

## Development of In-Hospital and Discharge Protocols for Optimal Lipid-Lowering Strategies in Patients with Acute Coronary Syndrome in Türkiye: Expert Guidance

Türkiye'de Akut Koroner Sendromlu Hastalarda Optimal Lipid Düşürücü Stratejiler için Hastane İçi ve Taburculuk Protokollerinin Geliştirilmesi: Uzman Rehberi

### ABSTRACT

Although guidelines strongly recommend low levels of low-density lipoprotein cholesterol (LDL-C) in patients with acute coronary syndrome (ACS), these goals are not achieved in many patients. We present expert recommendations for the in-hospital and post-discharge management of lipid-lowering therapy in ACS patients in Türkiye. A group of expert cardiologists comprising members of the Turkish Society of Cardiology and leading lipidologists who have all worked in national cardiology lipid working groups for at least 4 years, considered the optimal approach to lipid management in ACS patients in Türkiye, taking into account Turkish healthcare infrastructure and issues from real-world practice. Novel standardized algorithms covering the first year after an ACS event were developed. The main elements of the proposed approach are summarized. The in-hospital strategy includes lipid profile assessments and commencement of statin therapy, including appropriate measures for patients with possible familial hypercholesterolemia or with a history of recurrent cardiovascular events. The role of a specially-trained nurse, use of a patient follow-up card, and the provision of patient information and referrals to affiliated healthcare professionals, are covered. The post-discharge strategy covers follow-up visits to monitor the patient's progress and recommends timepoints at which modifications to treatment (based on LDL-C levels) should be made. A country-specific approach to lipid management in ACS patients in Türkiye is proposed. Further work is needed to determine the best way to implement the strategy, and to validate the recommendations and their application in daily practice.

**Keywords:** Acute coronary syndrome, dyslipidemia, lipid-lowering therapy, Türkiye


### ÖZET

Kılavuzlar, akut koroner sendromlu (AKS) hastalarda düşük yoğunluklu lipoprotein kolesterolün (LDL-K) düşük düzeylerini kuvvetle tavsiye etse de birçok hastada bu hedeflere ulaşılamamaktadır. Türkiye'deki AKS hastalarında lipid düşürücü tedavinin hastane içi ve taburculuk sonrası yönetimi için uzman önerileri sunuyoruz. Türk Kardiyoloji Derneği üyelerinden olan ve ulusal kardiyoloji lipid çalışma gruplarında en az 4 yıl çalışmış önde gelen lipidologlardan oluşan bir grup uzman kardiyolog, Türkiye'deki AKS hastalarında lipid yönetimi için en uygun yaklaşım Türk sağlık altyapısı ve gerçek dünyadaki uygulamalardaki sorunlar dikkate alınarak değerlendirildi. Bir AKS olayından sonraki ilk yılı kapsayan yeni standartlaştırılmış algoritmalar geliştirildi. Önerilen yaklaşımın ana unsurları özetlenmiştir. Hastane içi strateji, olası ailesel hiperkolesterolemisi olan veya tekrarlayan kardiyovasküler olay öyküsü olan hastalar için uygun önlemler de dahil olmak üzere, lipid profili değerlendirmelerini ve statin tedavisinin başlatılmasını içerir. Özel eğitilmiş bir hemşirenin rolü, hasta takip kartının kullanımı ve hasta bilgilerinin sağlanması ve ilgili sağlık profesyonellerine yönlendirme konularını kapsamaktadır. Taburculuk sonrası strateji, hastanın ilerlemesini izlemek için takip ziyaretlerini kapsar ve tedavide (LDL-K düzeylerine dayalı olarak) değişikliklerin yapılması gereken zamanları önerir. Türkiye'deki AKS hastalarında lipid yönetiminde ülkeye özgü bir yaklaşım önerilmektedir. Bu stratejiyi uygulamanın en iyi yolunu belirlemek ve tavsiyeleri ve bunların günlük uygulamalardaki yerini doğrulamak için daha fazla çalışmaya ihtiyaç vardır.

