

Clinical review

Recent advances

Geriatric medicine

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BMJ 2001;322:86-9

The number of people older than 65 years is increasing, and the proportion of people older than 85 is increasing exponentially.^{1,2} In response to this challenge, clinicians need to assess and optimise health care for this group.

Methods

I reviewed the contents of *ACP Journal Club* and *Evidence Based Medicine* from 1998 to 2000 and, after discussion with colleagues, selected articles that I believed to be relevant to the care of geriatric patients. It is not possible to give a comprehensive review of all recent advances here, but additional articles are listed on the *BMJ's* website.

Cardiovascular risk

Several studies have shown the benefits of angiotensin converting enzyme inhibitors in patients with left ventricular dysfunction, but the findings of the heart outcomes prevention evaluation study provide evidence for the use of ramipril in patients at high risk of cardiac events who do not have left ventricular dysfunction. Treatment with ramipril decreased the risk of death (number needed to treat 56, 95% confidence interval 32 to 195), myocardial infarction (42, 27 to 89), and stroke (67, 43 to 145) compared with placebo.³

Cholesterol

A subgroup analysis of data on patients older than 65 from the cholesterol and recurrent events trial has been published recently.⁴ The study was a randomised, double blind, placebo controlled trial in which patients with a recent history of myocardial infarction and average cholesterol concentrations were allocated to either pravastatin 40 mg/day or placebo and subsequently followed for the development of major coronary events. Among the 1283 patients aged between 65 and 75 years, those randomised to pravastatin had reduced risks of major coronary events (number needed to treat 11, 95% confidence interval 8 to 24) and stroke (34, 22 to 333) at a median follow up of five years compared with patients who received placebo.⁴ This study provides an example of how a constant reduction in relative risk of morbidity or mortality across different age groups will result in a greater absolute risk reduction (and a smaller number needed to treat) in elderly people because they have a higher baseline risk of the outcome event.

Recent advances

Statins decrease the risk of stroke and major coronary events in elderly people

Diuretics are effective first line drugs for hypertension but are underused

Stroke units decrease the risk of long term institutional care, dependency, and death

Calcium and vitamin D decrease the risk of non-vertebral fractures in healthy people over 65

A recent systematic review of randomised trials evaluating the use of statins to reduce cholesterol concentrations has shown that these drugs decrease the risk of stroke (number needed to treat 186, 109 to 662) and death (151, 78 to 2302) at a mean follow up of 3.3 years.⁵ However, although there is good evidence for using lipid lowering drugs in elderly people, they are consistently underused.⁶

Hypertension

Clinical practice guidelines for the management of hypertension prepared by various organisations suggest use of diuretics or β blockers as first line treatment for patients with hypertension unless they have coexistent illnesses or other contraindications.^{7,8} However, as with lipid lowering drugs, diuretics are underused despite evidence that they reduce the risk of stroke and cardiovascular mortality.⁹ A recent systematic review of randomised trials evaluating diuretics and β blockers as first line drugs in patients aged 60 years or older found that diuretics reduced the risk of stroke, coronary heart disease, and all cause mortality whereas β blockers reduced only the risk of stroke.¹⁰ Thiazides were also found to be the most effective first line drugs for hypertension in a systematic review that looked at randomised trials of diuretics, β blockers, calcium channel blockers, and angiotensin converting enzyme inhibitors.¹¹

Heart failure

Congestive heart failure is a common cause of morbidity and mortality in elderly people. Two systematic reviews of 18 randomised trials that evaluated β blockers

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Further references
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osteoporosis are
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BMJ's website

in patients with congestive heart failure who were already receiving diuretics and angiotensin converting enzyme inhibitors showed a decrease in mortality and hospital admission (table).^{12, 13} In a recently published randomised trial of extended release metoprolol versus placebo in patients with symptomatic chronic heart failure and stabilised with standard treatment (ejection fraction of $\leq 40\%$), metoprolol was found to decrease the risk of death and of the combined end point of total mortality and all cause hospital admissions.^{14, 15} In a pre-defined subgroup analysis, no significant increase in total mortality was observed in patients older than 70 years, although the confidence intervals for this estimate were wide. This evidence supports the use of β blockers in patients with heart failure who are receiving diuretics and angiotensin converting enzyme inhibitors.

