Changing age pattern – more young strokes?

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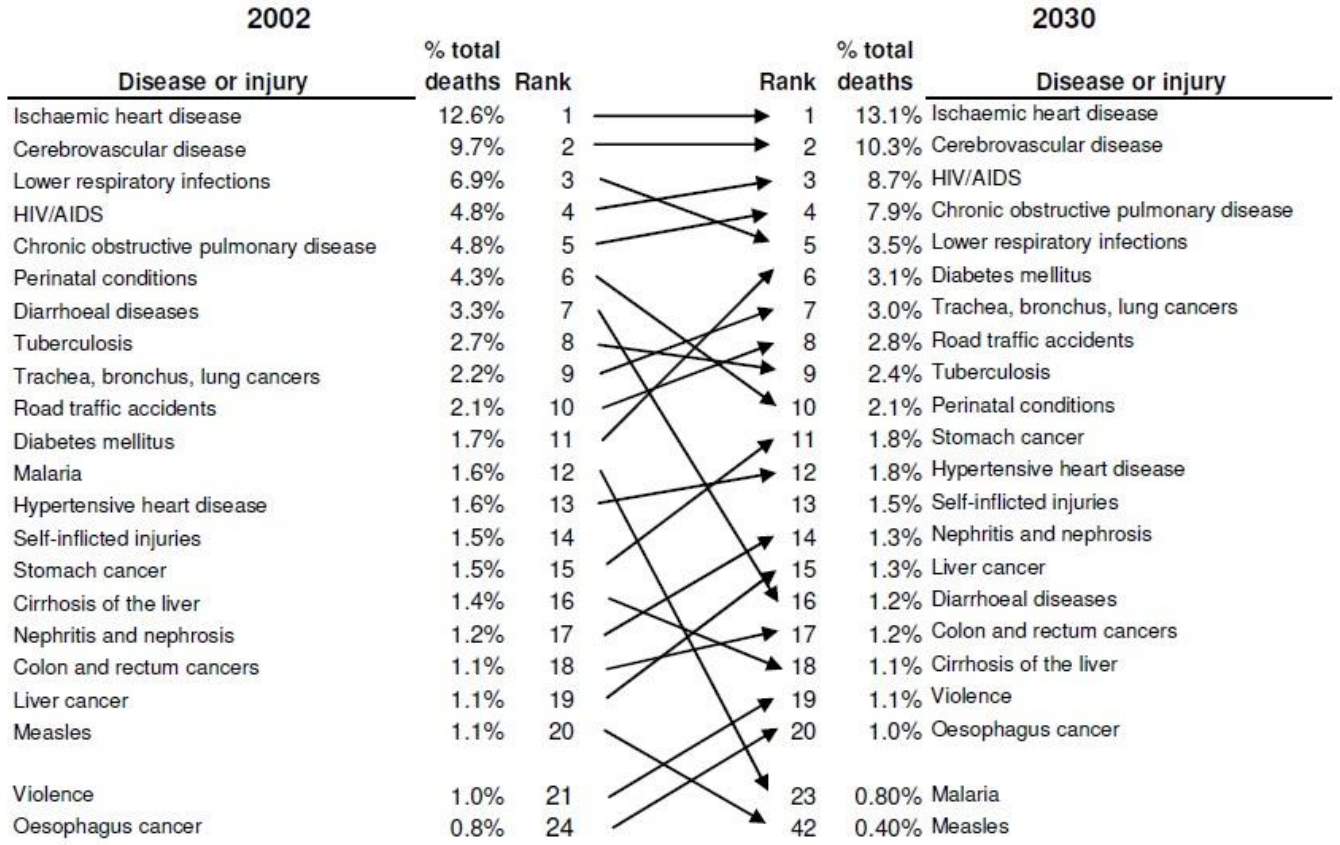
(Mega) trends in stroke epidemiology

- Stroke continuous to represent a major global public health treat due to the high mortality and loss of disability-adjusted life years.
- The development have been positive in the developed countries during the last decades with a substantially lowering of the mortality and a stabilized or even declining overall incidence of stroke aging populations.