**Anahtar Kelimeler:** Akut koroner sendrom, dislipidemi, lipid düşürücü tedavi, Türkiye

### EXPERT OPINION UZMAN GÖRÜŞÜ

Öner Özdoğan<sup>1</sup> 

Meral Kayıkçıoğlu<sup>2</sup> 

Barış Güngör<sup>3</sup> 

Ceyhan Ceyhan<sup>4</sup> 

Özcan Başaran<sup>5</sup> 

Mithat Selvi<sup>6</sup> 

Lale Tokgözoğlu<sup>7</sup> 

<sup>1</sup>Department of Cardiology, University of Health Sciences, Izmir Faculty of Medicine, Izmir, Türkiye

<sup>2</sup>Department of Cardiology, Ege University School of Medicine, Izmir, Türkiye

<sup>3</sup>Department of Cardiology, Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Center, Istanbul, Türkiye

<sup>4</sup>Department of Cardiology, Adnan Menderes University Faculty of Medicine, Aydın, Türkiye

<sup>5</sup>Department of Cardiology, Mugla University Faculty of Medicine, Muğla, Türkiye

<sup>6</sup>Novartis Turkey, Istanbul, Türkiye

<sup>7</sup>Department of Cardiology, Hacettepe University Medical Faculty, Ankara, Türkiye

### Corresponding author:

Öner Özdoğan

✉ onerozdogan@yahoo.com

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Globally, non-communicable diseases account for approximately 41 million deaths each year, with cardiovascular (CV) diseases responsible for 17.9 million (38%) of these, making them one of the leading causes of mortality worldwide.<sup>1</sup> According to the World Health Organization (WHO), coronary artery disease (CAD) was the leading cause of death globally in 2019, with 8.9 million fatalities.<sup>2</sup> Based on these statistics, mortality from CAD and acute coronary syndrome (ACS) continues to be a significant problem for healthcare systems worldwide, even with notable reductions in morbidity and mortality from atherosclerotic CV disease over the past twenty years.<sup>3,4</sup> Research, such as a large population study by Mannsverk et al.,<sup>4</sup> indicates that primary prevention efforts like reducing hypercholesterolemia, improving blood pressure (BP) control, and promoting smoking cessation have markedly decreased the incidence of coronary heart disease (CHD) and sudden deaths outside of hospitals.

There is a well-established link between high levels of low-density lipoprotein cholesterol (LDL-C) and myocardial infarction (MI).<sup>5</sup> Moreover, increased levels of non-high-density lipoprotein cholesterol (non-HDL-C; total cholesterol minus HDL-C), which reflects the total cholesterol carried by atherogenic lipoproteins (LDL, intermediate-density lipoprotein, very-low-density lipoprotein, remnants, lipoprotein(a) [Lp(a)]), are now recognized as a more accurate predictor of atherosclerotic CV disease than elevated LDL-C alone.<sup>6-8</sup> The 2021 European Society of Cardiology (ESC) guidelines on CV disease prevention emphasize risk classification using the Systematic Coronary Risk Estimation (SCORE-2) algorithm, which includes non-HDL-C levels.<sup>9</sup> For patients in the post-ACS phase, who are categorized as "very high risk," current dyslipidemia guidelines advocate for a target LDL-C level below 55 mg/dL (1.4 mmol/L) and a minimum 50% reduction from the baseline LDL-C level, with a Class I recommendation for these patients.<sup>10,11</sup> Thus, life-long lipid-lowering therapy should be implemented carefully and rigorously in this "very high risk" patient group.

In the practical environment of everyday clinical practice, managing patients with CAD is increasingly complex, particularly in an aging population with frequent comorbidities. This complexity is pronounced in post-ACS patients, who often receive care from multiple healthcare providers, which can lead to fragmented or insufficient follow-up. The effectiveness of care may further be diminished by physicians' non-adherence to guidelines and patient non-compliance with treatment regimens.<sup>12,13</sup>

