

FIBRILLAZIONE ATRIALE E ICTUS CARDIOEMBOLICO

PROSPETTIVE TERAPEUTICHE E SOSTENIBILITÀ ECONOMICA

Le conseguenze della Fibrillazione Atriale: ictus, disabilità e costi sociali

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Outline

- Quale è la proporzione di ictus ischemici attribuibile a cardioembolismo
- Il peso assistenziale ed i costi dell'ictus
- Le caratteristiche dell'ictus cardioembolico
- La necessità di migliorare la prevenzione

L'ictus è una complicanza frequente della FA

La FA si associa a un rischio globale di ictus 5 volte maggiore[1].
Se corretta per altri fattori di rischio, la FA raddoppia il rischio di ictus[2]

Senza trattamento preventivo, ogni anno circa 1 paziente su 20 (5%) con FA permanente avrà un ictus[3]

Se si considerano gli attacchi ischemici transitori e gli ictus clinicamente 'silenti', il tasso di ischemie cerebrali associate a FA non valvolare supera il 7% annuo[4]

1. Savelieva I et al. Ann Med 2007;39:371–91;
2. ACC/AHA/ESC guidelines: Fuster V et al. Circulation 2006;114:e257–354 & Eur Heart J 2006;27:1979–2030;
3. Atrial Fibrillation Investigators. Arch Intern Med 1994;154:1449–57;
4. Carlson M. Medscape Cardiology. 2004;8; available at http://cme.medscape.com; accessed Feb 2010;

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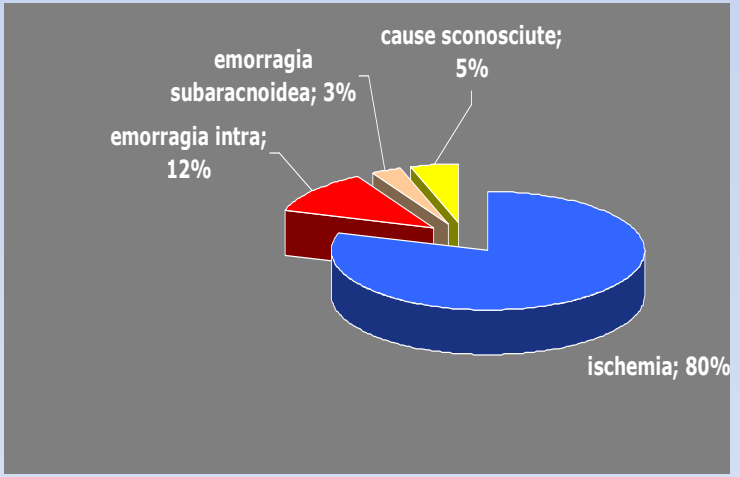
La maggioranza degli ictus è di natura ischemica

L'ictus ischemico rappresenta la forma più frequente di ictus (80% circa), le emorragie intraparenchimali riguardano il 15%-20% e le emorragie subaracnoidee il 3% circa.

SPREAD 10 anni



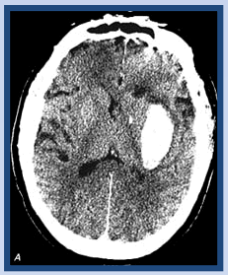
Negli USA

- 87% ischemic stroke
- 10% intracerebral hemorrage
- 3% subaracnoid hemorrage

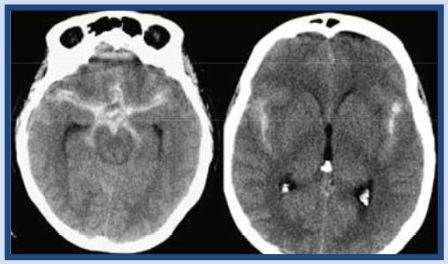
Heart Disease and Stroke Statistics—2012 Update
A Report From the American Heart Association
Circulation published online December 15, 2011

Sottotipi di ictus

Ictus emorragico

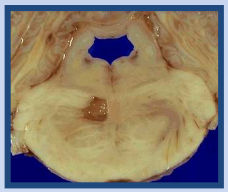


Emorragia cerebrale (59%)

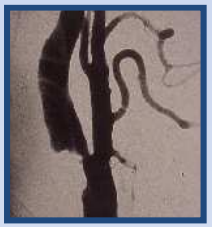


Emorragia subaracnoidea (41%)

Ictus ischemico



Ictus lacunare (23-25%)



Ictus aterotrombotico (13-20%)



Ictus Embolico (20-27%)

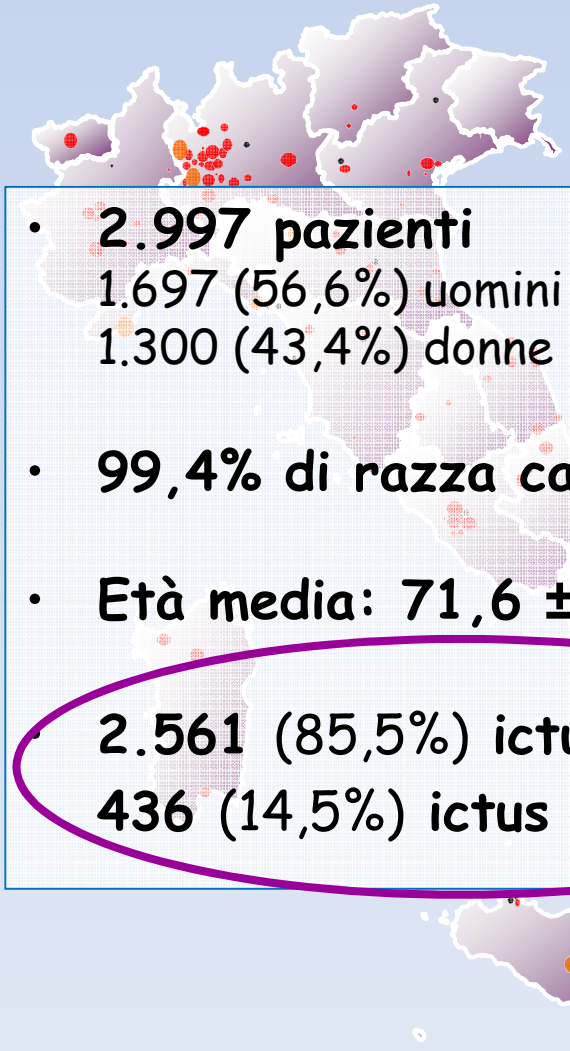
Non attribuibile Non identificato

Ictus Criptogenetico (30-35%)