Spirolactone has also been shown to reduce mortality in patients with congestive heart failure.¹⁶ A trial was conducted in 1663 patients with severe heart failure and an ejection fraction less than 35% and who were receiving angiotensin converting enzyme inhibitors and loop diuretics (if tolerated). Spirolactone reduced all cause mortality (number needed to treat 9, 7 to 16) and hospital admissions for cardiac causes (13, 8 to 27).¹⁶ Clinicians and patients need to consider the severity of heart failure, the risks and benefits of treatments, and the patient's values when making decisions about the use of spironolactone and β blockers in the management of heart failure.

Stroke

A systematic review published in 1997 showed that specialised stroke units decrease the risk of death, dependency, and the need for long term institutional care compared with care on a general medical ward.¹⁷ One of the studies included in this review has recently published the long term effects of admission to a stroke unit. Two hundred and twenty patients with acute stroke were randomised to care in a specialised stroke unit or to usual care on a general medical ward.¹⁸ Stroke unit care improved long term survival and quality of life and increased the number of patients living at home (number needed to treat 6, 4 to 21) at five years. Stroke units also improved survival and increased the proportion of patients able to live at home 10 years after their stroke.¹⁹

Dementia

The association between apolipoprotein E and Alzheimer's disease is well established. A blinded comparison of the diagnostic accuracy of Apo E genotypes and clinical findings with pathological findings at necropsy found that although Apo E testing increased the specificity of the clinical diagnosis it decreased the sensitivity.²⁰ Given the current state of the evidence, genotype testing cannot be recommended for routine clinical use.

Various drugs have been evaluated for treating this disorder, but most of the evidence is on the use of cholinesterase inhibitors. Tacrine was the first of these drugs to be assessed, but many patients cannot tolerate it because of severe adverse effects.²¹ Several studies have looked at other cholinesterase inhibitors including donepezil,²² metrifonate,²³ and rivastigmine.²⁴ All these drugs produce similar, small improvements in cognition

Effect of β blockers on mortality and hospital admission in patients aged over 75 with congestive heart failure¹³

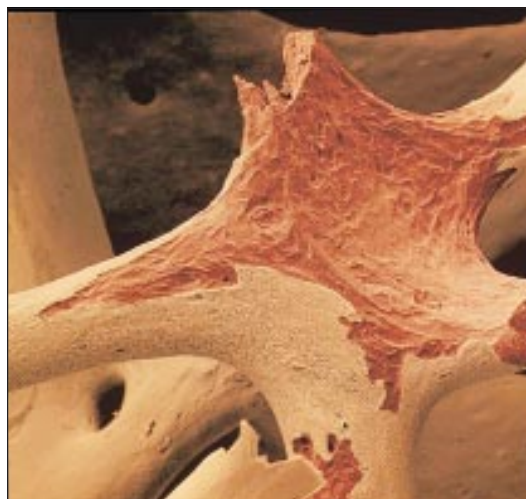
Outcome	weighted event rate (%)		% reduction in relative risk (95% CI)	No needed to treat (95% CI)
	Placebo	β blocker		
Mortality at 13 months	12.6	8.2	25 (7 to 40)	32 (19 to 93)
Hospital admission at 20 months	28.8	18.1	37 (24 to 48)	11 (8 to 18)

and behaviour. Further research is needed to look at longer follow up periods and at how patients should be selected for these treatments. If patients with mild to moderate Alzheimer's disease are interested in treatment with a cholinesterase inhibitor, clinicians should discuss the potential risks and benefits of treatment with them and explore the patients' values and the outcomes that are important to them before starting treatment.

Osteoporosis

Osteoporosis is an important public health concern in older women. Several advances have been made in the prevention and treatment of this condition over the past few years. A randomised, double blind, placebo controlled study of 445 people older than 65 living in the community evaluated the effectiveness of calcium and vitamin D supplementation in reducing non-vertebral fractures.²⁵ Participants were randomised to either elemental calcium 500 mg/day and vitamin D 700 IU/day or to placebo and were followed up for three years. The risk of non-vertebral fractures was decreased in people who received calcium and vitamin D compared with patients who received placebo (number needed to treat 15, 8 to 12).

The fracture intervention trial assessed 2027 postmenopausal women with osteoporosis who were randomised to alendronate or placebo.²⁶ All women who had a daily calcium intake of less than 1000 mg/day were also given calcium and vitamin D supplementation. The study showed that alendronate decreased the risk of fracture (vertebral and hip) compared with placebo. A subgroup analysis reported that alendronate was effective across all age groups (see *BMJ's* website for further details).²⁷ Alendronate can cause gastrointestinal side effects, and patients are therefore advised not to lie down for 30 minutes after



Fractured brittle and spongy bone from patient with osteoporosis



Elderly people benefit from exercise

taking the drug. This may make it difficult for some people to adhere to treatment.

