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Statin prescribing pattern and the outcomes for acute coronary syndrome as primary and secondary prevention: a comprehensive review

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ABSTRACT: Cardiovascular disease is the highest rate of total burden non-communicable disease worldwide in these 5 recent years. Reducing the LDL-c level is closely related to reducing the risk of cardiovascular events recurrences among Acute Coronary Syndrome (ACS) patients. This study aims to explore the statin prescribing pattern among the ACS population and population at risk of ACS and to sum up the reported clinical outcomes, cost-effectiveness, or quality of life-related to statin utilization. The literature searching was conducted by using PubMed and Scopus databases from January 2020 to December 2021. Ten eligible studies were included, examining outcomes such as Major Adverse Cardiovascular Events (MACE), quality of life, and cost-effectiveness. Atorvastatin emerged as the most frequently prescribed statin for both primary and secondary prevention. In high-risk ACS populations, the delayed or underutilization of high-intensity statins led to suboptimal cardiovascular outcomes. Conversely, early administration, particularly within 48 hours post-event or post-PCI, significantly reduced MACE. Importantly, low to moderate intensity statin regimens showed cost-effectiveness primarily among low-risk ACS groups only when treatment was fully subsidized. In settings without government coverage, statin inaccessibility may affect the increased of recurrent events and elevated healthcare costs. The strategic use of statins—especially timely initiation and risk-based intensity selection—offers measurable benefits in reducing cardiovascular events. However, the lack of universal healthcare coverage for statin therapy in low- to middle-income settings presents a substantial barrier to cost-effective care, particularly for high-risk individuals. These findings underscore the need for policy interventions and expanded access to guideline-directed statin therapy.

KEYWORDS: Acute coronary syndrome; statin; cost-effectiveness; quality of life; secondary prevention.

INTRODUCTİON

Cardiovascular disease is the highest rate of total burden non-communicable disease worldwide in these 5 recent years [1]. Some recent guidelines recommend the use of statins as the major therapy for atherosclerotic cardiovascular disease (ASCVD) including acute coronary syndrome (ACS) [2]. The use of statins as an important medication in the primary and secondary prevention of vascular diseases has been applied to patients with Acute Coronary Syndrome [3]. Reducing the LDL-c level is closely related to reducing the risk of cardiovascular events recurrences among ACS patients. The need for supporting data regarding the reported outcomes profile of using the prescribed statin during the ACS hospitalization and after discharge should be provided. The prescriber should observe not only the clinical outcomes data but also the cost aspect and the patient's quality of life during the ACS therapy.

Financial and humanistic aspects are becoming a pivotal concern for chronic diseases besides the clinical outcomes. These concerns are due to the patients will experience the therapy for a long period so the prescriber should be aware of how to optimize the statins therapy during the treatment period [4],[5]. Statin should be prescribed to High-Risk Cardiovascular Events patients. The High-Risk Cardiovascular Event is defined as an experienced prior atheromatous disease, diabetes, blood pressure, smoking status, age, and sex [6]. Patients at Low-Risk with an abnormal lipid profile should be considered not to receive statin and each of the patient's risk-benefit ratios must be assessed carefully [7],[8].

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Some studies revealed that statin is still underused for those populations in some countries [9],[10]. This condition is interesting to be further analyzed in a systematic review study so that can provide the supported data regarding the current statin's prescription pattern as well reported outcomes such as clinical outcomes, cost-effectiveness, and qualitative among the patients with Acute Coronary Syndrome either as primary or secondary intervention. This review aimed to explore the statin prescribing pattern among the ACS population and the population at risk of ACS. This review also intended to sum up the reported clinical outcomes, cost-effectiveness, or quality of life-related to statin utilization.