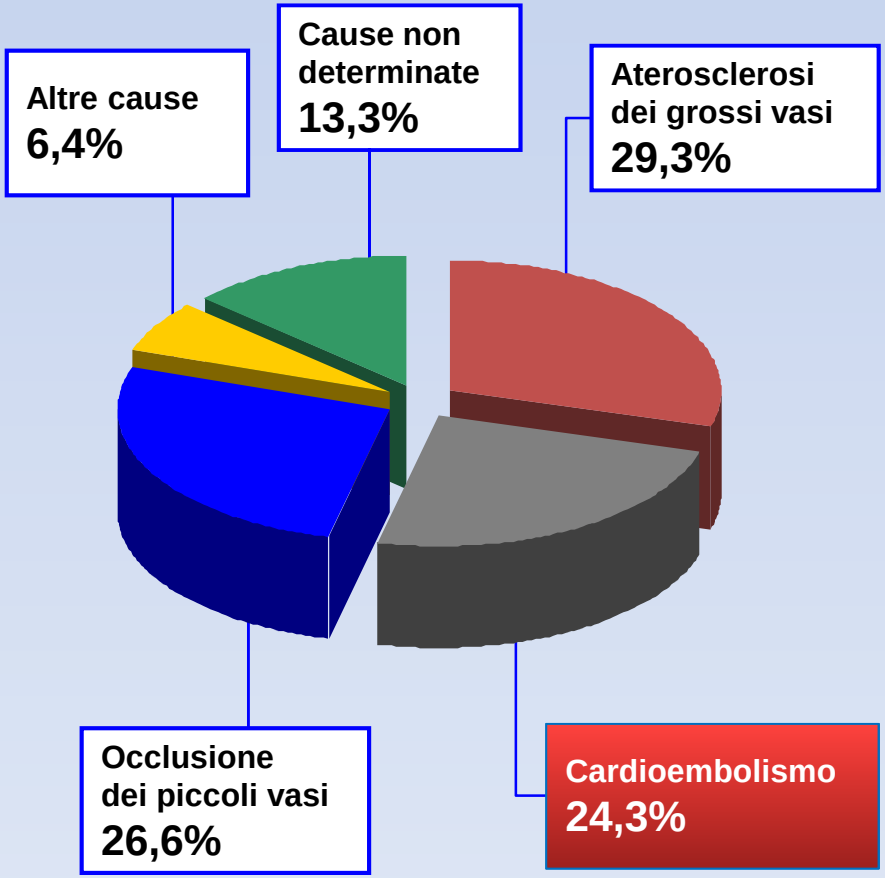
Albers GW et al. Chest. 1998
Rosamond WD et al. Stroke. 1999.
Kolominsky-Rabas PL et al. Stroke. 2001

Sottotipi di Ictus
Popolazione italiana

119 centri partecipanti



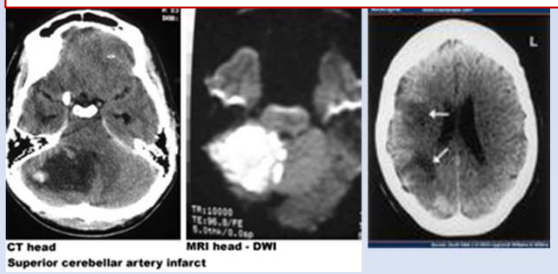
- **2.997 pazienti**
  1.697 (56,6%) uomini
  1.300 (43,4%) donne
- **99,4% di razza caucasica**
- **Età media: 71,6 ± 12,2 anni**
- **2.561 (85,5%) ictus ischemici**
  436 (14,5%) ictus emorragici



Toso V, et al. Neurol Sci 2006

Ictus cardioembolico

La FA è la principale causa degli ictus cardioembolici ed è responsabile da 1/5 a 1/4 di tutti gli ictus



Hannon N et al. Cerebrovasc Dis 2010;29:43–9;
Atrial fibrillation; available at http://www.americanheart.org/presenter.jhtml?identifier=4451;

Ictus criptogenetico

Almeno una parte degli ictus criptogenetici è attribuibile a FA misconosciuta

Up to 20% of patients labelled as "cryptogenic" may have PAF

Jabaudon D. Stroke 2004
Elijovich et al. J of Stroke and Cerebrovasc Dis 2009
International Stroke Conference (ISC) 2012

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Problema assistenziale e sociale

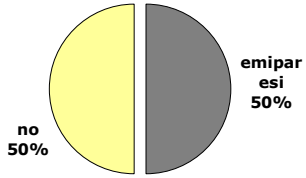
- In Italia l'ictus è la terza causa di morte dopo le malattie cardiovascolari e le neoplasie, causando il 10%-12% di tutti i decessi per anno, e rappresenta la principale causa d'invalidità.

- Essendo la **prima causa di disabilità** a lungo termine, l'ictus rappresenta un **rilevante problema sanitario** che assorbe una grande quantità di risorse nell'ambito del SSN
- Con l'invecchiamento della popolazione costituirà sempre più un problema primario assistenziale e sociale

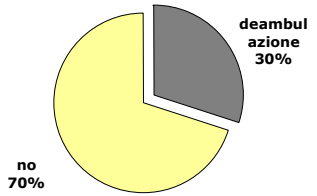
Gli esiti e la disabilità

Nei pazienti sopravvissuti (a 6 mesi)

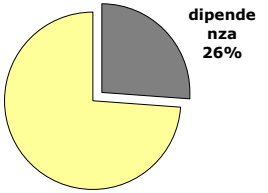
- 50% had some hemiparesis



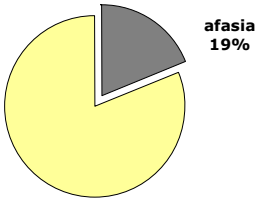
- 30% were unable to walk without some assistance



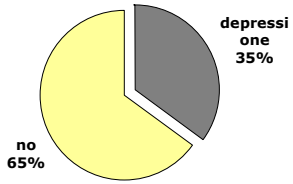
- 26% were dependent in activities of daily living



