Strokes in the Young and Middle-aged: Consequences to the Family and to Society

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Strokes are the commonest cause of chronic disability in the Western world (*British Medical Journal*, 1976; Capildeo *et al.*, 1978), consequently, a considerable part of Health Service resources is directed towards meeting the needs of such patients. While stroke is commonest among the old, between 25 and 33 per cent of all strokes occur in the economically active section of the community aged 65 years and under (Acheson and Fairbairn, 1970).

The present study explores factors that may predispose to the stroke in these younger patients, and examines the ensuing costs to the patient, his family, the hospital services and society.

Methods

The Patients

One hundred patients aged 65 years or less, presenting with a stroke, have been studied. For this study the arbitrary definition of Capildeo et al. (1978) has been used; a stroke is 'An acute disturbance of cerebral function of vascular origin causing disability lasting more than, or death within, 24 hours'. This corresponds to the International Statistical Classification of Diseases, Injuries and Causes of Death (Manual of the ISCD, 1967) rubrics 430-434. It includes subarachnoid haemorrhage (430), cerebral, cerebellar and brain stem haemorrhage (431), occlusion of precerebral arteries (432), cerebral thrombosis (433) and cerebral embolism (434). In this study no attempt has been made to separate individual causes of the stroke, except for subarachnoid haemorrhage; each of the 10 patients in this last group had sudden onset of headache and/or sudden loss of consciousness with subsequent neck rigidity and a lumbar puncture showing blood in the cerebrospinal fluid.

The patients were consecutive admissions from the Emergency Department of the Western Infirmary and Gartnavel General Hospital, Glasgow. The single department is shared by both hospitals. Patients were identified by daily review of all admissions. Also included in the study were three patients having a stroke while in hospital for other reasons. As a test of completeness of the survey, when 100 patients had been collected from 15th January to 6th December 1977, the inpatient records of one of the six receiving medical units were scrutinised; no further patients with strokes admitted during that time came to light.

Excepting the relatives of patients who died shortly

after admission, all patients and/or their relatives were interviewed within 72 hours of admission. All interviews were conducted by the first author, who was independent of clinicians concerned with the patient's management. Details of the presenting illness, past medical history, family history, drug treatment and compliance, and social history, were obtained while in the ward, using a special proforma. Further details of past medical history, particularly hypertension (with the readings) and drug treatment, were obtained from GPs' records, using a mailed questionnaire (88 per cent response) or, where this failed, by telephone. Hospital notes of previous admissions or attendances were also scrutinised. Thereafter the inpatient's clinical progress was followed. Use of hospital resources was assessed in terms of bed occupancy, investigations done and drug treatment, physiotherapy, speech therapy and occupational therapy given.

Following discharge from hospital, patients or their family recorded the number of outpatient attendances, visits from their GP, district nurse and health visitor, and hours of attendance by a home help. This and other information (*see* below) was checked when the author visited the patients' homes six months after the onset of the stroke. Sixty-five survivors were personally contacted; three survivors had gone abroad and the necessary information about them was obtained from relatives. At the follow-up interview, any continuing physical or mental disability was noted and details of financial and occupational changes were discussed.

Relatives of patients who had been returned home incapacitated and in need of care were interviewed about their own social, economic and emotional problems consequent on the patient's stroke.

The Controls

Of the 90 patients suffering a stroke (those with subarachnoid haemorrhage being excluded) 88 were compared for blood pressure, obesity and smoking habits with a control population. These controls, matched for age and sex, were randomly selected by computer from data on the Renfrew Mid-Span Scheme (Hawthorne *et al.*, 1974). Of the 90 patients, 2 were teenagers and could not be matched with the middle-aged controls. Information on the controls was collected in 1972, but the control population is geographically and socially similar to that of the patients seen in hospital.

The Stroke

Ninety of the 100 patients suffered a cerebral haemorrhage/infarction (ISCD, 1967, rubrics 431-434) and 10 had a subarachnoid haemorrhage (ISCD, 1967, rubric 430).

Figure 1. Age, sex and mortality of 100 strokes: A. 90 cases of cerebral haemorrhage/infarction, B. 10 cases of subarachnoid haemorrhage. Cross-hatching represents fatalities.