The multiple outcomes of the raloxifene evaluation study recently showed that raloxifene, a selective oestrogen receptor modulator, can decrease the risk of fracture in postmenopausal women with osteoporosis (number needed to treat 29, 20 to 52).²⁸ Raloxifene was shown to decrease the risk of vertebral fractures but not non-vertebral fractures. The investigators also found that raloxifene decreased the risk of breast cancer (123, 74 to 253).²⁹ However, the drug increased the risk of venous thromboembolism (number needed to harm 155, 101 to 363), which makes it an unsuitable alternative to alendronate for the treatment of osteoporosis alone. Additionally, women who want the vasomotor and urogenital effects of oestrogen may not wish to take raloxifene.

Falls

Falls are the leading cause of accidental death among people aged 75 years or older and are also responsible for appreciable morbidity including fracture, impaired mobility, fear of falling, and admission to long term care facilities.³⁰⁻³² The morbidity and mortality associated with falls result in large costs for the healthcare system, and they are a major public health concern.³³ A recent systematic review suggested that compared with usual care, complex interventions that targeted modification of multiple risk factors on the basis of individual health assessments decreased the number of people who fell.³⁴ However, the limited number and size of the studies makes it difficult to determine which components are the most effective in decreasing the risk of falls. Indeed, a systematic review recently identified over 400 variables that have been investigated as potential risk factors including sensory impairment, dizziness, mobility impairment, and cognitive impairment.³⁵ Further evidence is also needed to determine which interventions can decrease the risk of injury (including fractures) from falls. Parker and colleagues have suggested that external hip protectors may decrease hip fractures among elderly people in nursing homes.³⁶ However, compliance with these cumbersome devices is low.

Conclusions

Although we have evidence about the effectiveness of some interventions in elderly people, and many advances have been made in the care of elderly people,

many gaps in our knowledge remain. We need to encourage research in elderly people and encourage our elderly patients to participate in this research. In particular, we need to encourage the inclusion of frail elderly people (those with complex medical and psychosocial problems) in studies assessing interventions, prognosis, and quality of life.

I thank Ken Locke for his comments on earlier drafts of the manuscript and Aleksandra Lalovic for secretarial help. SES is funded by a career scientist award from the Ontario Ministry of Health and Long Term Care.

Competing interests: None declared.

