The incidence of stroke and transient ischaemic attacks is falling: a report from the Belgian sentinel stations

Frank Buntinx, Dirk Devroey and Viviane Van Casteren

SUMMARY

Background: *Increasing as well as decreasing trends in stroke incidence have been described.*

Aim: *To examine time trends associated with the incidence of stroke and transient ischaemic attacks (TIAs) within an ongoing registration network.*

Design of study: *Analysis of data from a network of sentinel practices.*

Setting: *Sentinel practice population (approximately 1.4% of the total Belgian population.*

Method: *Attack incidence rates of both stroke and TIA were studied at four one-year registration periods between 1984 and 1999.*

Results: *The number of events identified as stroke was 1097 (513 in males and 584 in females). The percentage of first-ever stroke was 69%, 64%, and 70% in 1989, 1998, and 1999 respectively. The number of events identified as TIAs was 382 (165 in males and 217 in females). The percentage of first-ever TIA was 65%, 69%, and 75% in 1989, 1998, and 1999 respectively. Yearly age-standardised attack rates of stroke significantly decreased during the registration period, from 2.86 per 1000 in 1984, to 1.62 per 1000 in 1999 (χ^2 for trend, P = 0.04) in males and from 2.97 per 1000 to 1.96 per 1000 (P = 0.007) for females. The decrease was restricted to subjects aged over 60 years. For TIA, a significant decrease (P = 0.014) was identified in females, but not in males (P = 0.61). Crude attack rates of stroke also significantly decreased, with an overall decrease between 1984 and 1999 of 37% in males and 26% in females. No such trend was found for TIA (P = 0.63 for males and P = 0.35 for females).*

Conclusion: *Both crude and age-standardised attack rates of stroke show a clear and significant decrease between 1984 and 1999. For TIA, a weaker trend was identified.*

Keywords: *cerebrovascular accident; incidence; morbidity.*

F Buntinx, MD, PhD, professor, Department of General Practice, Catholic University of Leuven, Belgium; D Devroey, MD, epidemiologist; and V Van Casteren, MD, epidemiologist, Unit of Epidemiology, Scientific Institute of Public Health, Brussels, Belgium.

Address for correspondence

Professor Frank Buntinx, ACHG-KU Leuven, Kapucijnenvoer 33 – Blok J, 3000 Leuven, Belgium. E-mail: Frank.Buntinx@med.kuleuven.ac.be

Submitted: 26 November 2001; Editor's response: 18 February 2002; final acceptance: 22 April 2002.

Introduction

ALL over the world, stroke is a disease with a high impact on patients. In Europe, one-year case-fatality rates are around 35%[1] and stroke is ranked between first and fourth among the nations' main causes of death.[2]

Most survivors are confronted with the need for long and difficult rehabilitation periods, have significant functional deficits, and an increased risk of institutionalisation.[3] National incidence rates in European population surveys range between one and 5 per 1000 inhabitants and are almost twice as high in eastern Europe compared with western Europe. Time trends in incidence rates of stroke and transient ischaemic attack (TIA) have rarely been studied. Both decreases[4-6] and increases[7] have been identified. In some cases, different trends were identified according to sex[8-9] or age.[4] Decreasing age-specific incidences have been described in association with constant crude incidences as a result of increasing mean age.[8] Even less information is available with respect to trends in TIA incidence.

Against this background we studied the age and sex-specific incidence, as well as the crude incidence, of both stroke and TIA at four one-year registration periods between 1984 and 1999 in an ongoing general practice-based network of sentinel practices in Belgium.

Method

Definition of stroke

In agreement with the WHO definition, stroke was defined as a sudden onset of clinical signs of focal (or global) disturbance of cerebral function, which lasts more than 24 hours.[10] Cases were excluded if they were related to a non-vascular cause, e.g. trauma, malignancy or intoxication. Similar cases that recovered within 24 hours were coded as TIAs.

