac death) as well as for low doses of diclofenac, compared with non-initiators. Although the relative risk of major adverse cardiovascular events was highest in individuals with low or moderate baseline risk (that is, diabetes mellitus), the absolute risk was highest in individuals with high baseline risk

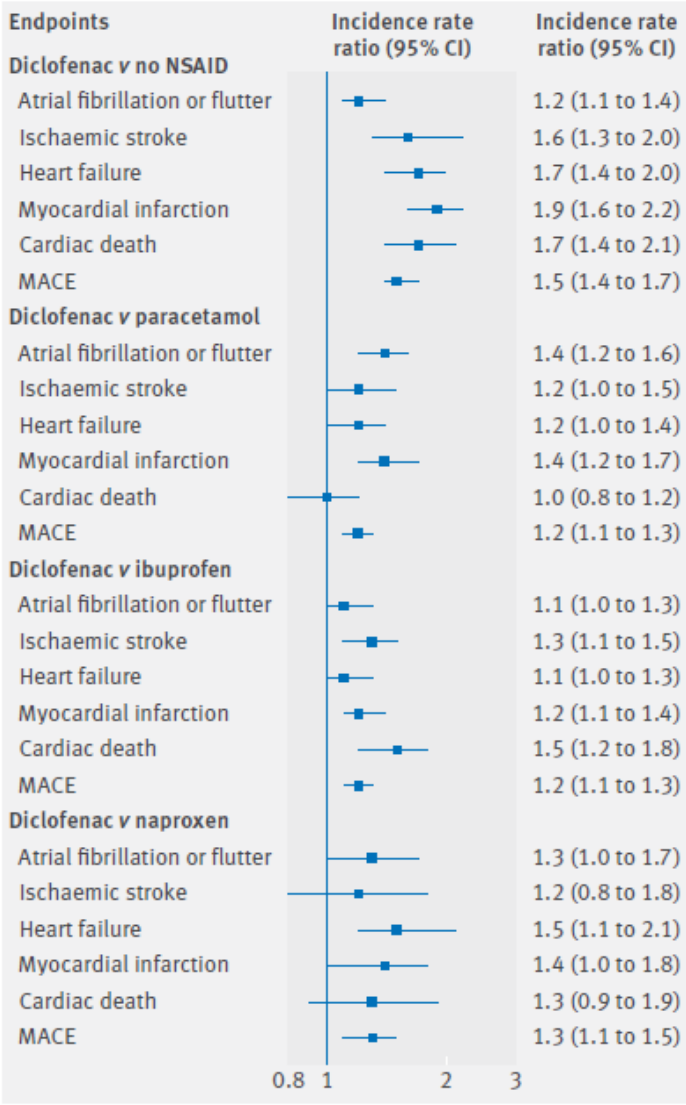

Fig 2 | Cardiovascular risks at 30 days associated with diclofenac initiation compared with no NSAID initiation and initiation of paracetamol, ibuprofen, or naproxen. NSAID=non-steroidal anti-inflammatory drug; MACE=major adverse cardiovascular event

