

## NEWSLETTER

Supporting the Derbyshire Health Community

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### JAPC Update

The Joint Area Prescribing Committee (JAPC) is a countywide group covering Derbyshire County PCT and Derby City PCT. It provides recommendations on drugs and medicines management issues.

RED drugs are those where prescribing responsibility lies with a hospital consultant or a specialist. AMBER drugs are those that are initiated within a hospital/specialist setting but are suitable for shared care with a GP under a shared care agreement. GREEN drugs are regarded as suitable for primary care prescribing. BROWN drugs are those that JAPC does not recommend for use, except in exceptional circumstances, due to lack of data on safety, effectiveness, and/or cost-effectiveness.

The most recent updates are in the table below; the full list is available at

<http://www.derbyshirecountypct.nhs.uk/guidelines/default.asp>

The guidelines, formulary chapters, newsletters, etc can now be found via this link.

<b>Drug</b>	<b>Date considered</b>	<b>Decision</b>
Lacosamide	February 2008	RED
NuvaRing	February 2008	BROWN
Ropinirole XL	February 2008	GREEN (only on consultant recommendation)
Lanthanum	January 2009	AMBER (with Derby hospitals only: remains RED with Sheffield)
Eplerenone	December 2008	GREEN (only if spironolactone not tolerated)
Liothyronine	December 2008	AMBER (for depression)
Alitretinoin	November 2008	RED
Amantadine	November 2008	BROWN
Promixin	November 2008	BROWN
Rivaroxaban	November 2008	RED
Rosiglitazone	November 2008	BROWN

### Prevention of osteoporotic fragility fractures

After much consultation NICE has produced its guidance on the primary<sup>1</sup> and secondary<sup>2</sup> prevention of osteoporotic fragility fractures. They cover the use of bisphosphonates, strontium, raloxifene and teriparatide. These are complicated and we have tried to simplify the guidance as much as possible in the form of algorithms (see pages 7 and 8). The new guidance is more restrictive than the old NICE guidance but as they are in the form of Technology Appraisal Guidance, they are mandatory on the NHS.

Alendronate is the first-line drug for both primary and secondary prevention, provided certain criteria are met. Other bisphosphonates, strontium ranelate, raloxifene (secondary prevention only), and teriparatide (secondary prevention only) can only be used if further criteria are met. Raloxifene and teriparatide are not recommended at

all for the primary prevention of fractures in postmenopausal women. JAPC recommends that patients should be assessed against this new NICE guidance at their next review, and consulted to see whether they wish to continue with their current medication, if they do not meet the new criteria.

NICE has produced patient information leaflets, which can be found here

[www.nice.org.uk/nicemedia/pdf/TA160publicinfo.pdf](http://www.nice.org.uk/nicemedia/pdf/TA160publicinfo.pdf) and [www.nice.org.uk/nicemedia/pdf/TA161publicinfo.pdf](http://www.nice.org.uk/nicemedia/pdf/TA161publicinfo.pdf) .

This guidance does not apply to steroid-induced osteoporosis, which will be the subject of future NICE guidance.

1. [www.nice.org.uk/nicemedia/pdf/TA160quickrefguide.pdf](http://www.nice.org.uk/nicemedia/pdf/TA160quickrefguide.pdf)

2. [www.nice.org.uk/nicemedia/pdf/TA161quickrefguide.pdf](http://www.nice.org.uk/nicemedia/pdf/TA161quickrefguide.pdf)

### **Red drug audit**

You may have already participated in a PCT Medicines Management Team led audit on the prescribing of red drugs (specialist only) in primary care. JAPC has considered the results of this audit and were concerned that as the commissioning of these treatments is covered by contracts, primary care prescribing results in the PCTs paying twice. Red drugs are determined as specialist only for clinical and safety reasons. Some of the commonest red drugs prescribed were mycophenolate, tacrolimus and hydroxycarbamide, which are highly specialised drugs.

Requests for prescribing of red drugs in primary care should be politely referred back to the specialist/hospital trust. The PCT Medicines Management Teams are developing a template letter to support returning these requests. Please report any regular patterns of request for red drugs to your local PCT medicines management pharmacist or technician. The up to date traffic light list can be found here

<http://www.derbyshirecountypct.nhs.uk/traffic-light-classification-.asp> .