According to these definitions the study is based on clinical diagnoses, which have nevertheless been shown to be reliable,[11,12] although less so for TIA.[13]

Study population

The recordings for this study were made by the Belgian network of general practitioners (GPs). This network has been functioning since 1979 with similar methods and serves as a reliable source on the surveillance of morbidity in Belgium.[14,15] Such a surveillance system has already been tested and proved effective[16] and is currently applied in a number of countries.[17] It has been adequately proven that the Belgian sentinel general practices form an important source of data over a wide range of both infectious and non-

HOW THIS FITS IN

What do we know?

Both increasing and decreasing time trends in incidence rates of stroke have been reported. Information on TIA trends is scarce.

What does this paper add?

Both crude and age-standardised attack rates of stroke decreased between 1984 and 1999. For TIA the picture is less clear. This combination suggests an effect of secondary prevention measures, maybe in association with an effect of primary prevention measures and lifestyle changes.

infectious diseases. The network of sentinel general practices consists of physicians who, with respect to age and sex, are representative of GPs in Belgium. The general practices are distributed evenly over the territory by means of a cluster analysis based on epidemiological criteria.[14-15] The yearly sentinel population was estimated to be slightly over 1.4% of the total Belgian population.

Case ascertainment

The registration covered the years 1984, 1989, 1998, and 1999 respectively. The choice of these periods was made for pragmatic reasons only. Results covering each of the first three registration periods have been published previously.[6,18,19] GPs in the sentinel network registered all cases that complied with the definition of stroke or TIA and sent the forms to the central database, where the data were coded and entered. One month after the initial recording on the weekly registration form, the GP was sent an additional in-depth questionnaire. Questions on this form were intended to confirm or deny the initial diagnosis and to provide additional or more detailed information.

Analysis

Attack incidence rates were calculated per 1000 person years, specific for sex and for ten-year age categories. Age groups of patients aged up to 50 years and patients aged over 89 years were grouped. Crude attack rates for the study population were stratified for sex.

Sex-specific and age-stratified attack rates were calculated by direct standardisation, using the 1999 study population as reference. For all rates, 95% confidence intervals (95% CI) were calculated. The presence of a linear trend over years was tested using χ^2 test for trend in the case of non-standardised measures, and by linear regression analysis in the case of standardised measures. Crude and standardised attack rates were calculated with their 95% CIs using CIA software, and SPSS v10 was used for regression analysis.

Results

The total number of person years studied exceeded 500 000 (253 107 person years in males and 265 344 in females). During the registration period, 1097 events were classified as stroke (513 in males and 584 in females). The percentage of first-ever strokes was 69%, 64%, and 70% in the years 1989, 1998, and 1999 respectively. For 1984 this percentage is no longer retrievable.

As TIA was not registered during the first year of registration, the study population for TIA consists of 197 226 person years in males and 205 944 in females, during which 382 events were classified as TIA (165 in males and 217 in females). The percentage of first-ever TIA was 65%, 69%, and 75% in 1989, 1998, and 1999 respectively. For a total of 11 cases (over all four registrations) the age of the patient was missing. These patients were assigned to the median age group of the year's cases.

Careful examination of the ten-year age groups reveals that the group aged between 60 and 69 years follows the trend of the older age group for stroke and the trend of the younger age group for TIA (Table 1).

Age-standardised attack rates of stroke significantly decreased during the registration period, from 2.86 per 1000 in 1984, to 1.62 per 1000 in 1999 (χ^2 for trend, $P = 0.04$) in males and from 2.97 per 1000 to 1.96 per 1000 ($P = 0.007$) for females (Figure 1). For TIA, a significant decrease ($P = 0.014$) was identified in females. However, this could not be found in males ($P = 0.61$).

Differences in the evolution of the incidence of stroke attacks occur according to age (Table 2). Above the age of 70 years, stroke incidence is progressively and significantly decreasing in both males and females. For TIA the same trend was present, although it is not statistically significant in our study. However, in the under-70 years age group, no such trend could be found. TIA incidence in females even had a (non-significant) tendency to increase.