Cite this as: *BMJ* 2018;362:k3426
http://dx.doi.org/10.1136/bmj.k3426

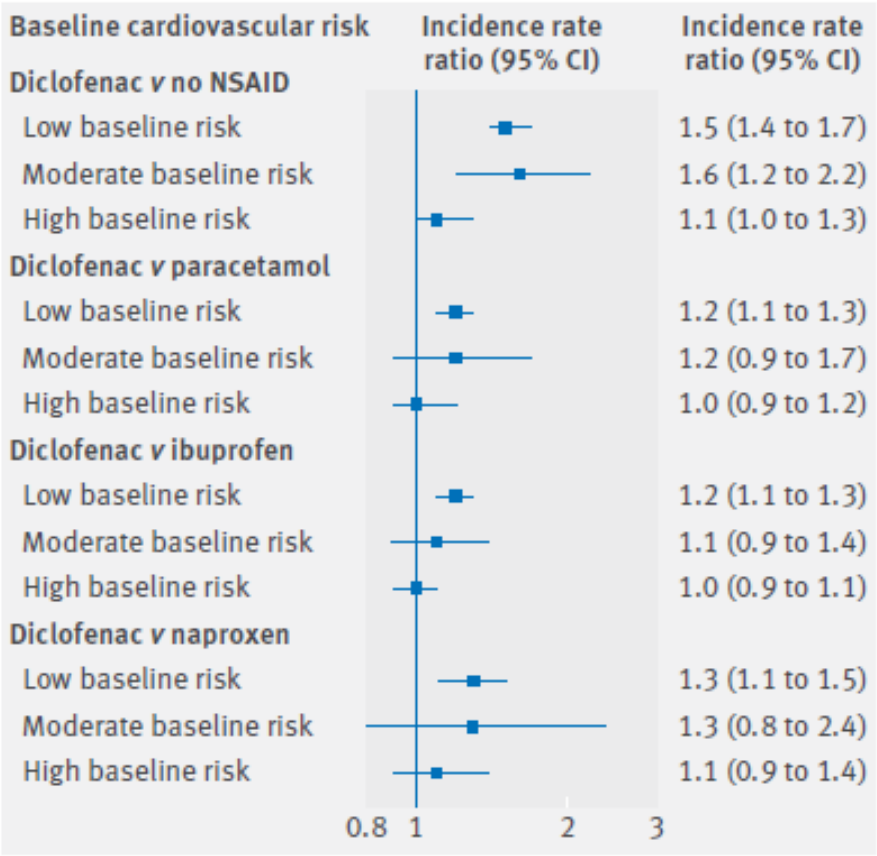

Fig 4 | Risk of major adverse cardiovascular events after diclofenac initiation according to baseline cardiovascular risk. NSAID=non-steroidal anti-inflammatory drug

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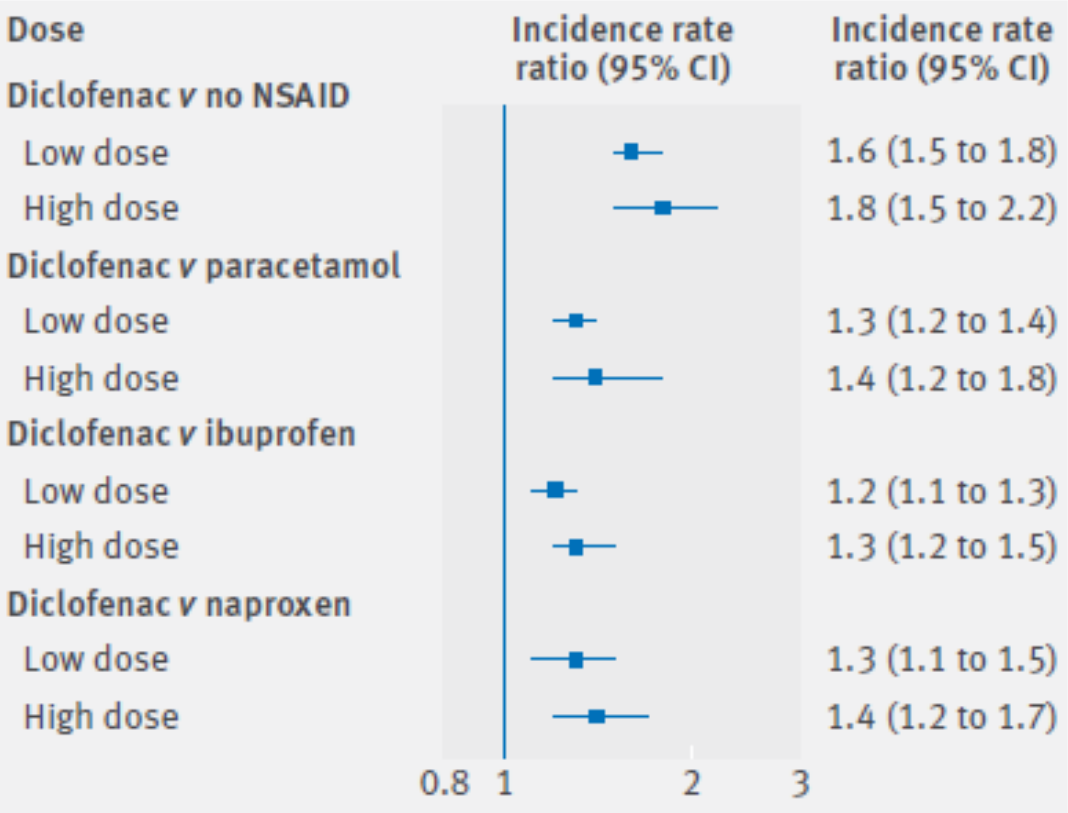

