GERIATRIC MEDICINE: AT THE LIMITS OF EVIDENCE-BASED PRACTICE*

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Many clinical trials and observational studies exclude elderly subjects through an assumption (often mistaken) that such patients are less likely to display a benefit from the intervention under study or that their inclusion may prejudice observations through co-morbidity. Such exclusions often have little clinical or scientific justification, and result in data that are poorly generalisable to an elderly population. As a consequence, in an era when clinical governance and evidence-based practice are becoming increasingly important, practitioners of geriatric medicine are left disadvantaged as the evidence base necessary for informed practice is often inadequate. The purpose of the symposium was to review the current state of evidence concerning the assessment and treatment in the elderly of a number of common, serious conditions, and to stress the importance of the development of a more comprehensive knowledge bank in conditions peculiar to an elderly population. Presentations were made on various topics of controversy within geriatric medicine.

A patient scenario relevant to the subject being presented preceded each review session; the audience was given the opportunity to vote for a selection of treatment options before and after each presentation. The scenarios precede reviews of each presentation, with the results of the audience vote both before and after the presentations being recorded in an Appendix at the end of the paper.

ATRIAL FIBRILLATION – NEW DILEMMAS FOR OLD AGE MEDICINE
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Scenario 1: An 86-year-old woman is admitted with delirium due to a urinary tract infection. She is in atrial fibrillation (AF), and the GP confirms this has been present for two years and treated with digoxin alone. She recovers completely and has an MMSE of 27/30 at discharge. Her apical heart rate is 70/min, she has sustained two falls in the last year and lives alone. She has a symptomatic hiatus hernia treated with omeprazole. There was an episode of right arm weakness one year prior, which lasted less than 24 hours. There is no close family and it is planned to discharge her with home help twice a week.

Current evidence would suggest that the best management of this patient's AF would be:

1. attempted cardioversion with warfarin cover;
2. no attempt at cardioversion: continue digoxin and add aspirin;
3. no attempt at cardioversion: continue digoxin and anticoagulate with warfarin;

4. no attempt at cardioversion: continue digoxin, and add aspirin and warfarin;
5. no attempt at cardioversion: continue digoxin, no other treatment change.

AF is common in the elderly; a prevalence of 4.7%[1] in over 65 year olds was recorded in one recent UK community study. In those aged 75 years and over, 10% of men and 5.7% of women were found to have AF, and this arrhythmia was present in up to 23% of the institutionalised elderly.[2] The priorities in the management of AF are the alleviation of symptoms, the reduction of cardioembolic risk and the reduction of associated cardiovascular morbidity and mortality. However, about two-thirds of patients with new onset[3] AF will undergo spontaneous cardioversion within 72 hours, the majority within 24 hours. Factors such as age, gender and left ventricular dysfunction have not been found to influence the likelihood of spontaneous cardioversion.

If patients do not spontaneously revert to sinus rhythm (SR), attempts at electrical cardioversion may need to be considered. The incidence of failure of cardioversion increases exponentially with the time the AF has been present, and the energy required to successfully cardiovert also rises with time. Other factors reported as being associated with failure of cardioversion include presence of underlying heart disease, NYHA grade 3 or 4 heart failure and an enlarged left atrium (>45 mm). Van Gelder[4] *et al.* demonstrated successful cardioversion in 70% of patients with persistent AF and 96% of patients with atrial flutter. The population studied had a high prevalence of heart disease, only 15% having lone AF. Negative predictive factors for successful reversion to SR were duration of AF and age, although the latter does not preclude electrical cardioversion in the elderly. Type of heart disease and NYHA functional class were not predictors of cardioversion but did predict likelihood of reverting to AF. Only 40% of subjects initially cardioverted remained in sinus rhythm (SR) at one year. Of note, patient age was not a predictor of reversion to AF.

