Les complications cardiovasculaires IV

- Tabagisme
- Diabète sucré
- HTA

Prévention primaire

Tabagisme

Cite this article as: BMJ, doi:10.1136/bmj.38142.554479.AE (published 22 June 2004)

Papers

Mortality in relation to smoking: 50 years' observations on male British doctors

Richard Doll, Richard Peto, Jillian Boreham, Isabelle Sutherland

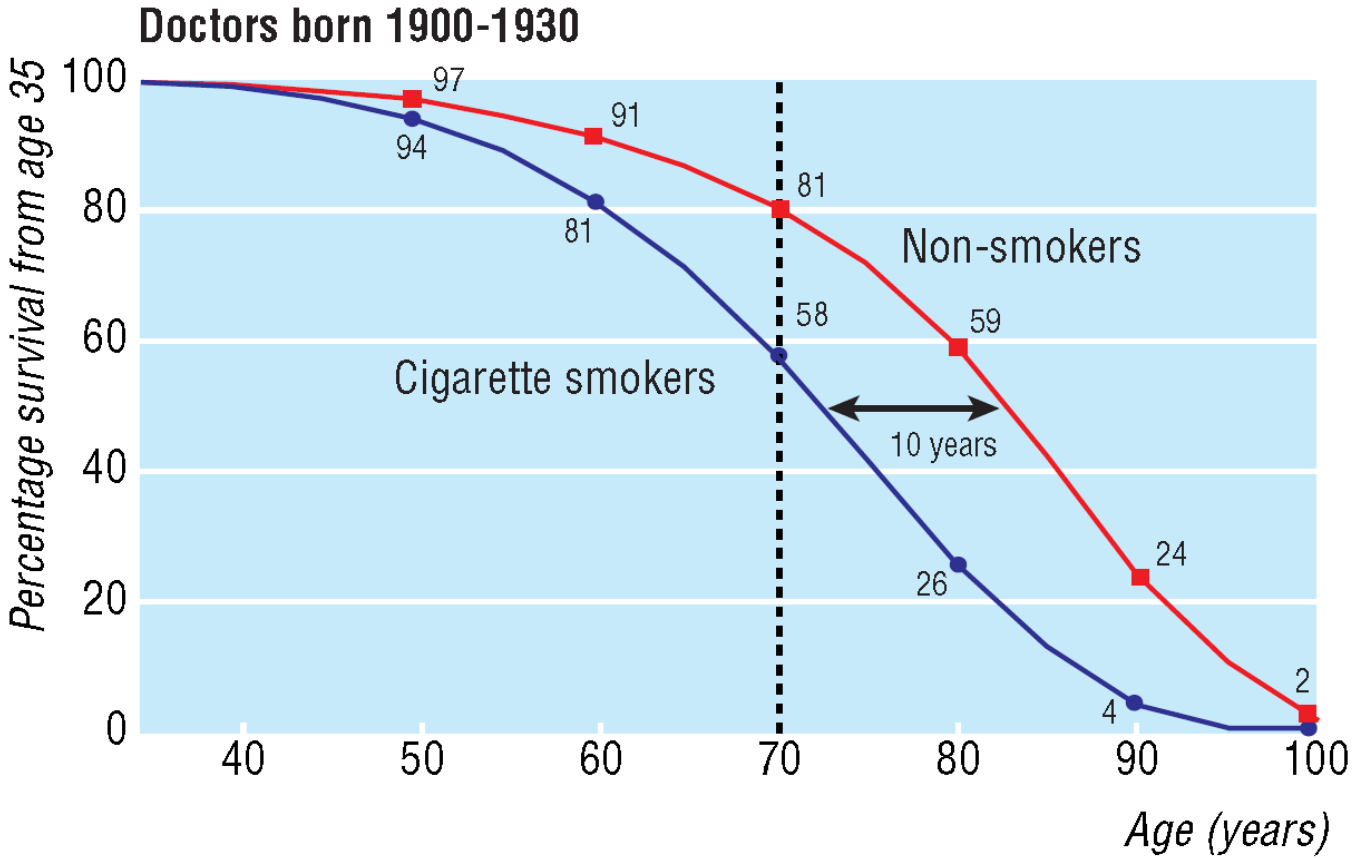

Fig 3 Survival from age 35 for continuing cigarette smokers and lifelong non-smokers among UK male doctors born 1900-1930, with percentages alive at each decade of age

BMJ, doi:10.1136/bmj.38142.554479.AE (published 22 June 2004)

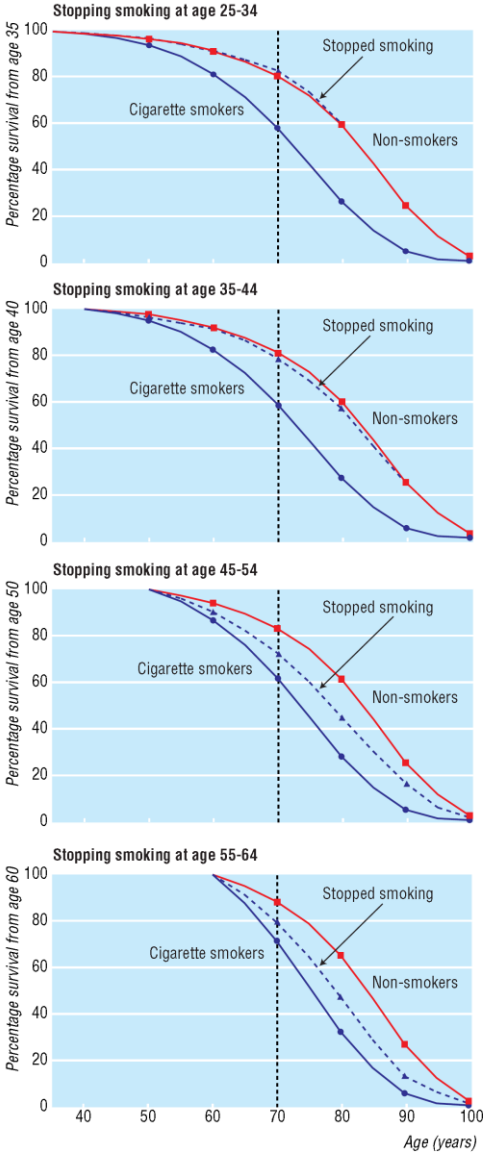

Fig 4 Effects on survival of stopping smoking cigarettes at age 25-34 (effect from age 35), age 35-44 (effect from age 40), age 45-54 (effect from age 50), and age 55-64 (effect from age 60)

BMJ, doi:10.1136/bmj.38142.554479.AE (published 22 June 2004)

Richard Doll. Une surprenante histoire de conflits d'intérêt

Richard Doll. A surprising story of conflicts of interest

J.-P. Sculier
Service des Soins intensifs et Urgences oncologiques & Oncologie thoracique,
Institut Jules Bordet, Centre des Tumeurs de l'ULB

RESUME

Richard Doll est un médecin épidémiologiste anglais très célèbre. On lui attribue la découverte du lien entre tabagisme et cancer bronchique. Sa réputation a été récemment entachée par deux faits, l'ignorance des études allemandes antérieures à ses travaux et l'existence de conflits d'intérêt majeurs avec l'industrie l'ayant conduit à minimiser le rôle des produits chimiques dans la carcinogenèse.

Rev Med Brux 2012 ; 33 : 487-90

ABSTRACT

Richard Doll is a very famous English physician epidemiologist. He is credited with discovering the link between smoking and lung cancer. His reputation was recently vitiated by two facts, ignorance of German studies prior to his work and the existence of major conflicts of interest with industry that led him to minimize the role of chemical products in carcinogenesis.

Rev Med Brux 2012 ; 33 : 487-90

Key words : conflicts of interest, Richard Doll

OPEN ACCESS

Impact of smoking and smoking cessation on cardiovascular events and mortality among older adults: meta-analysis of individual participant data from prospective cohort studies of the CHANCES consortium

Ute Mons,[1] Aysel Müezzinler,[1,2] Carolin Gellert,[1] Ben Schöttker,[1] Christian C Abnet,[3] Martin Bobak,[4] Lisette de Groot,[5] Neal D Freedman,[3] Eugène Jansen,[6] Frank Kee,[7] Daan Kromhout,[5] Kari Kuulasmaa,[8] Tiina Laatikainen,[8,9,10] Mark G O'Doherty,[7] Bas Bueno-de-Mesquita,[11,12,13,14] Philippos Orfanos,[15,16] Annette Peters,[17,18] Yvonne T van der Schouw,[19] Tom Wilsgaard,[20] Alicja Wolk,[21] Antonia Trichopoulou,[15,16] Paolo Boffetta,[15,22] Hermann Brenner,[1] on behalf of the CHANCES consortium

For numbered affiliations see end of article.

Correspondence to: U Mons, Division of Clinical Epidemiology and Aging Research, German Cancer Research Center (DKFZ), Im Neuenheimer Feld 581, 69120 Heidelberg, Germany
u.mons@dkfz.de

Cite this as: *BMJ* 2015;350:h1551
doi:10.1136/bmj.h1551

Accepted: 6 February 2015

ABSTRACT

OBJECTIVE

To investigate the impact of smoking and smoking cessation on cardiovascular mortality, acute coronary events, and stroke events in people aged 60 and older, and to calculate and report risk advancement periods for cardiovascular mortality in addition to traditional epidemiological relative risk measures.

DESIGN

Individual participant meta-analysis using data from 25 cohorts participating in the CHANCES consortium. Data were harmonised, analysed separately employing Cox proportional hazard regression models, and combined by meta-analysis.

RESULTS

Overall, 503 905 participants aged 60 and older were included in this study, of whom 37 952 died from cardiovascular disease. Random effects meta-analysis dose-response manner, and decreased continuously with time since smoking cessation in former smokers. Relative risk estimates for acute coronary events and for stroke events were somewhat lower than for cardiovascular mortality, but patterns were similar.

CONCLUSIONS

Our study corroborates and expands evidence from previous studies in showing that smoking is a strong independent risk factor of cardiovascular events and mortality even at older age, advancing cardiovascular mortality by more than five years, and demonstrating that smoking cessation in these age groups is still beneficial in reducing the excess risk.

Background

In 1964, the first of a series of the US Surgeon General's reports on the health consequences of smoking concluded that male smokers had a higher death rate from

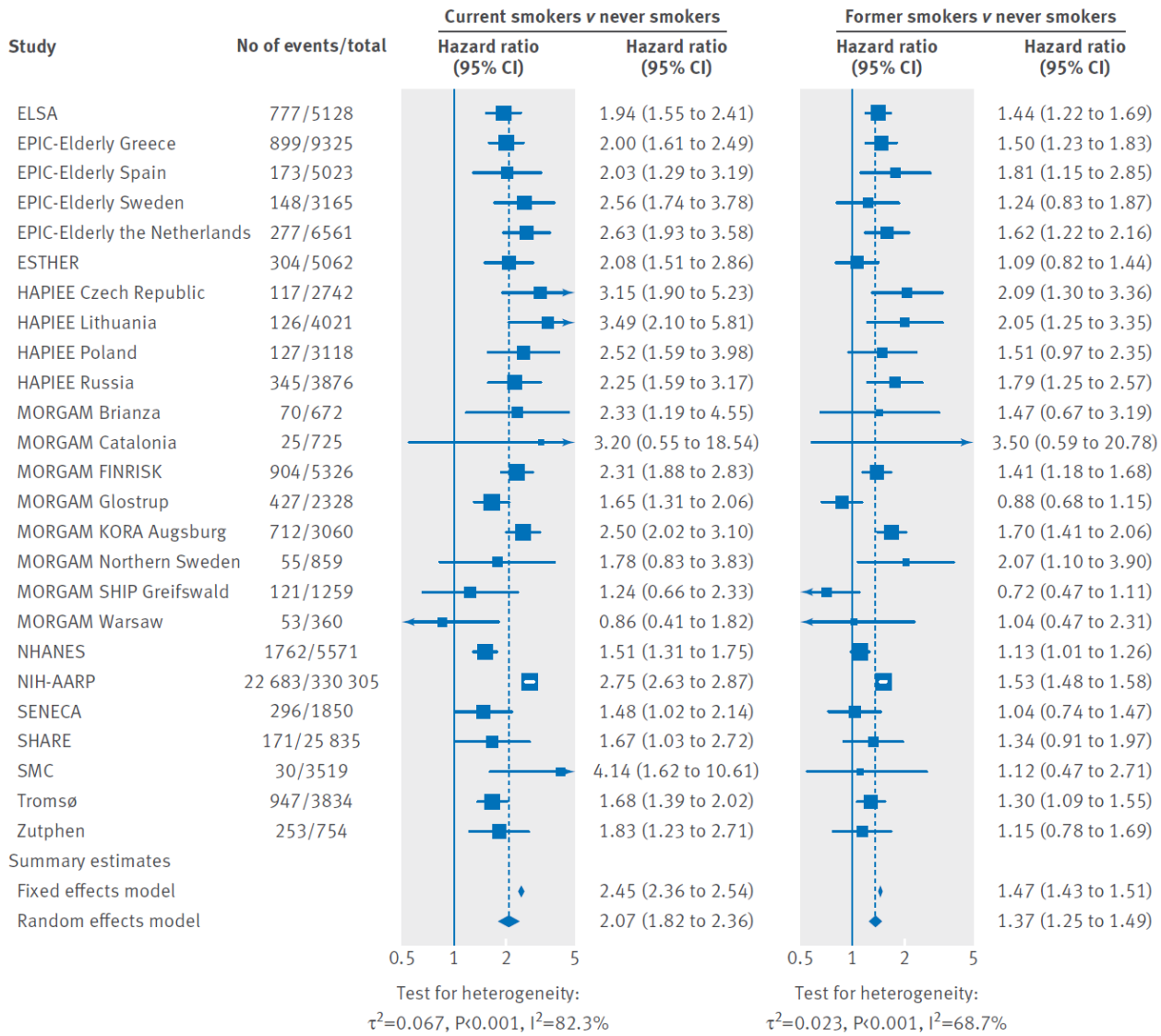

Fig 1 | Meta-analysis of the association of current smoking status with cardiovascular mortality

Cite this as: *BMJ* 2015;350:h1551
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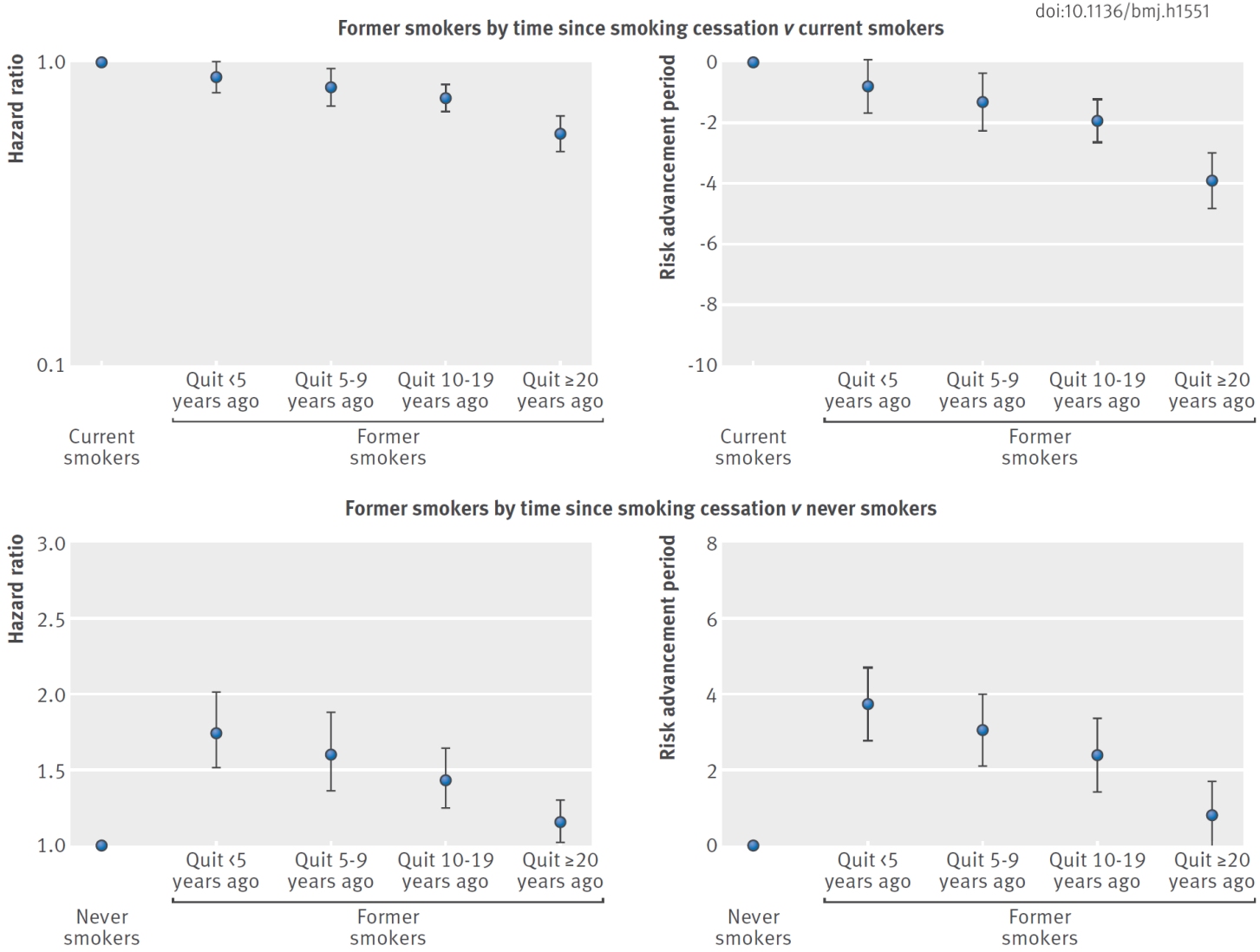


Fig 3 | Cardiovascular mortality summary estimates (random effects model) of hazard ratios and risk advancement periods for categories of cigarette consumption and time since smoking cessation

La période d'avancement du risque (RAP) donne le délai moyen auquel la survenue d'un événement (comme l'incidence de la maladie ou le décès) dû à un facteur de risque est avancée chez les personnes exposées par rapport aux personnes non exposées.