Fig 5 | Risk of major adverse cardiovascular events comparing initiation of low and high dose diclofenac with no NSAID initiation or initiation of paracetamol, ibuprofen, or naproxen. NSAID=non-steroidal anti-inflammatory drug

Cite this as: *BMJ* 2018;362:k3426
http://dx.doi.org/10.1136/bmj.k3426

Conclusion

Cette étude fournit une vue d'ensemble du spectre et de l'ampleur des risques cardiovasculaires liés à l'initiation du diclofénac. Elle a également montré que les initiateurs du diclofénac présentaient un risque hémorragique gastro-intestinal supérieur similaire à celui des initiateurs du naproxène et plus de deux fois plus de risques que les initiateurs d'ibuprofène. Le traitement de la douleur et de l'inflammation avec des AINS peut être intéressant pour certains patients afin d'améliorer leur qualité de vie malgré les effets secondaires potentiels. Compte tenu de ses risques cardiovasculaires et gastro-intestinaux, il n'est guère justifié d'instaurer un traitement par le diclofénac avant les autres AINS classiques.

Le Syndrome d'apnées obstructives du sommeil (SAS)

Respiratory Disturbance Index

An Independent Predictor of Mortality in Coronary Artery Disease

YÜKSEL PEKER, JAN HEDNER, HOLGER KRAICZI, and STEEN LÖTH

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Am J Respir Crit Care Med Vol 162. pp 81–86, 2000
Internet address: www.atsjournals.org

TABLE 4

OUTCOME VARIABLES DURING A 5-yr FOLLOW-UP PERIOD*

Variable	OSA (+) (*n = 16*)	OSA (−) (*n = 43*)	p Values
Myocardial infarction, n (%)	5 (31.3)	8 (18.6)	NS
Stroke, n (%)	1 (6.3)	5 (11.6)	NS
Mortality, n (%)	6 (37.5)	4 (9.3)	0.018

Definition of abbreviation: NS = not significant.

* Comparison of groups by Fisher exact test (two-tailed).

Am J Respir Crit Care Med Vol 162. pp 81–86, 2000
Internet address: www.atsjournals.org

TABLE 6

SIGNIFICANT PREDICTORS OF CARDIOVASCULAR MORTALITY IN CAD PATIENTS DURING 5 yr AFTER DISCHARGE FROM THE ICU

	p Values (two sided)
In univariate analysis	
RDI	0.007
OSA (RDI $\geqslant$ 10/h)	0.014
Age at baseline	0.028
Hypertension at baseline	0.036
History of never-smoking	0.031
Digoxin treatment during the observation period	0.013
In multivariate analysis	
RDI	< 0.001*

* Using Cox multiple conditional regression model (exp $\beta = 1.13$, 95% CI 1.05 to 1.21).

Am J Respir Crit Care Med Vol 162. pp 81–86, 2000
Internet address: www.atsjournals.org

Obstructive Sleep Apnea as a Risk Factor for Stroke and Death

H. Klar Yaggi, M.D., M.P.H., John Concato, M.D., M.P.H., Walter N. Kernan, M.D., Judith H. Lichtman, Ph.D., M.P.H., Lawrence M. Brass, M.D., and Vahid Mohsenin, M.D.

ABSTRACT

BACKGROUND

Previous studies have suggested that the obstructive sleep apnea syndrome may be an important risk factor for stroke. It has not been determined, however, whether the syndrome is independently related to the risk of stroke or death from any cause after adjustment for other risk factors, including hypertension.

