Review Article

The Cost-Effectiveness and Cost-Utility of Statin Drug for the Treatment of Patients with Cardiovascular Disease, A Systematic Review

Mahmoud Eisavi*, Elaheh Mazaheri[1]*, Aziz Rezapour[2], Sajad Vahedi[3], Marziye Hadian[4], Abdosaleh Jafari[5]

Assistant Professor, Faculty of Economics, Allameh Tabataba'i University, [2]Health Management and Economics Research Center, Iran University of Medical Sciences, Tehran, [1]Department of Medical Library and Information Sciences, Health Information Technology Research Center, Student Research Committee, School of Management and Medical Information Sciences, Isfahan University of Medical Sciences, Isfahan, Iran, [4]Department of Health Care Management, Health Management and Economics Research Center, Student Research Committee, School of Management and Medical Information Sciences, Isfahan University of Medical Sciences, Isfahan, [3]Department of Health Services Management, School of Health, Ahvaz University of Medical Sciences, Ahvaz, [5]Health Human Resources Research Centre, School of Management and Medical Information Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

** contributed equally to this work*

Abstract

Cardiovascular diseases impose a burden of disease and economic burden on society. With regard to different drugs are used to treat cardiovascular disease; these interventions should be economically evaluated and them that the most cost-effective were selected. The aim of this study was to investigate the studies carried on the cost-effectiveness and cost-utility of statin drugs for the treatment of patients with cardiovascular disease between 2004 and 2020. Quality assessment of the articles was examined by Drummond's checklist. Given that the inclusion criteria, 26 articles included in the review. The results of this review showed that many articles related to the economic evaluation of statin drugs adhered international standards for performing economic evaluation studies. All the studies mentioned the source of effectiveness (the second criteria) and alternative options for the comparison (the third criteria). Atorvastatin and rosuvastatin drugs were the main options for the comparison in the studies. Although the results of the studies were different in some aspects, such as the type of modeling, costs items and the study perspective, they reached the same results which the use of statin drugs versus no-drug can decrease cost, cardiovascular events and deaths and increase QALY. The results were nearly different due to study design, time horizon, efficacy, and drug prices.

Keywords: *Cost-benefit analysis, cardiovascular diseases, statin drugs, systematic review*

Introduction

Cardiovascular diseases (CVDs) have been accounted as a leading cause of rehospitalization and mortality in the World.[1,2] Unfortunately, the large numbers of mortalities related to CVDs occur in low-and middle-income countries (LMICs). Heart attacks and strokes accounted as 80% of CVDs mortalities.[3-5] Global burden of diseases (GBD) studies showed that CVDs induce remarkable burden of disease, especially in LMICs. It is estimated that in 2020, ischemic heart disease (IHD) for example will be accounted as the first cause of mortality in the World.[2,6] Causing 10% of the burden of disease, after accidents and mental disorders, CVDs accounted for the third important contributor of the burden of disease in Iran.[7] CVDs also impose remarkable expenditures on both patients and healthcare systems.[8] In the personal and household levels, studies showed that households that affected by CVDs have larger medical expenditures. This may lead these households to face catastrophic healthcare expenditure.[9] Alongside primary prevention strategies such as tobacco control policies, taxation to reduce harmful food, increasing physical activity, alcohol reduction strategies and providing healthy school meals to children, evidence show that using medicines such as aspirin, beta-blockers, angiotensin-converting enzyme inhibitors and statins as secondary prevention may reduce the burden of CVDs.[5,10] Statins, a class of lipid-lowering medications, by reducing the production of cholesterol in the liver and reabsorbing cholesterols from the walls of the arteries reduce CVDs and mortality attributed to it. Because of their efficacy, the World Health Organization (WHO) included these medicines in the Essential Medicines 2015 list.[11]

Address for correspondence: *Dr. Abdosaleh Jafari, Health Human Resources Research Centre, School of Management and Medical Information Sciences, Shiraz University of Medical Sciences, Shiraz, Iran.*
E-mail: abdosaleh.jafari@gmail.com
Mrs. Marziye Hadian,
Department of Health Care Management, Health Management and Economics Research Center, Student Research Committee, School of Management and Medical Information Sciences, Isfahan University of Medical Sciences, Isfahan, Iran
E-mail: m.hadian68@gmail.com

How to cite this article: Eisavi M, Mazaheri E, Rezapour A, Vahedi S, Hadian M, Jafari A. The cost-effectiveness and cost-utility of statin drug for the treatment of patients with cardiovascular disease, a systematic review. Int J Prev Med 2021;12:39.