Monitoring and follow-up are crucial to achieve the LDL-C target levels recommended by guidelines. For instance, the EUROASPIRE-V (European Action on Secondary and Primary Prevention by Intervention to Reduce Events V) study revealed that only 30% of European ACS patients reached the LDL-C target of 70 mg/dL (1.8 mmol/L) one year after discharge.<sup>14</sup> In Türkiye, initial post-discharge statin use was approximately 82%, slightly higher than the ~81% observed in Europe, according to the EUROASPIRE-III study, which spanned the past 15 years.<sup>15</sup> Data from follow-up studies show that one year after discharge, statin use in Türkiye decreased from 82% to 65% according to EUROASPIRE-III findings, and from 88% to 81% as reported in EUROASPIRE-IV.<sup>15,16</sup> This decline is particularly alarming

considering that only about 10% of ACS patients receiving high-intensity statin monotherapy are able to achieve the target LDL-C level of 55 mg/dL.<sup>17-19</sup> These statistics underline the need for a more assertive approach in treating these patients, including the early adoption of combination therapies with statins and sustained, guideline-directed follow-up throughout their lives.

Significantly, the incidence of familial hypercholesterolemia (FH) among hospitalized ACS patients is up to 8%, which is significantly higher than the incidence in the general population.<sup>20</sup> In Türkiye, a retrospective study assessing 2-year cardiovascular outcomes reported a similar FH incidence of approximately 7.6% among ACS patients.<sup>21</sup>

Variations in healthcare systems and reimbursement policies for lipid-lowering medications can impact the effectiveness of dyslipidemia management in post-ACS patients. This underscores the necessity for country-specific guidelines and protocols tailored to the in-hospital and post-discharge care of ACS patients in practical settings, to enhance adherence to lipid-lowering therapies and ensure the attainment of optimal target LDL-C levels. The need for country-specific recommendations and guidance is a recognized priority across various European nations.<sup>12,22</sup>

In this paper, we propose recommendations formulated by a consensus of experts for a country-specific protocol designed for the in-hospital and post-discharge management of lipid-lowering therapy in ACS patients within the Turkish healthcare context.

## Materials and Methods

A panel of nine experts, including members from the Turkish Society of Cardiology and leading lipidologists, was convened to develop strategies for optimal lipid management in ACS patients, considering the unique aspects of Türkiye's healthcare infrastructure. The panel reviewed key recommendations from major dyslipidemia guidelines, addressing practical challenges in Türkiye, such as medication costs, reimbursement systems, educational needs, and healthcare practitioners' attitudes towards treatment intensification. Innovative, standardized algorithms intended for use during the first year following an ACS event were created. All authors are expert cardiologists with at least four years of experience in national cardiology lipid working groups.

