

**BEST PRACTICE****STATINS IN OLDER PATIENTS****Introduction**

The risk of atherosclerotic cardiovascular disease increases with age. Over time, age becomes the dominant risk factor for cardiovascular events with patients older than 65 years experiencing the highest incidence rates and number of events.

Although the South African population is predominately young (under the age of 49 years), the population of older persons is increasing. In 2011, according to the South African Census, there were 4 million adults over the age of 60 years in the country; 1.5 million were over the age of 70 years.<sup>1</sup>

Statins are relatively cheap and have been shown to reduce cardiovascular events in multiple studies in a wide spectrum of patients. A recent subgroup analysis of the Cholesterol Treatment Trialists (CTT) study showed that statins were effective across a wide age range.<sup>2</sup> The numbers needed-to-treat to prevent one event per 1mmol/L reduction in low-density lipoprotein cholesterol (LDLC) was 37 for people under the age of 60 years, 29 for patients aged 60 to 69 years, and 36 for those aged more than 70 years.

Clinical insights from



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*“While the evidence from sub-group studies within RCTs up to the age of 75 years points to continued benefit, there is no indication in the published literature that statin therapy above the age of 75 years will not continue to provide benefit in terms of reducing cardiovascular events.”*

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**Cipla****KEY MESSAGES**

- Clinicians need to set aside rigid guidelines when considering statin therapy in older patients
- Each patient should be assessed individually, carefully evaluating benefit versus risk and considering issues such as frailty, performance status and underlying cardiovascular risk
- When statins are prescribed, the clinician needs to communicate the individual benefit to the patient and family/caregiver to encourage compliance.

**Elderly at increased risk, but untreated**

Paradoxically, older patients (>75 years) are often less likely to receive statins for both primary and secondary prevention.<sup>3</sup> The likelihood of receiving a statin prescription has been shown by an American Registry study to be reduced by more than 6% for each yearly increase in age (after 66 years), despite the concomitant

1% increase in predicted 3-year mortality risk.<sup>4</sup>

Likely reasons for this include misconceptions of the benefit-harm balance and physician assumptions about medication compliance in older patients who are already taking other medications for comorbidities.

**What do we know about risk-benefit in the very elderly?**

The Framingham Risk Score (FRS-CVD) is commonly used in South Africa to assess cardiovascular risk but is not well validated for persons older than 75 years of age. This is due to older patients

often not being adequately represented in the databases from which these risk estimation algorithms are derived.

As many randomised clinical trials (RCTs) of statins excluded older patients

(Table 1), it is useful to look more closely at two trials concerning statin treatment

specifically in the above 70-year-old group.

*“I don’t think we should discriminate against older adults, with regard to primary prevention, simply because we do not have all the supportive data we would like to have.”*

### Primary prevention and secondary prevention in the above 70-year-old group

The PROSPER study<sup>5</sup> (pravastatin in elderly individuals at risk of vascular disease) randomised 5 804 patients aged 70 to 82 years at high risk for or with existing vascular disease. Prior to this study, lower cholesterol levels in the elderly were thought to be associated with increased mortality. In the PROSPER study,

patients were treated with a low potency statin (pravastatin 40mg daily). After 3.2 years there was a 15% relative risk reduction in primary end-points of coronary death, non-fatal myocardial infarction (MI) and stroke. The statin therapy reduced coronary events by 19% and coronary deaths by 24%.

**Table 1. Enrolment of elderly and very elderly in primary prevention statin trials<sup>7</sup>**

Study Name, Year	No.	Mean age (yrs)	Age Range (yrs)	Elderly (yrs)	Very elderly (≥75yrs of age)
WOSCOPS, <sup>8</sup> 1995	6 595	55	Men 45–64	0	0
AFCAPS/TexCAPS, <sup>9</sup> 1998	6 605	Men 58 Women 62	Men 45–73 Women 55–73	Men 20% ≥65 Women 33% ≥65	0
ALLHAT-LLT, <sup>10</sup> 2002	10 355	66	≥55	28% ≥65*	7%*
PROSPER, <sup>11</sup> 2002	3 239 (no ASCVD)	75 (whole cohort)	70–82 (whole cohort)	100% ≥70	NR
ASCOT-LLA, <sup>12</sup> 2003	10 305	63	40–79	64% >60 23% >70	NR
CARDS, <sup>13</sup> 2004	2 838	62	40–75	40% ≥65 12% >70	0
MEGA, <sup>14</sup> 2006	7 832	58	40–70	23% >65	0
JUPITER, <sup>15</sup> 2008	17 802	66	Men ≥50 Women ≥60	58% ≥65 <sup>†</sup> 32% ≥70 <sup>†</sup>	NR
HOPE-3, <sup>16</sup> 2016	12 705	66	Men ≥55 Women ≥65/60	52% ≥65 <sup>†</sup> 24% ≥70 <sup>†</sup>	NR