Access this article online

Website: www.ijpvmjournal.net/www.ijpm.ir

DOI: 10.4103/ijpvm.IJPVM_125_20

Quick Response Code:

Various interventions at the levels of prevention and treatment for CVDs have different cost and effectiveness. Hence, these interventions need to be evaluated regards to their cost and effectiveness. This fact highlighted the necessity of using economic evaluation techniques in this field. Economic evaluation is one of the scientific techniques that policy-makers use to determine the most possible cost-effective intervention.[12] Since there are numerous economic evaluation studies about statin drugs, present study tries to review these economic evaluation researches to inform both the public and policy-makers about their quality of methods, their results and to facilitate knowledge translation regarding statin drugs.

Methods

Literature search

Applying systematic review approach,[13] present research reviewed and extracted previous economic evaluation studies about statin drugs between 2004 and 2020 from scientific database such as Cochrane library, NHS Economic Evaluations Database Medline, PubMed, Google scholar, science direct, Scopus. Given that most studies on the economic evaluation of statin drugs were published after 2004, the time interval for the present study was chosen between 2004 and 2020.

The following keywords were applied:

Cost-effectiveness OR cost-utility OR economic evaluation AND cardiovascular disease OR coronary heart disease OR peripheral arterial disease AND statin drugs.

Inclusion and exclusion criteria

The inclusion criteria were based on the PICOTS framework: population: patients with cardiovascular disease. Intervention: statin drugs. Comparator: not restricted. Outcome: quality-adjusted life year (QALY), Life years gained (LYG) and clinical outcome. Time: articles published between 2004 and 2020. Study design: full economic evaluation studies.

Quality assessment

After searching for studies, the methodological quality of articles was examined by Drummond's checklist.[14] As Table 1 shows, this checklist included ten questions that examine the methodological quality of economic evaluation studies regards to the objective of studies, evidence of the effectiveness of the studied program, presence of competing alternatives, identifying important cost and consequences, measuring and valuing of identified cost and consequences, using incremental analysis, using sensitivity analysis, well discussion and conclusion about ICER and usefulness of the results for study context.

Table 1: Drummond's criteria for the quality assessment of economic evaluation studies

Row	Criteria
1	Was the main question of the study asked in an appropriate way?
2	Were the competitor options presented in a comprehensive manner?
3	Were evidences of the effectiveness program presented?
4	Were all significant costs and relevant outcomes identified?
5	Were all significant costs and relevant outcomes properly measured?
6	Were all significant costs and relative outcomes properly valued?
7	Were costs and outcomes adjusted for different time?
8	Were an incremental analysis of the costs and outcomes of competitor options carried out?
9	Were the effects of uncertainty (sensitivity analysis) investigated for all costs and outcomes?
10	Were all problems related to the users of the results of the study investigated during analysis and presentation of results?

Data extraction

Using designed tables, the data were extracted and summarized. To arrange the studies, read the titles and abstracts, and identify duplicates, Endnote X5 software was applied.

Results

After searching pre-identified scientific databases, totally 576 articles were found. Subsequently, according to the inclusion and exclusion criteria, the found articles decreased to the 125 articles. Finally, after reviewing full text, the screened articles decreased to 26 articles that performed full economic evaluation analysis.[15-40] The results of the systematic review have shown in the Figure 1.

