

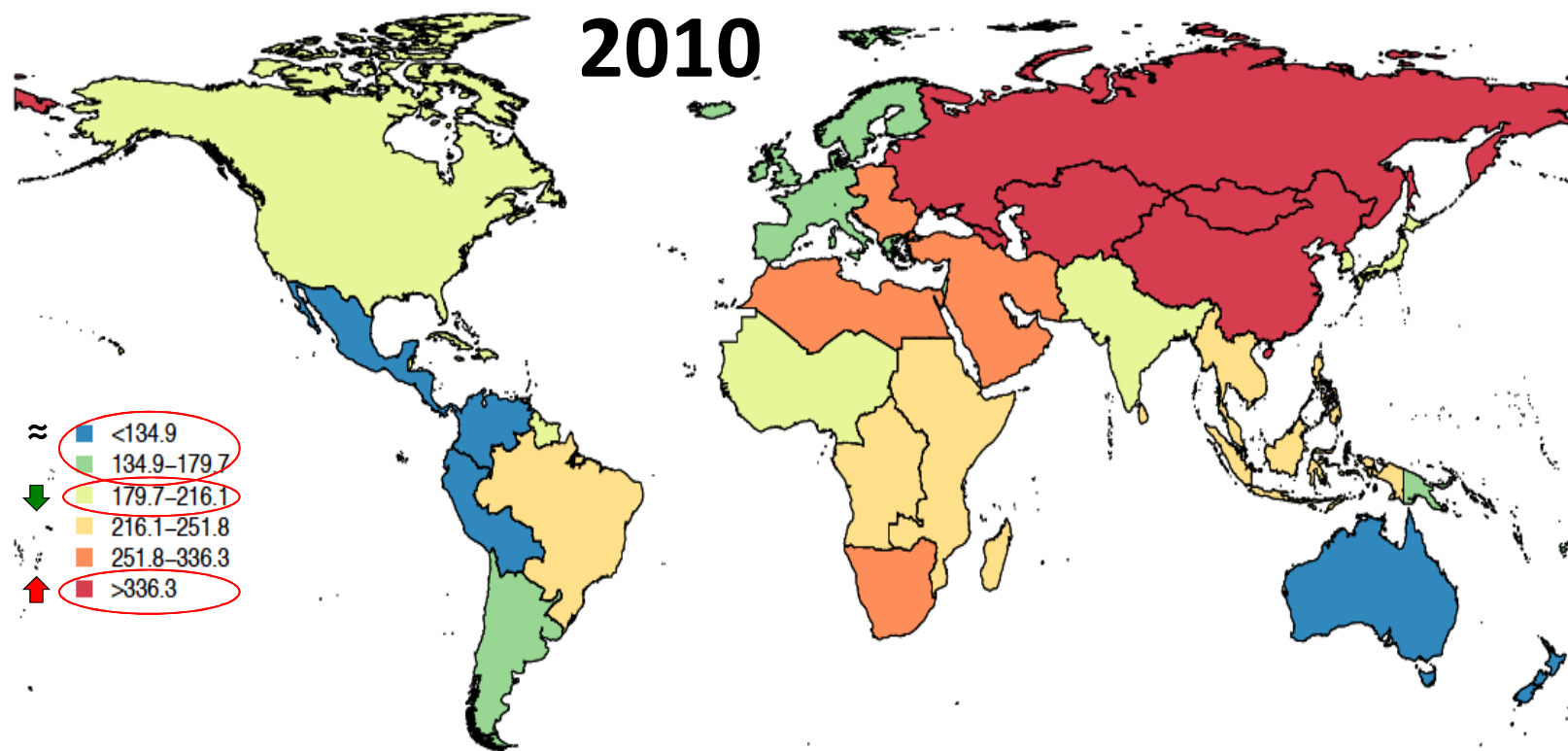
"The Burden of Stroke in Europe": nuovi e vecchi fattori di rischio per l'ictus cerebrale