Cerebral Haemorrhage/Infarction. There were 56 male and 34 female patients (Fig. 1), with ages ranging from 33 to 65 and 16 to 65 respectively, mean 55.4 years and 55.1 years respectively. Mortality was significantly greater among the women -16 (47 per cent) died – than among the men -11 (20 per cent) died ($\chi^2 = 6.3228$, p<0.025). Among those who died, women survived longer (mean 29.8 days) than did men (mean 9.4 days). At the end of the six-months follow-up period 63 (70 per cent) of this group were still alive.

Subarachnoid Haemorrhage. There were 5 male and 5 female patients with a subarachnoid haemorrhage. Mean ages were 46.0 years for the men, 51.6 years for the women, overall 48.8 years, younger than the cerebral haemorrhage/infarction group. Five died (3 women, 2 men) after a mean interval of 7 days. Because of the small numbers in this subarachnoid group, hereafter, unless specifically stated, data on stroke refer to the 90 patients with cerebral haemorrhage/infarction.

Hypertension

Forty patients (44.5 per cent) in the cerebral haemorrhage/infarction group (21 men, 19 women) had a diastolic blood pressure greater than or equal to 90 mmHg on the last recording before their stroke; 40 (44.5 per cent) had readings lower than this; 10 (11 per cent) had not previously had their blood pressure recorded.

Comparison of the diastolic blood pressure in patients before the stroke with the pressure in matched controls reveals pre-existing hypertension more frequently in the stroke group (Table 1). Only one control subject had a diastolic pressure greater than 110 mmHg, while 18 of the people who subsequently had a cerebral haemorrhage/infarction equalled or exceeded that level ($\chi^2 = 17.051$, p<0.001).

The mortality rate (37.5 per cent) was higher among those with a diastolic pressure of 90 mmHg and greater than among those known to have a pressure lower than this (25 per cent) ($\chi^2 = 2.0945$, p>0.05). Among those who died in the former group there were 6 in whom the last diastolic blood pressure recorded before their stroke was greater than or equal to 110 mmHg.

Diastolic Blood Pressure	Controls	Strokes	
150 + mm Hg	0	1	
140-149 mm Hg	0	0	
130-139 mm Hg	0	1	
120-129 mm Hg	1	4	
110-119 mm Hg	0	12	
100-109 mm Hg	9	7	
90- 99 mm Hg	22	15	
Below 90 mmHg*	56	38	
No recordings	0	10	
Total	88	88	

*Data for the stroke group in the category 'Below 90 mmHg' include those found to be below 90 mmHg and those in whom blood pressure has been recorded as 'normal'. Of the 40 patients with blood pressure readings of 90 mmHg and greater, 23 were not receiving any drug treatment at the time of their stroke. Diastolic pressures in these varied from 90 to 130 mmHg (mean 98.2 mmHg). Furthermore, 5 of the patients who had been prescribed antihypertensive drugs by their GP or by a hospital had defaulted from their treatment, and in these, the last recorded diastolic pressures varied from 100 to 120 mmHg (mean 107.5 mmHg).

Smoking

Of the 88 matched patients with cerebral haemorrhage/ infarction 62 (70 per cent) were smokers, compared with 36 of the 88 matched controls (41 per cent)—see Table 2 —this difference being statistically significant (χ^2 = 15.565, p<0.001). There were more male than female smokers in both patient and control groups, but the percentage of female smokers among the strokes (59 per cent) even exceeded the percentage of male smokers among controls (48 per cent). Smoking was also heavier among stroke patients; 68 per cent of the stroke patients who smoked, smoked 20 or more cigarettes a day, compared with 44 per cent of the control smokers (χ^2 = 3.901, p<0.05).

Obesity

Using Metropolitan Life Insurance Company (1959) statistics for desirable weight, 32 per cent of the male patients and 53 per cent of the female patients were overweight. However, figures for controls were similar (43 per cent and 53 per cent respectively).

Family History

Of the cerebral haemorrhage/infarction patients 30 (33 per cent) had a first degree relative who had suffered a stroke. In 44 (49 per cent) there was a history of ischaemic heart disease and in 16 (18 per cent) a history of a

Table 2. Smoking Habits (%).

hypertensive relative. Sixty-one patients (68 per cent) had a first degree relative who had suffered, or was suffering, from one of these three conditions.