The results of the quality assessment of the screened articles by using Drummond checklist were represented in Table 2. Based on Table 2, many articles related to the economic evaluation of statin drugs adhered international standards for performing economic evaluation studies. Totally, 80% of the studies clearly mentioned the main research question of the study (first criteria). All the studies mentioned the source of effectiveness (the second criteria) and alternative options for the comparison (the third criteria). Atorvastatin and rosuvastatin drugs were the main options for the comparison in the studies. Although the results of the studies were different in some aspects, such as the type of modeling, costs items, and the study perspective, they reached the same results which the use of statin drugs versus no-drug can decrease cost, cardiovascular events and deaths and increase QALY. In Table 3, the economic characteristic of the studies was represented. As depicted in this table, 6 articles and 19 articles used cost-effectiveness analysis and cost-utility analysis, respectively. 1 study

Table 2: Qualitative assessment of English articles using Drummond's checklist

Study	1- Was the main question of the study asked in an appropriate way?	2- Were the competitor options presented in a comprehensive manner?	3- Were evidences of the effectiveness program presented?	4- Were all significant costs and relevant outcomes identified?	5- Were all significant costs and relevant outcomes properly measured?	6- Were all significant costs and relative outcomes properly valuated?	7- Were costs and outcomes adjusted for different times?	8- Were an incremental analysis of the costs and outcomes of competitor options carried out?	9- Were the effects of uncertainty (sensitivity-analysis) investigated for all costs and outcomes?	10- Were all problems related to the users of the results of the study investigated during analysis and presentation of results?
Amirsadri[18]	+	+	+	+	+	+	+	+	+	n/a
Pandya[33]	+	+	+	-	n/a	n/a	+	+	+	n/a
Pandya[34]	n/a	+	+	n/a	n/a	n/a	+	+	+	n/a
Ribeiro[37]	+	+	+	+	+	+	+	+	+	n/a
Vegter[40]	+	+	+	+	+	+	+	+	+	n/a
Burger[23]	+	+	+	+	+	+	+	+	+	n/a
Barrios[22]	+	+	+	+	+	+	+	+	+	n/a
Gandhi[25]	+	+	+	+	+	+	+	+	+	n/a
Fragoulakis[24]	+	+	+	+	+	+	+	+	+	+
Ademi[16]	+	+	+	+	+	+	+	+	+	+
Reckless[36]	+	+	+	+	+	+	+	+	+	+
Ara[19]	+	+	+	+	+	+	+	+	+	+
Ara[20]	+	+	+	+	+	+	+	+	+	n/a
Mullins[32]	+	+	+	+	+	+	+	+	+	n/a
Pinto[35]	+	+	+	+	+	+	+	+	+	n/a
Armstrong[21]	+	+	+	+	+	+	+	+	+	n/a
Arnio[15]	+	+	+	+	+	+	+	+	+	+
Stomberg[39]	+	+	+	+	+	+	+	+	+	n/a
Stam-Slob[38]	+	+	+	+	+	+	+	+	+	+
Agus[17]	+	+	+	+	+	+	+	+	+	+
Grabner[26]	N/A	+	+	N/A	N/A	N/A	+	+	+	+
Heller[27]	N/A	+	+	N/A	N/A	N/A	+	+	+	N/A
Hong[28]	+	+	+	+	+	+	+	+	+	+
Jeong[29]	N/A	+	+	N/A	N/A	N/A	-	-	-	N/A
Lin[30]	+	+	+	+	+	+	+	+	+	+
Lum[31]	N/A	+	+	N/A	N/A	N/A	-	-	N/A	+