Francesca Romana Pezzella MD, PhD, BSc

Stroke Unit

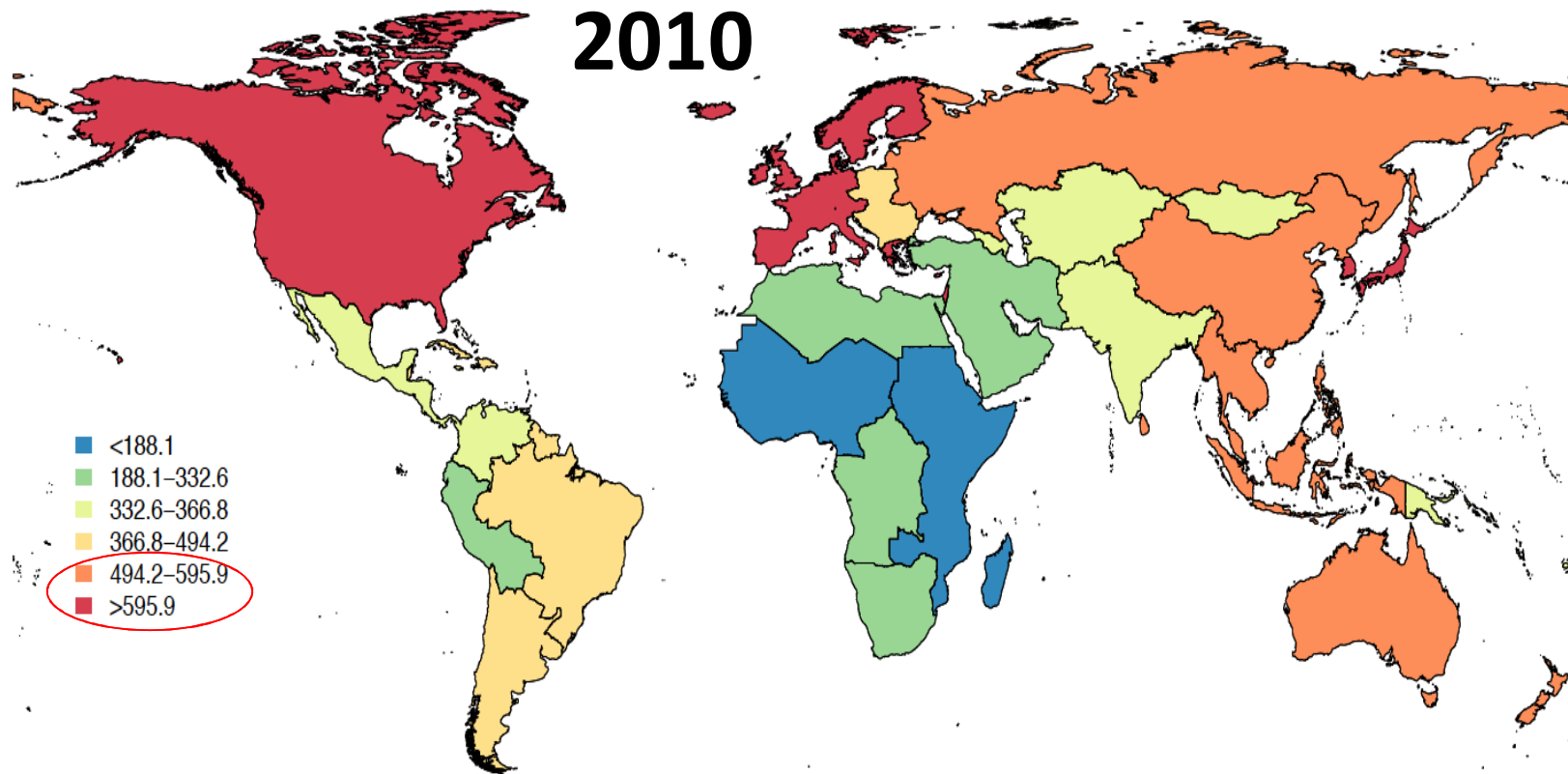
AO S Camillo Forlanini

**Age-adjusted stroke incidence rates per 100,000 person-years
in GBD regions in 1990 & 2010**



Global incidence rates slightly increased from 251 to 258/100,000 person-years: up 12% in LMIC and down 12% in HIC

Age-adjusted stroke prevalence per 100,000 people in GBD regions in 1990 & 2010



Global prevalence increased from 435 to 502/100,000 people: up by 10% in LMIC and 24% in HIC