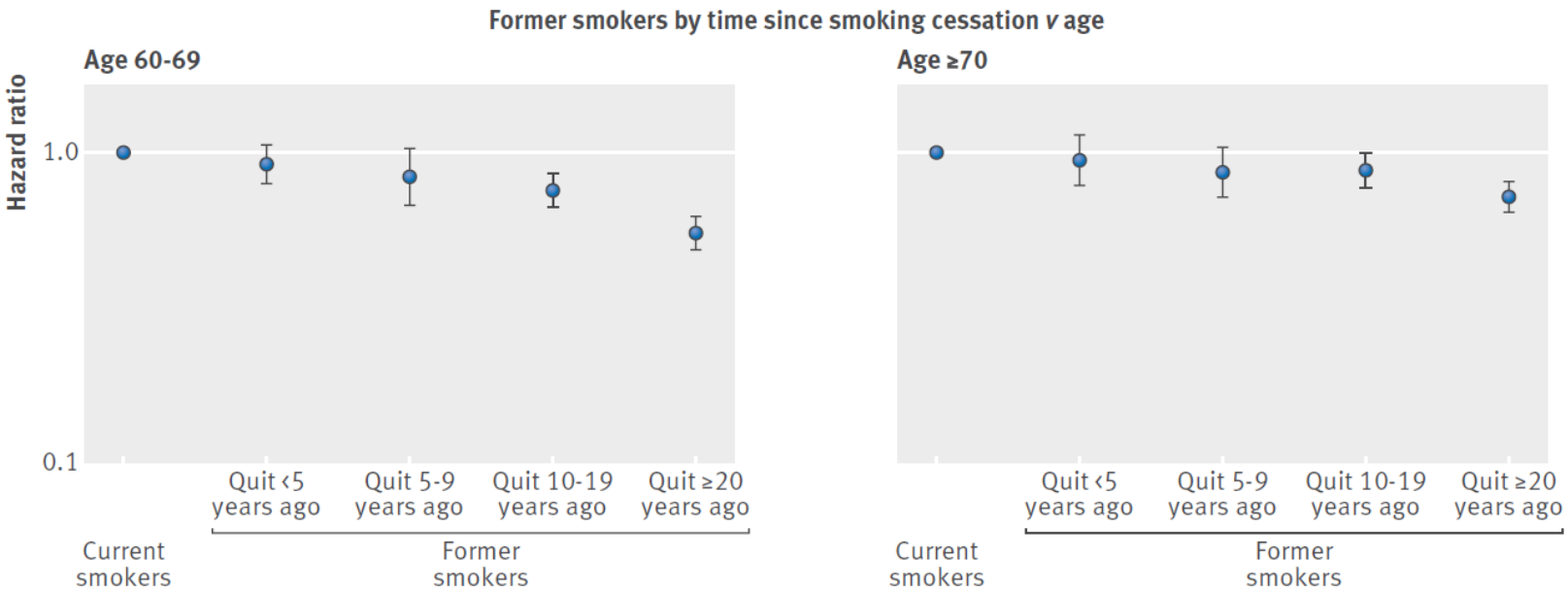


Fig 4 | Cardiovascular mortality summary estimates (random effects model) of hazard ratios for categories of time since smoking cessation by sex and age

Cite this as: *BMJ* 2015;350:h1551
doi:10.1136/bmj.h1551

Table 2 | Cardiovascular deaths, acute coronary events, and stroke events summary estimates (random effects model) of hazard ratios (HR) for current smoking status, from sex and age stratified analyses

		Cardiovascular deaths		Acute coronary events		Stroke events	
Population	Smoking status	HR	95% CI	HR	95% CI	HR	95% CI
Men	Never smokers	1.00		1.00		1.00	
	Former smokers	1.33	1.20 to 1.48	1.18	1.00 to 1.38	1.08	0.97 to 1.21
	Current smokers	1.95	1.69 to 2.25	1.80	1.51 to 2.15	1.44	1.23 to 1.68
Women	Never smokers	1.00		1.00		1.00	
	Former smokers	1.40	1.25 to 1.57	1.24	1.07 to 1.41	1.20	1.06 to 1.36
	Current smokers	2.22	1.86 to 2.65	2.26	1.98 to 2.59	1.78	1.46 to 2.17
Age 60–69	Never smokers	1.00		1.00		1.00	
	Former smokers	1.57	1.43 to 1.72	1.25	1.10 to 1.43	1.22	1.10 to 1.35
	Current smokers	2.45	2.22 to 2.69	2.02	1.78 to 2.28	1.68	1.46 to 1.94
Age 70+	Never smokers	1.00		1.00		1.00	
	Former smokers	1.21	1.08 to 1.36	1.12	0.95 to 1.32	1.10	0.95 to 1.28
	Current smokers	1.70	1.42 to 2.04	1.88	1.41 to 2.52	1.49	1.22 to 1.82

Cite this as: *BMJ* 2015;350:h1551
doi:10.1136/bmj.h1551

Prévention secondaire en cas de CMI

Smoking cessation for secondary prevention of cardiovascular disease (Review)

Wu AD, Lindson N, Hartmann-Boyce J, Wahedi A, Hajizadeh A, Theodoulou A, Thomas ET, Lee C, Aveyard P

Cochrane Database of Systematic Reviews 2022, Issue 8. Art. No.: CD014936.
DOI: 10.1002/14651858.CD014936.pub2.

68 études avec 80.702 participants

Summary of findings 1. Smoking cessation compared to continuous smoking for prevention of secondary cardiovascular disease events

Smoking cessation compared to continuous smoking for prevention of secondary cardiovascular disease events

Patient or population: people with coronary heart diease

Setting: hospital and community
Intervention: smoking cessation
Comparison: continuous smoking

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with continuous smoking	Risk with smoking cessation			
Death from cardiovascular disease at 19 months to 126 months	Study population		HR 0.61 (0.49 to 0.75)	17,982 (18 observational studies)	⊕⊕⊕⊖ Moderate[a,b]
	210 per 1000	134 per 1000 (109 to 162)			
Major adverse cardiovascular events (MACE) at 19 months to 110 months	Study population		HR 0.57 (0.45 to 0.71)	20,521 (15 observational studies)	⊕⊕⊖⊖ Low[c,d,e]
	323 per 1000	227 per 1000 (196 to 262)			

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

Cochrane Database of Systematic Reviews 2022, Issue 8. Art. No.: CD014936.
DOI: 10.1002/14651858.CD014936.pub2.

TABLEAU 1

Nombre et pourcentage de décès attribuables au tabagisme *

Causes des décès (nombre)	Hommes		Femmes	
	30-69 ans	> 70 ans	30-69 ans	> 70 ans
Cancer du poumon (848 000)	77 %	82 %	44 %	54 %
BPCO	54 %	52 %	24 %	19 %
Cardio-vasculaire (1 690 000)	24 % 848 000	12 % 476 000	6 % 143 000	4 % 223 000
Mortalité totale (4 833 000)	19 % 2 280 000	18 % 1 556 000	5 % 410 000	5 % 587 000

* Nombre de décès attribuables au tabagisme pour différentes pathologies et pourcentage de mortalité attribuable au tabagisme pour chacune de ces pathologies, par tranches d'âge (estimation à l'échelle mondiale en 2000). Le nombre de décès cardiovasculaires dus au tabagisme est le double de celui des décès par cancer du poumon. Environ 25 % des décès cardiovasculaires des hommes de moins de 70 ans sont attribuables au tabagisme. Contrairement aux décès par cancer du poumon, ce risque de décès cardiovasculaire attribuable au tabagisme est maximal chez les sujets jeunes. BPCO : bronchopneumopathie chronique obstructive. *D'après la réf. 1.*

Diabète sucré

Définition diabète type 2

critères biologiques :

- soit lors de 2 dosages effectués 2 jours différents, avec :
  - soit une glycémie à jeun ≥ 1,26 g/l (7 mmol/l)
  - soit une glycémie non à jeun ≥ 2 g/l (11,1 mmol/l)
- soit un taux d'hémoglobine glyquée (HbA1c) ≥ 6,5 %

Type 2 diabetes and incidence of cardiovascular diseases: a cohort study in 1·9 million people

Anoop Dinesh Shah, Claudia Langenberg, Eleni Rapsomaniki, Spiros Denaxas, Mar Pujades-Rodriguez, Chris P Gale, John Deanfield, Liam Smeeth, Adam Timmis, Harry Hemingway

Summary

Background The contemporary associations of type 2 diabetes with a wide range of incident cardiovascular diseases have not been compared. We aimed to study associations between type 2 diabetes and 12 initial manifestations of cardiovascular disease.

Methods We used linked primary care, hospital admission, disease registry, and death certificate records from the CALIBER programme, which links data for people in England recorded in four electronic health data sources. We included people who were (or turned) 30 years or older between Jan 1, 1998, to March 25, 2010, who were free from cardiovascular disease at baseline. The primary endpoint was the first record of one of 12 cardiovascular presentations in any of the data sources. We compared cumulative incidence curves for the initial presentation of cardiovascular disease and used Cox models to estimate cause-specific hazard ratios (HRs). This study is registered at ClinicalTrials.gov (NCT01804439).

Lancet Diabetes Endocrinol 2015; 3: 105–13

Published Online November 11, 2014 http://dx.doi.org/10.1016/S2213-8587(14)70219-0

See Comment page 92

Farr Institute of Health Informatics Research at London, London, UK (A D Shah MRCP, E Rapsomaniki PhD, S Denaxas PhD,

Ne pas se focaliser sur les troubles coronaires

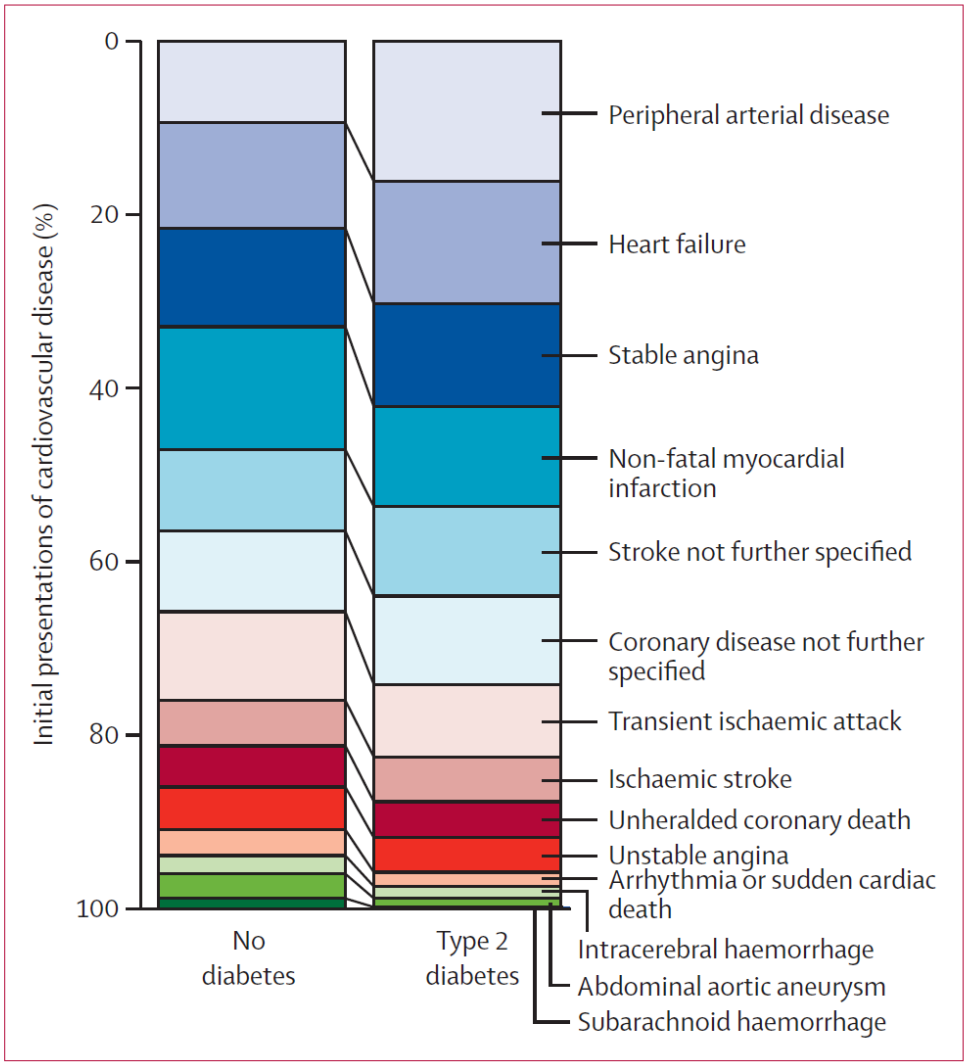


***Figure 1*: Distribution of initial presentations of cardiovascular diseases**
Distribution of initial presentations of cardiovascular disease in participants with and without type 2 diabetes and no history of cardiovascular disease.