▪ MATERIALS AND METHODS

Materials

The selected studies were extracted from PubMed and Scopus databases during January 2020 to December 2021. PubMed and Scopus were chosen for their extensive coverage in terms of their outstanding publication quality with peer-reviewed research articles that could ensure a comprehensive retrieval of relevant studies. The relevant studies were collected by using the combination of Medical Subject Heading (MeSH) terms and keywords of population domain (Acute Coronary Syndrome) and intervention domain (Statin Prescription). Prescribing pattern, drug prescription, clinical outcome, major adverse cardiovascular events, cholesterol, quality of life, quality adjusted life year, cost analysis, and cost were combined with anykind of statin as the searching strategy to find the desired studies. One reviewer (PM) was performing the searching process then verified by the other reviewers (FC, WH, MT, BR). All the results are then discussed among all the authors for finishing the final report to evaluate the quality of each selected articles by also using related quality assessment checklist such as Newcastle-Ottawa Scale (NOS) or AXIS checklist The final report and revision process were conducted by 2 authors (PM, WH).

Methods

This systematic review included all references reporting the prescribed statin for ACS patients either for primary or secondary prevention. This review also collected the report about the clinical outcomes, cost-effectiveness, or quality of life assessed among ACS patients or patients at risk of ACS. The selected study should involve participants with ACS or participants known as ACS risk. There are no limited ages for the participants. The selected references should involve participants who use statins and the used statin should be mentioned clearly in the study. This study set the list of criteria which should meet with all the included articles in the inclusion and exclusion criteria. Studies that reporting the type of prescribed statin, reporting the outcome as a clinical or cost-effectiveness or quality of life, involving participants with ACS or in the risk of ACS and full-text article, were included in this review. Studies that use the patient's adherence profile to measure the outcome, a review study, protocol study, and expert opinion were excluded from current review. The selection process was conducted thoroughly by all the authors.

Data analysis

Data from the selected articles that consisted of authors, study design, year of publication, country, type of statin, prescribing pattern and outcomes (clinical and economic), were extracted by 3 independent reviewers (WH, FC, BR).

▪ RESULTS

This study identified 239 articles from PubMed and 234 articles from Scopus. Duplication of the articles between two databases were found as much as 289 articles. We excluded 141 articles at the beginning due to unrelated title and abstract, then found 148 full-text articles for fully screening based on the eligibility criteria. Finally, 10 articles were met the criteria to be included in this systematic review (see Figure 1). The 10 selected studies, could sufficiently provide the scientific support about the use of high-intensity statin for the high-risk patients particularly as the secondary prevention in ACS patients. Moreover, those studies could consistently report the reduction in MACEs and positive short-term health outcomes post-PCI.

