South African National Essential Medicine List
Primary Healthcare and Adult Hospital Level Medication Review Process
Component: Cardiovascular

SIMVASTATIN FORECASTING AND BUDGET IMPACT ANALYIS (MODEL)
Date: 7 May 2018

Objective:

At the National Essential Medicines List Committee (NEMLC) meeting of 2 February 2018, the NEMLC had accepted intermediate statin dose for secondary prevention of ischaemic events, based on clinical evidence and a cost-effectiveness analysis. However, as there is a paucity of local epidemiological data, a budget impact analysis could not be conducted. Thus, a report was developed in order to assist with the forecasting of tender estimates and to advise contract management that continuous monitoring of consumption is essential.

Background:

Historically, the PHC and Adult Hospital Level STGs and EML (2014 and 2015 editions) recommended low dose statin (i.e. simvastatin 10 mg) for both primary and secondary prevention of ischaemic events. This recommendation was informed by a meta-regression[1] analysis that showed a dose-response curve with little additional benefit beyond a decrease of 1 mmol of plasma low-density (LDL) cholesterol (which can be achieved with a simvastatin dose of 10 mg daily)[2].

However, several other meta-analyses showed a linear relationship between statin dose and prevention of ischaemic events, and concluded that the higher the statin dose the better[3]. Several international guidelines[4] recommend high dose statins at a fixed dose, rather than dose titration based on plasma LDL cholesterol concentrations. Several external stakeholders reviewed the PHC and AHL STGs, and asked the expert review committees to consider higher statin doses. NEMLC agreed that higher doses for the secondary prevention of cardiovascular disease should be investigated.

Subsequently, a cost-effectiveness analysis was done, based on the Cholesterol Treatment Trialists' Collaboration meta-analysis[5] in order to inform a decision on a higher dose statin for secondary prevention.

[1] Takagi H, Umemoto T; for the ALICE (All-Literature Investigation of Cardiovascular Evidence) Group. Limit to Benefits of Large Reductions in Low-Density Lipoprotein Cholesterol Levels: Use of Fractional Polynomials to Assess the Effect of Low-Density Lipoprotein Cholesterol Level Reduction in Metaregression of Large Statin Randomized Trials. *JAMA Intern Med.* 2013 Apr 29:1-2.http://www.ncbi.nlm.nih.gov/pubmed/23700132
[2] Naci H, Brugts JJ, Fleurence R, Ades AE. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. Eur J Prev Cardiol. 2013 Aug;20(4):658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608
[3] Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, Kirby A, Sourjina T, Peto R, Collins R, Simes R; Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet. 2005 Oct 8;366(9493):1267-78. Epub 2005 Sep 27. Erratum in: Lancet. 2008 Jun 21;371(9630):2084. Lancet. 2005 Oct 15-21;366(9494):1358. http://www.ncbi.nlm.nih.gov/pubmed/16214597
[4] NICE: Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline, 18 July 2014. www.nice.org.uk/guidance/cg181
[5] Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, Kirby A, Sourjina T, Peto R, Collins R, Simes R; Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised

Simvastatin 40 mg was shown to be the most cost-effective of the options investigated for secondary prevention (as indicated in the table 1, below). Therefore, the NEMLC recommended that the intermediate intensity statin be recommended in the relevant STGs for secondary prevention.

Table 1: Costs, outcomes and cost-effectiveness ratios of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease:

	Cost	Life years	ICER
Simvastatin 10mg	42829.40	4.31	Dominated
Simvastatin 20 mg	42024.12	4.32	Dominated
Atorvastatin 40 mg	40500.50	4.34	Dominated
Simvastatin 40 mg	39773.00	4.34	
Atorvastatin 80 mg	40737.80	4.34	128142.33

ICER: incremental cost effectiveness ratio

(Refer to the cost effectiveness analysis report for detailed information, accessible at: http://www.health.gov.za/index.php/standard-treatment-guidelines-and-essential-medicines-list/category/405-phc-costings).

A budget assessment was recommended to determine the impact of increasing the dose of simvastatin from 10 mg to 40 mg for secondary prevention. However, local prevalence data is not available and using contract estimates was unreliable. Thus, it was recommended that consumption data be used to model the estimated increase in expenditure.

Forecast and budget impact model:

Assumptions for quantification:

Consumption data cannot be disaggregated by indication (primary or secondary prevention) or by prescription at primary or secondary level of care. Despite simvastatin 20 mg not being on the EML, historically there has been national consumption of this product.