- 19% had aphasia



- 35% had depressive symptoms



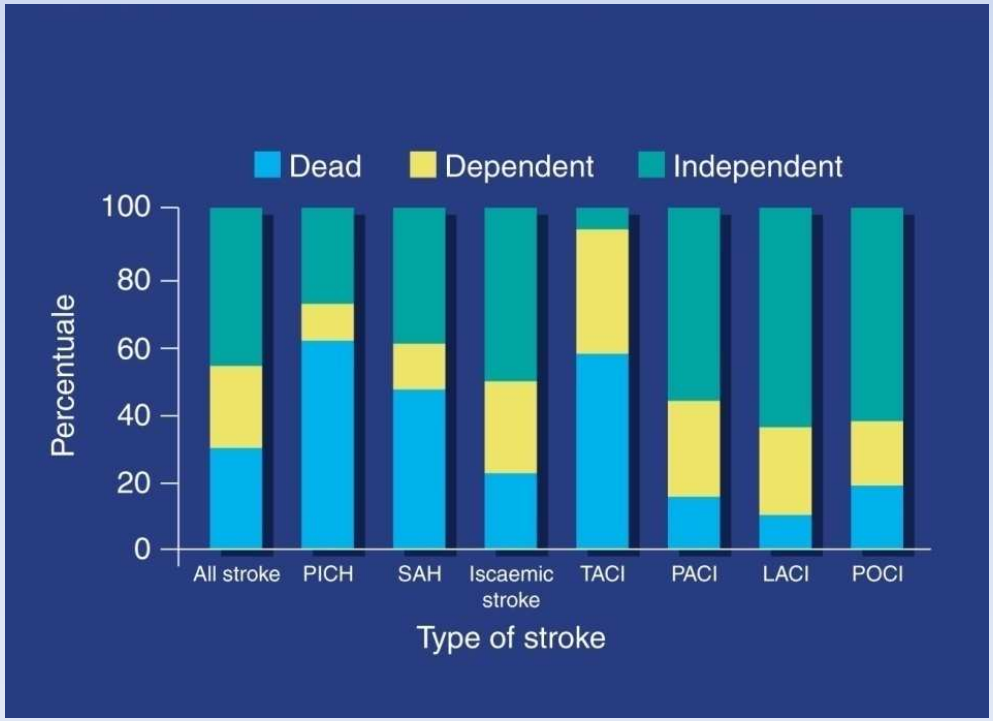
- 26% were institutionalized in a nursing home



Kelly-Hayes M, et al. J Stroke Cerebrovasc Dis. 2003

1/3 di ictus con disabilità/dipendenza

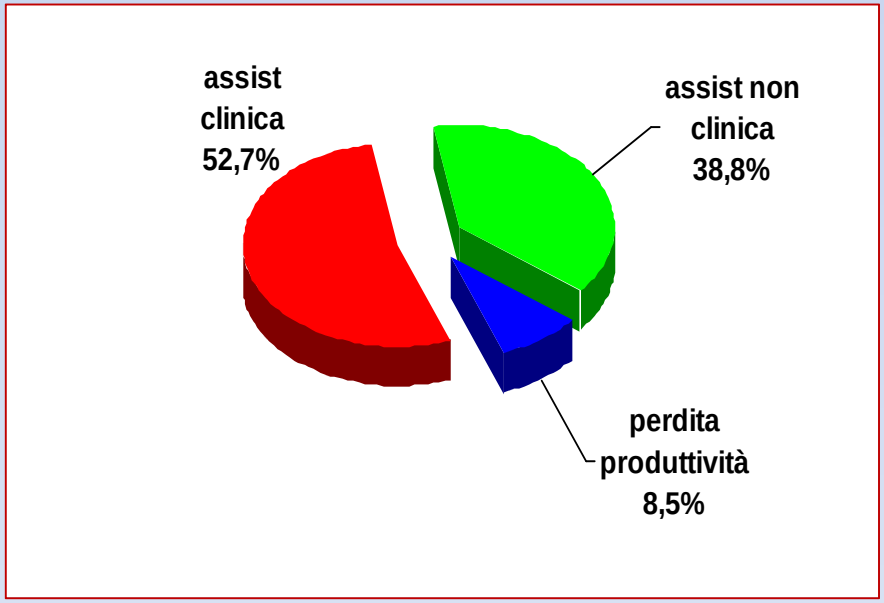
- Ad 1 anno circa dall'evento acuto, **un terzo** circa dei soggetti sopravviventi ad un ictus - indipendentemente dal fatto che sia ischemico o emorragico - presenta un grado di **disabilità elevato**, tanto da poterli definire **totalmente dipendenti**.



I costi a 6 mesi (Italia)

449 pz. (386 al follow-up a 6 mesi)

- **Costo medio/pz € 11.600**
- **Ogni punto in più di FIM diminuzione costo 0.5%**
- **Stroke unit e reparti neurologici più costosi rispetto a reparti medicina generale**



Studio ECLIPSE. Gerzeli. Neurol Sci 26: 72-80, 2005

I costi a 12 mesi (Italia)

Fattore *et al. BMC Neurology* 2012, **12**:137
http://www.biomedcentral.com/1471-2377/12/137

BMC Neurology

RESEARCH ARTICLE Open Access

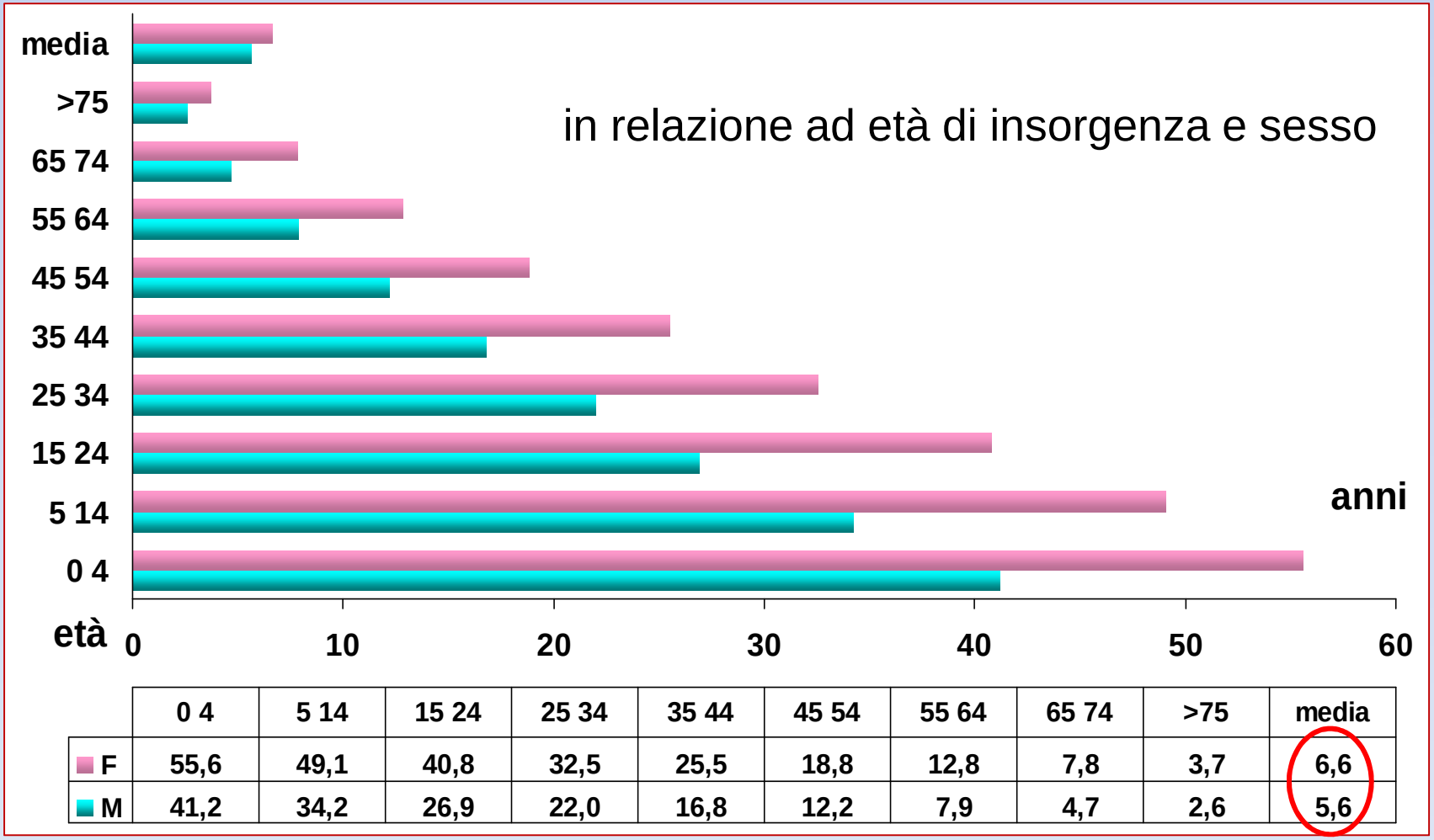
The social and economic burden of stroke survivors in Italy: a prospective, incidence-based, multi-centre cost of illness study