### **The ACCOMPLISH trial (N Engl J Med; 359: 2417-28)**

Hypertension is one of the most important risk factors for cardiovascular and renal diseases. Many clinical trials have examined the effects of antihypertensive drugs. One might ask whether we need another one? Studies comparing antihypertensive drugs with placebo have shown consistently that lowering blood pressure is associated with reductions in the incidence of coronary events, strokes, and congestive heart failure. The results of trials comparing the effects of different antihypertensive drugs or drug regimens have not been as consistent. Based on evidence and cost-effectiveness, thiazide diuretics are the first-line option for many people, although more than one drug may be needed to achieve targets.<sup>1</sup> ACCOMPLISH was designed to test the hypothesis that treatment with an ACE inhibitor combined with amlodipine would result in better CV outcomes than treatment with the same ACEI combined with a thiazide diuretic.

#### *Method*

- 11,506 participants from the U.S., Sweden, Norway, Denmark and Finland, representing 548 centres, were included in the trial.
- All patients had hypertension and were at high risk for CV events because of a history of coronary events, MI, revascularisation, stroke, impaired renal function, PAD, left ventricular hypertrophy or diabetes mellitus.
- Immediately on entering the study (without a washout period), patients were randomly assigned in a global one-to-one ratio to either of the two treatment groups, with assignments made centrally by telephone. Patients began treatment with either a combination of 20 mg of benazepril and 5 mg of amlodipine or a combination of 20 mg of benazepril and 12.5 mg of hydrochlorothiazide, once daily. As dictated by the protocol, the benazepril component in both groups was increased to 40 mg daily one month after randomisation. Thereafter, investigators could increase the amlodipine dose to 10 mg daily and increase the hydrochlorothiazide dose to 25 mg daily, if necessary, to attain a target blood pressure of less than 140/90 mm Hg (or a recommended target of 130/80 mm Hg for patients with diabetes or kidney disease).
- The addition of other antihypertensive agents was permitted (excluding any calcium-channel blockers, any ACE inhibitors, any angiotensin II-receptor blockers, and any thiazide diuretics but including beta-blockers, alpha-blockers, clonidine, and spironolactone). Loop diuretics taken once daily were permitted for volume management.
- The primary end point was measured as the time to the first event (which was defined as the composite of a cardiovascular event and death from cardiovascular causes). A cardiovascular event was defined as a nonfatal myocardial infarction, stroke, hospitalisation for unstable angina, coronary revascularisation, or resuscitation after sudden cardiac arrest.
- The study was funded by Novartis.

## Results

- 5,744 patients were assigned to the benazepril-amlodipine (BA) group and 5,762 to the benazepril-hydrochlorothiazide (BH) group.
- There were no significant differences in baseline characteristics between patients in the two treatment groups. The mean age was 68.4 years and 39.5% were women. Of note, 60.4% of the patients had a diagnosis of diabetes and 23.5% had a previous MI.
- At enrolment, most patients (97.2%) were being treated for hypertension, and 74.7% were taking two or more classes of antihypertensive medications, though only 37.3% had blood pressure below 140/90 at baseline.
- For the patients in the BA group, the mean daily dose was 36.3 mg of benazepril and 7.7 mg of amlodipine. For patients in the BH group, the mean daily dose was 36.1 mg of benazepril and 19.3 mg of hydrochlorothiazide.
- In each group, 32.3% of the patients received approved antihypertensive agents in addition to the highest dose of study medication after one year in the study.
- After a mean of 30 months of treatment exposure the data and safety monitoring committee observed a difference between the two groups that exceeded the boundary of the prespecified stopping rule and recommended early termination of the study.
- The baseline blood pressures were similar between the two groups and the reduction in blood pressure from baseline was similar over the course of the trial. The mean difference in blood pressure between the two groups (higher in the BH group) was 0.99 mmHg systolic and 1.1 mmHg diastolic ( $p < 0.001$  for both comparisons). Blood pressure control (BP < 140/90) was attained in an average of 75.4% of patients in the BA group and 72.4% in the BH group (no p-value given).
- A primary-outcome event occurred in 9.6% in the BA group compared with 11.8% in the BH group; HR 0.80 (95% CI 0.72 to 0.90),  $p < 0.001$ . The absolute risk reduction is 2.2% giving an NNT of 45.