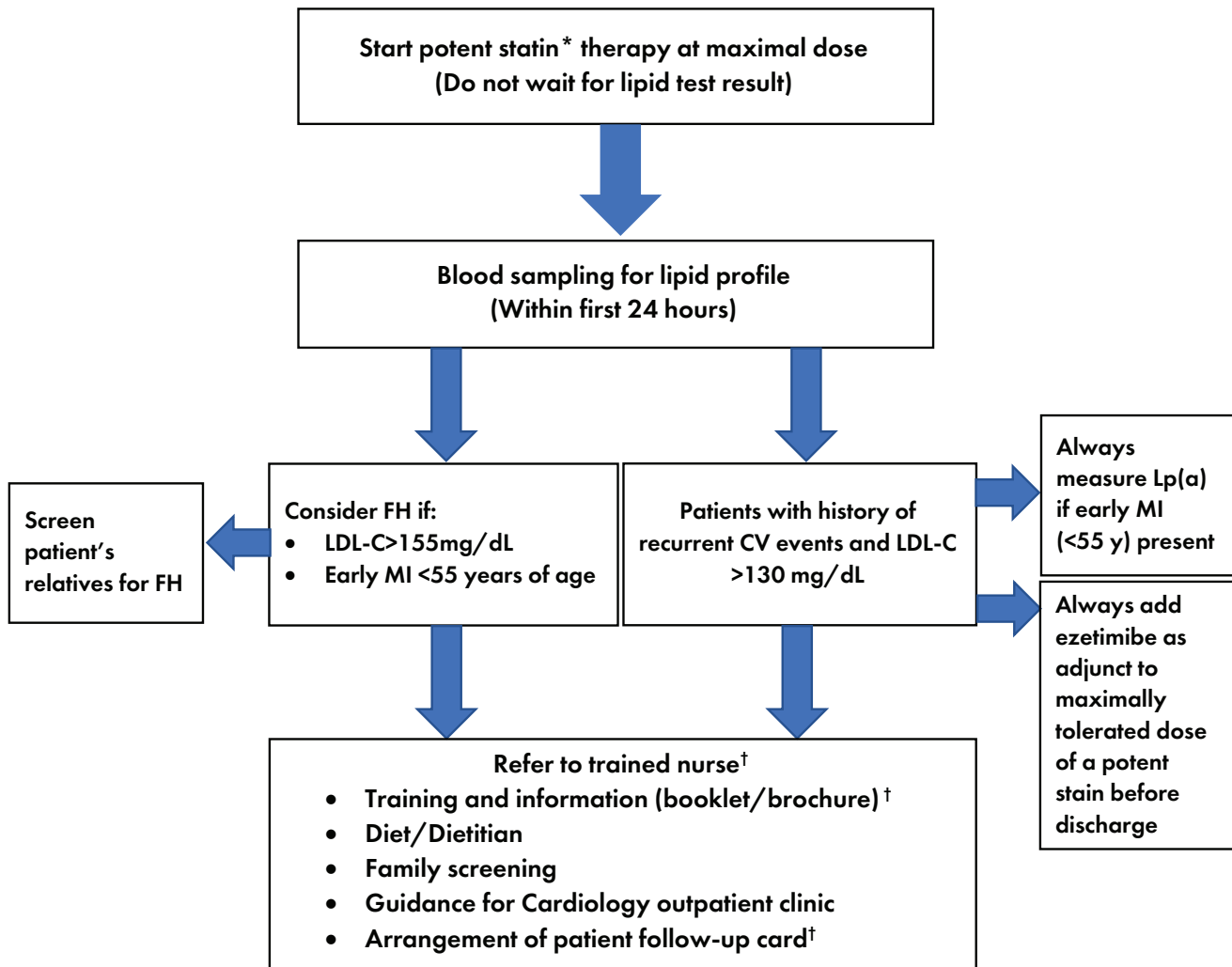
Separate recommendations have been developed for both the in-hospital and post-discharge phases of lipid-lowering therapy management in ACS patients in Türkiye.

## Recommendations for the In-Hospital Management of Dyslipidemia in ACS Patients

This section presents the recommendations for managing dyslipidemia in ACS patients during their hospital stay. An algorithm summarizing these recommendations is shown in Figure 1.

### 1. Lipid Profile Evaluation

It is noted that in the initial days following an ACS event, levels of LDL-C may decrease, and triglyceride levels may increase.<sup>10</sup> The panel recommends that the lipid profile be measured within the first 24 hours post-ACS to capture these changes.



**Figure 1. In-hospital dyslipidemia management strategy for patients with ACS.**

**Note:** In addition to managing dyslipidemia, the primary responsible physician should evaluate and optimize other risk factors for CAD and ACS, such as diabetes mellitus, smoking, and hypertension.

\* High-intensity statin therapy refers to rosuvastatin 20-40 mg or atorvastatin 40-80 mg.

† Trained nurse, booklet/brochure, and follow-up card will be defined based on outcomes from a future clinical trial.

ACS, Acute Coronary Syndrome; CAD, Coronary Artery Disease; CV, Cardiovascular; FH, Familial Hypercholesterolemia; LDL-C, Low-Density Lipoprotein Cholesterol; LP(a), Lipoprotein(a); MI, Myocardial Infarction; y, Years.

Additionally, Lp(a) levels should be measured once for all patients to assist with risk stratification. This test should be performed accurately and, if feasible, results should be reported in nmol/L. An Lp(a) level above 125 nmol/L is considered indicative of high risk for atherosclerotic CV disease.<sup>23</sup>

Patients with an LDL-C level >155 mg/dL and a history of early MI before the age of 55 should be considered likely to have familial hypercholesterolemia (FH). It is recommended that arrangements be made to screen their relatives for elevated LDL-C levels.