Worldwide stroke epidemic continues to increase

1990-2010

- ↑ **25%** in strokes in people 20-64 years
- ↑ **113%** in stroke prevalence
- ↑ **70%** in the number of strokes each year
- ↑ **36%** in the number of deaths from stroke
- ↑ **31%** in DALYs (Disability Adjusted Life Years)

In most LMIC mortality from stroke greater than that from IHD
>60% of all strokes occur in people younger than 75 yr
(68% in LMIC and 50% in HIC)

TO REDUCE THE NUMBER OF PREMATURE DEATHS OF CVD by 25% in 2025



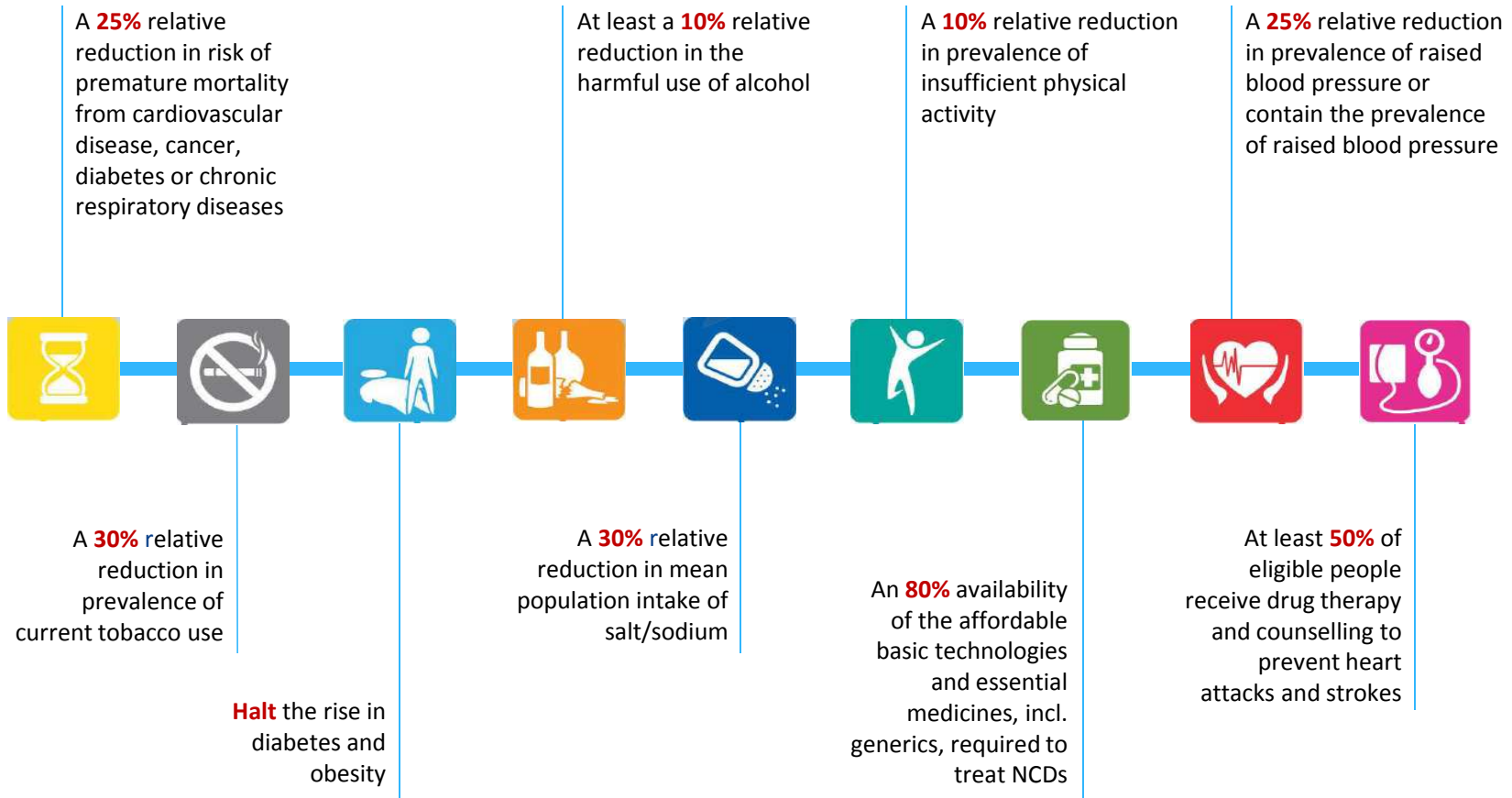
World Health
Organization

GLOBAL ACTION PLAN

FOR THE PREVENTION AND CONTROL OF NONCOMMUNICABLE DISEASES

2013-2020

9 global NCD targets to be attained by 2025 (against a 2010 baseline)