Discussion

Age-standardised attack rates of stroke show a clear and significant average decrease between the years 1984 and 1999. The decrease was found in both males and females, but seems to be restricted to subjects aged over 60 years. In males the overall decrease in crude rates is one-third, in females one-quarter. This corresponds to a yearly decrease of 2.5% and 1.7% respectively. Elsewhere, decreases as well as increases have been reported for stroke incidence.[4-9] In some other countries, such as Sweden and New Zealand, no changes in stroke incidence were observed.[20,21]

For TIA, on the other hand, the trend to decrease is much smaller and non-significant. This may either result from an absence of such a trend or from the shorter time period that was studied (1989 to 1999), with three registration periods instead of four.

The co-occurrence of an important decrease over time of stroke incidence and only a limited decrease in TIA incidence suggests the influence of secondary prevention measures, maybe in addition to an effect of measures of primary prevention and lifestyle changes.

Analysis of trends in stroke attack incidence rates can provide data on the mechanisms responsible for stroke and the possible influence of changes in prevention and diagnostic features. In several countries, registrations in hospitals and in well-defined populations have been set up. In Belgium, the cases of stroke attacks in a network of sentinel general

*Table 1. Crude and age-standardised incidence of stroke and transient ischaemic attacks (TIAs) (*n *= number of cases).*

	1984			1989			1998			1999		
	Population	*n*	Incidence (95% CI)	Population	*n*	Incidence (95% CI)	Population	*n*	Incidence (95% CI)	Population	*n*	Incidence (95% CI)
Stroke												
Males												
Crude	55 881	144	2.86 (2.4–3.3)	62 228	128	2.27 (1.9–2.7)	67 652	132	1.96 (1.6–2.3)	67 346	109	1.62 (1.3–2.0)
Standardised			2.58 (2.2–3.0)			2.06 (1.7–2.4)			1.95 (1.7–2.3)			1.62 (1.3–2.0)
Females												
Crude	59 400	157	2.97 (2.5–3.4)	64 957	156	2.68 (2.3–3.1)	70 472	133	1.90 (1.6–2.2)	70 515	138	1.96 (1.7–2.3)
Standardised			2.64 (2.3–3.1)			2.40 (2.3–3.1)			1.89 (1.6–2.2)			1.96 (1.7–2.3)
TIA												
Males												
Crude				62 228	54	0.96 (0.7–1.2)	67 652	65	0.96 (0.7–1.2)	67 346	46	0.68 (0.5–0.9)
Standardised						0.87 (0.7–1.0)			0.96 (0.8–1.2)			0.68 (0.5–0.9)
Females												
Crude				64 957	75	1.28 (1.0–1.6)	70 472	70	1.04 (0.8–1.3)	70 515	72	1.02 (0.8–1.3)
Standardised						1.15 (0.9–1.5)			0.99 (0.8–1.3)			1.02 (0.8–1.3)

