

# Impact of the New Guidelines to Prescribe Statins in a University Hospital

## *Impacto de las nuevas guías para la indicación de estatinas en un hospital universitario*

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### ABSTRACT

**Background:** The application of the new guidelines for the use of statins has increased the number of new statin prescriptions; however, there are no investigations on this topic in our region.

**Objective:** The aim of this study was to compare in a population consisting of members belonging to a healthcare system, the proportion of persons that would be eligible for statin therapy under the new 2013 ACC-AHA guidelines versus the previous ATP III guidelines.

**Methods:** The ratio of subjects that would be eligible for statin therapy under both guidelines was analyzed in a simple random sample without replacement, and the results were extrapolated to the entire population of the healthcare system.

**Results:** A total of 226 patients were analyzed. Applying the ATP-III and the 2013 ACC/AHA guidelines, 35.8% and 52.2% of the population was eligible for statin therapy, respectively. The difference was higher in women (18.3%) and in subjects >60 years (27.1%). Applying the new guidelines to the entire hospital population (n=75,139) would imply an increase of 12,323 statin prescriptions.

**Conclusion:** The application of the new guidelines was associated with greater potential prescription of statins, particularly among women and older subjects.

**Keywords:** Cholesterol - Statins - Risk Scores - Guidelines

### RESUMEN

**Introducción:** De la aplicación de las nuevas guías sobre la indicación de estatinas surge un aumento considerable de su prescripción. No contamos con investigaciones que hayan abordado esta problemática en nuestra región.

**Objetivo:** Comparar en una población afiliada a un seguro de salud la proporción de sujetos con indicación de estatinas según las guías nuevas (ACC/AHA 2013) versus las antiguas (ATP III) para el manejo del colesterol.

**Material y métodos:** En una muestra aleatoria simple sin reposición se analizó la proporción de sujetos elegibles para recibir estatinas según ambas guías, extrapolando los hallazgos a toda la población del sistema de salud.

**Resultados:** Se analizaron 226 pacientes. La indicación de estatinas fue del 35,8% y 52,2% al aplicar las guías ATP III y ACC/AHA 2013, respectivamente. La diferencia fue mayor en las mujeres (18,3%), y en los sujetos > 60 años (27,1%). Aplicar las nuevas guías a toda la población hospitalaria (n = 75.139) implicaría un aumento de 12.323 prescripciones de estatinas.

**Conclusión:** La utilización de las nuevas guías se asoció con una potencial mayor indicación de estatinas, fundamentalmente en mujeres y en sujetos con mayor edad.

**Palabras clave:** Colesterol - Estatinas - Puntajes de riesgo - Guías

### Abbreviations

ACC	American College of Cardiology	ATP III	Adult Treatment Panel III
AHA	American Heart Association	LDL-C	Low-density lipoprotein cholesterol

### INTRODUCTION

The Framingham risk score is the most commonly used tool to predict cardiovascular risk in our country, recommended by the third report of the National Cholesterol Education Program expert panel [Adult Treatment Panel III (ATP III)]. (1)

By the end of 2013, the American College of Cardiology (ACC) and the American Heart Association (AHA) published the new guidelines, establishing new recommendations on the treatment of blood cholesterol. (2) These guidelines use a new risk score and, in general, a lower threshold to prescribe statins com-

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pared with the previous guidelines. A recent investigation from the United States showed that compared to the ATP III recommendations, the application of the new guidelines increased the number of new statin prescriptions; (3) however, there are no investigations on this topic in our region.

The goals of this study were: to compare in a sample of patients from a population belonging to the healthcare system of a University Hospital, the proportion of members that would be eligible for statin therapy if the new 2013 ACC/AHA and the old ATP III guidelines were applied and 2) to extrapolate the results to the entire population of the healthcare system, analyzing the impact of applying the recommendations established by both guidelines.

## METHODS

A cross-sectional study was performed by December 21, 2014, describing the proportion of members belonging to the healthcare system of a University Hospital that would be eligible for statin therapy according to each guideline. The cohort consisted of subjects between 40 and 75 years (the age that allows to estimate the scores recommended by both guidelines), excluding subjects with triglyceride levels >400 mg/dL (which could distort the LDL-C level calculated, and, in consequence, the prescription of statin therapy).

Sampling was done without replacement. The electronic clinical records of the patients included were revised, obtaining information about their history, cardiovascular risk factors and medication received over the past year.