## Discussion/implications

- The authors state that this trial shows that combination treatment with benazepril plus amlodipine is superior to treatment with benazepril plus hydrochlorothiazide in reducing the risk of CV events and of death among high-risk patients with hypertension and this has implications for clinical management of hypertension. They do go on to say that these results should not cast doubt on the efficacy of diuretics in reducing the risk of CV events but that approaches that do not include thiazides may be better for some populations.
- Many participants in this trial had diabetes and previous coronary disease and thus are not representative of the broad population of people with hypertension. This was not a trial of people being initiated on anti-hypertensives. Most were taking two or more blood pressure lowering drugs at enrolment. These were stopped, without a washout period, before randomisation to study drugs.
- Hydrochlorothiazide (except in combination products) and benazepril are not available in the UK.
- Both treatment regimes were effective at controlling blood pressure and the absolute difference in the proportion of patients who suffered a CV event was modest – 45 patients would have to be treated with the BA combination rather than the BH combination to prevent one event.
- There was no reduction in death from CV causes or overall mortality.
- One of the consequences of stopping the study early was that it had insufficient power to identify if the benefits were applicable to just some or all of the included sub-groups (e.g. diabetes).
- The accompanying editorial<sup>2</sup> states that treatment recommendation should be based on the total available evidence rather than on the results of any single trial. The evidence is overwhelming that the most important aspect of treatment is to reduce blood pressure to goal levels – how this is achieved is less important.<sup>2</sup>
- The NPC recommends that prescribers should not change practice<sup>3</sup> on the basis of this one clinical study.<sup>3</sup> Their advice from September 2006<sup>4</sup> is still appropriate, “prescribers may decide to use diuretics preferentially in view of their lower acquisition costs, unless there are good reasons to do otherwise.”

JAPC have discussed this study and agreed that it should not change practice and continue to endorse the hypertension algorithm in the cardiovascular system formulary (available here

[www.derbyshirecountypct.nhs.uk/template-practice-formulary-.asp](http://www.derbyshirecountypct.nhs.uk/template-practice-formulary-.asp) )

1. DTB 2008; 46 (9):65-9

2. N Engl J Med 2008; 359:2485-8

3. [www.npci.org.uk/blog/?p=250](http://www.npci.org.uk/blog/?p=250)

4. MeReC Bulletin 2006; 17(1): 1-2

## **Before you refer for hypertension**

The British Journal of Cardiology<sup>1</sup>, has published '10 steps before you refer for hypertension'. These are the highlights.

1. *Check that the measurement is correct*

Ensure that they really are poorly controlled by resting the patient for 10 minutes, with the cuff in place to discourage them from standing before taking at least two measurements, one to two minutes apart. Feel the radial pulse because in arrhythmias such as atrial fibrillation automatic sphygmomanometers are inaccurate and therefore traditional devices such as mercury sphygmomanometers must be used.

2. *Check compliance, establish concordance*

Warning the patient about side effects will often help to avoid them stopping new prescriptions, especially if you point out that many side effects are temporary. As a routine you should ask patients when they last took their medication. Seek agreement with the patient about their prescription and make sure they are doing this for themselves and not you! Many patients feel guilty about poor compliance and this is why they hide this from their practitioner.

3. *Encourage weight loss and salt reduction*

A weight loss of about 10 kg will result in a systolic blood pressure drop of up to 10 mmHg, depending on the level of a patient's obesity. Inform the patient of this fact and explain to them that most people can lose that amount of weight relatively easily. If they put it on again you can always encourage them to do it on an annual basis. A reduction in salt intake will result in a significant reduction in blood pressure and will maximise the blood pressure-lowering effect of many classes of drugs.

4. *Stop drugs that raise blood pressure*

Non-steroidal anti-inflammatory drugs and the combined oral contraceptive pill are drugs that commonly cause a rise in blood pressure. Ciclosporin has a hypertensive effect and you might bring this to the attention of the specialist prescribing it and ask if an alternative could be used. Drugs of abuse should also be considered such as cocaine and alcohol.

4. *Maximise medication using 'ACD'*

Step 3 of the hypertension algorithm is ACE inhibitor + calcium channel blocker + thiazide diuretic (see the cardiovascular formulary at [www.derbyshirecountypct.nhs.uk/template-practice-formulary-.asp](http://www.derbyshirecountypct.nhs.uk/template-practice-formulary-.asp))

6. *Spironolactone*

It is estimated that 21% of resistant hypertensive patients have hyperaldosteronism. Patients with resistance and a low serum potassium are particularly likely to have this problem. The diagnosis can sometimes be confirmed by measuring the renin to aldosterone ratio but this is not available to doctors in many areas and can provide false negatives. A low dose of spironolactone, half a 25 mg tablet, may well be very effective. Urea and electrolytes should be monitored regularly and you should warn patients to stop these drugs temporarily if they are suffering diarrhoea or are dehydrated. Watch for hypotension and often you may have to reduce the doses of the ACD drugs because the spironolactone is so effective.