La *prevenzione primaria* si riferisce al trattamento delle persone fisiche con nessuna storia di ictus. Prevenzione secondaria si riferisce al trattamento di persone che hanno già avuto un ictus o un attacco ischemico transitorio

Misure di riduzione del rischio in prevenzione primaria possono includere: l'uso di farmaci antipertensivi, anticoagulanti, antiaggreganti piastrinici, gli inibitori della 3-idrossi-3-metilglutaril coenzima A (HMG-CoA) reduttasi (statine), cessazione del fumo, intervento dietetico, perdita di peso, e l'esercizio fisico

AHA/ASA Guideline

Guidelines for the Primary Prevention of Stroke A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

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Wesley S. Moore, MD, FAHA; J.V. (Ian) Nixon, MD, FAHA; Thomas A. Pearson, MD, FAHA; on
behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council
on Epidemiology and Prevention, Council for High Blood Pressure Research, Council on Peripheral
Vascular Disease, and Interdisciplinary Council on Quality of Care and Outcomes Research

Background and Purpose—This guideline provides an overview of the evidence on established and emerging risk factors for stroke to provide evidence-based recommendations for the reduction of risk of a first stroke.

Methods—Writing group members were nominated by the committee chair on the basis of their previous work in relevant topic areas and were approved by the American Heart Association (AHA) Stroke Council Scientific Statement Oversight Committee and the AHA Manuscript Oversight Committee. The writing group used systematic literature reviews (covering the time since the last review was published in 2006 up to April 2009), reference to previously published guidelines, personal files, and expert opinion to summarize existing evidence, indicate gaps in current knowledge, and when appropriate, formulate recommendations using standard AHA criteria (Tables 1 and 2). All members of the writing group had the opportunity to comment on the recommendations and approved the final version of this document. The guideline underwent extensive peer review by the Stroke Council leadership and the AHA scientific statements oversight committees before consideration and approval by the AHA Science Advisory and Coordinating Committee.

Results—Schemes for assessing a person's risk of a first stroke were evaluated. Risk factors or risk markers for a first stroke were classified according to potential for modification (nonmodifiable, modifiable, or potentially modifiable) and strength of evidence (well documented or less well documented). Nonmodifiable risk factors include age, sex, low birth weight, race/ethnicity, and genetic predisposition. Well-documented and modifiable risk factors include hypertension, exposure to cigarette smoke, diabetes, atrial fibrillation and certain other cardiac conditions, dyslipidemia, carotid artery stenosis, sickle cell disease, postmenopausal hormone therapy, poor diet, physical inactivity, and obesity and body fat distribution. Less well-documented or potentially modifiable risk factors include the metabolic syndrome, excessive

Fattori di Rischio non modificabili

Factor	Incidence/Prevalence				Relative Risk
Age, y ²¹	Prevalence of first stroke (percent per 100 000)				...
18–44	0.5				
45–64	2.4				
65–74	7.6				
75+	11.2				
	Incidence of first stroke (per 1000) ^{1†}				
	White men	White women	Black Men	Black women	
45–54	1.4	1.0	3.5*	2.9	
55–64	2.9	1.6	4.9	4.6	
65–74	7.7	4.2	10.4	9.8	
75–84	13.5	11.3	23.3*	13.5	
85+	32.1	16.5	24.7*	21.8	
Sex (age adjusted) ²¹	Prevalence (percent per 100 000)				...
	Men: 2.9				
	Women: 2.3				
	Total: 2.6				
Low birth weight ^{30,31}	...				~2 for birth weight <2500 g vs >4000 g
Race/ethnicity (age adjusted) ²¹	Prevalence (percent per 100 000)				...
	Asian: 1.8				
	Blacks: 4.6				
	Hispanics: 1.9				
	Whites: 2.4				
Family history of stroke/TIA ²⁵	...				RR, paternal history: 2.4 (95% CI, 0.96–6.03) RR, maternal history 1.4 (95% CI, 0.60–3.25)

CI indicates confidence interval; RR, relative risk; and TIA, transient ischemic attack.