Oral Oestrogens

There were 9 women aged 50 years and under in the cerebral haemorrhage/infarction group. Two of these were teenagers and neither was on an oral oestrogen preparation as far as could be determined. The remaining 7 were aged 41 to 50 years and 5 were taking an oral oestrogen at the time of their stroke (patients 1 to 5, Table 3). Three had been on the oral contraceptive pill for 8-12 years and in the third the blood pressure had not been checked for almost 3 years before her stroke. The two who died did so within 24 hours of admission. Both had lateralising neurological signs without neck rigidity and a diagnosis of subarachnoid haemorrhage was not entertained.

A further patient (patient 6, Table 3), had been on the oral contraceptive pill for four years. She died 10 hours after presentation with severe headache of sudden onset and blood-stained cerebrospinal fluid was obtained at lumbar puncture. The clinical diagnosis of subarachnoid haemorrhage was confirmed at postmortem, where a posterior cerebral artery berry aneurysm was found.

Other Conditions

Eleven patients (12 per cent) subsequently having a cerebral haemorrhage/infarction had previously experienced from one to six transient ischaemic attacks. A transient ischaemic attack is defined as 'an acute disturbance of cerebral function of vascular origin, with disability lasting less than 24 hours' (Capildeo *et al.*, 1978). Sixteen patients (18 per cent) had previously suffered a stroke. Forty-two (48 per cent) had suffered from either a transient ischaemic attack, stroke, ischaemic heart disease, or peripheral vascular disease previously.

	Stroke Patients Men n = 56 Women n = 32 All n = 88			Controls Men n = 56 Women n = 32 All n = 88		
Non-smokers	13 (23)	13 (41)	26 (30)	29 (52)	23 (72)	52 (59)
Smokers	43 (77)	19 (59)	62 (70)	27 (48)	9 (28)	36 (41)
>20/day smokers	31 (55)	11 (34)	42 (48)	13 (23)	3 (9)	16 (18)

Table 3. Oral Oestrogens among 100 Young Strokes

	Oestrogen Content	Reason for 'Pill'	Duration of treatment	Last BP reading prior to stroke (interval between reading and stroke)	Smoking habits (cigs/day)	Age/yrs	Outcome
Patient 1	50 μ g ethinyloestradiol	Contraception	12 years	164/96 (2 months)	30	41	Alive
Patient 2		Contraception	10 years	130/75 (3 months)	25	42	Alive
Patient 3	50 µg ethinyloestradiol	Contraception	8 years	130/70 (2yr 10 months)	15	43	Dead
Patient 4	10 /	Dysmenorrhoea	1 year	200/110 (1 month)	0	50	Dead
Patient 5	2 mg oestradiol valerate	Menopausal symptoms	10 days	150/110 (10 days)	0	50	Alive
Patient 6		Contraception	4 years	None available	15	32	Dead

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Arrhythmias apparently played a small part. Three patients had atrial fibrillation at the time of their stroke (one ischaemic, one rheumatic and one thyrotoxic heart disease). None was receiving anticoagulants.

Three patients were suffering from a blood disorder leading to thrombocytopenia. Two, despite their presentation with a sudden onset of neurological deficit, subsequently proved to have a cerebral neoplasm (one primary, one secondary). The existence of cerebral haemorrhage/infarction was likely on clinical grounds but was not confirmed by postmortem.

Three patients had a stroke while in hospital. In each case the stroke occurred within 24 hours of surgery. One patient died. Operative procedures, anaesthetic agents and postoperative care were unremarkable. One patient had an oophorectomy, another had a vagotomy and pyloroplasty, while the third had a nasal polypectomy. No patient had a preoperative state likely to have predisposed to a stroke. Preoperative blood pressure was known to be normal in each case.

NHS Resources Used

Beds Occupied

Most patients occupied an acute medical bed for less than 3 weeks (Fig. 2). On average, the 90 patients with

Figure 2. Duration of stay in an acute hospital bed of 90 cases of cerebral haemorrhage/infarction. Open graph represents males, cross-hatching females.



cerebral haemorrhage or infarction remained in hospital for 24.0 days (range 1 to 143 days). This compares with a mean stay of 9.5 days for all acute medical admissions (1977 Western Infirmary returns), 27.3 days for strokes of all ages, and 28.0 days for strokes over 65 years of age.

