

Methods (detailed version)

A substantial proportion of stroke cases were believed not to receive specialist attention. ‘Hot pursuit’ methods were therefore deemed necessary in order for the ascertainment process to be sufficiently sensitive [1, 2].

The study was designed to ascertain incident (first ever in a lifetime) strokes, prospectively, in residents of the Primorski district of the city of Varna and the rural obstinae (local districts) of Provadia and Dolen Chiflik, some 30 to 70 Km to the south-west of the city. Approximately 45% of the populations of the rural districts live in the two towns after which the districts are named, and these towns are both classified as ‘urban’ by the statistical authorities. After a 3 month trial period, we sought to identify all first in lifetime strokes with dates of onset from May 1, 2000 to April 30, 2001.

Populations at risk were defined as persons aged 35 or more with an eligible address in the ‘current address’ field of the computerised population registers maintained and continuously updated by the municipal office for residential registration. The 10 digit personal identification number included in the registers, incorporates date of birth and sex, allowing easy calculation of the numbers of persons at risk at the study midpoint (taken as November, 2000). In the more restricted age range used for external comparisons that we report here – ages 45 to 84 — there were 37791 in the designated urban population and 18656 in the designated rural population.

Designated sources of notification for suspected eligible strokes included: the centres which processed emergency calls to the Ambulance and Emergency Services (in Varna, Dolen Chiflik and Provadia), the Varna District Hospital emergency room, duty doctors and nurses in the in-patient neurological units in the area (four urban and

one rural), local physicians practising within, or close to, the specified study areas, (identified from the list of contract holders with the Regional Health Insurance Fund: 43 urban and 28 rural general practitioners, 7 urban and 4 rural consultant neurologists), admission and discharge books for four hospitals, duty doctors in two residential homes (one for the elderly and one for persons with physical disabilities), death registrations lodged with the Regional Health Centre (typically within days of death for the urban population and taking up to a month for the rural population), and autopsy protocols from department of pathology at Varna University Hospital and Varna District Hospital. For strokes occurring in inpatient units other than neurological (in the four relevant hospitals), sources of notifications were the consultant neurologists, medical discharge records, other clinical records and records of specialist groups on disability within the hospital. These were checked monthly. The central records of the ambulance service were also scanned once a month for possible missed cases.

We aimed to conduct neurological assessments within a week of onset. The registrar phoned or visited contact persons in the main sources of information (ambulance call centres, emergency rooms, and neurological units) each working day. Primary care physicians were contacted by phone twice weekly in the urban area and three times per week in the rural area. Cooperating staff within all medical inpatient units and within all general and neurological medical practices were asked to notify all cases referred to them as possible stroke, including cases reported as transient ischaemic episode (TIA), vertebrobasilar insufficiency, epilepsy or dementia. A list of 'key words' prepared during the pilot period included ischaemic stroke, haemorrhagic stroke, subarachnoid haemorrhage, transient ischemic attack, cerebrovascular disease,

vascular dementia, vertebrobasilar or carotid insufficiency and these were used in guidance to notifiers.

Death certificates were scanned weekly, mostly before they were coded for underlying cause by the regional vital statistical office. Notification records were generated for all deaths in residentially eligible persons with any of the 'key words' mentioned above in any of the cause of death fields. For coded death certificates, all cases coded to ICD (9) 430-439 were also included. If the death certificate was issued following a forensic assessment, a copy of the forensic protocol was requested.

To maximise the sensitivity of ascertainment, redundant notification was deliberately sought. Up to 6 notification sources were recorded for each event. All notified events were initially assessed by the registrar (VA) to exclude from further investigation those who were residentially ineligible (i.e. without an eligible 'current address' in the population register), those which had unequivocal evidence that the event was not a stroke or, if a possible stroke, unequivocal evidence that it was not the first in the lifetime. The prior exclusion of stroke by an attending general practitioner or neurologist plus confirmation by the patient that they had experienced no neurological symptoms within 24 hours of the alleged event counted as unequivocal evidence that the event was not a stroke. A history from the GP or neurologist of a prior hemiplegic event, confirmed as a stroke by neurological assessment (with or without CT scan) counted as unequivocal evidence of prior stroke. Doubtful cases were always discussed with the study neurologists and usually referred for clinical assessment by them.

Persons not admitted as in-patients were contacted by telephone (where possible) in order to collect additional information and to obtain permission for a visit by the study neurologist. Where telephone contact could not be established, at least three visits to

the notified address plus other enquiries were made before further investigation was abandoned.

The processes by which potentially eligible events were assessed by study neurologists may be classified according to the nature of information available into:

1. *'Direct' neurological assessments*

Study neurologists (MS and PK) sought to examine all potentially eligible cases — inclusive of cases admitted to hospital. These assessments included a detailed history, and full neurological examination, including the components of the Glasgow Coma Scale [3]. Results from doppler sonography, echocardiography, CT scan, cerebral angiography and lumbar puncture were recorded whenever available.

2. *'Indirect' neurological assessments*

This category includes cases who had been clinically assessed by a service neurologist but who died before direct assessments by study neurologists could be carried out. The consulting neurologist was interviewed whenever possible and hospital and personal medical records abstracted. This category also includes cases confirmed by forensic autopsy.

3. *Assessments of fatal cases identified from death certificates only*

Cases only qualified for (and remained in) this third category if:

- a) the doctor certifying the cause of death had entered a stroke diagnosis in one of the Part I fields of the death certificate; and
- b) no information from an assessment by a service neurologist or pathologist could be obtained. (Where such information was obtained the assessment was reclassified as 'indirect'.)