Leading Global Causes of Death, 2002 and 2030



2002						2030
Disease or injury	% total deaths	Rank		Rank	% total deaths	Disease or injury
Ischaemic heart disease	12.6%	1		1	13.1%	Ischaemic heart disease
Cerebrovascular disease	9.7%	2		2	10.3%	Cerebrovascular disease
Lower respiratory infections	6.9%	3		3	8.7%	HIV/AIDS
HIV/AIDS	4.8%	4		4	7.9%	Chronic obstructive pulmonary disease
Chronic obstructive pulmonary disease	4.8%	5		5	3.5%	Lower respiratory infections
Perinatal conditions	4.3%	6		6	3.1%	Diabetes mellitus
Diarrhoeal diseases	3.3%	7		7	3.0%	Trachea, bronchus, lung cancers
Tuberculosis	2.7%	8		8	2.8%	Road traffic accidents
Trachea, bronchus, lung cancers	2.2%	9		9	2.4%	Tuberculosis
Road traffic accidents	2.1%	10		10	2.1%	Perinatal conditions
Diabetes mellitus	1.7%	11		11	1.8%	Stomach cancer
Malaria	1.6%	12		12	1.8%	Hypertensive heart disease
Hypertensive heart disease	1.6%	13		13	1.5%	Self-inflicted injuries
Self-inflicted injuries	1.5%	14		14	1.3%	Nephritis and nephrosis
Stomach cancer	1.5%	15		15	1.3%	Liver cancer
Cirrhosis of the liver	1.4%	16		16	1.2%	Diarrhoeal diseases
Nephritis and nephrosis	1.2%	17		17	1.2%	Colon and rectum cancers
Colon and rectum cancers	1.1%	18		18	1.1%	Cirrhosis of the liver
Liver cancer	1.1%	19		19	1.1%	Violence
Measles	1.1%	20		20	1.0%	Oesophagus cancer
Violence	1.0%	21		23	0.80%	Malaria
Oesophagus cancer	0.8%	24		42	0.40%	Measles

PLoS Med 2006;3:e442

Time trend in incidence of stroke in the young in Denmark

ORIGINAL RESEARCH

American Heart Association | American Stroke Association.

Increasing Incidence of Hospitalization for Stroke and Transient Ischemic Attack in Young Adults: A Registry-Based Study

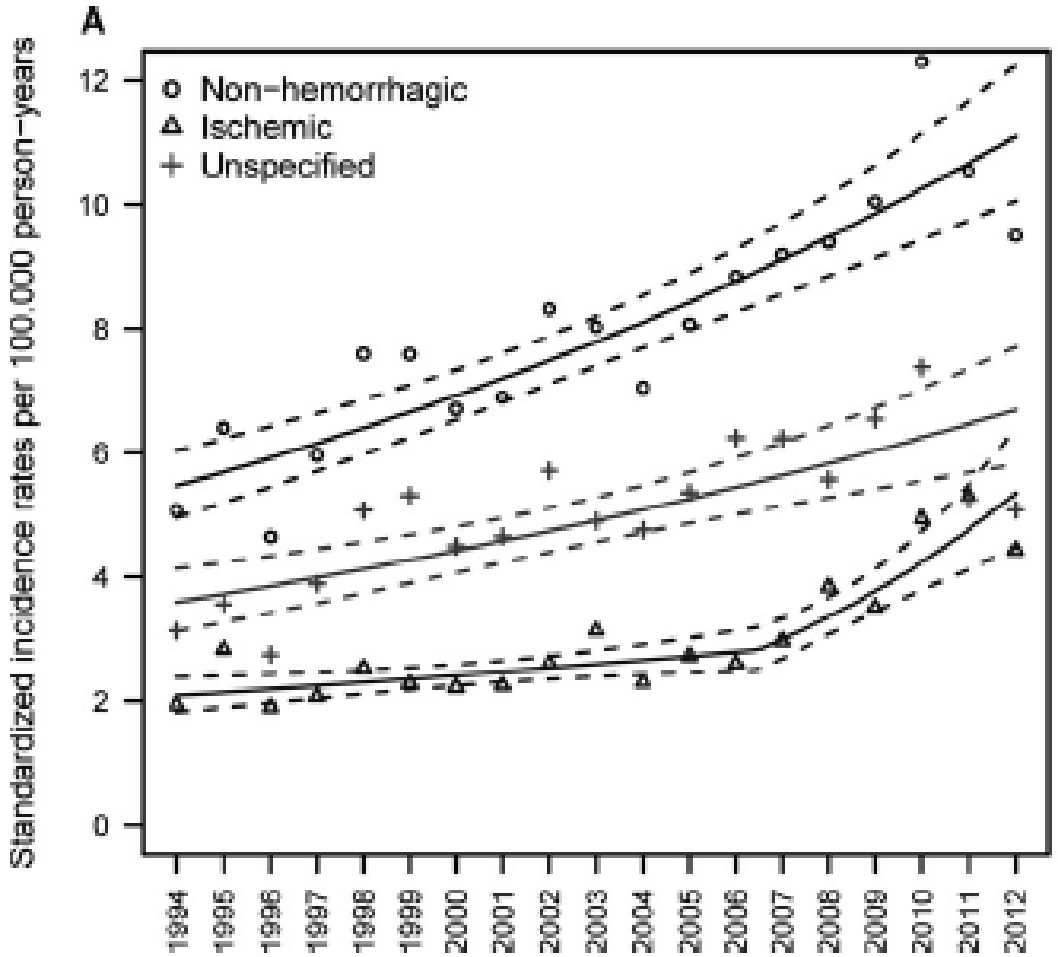
Maiken Tibæk, MD; Christian Dehlendorff, PhD, MS; Henrik S. Jørgensen, DMSc, MD; Hysse B. Forchhammer, PhD, NP; Søren P. Johnsen, PhD, MD; Lars P. Kammersgaard, DMSc, MD