Therefore, the following assumptions were made:

- 20 mg dose consumption data was assumed to be used for secondary prevention; whilst the 10 mg dose was assumed to be used for primary prevention.
- Simvastatin STG change is expected to double the prescribed dosage from 20 mg to 40 mg (i.e. 2x20 mg tablets) from July 2018.
- The uptake of the higher dosage is expected to be phased in over 9-month period i.e. July 2018 to March 2019. The projected forecast volume is based on estimated historic consumption data.
- Introduction of the simvastatin 40 mg tablet:
    - A 40mg tablet is expected to be introduced in April 2019, the estimated starting date for the new cycle of tablet tender. This tablet will be phased in over a 20-month period, assuming that 10% of patients on 2x20mg simvastatin would initially switch to simvastatin 40mg. After 20 months, it is assumed that all patients would have converted to simvastatin 40mg.
    - It is assumed that a patient on simvastatin 20 mg would default to 40 mg, presuming that the indication is for secondary prevention of ischaemic events.
    - The 2x20mg tablet will be phased out over the same period.

trials of statins. Lancet. 2005 Oct 8;366(9493):1267-78. Epub 2005 Sep 27. Erratum in: Lancet. 2008 Jun 21;371(9630):2084. Lancet. 2005 Oct 15-21;366(9494):1358. http://www.ncbi.nlm.nih.gov/pubmed/16214597

- No change expected for the simvastatin 10mg tablet, as it is assumed that 10 mg dose is used for primary prevention.

Fig 1: Phased in approach of double dosage of 20mg Simvastatin, over 9 months

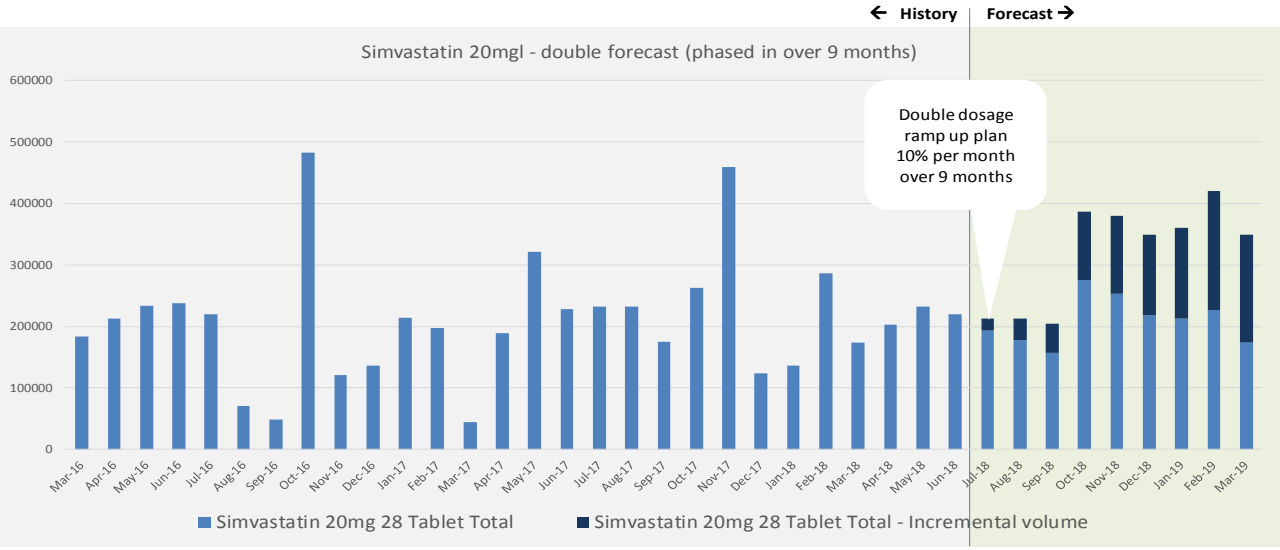
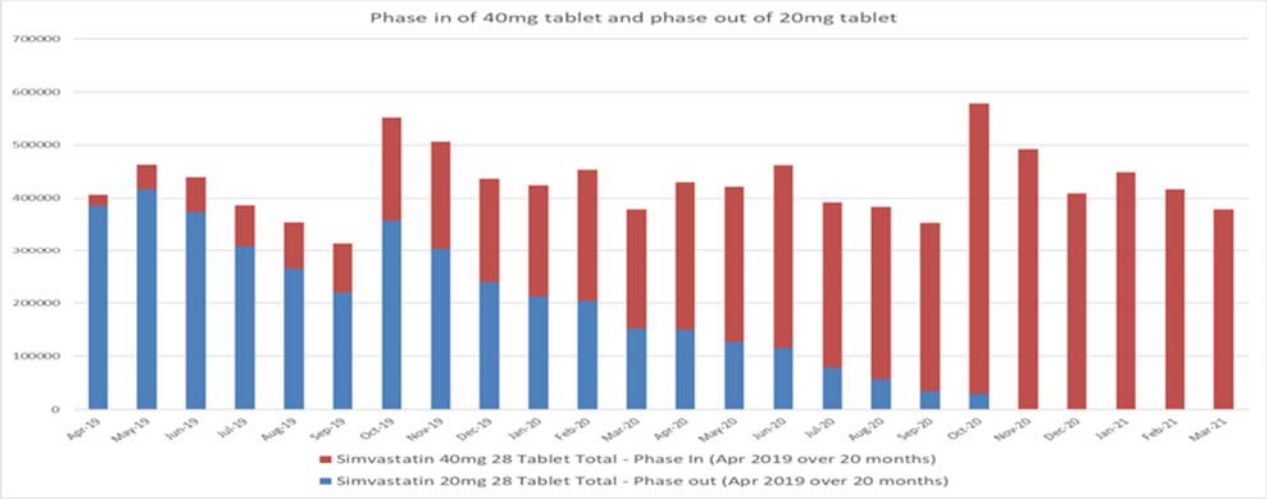