- 1 Bureau of the Census. *Current population reports. 65-plus in America*. Washington DC: US Government Printing Office, 1993.
- 2 *Partnerships in long-term healthcare*. Toronto: Ministry of Health, 1993.
- 3 The Heart Outcomes Prevention Evaluation Study Investigators. Effect of an angiotensin-converting-enzyme inhibitor, ramipril, on death from cardiovascular causes, myocardial infarction, and stroke in high-risk patients. *N Engl J Med* 2000;342:145-53.
- 4 Lewis SJ, Moye LA, Sacks FM. The effect of pravastatin on cardiovascular events in older patients with myocardial infarction and cholesterol levels in average range. Results of the Cholesterol in Recurrent Events Trial. *Ann Intern Med* 1998;129:681-9.
- 5 Hebert PR, Gaziano JM, Chan KS, Hennekens CH. Cholesterol lowering with statin drugs, risk of stroke, and total mortality. An overview of randomised trials. *JAMA* 1997;278:313-21.
- 6 Lemaitre RN, Furberg CD, Newman AB, Hulley SB, Gordon DJ, Gottdiener JS, et al. Time trends in the use of cholesterol-lowering agents in older adults: the cardiovascular health study. *Arch Intern Med* 1998;158:1761-8.
- 7 Ramsay LE, Williams B, Johnston GD, Macgregor GA, Boston L, Potter JF, et al. British Hypertension Society guidelines for hypertension management 1999: summary. *BMJ* 1999;319:630-5.
- 8 The sixth report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med* 1997;157:243-6.
- 9 Psaty BM, Savage PJ, Tell GS, Polak JF, Hirsch CH, Gardin JM, et al. Temporal patterns of antihypertensive medication use among elderly patients. The cardiovascular health study. *JAMA* 1993;270:1837-41.
- 10 Messerli FH, Grossman E, Goldbourt U. Are beta-blockers efficacious as first-line therapy for hypertension in the elderly? A systematic review. *JAMA* 1998;279:1903-7.
- 11 Gueyffier F, Bulpitt C, Boissel J-P et al for the INDANA Group. Antihypertensive drugs in very old people: a subgroup meta-analysis of randomised controlled trials. *Lancet* 1999;353:793-6.
- 12 Lechat P, Packer M, Chalon S, Cucherat M, Arab T, Boissel JP, et al. Clinical effects of beta-adrenergic blockade in chronic heart failure. A meta-analysis of double-blind, placebo-controlled, randomised trials. *Circulation* 1998;98:1184-91.
- 13 Review: Beta-blockers reduce mortality in morbidity in congestive heart failure. *ACP J Club* 1999;130:7. Abstract of: Avezum A, Tsuyuki RT, Pogue J, Yusuf S. Beta-blocker therapy for congestive heart failure: a systematic overview and critical appraisal of the published trial. *Can J Cardiol* 1998;14:1045-53.
- 14 Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF). Effect of metoprolol CR/XL in chronic heart failure. *Lancet* 1999;353:2001-7.
- 15 Hjalmarson A, Goldstein S, Fagerberg B, Wedel H, Waagstein F, Kjekhus J, et al. Effects of controlled release metoprolol on total mortality, hospitalisations, and well-being in patients with heart failure: the Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF). *JAMA* 2000;283:1295-1302.
- 16 Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, et al for the Randomised Aldactone Evaluation Study Investigators. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. *N Engl J Med* 1999;341:709-17.
- 17 Stroke Unit Trialists' Collaboration. Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke. *BMJ* 1997;314:1151-9.
- 18 Indredavik B, Sjordahl SA, Bakke F, Rokseth R, Haheim LL. Stroke unit treatment. Long-term effects. *Stroke* 1997;28:1861-6.
- 19 Indredavik B, Sjordahl SA, Bakke F, Rokseth R, Haheim LL. Stroke unit treatment. 10 year follow-up. *Stroke* 1999;30:1524-7.
- 20 Mayeux R, Sonders AM, Shea S, Mirra S, Evans D, Roses AD, et al. Utility of the apolipoprotein E in the genotype in the diagnosis of Alzheimer's disease. *N Engl J Med* 1998;338:506-11.
- 21 Lopez Arrieta J, Rodriguez Rantalejo F. Methodology, results and quality of clinical trials of tacrine in the treatment of Alzheimer's disease: a systematic review of the literature. *Age Ageing* 1998;27:161-79.
- 22 Rogers SL, Doody RS, Mohs RC, Friedhoff LT and the donepezil study group. Donepezil improves cognition and global function in Alzheimer disease: a 15-week, double-blind, placebo-controlled study. *Arch Intern Med* 1998;158:1021-31.
- 23 Raskind MA, Cyrus PA, Ruzicka BB, Gulanski BI for the metrifonate study group. The effects of metrifonate on the cognitive, behavioural, and functional performance of Alzheimer's disease patients. *J Clin Psychiatry* 1999;60:318-25.

- 24 Rosler M, Anand R, Cicin-Sain A, Gauthier S, Agid Y, Dal-Bianco P, et al. Efficacy and safety of rivastigmine in patients with Alzheimer's disease: international randomised controlled trial. *BMJ* 1999;318:633-40.
- 25 Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. *N Engl J Med* 1997;337:670-6.
- 26 Black DM, Cummings SR, Karpf DB et al. Randomised trial of effective alendronate on risk of fracture in women with existing vertebral fractures. Fracture intervention trial research group. *Lancet* 1996;348:1535-41.
- 27 Ensrud KE, Black DM, Palermo L, Bauer DC, Barrett-Connor E, Quandt SD, et al. Treatment with alendronate prevents fractures in women at highest risks. Results from the fracture intervention trial. *Arch Intern Med* 1997;157:2617-24.
- 28 Ettinger B, Black DM, Midlak BH, Knickerbocker RK, Nickelson T, Genant HK, et al for the Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene. Results from a three-year randomised clinical trial. *JAMA* 1999;282:637-45.
- 29 Cummings SR, Eckert S, Krueger KA et al. The effect of raloxifene on risk of breast cancer in postmenopausal women. Results from the MORE randomised trial. *JAMA* 1999;281:2189-97.
- 30 Cryer PC, Davidson L, Styles CP, Langley JD. Descriptive epidemiology of injury in the south east: identifying priorities for action. *Public Health* 1996;110:331-8.
- 31 Kannus P, Parkkari J, Koskinen S, Niewi S, Palvaneri M, Jarvinen M, et al. Fall-induced injuries and deaths among older adults. *JAMA* 1999;281:1895-9.
- 32 Tinetti ME, Williams CS. Falls, injuries due to falls and the risk of admission to a nursing home. *N Engl J Med* 1997;337:1279-84.
- 33 Rizzo JA, Friedkin R, Williams CS, Nabors J, Acampora D, Tinetti ME. Health care utilisation and costs in a Medicare population by fall status. *Med Care* 1998;36:1174-88.
- 34 Gillespie LD, Gillespie WJ, Cumming R, Lamb SE, Rowe BH. Interventions to reduce the incidence of falling in the elderly. In: Cochrane Collaboration. *Cochrane Library*. Issue 2. Oxford: Update Software, 2000.
- 35 NHS Centre for Reviews and Dissemination. Preventing falls and subsequent injury in older people. *Effective Health Care* 1996;2(4):1-16.
- 36 Parker MJ, Gillespie LD, Gillespie WJ. Hip protectors for preventing hip fractures in the elderly. In: Cochrane Collaboration. *Cochrane Library*. Issue 2. Oxford: Update Software, 2000.