Giovanni Fattore[1*], Aleksandra Torbica[1*], Alessandra Susi[2], Aguzzi Giovanni[1], Giancarlo Benelli[3], Marianna Gozzo[3] and Vito Toso[4]

44 hospitals across the country. Socio-demographic, clinical variables and resource consumption were prospectively surveyed for 411 stroke survivors at admission, discharge and 3, 6 and 12 months post the event

	Users		Resources per patient		Cost per patient (€)			
	N.	%	Mean	Sd	Mean	Sd	Median	IQR
Total healthcare costs					11,747	11,250	6,727	9,483
Non-healthcare costs								
Informal care (hours per day)	183	45%	7.8	5.2	6,656	11,051	1800	
Paid care (hours per day)	60	15%	1.2	0.1	758	2,232	0	0
Production losses	25	6.1%			[illegible]	28	0	78
Total societal costs					19,953	18,114	13,714	22,058

Durata disabilità



	0 4	5 14	15 24	25 34	35 44	45 54	55 64	65 74	>75	media
F	55,6	49,1	40,8	32,5	25,5	18,8	12,8	7,8	3,7	6,6
M	41,2	34,2	26,9	22,0	16,8	12,2	7,9	4,7	2,6	5,6

Francescutti. Disabil. Rehabil. 27: 229-40, 2005

I costi aumentano con il tempo

Stroke
Journal of the American Heart Association
American Stroke Association
A Division of American Heart Association

Costs of Stroke Using Patient-Level Data
A Critical Review of the Literature

Ramon Luengo-Fernandez, MSc; Alastair M. Gray, PhD; Peter M. Rothwell, FRCP

Table 3. Cost Estimates From the 71 Studies Reporting Costs for Stroke or Ischemic Stroke, Stratified by Length of Follow-Up

Follow-Up Duration	N	Mean, $	Median, $	Range, $
Hospital discharge	53	17 250	10 202	468–65, 25
3 months to <6 mo	40	10 216	8 312	763–25, 611
6 months to <12 mo	22	16 973	17 195	7473–25 341
12 mo	48	28 525	19 635	7342–146 149
>12 mo	2	36 213	36 213	25 509–46 516

Stroke.2009;40:e18-e23

Age and Ageing 2009; **38:** 27–32
doi: 10.1093/ageing/afn281
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Cost of stroke in the United Kingdom

ÖMER SAKA[1], ALISTAIR MCGUIRE[1,2], CHARLES WOLFE[1,3]

Results: the treatment of and productivity loss arising from stroke results in total societal costs of **£8.9 billion a year**, with treatment costs accounting for approximately **5% of total UK NHS costs**.

Direct care accounts for approximately 50% of the total, informal care costs 27% and the indirect costs 24%.

Table 2. Total costs

Cost item	Cost in £	Percentage
Diagnosis costs	45.604 m	0.51
Inpatient care costs	865.872 m	9.64
Outpatient costs	109.679 m	1.22
Outpatient drug costs	505.588 m	5.63
Community care costs	2, 857.113m	31.82
Annual care cost total	4, 383.858m	48.82
Informal care costs total	2, 420.921m	26.96
Income lost due to mortality	592.733m	6.6
Income lost due to morbidity	740.158m	8.24
Productivity loss total	1, 332.892m	14.85
Benefit payments	841.254 m	9.37
Total	8, 978.926 m	

EUROPEAN JOURNAL OF NEUROLOGY
THE OFFICIAL JOURNAL OF THE EUROPEAN FEDERATION OF NEUROLOGICAL SOCIETIES

Cost of stroke in France

Chevreul, K et al. 20, 1094–1100, 2013

The total healthcare cost of stroke patients in France in 2007 was € 5.3 billion, 92% of which was borne by statutory health insurance.

Healthcare costs representing 3% of total health expenditure in France.

The high cost of illness underscores the need for improved prevention and interventions to limit the disabling effects of stroke.

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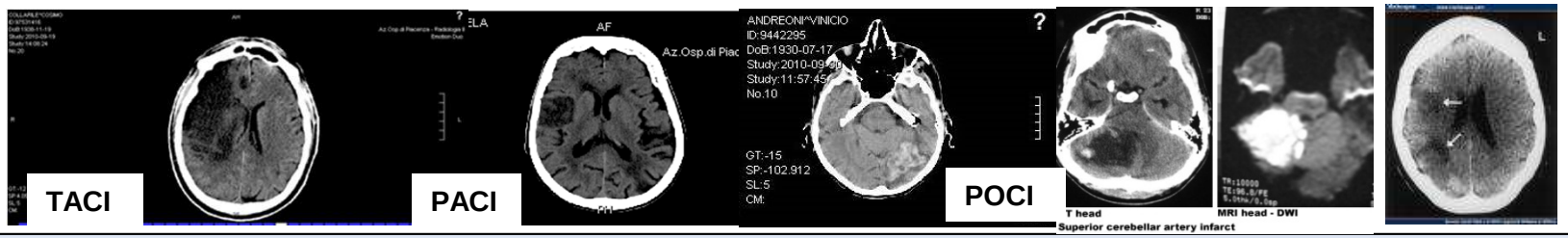
Cosa qualifica l'ictus cardioembolico: gravità e costi

Non solo la FA è la causa di un gran parte degli ictus ischemici, ma l'ictus cardioembolico è più grave e quindi più costoso in termini sanitari e sociali

Caratteristiche dell'ictus cardioembolico

- Più spesso di grandi dimensioni.
- Frequenti le ischemie totali /parziali di un distretto anteriore (TACI/PACI) o posteriore (POCI).
- Se ischemie silviane parziali, solitamente con interessamento corticale.
- Più frequente la presenza di infarcimento emorragico della lesione.
- Patognomonica la presenza di lesioni ischemiche contemporanee o in tempi ravvicinati in territori vascolari diversi o bilaterali.