Little evidence is available for choice of antiarrhythmic to maintain SR in the elderly once cardioversion is achieved. A recent study[5] has shown amiodarone more effective than a combination of sotalol and propafenone in maintenance of SR, although this study may have limited general applicability. Very limited evidence exists for chemical conversion of AF. The European Society for Cardiology (ESC) recommends that the optimal time for attempted chemical conversion of AF is within 48 hours of onset, despite the fact that spontaneous cardioversion is frequent in this time. The ESC's recommendation for first-line therapy is a Vaughan-Williams class Ic antiarrhythmic drug, e.g. flecanide, except in patients with underlying heart disease; however, abnormal echocardiograms are found in the majority of over 75s. The next agent of choice is

amiodarone, despite its unfavourable side-effects profile, and the newer class III agents, dofetalide and ibutalide may also be considered. Pre-treatment with ibutalide may also improve chances of successful DC cardioversion but does not improve chances of sustaining SR.[6] Digoxin has no role in the prophylaxis of recurrence of AF or in cardioversion to SR. It has a beneficial effect in rate control of persistent or permanent AF, but only a modest effect on rate at the onset of paroxysms of AF, and no effect on exercise-related tachyarrhythmia.

Evidence for functional benefit from cardioversion from AF in the elderly is limited. Patients undergoing successful cardioversion from AF have been shown to have improvements in exercise duration, peak oxygen consumption, heart rate and mean NHYA class.[7] These improvements, whilst statistically significant, may be of little clinical relevance in an elderly population.

As spontaneous cardioversion from new onset AF is very common, controversy exists about the need for immediate anticoagulation in these cases. A recent study[8] has shown an incidence of only three embolic episodes in 375 patients with new onset AF, all in very elderly patients. Whilst this argues against the commencement of immediate anti-thrombotic therapy, for patients who persist in AF or those in whom active cardioversion may be an option, anticoagulation should be commenced, and it is often easier to commence this therapy at diagnosis.

The use of warfarin and aspirin in persistent or permanent AF is associated with a relative risk reduction (RRR) for stroke prevention of 62% and 22% respectively versus placebo. The effect in secondary prevention is even more profound. In primary prevention the number needed to treat (NNT) for one year, to prevent one stroke, is 37 for warfarin and 67 for aspirin. In secondary prevention, the NNTs are 12 and 40 respectively for warfarin and aspirin. Major bleeding complications from warfarin therapy are rare (<1%), but do tend to occur mainly in the elderly.[9]

THE MANAGEMENT OF BLOOD CHOLESTEROL IN THE OLDER PERSON – SHOULD WE TREAT?
Dr J. Armitage, University of Oxford

Scenario 2: An 82-year-old hypertensive man is admitted with a Transient Ischaemic Attack (TIA). He does not smoke and takes bendrofluazide. He had an MI 20 years ago. He is not overweight. CT scan and doppler ultrasound of his carotids are normal. How would you manage his lipids?

1. Do not measure lipids.
2. Do measure lipids and treat if total cholesterol >5.5 mmol/l.
3. Do measure lipids and advise dietary modifications if total cholesterol >5.5 mmol/l.

Few disagree that hypercholesterolaemia in middle-aged patients merits treatment; large prospective studies have shown that a total cholesterol of >7.0 mmol/l is associated with a relative risk (RR) of mortality of 4.0.[10, 11] Some studies have suggested, however, that this benefit is not maintained in the elderly, the RR being only 1.3. This apparent reduction in efficacy may in fact represent an artifact of regression-dilution bias,[12] and the benefit to older people potentially higher than previously thought. Unfortunately, due to artificial upper age limits imposed in many studies, there are little prospective data for an elderly population to confirm this. Other data, which has suggested that low cholesterol is associated with excess mortality in the elderly, is now also felt to be questionable[13] because of confounding by disease,[14] where frail patients had lower cholesterol levels.

Trials of the effect of cholesterol lowering on coronary disease, particularly of the statins, have also often excluded elderly patients. The maximum age of patients in any of the larger studies is only 74.[15-17] However, the benefits shown for cholesterol lowering in patients over 60 years are very similar to those for younger patients[15, 16] and there is little evidence that these benefits will not persist in even older people.