Lesson of the week

Pulmonary Wegener's granulomatosis misdiagnosed as malignancy

S Uppal, N Saravanappa, J P Davis, C K T Farmer, D J A Goldsmith

Wegener's granulomatosis is a systemic vasculitis that primarily involves the upper and lower respiratory tracts and kidneys. Pulmonary Wegener's granulomatosis can present with multifocal lung involvement or solitary lung lesions with no evidence of extrapulmonary disease.¹ Diagnosing Wegener's granulomatosis on the basis of cytological material obtained from fine needle aspiration or sputum may present a challenging problem to the pathologist. A wrong diagnosis may lead to inappropriate treatment for the patient. We describe two patients with Wegener's granulomatosis originally diagnosed as malignancy.

Case reports

Case 1

A 70 year old woman presented with an 18 month history of intermittent productive cough and pain of the left lower chest. Clinical examination of the chest gave normal results. A chest x ray film showed a hazy left base with loss of radiological markings of the left hemidiaphragm and left heart border. A computed tomogram showed three nodules within the lungs: one at the right apex, one in the apical segment of the left lower lobe, and one in the posterobasal segment of the right lower lobe. The nodules were non-enhancing and had irregular margins. Fibreoptic bronchoscopy gave normal results. Bronchial washings showed no acid fast bacilli or malignant cells. Fine needle aspiration of the lesion in the right lower lobe guided by computed tomography showed foamy and epithelioid histiocytes together with a few groups of cells with an increased nuclear to cytoplasmic ratio. Prominent nucleoli were identified, which were suggestive but not diagnostic of adenocarcinoma. Positron emission tomography was performed, which showed multiple, bilateral lung nodules with no evidence of extrapulmonary lesions. A metastatic pulmonary adenocarcinoma from an unknown primary was diagnosed. A conservative "wait and watch" policy was adopted.

Twelve weeks later the patient presented to the department of otorhinolaryngology with nasal congestion which had failed to respond to nasal steroids and antibiotics. Examination showed a saddle nose deformity with bilateral rhinosinusitis. The cytoplasmic antineutrophil cytoplasmic antibody titre suggested Wegener's granulomatosis. A biopsy sample of the nasal mucosa showed features consistent with the condition. The patient responded well to treatment with cyclophosphamide and high dose prednisolone.

Case 2

A 52 year old man presented with a seven week history of cough, dull chest pain, increasing shortness of breath on exertion, loss of weight, fever, and night sweats. There was no haemoptysis or nasal symptoms. A chest x ray film showed irregular lesions of the left apical and upper lobe. No hilar lymphadenopathy was evident. Sinus x ray films showed thickening of the mucosa. Sputum cytology showed atypical cells suspicious of bronchogenic carcinoma. Bronchoscopy was performed with an intention to proceed to left upper lobectomy or pneumonectomy if required. During the preanaesthetic check the patient was found to have raised blood pressure, splinter haemorrhages under the fingernails, a vasculitic skin rash on his legs, and ulcerated left nasal mucosa. Subsequent investigations showed proteinuria and increased blood urea and serum creatinine concentrations. A renal biopsy sample showed segmental or complete necrosis of glomeruli with fibrocellular crescent formation. Nothing was seen on immunofluorescence. The cytoplasmic antineutrophil cytoplasmic antibody titre gave a strongly positive result, and Wegener's granulomatosis was diagnosed. The patient was treated with cyclophosphamide and prednisolone. Over the following four months the lesion in the left apical chest resolved completely, and the patient improved.

Cytoplasmic antineutrophil cytoplasmic antibody tests can prevent misdiagnosis of Wegener's granulomatosis as malignancy

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BMJ 2001;322:89-90