Lancet Diabetes Endocrinol
2015; 3: 105–13

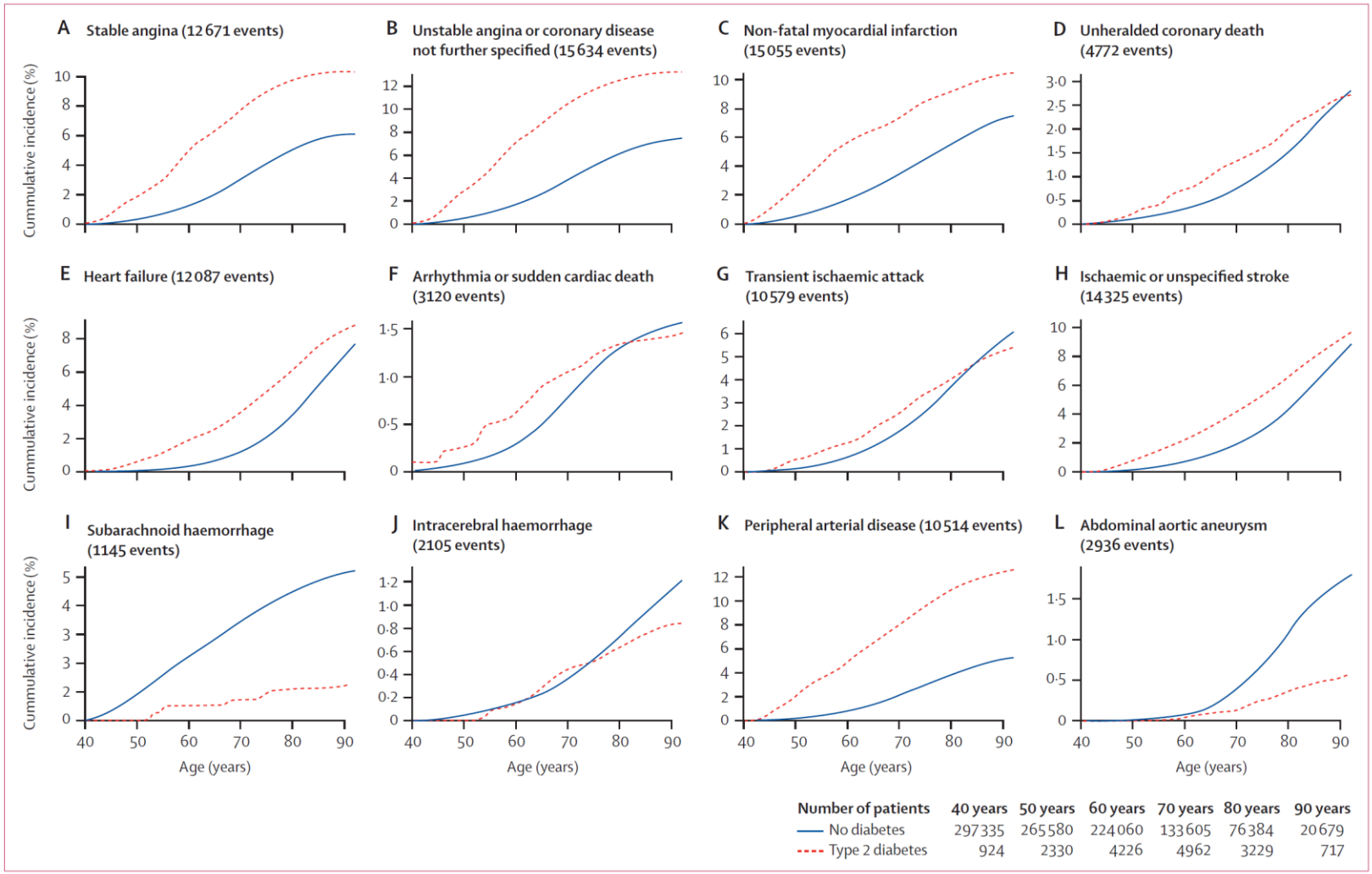


***Figure 2*: Cumulative incidence curves for the incidence of first presentation of 12 cardiovascular diseases in patients aged ≥40 years, by diabetes status**
The curves begin at age 40 years rather than 30 years because 40 years is a typical age for a patient to develop type 2 diabetes.

Lancet Diabetes Endocrinol
2015; 3: 105–13

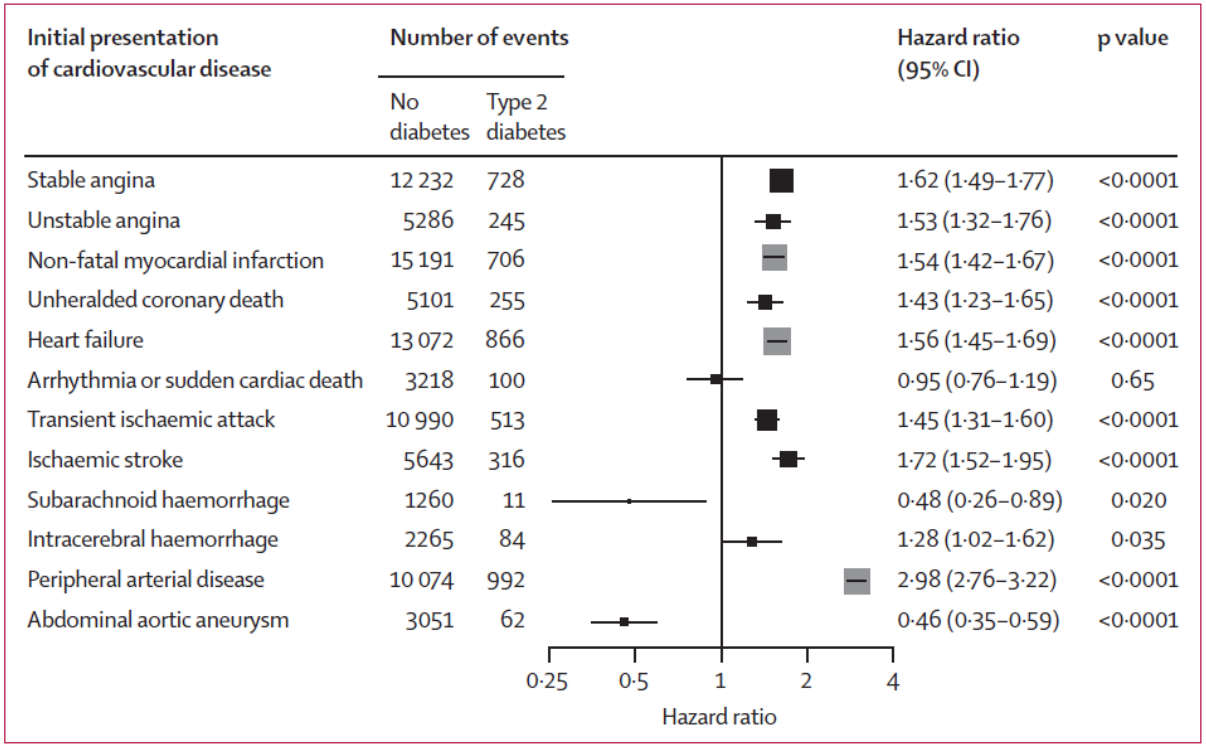
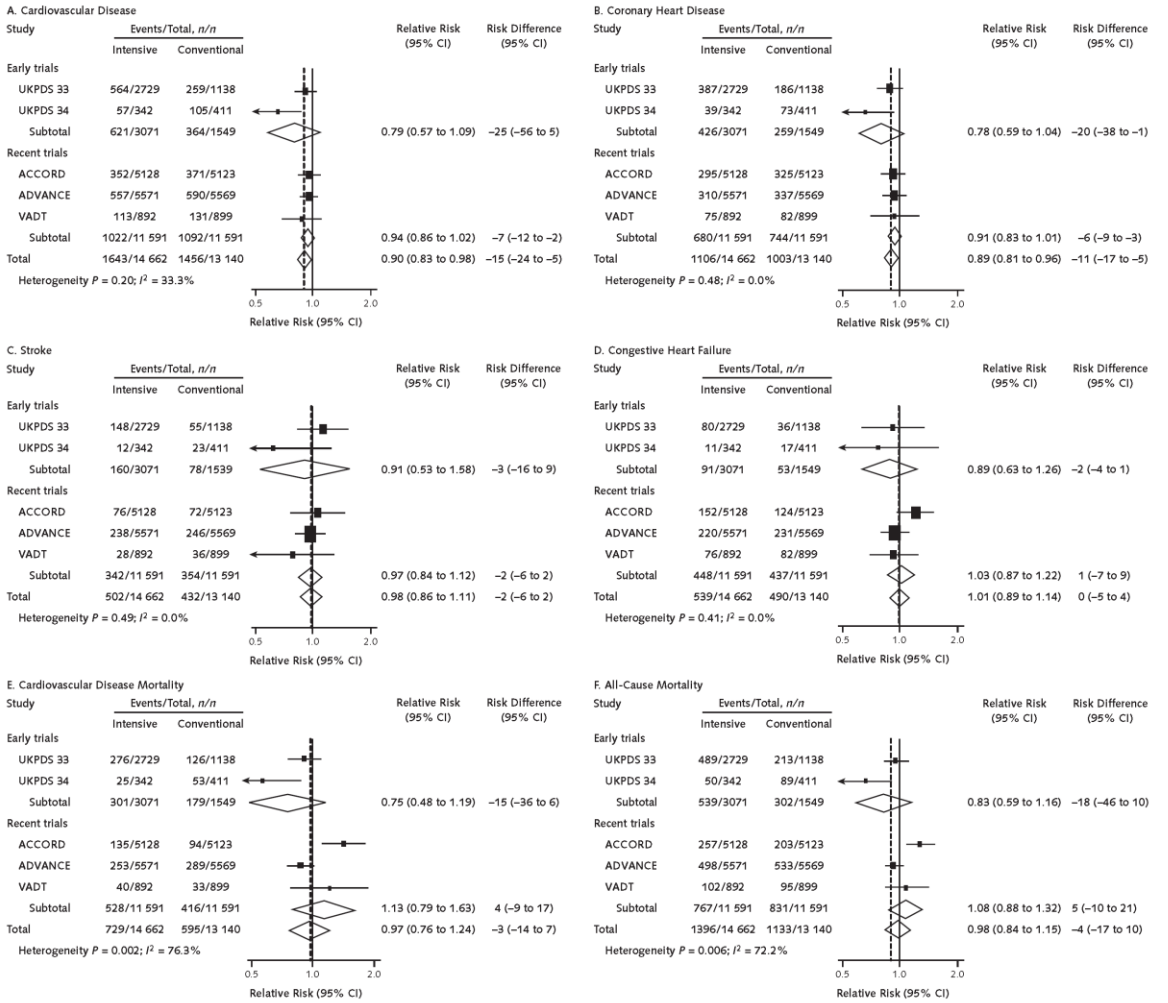


***Figure* 3: Association of type 2 diabetes with 12 cardiovascular diseases in patients aged ≥30 years**
Adjusted hazard ratios (HRs) for different initial presentations of cardiovascular diseases associated with type 2 diabetes, adjusted for age, sex, BMI, deprivation, HDL cholesterol, total cholesterol, systolic blood pressure, smoking status, and statin and antihypertensive drug prescriptions. Two non-specific components of the primary endpoint are not shown in the figure for simplicity (they are inprecisely recorded versions of one of the 12 initial presentations): coronary disease not further specified, HR 1·58 (95% CI 1·45–1·73), p<0·0001; stroke not further specified 1·64 (1·48–1·81), p<0·0001.

Lancet Diabetes Endocrinol
2015; 3: 105–13

Systematic Review: Glucose Control and Cardiovascular Disease in Type 2 Diabetes

Tanika N. Kelly, PhD; Lydia A. Bazzano, MD, PhD; Vivian A. Fonseca, MD; Tina K. Thethi, MD; Kristi Reynolds, PhD; and Jiang He, MD, PhD



ACCORD = Action to Control Cardiovascular Risk in Diabetes (12); ADVANCE = Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (13); UKPDS = United Kingdom Prospective Diabetes Study (8, 11); VADT = Veterans Affairs Diabetes Trial (14).

Diabète sucré : prévention des complications

- **pour les complications micro-vasculaires** (rétinopathie diabétique, néphropathie diabétique, neuropathie diabétique) : **contrôle strict de la glycémie** (suivre l'hémoglobine glycosée : essayer de la maintenir à 7%) et de l'albuminurie
- **pour les complications macro-vasculaires** (infarctus myocardique, AVC, insuffisance cardiaque, artériopathie MI) :
  - arrêt du tabagisme
  - contrôle de PA (< 130/80 mmHg)
  - blocage du système rénine-angiotensine (IEC)
  - contrôle du LDL-cholestérol (<100 mg/dl)

Importance de l'hémoglobine glyquée

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

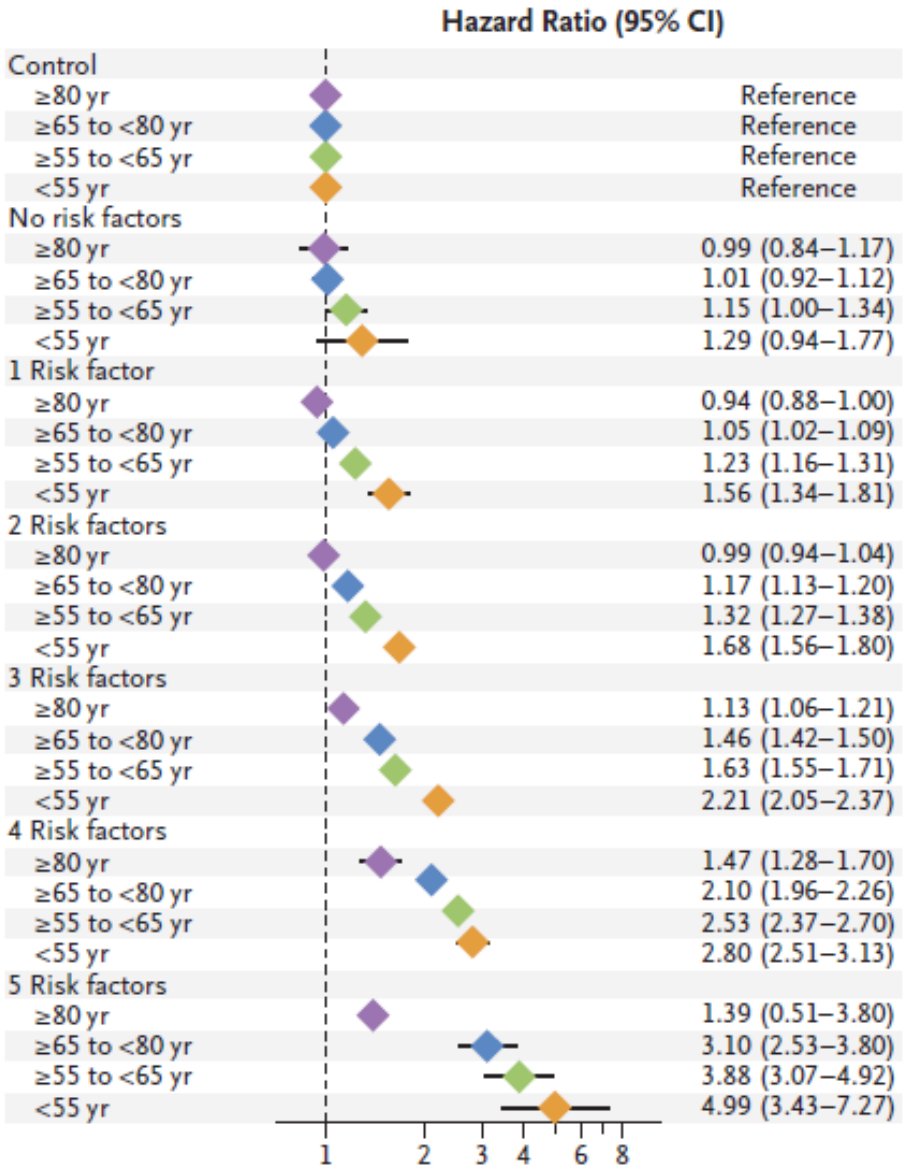
Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes

Aidin Rawshani, M.D., Araz Rawshani, M.D., Ph.D., Stefan Franzén, Ph.D., Naveed Sattar, M.D., Ph.D., Björn Eliasson, M.D., Ph.D., Ann-Marie Svensson, Ph.D., Björn Zethelius, M.D., Ph.D., Mervete Miftaraj, M.Sc., Darren K. McGuire, M.D., M.H.Sc., Annika Rosengren, M.D., Ph.D., and Soffia Gudbjörnsdottir, M.D., Ph.D.