Furthermore, there is no strong evidence of adverse effects related to cholesterol lowering. There is also some evidence from the statin trials[15, 16] of a reduction in incidence of stroke associated with cholesterol lowering. A relative risk reduction of about 20% is evident but the numbers studied are relatively small and the analysis performed on a *post hoc* basis. Three studies, the Heart Protection Study (HPS),[18] PROSPER[19] and RESPECT, will hopefully clarify these issues over the next few years. A collaborative meta-analysis to incorporate all data on completion of these studies is also planned. In the meantime the evidence that exists suggests that it may be reasonable to measure and treat serum cholesterol in the over 80s until further data becomes available.

BONE PROTECTION AFTER HIP FRACTURE
Dr F. Anderson, Southampton General Hospital

Scenario 3: A 76-year-old woman is admitted with a fractured neck of the femur. This occurred after the third in a series of falls. Each fall occured in the street, without warning, no associated symptoms, no loss of consciousness and no other injuries. There are no abnormalities on CVS and CNS examination. Her bone biochemistry is normal. How should her bones be treated?

1. No treatment or investigation needed.
2. Calcium and vitamin D.
3. Bisphosphonates.
4. Hormone replacement therapy.
5. Needs further investigation to determine therapy.

The incidence of osteoporotic fracture is high and continues to rise. The lifetime risk of a 50-year-old suffering a fracture of hip, vertebra or forearm is 14%, 11% and 13% respectively for women and 6%, 5% and 2.5% respectively for men.[20] Women have a one in three lifetime chance of having one of these fractures. Risk factors associated with fracture include incidence of falls, quality of protective responses and bone quality (mineralisation and shape). Exercise appears to be a strong protective factor against osteoporotic fracture, although turning this into a viable intervention is difficult. Femoral fracture is associated with an excess mortality of 20% in women and 35% in men in the first year; this occurs particularly in the first six months. An excess mortality is also associated with vertebral fracture.

Consequences of osteoporotic factors include pain which is no less severe than in any other fracture, loss of mobility and social isolation. The cost of osteoporotic fractures in the UK has risen from £750m in 1995 to £950m in 1999. Most of this is due to the cost of hip fractures and is mainly due to out-of-hospital costs, especially nursing home care. Twenty per cent of the cost is attributable to fractures in men, amongst whom the incidence of osteoporotic fracture is now increasing faster than in women. The medical approach to patients with osteoporotic fractures should first of all be relief of symptoms, particularly pain relief, which may need to be prolonged. The next priority is prevention of falls injury, including investigation of falling tendency and environmental assessment. The final priority is the treatment of the osteoporosis itself.

Treatment studies include those measuring changes in bone density, which can be done quite quickly, and those recording fracture incidence, which tend to be larger and take more time. However, treatment studies have again frequently failed to include older individuals. All the large trials of bisphosponates have included less than 400 over 75-year-olds between them. Little evidence has been collected for the use of hormone therapy in this age group but there is more evidence for the use of calcium and vitamin D. Four major trials were published. Chapuy and Meunier showed a reduction of 30% in incidence of non vertebral and hip fracture over three years amongst nursing home residents given oral calcium and vitamin D.[21] Heikinheimo et al.[22] showed a 20% reduction in fracture with yearly administration of intramuscular vitamin D, and a Massachusetts community study[23] showed a 50% reduction in fractures compared with placebo in a population of active elderly treated with calcium and vitamin D. However, one well designed study from Amsterdam[24] has failed to demonstrate any benefit from vitamin D alone.