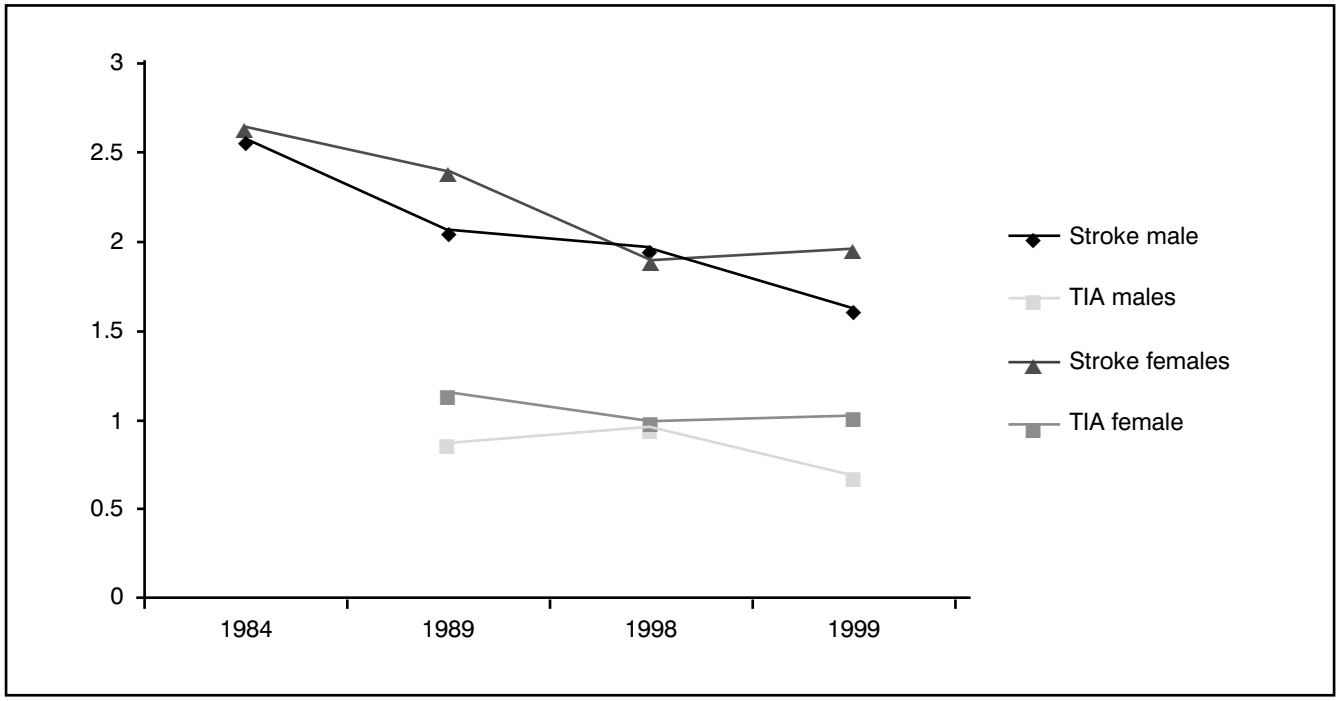

Figure 1. Age-standardised incidence of stroke and TIA.

practices were recorded. Our registration method, as well as the number of participating GPs, remained stable over the complete period of the registration. This should assure us that changing trends are probably not attributed to changes of data recording procedures.

Changes in diagnostic opportunities or diagnostic behaviour by clinicians have a tendency to influence incidence rates of diseases. It has been suggested that the increase in the 1980s coincided with the introduction of computed tomography (CT), which has given physicians the ability to detect less severe strokes. All incidence rates before the introduction of CT would therefore be underestimates.[29] After this period it is imagined that improved diagnostic and therapeutic abilities in hospitals resulted in a higher referral rate for patients who had had a stroke or TIA. However, as stroke and TIA are essentially clinical diagnoses, there is no reason to assume that this will substantially affect overall attack rates, which was confirmed by our results. The increasing use of CT since 1985 and magnetic resonance imaging since 1990 has apparently not influenced the incidence of stroke attacks in Belgium.

Comparing our data with other countries' is difficult. Adjustment for age and sex is often done in different ways in different countries. As crude incidences differ considerably in age and sex categories, only standardised incidences can be compared. The different environment of the registration (general population, hospital or GP) and age group limitations in some studies also need to be considered.

Table 2. Age-specific incidence rates of cerebrovascular accident (CVA) (stroke) and transient ischaemic attacks.