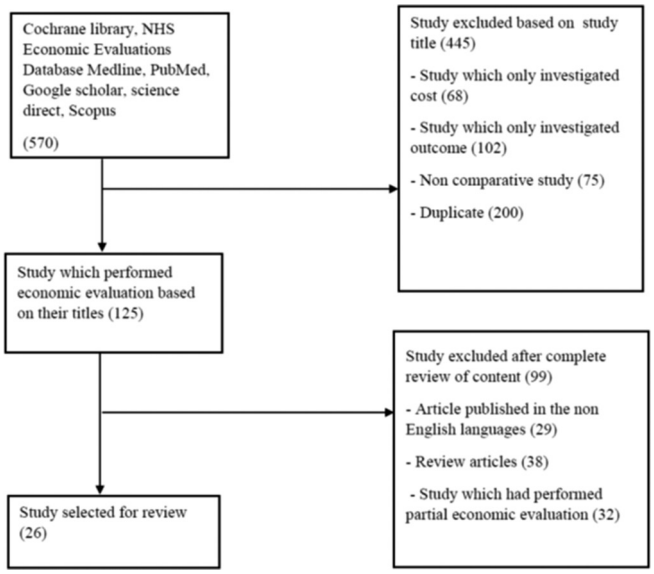

Figure 1: Result of systematic literature search

performed cost-benefit analysis. In the CEA articles, 2 articles used life year gain and 4 articles used clinical outcomes as effectiveness measure. Concerning design of the studies, 20 articles conducted by using Markov modeling, 1 article used decision tree modeling and 2 articles conducted alongside a clinical trial. Regarding sensitivity analysis, to decrease uncertainty in economic evaluation, 14 articles simultaneously have performed one-way and probabilistic sensitivity analysis and 2 articles used scenario analysis. Most of the studies (13 articles) applied lifetime approach as time horizon of study. In relation to discounting of future outcomes and costs, most of the studies (11 articles) used 1–3% discount rate and 3 studies used 3.5% discount rate. The number of economic evaluations studies about statin drugs in terms of year of publication was indicated in Figure 2. Based on this figure, most of the studies (27%) published in 2017.

Discussion

In the present study, 26 studies were reviewed, and the results indicated that the most of studies related to the economic evaluation of statin drugs adhered international standards for performing economic evaluation studies. The most weakness in these articles was associated with the 10th Drummond's criteria. Another shortcoming in the articles was related to perspective so that many articles were not able to measure costs based on the study viewpoint. For instance, in the Pandya's study, the study viewpoint was the society, but indirect costs were not estimated.[33] furthermore, most studies applied the Markov model for analysis. Regarding the type of sensitivity analysis, 54% of the studies conducted one-way and probabilistic analysis at the same time in order to handle uncertainty. Sensitivity analysis assists the researcher to determine which parameters are the main factors for the results of economic evaluation.[41,42]

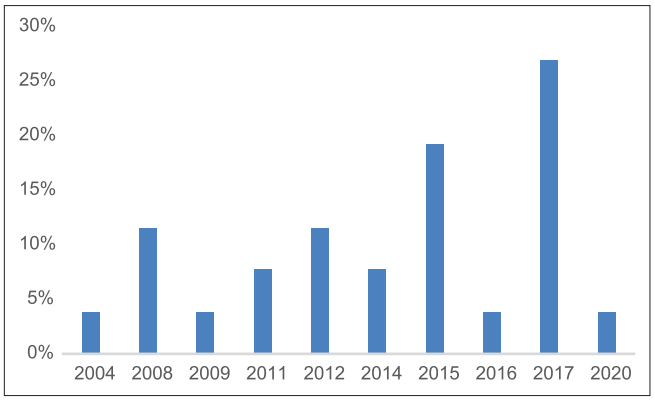

Figure 2: The Number of articles published on economic evaluation of statin drugs, by year

Table 3: Economic characteristics of reviewed articles

Characteristics	Number	Percentage
Type of Economical Evaluation		
Cost-effectiveness analysis	6	23
Cost-utility analysis	19	73
Cost-benefit analysis	1	4
Study Design		
Randomized controlled trial	2	8
Decision tree	1	4
Markov model	20	77
Retrospective	3	11
Perspective evaluated		
Social	3	11
Health system	17	65
Payer	1	4
Not stated	5	20
Type of Sensitivity Analysis		
One-way	3	11
Probabilistic	4	15
One-way and probabilistic	14	54
Scenario	2	8
Probabilistic and Scenario	2	8
Not performed	1	4
Time Horizon		
1-10 years	11	42
Over 10 years	2	8
Lifetime	13	50
Type of Outcome		
Quality-Adjusted Life Year (QALY)	13	50
Life Years Gained (LYG)	2	8
QALY and LYG	5	19
Clinical outcome	4	19
Clinical outcome and QALY	1	4
Discount rate for time horizons of more than 1 year		
1-3%	11	42
5%	3	11
3.5%	3	11
4% for cost and 1.5% for QALY	3	11