7. *Establish that better control is required*

Make sure that the patient is willing to take further medication and wants more investigation. The patient's opinion should be taken into account and recorded before using the exception code.

8. *Ensure that other preventive measures are in place*

Risk factors cluster so if you cannot fully control somebody's hypertension you should cover the other risk factors. If the patient has cardiovascular disease, diabetes or chronic kidney disease they should have all other relevant preventive measures in place. A prevention screen should have been carried out, as for all other patients, and if their cardiovascular risk is equal to or greater than 20% they should be considered for statin therapy. The new NICE guidelines also tell us to use statin therapy in people over 74 years who smoke or have hypertension.

9. *Are there any investigations that might be useful for the specialist?*

The specialist needs to have as many facts to hand as possible when they see the patient. If they have to arrange tests it just delays implementing treatment. You should have a good idea of the sort of tests your local specialist might like to have done. As previously mentioned, a prevention screen, including lipids and blood glucose are important. Have you carried out routine tests such as macroalbuminuria, 24-hour urine for sodium, urea and electrolytes, estimated glomerular filtration rate (eGFR), serum urate, thyroid-stimulating hormone and gamma gluteryl transferase? All hypertensive patients need a routine electrocardiogram (ECG) and a copy should ideally be sent with the referral.

10. *Are you referring to the correct consultant*

You may have a local hypertension clinic and it is obvious where you should refer, but not all general practitioners have such a local clinic. Where there is no specialist clinic it is common to refer to the local cardiologist. But does your local cardiologist have any specialist training or an interest in hypertension? Many do not and may actually have less overall experience of managing hypertension than you do. Patients with renal impairment may benefit from seeing a renal physician and many of them do have a specific interest in hypertension. There may be a local vascular or stroke physician with an interest and some elderly care physicians have such an interest.

1. Br J Cardiol 2008; 15:254-7

**Diuretics for patients with prediabetes or metabolic syndrome**

A BMJ article<sup>1</sup> asks the question 'should we prescribe diuretics for patients with prediabetes and hypertension?' After discussing the evidence the authors reach the following conclusion.

On the basis of current evidence, it is justifiable to use a thiazide diuretic as first line treatment in people with hypertension and prediabetes. In people without diabetes, people with impaired fasting glucose, and those who develop diabetes during trials, cardiovascular outcomes from treating hypertension with diuretics are at least as good as or better than with other antihypertensives. These results have been collected for up to 14 years and are mainly from those aged 55 or over. For younger patients with prediabetes the uncertainty remains, but the data from older patients are encouraging, and the key problem will probably be ensuring a consistently low blood pressure rather than deciding which drugs should be used to obtain it.

Thiazide diuretics are also an appropriate first-line choice in patients with hypertension and metabolic syndrome. A subgroup analysis of patients with metabolic syndrome in the ALLHAT study<sup>2</sup> (these comprised about half of the patients in the study, 23,000 people) identified similar findings to those of the whole ALLHAT study population. However, it found the incidence of heart failure were significantly higher in patients initially treated with amlodipine and lisinopril (and doxazosin) than in those initially treated with a diuretic. These findings were particularly apparent in black patients. Further advantages for diuretics were found in comparison with the other treatments for some other secondary outcomes.

The NPC concludes<sup>3</sup> "This analysis adds weight to the positioning of thiazide diuretics as first-line antihypertensive in the vast majority of patients with hypertension. This study fails to support the use of calcium channel blockers, ACE inhibitors (or alpha-blockers) ahead of diuretics in patients with metabolic syndrome."