The cost of primary prevention of fracture using oral calcium and vitamin D is high at £22,379 per hip fracture prevented. It is more economically attractive if one only targets therapy at high-risk groups such as nursing home residents, or if further trials of yearly intramuscular vitamin D proves its efficacy. Such a trial to determine the efficacy of yearly vitamin D injection given with the influenza vaccine is presently underway in Warwickshire. Multicentre trials of calcium carbonate and vitamin D for secondary prevention of fracture are also in progress. Hip protectors reduce the incidence of hip fractures by 44% when worn, but compliance is poor.[25]

THE LILLY LECTURE: ACHIEVING CLINICAL EVIDENCE IN THE OLDER PERSON
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Disability and cognitive decline are the twin scourges of old age. When questioned, 80% of women over 75 years of age stated that they would rather be dead than disabled and placed in a nursing home following a hip fracture. However, the prevalence of severe disability in the over 80s is over 13%. The prevalence of mild disability is even higher, with gait disturbance present in 24.2% of those aged between 75 and 84 years and 51.6% in those 85 years and over. In the US a 65-year-old man can expect a mean life expectancy of 14 years, of which 2.1 years will be spent disabled. The life expectancy of a woman of the same age is 17.8 years, of which 4.2 years on average will be associated with significant disability. Disability in the elderly is complex and multifactorial, but simple interventions may be available to address these. However, assessing the effectiveness of such interventions may be complicated by the arbitrary definitions of severe disability used.

Another challenge facing geriatric medicine is in the management of dementia. There is a prevalence of dementia of between 10% and 12% in the over 80s. However, this prevalence varies according to criteria used, with a ten-fold difference in prevalence found when using DSM-III criteria versus ICD-10.[26] The prevalence of cognitive impairment but no dementia (CIND) in the over 65s is 16.8%, more than twice the prevalence of frank dementia. It is arguable that the difference between cognitive impairment and dementia is more quantitative rather than qualitative and that cognitive deterioration in the elderly should be regarded as a continuum rather than a matter of 'Yes' or 'No'.

Whilst the problems of dementia and disability in the elderly are complex and multifactorial, simple interventions may be effective. What is essential in any study is to establish clear definitions of both objective and intervention prior to commencement. It is also important to ensure that the intervention studies, particularly lifestyle interventions, are sustainable in the long term and are therefore realistic.

Large treatment studies of hypertension and hyperlipidaemia have not examined disability and cognitive decline amongst their outcome measures. Exceptions to this include the SystEur study,[27] which demonstrated a significant reduction in the development of cognitive impairment following treatment of systolic hypertension with nitrendipine. The Scandinavian Simvastatin Survival Study (4S)[15] of the effects of cholesterol lowering demonstrated that the number of patients who required to be treated to prevent one vascular event in the over 60s was lower than in the younger age group, although the cost per year of life gained may not be as favourable. The new PROSPER[19] study has included disability and cognitive decline as end points.

Past studies of complex interventions in geriatric medicine frequently do not include sufficient specification of what has been done to permit replication. Whilst we know that interventions such as geriatric assessment units and stroke units significantly reduce the incidence of death and institutionalisation we do not exactly know why. Future studies examining clearly defined processes of care have been performed in delirium and have recently been commenced in stroke but such studies are necessary throughout geriatric medicine to achieve adequate standards of clinical evidence.

COLONIC CARCINOMA IN THE ELDERLY – WHO SHOULD HAVE SURGERY?
Mr M. Dunlop, Western General Hospital, Edinburgh

Scenario 4: An 86-year-old lady presents with distended abdomen and symptoms suggestive of large bowel obstruction. She gives a two year history of iron deficiency anaemia (diagnosed by FBC and ferritin by her GP). She has evidence of lymph node and liver metastases. She

goes for operation and undergoes resection and end colostomy (Hartmann's operation). When told the diagnosis she asks whether earlier investigation, done when she presented two years ago, would have made a difference. Despite her age she was given a colostomy which she cannot manage and was upset to be diagnosed with a terminal disease.

If you had seen this lady when she was 84 years old initially presenting with anaemia would you have:

1. checked her FBC and ferritin and treated her with iron, as did her GP?
2. checked her FBC, ferritin and tumor markers?
3. referred her to hospital for large bowel investigation for prognostic reasons?
4. referred her for investigation with a view to hemicolectomy?