Features of Stroke Patients With and Without AF

18,451 patients from the International Stroke Trial

Characteristics	Patients With AF n = 3,169	Patients Without AF n = 15,282
Age (mean, y)	77.8	70.6
Female	56%	45%
Impaired consciousness	37%	20%
Type of stroke: TACS	36%	21%
Ischemic stroke	90%	90%
Death (any cause) within 14 days	16.9%	7.5%
Death caused by neurological damage	9.6%	3.6%

Of patients with AF, 78.5% will be dead or dependent at 6 months

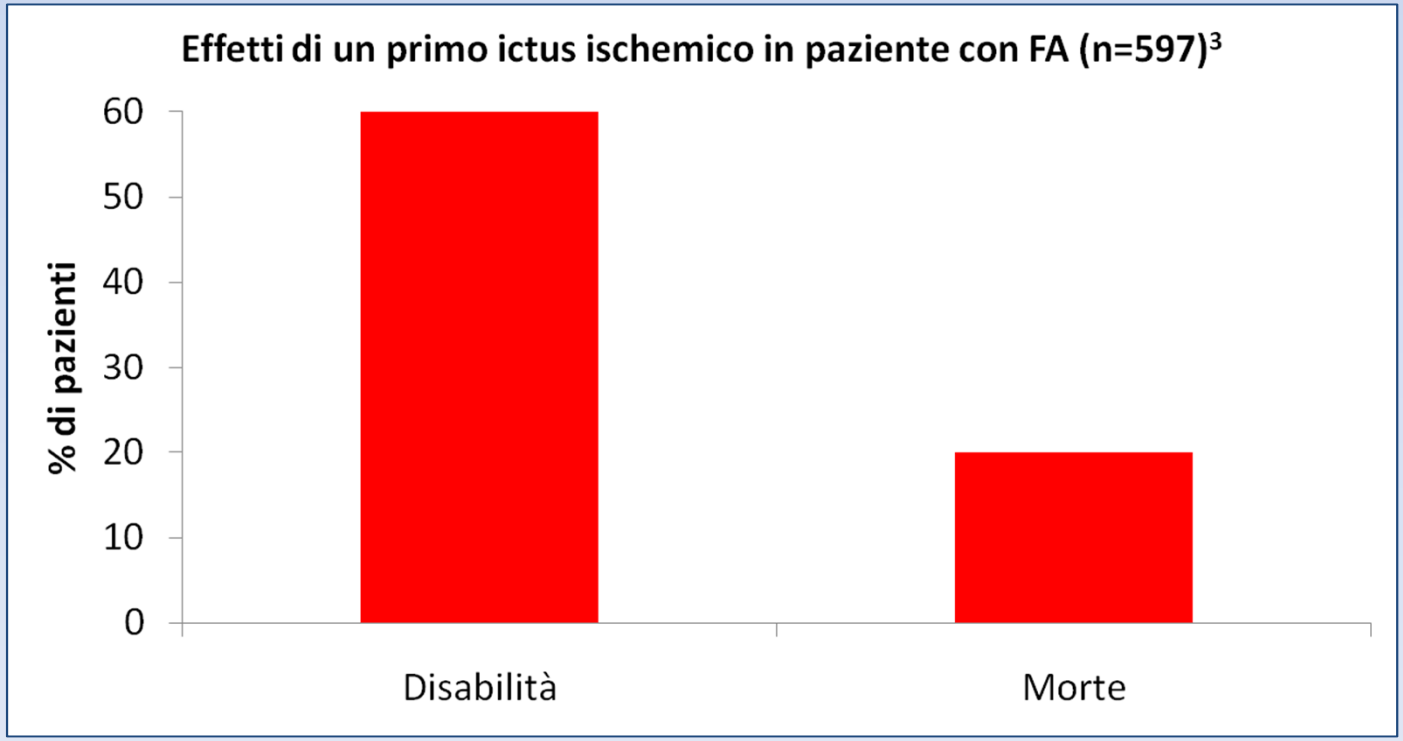
Saxena R, et al. *Stroke.* 2001;32:2333-2337.

Medscape EDUCATION

FA aumenta il rischio di ictus … grave

Il rischio di ictus è aumentato indipendentemente dal tipo di FA (parossistica vs. persistente) [1,2]

Gravità dell'ictus in paziente con FA



1. Rosamond W et al. *Circulation*. 2008;117:e25–146; 2.Hart RG, et al. *J Am Coll Cardiol* 2000;35:183-187;
3. Gladstone DJ et al. *Stroke*. 2009;40:235-240

… anche nel «Minor Stroke»

Hao et al. BMC Neurology 2013, 13:154
http://www.biomedcentral.com/1471-2377/13/154

BMC Neurology

RESEARCH ARTICLE Open Access

Etiologic subtype predicts outcome in mild stroke: prospective data from a hospital stroke registry

Zilong Hao[1], Ming Liu[2*], Deren Wang[1], Bo Wu[1], Wendan Tao[1] and Xueli Chang[1]

The rate of case fatality and death/disability was 2.2% and 10.1% respectively at 3 months.

After adjustment of potential confounders, such as age, sex, NIHSS on admission and vascular risk factors et al.,