*Incidence rates for black men and women 45 to 54 y of age and black men >75 y of age are considered unreliable.

†Unpublished data from the Greater Cincinnati/Northern Kentucky Stroke Study.

Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study



*Martin J O'Donnell, Siu Lim Chin, Sumathy Rangarajan, Denis Xavier, Lisheng Liu, Hongye Zhang, Purnima Rao-Melacini, Xiaohe Zhang, Prem Pais, Steven Agapay, Patricio Lopez-Jaramillo, Albertino Damasceno, Peter Langhorne, Matthew J McQueen, Annika Rosengren, Mahshid Dehghan, Graeme J Hankey, Antonio L Dans, Ahmed Elsayed, Alvaro Avezum, Charles Mondo, Hans-Christoph Diener, Danuta Ryglewicz, Anna Czlonkowska, Nana Pogossova, Christian Weimar, Romaina Iqbal, Rafael Diaz, Khalid Yusoff, Afzalhussein Yusufali, Aytekin Oguz, Xingyu Wang, Ernesto Penaherrera, Fernando Lanas, Okechukwu S Ogah, Adesola Ogunniyi, Helle K Iversen, German Malaga, Zvonko Rumboldt, Shahram Oveisgharan, Fawaz Al Hussain, Daliwonga Magazi, Yongchai Nilanont, John Ferguson, Guillaume Pare, Salim Yusuf; on behalf of the INTERSTROKE investigators**

www.thelancet.com Published online July 15, 2016

INTERSTROKE è un grande studio caso-controllo internazionale. I partecipanti sono stati reclutati tra il 11 Gennaio 2007, e 8 Agosto 2015, da 142 centri in 32 paesi in **Asia** (Cina, India, Pakistan, Filippine, Thailandia e Malesia), **Africa** (Mozambico, Nigeria, Sud Africa, Sudan e Uganda), **Europa** (Croazia, Danimarca, Germania, Polonia, Russia, Svezia, Regno Unito, Irlanda e Turchia), **Medio Oriente** (Iran, Arabia Saudita, Kuwait, e Emirati Arabi Uniti), **Nord America** (Canada), **Australia e Sud America** (Argentina, Brasile, Cile, Colombia, Ecuador e Perù)

Secondo lo studio INTERSTROKE, circa il 90% del ***burden of stroke*** di tutto il mondo può essere attribuito ai seguenti 10 fattori di rischio potenzialmente modificabili, collettivamente:

- Storia di ipertensione o pressione arteriosa di almeno 140/90 mmHg
- Attività fisica regolare
- Apolipoproteina B / apolipoproteina A-I rapporto
- Dieta
- Circonferenza addominale
- Fattori psicosociali
- Tabagismo
- Condizioni cardiache (Fibrillazione atriale)
- Consumo di alcool
- Diabete mellito

Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study

Martin J O'Donnell, Siu Lim Chin, Sumathy Rangarajan, Denis Xavier, Lisheng Liu, Hongye Zhang, Purnima Rao-Melacini, Xiaohu Zhang, Prem Pais, Steven Agapay, Patricio Lopez-Jaramillo, Albertino Damasceno, Peter Langhorne, Matthew J McQueen, Annika Rosengren, Mahshid Dehghan, Graeme J Hankey, Antonio L Dans, Ahmed Elsayed, Alvaro Avezum, Charles Mondo, Hans-Christoph Diener, Danuta Ryglewicz, Anna Czlonskowska, Nana Pogossova, Christian Weimar, Romaina Iqbal, Rafael Diaz, Khalid Yusoff, Afzalhussein Yusufali, Aytekin Oguz, Xingyu Wang, Ernesto Penaherrera, Fernando Lanas, Okechukwu S Ogah, Adesola Ogunniyi, Helle K Iversen, German Malaga, Zvonko Rumboldt, Shahram Oveisgharan, Fawaz Al Hussain, Daliwonga Magazi, Yongchai Nilanont, John Ferguson, Guillaume Pare, Salim Yusuf; on behalf of the INTERSTROKE investigators*