	P-value	1984	1989	1998	1999
Males aged <70 years					
CVA	0.42	0.80 (0.55–1.04)	0.87 (0.63–1.11)	0.91 (0.67–1.14)	0.57 (0.38–0.76)
TIA	0.85	–	0.30 (0.16–0.44)	0.37 (0.22–0.52)	0.21 (0.10–0.33)
Females aged <70 years					
CVA	0.16	0.60 (0.39–0.81)	0.46 (0.28–0.63)	0.51 (0.33–0.69)	0.34 (0.20–0.49)
TIA	0.42	–	0.18 (0.07–0.28)	0.20 (0.09–0.31)	0.26 (0.13–0.39)
Males aged ≥70 years					
CVA	<0.0001	23.60 (19.1–28.1)	17.2 (13.4–21.0)	13.1 (10.2–16.1)	12.8 (9.9–15.7)
TIA	0.22	–	8.15 (5.5–10.8)	7.26 (5.1–9.5)	5.7 (3.8–7.7)
Females aged ≥70 years					
CVA	<0.0001	16.9 (13.9–19.8)	16.6 (13.8–19.4)	10.8 (8.7–12.9)	12.3 (10.1–14.5)
TIA	0.05	–	8.3 (6.3–10.3)	6.5 (4.8–8.1)	5.9 (4.3–7.4)

Basically, risk factors for stroke and TIA are the same. Age and sex are the most important but are not modifiable. Modifiable risk factors are: hypertension, atrial fibrillation, smoking, diabetes, alcohol misuse, and hyperlipidaemia. The decreased incidence in stroke attacks in Belgium could partially be explained by a decrease in the proportion of smokers in the population, by improved treatment of hypertension, and by the abundant use of statins to lower lipid levels, especially after a previous cardiovascular event.[22-24] Epidemiological studies have shown a clear and linear relationship between the diastolic blood pressure and the incidence of primary stroke.[25-27] The relative risk reduction by improved diastolic blood pressure control is less extreme in old age than in middle age.[28] Epidemiological studies in the United States, Japan, Germany, and Finland have shown declining incidence rates for stroke between the 1950s and the 1970s in all age and sex groups[29-33] for TIA which coincided with the introduction of effective antihypertensive drugs. However, while the control of hypertension continued to improve during the 1970s and 1980s, the rates stabilised in the 1970s and increased again from the second half of the 1980s onwards, especially in the older age groups.[29-33] Although serum cholesterol is a strong risk factor for coronary artery disease, its predictive power for stroke is weak and controversial.[28,34] Lipid-lowering drugs can only reduce the incidence of stroke after myocardial infarction.[24]

As well as the risk factor reduction, the use of aspirin as secondary prevention after TIA should be considered. For 1000 patients treated for three years and compared with controls, around 20 recurrent strokes were prevented by the use of low doses of aspirin.[35] Additional unpublished data from our study indicate that in 1999 four out of the five patients with TIA were prescribed aspirin on a long-term basis. Although this cannot be considered sufficient proof, we assume that the decrease over time in stroke attack rates in this study may largely result from the use of aspirin after a previous CVA or TIA. This is possibly associated with continuously improving antihypertensive therapy and the increased treatment.