cardioembolism (RR = 3.395) was the predictor of death or disability at 3 months

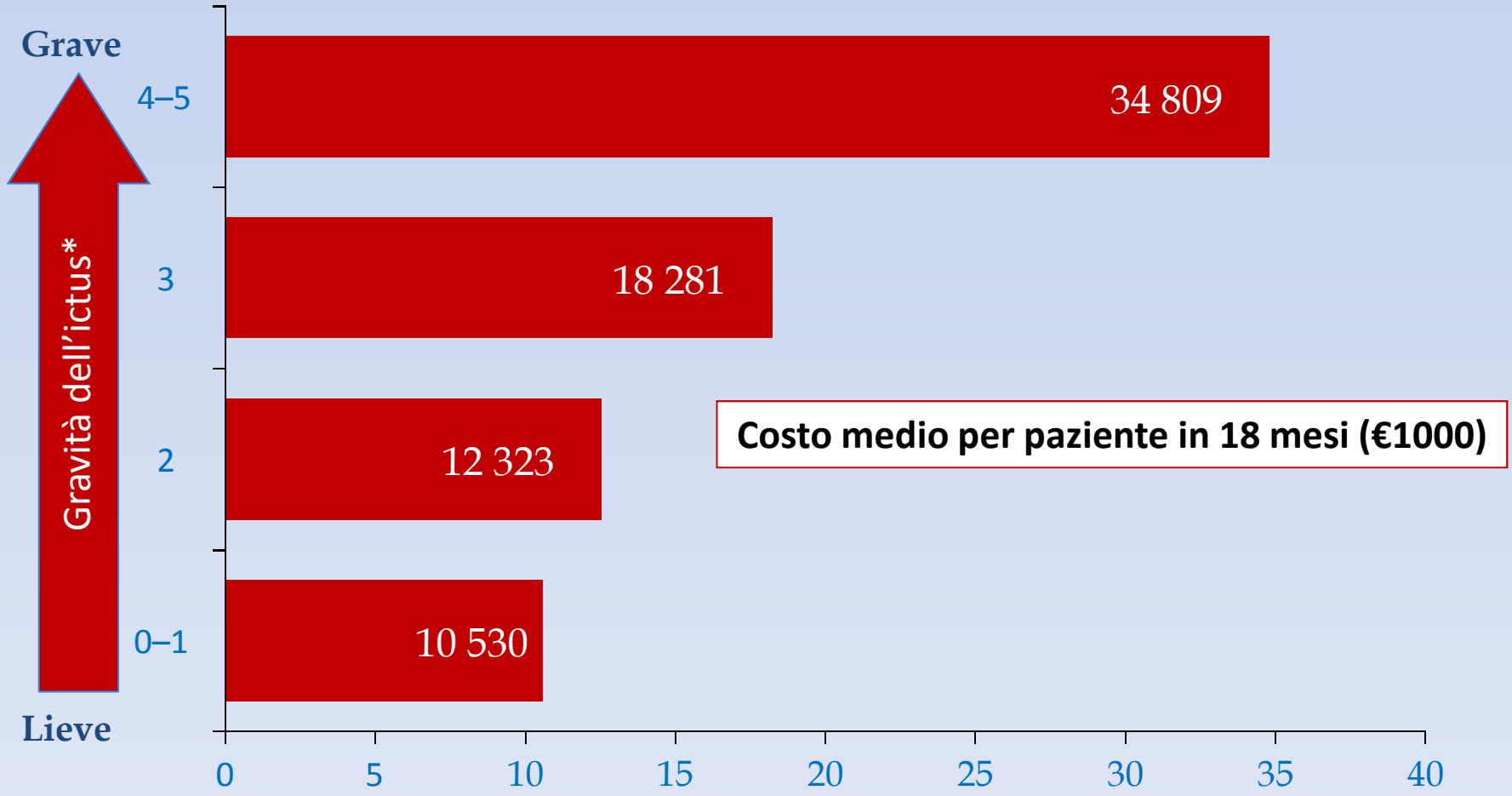
small vessel occlusion (RR = 0.412 was the protective factor of death or disability at 3 months.

Table 2 Multivariate logistic analysis of the influence of cardioembolism on death/disability

Variates	RR	95% CI	P value
Age	1.037	1.003 ~ 1.073	.031
Gender	.628	.276 ~ 1.426	.266
Time from onset	1.002	1.000 ~ 1.004	.107
SBP on admission	.992	.969 ~ 1.015	.486
DBP on admission	1.008	.972 ~ 1.045	.668
Hypertension	1.313	.610 ~ 2.826	.486
Diabetes mellitus	1.263	.533 ~ 2.989	.596
Hypercholesterolemia	1.188	.317 ~ 4.448	.798
Coronary heart diseas	.321	.060 ~ 1.708	.183
History of ischemic stroke	.228	.025 ~ 2.070	.189
History of hemorrhagic stroke	11.297	1.469 ~ 86.889	.020
Alcohol	.619	.208 ~ 1.848	.390
Smoking	1.620	.644 ~ 4.072	.305
CE VS. Non-CE	3.395	1.257 ~ 9.170	.016
Complications	3.405	1.527 ~ 7.596	.003

CE: cardioembolism.

I costi aumentano con la gravità dell'ictus



Dati relativi a 494 pazienti consecutivi con ictus in Francia; *Scala di Rankin a 10 giorni modificata

Spieler JF et al. Cerebrovasc Dis 2002;13:132–41c

Review

Neuro
-epidemiology

Neuroepidemiology 2013;40:227–239
DOI: 10.1159/000343667

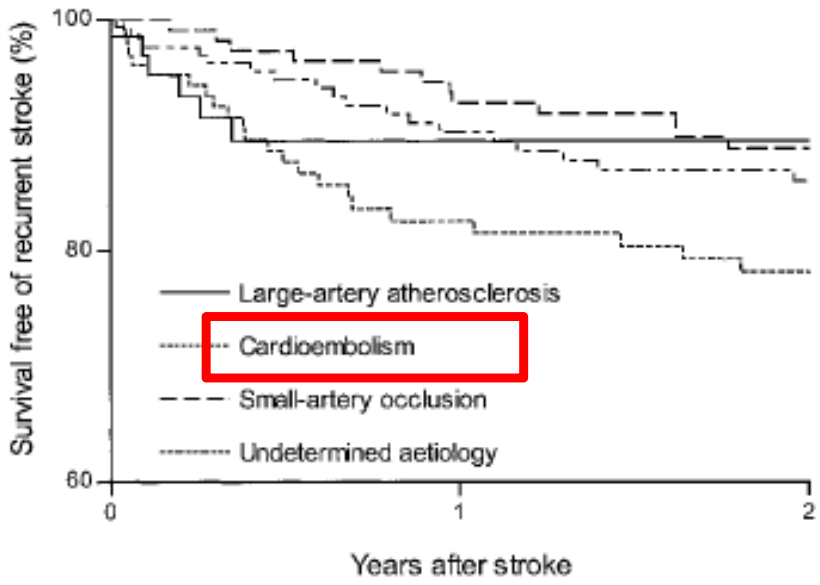
The Prevalence, Impact and Economic Implications of Atrial Fibrillation in Stroke: What Progress Has Been Made?