Background—Studies have reported increasing incidence of ischemic stroke in adults younger than 50 to 55 years. Information on temporal trends of other stroke subtypes and transient ischemic attack (TIA) is sparse. The aim of this study was to investigate temporal trends of the incidence of hospitalizations for TIA and stroke including sex- and subtype-specific trends in young adults aged 15 to 30 years.

Methods and Results—From the Danish National Patient Register, we identified all cases of first-ever stroke and TIA (age 15–30 years) in Denmark, who were hospitalized during the study period of 1994 to 2012. Incidence rates and estimated annual percentage changes (EAPCs) were estimated by using Poisson regression. During the study period, 4156 cases of first-ever hospitalization for stroke/TIA were identified. The age-standardized incidence rates of hospitalizations for stroke increased significantly (EAPC 1.83% [95% CI 1.11–2.55%]) from 11.97/100 000 person-years (PY) in 1994 to 16.77/100 000 PY in 2012. TIA hospitalizations increased from 1.93/100 000 PY in 1994 to 5.81/100 000 PY in 2012 and after 2006 more markedly in men than in women (EAPC 16.61% [95% CI 10.45–23.12%]). The incidence of hospitalizations for ischemic stroke was markedly lower among men, but increased significantly from 2006 (EAPC 14.60% [95% CI 6.22–23.63%]). The incidences of hospitalizations for intracerebral hemorrhage and subarachnoid hemorrhage remained stable during the study period.

Conclusions—The incidence rates of first-time hospitalizations for ischemic stroke and TIA in young Danish adults have increased substantially since the mid 1990s. The increase was particularly prominent in the most recent years. **(*J Am Heart Assoc.* 2016;5: e003158 doi: 10.1161/JAHA.115.003158)**