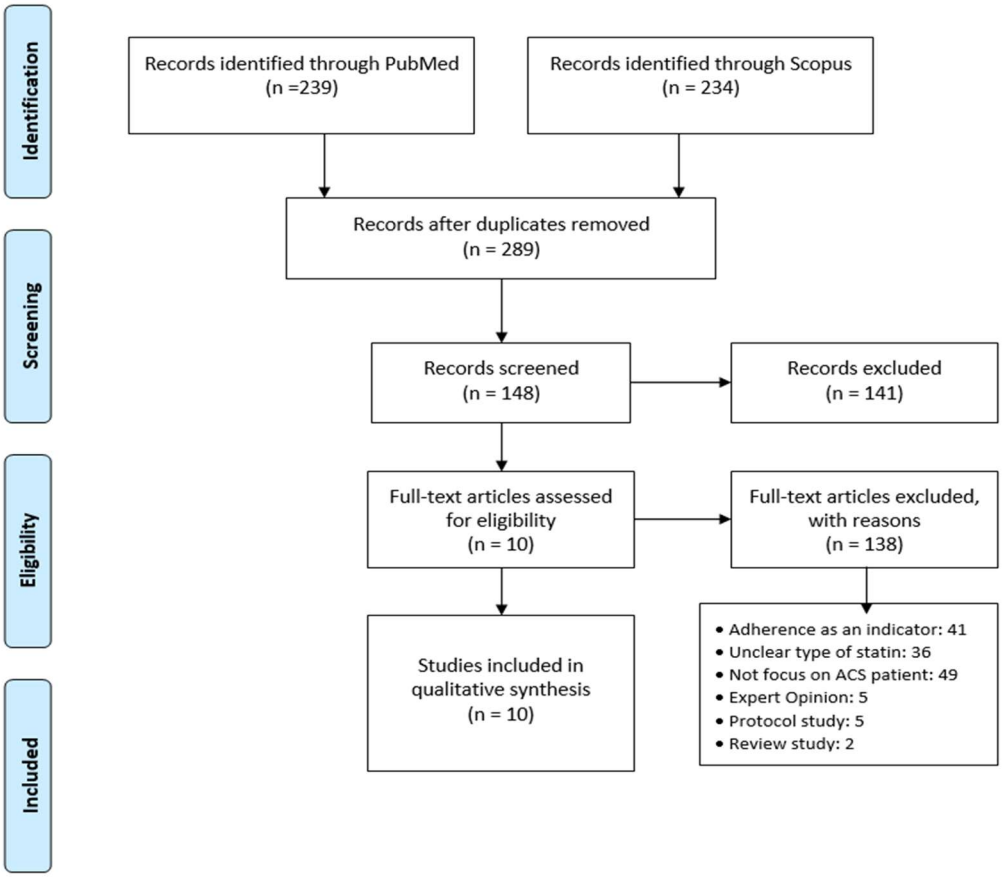

Figure 1. PRISMA diagram showing the selection of studies for inclusion in the review.

Prescribing pattern

There were some factors influencing the physician's prescribing pattern for patients with ACS, such as blood cholesterol levels and patients with STEMI. The lower dose of those statins was given to the patients mostly after they experienced PCI [11]. Among India population, atorvastatin most likely to be given to ACS patients (92%-100%) during their stay at ICCU as secondary prevention purpose [12],[13], while all type of ACS patients (STEMI, NSTEMI, UA) were given Atorvastatin (100%) for primary prevention purpose [14]. The low adherence using HIS among ACS patients also reported by a study in 2018 [15] which can lead to the risk of cardiovascular events. Surprisingly, the similar population in USA who has experienced ACS before mostly didn't take any statin until the ACS recurrence happened [15]. Based on the selected references in Table 1, there were 4 of 6 studies reporting the use of statin that more preferable to be prescribed for ACS patients as secondary prevention than primary prevention [12],[13],[14]. However, a prospective study in Denmark reported the use of Simvastatin as primary prevention mostly among low-risk patients [16]. The category of low to moderate and high intensity statin was following the 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease and the 2018 AHA/ACC Multi-society Guideline on the Management of Blood Cholesterol. High-intensity statin therapy is defined as the administration of Atorvastatin at doses of 40-80 mg or Rosuvastatin at doses of 20-40 mg; any other statin usage is categorized as low to moderate intensity statin.

Table 1. Reported statin prescribing pattern.

Study	Year	Country	Study design	Type of population	Statin regimen	Primary prevention	Secondary prevention
Malleshappa	2017	India	Prospective observational study	ACS patients in ICCU setting	Atorvastatin 92% Rosuvastatin 8%		V
Avula Naveen	2017	India	Retrospective observational study	ACS patients with STEMI, NSTEMI, or Unstable Angina	Atorvastatin 100%	V	V
Boklage, Malangone-Monaco	2018	USA	Retrospective observational study	ACS patients with STEMI, NSTEMI, or Unstable Angina	A higher number of LMIS is given to ACS patients compared with HIS in the setting of before (14.9% vs 3.4%), during (30.7% vs 13.2%), and after hospitalizatio n (45.1% vs 16.4%)	V	
Kulenovic, Mortensen	2016	Denmark	Prospective observational study	ACS patients with STEMI or NSTEMI	Simvastatin was consumed by 69.8% of participants before experiencing the first MI, but only 37% of them had SCORE ≥5% (defined as High or Very High Risk)	V	
Kim, Mi-Jeong	2012	Korea	Prospective observational study	ACS patients underwent PCI	HIS gave to STEMI and NSTEMI patients on Pre-PCI and 30 days after PCI		V
Lakshmi, Gowda	2017	India	Prospective observational study	ACS patients in ICCU setting	Atorvastatin 100% prescribed for ACS patients since the initial 48 hours admitted in ICCU	V	V