Attempts were always made to obtain confirmatory information from the general practitioners and ambulance and other professional staff concerning signs present during the last illness. In addition, and especially where information from the general practitioner was not available, relatives and witnesses were also interviewed. In the small number of instances where the latter were the only source of information additional to the death certificate entries, study neurologists applied conservative criteria before classifying events as ‘probable’ strokes and as first ever in a lifetime. Resort, in these instances, to ‘verbal autopsies’ was preferred to the alternative policy of assuming that none of these cases were true strokes because:

- c) It was consistent with established protocols such as that for MONICA (<http://www.ktl.fi/publications/monica/manual/part4/iv-2.htm>) which specify that death certificates should be scanned as one of the means for identifying potentially eligible events. Some fatal cases identified this way will inevitably lack records of specialised diagnostic assessments even though the balance of available evidence points clearly towards a stroke. The MONICA protocol specifies that all such cases must have been assessed clinically within 28 days of onset. Among the MONICA stroke registries, up to 69% of fatal cases had not been examined by a physician of any kind [4].
- d) Conservative use of these procedures was likely to yield an incidence estimate closer to the truth, than the highly improbable assumption that none of the potential cases falling into this category were true strokes.

The procedures adopted in the third category of assessments were not specified in a prior protocol but were developed and formalised ‘in the field’

during the 3 months of the pilot phase. They are illustrated in the figure attached at the end of this additional file.

Additional file 2: ascertainment and classification procedures.pdf gives the number of events assessed by each type of assessment.

The WHO clinical definition of a stroke as ‘rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting more than 24 hours (unless interrupted by surgery or death) with no apparent cause other than a vascular origin’[5] was applied. Global clinical signs were accepted only for patients with deep coma or subarachnoid haemorrhage. Strokes were distinguished from transient ischaemic attacks (which were excluded from the study) by duration of functional loss or symptoms of greater than 24 hours.

All cases classified as first ever in lifetime strokes were followed up at day 28 (where day of occurrence counted as day 0). Previously unrecorded CT scans or autopsy reports were noted.

Study priorities were determined by the study’s main aim: to test hypotheses derived from death certificate based information and local clinical experience that the incidence of total stroke was truly very high in this region and that it was higher in rural than urban populations. Priorities were therefore to maximise ascertainment of potentially eligible events, to maximise the validity of the clinical distinction between stroke and ‘non-stroke’ and to determine whether there had been a prior history of stroke. It was anticipated that classification by pathological sub-type would only be possible, with confidence, for the minority of confirmed incident cases that had received appropriate ancillary investigations and that this could not therefore be an important objective of the study.

External comparisons

Study priorities also influenced the choice of incidence reports used for external comparisons. The collation of Sudlow and Warlow [6] was selected because:

- a) the studies employed comparable ascertainment procedures to those employed in this study;
- b) they included at least one study in a high risk east European population (that from Novisibirsk).

For the external comparisons rates were age-standardised by 5-year age groups from 45-9 to 80-4, using the world standard age weights, following Sudlow et al [6].

Analyses of case fatality

On discovering that case fatality appeared to be higher in village residents, its relation to age, sex, residence and severity (as indexed by the Glasgow Coma Score) was explored using stratified analyses.

Comparisons (for fatal cases) with coding of cause of death by the vital statistics office

For all persons giving rise to the 742 assessed events, vital status was followed up to May 31, 2001. For those known to have died, the underlying cause of death, as coded by the vital statistics office, was always sought. To assess the comparability of study classifications with those of the vital statistics office, study classification as stroke or not was compared with the vital statistics office classification, stratifying by type of study assessment procedure.

Statistical methods

Confidence intervals for standardised rates and for ratios were calculated by standard methods [7] and for case fatality using the Wald method [8]. For testing whether case

fatality was higher in village residents one tailed p values were estimated using a score statistic [9].

Ethical approval was granted by the Ethics Committee of the Varna Medical University. Informed consent was obtained for all patients directly assessed by study neurologists — where necessary from their next of kin.

References for this additional file

1. R Malmgren, C Warlow, J Bamford, P Sandercock. **Geographical and secular trends in stroke incidence.** *Lancet* 1987; ii: 1196-9
2. CL Sudlow, CP Warlow: **Comparing stroke incidence worldwide: what makes studies comparable?** *Stroke* 1996, **27**: 550-558
3. G Teasdale, B Jennet: **Assessment of coma and impaired consciousness: a practical scale.** *Lancet* 1974, **2**: 81-84
4. K Asplund, R Bonita, K Kuulasmaa, AM Rajakangas, V Feigin, H Schaedlich, K Suzuki, P Thorvaldsen, J Tuomilehto: **Multinational comparisons of stroke epidemiology: Evaluation of case ascertainment in the WHO MONICA stroke study.** *Stroke* 1995, **26**: 355-360
5. MONICA definition, available at <http://www.ktl.fi/publications/monica/manual/part4/iv-2.htm#s2-2> (accessed 7/7/01)
6. CL Sudlow and CP Warlow for the International Stroke Incidence Collaboration: **Comparable studies of the incidence of stroke and its pathological types: results from an international collaboration..** *Stroke* 1997, **28**: 491-499
7. KJ Rothman, S Greenland: **Modern Epidemiology**, 2 edn. Philadelphia: Lippincott Raven, 1998 p 260-4.
8. *ibid.*, p 239-41.
9. *ibid.*, p 241-4.

PROTOCOL FOR NEUROLOGICAL ASSESSMENT OF LATE NOTIFIED POTENTIALLY ELIGIBLE FATAL CASES

Classification pathways: 2 = 'indirectly assessed fatal events'; 3 = 'fatal events lacking specialist assessment before death'