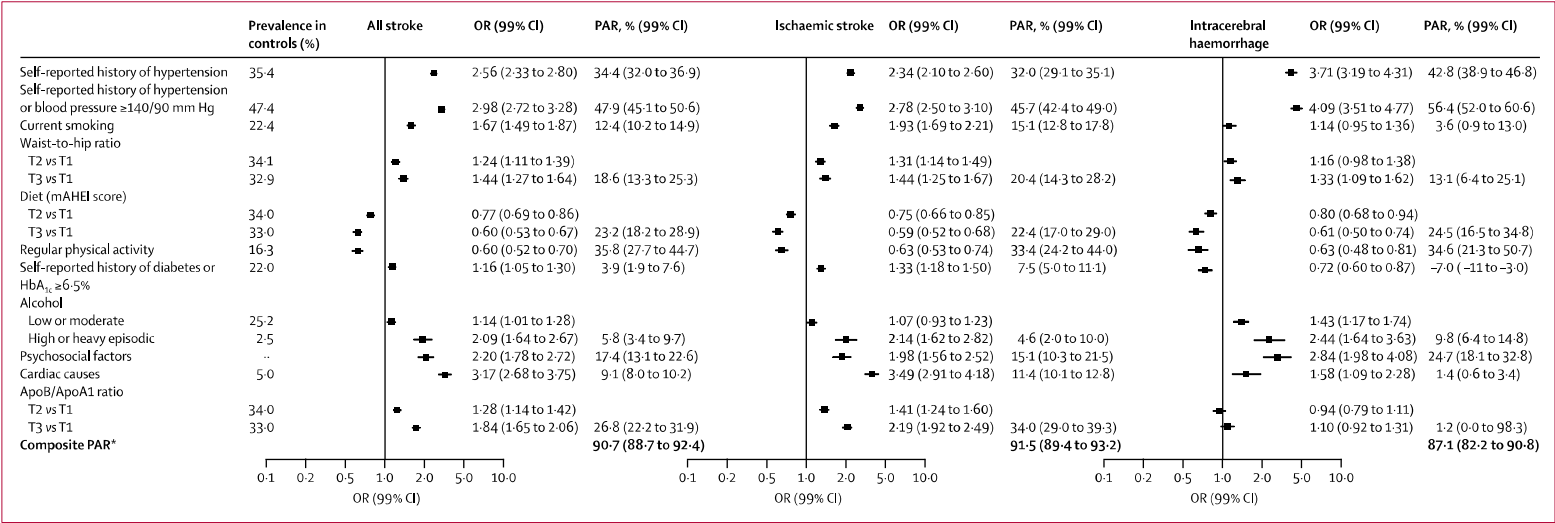
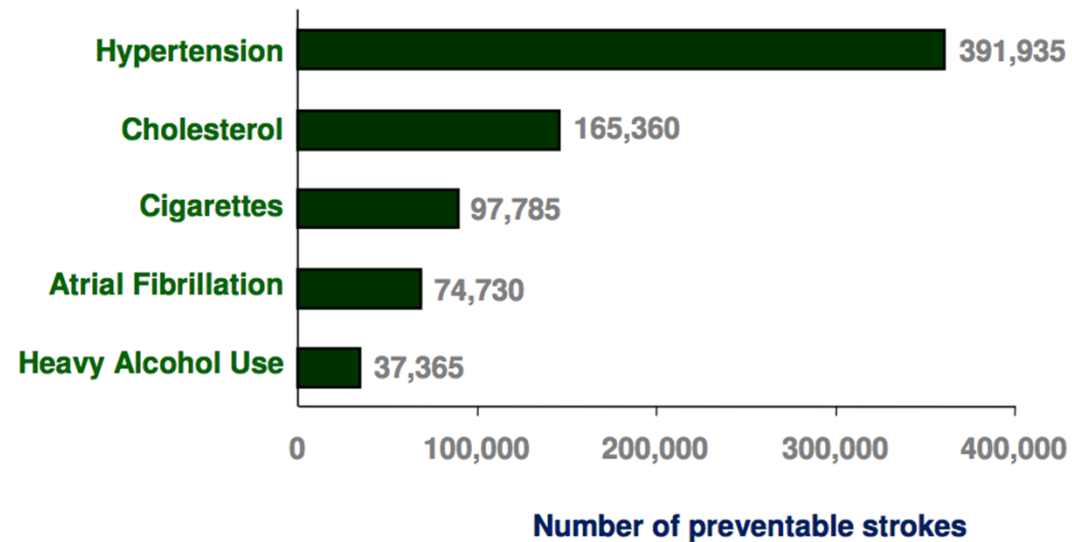