Clinical outcome

The study reported the use of high-dose statin (Atorvastatin ≥40mg/day or Rosuvastatin ≥20 mg/day) can be able to reduce the adverse clinical events during 30 days post-PCI if only administered the patients with NSTEMI before they receiving PCI [11]. Practically, the use of high-dose statin is mostly found in patients with STEMI with a smoking history and hypercholesterolemia. The large registry-based Chinese ACS conducted by [17], was involving participants with LDL-c <70 mg/dl at baseline and received low to moderate statin (Atorvastatin 5, 10, 20 mg/day), they then significantly experienced a lower risk of MACEs and other cases related to mortality factors during 12 months follow up after discharge. This condition was compared to the non-statin group. There are 2 of 3 studies that found that the use of any intensity of statin as secondary prevention among ACS patients could reduce MACEs when compares to no statin group [17],[18]. The use of High-Intensity Statin (HIS) remains underutilized among patients with ACS even though the guidelines have suggested the use of HIS during and after ACS events. Although concerns have been raised about the adverse events due to using statins, generally the events are considered to be well tolerated and to have a good safety profile. This view is generally supported by the evidence of the trials included in this review. Although increases in creatine kinase and myopathy have been reported, rhabdomyolysis and hepatotoxicity rarely happen. However, some patients may receive lipid-lowering therapy for as long as 50 years, and long-term safety over such a timespan remains unreported adequately by recent studies [19]. Based on the included references for this review as presented in Table 2, the desired clinical outcome of using statin among ACS patients is to reduce the total Major Adverse Cardiovascular Events (MACEs). They reported about the use of High and Moderate Intensity Statin could reduce the total MACEs if it's given as early as the patient got the first ACS.

Table 2. Reported clinical outcomes in using statin.

Study	Year	Country	Number of participants	Statin	Outcome	Time of statin administration	Study design	Secondary prevention
Kim, Mi-Jeong	2012	Korea	3362	High-Intensity Statin	Total MACEs reduced	30 days post PCI for NSTEMI patients	Prospective Observational Study	V
Yihong Sun	2018	Japan	3374	Low to Moderate Intensity Statin	Total MACEs were lower than no statin group	At hospital discharge	Post Hoc Study	V
Gregory G Schwartz	2017	USA	3086	High-Intensity Statin	Total MACEs were lower than no statin group	1–4 days after ACS and continuing for 16 weeks.	Post Hoc Study	V

Cost analysis

The average cardiovascular-specific healthcare cost reported by previous study, consumed about 48% of the overall expenses Per Patient Per Month (PPPM) units or as much as $1111 for medical only and $1391 for medical and outpatient pharmacy [15]. By using the Markov Model conducted by previous study, the Low-Intensity Statin was projected to be cost-effective for the Low-Risk ACS population even with a modest level of LDL [19]. Furthermore, with a similar model used to evaluate the cost-effectiveness of using Low-Intensity Statin among Australian patients with CAD, A projected the use of Low-Intensity Statin is cost-effective as secondary prevention if it is fully covered by the government [20]. Based on the ICER in Japan, a study conducted by previous study claimed Atorvastatin as the more cost effective than other kinds of statin [21]. A literature review from the UK reported about the cost-effectiveness of statins as a coronary heart disease prevention will decrease due to the ages range 45-85 which is indicated by the inclining of ICER [22]. Some factors such as the treated population due to CHD risk as well as the age and gender should be considered to assess the financial aspect of statin utilization among the populations. Cost studies conducted in UK in 2007 reported the cost-effectiveness of statin utilization as the primary prevention was between £8000-30000 per life-year gained (LYG) and depending on the examined baseline risk. On the other hand, the cost-effectiveness of secondary treatment was estimated £6000 to £40,000 per LYG. The selected studies in Table 3 reported the cost-effectiveness of using Low-Intensity Statin among Low-Risk ACS patients and fully covered by the government for the direct medical cost.

Table 3. Reported cost effectiveness of using statin.