A sample of 174 members was estimated to provide 80% power (beta error of 0.2) and an alpha error of 0.05 to detect an absolute difference  $\geq 15\%$  between the proportion of members eligible for statin therapy according to the recent guidelines compared with the previous recommendations. (3) Assuming that the information could be incomplete in some of the subjects randomized, we requested the sample to be 20% larger. In case of missing data, the patient was contacted by telephone.

Different criteria were used to determine whether the subjects were eligible for statin therapy: 1) For the ATP III guideline: a) History of cardiovascular disease and LDL-C  $\geq 100$  mg/dL; b) LDL-C  $\geq 190$  mg/dL; c) Diabetes and LDL-C  $\geq 100$  mg/dL; d) Framingham risk score  $\geq 20\%$  and LDL-C  $\geq 100$  mg/dL; Framingham risk score between 10% and 20% with LDL-C  $\geq 130$  mg/dL and two additional risk factors [smoking, hypertension, high density lipoprotein-cholesterol (HDL-C) <40 mg/dL, family history of premature coronary artery disease, and age  $\geq 45$  years in men and  $\geq 55$  in women]; Framingham risk score <10% with LDL-C >160 mg/dL and two additional risk factors. 2) For the 2013 ACC/AHA guideline: a) Cardiovascular disease; b) LDL-C  $\geq 190$  mg/dL; c) Diabetes and LDL-C  $\geq 70$  mg/dL; d) Estimated risk at 10 years by the new score  $\geq 7.5\%$  and LDL-C  $\geq 70$  mg/dL. Those patients already receiving statin therapy were considered as subjects with appropriate prescription according to both guidelines, as in previous studies. (3)

## Statistical analysis

The concordance between both guidelines was analyzed using Cohen's kappa index and the Bland-Altman graph plot for graphical representation. A two-tailed p value < 0.01 was considered statistically significant.

## Ethical considerations

The study protocol was approved by the Institutional Ethics Committee.

## RESULTS

The clinical records of 226 patients (mean age 60.3 years; 60.6% women) were analyzed. A history of cardiovascular disease was present in 5.8% of the subjects, 9.3% were diabetics and 5.3% had very high LDL-C levels (>190 mg/dL); 36.1% of the population was receiving statins. The median Framingham risk score was 3% (interquartile range 2-7) while the median new score was 5% (interquartile range 1.9-10.5).

Applying the ATP III and the 2013 ACC/AHA guidelines, 35.8% and 52.2% of the population were eligible for statin therapy, respectively (difference of 16.4%) The concordance between both guidelines was moderate to select the population eligible for statin therapy (kappa coefficient 0.57). Only 6 of the 81 patients eligible for statin therapy according to the ATP III should not receive statins applying the new guidelines. On the other hand, of the 118 subjects who would be eligible for statin therapy according to the new recommendations, 43 would not receive it applying the ATP III. The concordance between both strategies was also moderate when considering only those subjects who would be eligible for statin therapy depending on the risk score (Figure 1).

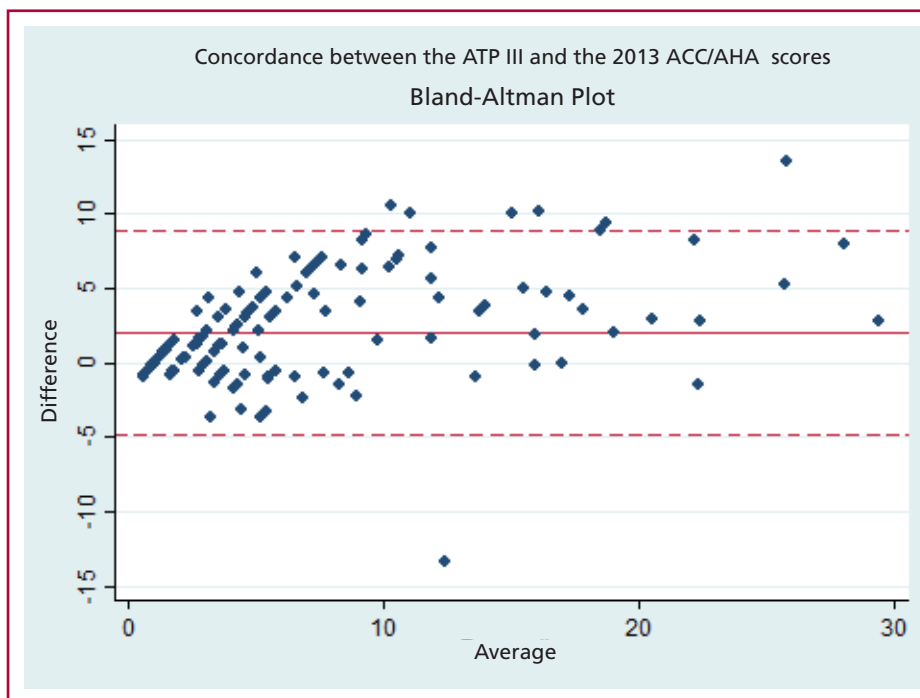
Eighty-four percent of the patients in secondary prevention were receiving statins. In primary prevention, the proportion of subjects eligible for statin therapy according to the risk score was greater applying the 2013 ACC/AHA guidelines. Figure 2 shows the reasons to prescribe statin therapy in primary prevention.