The results of the present study indicated that the use of statin drugs versus no-drug for primary prevention of

cardiovascular disease can be cost-effective and reduce cost, cardiovascular events and deaths and increase QALY. Lin *et al*., in their study in Taiwan, showed that lowering the target low-density lipoprotein cholesterol (LDL-C) level from 100 to 70 mg/dL using statin therapy could be cost-effective. their study also indicated that The probabilities of being cost-effective at willingness-to-pay thresholds of one and three gross domestic product per capita ($24,329 in 2017) per QALY were 51.1% and 94.2%, respectively.[30] Jeong *et al*. in their study in Korea also found that at baseline LDL-C levels of 130–159 mg/dL, the cost-effectiveness analysis (CEA) based on the LDL-C reduction rate (CEA-RR) value of rosuvastatin (20 mg) was three times lower than that of atorvastatin (40 mg).[29] In a similar study, about cost-utility analysis alongside RCT in the UK and Ireland, Agus *et al*. showed that simvastatin was cost-effective for the treatment of patients with acute respiratory distress syndrome, being related to both a significant QALY gain and a cost saving.[17] Amirsadr *et al*. also found that the use simvastatin 10 mg for the primary prevention of myocardial infarction (MI) in 45-year men with a 10-year CVD risk of 15% could be highly cost-effective in Iran.[18]

Study limitation

First, due to the heterogeneity of the results of studies, performing meta-analysis was impossible. Another limitation of this review was that unpublished studies such as reports from the department of health technology assessment and health economics department, medical schools, reports from pharmaceutical companies and academic thesis.

Conclusions

This systematic review indicated that that many articles related to the economic evaluation of statin drugs adhered international standards for performing economic evaluation studies. All the studies clearly stated the source of effectiveness (the second criteria) and alternative options for the comparison (the third criteria). Atorvastatin and rosuvastatin drugs were the main options for the comparison in the studies. Although the results of the studies were different in some aspects, such as the type of modeling, costs items, and the study perspective, they reached the same results which the use of statin drugs versus no-drug can decrease cost, cardiovascular events and deaths and increase QALY. The results were nearly different due to study design, time horizon, efficacy, and drug prices. Moreover, in most studies, the utility value was derived from the literature, which could cause an overvaluation or undervaluation of QALY.

Acknowledgments

The authors would like to thank all those who cooperated in collecting and analyzing the data.

Financial support and sponsorship

This article was extracted from a research project supported financially by Health Management and Economics Research Center, Iran University of Medical Sciences, grant's No. 94-04-163-26765.

Conflicts of interest

There are no conflicts of interest.

Received: 18 Mar 20 **Accepted:** 14 Jul 20
Published: 15 May 21

References

1. Roth GA, Huffman MD, Moran AE, Feigin V, Mensah GA, Naghavi M, *et al*. Global and regional patterns in cardiovascular mortality from 1990 to 2013. Circulation 2015;132:1667-78.
2. Joseph P, Leong D, McKee M, Anand SS, Schwalm JD, Teo K, *et al*. Reducing the global burden of cardiovascular disease, part 1: The epidemiology and risk factors. Circulation Res 2017;121:677-94.
3. Gupta S, Epari V, Bhatia S. Potential gains of screening family members of suspected coronary artery disease: A pilot study. Int J Prev Med 2019;10:148.
4. Javadi M, Jamalzehi A, Gerami H, Hosseini SK, Maljaei MB, Eslami M, *et al*. Association between dietary intakes of tea, coffee, and soft drinks in patients undergoing coronary angiography with coronary artery stenosis. Int J Prev Med 2019;10:172.
5. World Health Organization. Cardiovascular diseases (CVDs). 2017. Fact Sheet 2016(317).
6. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, *et al*. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. J Am College Cardiol 2017;70:1-25.
7. Forouzanfar MH, Sepanlou SG, Shahraz S, BESc PN, Pourmalek F, Lozano R, *et al*. Evaluating causes of death and morbidity in Iran, global burden of diseases, injuries, and risk factors study 2010. Arch Iran Med 2014;17:304.
8. Cook C, Cole G, Asaria P, Jabbour R, Francis DP. The annual global economic burden of heart failure. Int J Cardiol 2014;171:368-76.
9. Kankeu HT, Saksena P, Xu K, Evans DB. The financial burden from non-communicable diseases in low- and middle-income countries: A literature review. Health Res Policy Syst 2013;11:31.
10. Yusefi AR, Lankarani KB, Bastani P, Radinmanesh M, Kavosi Z. Risk factors for gastric cancer: A systematic review. Asian Pac J Cancer Prev 2018;19:591-603.
11. Leong DP, Joseph PG, McKee M, Anand SS, Teo KK, Schwalm JD, *et al*. Reducing the global burden of cardiovascular disease, part 2: Prevention and treatment of cardiovascular disease. Circ Res 2017;121:695-710.
12. Collins M, Mason H, O'Flaherty M, Guzman-Castillo M, Critchley J, Capewell S. An economic evaluation of salt reduction policies to reduce coronary heart disease in England: A policy modeling study. Value Health 2014;17:517-24.
13. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. J Clin Epidemiol 2009;62:e1-34.
14. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Health