## 2. Patients with an Index ACS Event

Immediate initiation of high-intensity lipid-lowering therapy is recommended for all patients, including those experiencing their first ACS event.<sup>11</sup> This approach should not be delayed

pending lipid profile results. A high-intensity regimen typically involves a statin dose that reduces LDL-C by ≥ 50%.<sup>10</sup> Examples of high-intensity statins include atorvastatin (40-80 mg) and rosuvastatin (20-40 mg).<sup>10,11,23</sup>

## 3. Patients with a History of Recurrent Cardiovascular Events

Patients with a history of recurrent CV events, who are stable regarding other risk factors, should be classified as "residual very high-risk." For those on a low dose of statin, the dosage should be modified and/or titrated to the maximally tolerated dose (MTD) of a high-intensity statin.

Lp(a) levels should be routinely measured in patients with a history of recurrent CV events, particularly those with an LDL-C level greater than 130 mg/dL and a history of early MI before the age of 55.

For patients with a history of recurrent CV events and an LDL-C level above 130 mg/dL, the addition of ezetimibe to the MTD of a high-intensity statin is recommended prior to hospital discharge. The addition of ezetimibe to statin therapy has been proven to further reduce LDL-C levels in patients, with or without existing coronary heart disease (CHD).<sup>10, 24</sup>

#### 4. Education and Information

Before discharge, all patients should receive comprehensive education about their condition. A specially trained nurse should provide detailed information on diet and lifestyle modifications. Additionally, patients should be given a booklet outlining the importance of lipid-lowering therapy post-ACS and detailing other secondary prevention strategies. The specifics of the nurse's training and the booklet's content will be established based on findings from upcoming clinical trials. Evidence from several randomized controlled trials suggests that nurse-led education and follow-up of patients after an ACS event can enhance the achievement of target lipid levels.<sup>25-27</sup>

For patients with a history of recurrent CV events, it is important to address any gaps in the education, information, or instructions they have previously received. Patients diagnosed with FH, along with their relatives, should be educated about the condition and referred to a cardiology outpatient clinic for further evaluation.

#### 5. Referral

In Türkiye, routine follow-up for patients with dyslipidemia typically occurs in Cardiology departments.<sup>28</sup> Trained nurses should ensure that all ACS patients are referred to Cardiology outpatient clinics for follow-up (control) visits to monitor their dyslipidemia. A patient follow-up card should be created to streamline communication with the Cardiology outpatient clinic and ensure the first follow-up visit occurs between 3 to 6 weeks after discharge.

Before discharge, the nurse will collect the patient's contact details to send text messages or make phone calls, reminding them of their upcoming appointments. The follow-up card, provided to the patient at discharge, should be brought by the patient to all subsequent appointments.

#### 6. Optimization of Other Risk Factors

Alongside managing dyslipidemia, the primary responsible physician should assess and address any other risk factors for CAD and ACS present, such as diabetes mellitus, smoking, and hypertension.

#### Recommendations for the Post-Discharge Management of Dyslipidemia in ACS Patients

This section presents the recommendations for managing dyslipidemia in ACS patients following their discharge from the hospital. An algorithm summarizing these recommendations is illustrated in Figure 2.

##### 1. Follow-up and Assessment of Treatment Response

**First Control Visit:** It is crucial that ACS patients have their LDL-C levels measured within 3 to 6 weeks after discharge (ideally within one month) to determine if LDL-C control has been achieved. This assessment should be conducted in the Cardiology outpatient clinic. During this visit, the attending physician should discuss dietary habits, essential lifestyle

changes, and adherence to MTD statin therapy. A specially trained nurse should document this information on the patient's follow-up card.