Thirty thousand people are diagnosed with colorectal cancer annually in the UK, of whom half are over the age of 70. About 300,000 people are investigated for it annually. Whilst survival has improved from 33% to 44% in the last 30 years, 30% of patients still present with liver metastases and 30% of the remainder will develop them despite intervention.[28] The absolute five year risk for developing colonic cancer in patients in their 70s is 1.5%, and 2% for patients in their 80s. As many as one in ten patients in their 80s may have a bowel tumour *in situ*.

An increasing number of elderly patients are undergoing surgery for their colorectal carcinomas with the objective of cure rather than non-surgical management. There is also an increasing use of palliative resections in the elderly, as this proves more effective than non-surgical palliation. Although they do not present with more advanced cancer, the relative surgical mortality and morbidity for the over 80s is poor compared with the under 60s (28% versus 50%). This is mainly due to co-morbidity rather than age itself. Operative mortality in elective surgery in 80-year-olds is about twice that of the general population but is still less than 10%. Mortality in the over 80s undergoing emergency surgery may be as high as 33% and only 29% of these return to independent living, compared to 76% of those undergoing elective surgery returning to independence.[27] Patients who are independent prior to elective surgery tend to regain their independence.

In summary, emergency surgery in the elderly is associated with greatly increased mortality, morbidity and loss of independence, and accordingly should be avoided. Elderly patients presenting with anaemia or rectal bleeding are more likely to have colorectal carcinoma than younger patients and should be investigated accordingly. Presentation with anaemia has not been found to be associated with a worse prognosis. Staging investigations should be the same as in younger patients and thorough pre-operative assessment is essential. Tumour markers are unhelpful in the diagnosis of bowel cancer.

LUNG CANCER IN THE OLDER PERSON – HOW MUCH TREATMENT?
Dr D. Eraut, Southend Hospital

Scenario 5: A 75-year old man presents with a brief single haemoptysis. He is a smoker with mild COPD. Past medical history of MI ten years ago. Examination reveals finger clubbing. No other abnormal signs. CXR shows a cavitated lesion above right hilum. Blood tests reveal an isolated raised calcium of 2.7 mmol/l (corrected). FEV1/FVC: 1.75/3.4 (predicted 2.5/3.65). Bronchoscopy: tumour seen in RUL. Biopsies: poorly differentiated squamous carcinoma. CT: 3 cm tumour RUL with adjacent 1 cm enlarged hilar node. No other CT evidence of tumour. How should he be managed?

1. Referred for surgery?
2. Referred for radical radiotherapy?
3. Referred for palliative radiotherapy?
4. Referred for chemotherapy +/- radiotherapy?
5. Requires further investigation, e.g. bone scan/ mediastinoscopy/cardiology assessment?

Carcinoma of the bronchus is now the commonest form of internal cancer. Ninety-five per cent occurs in current or ex-smokers and over 40% in the over 75 age group.[29] Seventy per cent present with respiratory symptoms and 13% with metastatic disease. Ninety-eight per cent of patients have an abnormality on chest X-ray; in 43% an isolated mass is seen. Obtaining a histological diagnosis of tumour where practicable is important, as patients over 75 years with no histological diagnosis have only a 5.4% chance of receiving treatment compared with 37% of under 75s without histology. Current recommendations are that all patients with lung cancer, regardless of age, should be seen by a chest physician. Such patients are significantly more likely to receive both a histological diagnosis and treatment.

Two year survival for lung cancer is less than 10%, and only 10% to 12% of patients are referred for surgery. If a patient is aged over 65 the overall chance of their being referred for surgery is halved. Operative mortality is <10% in the over 70s, less than 3% in some centres, and is not significantly higher than in younger age groups. However, those chosen for surgery over the age of 70 represent a highly selected group.[30]

Radiotherapy is associated with a one year survival of between 60% and 80%, although three and five year survival is not as good as for surgery. Radiotherapy results in the elderly are similar to those in younger people but mortality and morbidity is higher as a result of co-morbidity. Palliative radiotherapy is given to nearly 50% of people with lung cancer. It is useful in the treatment of haemoptysis, superior venacaval obstruction, bronchial obstruction and sometimes cough or dysphagia. It is also useful in extra-thoracic disease.