Care Programmes. Oxford University Press; 2015.
15. Aarnio E, Korhonen MJ, Huupponen R, Martikainen J. Cost-effectiveness of statin treatment for primary prevention in conditions of real-world adherence–estimates from the Finnish prescription register. Atherosclerosis 2015;239:240-7.
16. Rezapour A, Hadian M, Ghasemi M, Vahedi S, Jafari A. Economic Evaluation of the Drugs Used In Treating Patients with Myocardial Infarction: A Systematic Review. Journal of Health Management & Informatics. 2019;6:7-14.
17. Agus A, Hulme C, Verghis R, McDowell C, Jackson C, O'Kane C, *et al*. Simvastatin for patients with acute respiratory distress syndrome: Long-term outcomes and cost-effectiveness from a randomised controlled trial. Critical Care 2017;21:108.
18. Amirsadri M, Hassani A. Cost-effectiveness and cost-utility analysis of OTC use of simvastatin 10 mg for the primary prevention of myocardial infarction in Iranian men. Daru 2015;23:56.
19. Ara R, Pandor A, Stevens J, Rafia R, Ward S, Rees A, *et al*. Prescribing high-dose lipid-lowering therapy early to avoid subsequent cardiovascular events: Is this a cost-effective strategy? Eur J Prev Cardiol 2012;19:474-83.
20. Ara R, Pandor A, Tumur I, Paisley S, Duenas A, Williams R, *et al*. Estimating the health benefits and costs associated with ezetimibe coadministered with statin therapy compared with higher dose statin monotherapy in patients with established cardiovascular disease: Results of a Markov model for UK costs using data registries. Clin Ther 2008;30:1508-23.
21. Jabbari A, Jafari A, Hadian M, Ghasemi M. Model-based Cost-effectiveness Analysis of Atorvastatin Drugs for Prevention of Cardiovascular Diseases in Iran. Int J Prev Med. 2020;11:57.
22. Barrios V, Lobos JM, Serrano A, Brosa M, Capel M, Álvarez Sanz C. Cost-effectiveness analysis of rosuvastatin vs generic atorvastatin in Spain. J Med Econ 2012;15(Sup 1):45-54.
23. Burgers L, Nauta S, Deckers J, Severens J, Redekop WK. Is it cost-effective to use a test to decide which individuals with an intermediate cardiovascular disease risk would benefit from statin treatment? Int J Cardiol 2014;176:980-7.
24. Fragoulakis V, Kourlaba G, Maniadakis N. Economic evaluation of statins in high-risk patients treated for primary and secondary prevention of cardiovascular disease in Greece. Clinicoecon Outcomes Res 2012;4:135-43.
25. Gandhi SK, Jensen MM, Fox KM, Smolen L, Olsson AG, Paulsson TJC, *et al*. Cost-effectiveness of rosuvastatin in comparison with generic atorvastatin and simvastatin in a Swedish population at high risk of cardiovascular events. Clinicoecon Outcomes Res 2012;4:1-11.
26. Grabner M, Winegar DA, Punekar RS, Quimbo RA, Cziraky MJ, Cromwell WC. Cost effectiveness of achieving targets of low-density lipoprotein particle number versus low-density lipoprotein cholesterol level. Am J Cardiol 2017;119:404-9.
27. Heller DJ, Coxson PG, Penko J, Pletcher MJ, Goldman L, Odden MC, *et al*. Evaluating the impact and cost-effectiveness of statin use guidelines for primary prevention of coronary heart disease and stroke. Circulation 2017;136:1087-98.
28. Hong JC, Blankstein R, Shaw LJ, Padula WV, Arrieta A, Fialkow JA, *et al*. Implications of coronary artery calcium testing for treatment decisions among statin candidates according to the ACC/AHA cholesterol management guidelines: A cost-effectiveness analysis. JACC Cardiovasc Imaging 2017;10:938-52.