References

1. Wolfe CD, Giroud M, Kolominsky-Rabas P, *et al*. Variations in stroke incidence and survival in three areas of Europe. European Registries of Stroke (EROS) Collaboration. *Stroke* 2000; **31:** 2074-2079.
2. Brainin M, Bornstein N, Boysen G, Demarin V. Acute neurological stroke care in Europe: results of the European Stroke Care Inventory. *Eur J Neurol* 2000; **7:** 5-10.
3. Schmidt R, Breteler MM, Inzitari D, *et al*. Prognosis with stroke in Europe: a collaborative study of population-based cohorts. Neurologic Diseases in the Elderly Research Group. *Neurology* 2000; **54:** S34-S37.
4. Jamrozik K, Broadhurst RJ, Lai N, *et al*. Trends in the incidence, severity, and short-term outcome of stroke in Perth, Western Australia. *Stroke* 1999; **30:** 2105-2111.
5. Morikawa Y, Nakagawa H, Naruse Y, *et al*. Trends in stroke incidence and acute case fatality in a Japanese rural area: the Oyabe study. *Stroke* 2000; **31:** 1583-1587.
6. Buntinx F, Van Casteren V, Wens J, *et al*. Cerebrovasculaire incidenten. Een registratie van het peilpraktijkennetwerk. [Cererbrovascular accidents: a registration of the sentinel network.] *Huisarts Nu* 1997; **26:** 28-35.
7. Johansson B, Norrving B, Lindgren A. Increased stroke incidence in Lund-Orup, Sweden, between 1983 to 1985 and 1993 to 1995. *Stroke* 2000; **31:** 481-486.
8. Jorgensen HS, Plesner AM, Hubbe P, Larsen K. Marked increase of stroke incidence in men between 1972 and 1990 in Frederiksberg, Denmark. *Stroke* 1992; **23:** 1701-1704.
9. Stegmayr B, Asplund K, Wester PO. Trends in incidence, case-fatality rate, and severity of stroke in northern Sweden, 1985-1991. *Stroke* 1994; **25:** 1738-1745.
10. WHO MONICA Project Principal Investigators. The World Health Organization MONICA Project (monitoring trends and determinants in cardiovascular disease): a major international collaboration. *J Clin Epidemiol* 1988; **41:** 105-114.
11. Sandercock P, Molyneux A, Warlow C. Value of computed tomography in patients with stroke: Oxfordshire Community Stroke Project. *BMJ* 1985; **290:** 193-197.
12. Dewey HM, Donnan GA, Freeman EJ, *et al*. Interrater reliability of the National Institutes of Health Stroke Scale: rating by neurologists and nurses in a community-based stroke incidence study. *Cerebrovasc Dis* 1999; **9:** 323-327.
13. Landi G. Clinical diagnosis of transient ischaemic attacks. *Lancet* 1992; **339:** 402-405.
14. Stroobant A, Van Casteren V, Thiers G. *Surveillance systems from primary-care data: surveillance through a network of sentinel general practitioners*. In: Eylenbosch WJ, Noah D (eds). *Surveillance in Health and Disease*. Oxford: Oxford University Press, 1988; 62-74.
15. Lobet M, Stroobant A, Mertens R, *et al*. Tool of validation of the network of sentinel general practitioners in the Belgian health care system. *Int J Epid* 1987; **16:** 612-618.
16. Grob PR. *A morbidity recording system for primary health care*. In: Leaverton PE (ed). *Environmental Epidemiology.* New York: Praeger Publishers, 1982; 131-139.
17. Van Casteren V. *Inventory of Sentinel Health Information Systems with general practitioners in the European Community. Situation up to March 1990*. Brussels: IHE, January 1991; 97.
18. Van Casteren V, Stroobant A, Lobet MP, Cornelis R. Cerebrovasculaire accidenten in België. Een epidemiologische studie. [Cerebrovascular accidents in Belgium: an epidemiological study.] *Tijdschr Geneesk* 1988; **44:** 1065-1070.
19. Buntinx F, Van Casteren V. Cerebrovasculare incidenten in België. Preliminaire resultaten uit een herhaalde registratie. [Cerebrovascular accidents in Belgium: preliminary results of a