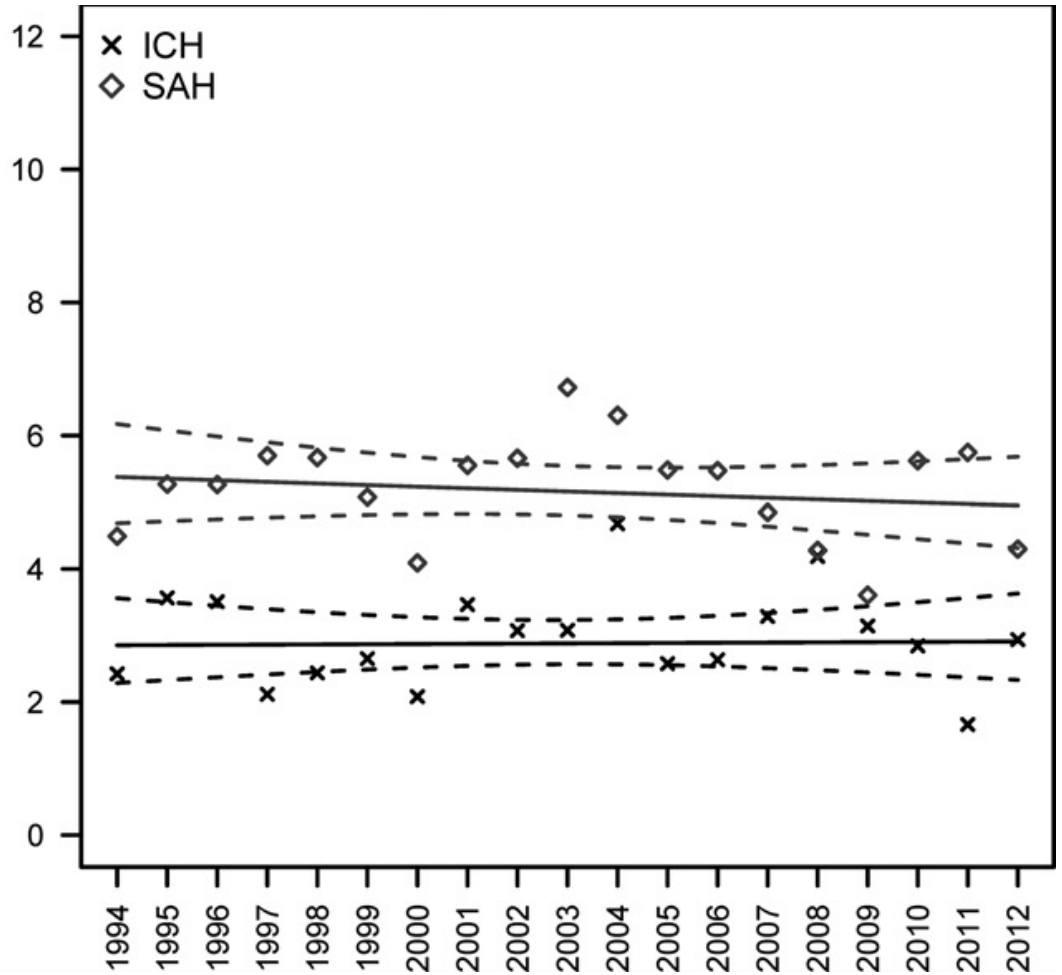
Time trend in incidence of stroke in the young in Denmark



Ischemic stroke:
1994-2005: EAPC 2.56%
2006-2012: EAPC 11.80%

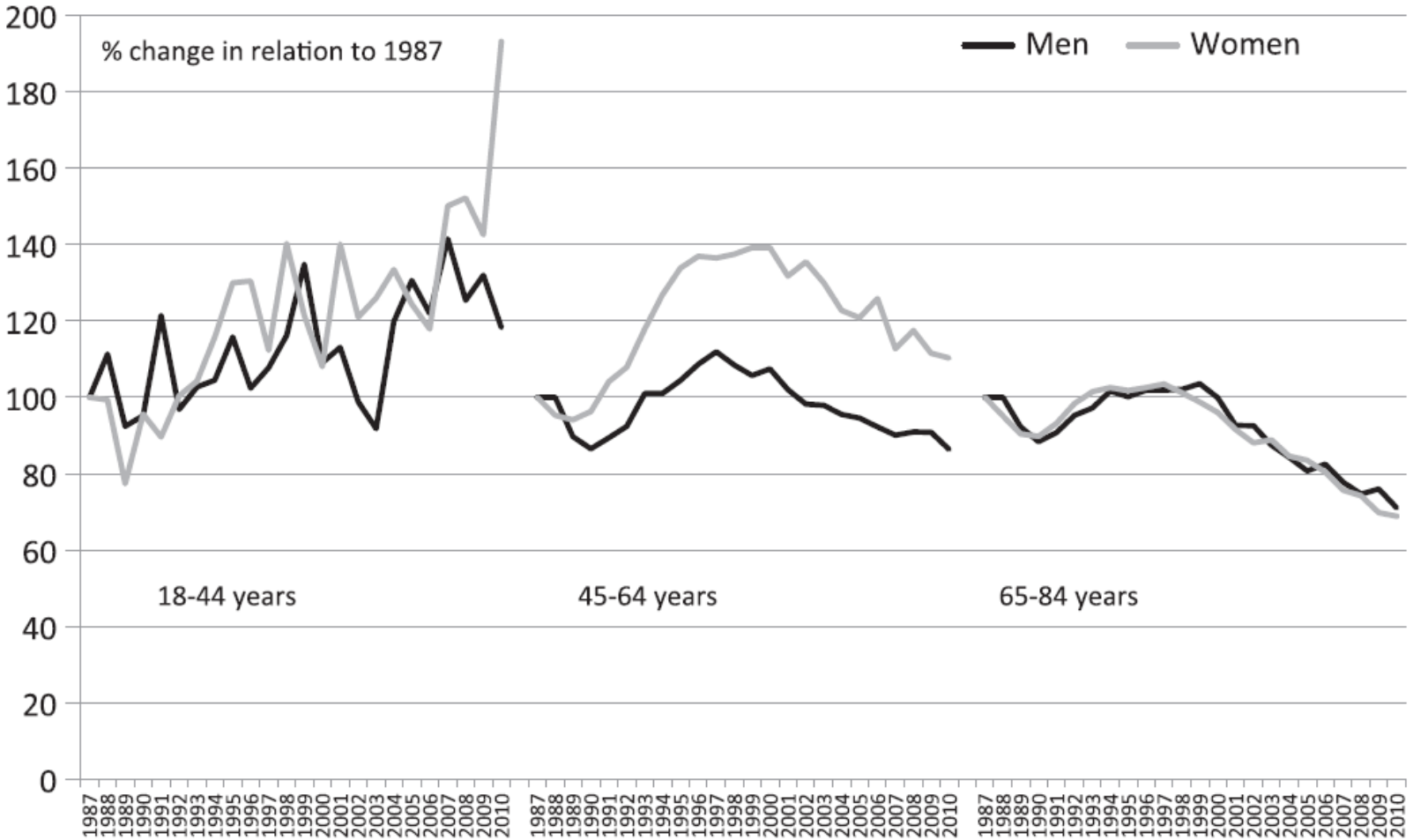
Tibæk M et al. J Am Heart Assoc 2016;5 pii: e003158