Figure 1: Multivariable analysis of prevalence of risk factors, OR, and PAR for ten risk factors
Cardiac sources include atrial fibrillation or flutter, previous myocardial infarction, rheumatic valve disease, or prosthetic heart valve. For tertiles, PAR was calculated using T2+T3 versus T1, other than diet, where PAR was calculated using T1+T2 versus T3. For physical activity, OR is reported for physically active versus other, and PAR is calculated for the inverse. For alcohol, OR is reported for high or heavy episodic, low or moderate vs former or never drinker, PAR is reported for current alcohol intake vs former or never drinker. For psychosocial factors, additional adjustment for education and income (purchasing power parity) reported a PAR 16.1% (95% CI 11.6–21.9) for all stroke. Apo=apolipoprotein. mAHLE=modified Alternative Healthy Eating Index. OR=odds ratio. PAR=population attributable risk. T=tertile. *Composite PAR includes all ten risk factors; self-reported history of hypertension or blood pressure ≥140/90 mm Hg was used for hypertension variable.

How Many US Strokes Can Be Prevented by Controlling Risk Factors?



Gorelick PB, et al. *Arch Neurol.* 1995;52:347-355.

Gorelick PB, et al. *Stroke.* 2002;33:862-875.

Ambient Air Pollution and the Risk of Acute Ischemic Stroke

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Background: The link between daily changes in level of ambient fine particulate matter (PM) air pollution (PM_{<2.5} μm in diameter [PM_{2.5}]) and cardiovascular morbidity and mortality is well established. Whether PM_{2.5} levels below current US National Ambient Air Quality Standards also increase the risk of ischemic stroke remains uncertain.

Methods: We reviewed the medical records of 1705 Boston area patients hospitalized with neurologist-confirmed ischemic stroke and abstracted data on the time of symptom onset and clinical characteristics. The PM_{2.5} concentrations were measured at a central monitoring station. We used the time-stratified case-crossover study design to assess the association between the risk of ischemic stroke onset and PM_{2.5} levels in the hours and days preceding each event. We examined whether the association with PM_{2.5} levels differed by presumed ischemic stroke pathophysiologic mechanism and patient characteristics.

Results: The estimated odds ratio (OR) of ischemic stroke onset was 1.34 (95% CI, 1.13-1.58) ($P < .001$) following a 24-hour period classified as *moderate* (PM_{2.5} 15-40 $\mu\text{g}/\text{m}^3$) by the US Environmental Protection Agency's (EPA) Air Quality Index compared with a 24-hour period classified as *good* ($\leq 15 \mu\text{g}/\text{m}^3$). Considering PM_{2.5} levels as a continuous variable, we found the estimated odds ratio of ischemic stroke onset to be 1.11 (95% CI, 1.03-1.20) ($P = .006$) per interquartile range increase in PM_{2.5} levels (6.4 $\mu\text{g}/\text{m}^3$). The increase in risk was greatest within 12 to 14 hours of exposure to PM_{2.5} and was most strongly associated with markers of traffic-related pollution.

Conclusion: These results suggest that exposure to PM_{2.5} levels considered generally safe by the US EPA increase the risk of ischemic stroke onset within hours of exposure.

Arch Intern Med. 2012;172(3):229-234

Original Contributions

Depressive Symptoms and Risk of Stroke The Framingham Study

Kimberly J. Salaycik, MA; Margaret Kelly-Hayes, EdD, RN; Alexa Beiser, PhD;
Anh-Hoa Nguyen, MA; Stephen M. Brady, PhD; Carlos S. Kase, MD; Philip A. Wolf, MD

Background and Purpose—Emerging evidence raises the possibility of an association between depression and stroke risk. This study sought to examine whether depressive symptoms are associated with an increased risk of cerebrovascular events in a community-based sample.