repeated registration.] *Huisarts Nu* 2000; **29:** 30-32.
20. Bonita R, Broad JB, Beaglehole R. Changes in stroke incidence and case-fatality in Auckland, New Zealand, 1981-91. *Lancet* 1993; **342:** 1470-1473.
21. Harnsen P, Tsipogianni A, Wilhelmsen L. Stroke incidence rates were unchanged, while fatality cases declined, during 1971-1987 in Goteborg, Sweden. *Stroke* 1992; **23:** 1410-1415.
22. De Henauw S, De Bacquer D, De Smet P, *et al*. Trends and regional differences in coronary risk factors in two areas in Belgium: final results from the MONICA Ghent-Charleroi Study. *J Cardiovasc Risk* 2000; **7:** 347-357.
23. De Henauw S, De Bacquer D, Fonteyne W, *et al*. Trends in the prevalence, detection, treatment and control of arterial hypertension in the Belgian adult population. *J Hypertens* 1998; **16:** 277-284.
24. Plehn JF, Davis BR, Sacks FM. Reduction of stroke incidence after myocardial infarction with Pravastatin. The Cholesterol and Recurrent Events (CARE) Study. *Circulation* 1999; **99:** 216-223.
25. MacMahon S. Blood pressure, stroke and coronary heart disease, Part I: Effects of prolonged differences in blood pressure — Evidence from nine prospective observational studies corrected for the regression dilation bias. *Lancet* 1990; **335:** 765-774.
26. Eastern Stroke and Coronary Heart Disease Collaborative Research Group. Blood pressure, cholesterol, and stroke in eastern Asia. *Lancet* 1998; **352:** 1801-1807.
27. UKTIA Study Group. The United Kingdom Transient Ischaemic Attack (UKTIA) aspirin trial: final results. *J Neurol Neurosurg Psychiatry* 1991; **54:** 1044-1054.
28. Prospective Studies Collaboration. Cholesterol, diastolic blood pressure, and stroke: 13,000 strokes in 450,000 people in 45 prospective cohorts. *Lancet* 1995; **346:** 1647-1653.
29. Broderick JP, Phillips SJ, Whisnant JP, *et al*. Incidence rates of stroke in the eighties: the end of the decline in stroke? *Stroke* 1989; **20:** 577-582.
30. Eisenblätter D, Heinemann L, Classen E. Community-based stroke incidence trends from the 1970s through the 1980s in East Germany. *Stroke* 1995; **26:** 919-923.
31. Tuomilehto J, Rastenyte D, Sivenius J, *et al*. Ten-year trends in stroke incidence and mortality in the FINMONICA stroke study. *Stroke* 1996; **27:** 825-832.
32. Ueda K, Omae T, Hirota Y, *et al*. Decreasing trend in incidence and mortality from stroke in Hishayama residents, Japan. *Stroke* 1981; **20:** 154-160.
33. Shimamoto T, Komachi Y, Inada H. Trends for coronary heart disease and stroke and their risk factors in Japan. *Circulation* 1989; **79:** 503-515.
34. Tell GS, Crouse JR, Furberg CD. Relation between blood lipids, lipoproteins, and cerebrovascular atherosclerosis. A review. *Stroke* 1988; **19:** 423-430.
35. Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy — I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. *BMJ* 1994; **308:** 81-106.