Time trend in incidence of stroke in the young in Denmark



Tibæk M et al. J Am Heart Assoc 2016;5 pii: e003158

Trends in incidence of ischemic stroke in Sweden



Rosengren A et al. Stroke. 2013;44:2388-93

Trends in risk profile of ischemic stroke patients in Sweden

	1987–1992	1993–1998	1999–2004	2005–2010	*P* Value	Total
Number, n (%)	94 681	108 345	100 318	87 737		391 081
Mean age, y (SD)	73.0 (9.2)	72.8 (9.6)	72.5 (10.0)	71.7 (10.5)	0.0001	72.5 (9.8)
Women, n (%)	44 335 (46.8)	51 110 (47.2)	47 100 (46.9)	39 636 (45.2)	0.0001	182 181 (46.6)
Diabetes mellitus, n (%)	16 040 (16.9)	19 070 (17.6)	17 608 (17.6)	16 651 (19.0)	0.0001	69 369 (17.7)
Hypertension, n (%)	18 074 (19.1)	27 870 (25.7)	32 721 (32.6)	44 513 (50.7)	0.0001	123 178 (31.5)
Prior AMI, n (%)	12 120 (12.8)	14 483 (13.4)	13 403 (13.4)	11 495 (13.1)	0.0001	51 501 (13.2)
Any IHD, n (%)	21 612 (22.8)	26 352 (24.3)	24 138 (24.1)	20 539 (23.4)	0.0001	92 641 (23.7)
Atrial fibrillation, n (%)	14 682 (15.5)	20 839 (19.2)	20 730 (20.7)	19 191 (21.9)	0.0001	75 442 (19.3)
Malignancy, n (%)	8423 (8.9)	11 231 (10.4)	11 039 (11.0)	10 853 (12.4)	0.0001	41 546 (10.6)