1. BMJ 2008; 337:1415-16
2. Arch Intern Med 2008; 168: 207-17
3. [www.npci.org.uk/blog/?p=61](http://www.npci.org.uk/blog/?p=61)

**Elevated blood pressure in the very elderly**

Risk of serious adverse cardiovascular events increases with advancing age and with higher blood pressure. Falls and other serious adverse events associated with postural hypotension also increase with age and with antihypertensive drug therapy. It is therefore important to know whether drug treatment improves not only cardiovascular outcomes, but also measures of net health which combine benefit and harm: total mortality and all patients with any serious adverse event. A recent Therapeutics Letter focuses on the best available evidence about drug treatment of elevated blood pressure in individuals over 79 years of age.<sup>1</sup>

The review starts off by pointing out that the evidence for treatment of systolic BP  $\geq 160$  mmHg in people mostly aged 60-79 is considered robust and well established. A meta-analysis showed that therapy reduced both total mortality, RR 0.88 (95% CI 0.82 to 0.98), ARR = 1.7%, NNT = 59 for five years; and combined total stroke and coronary heart disease, RR 0.73 (95% CI 0.68 to 0.77), ARR = 5%, NNT = 20 for five years.

The overall evidence for lowering blood pressure in people  $\geq 80$  years with systolic BP  $\geq 160$  mmHg relates to individuals recruited for clinical trials who are relatively healthy. **It is not relevant to the sick or frail elderly population.** Pooled evidence demonstrates a reduction in the incidence of stroke, but no decrease in total mortality. This is reasonable justification for offering drug treatment to relatively healthy hypertensive elderly, as such patients uniformly want to avoid stroke. The best drug choice for management is not resolved by meta-analysis. However, the largest trial (HYVET) and the only one that demonstrated a net health benefit by reducing both mortality and number of serious adverse events provides a relatively simple approach.

Start with a low-dose thiazide followed by a low-dose ACE inhibitor. Double the dose of the ACE inhibitor once, if necessary to achieve a blood pressure  $<150/80$  mmHg. Using this approach one can expect that about half of patients will achieve a blood pressure of  $<150/80$  mmHg. This conservative approach to blood pressure management is corroborated by the recent observational study in Swedish individuals  $\geq 85$  years old, which suggests that systolic blood pressure in the range of 140 to 160 mmHg is optimal for the very elderly.

### Conclusions:

*For patients  $\geq 80$  years:*

- Various antihypertensive therapies for primary prevention in relatively healthy patients with systolic BP  $>160$  mmHg reduced stroke, but had no proven effect on mortality.
- Using low-dose thiazide as first-line therapy followed by a low-medium dose ACE inhibitor reduced mortality as well as serious adverse events in one large RCT.
- With this regimen a blood pressure of  $<150/80$  mmHg can be expected in about 50% of patients.

1. Therapeutics letter, September-October 2008. [www.ti.ubc.ca/PDF/71.pdf](http://www.ti.ubc.ca/PDF/71.pdf)

### Aspirin for the prevention of type 2 diabetes

Subclinical inflammation has been linked with the development of type 2 diabetes. Until recently no randomised trials have directly evaluated the efficacy of low-dose aspirin in diabetes prevention. A study has evaluated whether chronic low-dose aspirin prevents the development of clinical diabetes among initially healthy American women.<sup>1</sup>

Subjects were enrolled in the Women's Health Study, a 10-year randomised double-blind, placebo-controlled trial of aspirin and vitamin E for primary prevention of cardiovascular disease and cancer. Between 1992 and 1995, 38,716 women aged  $\geq 45$  years and free of clinical diabetes were randomly assigned to either low-dose aspirin or placebo (median follow-up 10.2 years). Documented clinical type 2 diabetes was prospectively evaluated throughout the trial. The dose of aspirin was 100mg every other day and this was chosen to be the lowest dose that would have a cardioprotective effect while minimising gastrointestinal side effects.

Among women randomly assigned to receive aspirin (n = 19,326) or placebo (n = 19,390), there was no statistically significant difference in the incidence of type 2 diabetes. There were 849 cases of diabetes in the aspirin group and 847 in the placebo group (rate ratio 1.01 [95% CI 0.91 to 1.11]). Stratification by diabetes risk factors including age, BMI, family history of diabetes, physical activity, HbA1c, and high-sensitivity C-reactive protein did not support a modulating effect of these variables. Analyses accounting for treatment duration and adherence similarly found no beneficial effects.