METHODS

In this observational cohort study, consecutive patients underwent polysomnography, and subsequent events (strokes and deaths) were verified. The diagnosis of the obstructive sleep apnea syndrome was based on an apnea–hypopnea index of 5 or higher (five or more events per hour); patients with an apnea–hypopnea index of less than 5 served as the comparison group. Proportional-hazards analysis was used to determine the independent effect of the obstructive sleep apnea syndrome on the composite outcome of stroke or death from any cause.

From the Section of Pulmonary and Critical Care Medicine, Yale Center for Sleep Medicine (H.K.Y., V.M.), the Section of General Medicine (J.C., W.N.K.), and the Departments of Epidemiology and Public Health (J.H.L., L.M.B.) and Neurology (L.M.B.), Yale University School of Medicine, New Haven, Conn.; and the Section of Pulmonary and Critical Care Medicine (H.K.Y.), the Clinical Epidemiology Research Center (H.K.Y., J.C.), and the Section of Neurology (L.M.B.), Veterans Affairs Connecticut Healthcare System, West Haven, Conn. Address reprint requests to Dr. Mohsenin at the Yale Center for Sleep Medicine, 300 Cedar St., TAC 441, P.O. Box 208057, New Haven, CT 06520.

N Engl J Med 2005;353:2034-41.

Table 3. Trend Analysis for the Relationship between Increased Severity of the Obstructive Sleep Apnea Syndrome and the Composite Outcome of Stroke or Death from Any Cause (N=1022).*

Severity of Syndrome	Stroke or Death		Mean Follow-up Period	Hazard Ratio (95% CI)
	No. of Events	No. of Patients		
			yr	
AHI ≤3 (reference score)	13	271	3.08	1.00
AHI 4–12	21	258	3.06	1.75 (0.88–3.49)
AHI 13–36	20	243	3.09	1.74 (0.87–3.51)
AHI >36	34	250	2.78	3.30 (1.74–6.26)

* P=0.005 by the chi-square test for linear trend. AHI denotes apnea–hypopnea index, and CI confidence interval.

N Engl J Med 2005;353:2034-41.

Le Covid-19

nature medicine

ARTICLES

https://doi.org/10.1038/s41591-022-01689-3

Check for updates

OPEN

Long-term cardiovascular outcomes of COVID-19

Yan Xie[1,2,3], Evan Xu[1,4], Benjamin Bowe[1,2] and Ziyad Al-Aly[1,2,5,6,7] ✉

The cardiovascular complications of acute coronavirus disease 2019 (COVID-19) are well described, but the post-acute cardiovascular manifestations of COVID-19 have not yet been comprehensively characterized. Here we used national healthcare databases from the US Department of Veterans Affairs to build a cohort of 153,760 individuals with COVID-19, as well as two sets of control cohorts with 5,637,647 (contemporary controls) and 5,859,411 (historical controls) individuals, to estimate risks and 1-year burdens of a set of pre-specified incident cardiovascular outcomes. We show that, beyond the first 30 d after infection, individuals with COVID-19 are at increased risk of incident cardiovascular disease spanning several categories, including cerebrovascular disorders, dysrhythmias, ischemic and non-ischemic heart disease, pericarditis, myocarditis, heart failure and thromboembolic disease. These risks and burdens were evident even among individuals who were not hospitalized during the acute phase of the infection and increased in a graded fashion according to the care setting during the acute phase (non-hospitalized, hospitalized and admitted to intensive care). Our results provide evidence that the risk and 1-year burden of cardiovascular disease in survivors of acute COVID-19 are substantial. Care pathways of those surviving the acute episode of COVID-19 should include attention to cardiovascular health and disease.