Rosengren A et al. Stroke. 2013;44:2388-93

Incidence of ischemic stroke in France

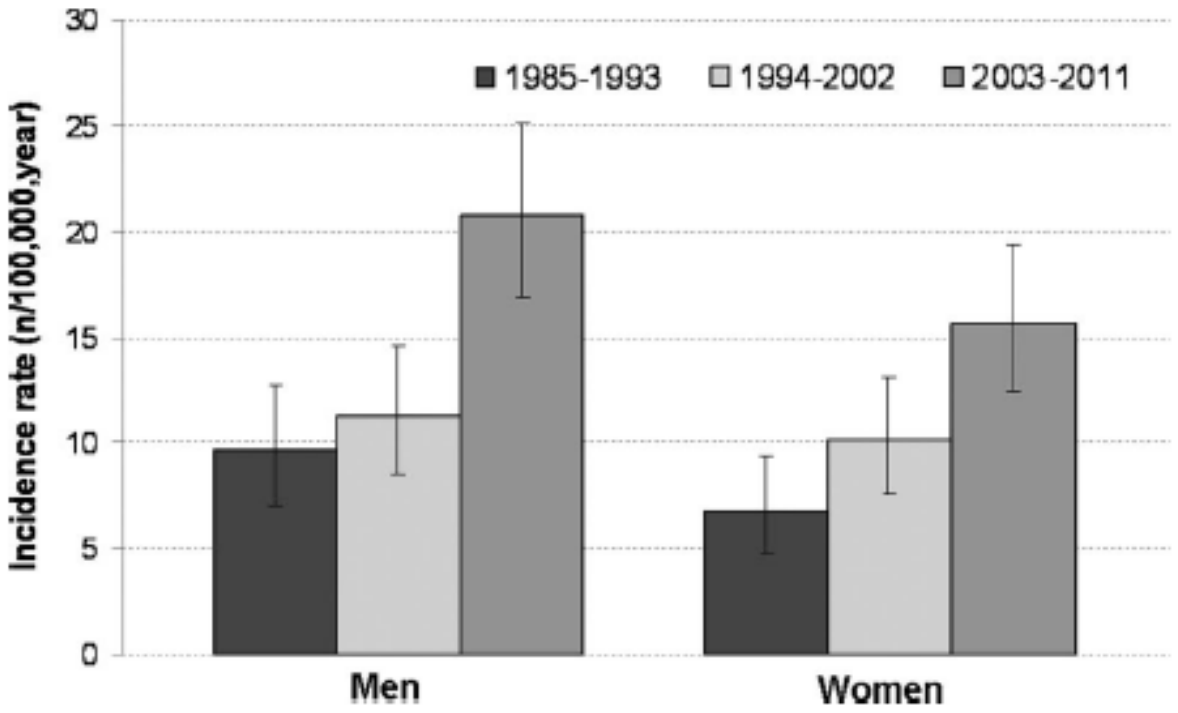


Figure 1 Trends in the incidence of ischaemic stroke in individuals <55 years old stratified by sex. Incidence rates expressed as n/100 000/ year. Bars represent 95% CI.

Béjot Y et al. J Neurol Neurosurg Psychiatry 2014;85:509–13.

Trends in stroke mortality and incidence in the Netherlands

Age Group		1997	1998	1999	2000	2001	2002	2003	2004	2005	Change* 1997–2005	Trend†
35–64	Mortality rate per 100 000	9.9	9.0	8.7	9.3	9.0	8.8	7.5	7.3	6.2	−0.37	0.01
	30-day case fatality (%)	7.4	7.0	5.9	6.6	7.5	6.3	5.4	4.3	4.3	−0.42	<0.05
	1-year mortality (%)	6.5	5.1	5.1	5.6	6.3	5.3	4.8	4.6	4.2	−0.35	<0.05
	Incidence per 100 000	65	67	67	64	65	70	73	74	78	0.20	0.01
65–74	Mortality rate per 100 000	129	134	123	120	111	120	102	93.4	81.9	−0.37	<0.01
	30-day case fatality (%)	12.5	12.3	9.7	10.9	11.0	10.4	8.0	7.8	6.9	−0.45	<0.01
	1-year mortality (%)	13.0	14.2	14.1	13.3	11.4	12.6	11.5	10.1	9.7	−0.25	0.01
	Incidence per 100 000	410	425	416	395	409	428	416	429	401	−0.02	n.s.
75–84	Mortality rate per 100 000	551	545	544	528	506	500	451	398	374	−0.32	<0.01
	30-day case fatality (%)	19.8	19.0	19.0	19.2	17.9	17.2	16.2	14.7	11.9	−0.40	<0.01
	1-year mortality (%)	22.9	24.1	22.2	22.0	22.3	20.3	19.8	19.4	17.5	−0.24	<0.01
	Incidence per 100 000	917	958	920	898	910	941	940	956	936	0.02	n.s.
85–94	Mortality rate per 100 000	1503	1559	1622	1487	1436	1560	1360	1298	1211	−0.19	<0.01
	30-day case fatality (%)	34.3	31.6	33.6	31.9	29.7	29.0	24.1	28.1	24.1	−0.28	<0.01
	1-year mortality (%)	28.6	32.0	27.1	26.0	29.5	26.2	29.0	27.4	26.8	−0.06	n.s
	Incidence per 100 000	1659	1788	1764	1637	1763	1785	1845	1797	1831	0.10	n.s

Mortality rate per 100 000, 30-day case fatality, 1-year mortality (31–365 days) after admission for ischemic stroke and incidence per 100 000 by age in the Netherlands, 1997–2005 for men aged >35 years.