Only 2 patients of the 90 required long-term institutional care—one man aged 61 years was transferred to geriatric care after occupying an acute bed for 120 days; the other, also male, aged 43 years, was transferred to a young chronic sick/rehabilitation bed after 90 days.

Investigations

During their hospital stay the 90 patients had the following investigations performed: full blood count, 109 times (1.2 times per patient); urea and electrolytes estimations, 152 times (1.7 times per patient); liver function tests, 110 times (1.2 times per patient); chest Xray, 80 times (0.9 times per patient); electrocardiogram, 128 times (1.4 times per patient), and bacteriological cultures, usually urine or sputum, 130 times (1.4 times per patient). More detailed investigations included skull X-ray (24 times), intravenous urography (5 times) and cerebral angiography (once), brain scan (18 times), electroencephalography (15 times) and lumbar puncture (5 times). One patient was transferred to another hospital for computerised axial tomography and subsequently had an intracerebral haematoma evacuated. A further patient, after ENT investigation, had a cricopharyngeal myotomy which helped to relieve the dysphagia accompanying a pseudobulbar palsy.

Treatment

Considerable use was made of physiotherapy, occupational therapy and speech therapy (Table 4), especially for inpatients, but treatment was often continued for outpatients. Drug therapy was monitored in hospital and at 6 months review. Of 63 survivors, 27 (42 per cent) required long-term drug treatment following their stroke. Five of these survivors required treatment with anti-depressant drugs because of their physical illness.

Table 4. Use of Physiotherapy, Occupational Therapy andSpeech Therapy.

	While inpatient	While outpatient
Physiotherapy		
Number of patients	64	28
Number of sessions	198	67
Number of sessions/week/patient	3.1	2.4
Occupational Therapy		
Number of patients	21	13
Number of sessions	59	30
Number of sessions/week/patient	2.8	2.3
Speech Therapy		
Number of patients	12	10
Number of sessions	22	21
Number of sessions/week/patient	1.8	2.1

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Follow-up Visits to Hospital

Of the survivors 47 were reviewed in a medical outpatient clinic a total of 86 times. Transport to and from these clinics and physiotherapy classes etc. and the extent that the ambulance services were utilised was not assessed.

Further Care at Home

Use of Health Service resources at home was not extensive. Of the 63 survivors 46 (73 per cent) consulted their GP at home or in his surgery a total of 156 times (mean 3.4 times per patient) in the 6-month period after their stroke. Seven of the survivors received visits from a district nurse, but only 4 needed this regularly. Two patients received a visit from a health visitor.

Local authority resources were used to the extent of providing domiciliary aids to 17 patients, such as banisters for stairs (5 patients), non-slip bathmats (15 patients), or walking aids (6 patients) though these were often lent by the hospital physiotherapy departments instead. Five patients had a home help who regularly attended for 6 hours a week.

The Costs

The following are approximate costs only. Some costs were much easier to assess than others but it does not follow that costs that were difficult to assess were necessarily small.

Table 5.	Cost to the NHS of the 90	Stroke Patients	in the First
6 Month	Period.		

	Total Cost	Cost/Patient	
Inpatient cost exclusive of investigations:			
i. Western Infirmary (45 patients ii. Gartnavel General Hospital	£41,653	£926	
(45 patients)	£44,198	£982	
Total inpatient cost in acute beds:	£85,851	£954	
Additional long-stay costs for 2 patients in the 6 months	£3,194		
Investigations	£4,814	£53	
Total	£93,860	£1,043	

Table 6. Work Status of Stroke Patients.

Direct Costs to the NHS

Over the 6-month period beginning with their stroke, the 90 cerebral haemorrhage/infarction patients cost the hospital services of the NHS £94,000, a mean of £1,043 per patient (Table 5). This figure is calculated from hospital running costs published by the Scottish Home and Health Department for the year ended 31st March 1977. It does not include the cost of investigations. This was estimated separately using, as a basis, costs agreed between the British Medical Association and the Departments of Employment and Health and Social Security for investigations performed for these departments but outside the auspices of the NHS (British Medical Association, 1978). This cost has then been added to produce a final inpatient total (Table 4). Investigations accounted for only 5.1 per cent of the total cost over this period.