In men, 46.1% and 59.6% of the patients were eligible for statin therapy according to the ATP III and the 2013 ACC/AHA guidelines, respectively (difference of 13.5%). In women, 29.2% and 47.5% of the population was eligible for statin therapy according to both guidelines (difference of 18.3%). The concordance between both guidelines was moderate in both sexes (women: kappa coefficient 0.54; men: kappa coefficient 0.60)

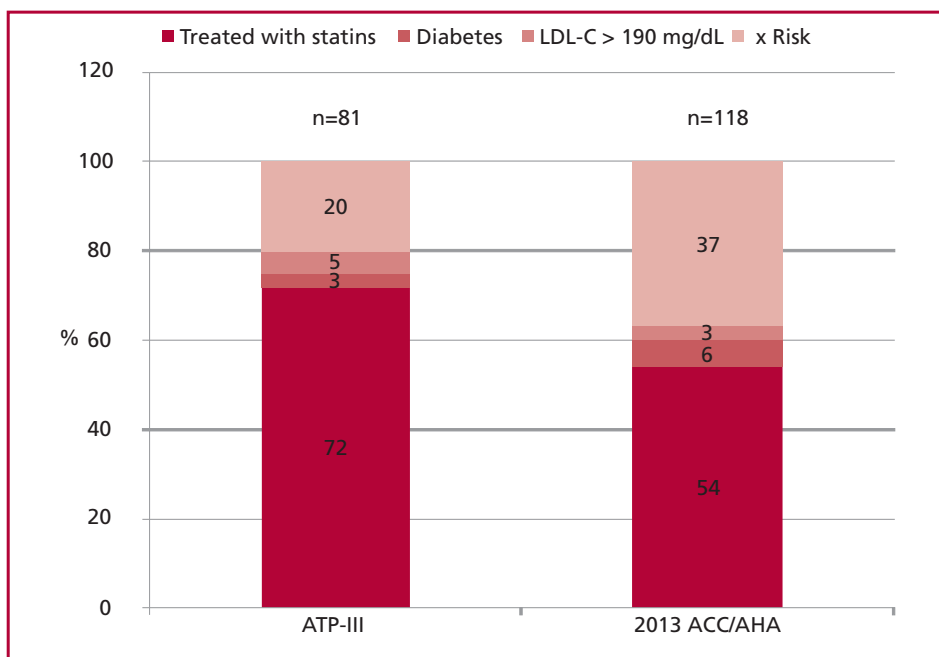
In subjects >60 years, 51.9% and 79% of the patients were eligible for statin therapy according to the ATP III and the 2013 ACC/AHA guidelines, respectively (difference of 27.1%). In subjects  $\leq 60$  years, 12.9% and 14.0% of the population was eligible for statins according to both guidelines (difference of 1.1%). The concordance between both guidelines was discrete in subjects >60 years (kappa coefficient 0.35) and significant in those  $\leq 60$  years (kappa coefficient 0.68)

The Health Insurance Program had 74,139 members between 40 and 75 years (44,819 women and 30,320 men). If we extrapolate the findings of this random sample to this entire universe, 26,900 and 39,223 subjects would be eligible for statin therapy applying the ATP III and the 2013 ACC/AHA guidelines, respectively, representing an increase of 12,474 prescriptions (Figure 3).

**Fig. 1.** Bland-Altman graph plot showing the concordance between the Framingham risk score (ATP III) and the 2013 ACC/AHA guideline score in a sample of members belonging to a University Hospital Health Insurance Program in Buenos Aires. The solid line shows the average difference between both scores (2%) and the dotted lines show the 95% limits of agreement (-5% to +9%).



**Fig. 2.** Proportion of the different reasons for “absolute statin indication” after applying both guidelines to a sample of members belonging to a University Hospital Health Insurance Program in Buenos Aires.