Chemotherapy is more useful for small-cell carcinoma either in combination with radiotherapy or without. Although not as well tolerated in the elderly as in younger people, chemotherapy has been found to be tolerated in over 40% of the over 75s.[31]

BREAST CANCER IN OLDER WOMEN – SHOULD WE BE SCREENING?
Dr D.J. Torgerson, University of York

Scenario 6: The mother of your consultant colleague has rung you up to ask why she has not had breast cancer screening. She is 75 years old and has just seen another consultant from the same hospital defend breast screening

following a report that it may not save lives after all. Do you tell her:

1. breast cancer screening is a waste of money and the early trials were hopelessly flawed, and efforts should concentrate on good treatment once cancer is diagnosed?
2. breast cancer screening does save lives and improve quality of life, but only for those less than 60 years?
3. breast cancer screening is even more beneficial for the older lady and she should receive an invitation soon from the expanded programme?
4. breast cancer screening is beneficial for older women but being rationed in the NHS so she should go privately?

A recent meta-analysis published in *The Lancet* has cast doubt on the effect of screening for breast cancer.[32] In particular it suggested evidence for subversion of randomisation in some of the controlled trials of screening. In only two of eight trials could properly conducted randomisation and unbiased comparison of screening be proven. Although 130,000 subjects were included in these two trials, no significant beneficial effect of screening could be identified. If baseline risk of breast cancer is higher than 0.4% per annum, however, some suggestion exists that screening may be of some benefit. This absolute risk is found in the older population who are currently excluded from breast cancer screening in the UK.

The stated reason for excluding elderly women is expected poor compliance. This would be important if it increased the cost of the programme or reduced detection. However, this is not the case for breast cancer where those most likely to develop breast cancer, i.e. those in the higher socio-economic groups, are those most likely to attend for screening. Costs can be controlled by inviting women called for screening to make their own appointments rather than sending out fixed appointments. This has the potential to reduce the number of missed appointments from 20% to 2%, and hence frees resources for older women. Pilot studies have shown an uptake of >60% amongst older women invited for screening. Unfortunately, the evidence for breast cancer screening must now be considered to be weak, and a further well conducted large randomised trial is necessary. If screening is to continue there is no evidence for the exclusion of older women; indeed it is in this age group that it appears likely to be most effective.

INTERACTIVE DEBATE: THROMBOLYSIS FOR ACUTE STROKE
Professor G.A. Ford vs. Dr K. Fullerton

Scenario 7: Intravenous thrombolysis with alteplase (rt-PA) for older patients with ischaemic stroke:

1. cannot be justified;
2. only in clinical trials;
3. useful but not a priority;
4. introduced immediately;
5. no views on the matter.

Scenario 8: If your elderly mother or father had an ischaemic stroke of moderate-to-severe severity and could be treated within three hours of symptom onset at a hospital with stroke thrombolysis expertise, should they receive treatment with intravenous alteplase (rt-PA)?

1. Yes.
2. No.
3. Randomised controlled trial.
4. Don't know/it depends.

SELECTED OLDER PEOPLE WITH STROKE SHOULD NOT BE DENIED THROMBOLYSIS
Professor G.A. Ford, University of Newcastle upon Tyne

Until now acute stroke has been considered untreatable, and whilst there is debate about the balance of risk and benefit from thrombolysis, it is clear that a reperfusion strategy modifies outcome in some patients. Greater than 80% of older people who suffer moderate-to-severe stroke are left dead or disabled. Prospective studies of intravenous rt-PA have included >2,700 patients to this point. Only the NINDS (n=624)[33] trial used a dose of 0.9 mg/kg in a time window of less than three hours from onset (mean: 90 minutes). The study showed a significant improvement in outcome and no increase in mortality. Others have shown no improvement in primary outcome but improvements in secondary outcome. ECASS 1[34] had a high proportion of protocol violators, particularly amongst patients with extensive early CT changes who had a higher rate of complications, and overall the study demonstrated no benefit for rt-PA in a six hour time window. ECASS 2[35] showed a positive effect on pre-morbid handicap on *post hoc* analysis in a six hour window. Meta-analysis of studies containing populations receiving rt-PA within a three hour time window demonstrate improved outcome in the treatment group.[36]

The evidence is much less clear for a three to six hour window. The number which have to be treated with rt-PA to obtain an additional patient with good outcome is only eight, and this compares favourably to thrombolysis for myocardial infarction. The NINDS results have been duplicated in practice in many centres, although a study from Cleveland, Ohio has recently shown excess mortality in the thrombolysed group.