Assessing the cost of the services outside hospital is even more difficult, but many of these expenses were relatively small. Physiotherapy, occupational therapy and speech therapy for outpatients has not been costed per capita by the Scottish Home and Health Department and has not been included here. Nevertheless, patients with a stroke constitute a substantial proportion of the workload of these hospital departments. Ambulance costs for outpatients are again difficult to assess since one patient may require an ambulance to himself while another more mobile individual can share with several patients. The cost of medical outpatient consultations has been assessed (SHHD statistics) and for the six months after the stroke this would have totalled £510.00 for the 90 patients, a mean of £5.66 per patient. GP and district nurse costs could not be assessed but GPs were already receiving capitation fees for the patients in their care and very few night calls were included in the 156 consultations recorded by the patients. Use of local authority resources was also small.

Overall then, the bulk of the direct cost concerns hospital inpatient care, and 95 per cent of that was directly proportional to the length of stay. The mean acute bed cost was twice that of a long-stay bed cost.

Indirect Costs to Industry

Table 6 shows the occupational status of the patients suffering a stroke 6 months from the time of onset. Only half of the patients had been working before their stroke. Nine of these died and the cost of this is probably very large but incalculable. None of the patients who died nad previously been an invalid receiving medical care. The

	Previously employed	Not previously employed	Total	Number who had returned to work by six months from the time of the stroke
Being cared for by relatives		1		
on discharge from hospital	16	12 (3 retired)	28	2
Independent on discharge				
from hospital	18	15 (4 retired)	33	15
Dead	9	18 (3 retired)	27	<u> </u>
Institutionalised	2	0	2	-
Total	45	45	90	17

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stroke, therefore, did not often terminate an expensive illness. Those 17 of the survivors who had returned to work within 6 months of their stroke lost a mean of 111 working days per working survivor. Nineteen others were incapable of returning to work after 6 months. Overall, the 63 survivors accounted for 5,364 days of certified sickness absence in the six-month period. It is important to emphasise that no assessment of cost beyond 6 months has been made, but indirect costs will continue.

Personal Costs

Of the 61 patients who returned home, 15 felt that they had sustained a financial loss because of their stroke. They had lost a mean of \pounds 494 (net) over the 6 months, range \pounds 80 to \pounds 1,000. Of the 15, 5 were self-employed and these sustained by far the greatest losses. Four others, not self-employed, were marginally better off when receiving all benefits than they were when working. It should be noted that this state of affairs would be reversed after 6 months, when half-pay from employers would stop. Assessment at two years follow-up would probably reveal a different pattern.

Costs in terms of loss of independence, social isolation in unsuitable homes, frustration, and depression resulting from a severely limiting illness are impossible to assess, but are nonetheless very important. This personal and psychological element varied in degree according to the personality of the patient and the support given by relatives. In some patients it had contributed by producing further costly illness such as depression or the physical consequences of immobility, or it had affected the earning capacity and physical and mental health of others.

Effects on the Relatives

Social and Economic Costs. Of the 90 cerebral haemorrhage/infarction patients, 28 returned home to be cared for by relatives. Of the 28 relatives (19 wives, 3 husbands, 4 daughters, 1 sister, 1 brother) 8 had to abandon their jobs to look after the patient, 2 had to work reduced hours and 2 others were able to work normal hours; the remaining 16 relatives were not working previously. Eight relatives considered themselves worse off financially. Their estimate of the loss for the sixmonth period varied from £84 to £700 (mean £314). Twenty-five relatives had to spend most or all of their time at home. Two had had to move house to accommodate the patient. Twelve abandoned their usual summer holiday.

Emotional Consequences for the Relatives. At the sixmonth follow-up, 20 of the relatives seemed moderately happy and confident. However, eight felt very depressed and were struggling to cope with their new problem. Three viewed the future with 'trepidation', three with 'despair', while eleven were 'taking a day at a time'. Eleven viewed the future 'hopefully'. Eighteen relations felt that the stroke had not changed their relationship with their relative, while seven felt a closer relationship had been bonded. However, three, all wives, felt that their relationship with the patient had deteriorated. Two of these patients were aphasic; the other was aggressive and frequently incontinent of urine. Eight relatives had required sedatives or hypnotics since the start of the patient's illness, and at the six-month follow-up six relatives still required tablets (5 having minor tranquillisers, 1 a hypnotic).