Study	Year	Country	Study design	Participants	Statin	Discount	Type of cost	Wtp	Primary prevention	Secondary prevention
Lawrence D. Lazar	2011	Usa	Decision analysis markov model	Acs	Low-intensity statin	3%/year	Direct medical cost	$50000/QALY	V	
				(low risk vs moderate to high risk)						
Zanfina Ademi	2011	Australia	Decision analysis markov model	Acs	Low-intensity statin	5%/year	Direct medical cost	$50000/QALY		V
				(Full vs 82% coverage)						

Quality of life

The ACS treatment, especially the use of statin among the patients should not only focus on the clinical outcome but also the humanistic aspects. The humanistic aspects refer to the quality of life (QoL) and risk-benefit assessments. For example, in an ACS patient setting, healthcare providers should pay attention to and understand individualized conditions. Treatment strategy selection is crucial, and many important factors must be taken into consideration, especially in the context of STEMI. Older patients with STEMI have a high risk of mortality, which is especially evident in the first 30 days. A similar situation is observed with NSTEMI [23]. Unfortunately, this review has only one reference which put the patient's quality of life aspect during statin treatment among ACS patients. Nevertheless, they only put limited results and explanations as the supplementary information of the studies. The selected study was measuring the functional status among the High-Intensity Statin patients using two kind of health-related quality-of-life (HRQOL) tools, the Seattle Angina Questionnaire (SAQ) and the Euro Quality of Life 5-Dimensional Classification (EQ-5D). The evaluation result reported a low score in each SAQ subscale but a high in EQ-5D score for the ACS patients for 30 days post Percutaneous Coronary Intervention and treated by High-Intensity Statin [11],[24].

Based on the reviewed evidence, quality of life (QoL) assessments using the Seattle Angina Questionnaire (SAQ) and EQ-5D consistently demonstrate that high-intensity statin therapy, compared to low- or moderate-intensity regimens, is associated with statistically significant improvements in both angina-related and general health-related QoL domains. Patients receiving high-intensity statins experienced greater reductions in angina frequency and physical limitations, as well as enhanced perceptions of treatment satisfaction and disease perception. This is complemented by EQ-5D data showing measurable gains in mobility, usual activities, and overall health utility scores. These findings reinforce the dual clinical and quality-of-life benefits of intensified lipid-lowering strategies post-ACS, particularly in elderly populations where frailty and comorbidity burden are significant. Notably, the impact of statin intensity on QoL remained significant even after adjusting for age, cognitive function, and functional status, indicating a robust benefit beyond survival alone.

▪ DISCUSSION

This review explores the prescribing pattern, clinical outcome, cost-effectiveness and quality of life aspects of statin utilization for primary and secondary prevention purposes. The results of this review indicate the dominant use of Atorvastatin in ACS therapy as both primary and secondary prevention. According to a recent meta-analysis, this could explain that using Atorvastatin as a high-intensity statin treatment could minimize MACE in ACS when compared to normal statin therapy, and major adverse events associated with high-intensity statin administration were uncommon [25],[26]. However, current review indicated that the use of High-Intensity Statin among the high-risk ACS population remains in low number compared with Low to Moderate Intensity Statin. A previous study found that the use of atorvastatin 20 mg/day was mostly given to the patients at discharge (secondary prevention purpose) who diagnosed with STEMI, NSTEMI, or UA from the secondary hospital but a higher dose was more likely to be prescribed for patients at the tertiary hospital [27],[28].

By comparing patients with NSTEMI in the Statin-naïve group, the incidence of adverse cardiovascular and renal events was found lower for those NSTEMI ACS in the statin group (Rosuvastatin) within 30 days after receiving contrast and a lower number of Non-fatal MI and death events based on 6 months follow up period [29],[30]. The use of High and Moderate Intensity Statins was mostly applied as secondary prevention and started from the admission day. A study reported the use of statin ≤48 hours after ACS admission could reduce the MACE rate during 12 months of follow-up compared to patients who received statin >48 hours after ACS admission [31],[32]. A retrospective study conducted by [33] reported a higher number of high-intensity statin was prescribed to statin users who experienced ACS at admission but less prescribed at discharge compared to the statin naïve patients. By comparing the recent guidelines [2],[34], this situation is considered as a delayed statin administration. The indicators to be used to consider the patient's risk in terms of ACS and the need for statin treatment have already been addressed in detail by the updated guidelines.