2022

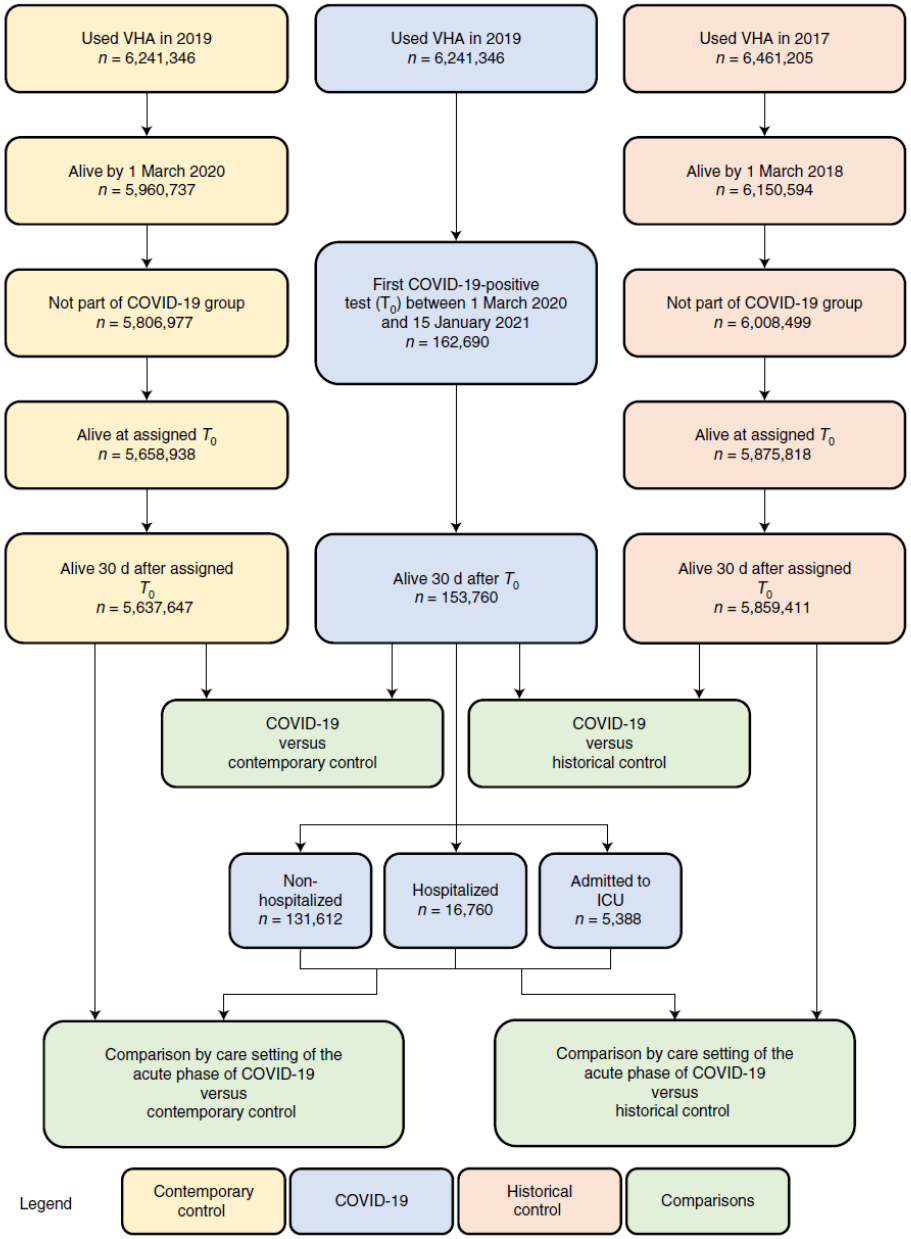

Fig. 1 | Flowchart of cohort construction. Cohort construction for COVID-19 group (blue), contemporary control group (yellow) and historical control group (orange). Comparisons between groups are presented in green.