For patients not on statin therapy, the reason should be identified. If statin intolerance is evident, the patient should be referred to a lipid clinic or lipidologist for further assessment and management.<sup>29</sup> If the target LDL-C level (< 55 mg/dL) has not been met despite MTD statin therapy, ezetimibe should be added in combination with the statin.<sup>10, 11</sup> For patients diagnosed with FH, the addition of a proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9i) to the existing therapy (MTD statin and/or ezetimibe) should be considered.<sup>10</sup> The trained nurse should update the treatment details on the patient's follow-up card and ensure that the patient is fully informed about any changes to their regimen. Additionally, the nurse should verify that the patient's contact details are current to facilitate reminders about future appointments via text messages or phone calls. In the future, it may be possible to develop an integrated technological infrastructure that utilizes digital tools to automate some of the administrative tasks performed by nurses, such as scheduling appointments and sending reminders.

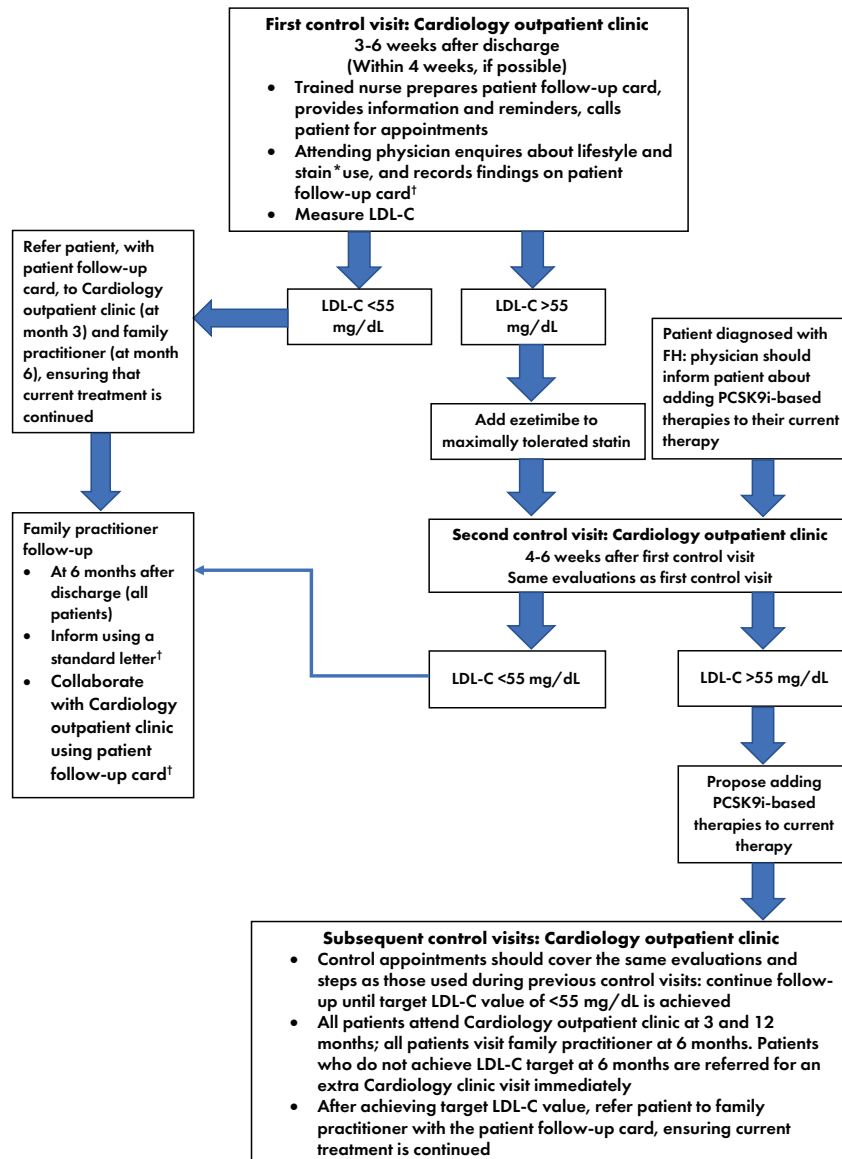
If the LDL-C target value is achieved at the first control visit, the patient should return to the Cardiology clinic at three months and then be referred to their family practitioner for a follow-up at six months, facilitated by a standard referral letter. The patient should bring their follow-up card to the family practitioner to ensure seamless communication and collaboration between the family practitioner and the Cardiology outpatient clinic. Meanwhile, the patient should maintain their current therapy.