N Engl J Med 2018;379:633-44.
DOI: 10.1056/NEJMoa1800256

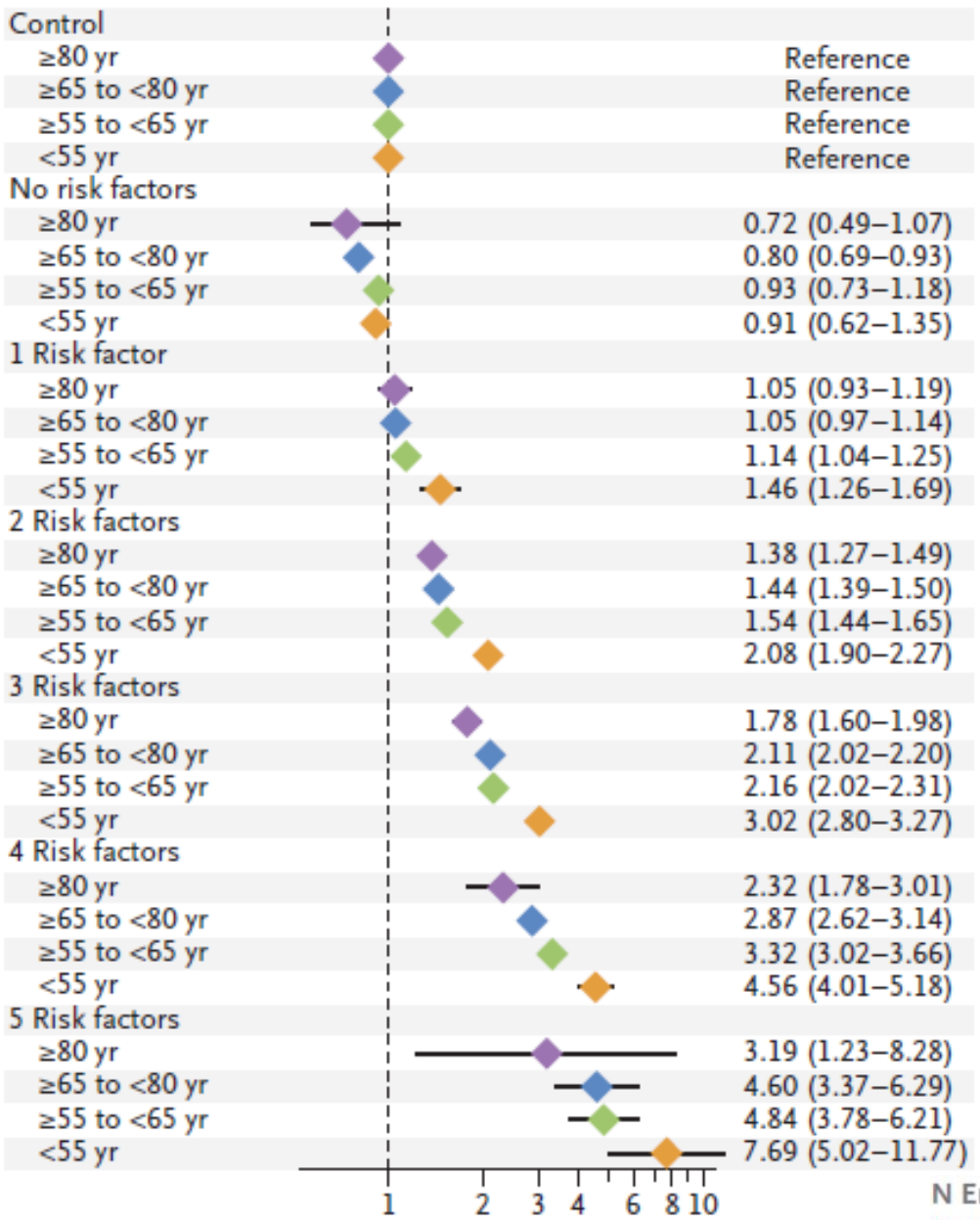
Dans une étude de cohorte, les auteurs ont inclus 271.174 patients atteints de diabète de type 2 inscrits au registre national suédois du diabète et les ont comparés à 1.355.870 témoins sur la base de l'âge, du sexe et du comté. On a évalué les patients diabétiques en fonction de leur âge et de la présence de cinq facteurs de risque (**taux élevé d'hémoglobine glyquée, taux élevé de LDL-cholestérol, albuminurie, tabagisme et tension artérielle élevée**). La régression de Cox a été utilisée pour étudier le risque excessif de conséquences (décès, infarctus aigu du myocarde, accident vasculaire cérébral et hospitalisation pour insuffisance cardiaque) associé au tabagisme et le nombre de variables hors des fourchettes cibles. Ont également été examinées les relations entre divers facteurs de risque et les résultats cardiovasculaires.

A Excess Mortality in Relation to Range of Risk-Factor Control



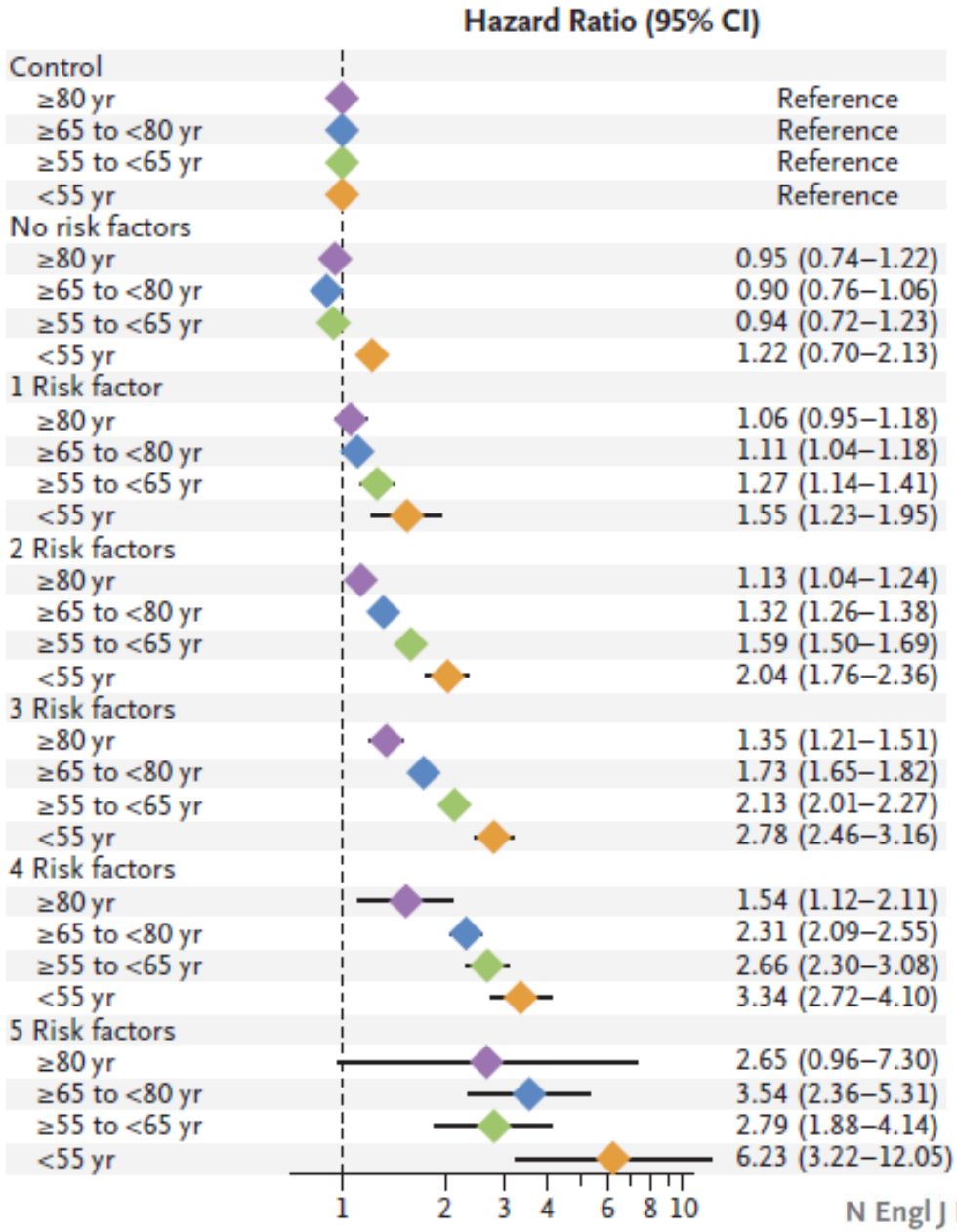
N Engl J Med 2018;379:633-44.
DOI: 10.1056/NEJMoa1800256

B Excess Acute Myocardial Infarction in Relation to Range of Risk-Factor Control



N Engl J Med 2018;379:633-44.
DOI: 10.1056/NEJMoa1800256

C Excess Stroke in Relation to Range of Risk-Factor Control



N Engl J Med 2018;379:633-44.
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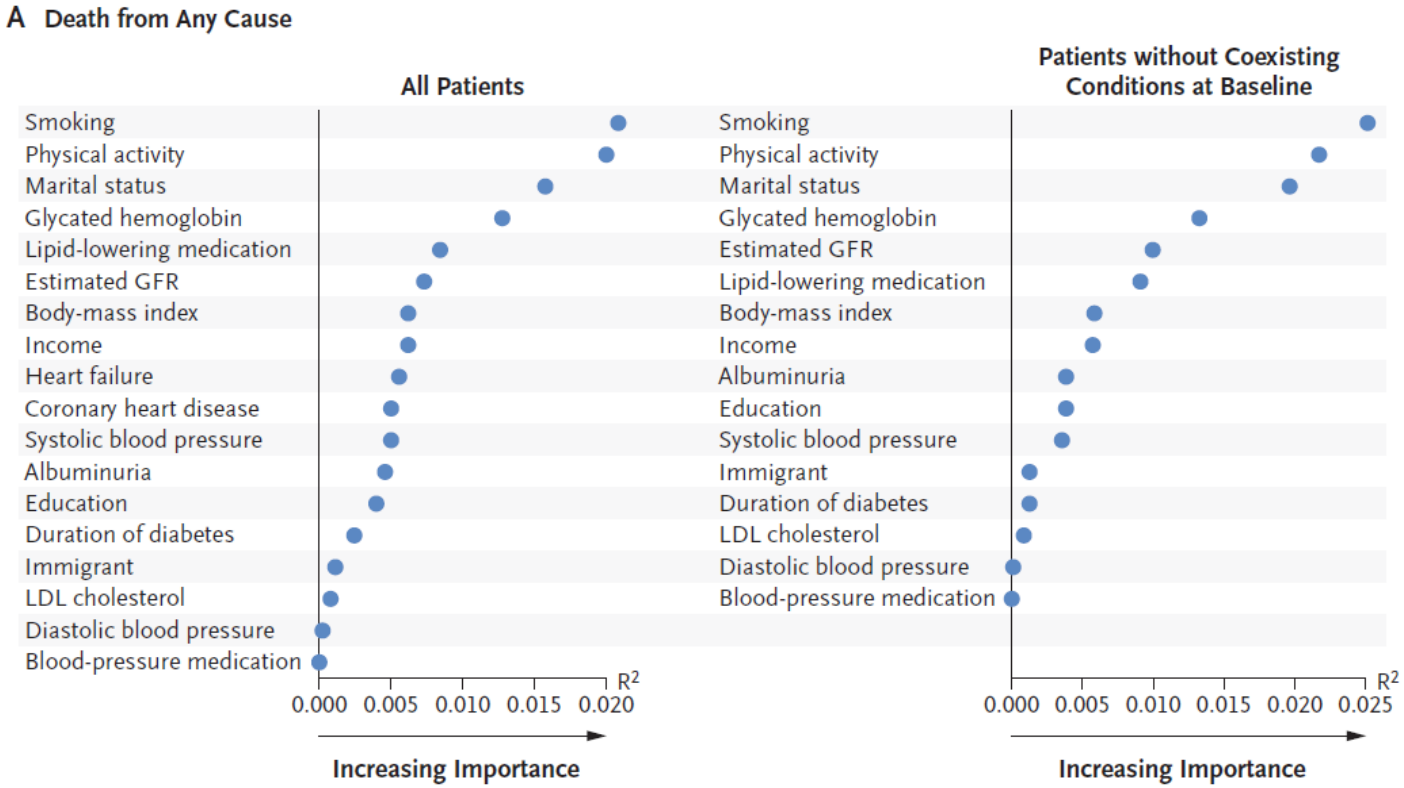

N Engl J Med 2018;379:633-44.
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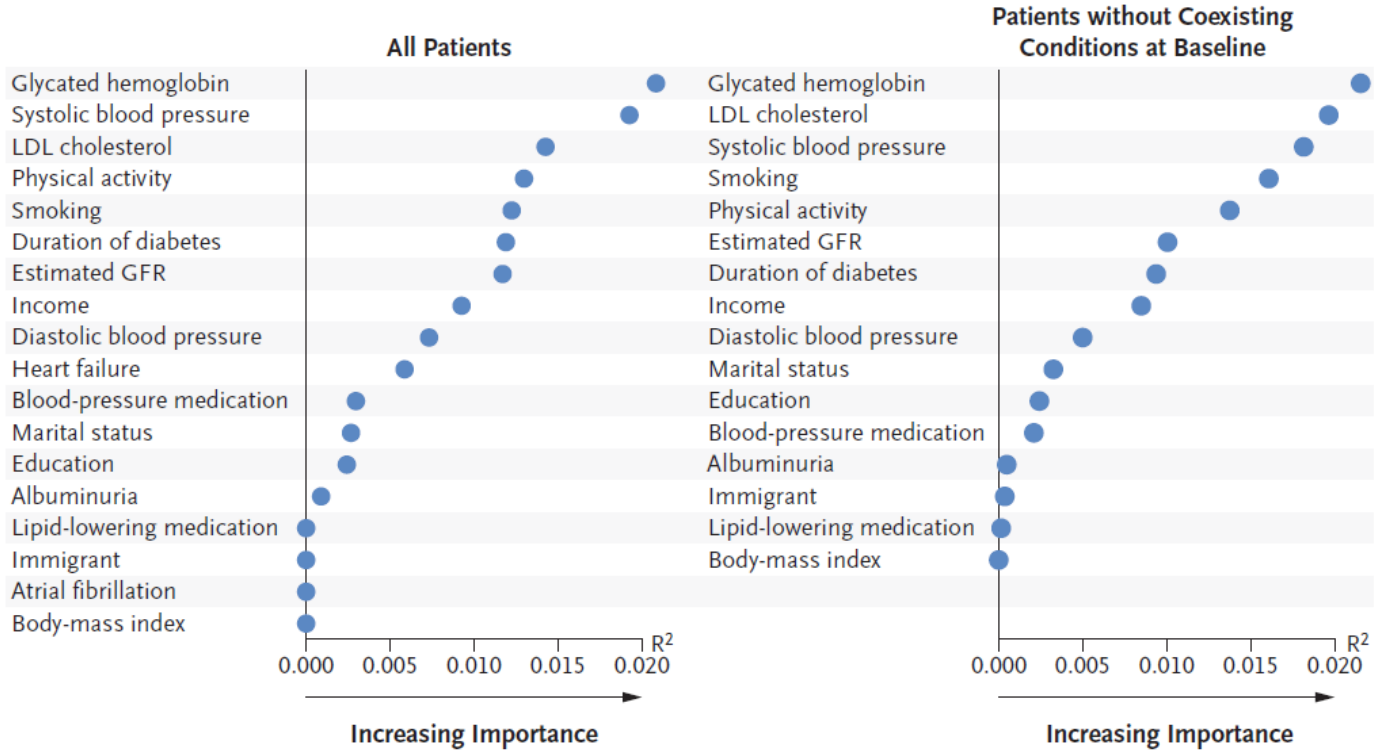
B Acute Myocardial Infarction



N Engl J Med 2018;379:633-44.
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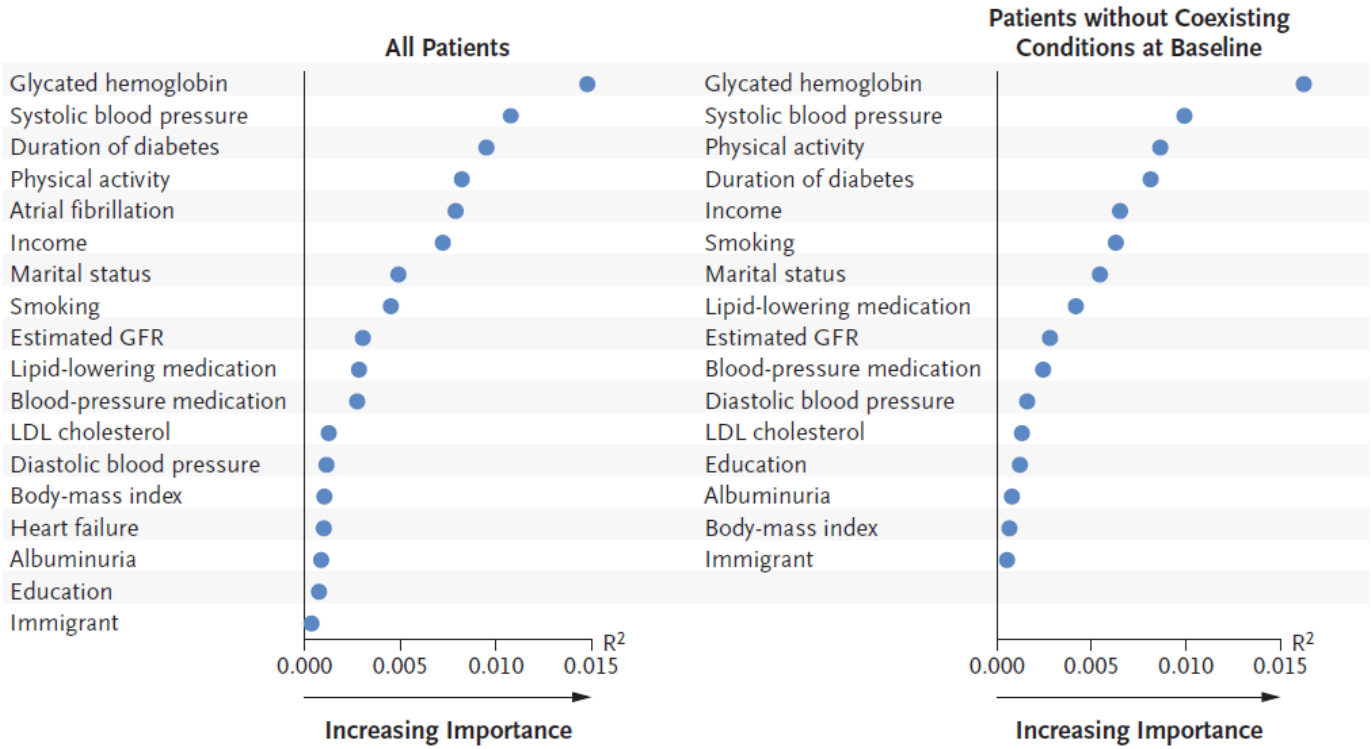
C Stroke



N Engl J Med 2018;379:633-44.
DOI: 10.1056/NEJMoa1800256

- « Parmi les patients diabétiques dont les cinq variables se situaient dans les limites de la cible, le ratio de risque de décès, quelle que soit la cause, est de 1,06 (comparé au groupe contrôle) (intervalle de confiance à 95% [IC], 1,00 à 1,12), le ratio de risque d'infarctus aigu du myocarde est de 0,84 (IC à 95%, 0,75 à 0,93) et le rapport de risque d'accident vasculaire cérébral est de 0,95 (IC à 95%, 0,84 à 1,07).
- Chez les patients atteints de diabète de type 2, un taux d'hémoglobine glyquée en dehors de l'intervalle cible est le principal facteur prédictif d'accident vasculaire cérébral et d'infarctus aigu du myocarde; le tabagisme est le plus puissant prédicteur de la mort ».