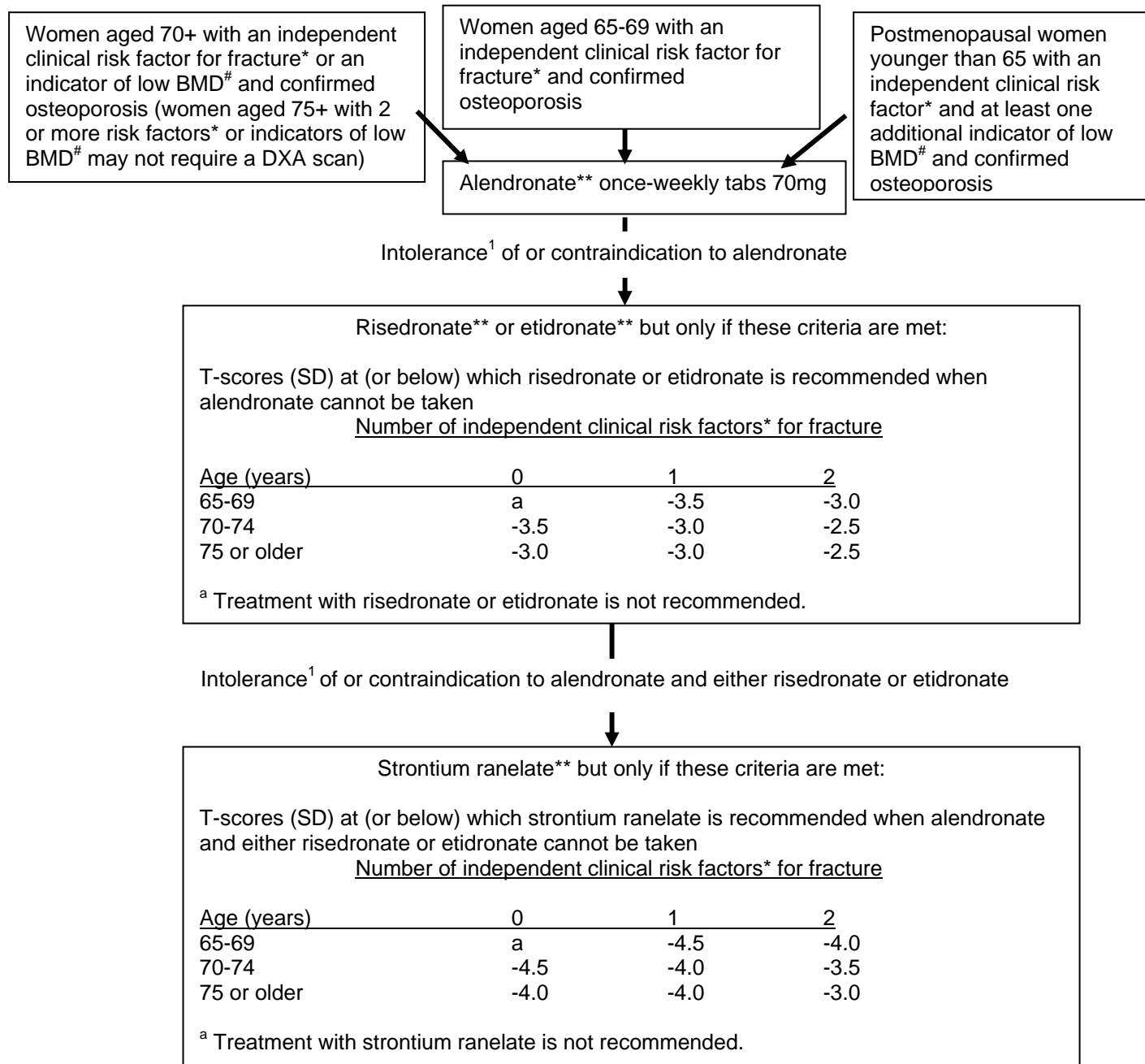
The authors conclude that these data suggest that long-term low-dose aspirin does not prevent the development of clinical type 2 diabetes in initially healthy women.

Even at the low dose evaluated in this trial, the use of aspirin was associated with a significant increase in clinically important bleeding events.

1. Diabetes Care 2009; 32:3-8

## **NICE TAG 160 – Primary prevention of osteoporotic fragility fractures**

- This guidance relates only to treatments for the primary prevention of fragility fractures in postmenopausal women who have osteoporosis. Osteoporosis is defined by a T-score of -2.5 standard deviations (SD) or below on dual-energy x-ray absorptiometry (DXA) scanning. However, the diagnosis may be assumed in women aged 75 years or older if the responsible clinician considers a DXA scan to be clinically inappropriate or unfeasible.



- Raloxifene is not recommended as a treatment option for the primary prevention of osteoporotic fragility fractures in postmenopausal women.

1. Unable to comply with the special instructions for administration or persistent upper gastrointestinal disturbance that is sufficiently severe to warrant discontinuation of treatment, and that occurs even though the instructions for administration have been followed correctly.