Discussion

A preponderance of males has been found in the younger section of the stroke population under study, a finding that is known to reverse in later decades (Kurtzke, 1969). It has also been noted that, in the period up to six months from the time of stroke, mortality among women is significantly greater than among men. This is in agreement with previous work (Robinson *et al.*, 1959; Marshall and Shaw, 1959), which also shows that longterm survival is better in females despite the higher initial mortality.

Several predisposing factors for stroke have been identified in this study—high blood pressure, smoking, oral oestrogens and a family history of stroke—as well as two conditions likely to cause a stroke more directly, thrombocytopenia and cerebral neoplasm. These associations are not new. The value of lowering blood pressure in reducing the incidence (Kannel *et al.*, 1970) and prognosis (Baker *et al.*, 1968; Hutchinson and Acheson, 1975) of stroke has been clearly shown. When high blood pressure was not lowered, poor compliance as well as inadequate or unsuccessful drug treatment seemed most responsible.

Smoking is less definitely recognised as a risk factor for cerebrovascular disease than for coronary artery disease. Some authors have found no association for the former (Crofton and Crofton, 1963; Doll and Hill, 1966) but data from the Framingham Study are suggestive of a connection (Kannel *et al.*, 1965). The present study indicates that not only do strokes occur more commonly in smokers but that patients with a stroke smoke more heavily than control subjects.

Despite the small numbers in this study, the fact that five of the seven females in the age range 41 to 50 were taking oral oestrogens at the time of their stroke was notable. Up to a nine-fold increase in the risk of stroke has been described in people taking oestrogens (Collaborative Group for the study of stroke in young women, 1973) and it has been further suggested that smoking may potentiate the risk. The short-term use of oestrogens for menopausal symptoms may also be dangerous (patient 5, Table 3). Illis *et al.* (1965) described three cases of cerebral infarction occurring within a few weeks of the start of oral oestrogens.

Data regarding family history are, unfortunately, not available for the control population in this series, but 33 per cent of patients with cerebral haemorrhage or infarction had a first degree relative who had suffered a stroke. Gifford (1966) found that four times as many parents of stroke patients as expected had also suffered strokes.

From this series the main scope for preventive efforts appears to lie in improved control of blood pressure and, as suggested in the recent report of the Royal College of General Practitioners' oral contraception study (1977), 'a careful re-assessment of pill usage by older women', especially where other risk factors co-exist.

Many stroke patients require lifelong inpatient care even where rehabilitation services are of the highest order. However, only 2 per cent of our younger patients required long-term care. This may mean that more capable younger relatives were willing to look after their spouses. However, it is also true that long-term beds for the young are in short supply and in this study 26 of the 28 relatives who looked after the patients at home were not offered the possibility of chronic sick care. Many of these relatives tell of a harrowing time spent looking after incontinent and depressed patients, features highlighted by Isaacs *et al.* (1976). Several relatives suffered financial loss. A particular problem is that long-term care may engender psychoneurotic illness, both in the patient and in the relative. Both may need drug treatment.

From the data presented above, young patients with strokes are expensive for the National Health Service. It also appears that the major determinant of costs is the duration of hospital stay. Two questions then arise. First, a suggestion more appropriate to the longer stay stroke patients: a large saving could be made by early transfer from an acute bed to a long-stay/rehabilitation bed, where the bed cost is less than half that of the acute bed (Scottish Home and Health Department, 1977). Second, excepting those cases where intensive nursing is required, those who are minimally disabled could be cared for at home, perhaps after initial hospital outpatient assessment and with continuing outpatient review. Patients are often retained in hospital for daily physiotherapy but it would be worth considering how much of this could satisfactorily and more cheaply be done out of hospital.

While the recognition of the cost of a stroke to the patient, his family and the Health Service is relatively easy, a further major cost to society is indirect. In this sixmonths' study, the 63 survivors accounted for 5,364 days of certified sickness absence. Such temporary or permanent loss of skilled workers cannot fail to have a deleterious economic effect, difficult as this is to assess accurately. The loss of working time due to stroke is substantial, although more time is lost due to ischaemic heart disease and hypertension (Office of Health Economics, 1971).

Strokes are expensive. It would undoubtedly be better, economically and medically, if they did not occur. Industry, the family and the potential patient will surely ask how they can be prevented. The sad fact is that prevention is seldom possible. However, from this study, as from others, three clear directives emerge: treat hypertension adequately; stop smoking; and, where possible, limit oestrogen therapy.

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