Conclusion

« Les patients atteints de diabète de type 2 présentant cinq facteurs de risque dans les fourchettes cibles semblent présenter peu ou pas de risque supplémentaire de décès, d'infarctus du myocarde ou d'accident vasculaire cérébral, par rapport à la population générale. »

Principes du traitement

- Mesures diététiques associées à une activité physique, pour diminuer l'excès pondéral souvent présent
- Metformine si insuffisant
  - Posologie chlorhydrate de metformine : 500 mg, 2 à 3 fois par jour ; ou 850 mg, 1 à 2 fois par jour, à augmenter progressivement par paliers de 500 mg jusqu'à 2.000 à 3.000 mg par jour)
  - effets secondaires : troubles digestifs, goût métallique, acidose lactique, carence en vit B12 (surtout si IPP)
- Objectif : taux d'HbA1c aux alentours de 7 %

Alternatives si intolérance ou contre-indication à la metformine

- Sulfamidé hypoglycémiant : glibenclamide, gliclazide, glimépiride ou glipizide
  - risque d'hypoglycémie
- Insuline

Quand la metformine ne suffit pas

- Incrétinomimétiques agonistes du GLP1 (glucagon-like peptide-1) en ajout à la metformine : liraglutide, dulaglutide ou sémaglutide par voie sous-cutanée
- Gliflozine (anti-SGLT2 = inhibiteur du co-transporteur rénal de sodium-glucose) en ajout à la metformine : en cas d'insuffisance cardiaque ou d'insuffisance rénale modérée avec protéinurie : dapagliflozine ou empagliflozine
- Insuline en ajout à la metformine : lorsque le taux d'hémoglobine glyquée (HbA1c) est très élevé

Agonistes du GLP1 : effets secondaires

- ralentissements de la vidange gastrique : nausées dose-dépendantes, surtout en début de traitement, vomissements, reflux gastro-œsophagiens, dyspepsies
- constipations sévères, voire obstructions intestinales
- insuffisances rénales
- pertes de poids excessives
- lithiases biliaires et cholécystites
- pancréatites aiguës

Gliflozines : effets secondaires

- démangeaisons génitales
- rares fasciites nécrosantes du périnée (gangrènes de Fournier)
- déshydratations, hypovolémies, hypotensions artérielles
- insuffisances rénales
- acidocétoses diabétiques, parfois même en l'absence de glycémies élevées

Diabète de type 1

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Julie R. Ingelfinger, M.D., *Editor*

Prevention of Cardiovascular Disease in Type 1 Diabetes

Camila Manrique-Acevedo, M.D., Irl B. Hirsch, M.D., and Robert H. Eckel, M.D.

TYPE 1 DIABETES MELLITUS IS A CHRONIC METABOLIC DISEASE RESULTING from autoimmune destruction of pancreatic beta cells. More than half the cases of type 1 diabetes are diagnosed in adulthood; 62% of new cases in 2021 were diagnosed in patients over the age of 20 years.[1] There are key genetic, immune, and metabolic differences between childhood- and adult-onset type 1 diabetes.[2] As a result of both a later age at diagnosis and longer life span, the mean age of a person living with type 1 diabetes is now 40 years.[1]

N Engl J Med 2024;390:1207-17.
DOI: 10.1056/NEJMra2311526

Table 1. Recommendations for Lipid-Lowering Therapy as Primary Prevention for Cardiovascular Disease in Patients with Type 1 Diabetes.*

Source	Recommendations
American Diabetes Association[36,41]	For people 40 to 75 years of age without atherosclerotic cardiovascular disease, use moderate-intensity statin therapy in addition to lifestyle changes. For people 40 to 75 years of age at higher cardiovascular risk, including those with ≥1 risk factor for atherosclerotic cardiovascular disease, use high-intensity statin therapy to reduce LDL cholesterol by ≥50% of baseline value and to target an LDL cholesterol goal of <70 mg/dl. After the age of 10 years, addition of a statin can be considered in youth with type 1 diabetes who, despite medical nutrition therapy and lifestyle changes, continue to have LDL cholesterol >160 mg/dl or >130 mg/dl with ≥1 cardiovascular disease risk factor.
American College of Cardiology–American Heart Association[38]	In adults 40 to 75 years of age, regardless of estimated risk of atherosclerotic cardiovascular disease, moderate-intensity statin therapy is indicated. For adults with multiple atherosclerotic cardiovascular disease risk factors, it is reasonable to prescribe high-intensity statin therapy with the aim to reduce LDL cholesterol by ≥50%.
European Society of Cardiology[37]	Statins should be considered in adults >40 years of age without a history of cardiovascular disease to reduce risk. For younger patients, statins should be considered if the patient has other cardiovascular risk factors, microvascular disease, or a 10-year cardiovascular disease risk ≥10%.
International Society of Pediatric and Adolescent Diabetes	If the implementation of lifestyle interventions for 6 months does not lower LDL cholesterol to 130 mg/dl, statins should be considered in children >10 years of age, with an ideal LDL cholesterol target of <100 mg/dl. Simvastatin, lovastatin, and pravastatin are effective and safe in children and adolescents.

N Engl J Med 2024;390:1207-17.
DOI: 10.1056/NEJMra2311526

Table 2. Recommendations for Glycemic Control, Blood-Pressure Control, Antithrombotic Therapy, and Obesity in Patients with Type 1 Diabetes.

Purpose	Recommendations
Glycemic control	Glycated hemoglobin <7%, if attainable without increased hypoglycemia[37]
Hypertension or blood-pressure control	Lifestyle interventions, with consideration of ambulatory blood-pressure monitoring[37] Blood pressure of <130/80 mm Hg[36] (and ideally, <120/80 mm Hg[37,51]) is recommended as a goal of treatment in adults and adolescents >13 years of age[44] Treatment should include blockade of renin–angiotensin–aldosterone system, unless patient is planning pregnancy or is pregnant or lactating[36,37]
Antithrombotic therapy	Aspirin (75–162 mg) can be considered as primary prevention in patients >50 years of age who have additional risk factors[36,37] Aspirin (75–162 mg) is indicated as secondary prevention in patients with established atherosclerotic cardiovascular disease (clopidogrel indicated for aspirin intolerance)[36,37]
Obesity	Lifestyle modifications, including caloric restriction and increased physical activity, recommended to achieve minimal weight reduction of 5–10% Consider referral to an intensive lifestyle modification program Consider GLP-1 receptor agonist therapy, with shared decision making with the patient regarding potential side effects*

* GLP-1 denotes glucagon-like peptide 1.

N Engl J Med 2024;390:1207-17.
DOI: 10.1056/NEJMra2311526

Hypertension artérielle

HTA : seuils justifiant un traitement

mesure au manomètre au cabinet médical :

- 160/95 mm Hg : population générale
- 140/80 mm Hg : diabétiques, après AVC

la notion de " pré-hypertension artérielle " n'est pas validée pour être une cible thérapeutique

Le problème du seuil

Articles

Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies

*Prospective Studies Collaboration**

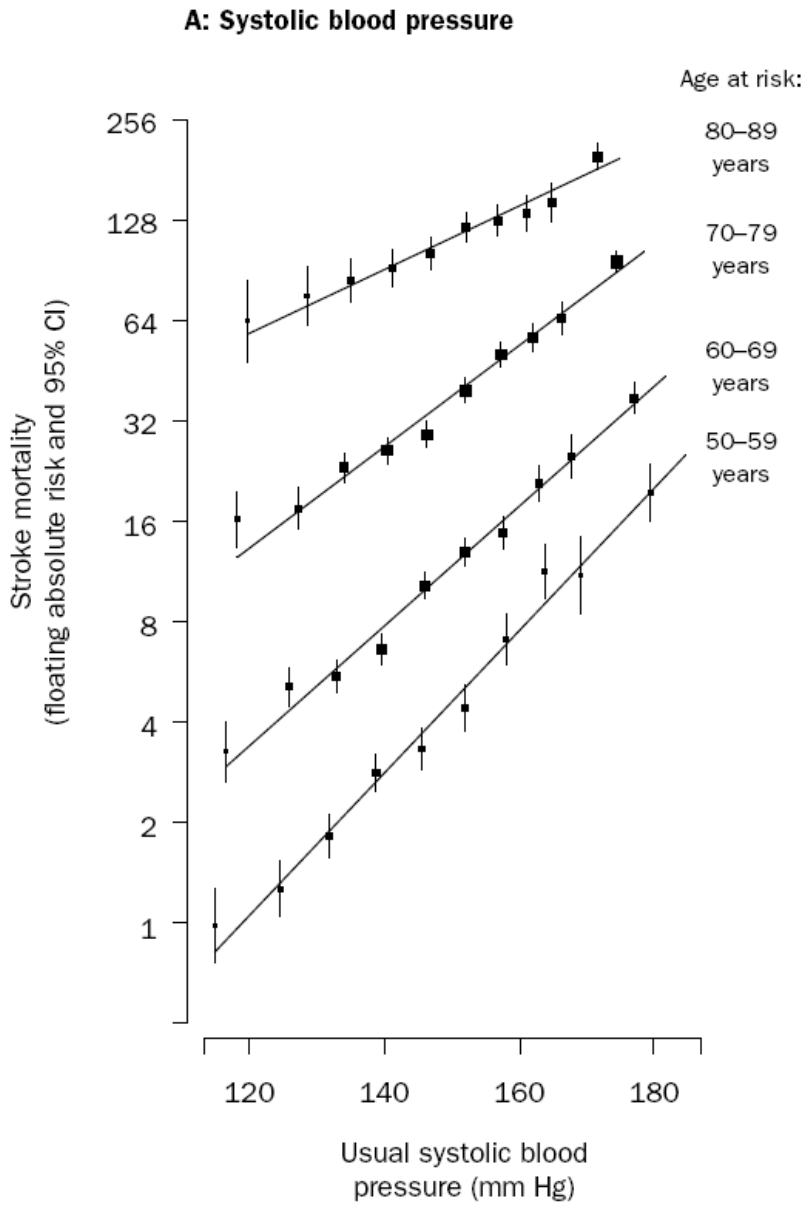
Lancet 2002; **360:** 1903–13

Age at risk (years)	Person-years at risk ($\times 10^3$)	Number of deaths by attributed cause					
		Stroke	IHD	Other vascular	Non-vascular	Unknown cause	All causes
<40	2020	74	98	57	1302	91	1622
40–49	3269	414	1322	386	4386	265	6773
50–59	3843	1372	5594	1377	12 228	847	21 418
60–69	2482	2939	10 450	2549	18 771	1686	36 395
70–79	913	4327	10 852	3227	16 112	1716	36 234
80–89	177	2636	5649	2251	7436	895	18 867
⩾90	7	198	318	245	562	84	1407
Total*	12 711	11 960	34 283	10 092	60 797	5584	122 716

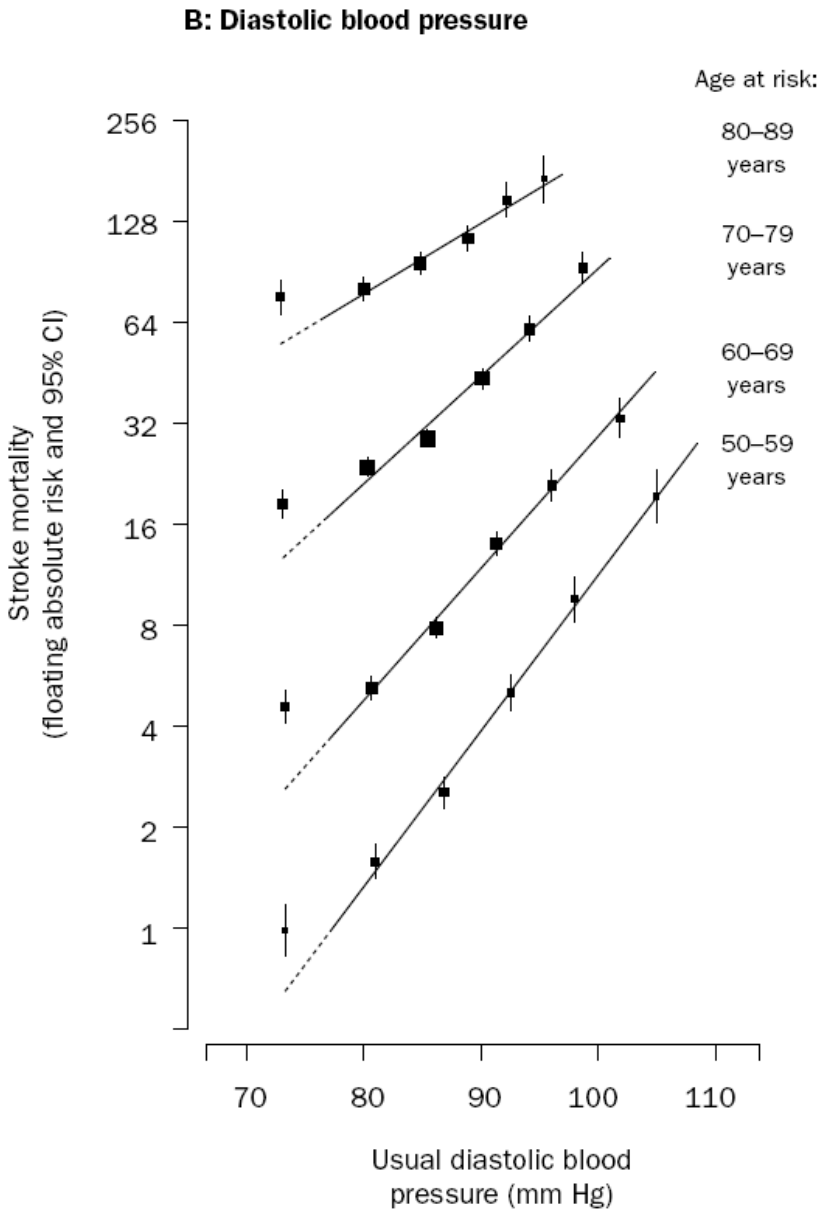
*For parallel analyses of the MRFIT study, which involved men dying only at ages 40–49, 50–59, and 60–69 years, respectively, there were 107, 461, and 717 stroke deaths; 1084, 4597, and 5679 IHD deaths; and 296, 1484, and 2359 other vascular deaths.