Intracerebral haemorrhage is a concern following administration of rt-PA. In the NINDS study 6% of patients in the treatment group suffered an intracerebral haemorrhage, compared with 0.6% in the non-treatment group, and half of these patients died. However, overall mortality was not increased, mainly because the rate of development of cerebral oedema and trans-tentorial herniation was greatly reduced. Consensus exists for a lack of a role for streptokinase as a thrombolytic in stroke. All studies examining its use have shown increased mortality in the treatment group. It has a long half-life and causes hypotension, which is almost certainly an undesirable complication in the early stages of acute stroke.

THROMBOLYSIS SHOULD NOT BE IMPOSED ON OLDER PEOPLE WITH STROKE
Dr K. Fullerton, Queen's University, Belfast

Whilst the NINDS[33] trial was positive, all other trials of rt-PA following stroke have been equivocal and positive results

were only found on *post hoc* analysis. When meta-analysis is performed on all rt-PA studies [37] administered in all time windows, a clear increase in the rate of intracerebral haemorrhage is demonstrable, including fatal haemorrhage, and whilst there is no statistically significant difference in mortality between groups, there is a slight trend to increased early and overall mortality in the treatment group. This trend may become significant with further studies. Patients receiving rt-PA derive a very small benefit in terms of death or dependency, but the risks associated with it are very considerable.

The resources necessary to provide a thrombolysis service are considerable[38] and require considerable expenditure in terms of staffing and infrastructure. The proportion of patients eligible to receive thrombolysis is very small, maybe as small as 2%. It is hard to justify such expenditure for such a small number of patients given the competing demands within the health service, and even within stroke care and prevention. Far more effect may be achieved by expending these resources into more and improved stroke units and in primary and secondary prevention.

APPENDIX: AUDIENCE VOTES ON SCENARIOS PROVIDED

	Scenario 1 Atrial fibrillation		Scenario 2 Lipid lowering		Scenario 3 Hip fracture		Scenario 4 Colorectal carcinoma	
Choice	Pre-lecture	Post-lecture	Pre-lecture	Post-lecture	Pre-lecture	Post-lecture	Pre-lecture	Post-lecture
n	115	114	123	126	122	123	106	115
1	7.0%	14.9%	40.7%	34.9%	4.1%	4.1%	4.7%	0.9%
2	53.0%	56.1%	37.4%	53.2%	31.1%	67.5%	9.4%	0.9%
3	29.6%	22.8%	22.0%	11.9%	27.0%	7.3%	44.3%	46.1%
4	1.7%	0.9%			0.8%	0.0%	41.5%	52.2%
5	8.7%	5.3%			36.9%	21.1%		

	Scenario 5 Lung cancer		Scenario 6 Breast cancer screening		Scenario 7 Thrombolysis for stroke (1)		Scenario 8 Thrombolysis for stroke (2)	
Choice	Pre-lecture	Post-lecture	Pre-lecture	Post-lecture	Pre-debate	Post-debate	Pre-debate	Post-debate
n	112	109	112	109	75	72	76	71
1	17.9%	53.2%	17.9%	53.2%	0%	2.8%	48.7%	39.4%
2	7.1%	19.3%	7.1%	19.3%	42.7%	59.7%	6.6%	21.1%
3	18.8%	8.3%	18.8%	8.3%	21.3%	22.2%	30.3%	33.8%
4	48.2%	6.4%	48.2%	6.4%	25.3%	13.9%	14.5%	5.6%
5					10.7%	1.4%		

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