* (last year−first year)/first year; † Mann–Kendall trend test; n.s. indicates nonsignificant.

Vaartjes I et al. Stroke. 2013;44:591-7

Mechanisms of increased ischemic stroke incidence

- Changes in risk factor profile:
  - Increasing burden of obesity
- Increased diagnostic awareness/possibilities
  - Increased use of brain imaging, in particular MRI
  - Increased awareness of coding of hospital diagnoses due to financial incentives

Studies on stroke etiology in young patients

Reference	Country	LAA	CE	SVD	ODE	UE
Cerrato et al[20]	Italy	16	24	17	19	24
Nedeltchev et al[2]	Switzerland	4	30	9	24	33
Rasura et al[15]	Italy	12	34	3	28	24
Varona et al[3]	Spain	20	18	5	22	36
Jovanovic et al[21]	Serbia	8	20	22	24	26
Putaala et al[7]	Finland	8	20	14	26	33
Spengos and Vemmos[22]	Greece	9	13	17	27	34
Smajlovic et al[6]	Bosnia and Herzegovina	15	10	26	9	40
Tancredi et al[23]	Italy	9	19	16	29	27
Yesilot Barlas et al[24]	Europe	9	17	12	22	40

Note: All numbers are percentages.

Abbreviations: LAA, large artery atherosclerosis; CE, cardiac embolism; SVD, small vessel disease; ODE, other determined etiology; UE, undetermined etiology.

Smajlović D.Vascular Health and Risk Management 2015:11 157–164

(Uncommon) causes of stroke in the young

Nonatherosclerotic angiopathies	Cervicocephalic arterial dissection
	Cerebral amyloid angiopathy
	Moyamoya disease
	Fibromuscular dysplasia
	Reversible cerebral vasoconstriction syndrome
	Susac's syndrome
	Sneddon's syndrome
	Migraine-induced stroke
Hematologic conditions	Hypercoagulable state due to deficiencies of protein S, protein C, or antithrombin; factor V Leiden mutation, prothrombin gene G20210A mutation
	Acquired hypercoagulable state (eg, cancer, pregnancy, hormonal contraceptive use, exposure to hormonal treatments such as anabolic steroids and erythropoietin, nephrotic syndrome)
	Antiphospholipid syndrome
	Hyperhomocysteinemia
	Sickle cell disease
	Myeloproliferative disorders (eg, leukemia, lymphoma)
Genetic	Fabry disease
	CADASIL
	MELAS
	Marfan syndrome
	Neurofibromatosis
	Sturge-Weber disease
Inflammatory and infectious	Vasculitis (primary angiitis of the CNS, Sjögren syndrome, Wegener's granulomatosis)
	Temporal arteritis
	Takayasu disease
	Behçet's syndrome
	Neurosarcoidosis
	Neurocysticercosis
	HIV
	Varicella zoster virus
	Neurosyphilis
	Tuberculous meningitis

