



# Overenthusiastic stroke risk factor modification in the over-80s: Are we being disingenuous to ourselves, and to our oldest patients?

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## Abstract

Statins and antihypertensive therapy are widely used in our oldest patients (ie, those aged over 80 years). The epidemiology suggests that, by this age, hypertension is not an attributable risk factor for stroke, and hypercholesterolaemia has little effect on stroke risk overall. The largest trials of antihypertensive therapy and statins in this age group show at best a marginal clinical reduction in stroke and very modest clinical reductions in other cardiovascular end points. Older patients have very diverse views on the relative importance of stroke and death as end points, and these differ from physicians' views. Informed consent principles (full relevant information in an accessible form, and autonomy of decision-making) suggest that these medications are greatly over-prescribed in the healthy elderly and largely irrelevant in the frail elderly, but require that the patient should be actively involved in the process.

## Introduction

Statins and antihypertensives were the most prescribed UK cardiovascular drugs in 2006.<sup>1</sup> Many older patients (75% in one US study<sup>2</sup>) are on statins for primary prevention. I challenge this orthodoxy.

## Epidemiology

Although stroke incidence increases exponentially with age from about 40, Framingham data confirm that the attributable risk from hypertension falls after 60, from a relative risk of 3.5 then, to statistically indistinguishable from 1 in the 80s.<sup>3</sup> In a study of over 4000 ambulatory hypertensive patients over the age of 80 years, mortality was higher in the 5-year follow-up period in those with lower systolic and diastolic blood pressure (BP).<sup>4</sup> Epidemiological evidence shows little effect of cholesterol on stroke risk.<sup>5</sup> Data from 61 prospective observational studies yielded nearly 12 million person-years at risk between the ages of 40 and 89 years. The risk for *ischaemic heart disease* death, for any given level of cholesterol, fell with age and in participants over 70 years (and particularly for those with systolic BP over about 145 mm Hg) total cholesterol was negatively related to both haemorrhagic and total stroke mortality.

## Trial data

A 2004 review of hypertension in the very elderly concluded that the then unreported HYVET study should answer lingering questions concerning whether antihypertensives would work as well as in younger hypertensives.<sup>6</sup> The HYVET study, arguably the definitive antihypertensive trial in older patients, involved nearly 4000 patients. Rigorously designed, it had a 90% power at 1% level to detect a 35% reduction in the rate of any

stroke, assuming an event rate of 40/1000 patient-years.<sup>7</sup> With nearly 4000 patient-years of follow-up in each arm, the primary end point (all strokes, fatal or non-fatal) showed a 30% relative reduction in the treated group, with a number needed to treat (NNT) of 94 over 2 years to prevent one stroke, although this just failed to achieve significance at 5% level. Calculating the number of *non-fatal* strokes from their data yields an NNT just exceeding 450 over 2 years. Even the largest clinical improvement, an impressive-sounding 64% HR reduction in fatal or non-fatal cardiac failure, yielded an NNT in excess of 50 over 2 years. There are also unresolved questions relating to the study's premature termination, and the fact that 40% of the participants were from China (whose stroke epidemiology is different from that of Western Europe's<sup>8</sup>).

Analogously, the PROSPER study is arguably the definitive study of statins for stroke prevention in older people.<sup>9</sup> Nearly 6000 participants aged 70–82 years and with a history of, or risk factors for, vascular disease were followed for just over 3 years on an average and given either 40 mg of pravastatin or placebo each day. There was a significant reduction in the composite primary end point (all *fatal or non-fatal* strokes or cardiac events). However, this included no statistically significant reduction in stroke, and the relative risk reduction of all cardiovascular end points of 33% (from 5.1% to 3.4%) gave a crude NNT of 59 over 3 years. The reduction of *non-fatal* cardiovascular end points (calculated from the published data) from 2% to 1% yields an NNT of 100.

Minor morbidity with statins is reported as up to 10%. However, there is evidence that these risks have been underestimated,<sup>10</sup> possibly because of publication bias.<sup>11</sup> Since most people believe that their statins are preventing serious and likely problems, their threshold for discontinuing statins tends to be high.

## Importance of morbidity versus mortality in older patients

A large number of my older patients have expressed the view made public last year by a major UK soap celebrity<sup>12</sup> that they would rather die than end up incapacitated by a stroke. It is often as much for altruistic reasons of not wanting to be a burden on partners, loved family or society (which is the reality<sup>13</sup>), as it is for personal reasons of not wanting to be dependent. Indeed, in my experience, it is not uncommon in the oldest of these often frail but relatively disease-free patients to see death as the next natural event in their life, especially welcome if they have outlived all their peers. However, this cohort is often deferential to 'the doctor' whom they frequently want to please, or at least not upset.

Studies show that patients' values and preferences relating to stroke vary enormously, and differ significantly from physicians'.<sup>14-15</sup> People entering trials probably have a lower threshold for treatment than those who do not.<sup>16</sup> Deciding what to focus on in frail older patients with multiple pathology is much more challenging than these 'single problem' cases<sup>17-18</sup> and a complex interaction of factors influence these decisions.<sup>19</sup> Informed consent requires information to be presented to the patient accessibly (eg, using decision aids<sup>20</sup>).

### Conclusion

The data strongly suggest that we are over-treating many healthy patients aged 80+ regarding stroke prevention. Should we ever use these medications in frail older patients with multimorbidity? We need actively to rethink our priorities and beliefs about stroke prevention, actively informing and involving the views of the key person, the patient. Most of the patients will probably eschew the modest potential benefit, preferring the reduced burden of polypharmacy and side effects judged as 'minor' by the prescriber.

Competing interests None.

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