This study found that the use of Low-Intensity Statin is considered as Cost Effective in terms of direct medical cost if it is applied among the Low-Risk ACS and fully supported by the government for both primary and secondary prevention. More studies about quality of life among ACS patients should be conducted to provide more social preference, especially about their discomforts profile during the treatment. Last study about the incremental benefit of using high-dose statin among high-risk CAD patients was conducted in 2007-2009 and reported that the use of high-dose statin therapy among ACS patients has the potential to be both highly efficacious and cost-efficient [35]. Thus, more studies regarding statin utilization are needed to provide more details about the use of statin in the worldwide practice among the no-risk, low-risk, moderate-risk, and high-risk ACS population. However, not all selected articles reported the dosage of prescribed statin. Some of the selected articles reported the statin based on its intensity. Only one finding was reported about the quality of life among the ACS patients without comparing it to another statin group. No selected articles reported the cost-effectiveness of using high-intensity statin among the ACS patients. High-intensity statin therapy, while effective in reducing cardiovascular events, may pose quality-of-life concerns in elderly or frail patients due to increased risks of functional decline and adverse effects. A study in an Australian geriatric unit found that statins were often discontinued in octogenarians or those with poor functional recovery, cognitive impairment, or primary prevention indications—highlighting the need to weigh the benefits of prevention against the burdens on daily functioning and wellbeing. Furthermore, frailty and functional status were found to significantly impact post-ACS quality of life, suggesting that statin decisions should consider multidimensional patient factors, not just clinical guidelines. However, real-world data show underutilization of HIS despite their proven benefits, with low- to moderate-intensity statins being more commonly prescribed—especially in low-risk or resource-limited settings—primarily due to cost-effectiveness when fully government-funded.

Based on the presented findings, this study could suggest the need for more targeted and optimized statin prescribing practice, especially emphasizing the underutilization of high-intensity statins (HIS) among the high-risk ACS patients. Despite guideline recommendations advocating for early and aggressive lipid-lowering therapy in high risk populations, this review reveals that moderate- to low-intensity statins remain more commonly prescribed—even in cases where the high intensity statin approach might yield greater cardiovascular protection. This situation points to a potential gap between evidence-based guidelines and real-world clinical practice, warranting a shift toward more consistent use of HIS for secondary prevention in high-risk individuals, while reserving low-intensity statins for low-risk populations or those with tolerability concerns. However, the authors also acknowledge several important limitations of this review that must temper the interpretation of its conclusions. First, publication bias cannot be ruled out, as studies with favorable or statistically significant outcomes are more likely to be published and included. Second, heterogeneity across study designs, populations, and outcome measures—especially in how statin intensity and clinical endpoints were reported—may limit the comparability of the included evidence. Lastly, the review appears to draw heavily from studies conducted in specific regions such as India, Korea, the USA, and Denmark, potentially reducing the global generalizability of its findings. Differences in healthcare infrastructure, statin availability, and prescribing culture across countries may influence both the implementation and effectiveness of statin therapies. These limitations highlight the need for further multicenter, globally representative studies with standardized outcome reporting to inform more equitable and precise prescribing guidelines.

CONCLUSION

High-intensity statins, especially Atorvastatin, could significantly reduce major adverse cardiovascular events (MACEs) when initiated immediately as secondary prevention for patients with ACS and receiving PCI. This review highlights the clinical importance of early and aggressive lipid-lowering strategies by prescribing the high-intensity statin among the high-risk individuals. Additionally, tailored use of low-intensity statins in low-risk patients, complemented by cost-effective measures, offers a pragmatic approach to treatment allocation within diverse patient cohorts. These findings could reinforce a stratified, evidence-based approach to ACS management that can improve patient's outcomes while ensuring the economic aspect.

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