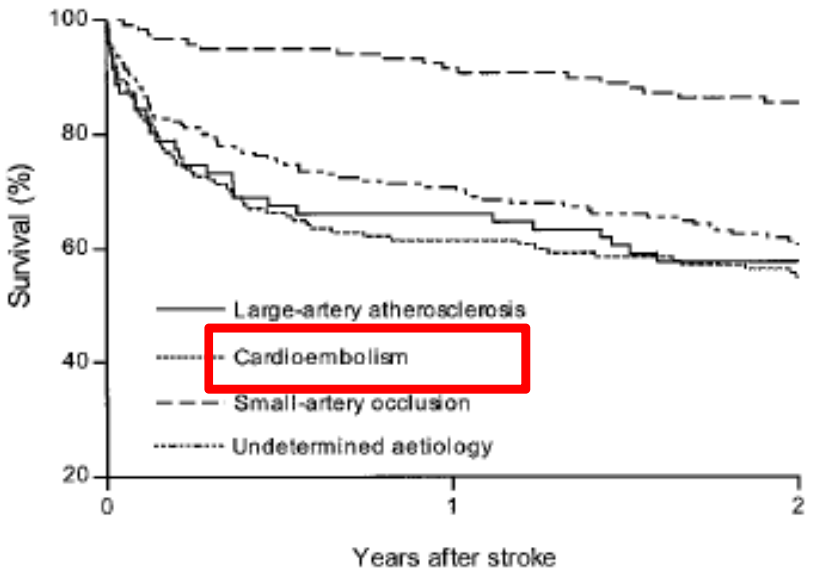
Nadine E. Andrew[a] Amanda G. Thrift[a, b] Dominique A. Cadilhac[a–c]

AF-related stroke cost an average of **between 7 and 20% more** than non-AF-related stroke [41–43] .
The excess cost was primarily attributable to longer lengths of hospital stay, but also to a greater frequency of recurrent stroke events over a 3-year period [42] .
Acute hospital costs remained greater for AF-related stroke when adjustment was made for potentially confounding variables such as gender, age and co-morbidities [41]

41. Bruggenjurgen B, et al. Value Health 2007.
42. Ghatnekar O, Glader E-L. Value Health 2008.
43, Meretoja A, et al. Stroke 2011.

Rischio di **recidive** e mortalità a due anni, per tipo di ictus (n= 531)





PL Kolominsky-Rabas et al. Stroke. 2001;32:2735-2740

Il maggior rischio di recidive aumenta il peso assistenziale ed i costi

Atrial fibrillation and incidence of **dementia**:
A systematic review and meta-analysis.

Table. Risk for Incident Dementia With AF vs No AF

Comparison	Odds Ratio (95% CI)	*P*	Heterogeneity, % (I^2)
AF vs no AF overall (14 studies)	2.0 (1.4 – 2.7)	<.0001	75
AF vs no AF in stroke patients (7 studies)	2.4 (1.7 – 3.5)	<.001	10
AF vs no AF in other populations (7 studies)	1.6 (1.0 – 2.7)	.05	87

AF = atrial fibrillation; CI = confidence interval

There is consistent evidence supporting an association between AF and increased incidence of dementia in patients with stroke whereas there remains considerable uncertainty about any link in the broader population

Kwok CS, et al. Neurology. 2011;76(10):914-22

Increased risk of cognitive and functional decline in patients with atrial fibrillation

results of the ONTARGET and TRANSCEND studies

- AF was associated with an increased risk of cognitive decline (hazard ratio [HR] 1.14), new dementia (HR 1.30), loss of independence in performing activities of daily living (HR 1.35) and admission to long-term care facilities (HR 1.53).
- **Cognitive and functional decline are important consequences of atrial fibrillation, even in the absence of overt stroke.**

– Marzona I, et al. Canadian Medical Association Journal (CMAJ), Feb 2012

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L'incidenza dell'ictus è in diminuzione negli USA

- Incidence of stroke has decreased over the past 50 years but the lifetime risk has not declined to the same degree, perhaps due to improved life expectancy.
- The results of this study suggest that *improved control of risk factors has lowered stroke incidence but emphasize the need for continued primary prevention efforts*.

FULL text at JAMA

Trends in incidence, lifetime risk, severity, and 30-day mortality of stroke over the past 50 years.
Carandang R, et al. JAMA. 2006 Dec 27;296(24):2939-46.

Ed anche nel Regno Unito

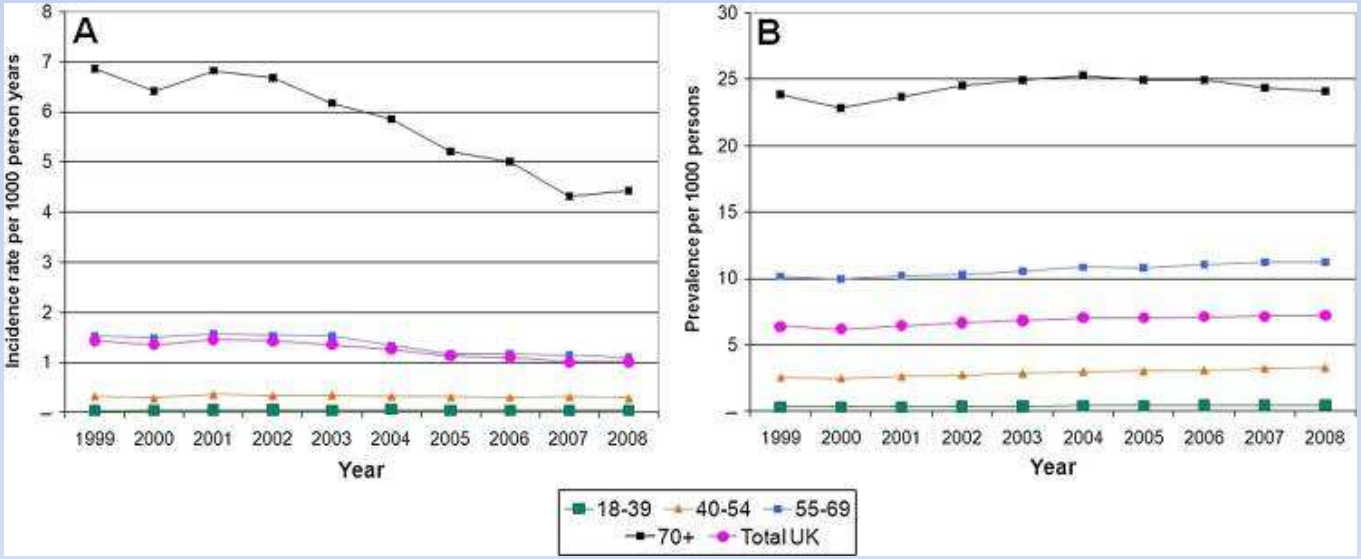
Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004

- Despite more complete case ascertainment than in OCSP, age-adjusted and sex-adjusted **incidence of first-ever stroke fell by 29%**
- Although 28% more incident strokes (366 vs 286) were expected due to demographic change alone (33% increase in those aged 75 or older), the observed number fell (262 vs 286).
- However, 30-day case-fatality remained the same: 17·2% (45/262) in 2002–04 versus 17·8% (99/557) in 1981–84
- Comparison of premorbid **risk factors revealed substantial reductions** in the proportion of smokers, mean total cholesterol, and mean systolic and diastolic blood pressures and major increases in premorbid treatment with antiplatelet, lipid-lowering, and blood pressure lowering drugs

P M Rothwell, A J Coull, et al for the Oxford Vascular Study. *Lancet* 2004

Incidenza e prevalenza (UK 1999-2008)

Incidence (A) and prevalence (B) of stroke in the UK adult population by age group.