**DISCUSSION**

The main finding of our study was that the proportion of patients eligible for statin therapy increased by about 46% applying the new guidelines for cholesterol management instead of the traditional guidelines.

Similarly, Pencina et al. evaluated the impact of applying both guidelines for statin prescription in a sample of 3,773 subjects. (3) Their results were similar to ours: the proportion of subjects who were receiving or were eligible for statin therapy increased from

42% to 56.6% (37.5% to 48.6% in those who were not previously receiving statins) when the new guidelines were applied versus the traditional recommendations.

In our setting, a recent study showed that the concordance between several risk scores was poor, and that the prescription of statins had a significant variation depending on the tool used. Interestingly, the indication of statins was greater applying the 2013 ACC/AHA score. (4)

In the same sense, Ray et al. evaluated the impact

of applying the new guidelines in a European cohort, concluding that 65% of the adult population would be eligible for statin therapy applying these recommendations. (5)

In our study, and in agreement with the article by Pencina et al., (3) the greatest impact of the application of the new guidelines on statin therapy was seen in subjects >60 years. While eligibility for statin therapy increased by 8.5% in young subjects, this indication increased by 52% in persons between 60 and 75 years.

The predictive capability of the new risk score is a common query about new guidelines. (6) The application of the new score could overestimate the risk of the population, showing a problem of calibration and discrimination. (7) Two recently published studies confirmed that the new guidelines overestimate the risk in primary prevention, (8, 9) a limitation that could generate increased prescription of statins.

Our findings emphasize the problem in older subjects. Age, per se, dominates the risk calculator, and the risk threshold of 7.5% is easily exceeded. (10) Moreover, a risk score dominated by chronological age favors late treatment and hinders early prevention of atherosclerosis.

Finally, we do not question the extraordinary benefit and the countless evidence supporting the use of statins, but the tools used to select subjects who could benefit from this medication.

## CONCLUSION

The application of the new 2013 ACC/AHA guidelines was associated with a potential increase in the indication of statin therapy, particularly in older subjects and women.

## Conflicts of interest

None declared. (See authors' conflicts of interest forms on the website/Supplementary material).

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## REFERENCES

1. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486-97. <http://doi.org/d39kqv>
2. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, et al. ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014;63:2889-934. <http://doi.org/f2skw5>
3. Pencina MJ, Navar-Boggan AM, D'Agostino RB, Williams K, Neely B, Sniderman AD, et al. Application of new cholesterol guidelines to a population-based sample. *N Engl J Med* 2014;370:1422-31. <http://doi.org/vck>
4. Masson W, Lobo M, Huerín M, Molinero G, Manente D, Pángaro M, et al. Use of Different Scores for Cardiovascular Risk Stratification in Primary Prevention and Their Implications in Statin Indication. *Rev Argent Cardiol* 2014;82:480-6. <http://doi.org/bc4r>
5. Ray KK, Kastelein JJ, Matthijs Boekholdt S, Nicholls SJ, Khaw KT, Ballantyne CM, et al. The ACC/AHA 2013 guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease risk in adults: the good the bad and the uncertain: a comparison with ESC/EAS guidelines for the management of dyslipidaemias 2011. *Eur Heart J* 2014;35:960-8. <http://doi.org/f5x9tf>
6. Morris PB, Ballantyne CM, Birtcher KK, Dunn SP, Urbina EM. Review of clinical practice guidelines for the management of LDL-related risk. *J Am Coll Cardiol* 2014;64:196-206. <http://doi.org/f2sxd5>
7. De Filippis AP, Young R, Carrubba CJ, McEvoy JW, Budoff MJ, Blumenthal RS. An analysis of calibration and discrimination among multiple cardiovascular risk scores in a modern multiethnic cohort. *Ann Intern Med* 2015;162:266-75. <http://doi.org/f6286q>
8. Ridker PM, Cook NR. Statins: new American guidelines for prevention of cardiovascular disease. *Lancet* 2013;382:1762-5. <http://doi.org/f2n38p>
9. Rana JS, Tabada GH, Solomon MD, Lo JC, Jaffe MG, Sung SH, et al. Accuracy of the atherosclerotic cardiovascular risk equation in a large contemporary, multiethnic population. *J Am Coll Cardiol* 2016;67:2118-30. <http://doi.org/f8jrgg>
10. Botet JP, Chillarón JJ, Benaiges D, Flores Le-Roux JA. Las guías estadounidenses de dislipemia. Fortalezas y debilidades. *Rev Esp Cardiol Supl* 2015;15(A):18-21.