29. Jeong Y, Kim H, Baik S, Kim T, Yang S, Lee SH, *et al*. Analysis and comparison of the cost-effectiveness of statins according to the baseline low-density lipoprotein cholesterol level in Korea. J Clin Pharm Ther 2017;42:292-300.
30. Lin F-J, Shyu K-G, Hsieh I-C, Sheu WH-H, Tu S-T, Yeh S-J, *et al*. Cost-effectiveness of statin therapy for secondary prevention among patients with coronary artery disease and baseline LDL-C 70–100 mg/dL in Taiwan. J Formos Med Assoc 2020;119:907-16.
31. Lum CJ, Nakagawa K, Shohet RV, Seto TB, Taira DA. The cost-benefit balance of statins in Hawai'i: A moving target. Hawaii J Med Public Health 2017;76:99-102.
32. Mullins CD, Rattinger GB, Kuznik A, Koren MJ. Cost-effectiveness of intensive atorvastatin treatment in high-risk patients compared with usual care in a postgeneric statin market: Economic analysis of the aggressive lipid-lowering initiation abates new cardiac events (ALLIANCE) study. Clin Ther 2008;30:2204-16.
33. Pandya A, Sy S, Cho S, Weinstein MC, Gaziano TA. Cost-effectiveness of 10-year risk thresholds for initiation of statin therapy for primary prevention of cardiovascular disease. JAMA 2015;314:142-50.
34. Pandya A, Weinstein MC, Salomon JA, Cutler D, Gaziano TA. Who needs laboratories and who needs statins?: Comparative and cost-effectiveness analyses of non–laboratory-based, laboratory-based, and staged primary cardiovascular disease screening guidelines. Circ Cardiovasc Qual Outcomes 2014;7:25-32.
35. Pinto CG, Carrageta MO, Miguel LS. Cost-effectiveness of rosuvastatin in the prevention of ischemic heart disease in Portugal. Value Health 2008;11:154-9.
36. Reckless J, Davies G, Tunceli K, Hu XH, Brudi PJ. Projected cost-effectiveness of ezetimibe/simvastatin compared with doubling the statin dose in the United Kingdom: Findings from the INFORCE study. Value Health 2010;13:726-34.
37. Ribeiro RA, Duncan BB, Ziegelmann PK, Stella SF, Vieira JLdC, Restelatto LMF, *et al*. Cost-effectiveness of high, moderate and low-dose statins in the prevention of vascular events in the Brazilian public health system. Arq Bras Cardiol 2015;104:32-44.
38. Stam-Slob MC, van der Graaf Y, Greving JP, Dorresteijn JA, Visseren FL. Cost-effectiveness of intensifying lipid-lowering therapy with statins based on individual absolute benefit in coronary artery disease patients. J Am Heart Assoc 2017;6:e004648.
39. Stomberg C, Albaugh M, Shiffman S, Sood N. A cost-effectiveness analysis of over-the-counter statins. Am J Manag Care 2016;22:e294-303.
40. Vegter S, Oosterhof P, van Boven JF, Stuurman-Bieze AG, Hiddink EG, Postma MJ. Improving adherence to lipid-lowering therapy in a community pharmacy intervention program: A cost-effectiveness analysis. J Manag Care Spec Pharm 2014;20:722-32.
41. Andronis L, Barton P, Bryan S. Sensitivity analysis in economic evaluation: An audit of NICE current practice and a review of its use and value in decision-making. Health Technol Assess; 2009;13:iii.
42. Bojke L, Claxton K, Sculpher M, Palmer S. Characterizing structural uncertainty in decision analytic models: A review and application of methods. Value Health 2009;12:739-49.