Table 2: **Numbers of deaths attributed to stroke, ischaemic heart disease (IHD), other vascular causes, and non-vascular causes, by age at risk**

Lancet 2002; **360:** 1903–13



Lancet 2002; **360:** 1903–13



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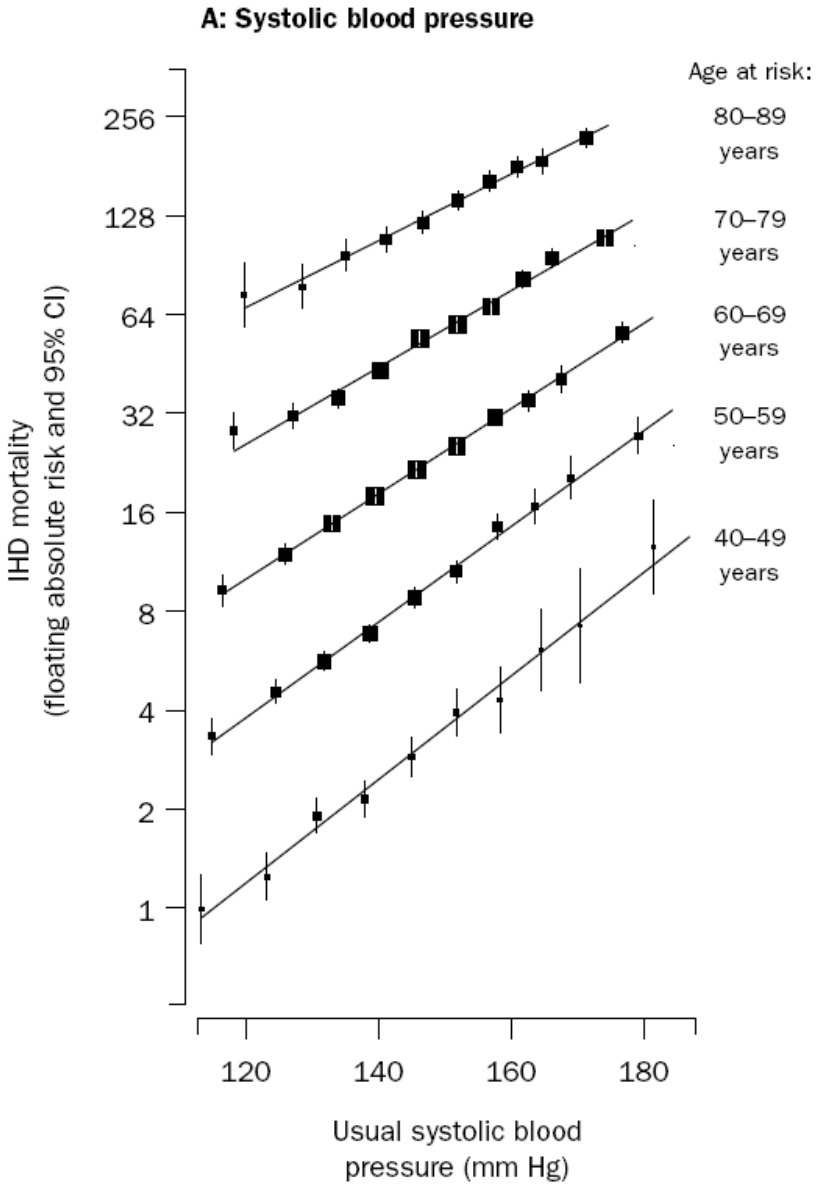

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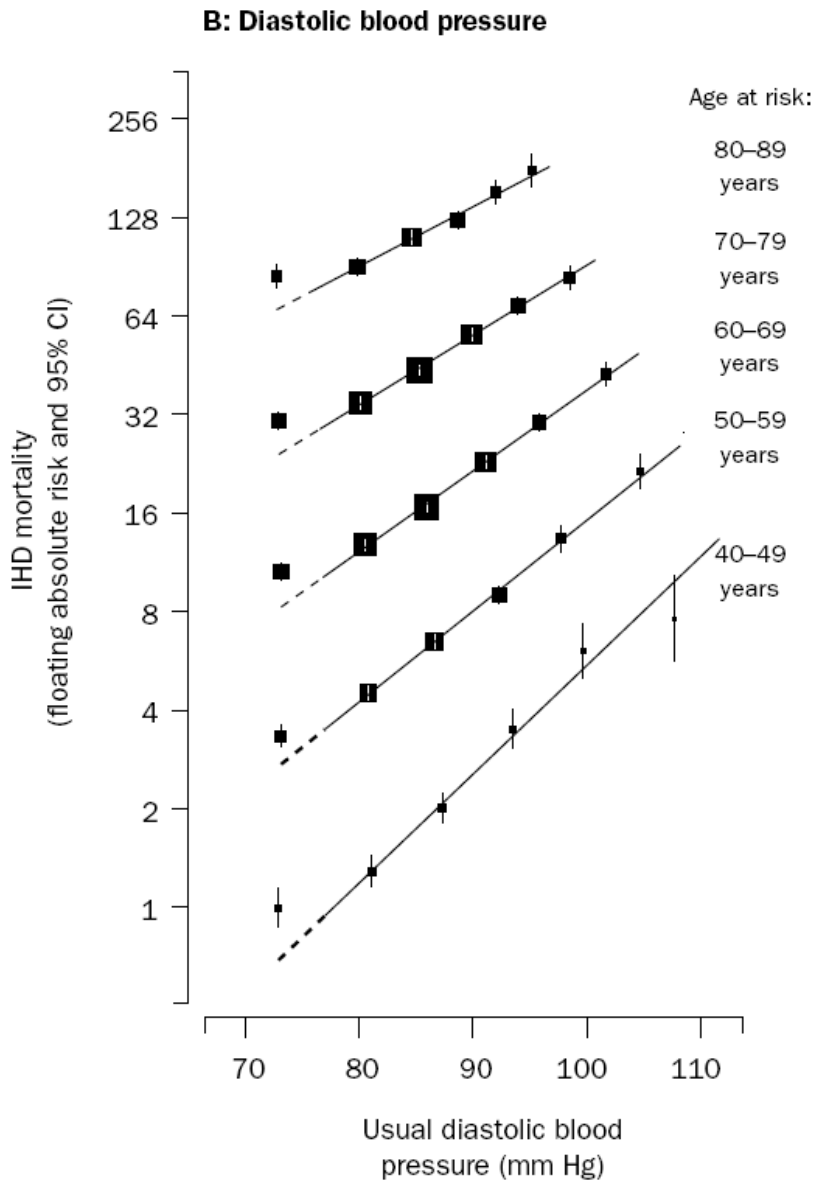

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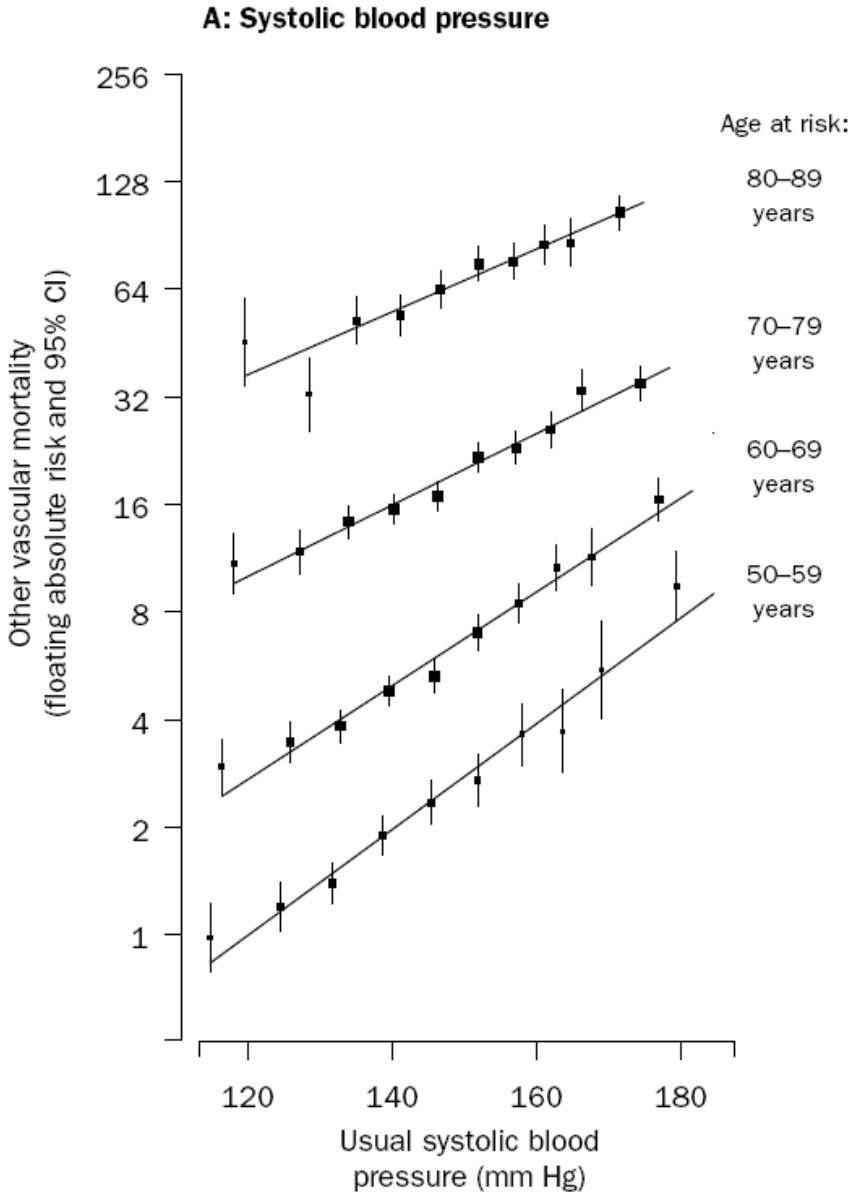

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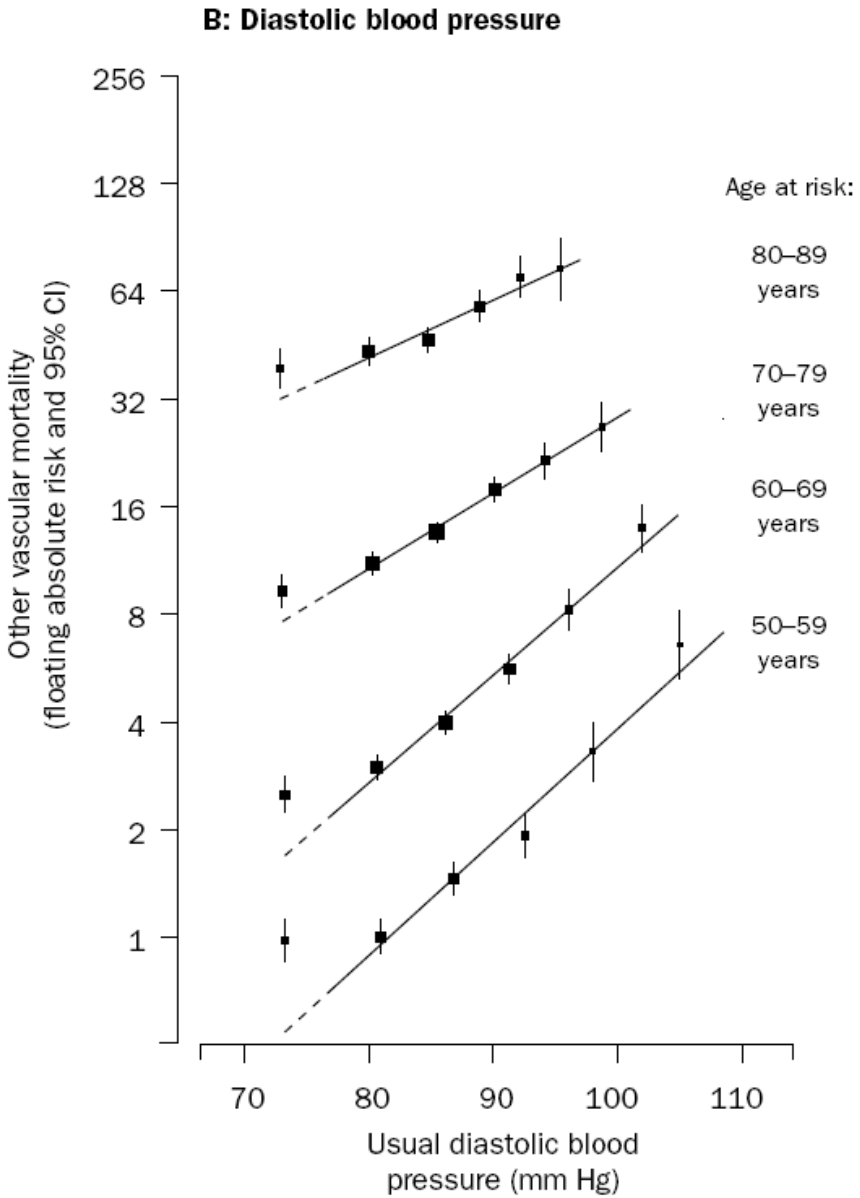


Lancet 2002; **360:** 1903–13

Tout au long du milieu de la vie et de la vieillesse, la pression artérielle habituelle est fortement et directement liée à la mortalité vasculaire (et globale), sans aucune preuve d'un seuil jusqu'à au moins 115/75 mm Hg.

Seuil pour instaurer le traitement

Pour l'hypertension artérielle, l'indication et le choix du traitement dépendent surtout de la présence de complications cérébrovasculaires, cardiaques ou rénales, de l'association à un diabète, et des chiffres systoliques et diastoliques.

Un médicament antihypertenseur est habituellement indiqué lorsque la pression artérielle au repos dépasse 160/95 lors de plusieurs mesures. Ce traitement est indiqué à partir d'une pression artérielle de 140/80 en cas de diabète associé ou après accident vasculaire cérébral (**a**).

JAMA Internal Medicine | Original Investigation

Association of Blood Pressure Lowering With Mortality and Cardiovascular Disease Across Blood Pressure Levels

A Systematic Review and Meta-analysis

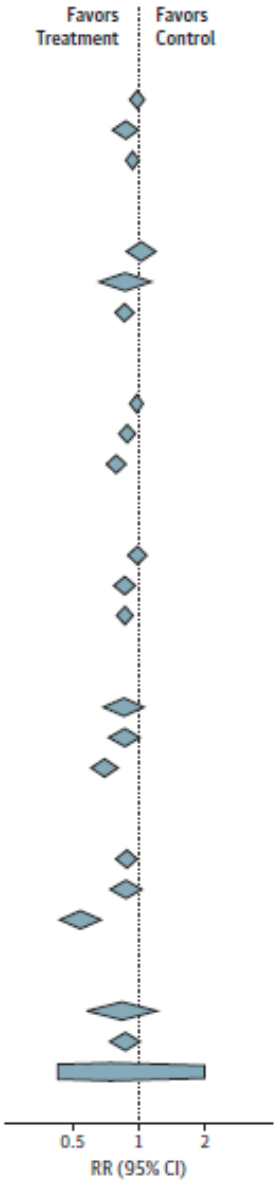
Mattias Brunström, MD; Bo Carlberg, MD, PhD

JAMA Intern Med. 2018;178(1):28-36. doi:10.1001/jamainternmed.2017.6015
Published online November 13, 2017. Corrected on January 2, 2018.

Soixante-quatorze essais uniques, représentant 306.273 participants uniques (39,9% de femmes et 60,1% d'hommes; âge moyen, 63,6 ans) et 1,2 million d'années-personnes, ont été inclus dans les méta-analyses. En prévention primaire, l'association d'un traitement hypotenseur à des événements cardiovasculaires majeurs dépendait de la PA systolique de base (TAS).