Fig 2: Phase in of 40mg tablet and phase out of 2x20mg tablet, over 24 months



Note: Assumption made that a patient on simvastatin 20 mg would default to 40 mg, presuming that the indication is for secondary prevention of CVD.

Projected forecasts:

The forecasts for the rest of the current financial year (9 months) 20mg is shown in table 1 and for the period, April 2019 to March 2020 in table 2 below.

It should be noted that the adjusted forecast, with the phase in of double dosage 20mg Simvastatin (2x20mg), is still lower than the original contracted values as shown in Table 1. This is largely driven by the lower actual usage rate over the last 18 months.

Table 1: Double dosage forecast of 2x20mg simvastatin July 2018 to March 2019

	Jul-18	Aug-18	Sep-18	Oct-18	Nov-18	Dec-18	Jan-19	Feb-19	Mar-19	**TOTAL**
Original contract estimates (4,426mil over 1 yr)	368,798	368,798	368,798	368,798	368,798	368,798	368,798	368,798	368,798	**3,319,184**
Forecast based on consumption data (2x20mg)	212,561	212,796	204,832	386,109	380,091	349,474	360,958	419,893	348,512	**2,875,224**

Note:

» Units are 28-day calendar packs i.e. per patient.

» Contract estimates described to show the variance between projected forecasts based on contract estimates versus consumption data.

Table 2: Forecasted volume for 2x20mg and 40mg for Apr 2019 to Mar 2020

	Apr-19	May-19	Jun-19	Jul-19	Aug-19	Sep-19	Oct-19	Nov-19	Dec-19	Jan-20	Feb-20	Mar-20	**TOTAL**
Simvastatin 2x20mg forecasted vol - Phase out	385,687	416,947	373,883	309,179	265,995	220,588	358,530	304,073	240,263	212,328	204,272	151,690	**3,443,434**
Simvastatin 40mg forecasted vol - Phase In	20,299	46,327	65,979	77,295	88,665	94,538	193,054	202,715	196,579	212,328	249,666	227,534	**1,674,980**

Note:

» Units are 28-day calendar packs i.e. per patient.

Estimated budget impact:

Based on the above forecasts and using the current contract prices for simvastatin, the anticipated - expenditure on simvastatin 20 mg is R19,638 million over the period from July 2018 to April 2019[6], using direct medicines costs; and the estimated incremental budget impact is projected to be R6,734 million[7] over the 12-month period (July 2018 to April 2019).

As there is paucity of local epidemiological data pertaining to the prevalence of acute coronary syndrome, historic consumption data of simvastatin was used to predict estimates for the higher dose simvastatin. However, going forward, close monitoring of the use of both 20mg and 40mg simvastatin is required to ensure appropriate measures are taken to adjust supply accordingly.

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[6] Based on contract circular HP09-2016SD, simvastatin 20 mg, 28 tabs at a price of R6.83 – Total budget impact = 2,875 mil units x R6.83 = R 19.638 mil.

[7] Based on historic consumption of simvastatin 20 mg, the estimated forecast is 1,889 mil units, and this equates to an estimated cost of R12,904 mil (i.e. 1,889 mil units x R6.83). The incremental estimated cost is R19.638 mil – R12,904 mil = R6,734 mil.