Acknowledgements

This study would not have been possible without the continuous efforts of the sentinel GPs: Dr Jean-Francois Adant, Dr Eric Alardeau, Dr Veronique Albert, Dr Guy Armand, Dr Dirk Avonts, Dr Baivier, Dr Pascale Bastin, Dr Nicole Bayers, Dr Fabienne Belvaux, Dr Sonja Berael, Dr Q Blonda, Dr Pierre Boudolf, Dr Dominique-Jean Bouilliez, Dr Monique Boulad, Dr Jozef Boulonne, Dr Bruynseels, Dr Pierre Buchin, Dr M. Buttiens, Dr Patrick Buytaert, Dr Nadine Carette, Dr J-M Caroyer, Dr P Cassiman, Dr Francoise Chapeaux, Dr J Charles, Dr M Chiang, Dr Christine Beirens, Dr Pierre Claerhout, Dr Geert Clauwaert, Dr Henri Clinquart, Dr Jose Coppine, Dr Cornelli Koen, Dr Myrjam Cramm, Dr Charles Cuypers, Dr Marc Daans, Dr Agnes De Graef, Dr Eric De Graef, Dr T De Lannoy, Dr J De Loof, Dr Dirk De Pauw, Dr Hilde De Ridder, Dr W De Schepper, Dr Frans De Smedt, Dr Jos De Smedt, Dr Maurice Debarre, Dr Marie Debry, Dr Frank Declercq, Dr Inge Decock, Dr Ludovic Deferm, Dr Steven Delcour, Dr Jean Delespaul, Dr E Delvaux, Dr Nadine Deraux-Carette, Dr Christian Deruyck, Dr Marc Dethier, Dr Jean-Jacques Detiege, Dr J Devries, Dr Francis Dils, Dr Jan Dominicus, Dr Jean-LucDubuisson, Dr Johan Dupont, Dr Yves Durez, Dr Catherine Durieux, Dr Luc Eraly, Dr Rudy Faelens, Dr Dominique Filee, Dr Robert Flon, Dr Fabien Fondu, Dr Francois Annick, Dr Philippe Fremy, Dr Chris Geens, Dr Walt Geeraert, Dr Willy Geldhof, Dr Bertine Gemen, Dr Francoise Gerard, Dr Isabelle Geudevert, Dr Bernardf Geuse, Dr Philippe Gilbert, Dr Jean-Marie Gilles, Dr Jules Goffin, Dr Patrick Govaert, Dr Yves Gueuning Dr Francoise Hanon, Dr L Hardy, Dr Kristien Hendrickx, Dr Jean Henrotin, Dr Ivo Herbots, Dr Jean-Pierre Hoengenaert, Dr Raymond Hovinne, Dr Pierre Huart, Dr Patrick Jadoulle, Dr Raoul Joos, Dr Michel Kaesemans, Dr C La Haye, Dr Hilde Lagasse, Dr Jan Lamberts, Dr Pierre Larue, Dr Renate Lauwers, Dr V Lebrun, Dr L Leconte, Dr Antoine Ledent, Dr Alain Ledoux, Dr Leonard Roger, Dr Philip Libaut, Dr Rik Lietaer, Dr Godelieve Lindemans, Dr Linden Baudouin, Dr Martine Luwel, Dr E Luyten, Dr Michel Mahieu, Dr C Maindiaux, Dr Pierre Malfait, Dr Jacques Marin, Dr Jean Marysael, Dr Christian Massart, Dr Jan Matthys, Dr A-C Mehu-Wegria, Dr J-J Mestdagh, Dr Francois Michaelis, Dr Jean-Philippe Monette, Dr Guido Nicolai, Dr P Noppe, Dr D Notte, Dr P Nuytemans, Dr P Nys, Dr Jean Parmentier, Dr Karine Pelicaen, Dr Yolanda Pil, Dr Wim Raes, Dr Martine Renard, Dr Marc Rijckaert, Dr Frank Robijn, Dr Jean Rosillon, Dr Francois Ossion, Dr Marc Royackers, Dr Jules Saerens, Dr Schillemans, Dr Hubert Schoofs, Dr Karl Segers, Dr Jan Sette, Dr Ghislain Spitaels, Dr Thierry Storme, Dr Peter Strobbe, Dr Jozef Thys, Dr Marcel Toye, Dr Jan Van Assche, Dr C Van Cauwenberge, Dr Francois Van Der Meersch, Dr Van Doren, Dr Jean-Luc Van Duyse, Dr A Van Erum, Dr Anne Van Hoof, Dr Christine Van Hoof, Dr Yvan Van Maele, Dr T Van Mullem, Dr Van Riet, Dr P Van Royen, Dr Philippe Van Vlaenderen, Dr Anne-Marie Vanderborght, Dr Daniel Vandeweghe, Dr Christiaan Vanhercke, Dr Freddy Vantomme, Dr Karolien Vantomme, Dr Thierry Vanwersch, Dr Jacques Vedrin, Dr Karleen Vercruysse, Dr F Verduyckt, Dr Cecile Verheugen, Dr Koen Verhofstadt, Dr M Vervenne, Dr Werner Vleugels, Dr Ch Vrijsen, Dr Luc Vuylsteke, Dr Marc Vydt, Dr Sylviane Wargny, Dr Johan Wens, Dr Gerlinde Wijnen, Dr Spiros Xanthos, Dr Els Yperman Els. We are also grateful to Marina Devis for logistic assistance and to Jan Heyrman for his helpful comments to a previous version of the manuscript.