Methods—A prospective study was conducted on 4120 Framingham Heart Study participants aged 29 to 100 years with up to 8 years of follow-up. The Center for Epidemiologic Studies Depression Scale was used to measure depressive symptoms. Incident stroke and transient ischemic attack (TIA) events were assessed by uniform diagnostic criteria. The association between depressive symptoms and risk of stroke/TIA was analyzed with Cox proportional-hazards models, after adjusting for traditional stroke risk factors.

Results—In participants <65 years, the risk of developing stroke/TIA was 4.21 times greater ($P<0.001$) in those with symptoms of depression. After adjusting for components of the Framingham Stroke Risk Profile (hazard ratio=3.43, 95% CI=1.60 to 7.36, $P=0.002$) and education (hazard ratio=4.89, 95% CI=2.19 to 10.95), similar results were obtained. In subjects aged 65 and older, depressive symptoms were not associated with an increased risk of stroke/TIA. Taking antidepressant medications did not alter the risk associated with depressive symptoms.

Conclusions—In this community-based study, depressive symptoms were an independent risk factor for incident stroke/TIA in individuals <65 years. These data suggest that identification of depressive symptoms at younger ages may have an impact on the primary prevention of stroke. (*Stroke*. 2007;38:16-21.)

Key Words: depressive symptoms ■ stroke ■ transient ischemic attack ■ risk factors

In questo studio, i sintomi depressivi erano un fattore di rischio indipendente di ictus / TIA nei soggetti di 65 anni.

Questi dati suggeriscono che l'identificazione di sintomi depressivi in giovane età può avere un impatto sulla prevenzione primaria dell'ictus

Psychosocial Distress, an Underinvestigated Risk Factor for Stroke

Michael Brainin and Alexandra Dachenhausen

Stroke. 2013;44:305-306; originally published online January 15, 2013;

doi: 10.1161/STROKEAHA.112.680736

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0039-2499. Online ISSN: 1524-4628

Psychosocial Distress and Stroke Risk in Older Adults

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Carlos F. Mendes de Leon, PhD; Denis A. Evans, MD; Susan A. Everson-Rose, PhD, MPH

Background and Purpose—To investigate the association of psychosocial distress with risk of stroke mortality and incident stroke in older adults.

Methods—Data were from the Chicago Health and Aging Project, a longitudinal population-based study conducted in 3 contiguous neighborhoods on the south side of Chicago, IL. Participants were community-dwelling black and non-Hispanic white adults, aged 65 years and older (n=4120 for stroke mortality; n=2649 for incident stroke). Psychosocial distress was an analytically derived composite measure of depressive symptoms, perceived stress, neuroticism, and life dissatisfaction. Cox proportional hazards models examined the association of distress with stroke mortality and incident stroke over 6 years of follow-up.

Results—Stroke deaths (151) and 452 incident strokes were identified. Adjusting for age, race, and sex, the hazard ratio (HR) for each 1-SD increase in distress was 1.47 (95% confidence interval [CI]=1.28–1.70) for stroke mortality and 1.18 (95% CI=1.07–1.30) for incident stroke. Associations were reduced after adjustment for stroke risk factors and remained significant for stroke mortality (HR=1.29; 95% CI=1.10–1.52) but not for incident stroke (HR=1.09; 95% CI=0.98–1.21). Secondary analyses of stroke subtypes showed that distress was strongly related to incident hemorrhagic strokes (HR=1.70; 95% CI=1.28–2.25) but not ischemic strokes (HR=1.02; 95% CI=0.91–1.15) in fully adjusted models.

Conclusions—Increasing levels of psychosocial distress are related to excess risk of both fatal and nonfatal stroke in older black and white adults. Additional research is needed to examine pathways linking psychosocial distress to cerebrovascular disease risk. (*Stroke*. 2013;44:367-372.)

Key Words: epidemiology ■ psychosocial stress ■ risk factors ■ women and minorities

Livelli crescenti di stress psico-sociale sono legati ad un aumento di rischio di ictus fatale e non fatale nei soggetti adulti più anziani.

Ulteriori ricerche sono necessarie per esaminare i percorsi che collegano disagio psico-sociale al rischio di malattie cerebrovascolari

Distress psicosociale: sintomi depressivi, stress vitale, nevrosi, soddisfazione per la propria vita

Chicago Health and Aging Project

NCD development and costs