Figure 1. Effect of Treatment to Lower Blood Pressure (BP) at Different BP Levels in Primary Prevention

Baseline SBP, mm Hg	No. of Events/ Participants/Trials	RR (95% CI)	Heterogeneity I^2 Value, %
All-cause mortality			
<140	4897/68816/16	0.98 (0.90-1.06)	11.6
140-159	2731/41049/15	0.87 (0.75-1.00)	43.2
≥160	4361/79900/18	0.93 (0.87-1.00)	17.0
SBP interaction, $P = .18$			
Cardiovascular mortality			
<140	2633/66480/12	1.03 (0.87-1.20)	43.4
140-159	1465/42587/15	0.86 (0.65-1.14)	57.9
≥160	2290/78789/17	0.85 (0.77-0.95)	18.0
SBP interaction, $P = .02$			
Major cardiovascular events			
<140	7354/67928/13	0.97 (0.90-1.04)	30.6
140-159	3951/43489/16	0.88 (0.80-0.96)	31.0
≥160	4627/77733/16	0.78 (0.70-0.87)	53.8
SBP interaction, $P = .004$			
Coronary heart disease			
<140	1618/62617/11	0.98 (0.88-1.09)	0.0
140-159	1369/42543/14	0.86 (0.76-0.96)	0.0
≥160	2018/78617/17	0.86 (0.78-0.94)	0.0
SBP interaction, $P = .13$			
Stroke			
<140	1775/62751/11	0.85 (0.68-1.06)	54.1
140-159	1429/41641/13	0.86 (0.72-1.01)	21.4
≥160	1929/79900/18	0.69 (0.60-0.80)	47.3
SBP interaction, $P = .16$			
Heart failure			
<140	2261/60879/9	0.88 (0.78-0.98)	29.8
140-159	1113/35254/10	0.87 (0.73-1.04)	5.3
≥160	520/23395/10	0.53 (0.42-0.67)	17.6
SBP interaction, $P = .005$			
End-stage renal disease			
<140	488/24512/5	0.84 (0.57-1.24)	42.5
140-159	870/32984/7	0.88 (0.74-1.04)	0.0
≥160	32/5566/2	0.73 (0.01-6.45)	0.0
SBP interaction, $P = .32$			



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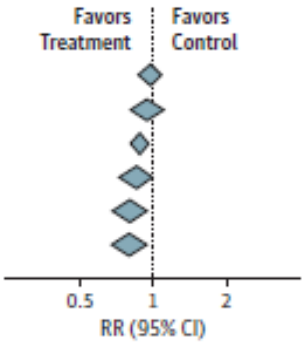
Published online November 13, 2017. Corrected on January 2, 2018.

Figure 2. Effect of Treatment to Lower Blood Pressure (BP) in Coronary Heart Disease Trials

Outcome	No. of Events/ Participants/Trials	RR (95% CI)	Heterogeneity I^2 Value, %
All-cause mortality	7061/77 562/12	0.98 (0.89-1.07)	49.1
CV mortality	4156/76 737/11	0.95 (0.84-1.09)	55.3
MACE	13 075/77 562/12	0.90 (0.84-0.97)	65.1
Coronary heart disease	4112/68 305/10	0.88 (0.77-1.00)	55.8
Stroke	2412/75 812/11	0.83 (0.73-0.96)	31.8
Heart failure	2905/74 385/9	0.83 (0.72-0.96)	38.4



MACE: major cardiovascular events

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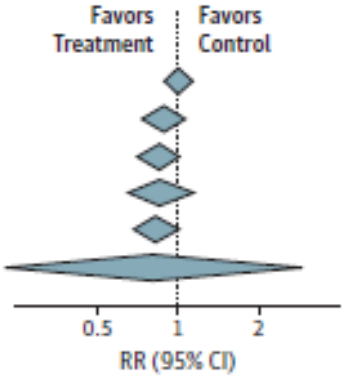
Figure 3. Effect of Treatment to Lower Blood Pressure (BP) in Poststroke Trials

Outcome	No. of Events/ Participants/Trials	RR (95% CI)	Heterogeneity I^2 Value, %
All-cause mortality	2610/32 102/6	1.00 (0.91-1.10)	0.0
CV mortality	1179/32 102/6	0.91 (0.78-1.05)	0.0
MACE	4731/32 102/6	0.88 (0.76-1.01)	62.1
Coronary heart disease	844/32 102/6	0.89 (0.72-1.11)	1.7
Stroke	3167/32 102/6	0.86 (0.74-1.01)	53.5
Heart failure	508/26 889/3	0.85 (0.32-2.29)	68.1



JAMA Intern Med. 2018;178(1):28-36. doi:10.1001/jamainternmed.2017.6015
Published online November 13, 2017. Corrected on January 2, 2018.

Etude de cohorte

Research

JAMA Internal Medicine | Original Investigation

Benefits and Harms of Antihypertensive Treatment in Low-Risk Patients With Mild Hypertension

James P. Sheppard, PhD; Sarah Stevens, PhD; Richard Stevens, PhD; Una Martin, FRCP; Jonathan Mant, MD; F. D. Richard Hobbs, FMedSci; Richard J. McManus, FRCGP

140/90-159/99 mmHg

JAMA Intern Med. 2018;178(12):1626-1634. doi:10.1001/jamainternmed.2018.4684
Published online October 29, 2018.

Table 2. Primary (Mortality) and Secondary Outcomes

Outcome	No. Not Treated		No. Treated		Hazard Ratio (95% CI)	*P* Value	NNH (95% CI)[a]	
	No Event	Event	No Event	Event			5 Years	10 Years
Treatment benefit outcomes								
Mortality	18 362	781	18 283	860	1.02 (0.88-1.17)	.81	NA	NA
Cardiovascular disease[b]	18 443	700	18 425	718	1.09 (0.95-1.25)	.23	NA	NA
Stroke	18 858	285	18 851	292	0.97 (0.78-1.21)	.76	NA	NA
MI	18 864	279	18 867	276	1.00 (0.80-1.25)	.98	NA	NA
Non-MI acute coronary syndrome	19 087	56	19 082	61	1.19 (0.74-1.91)	.47	NA	NA
Heart failure	19 012	131	18 974	169	1.34 (0.96-1.86)	.09	NA	NA
Treatment harm outcomes								
Hypotension	18 982	161	18 875	268	1.69 (1.30-2.20)	<.001	219 (127-501)	41 (24-93)
Syncope	18 670	473	18 534	609	1.28 (1.10-1.50)	.002	135 (77-385)	35 (20-100)
Bradycardia	19 067	76	19 040	103	1.11 (0.75-1.65)	.59		
Electrolyte abnormalities	19 089	54	19 048	95	1.72 (1.12-2.65)	.01	580 (253-3610)	111 (49-687)
Falls	19 104	39	19 098	45	1.15 (0.63-2.09)	.65		
Acute kidney injury	18 999	144	18 949	194	1.37 (1.00-1.88)	.048	467 (198-75 225)	91 (39-14 552)
Cancer (negative control)	17 550	1593	17 464	1679	1.01 (0.92-1.11)	.79	NA	NA

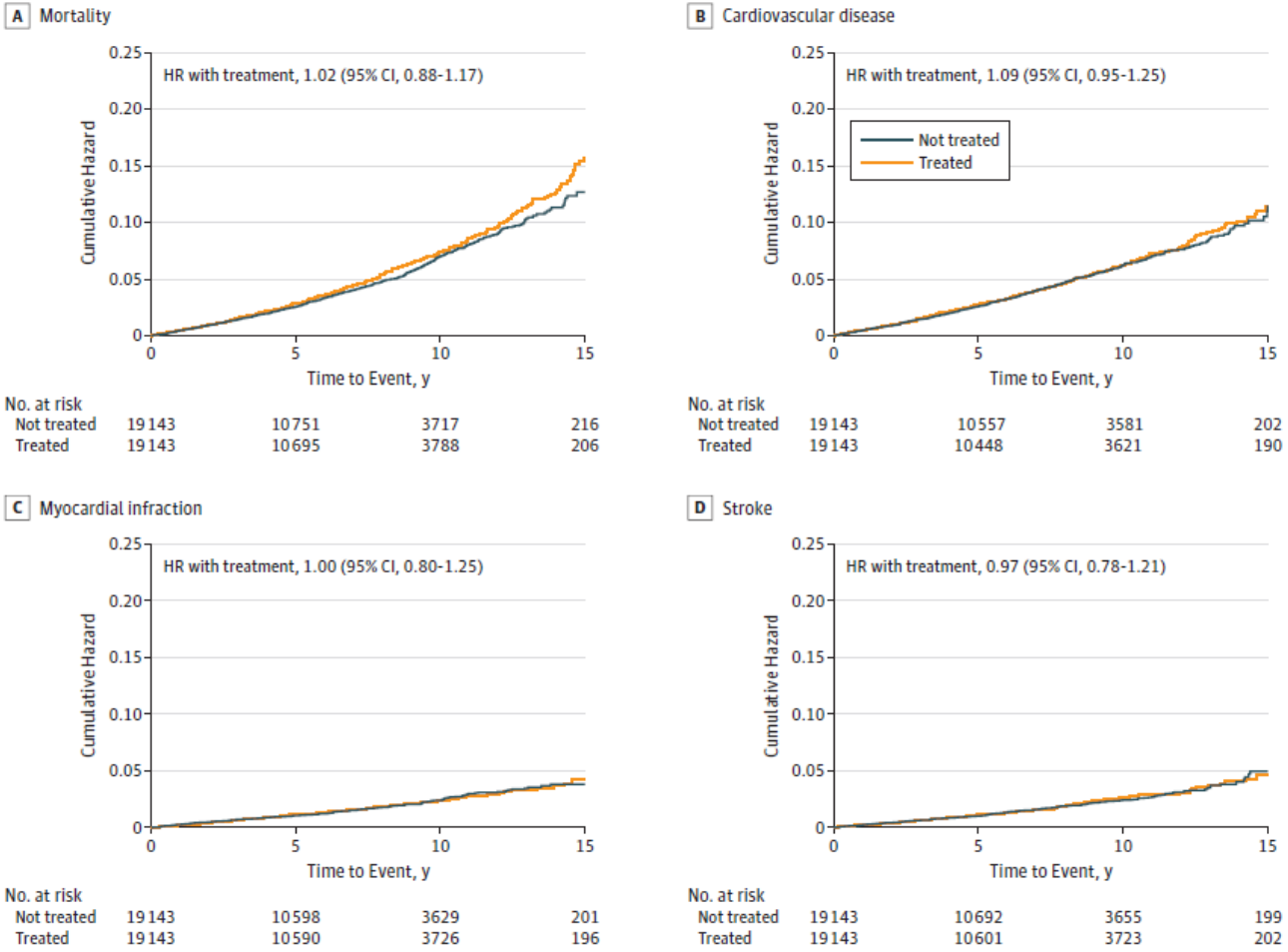
Abbreviations: MI, myocardial infarction; NA, not applicable; NNH, number needed to harm.

[a] The NNH was only estimated when there was a single direction of treatment effect (ie, CIs do not cross 1).

[b] Cardiovascular disease was defined as any code for fatal and nonfatal stroke, MI, non-MI acute coronary syndrome, or heart failure.

JAMA Intern Med. 2018;178(12):1626-1634. doi:10.1001/jamainternmed.2018.4684
Published online October 29, 2018.

Figure 1. Cumulative Hazard Plots Comparing Risk of Mortality and Cardiovascular Disease With Treatment Exposure



HR indicates hazard ratio.

JAMA Intern Med. 2018;178(12):1626-1634. doi:10.1001/jamainternmed.2018.4684
Published online October 29, 2018.

CONCLUSIONS ET PERTINENCE

- Cette analyse pré-spécifiée n'a trouvé **aucune preuve à l'appui des recommandations avec des lignes directrices qui encouragent l'initiation du traitement chez les patients souffrant d'hypertension légère à faible risque.**
- Il y avait des preuves d'un risque accru d'événements indésirables, ce qui suggère que les médecins devraient faire preuve de prudence lorsqu'ils suivent les lignes directrices qui généralisent les résultats des essais menés sur des personnes à haut risque à celles à faible risque.

Objectif du traitement de l'HTA

Réduire la pression artérielle :

en dessous de 140/90 mmHg

Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies

M R Law, professor of epidemiology J K Morris, professor of medical statistics N J Wald, professor of environmental and preventive medicine

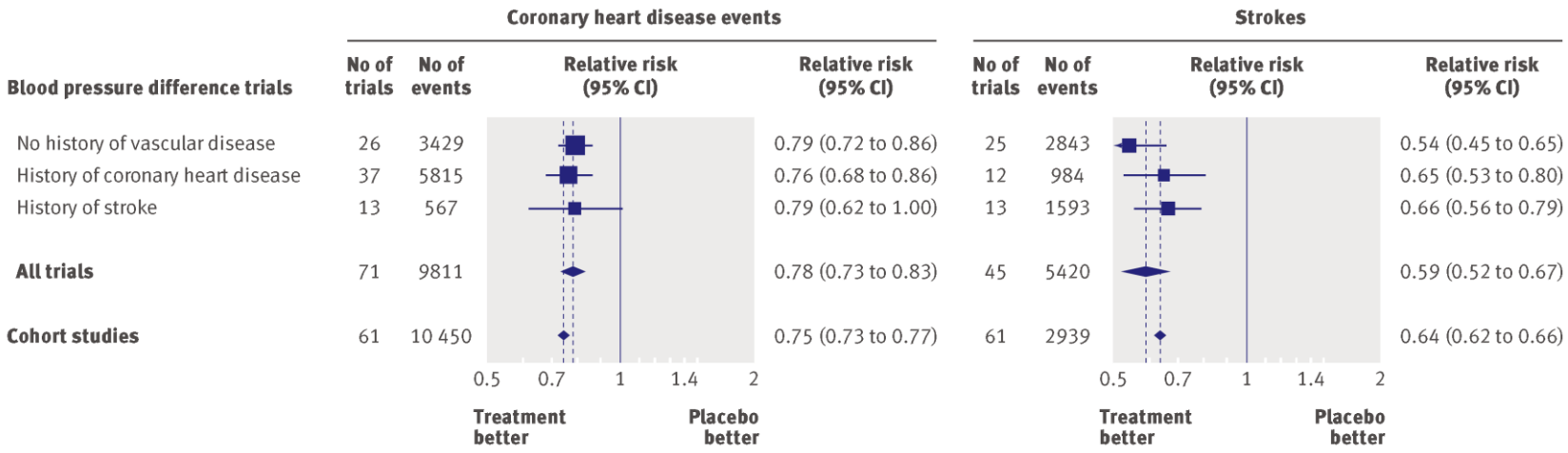


Fig 2 | Relative risk estimates of coronary heart disease events and stroke for a blood pressure reduction of 10 mm Hg systolic or 5 mm Hg diastolic in the blood pressure difference trials and in epidemiological cohort studies. (Total number of trials is fewer than the sum of the three categories as five included participants with and without vascular disease; see web extra figures 2a-f for individual trial results and summary estimates)

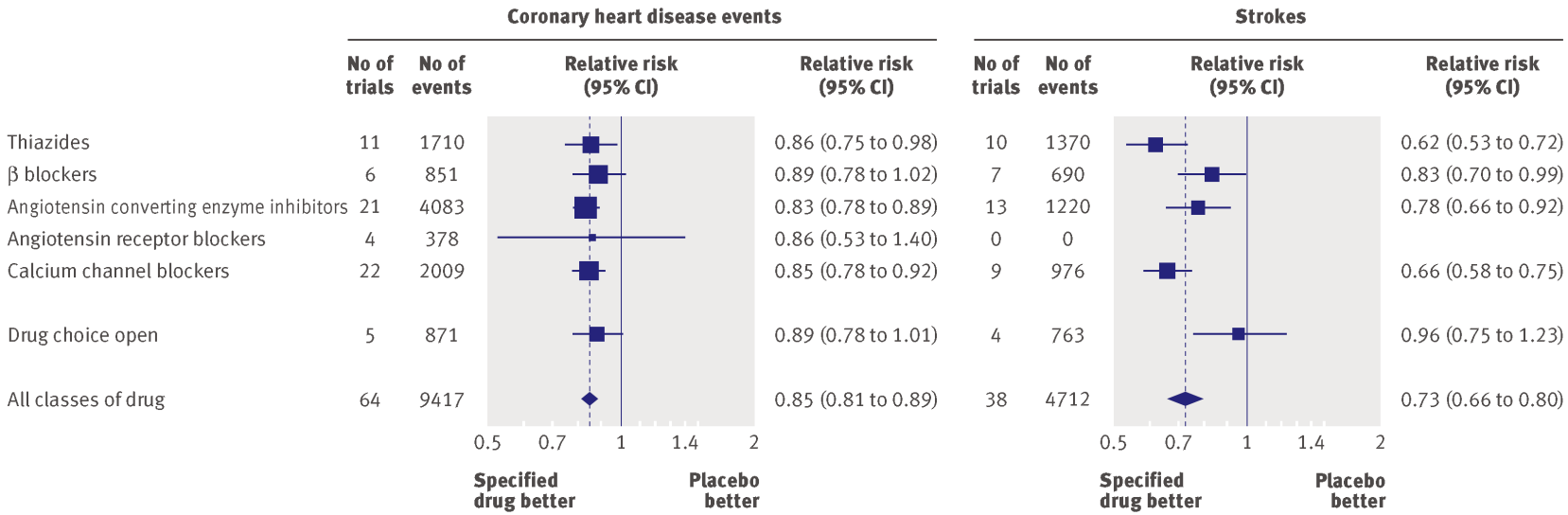


Fig 3 | Relative risk estimates of coronary heart disease events and stroke in single drug blood pressure difference trials according to class of drug (excluding CHD events in trials of β blockers in people with history of coronary heart disease). (Totals are less than the sum of the individual categories because some trials include more than one category; see web extra figures 3a-i for individual trial results and summary estimates)

Diabète : seuil pour traiter à 14/8 cm Hg

Research

Original Investigation

Blood Pressure Lowering in Type 2 Diabetes
A Systematic Review and Meta-analysis

Connor A. Emdin, HBSc; Kazem Rahimi, DM, MSc; Bruce Neal, PhD; Thomas Callender, MBChB; Vlado Perkovic, PhD; Anushka Patel, PhD

IMPORTANCE Lowering blood pressure (BP) is widely used to reduce vascular risk in individuals with diabetes.