\* Independent clinical risk factors for fracture are parental history of hip fracture, alcohol intake of 4 or more units per day, and rheumatoid arthritis (RA).

# indicators of low BMD are low BMI (<22kg/m<sup>2</sup>), medical conditions such as ankylosing spondylitis, RA, Crohn's disease, conditions that result in prolonged immobility, and untreated premature menopause.

\*\* This guidance assumes that women who receive treatment have an adequate calcium intake and are vitamin D replete. Unless clinicians are confident that women who receive treatment meet these criteria, calcium and/or vitamin D supplementation should be considered (calcium 1200mg + vit D<sub>3</sub> 800 units daily recommended locally).

## **NICE TAG 161 – Secondary prevention of osteoporotic fragility fractures**

- This guidance relates only to treatments for the secondary prevention of fragility fractures in postmenopausal women who have osteoporosis and have sustained a clinically apparent osteoporotic fragility fracture. Osteoporosis is defined by a T-score of -2.5 standard deviations (SD) or lower on dual-energy X-ray absorptiometry (DXA) scanning. However, the diagnosis may be assumed in women aged 75 years or older if the responsible clinician considers a DXA scan to be clinically inappropriate or unfeasible.

Alendronate<sup>#</sup> once-weekly tabs 70mg

Intolerance<sup>1</sup> of or contraindication to alendronate

1. Unable to comply with the special instructions for administration or persistent upper gastrointestinal disturbance that is sufficiently severe to warrant discontinuation of treatment, and that occurs even though the instructions for administration have been followed correctly.

2. Intolerance of strontium ranelate is defined as persistent nausea or diarrhoea, either of which warrants discontinuation of treatment.

3. An unsatisfactory response is defined as occurring when a woman has another fragility fracture despite adhering fully to treatment for 1 year and there is evidence of a decline in BMD below her pre-treatment baseline.

Risedronate<sup>#</sup> or etidronate<sup>#</sup> but only if these criteria are met:

T-scores (SD) at (or below) which risedronate or etidronate is recommended when alendronate cannot be taken

Number of independent clinical risk factors for fracture\*

Age (years)	0	1	2
50-54	a	-3.0	-2.5
55-59	-3.0	-3.0	-2.5
60-64	-3.0	-3.0	-2.5
65-69	-3.0	-2.5	-2.5
70 or older	-2.5	-2.5	-2.5

<sup>a</sup> Treatment with risedronate or etidronate is not recommended.

Intolerance<sup>1</sup> of or a contraindication to alendronate and either risedronate or etidronate

Strontium ranelate<sup>#</sup> or raloxifene<sup>#</sup> but only if these criteria are met:

T-scores (SD) at (or below) which strontium ranelate or raloxifene is recommended when alendronate and either risedronate or etidronate cannot be taken

Number of independent clinical risk factors for fracture\*

Age (years)	0	1	2
50-54	a	-3.5	-3.5
55-59	-4.0	-3.5	-3.5
60-64	-4.0	-3.5	-3.5
65-69	-4.0	-3.5	-3.0
70-74	-3.0	-3.0	-2.5
75 or older	-3.0	-2.5	-2.5

<sup>a</sup> Treatment with raloxifene or strontium ranelate is not recommended.

\* Independent clinical risk factors for fracture are parental history of hip fracture, alcohol intake of 4 or more units per day, and rheumatoid arthritis.

# This guidance assumes that women who receive treatment have an adequate calcium intake and are vitamin D replete. Unless clinicians are confident that women who receive treatment meet these criteria, calcium and/or vitamin D supplementation should be considered (calcium 1200mg + vit D<sub>3</sub> 800 units daily recommended locally).

- Teriparatide<sup>#</sup> is recommended as an alternative treatment option for secondary prevention only in those
  - who are unable to take alendronate and either risedronate or etidronate, or have a contraindication to or are intolerant<sup>1</sup> of alendronate and either risedronate or etidronate, **or** who have a contraindication to, or are intolerant<sup>2</sup> of strontium ranelate, **or** who have had an unsatisfactory response<sup>3</sup> to treatment with alendronate, risedronate or etidronate **and**
  - who are 65 years or older and have a T-score of -4.0 SD or below, or a T-score of -3.5 SD or below plus more than two fractures, **or** who are aged 55-64 years and have a T-score of -4 SD or below plus more than two fractures.