Smajlović D.Vascular Health and Risk Management 2015:11 157–64

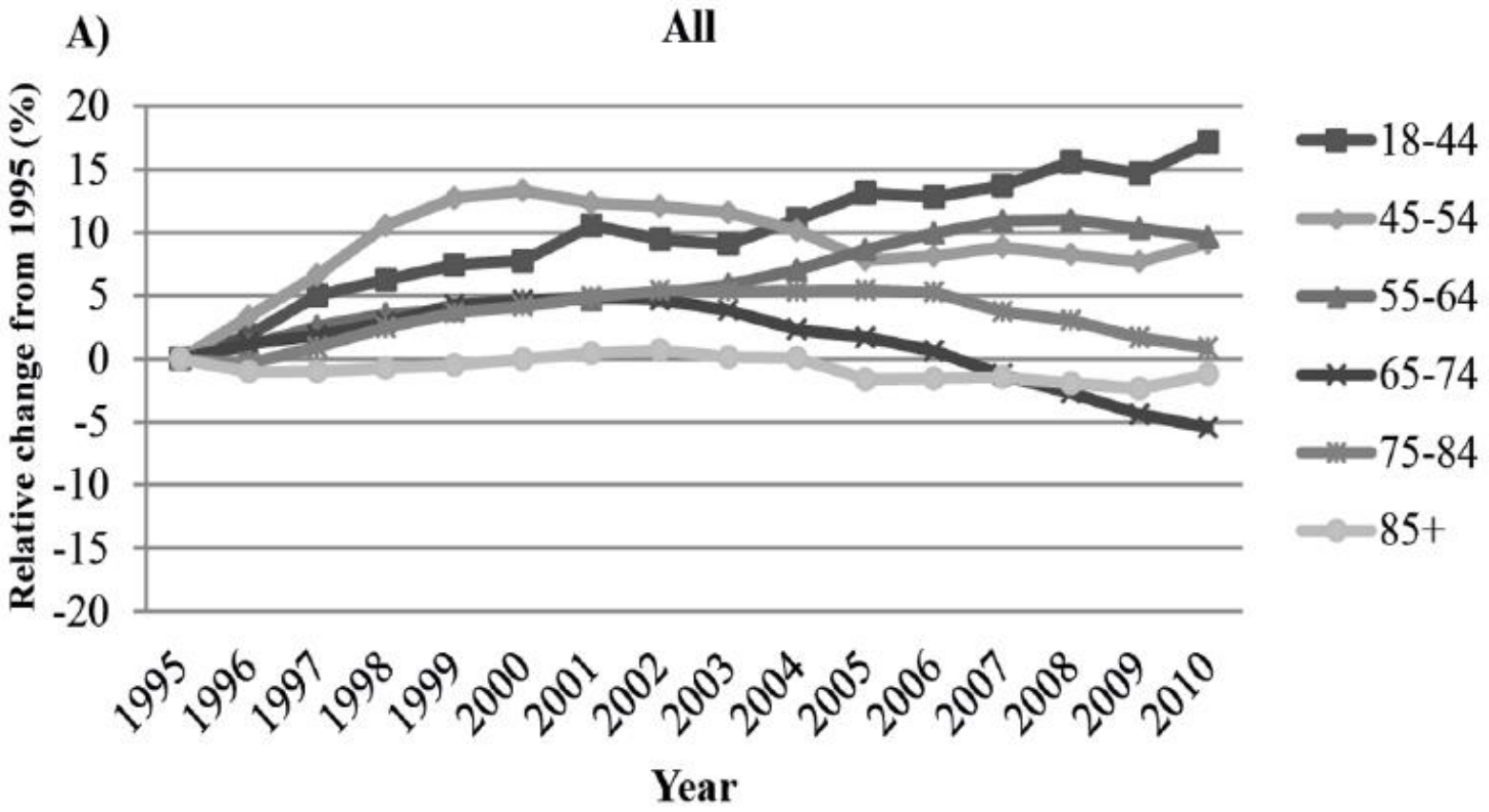
Rates of CT and MRI obtained in first-ever stroke patients

Overall	1993/1994	1999	2005
No.	1,907	1,995	1,883
CT done	1,775 (88.4)	1,932 (89.3)	1,797 (86.9)
MRI done	351 (18.7)	563 (27.6)	1,115 (56.7)
MRI by age, y			
20–44	33 (37.5)	45 (40.5)	98 (70.0)
45–54	42 (31.0)	78 (46.7)	170 (63.4)
55–64	77 (27.8)	101 (38.7)	220 (69.4)
65–74	103 (18.0)	159 (27.3)	265 (63.0)
75–84	84 (16.8)	140 (24.3)	255 (51.7)
85+	12 (3.8)	40 (13.5)	107 (33.2)

[a] p Value for trends all <0.0001 except for CT where p for trend = 0.71. Using logistic change over time by age interaction 0.13. Difference overall between ages, $p < 0.0001$, and change over time, $p < 0.0001$.

Kissela BM et al. Neurology. 2012;79:1781-7

Annual change in prevalence of ischemic stroke in Sweden



Giang KW et al. PLoS One. 2017;12:e0179658

Conclusion

- The incidence of ischemic stroke and TIA appears to be increasing among the young.
- The background is not clear, but the development is disturbing and more insight is essential if effective preventive measures are to be taken.