Between 1999 and 2008, first strokes …. incidence fell by 30%, from 1.48/1000 person-years in 1999 to 1.04/1000 person-years in 2008 ($p<0.001$). In patients aged 80 years and over (the group at highest risk), incidence fell by 42%.

Prevalence of stroke increased by 12.5% over the same period from 6.4/1000 persons to 7.2/1000 persons ($p<0.001$)

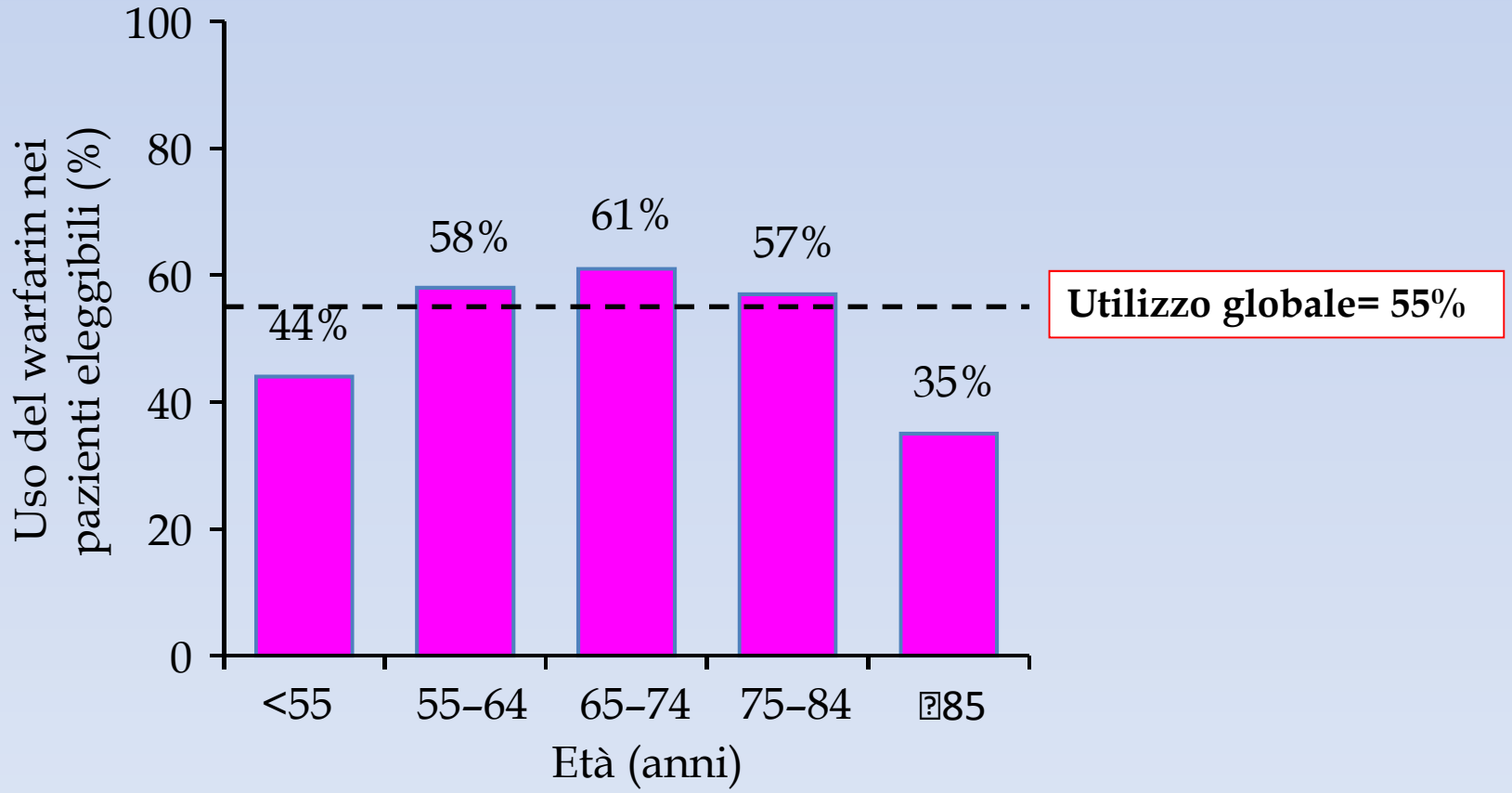
Lee S, Shafe AC, Cowie MR. BMJ Open. 2011

UK stroke incidence, mortality and cardiovascular risk management 1999-2008: time-trend analysis from the General Practice Research Database.

- Stroke incidence in the UK has decreased and survival after stroke has improved in the past 10 years.
- Improved drug treatment in primary care is likely to be a major contributor to this, with better control of risk factors both before and after incident stroke.
- **There is, however, scope for further improvement in risk factor reduction in high-risk patients with atrial fibrillation**

Lee S, Shafe AC, Cowie MR. BMJ Open. 2011

Warfarin è utilizzato solo in metà dei pazienti con FA



Warfarin è sotto-utilizzato, soprattutto nei pazienti anziani che sono quelli a più alto rischio di ictus

Go A et al. Ann Intern Med 1999;131:927

Review

Neuro
-epidemiology

Neuroepidemiology 2013;40:227–239
DOI: 10.1159/000343667

The Prevalence, Impact and Economic Implications of Atrial Fibrillation in Stroke: What Progress Has Been Made?

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Increased public health efforts are required to identify symptomatic and asymptomatic AF through population screening programmes and to implement strategies to improve prescription of and compliance with taking anticoagulant medications.

Conclusioni

- L'ictus CE dovuto a FA rappresenta una quota considerevole degli ictus ischemici (20-25%) ed è spesso misconosciuto (FAP, FA silente)
- L'ictus CE è più grave in termini di mortalità e di disabilità, di costi assistenziali e sociali
- L'ictus CE è prevenibile in misura superiore rispetto agli altri ictus ischemici
- La prevenzione con TAO è tuttora insufficientemente praticata, specie nell'anziano
- I nuovi anticoagulanti orali consentiranno di estendere la prevenzione ad un maggior numero di pazienti

Mr. Toad and Ratty From *Wind in the Willows*



Grazie per l'attenzione

Image courtesy of A Dalby.

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