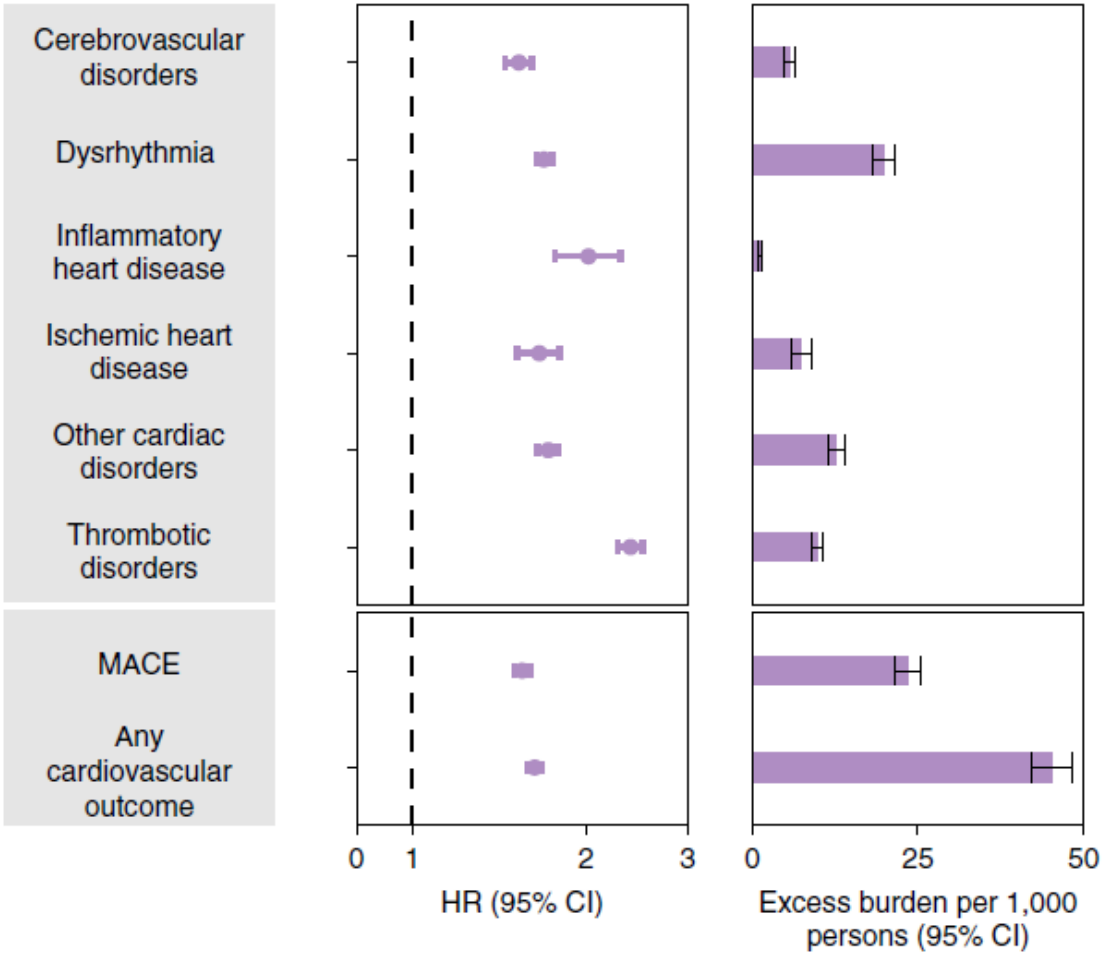

Fig. 3 | Risks and 12-month burdens of incident post-acute COVID-19 composite cardiovascular outcomes compared with the contemporary control cohort. Composite outcomes consisted of cerebrovascular

MACE : major adverse cardiovascular event (mortality, stroke and myocardial infarction)