\*Primary prevention data reported by Han et al. (17). †Reported by Ridker et al (18). AFCAPS/TexCAPS: Air Force/Texas Coronary Atherosclerosis Prevention Study; ALLHAT-LLT: Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial–Lipid Lowering Trial; ASCOT-LLA: Anglo-Scandinavian Cardiac Outcomes Trial–Lipid Lowering Arm; CARDS: Collaborative Atorvastatin Diabetes Study; HOPE-3: Heart Outcomes Prevention Evaluation-3; JUPITER: Justification for the Use of Statins in prevention: An Intervention Trial Evaluating Rosuvastatin; MEGA: Management of Elevated Cholesterol in the Primary Prevention Group of Adult Japanese; NR: not reported; PROSPER: Pravastatin in elderly individuals at risk of vascular disease; WOSCOPS: West of Scotland Coronary Prevention Study.

### Secondary prevention in the over 80-year-old group

An observational Swedish study of 14 907 patients over the age of 80 years with an acute MI followed these patients for a median of 296 days and a maximum of 5 years, evaluating outcomes according to statin use.<sup>6</sup> Excluding those patients who died in the first year (in whom statins may not have been able to influence prognosis), the patients on statin therapy showed a 37% reduction in cardiovascular mortality and acute MI mortality. Because this

was an observational study, results should be interpreted with caution because of the potential for confounding.

“While the evidence from sub-group studies within RCTs up to the age of 75 years points to continued benefit, there is no indication in the published literature that statin therapy above the age of 75 years will not continue to provide benefit in terms of reducing cardiovascular events”, Prof Blom noted (Table 1).<sup>7</sup>

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## Practical clinical situations

### The older patient not on statins

“In addressing the cardiovascular risk in an older patient, the clinician should use a risk chart with which he/she is familiar”.

Possibilities that can be used to assess the 5- and 10-year risk are:

- The revised SCORE (Systematic COronary Risk Evaluation) tool referred to as SCORE-OP<sup>19</sup> ([www.heartscore.org](http://www.heartscore.org))
- The Framingham risk score model for 10-year CVD incidence/death<sup>20</sup>

According to most risk assessment charts, the older patient (>65 years) is at high or very high risk, implying that most elderly patients are eligible for lipid-lowering treatment, even if they have not experienced an adverse cardiovascular event.

So, do you prescribe a statin? And should it be a moderate or high-intensity statin?

If you have an older patient with good functional status, without a history of

vascular disease and he/she has raised cardiovascular risk mediated at least in part by lipids, then the patient may benefit from statin treatment.

“I don’t think we should discriminate against older adults, with regard to primary prevention, simply because we do not have all the supportive data we would like to have.” Prof Blom stressed.

It is important to evaluate the number and quality of life years that can be gained for an individual patient prior to introduction of therapy. The level of benefit that can be expected is illustrated in Table 2. These calculations, which estimate the absolute treatment effect of statin therapy on major adverse cardiovascular events (MACE) for an individual patient aged ≥70 years, used data from the PROSPER, SMART and ASCOT-LLA studies.<sup>21</sup> These values provide clinicians with a useful barometer of the benefit of treatment versus non-treatment (Table 2).

*“In older patients, an initial lower dose of the selected statin may be advisable.”*

**Table 2. Estimation of absolute risk reduction (ARR) in individuals over 70 years of age on statin treatment versus non-treatment.<sup>21</sup>**

ARR	Patients with vascular disease	Patients without vascular disease
5-year	5.1% (4-6.2%)	1.7% (1.3-2.1%)
10-year	7.8% (6.8-8.6%)	2.9% (2.3-3.6%)

Other considerations before prescribing statin therapy include an assessment of comorbidities, risk of drug interactions and finally cost, which may influence the

decision on initiating statin therapy.

“In older patients, an initial lower dose of the selected statin may be advisable,” Prof Blom noted.

### The older patient already on a statin

The new South African Lipid Guidelines, currently in press, recommend that the patient who has been taking a statin for numbers of years, and is now above 70 years of age, should continue treatment

unless there is a specific reason for discontinuing therapy (he/she develops intolerance, a life-limiting disease intervenes, or he/she cannot cope with taking the statins anymore).

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