OBJECTIVE To determine the associations between BP-lowering treatment and vascular disease in type 2 diabetes.

DATA SOURCES AND STUDY SELECTION We searched MEDLINE for large-scale randomized controlled trials of BP-lowering treatment including patients with diabetes, published between January 1966 and October 2014.

Editorial page 573

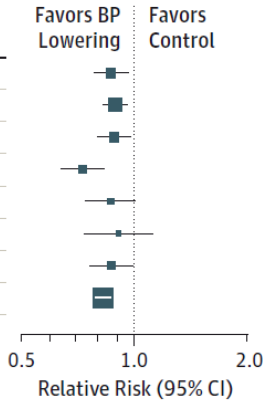
Supplemental content at jama.com

CME Quiz at jamanetworkcme.com and CME Questions page 622

JAMA. 2015;313(6):603-615. doi:10.1001/jama.2014.18574

Figure 2. Standardized Associations Between 10-mm Hg Lower Systolic BP and All-Cause Mortality, Macrovascular Outcomes, and Microvascular Outcomes in Diabetic Patients

Outcome	No. of Studies	BP Lowering		Control		Relative Risk (95% CI)
		Events	Participants	Events	Participants	
Mortality	20	2334	27693	2319	25864	0.87 (0.78-0.96)
Cardiovascular disease	17	3230	25756	3280	24862	0.89 (0.83-0.95)
Coronary heart disease	17	1390	26150	1449	24761	0.88 (0.80-0.98)
Stroke	19	1350	27614	1475	26447	0.73 (0.64-0.83)
Heart failure	13	1235	21684	1348	20791	0.86 (0.74-1.00)
Renal failure	9	596	19835	560	18912	0.91 (0.74-1.12)
Retinopathy	7	844	9781	905	9566	0.87 (0.76-0.99)
Albuminuria	7	2799	13804	3163	12821	0.83 (0.79-0.87)

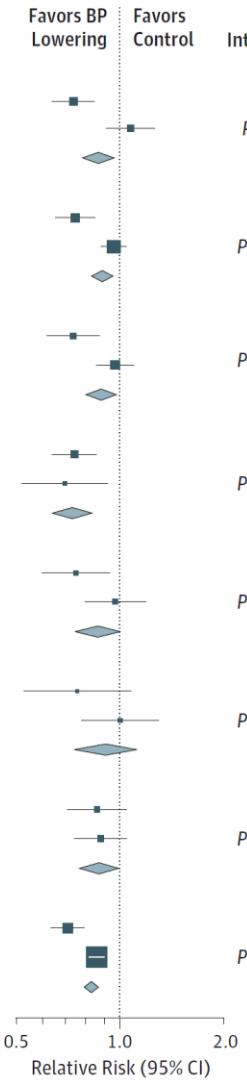


Macrovascular outcomes include cardiovascular events, coronary heart disease, stroke, and heart failure; and microvascular outcomes include renal failure, retinopathy, and albuminuria. The area of each square is proportional to the inverse variance of the estimate. Horizontal lines indicate 95% CIs of the estimate. BP indicates blood pressure.

JAMA. 2015;313(6):603-615. doi:10.1001/jama.2014.18574

Figure 3. Standardized Associations Between 10-mm Hg Lower Systolic BP and All-Cause Mortality, Macrovascular Outcomes, and Microvascular Outcomes Stratified by Mean Systolic BP of Trial Participants at Entry

Outcome	No. of Studies	Baseline SBP, Mean, mm Hg	BP Lowering, No. Events	BP Lowering, No. Participants	Control, No. Events	Control, No. Participants	Relative Risk (95% CI)	P for Interaction
Mortality, mm Hg								
≥140[16, 18, 19, 27-30, 35, 39-41, 51, 55, 56, 64, 65, 77-80]	13	149	1614	16418	1626	14580	0.73 (0.64-0.84)	
<140[17, 31, 36-38, 58-60, 80, 81]	7	137	720	1275	693	11284	1.07 (0.92-1.26)	P<.001
Overall							0.87 (0.78-0.96)	
Cardiovascular disease, mm Hg								
≥140[16, 18, 19, 27-30, 35, 39-41, 46, 47, 51-53]	11	148	1861	14976	1918	14068	0.74 (0.65-0.85)	
<140[17, 31, 36-38, 58-60, 80, 81]	6	137	1369	10780	1362	10794	0.96 (0.88-1.05)	P=.001
Overall							0.89 (0.83-0.95)	
Coronary heart disease, mm Hg								
≥140[16, 18, 27, 29, 30, 35, 39-41, 47, 51, 64, 65]	10	148	858	14875	931	13477	0.73 (0.61-0.87)	
<140[17, 31, 36-38, 43, 58-60, 80, 81]	7	137	532	11275	518	11284	0.97 (0.86-1.10)	P=.01
Overall							0.88 (0.80-0.98)	
Stroke, mm Hg								
≥140[16, 18, 19, 27, 29, 30, 35, 39-41, 45-47, 51, 55, 56, 63-65]	14	148	1129	19066	1245	17868	0.74 (0.64-0.86)	
<140[31, 36-38, 58-60, 80, 81]	5	137	221	8548	230	8579	0.69 (0.52-0.92)	P=.70
Overall							0.73 (0.64-0.83)	
Heart failure, mm Hg								
≥140[16, 18, 29, 30, 35, 39-41, 46, 47, 64, 65]	8	146	774	13592	814	12676	0.75 (0.59-0.94)	
<140[31, 42, 43, 58-60, 80, 81]	5	137	461	8092	534	8115	0.97 (0.79-1.19)	P=.09
Overall							0.86 (0.74-1.00)	
Renal failure, mm Hg								
≥140[16, 18, 29, 30, 35, 40, 41, 64, 65]	6	147	389	12475	346	11530	0.75 (0.52-1.08)	
<140[31, 58-60]	3	138	207	7360	214	7382	1.00 (0.77-1.29)	P=.21
Overall							0.91 (0.74-1.12)	
Retinopathy, mm Hg								
≥140[16, 29, 30, 64, 65, 77-80]	4	146	564	7946	586	7753	0.86 (0.70-1.04)	
<140[36-38, 59, 60, 80, 81]	3	137	280	1835	319	1813	0.88 (0.74-1.05)	P=.85
Overall							0.87 (0.76-0.99)	
Albuminuria, mm Hg								
≥140[16, 28-30, 64, 65]	4	146	1681	8447	1898	7647	0.71 (0.63-0.79)	
<140[17, 36-38, 59, 60]	3	137	1118	5357	1265	5174	0.86 (0.81-0.90)	P=.002
Overall							0.83 (0.79-0.87)	



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Bénéfice escompté du traitement antihypertenseur

- Diminution de 2 AVC pour 100 patients traités pendant 4 à 5 ans
- Diminution de 2 à 5 IDM pour 1000 patients traités pendant 2 à 6 ans
- Diminution de 2 à 3 décès pour 100 patients traités pendant 4 à 5 ans

Traitement non médicamenteux

- activité physique de loisir régulière
- **réduire l'apport sodé**
- réduction de la consommation d'alcool (< 3 verres standard chez l'homme et < 2 verres standard chez la femme)
- perte de poids en cas d'obésité (>30 kg/m²)
- **arrêt du tabagisme**

TABLEAU 1. EXEMPLES D'ALIMENTS RICHES EN « SEL CACHÉ »

	Produit	Quantité	Sel
Sauces et aides culinaires	Bouillon cube	1 unité	1 g
	Moutarde, sauce soja	1 cuillère à soupe	1 g
	Mayonnaise, ketchup	2 cuillères à soupe	1 g
Produits proposés à l'apéritif	Chips	60 g (2 petits paquets)	1 g
	Cornichons	10 petits	1 g
	Olives	1 petite poignée	1 g
	Saucisson sec	20 g, soit environ 5 tranches	1 g
	Jambon blanc	1 tranche épaisse (60 g)	1 g
	Pâté	1 tranche (50 g)	1 g
	Fromage	40 g	1 g
Produits de panification	Croissant	1 unité	1 g
	Pain baguette	¼ baguette (60 g)	1 g
Produits de la mer	Saumon fumé	1 tranche (40 g)	1 g
	Thon en boîte	100 g	1 g
	Huîtres	6 unités	1 g
Plats préparés	Pizza, quiche	¼ soit environ 100 g	1 g
	Plats cuisinés	100 g (1/3 de barquette individuelle)	0,5-1 g (voire plus)

Traitement médicamenteux chez l'adulte sans pathologie associée

- en 1ère ligne : diurétique thiazidique.
  chlortalidone : 12,5 à 25 mg/j ou hydrochlorothiazide (associé à triamtérène) : 1 co/j
  NB : à introduire à dose réduite chez le sujet âgé en raison du risque d'hypotension orthostatique
- Première alternative : inhibiteur de l'enzyme de conversion (IEC): captopril, énalapril, lisinopril, ramipril
- Sinon:
  - un β-bloquant : aténolol, métoprolol
  - un inhibiteur calcique : amlodipine, diltiazem, vérapamil
  - un sartan : losartan, valsartan

Essais comparatifs randomisés ayant évalué, chez des adultes hypertendus, la chlortalidone ou l'hydrochlorothiazide en termes de mortalité ou de complications cardiovasculaires (d'après réf. 1,7)

	Essai	Principaux critères d'inclusion			Traitements comparés (a)	Nombre de patients	Durée (ans)	Nombre d'événements évités, pour 1 000 patients traités par diurétique pendant un an			
		Âge (ans)	Pression artérielle (mm Hg)	Autres critères				AVC	IDM et décès coronarien	Insuffisance cardiaque	Mortalité totale
Essais chlortalidone	SHEP	> 60	PAS 160-220 et PAD < 90	–	*chlortalidone* ± aténolol versus placebo	4 736	4,5	5,2	3,4	5	NS
	Allhat-HTA	> 55	PA > 140/90 ou déjà sous hypertenseur	Au moins un autre facteur de risque cardiovasculaire	*chlortalidone* versus *amlodipine*	24 303	4,9	NS	NS	4,2	NS
					chlortalidone versus *lisinopril*	24 309	4,9	1,2	NS	1,7	NS
					chlortalidone versus *doxazocine*	24 335	3,3	1,6	NS	9,2	NS
	Shell	> 60	PAS ≥ 160 et PAD < 90	–	*chlortalidone* versus *lacidipine*	1 882	1,7	NS	NS	NS	NS
Essais hydrochlorothiazide	Ewphe	> 60	PAS 160-240 et PAD 90-120	–	*hydrochlorothiazide* + *triamtérène* versus placebo	840	3,2	13 décès cardiovasculaires			NR
	Insight	55 à 80	PA ≥ 160 ou (PAS > 150 et PAD > 95	Au moins un autre facteur de risque cardiovasculaire	*hydrochlorothiazide* + *amiloride* versus *nifédipine*	6 321	3,5	NS	NS	NS	NS
	MRC 65-74 ou MRC-OLD	65 à 74	PAS 160 - 210	–	*hydrochlorothiazide* + *amiloride* versus *aténolol*	2 183	5,8	NS	5,1	NR	NS

AVC : accident vasculaire cérébral ; IDM : infarctus du myocarde ; IEC : inhibiteurs de l'enzyme de conversion ; NR : non rapporté ; NS : absence de différence statistiquement significative ; PAS : pression artérielle systolique ; PAD : pression artérielle diastolique.

a- *Dans plusieurs essais, d'autres antihypertenseurs étaient éventuellement ajoutés quand les valeurs-cibles de pression artérielle n'étaient pas atteintes.*

Diurétiques thiazidiques

Probablement moins d'arrêts pour effets indésirables qu'avec d'autres hypotenseurs

Chez les patients traités pour une hypertension artérielle, les arrêts de traitement hypotenseur liés à des effets indésirables paraissent moins fréquents avec les diurétiques thiazidiques qu'avec les inhibiteurs de l'enzyme de conversion, les bêta-bloquants et les inhibiteurs calciques : environ 1 à 2 arrêts en moins pour 100 patients traités pendant 1 à 6 ans, selon une synthèse méthodique avec méta-analyses d'essais cliniques randomisés.

En cas d'échec

- rechercher des causes :
  - effet « blouse blanche »
  - période d'anxiété ou stress
  - mauvaise compliance
  - posologie insuffisante
  - obésité ou prise de poids
  - consommation excessive de sel, alcool, tabac, réglisse
  - drogues (amphétamine, cocaïne)
  - médicaments (corticoïdes, AINS, bupropion, sibutramine, vasoconstricteurs nasaux, tryptans, lévothyroxine, sympathomimétiques, etc.)
  - ou une HTA secondaire

- ensuite :
  * en deuxième ligne : autre monothérapie
  * en troisième ligne : bithérapie
  - en évitant certaines associations:
    - IEC ou sartan + diurétique hyperkaliémiant
    - β-bloquant + inhibiteur calcique bradycardisant
  - en tenant compte de certaines interactions médicamenteuses :
    - risque d'insuffisance rénale si association IEC ou sartan + diurétique
    - risque d'arythmie si diurétique hypokaliémiant + inhibiteur calcique bradycardisant ou β-bloquant

Traitement médicamenteux chez l'adulte avec pathologie associée

- diabète de type 2
  en 1ère ligne : IEC, sartan; diurétiques thiazidiques,
  en 2ème ligne : β-bloquant
- AVC
  en 1ère ligne : diurétiques ou association périndopril + indapamide
- infarctus myocardique
  en 1ère ligne : β-bloquant (aténolol, métoprodol, propranolol)
- insuffisance cardiaque
  en 1ère ligne : IEC
  inhibiteurs calciques à éviter (aggravent l'insuffisance cardiaque)
- insuffisance rénale
  IEC avec contrôle de la fonction rénale et de la kaliémie (captopril, énalapril)

TABLEAU 2

Interactions médicamenteuses des antihypertenseurs

Classe médicamenteuse	Interactions	Conséquences
Inhibiteurs du système rénine-angiotensine	Lithium	Augmentation de la lithémie par diminution de l'excrétion
	Diurétiques épargneurs de potassium	Hyperkaliémie
	Anti-inflammatoires non stéroïdiens	Insuffisance rénale aiguë
Inhibiteurs des canaux calciques non dihydropyridines	Inhibiteurs CYPA3A4 et CYP3A5	Surdosage ou sous-dosage de médicaments associés métabolisés par ces voies
Thiazidiques	Lithium	Augmentation de la lithémie par diminution de l'excrétion
	Antiarythmiques	Majoration du risque de torsades de pointes si hypokaliémie
Alphabloquants	Inhibiteurs calciques	Potentialisation hypotension orthostatique
Bêtabloquants	Antiarythmiques, Inhibiteurs des canaux calciques non dihydropyridines, digitaliques	Troubles de conduction et de contractilité