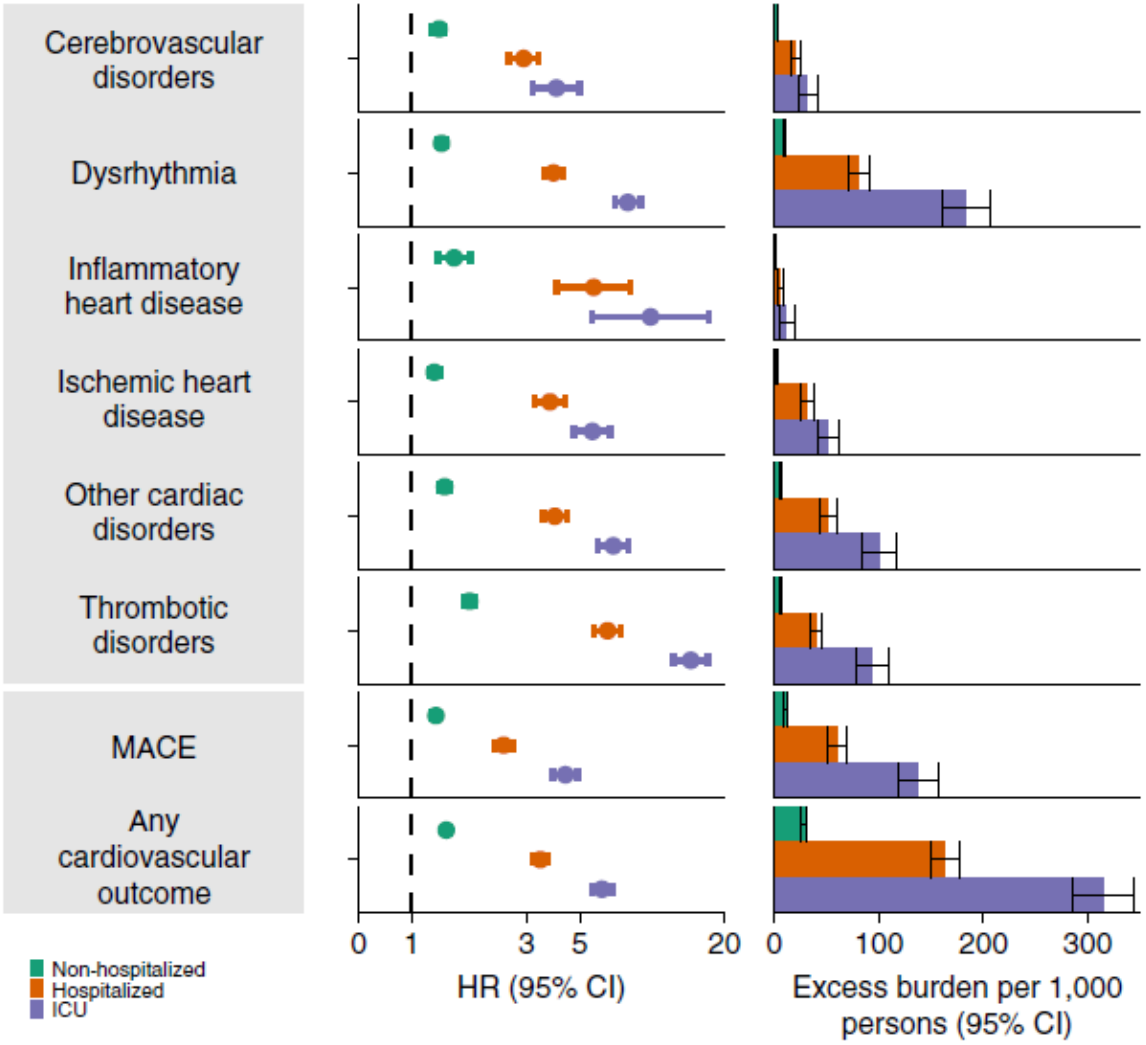

Fig. 6 | Risks and 12-month burdens of incident post-acute COVID-19 composite cardiovascular outcomes compared with the contemporary control cohort by care setting of the acute infection. Risks and burdens

Conclusions

- Par rapport aux contrôles « contemporains », les personnes ayant eu le Covid-19 avaient un surrisque (hazard ratio : 1,63) de survenue d'événements cardiovasculaires dans l'année suivant l'infection.
- Le surrisque d'événement cardiovasculaire était d'autant plus important que la sévérité du Covid avait été grande.
- Le surrisque persiste chez les patients ayant eu des épisodes non graves.
- Cette augmentation du risque CV était observée dans tous les sous-groupes, quels que soient les autres facteurs de risque cardiovasculaire connus.
- Des résultats similaires ont été obtenus en comparant la cohorte Covid au groupe contrôle « historique », soulignant que l'excès de risque existe indépendamment de la période analysée.
- Attention : cette étude a inclus des personnes infectées lors de la première année pandémique et la période considérée précède la mise à disposition des vaccins

https://www.larevuedupraticien.fr/article/covid-un-surrisque-cv-apres-infection-pendant-au-moins-1?t