**Second Control Visit:** Patients who did not meet LDL-C goals at the first control visit should undergo another LDL-C test 4-6 weeks later during a second visit to the Cardiology outpatient clinic. The trained nurse should review the patient's follow-up card for compliance with the previously prescribed lipid-lowering therapy.

If the patient has not achieved the LDL-C target level (< 55 mg/dL) despite receiving maximum-dose statin and ezetimibe combination therapy, initiating PCSK9i-based therapy is advised.<sup>10</sup> This is particularly crucial for patients with FH who have not yet started PCSK9i-based therapy; such treatment should be initiated without delay. The trained nurse should document this update on the patient's follow-up card and ensure that the patient is informed of any changes in their treatment regimen.

If target LDL-C values are met, the patient should be discharged from the Cardiology outpatient clinic and referred to their family practitioner. They should bring their follow-up card, which includes instructions to continue their current therapy.

**Subsequent Control Visits:** All patients should be monitored for at least one year, and all patients should have a consultation with their family practitioner at 6 months. Patients who achieve target LDL-C levels will have additional visits at the Cardiology outpatient clinic at 3 and 12 months, and see their family practitioner at 6 months. Patients who do not meet the LDL-C target during their 6-month visit with the family practitioner



**Figure 2. Post-discharge dyslipidemia management strategy for patients with ACS.**

**Note:** If a history of recurrent cardiovascular events (e.g., PAD, MI, stroke) is detected during follow-up and the patient is otherwise stable regarding other risk factors, adopt the following process:

- 1) Classify the patient as "residual very high-risk." Record this classification on the patient's follow-up card and adopt a more aggressive therapeutic approach, aiming for an LDL-C target of < 40 mg/dL.
  - 2) If the statin dose is low, escalate to a high-intensity statin<sup>§</sup> at the maximum tolerated dose (MTD). If LDL-C remains > 130 mg/dL, always add ezetimibe to MTD high-intensity statin, and consider PCSK9i-based therapy if there is a greater than 50% difference from the target LDL-C level.
  - 3) Patients with FH should receive PCSK9i-based therapy without delay.
  - 4) In cases of early MI (age < 55 years), always measure Lp(a) levels to assess predisposition to thrombosis (an Lp(a) threshold of 50 mg/dL/125 nmol/mL indicates high-risk for atherosclerotic cardiovascular disease).
- \* If the patient is not on statin therapy, investigate the reasons. The attending physician should be vigilant for any signs of statin intolerance. For further information, refer to Fitchett et al.<sup>29</sup> <https://doi.org/10.1161/CIRCULATIONAHA.114.013189>.
- † Patient follow-up card and standard letter will be defined in a future clinical trial.
- § High-intensity statin therapy refers to rosuvastatin 20-40 mg or atorvastatin 40-80 mg.

FH, Familial Hypercholesterolemia; Lp(a), Lipoprotein(a); MI, Myocardial Infarction; PAD, Peripheral Artery Disease.



should be immediately referred back to the Cardiology outpatient clinic for an additional assessment. This is in addition to the scheduled Cardiology outpatient visits at months 3 and 12. The trained nurse will contact patients via text messages or phone calls to remind them about their appointments.

During the Cardiology outpatient visits, the trained nurse should review the information recorded on the patient's follow-up card and assess the patient's adherence to their lipid-lowering treatment. If the patient does not achieve the LDL-C target level ( $< 55$  mg/dL) despite maximum-dose statin and ezetimibe therapy, initiating PCSK9i-based therapies is recommended.

## 2. Patients with a History of Recurrent Cardiovascular Events

Patients who experience a new CV event during follow-up after the initial event and are stable regarding other risk factors should be classified as "residual very high-risk." This classification should be documented on the patient's follow-up card, and a more aggressive treatment approach should be adopted, aiming for an LDL-C target value of  $< 40$  mg/dL.<sup>10</sup>

If the patient is on a low dose of statin, the dosage should be adjusted and/or titrated to the MTD of statin. If the LDL-C level exceeds 130 mg/dL, ezetimibe should be added as an adjunct to the statin MTD, and PCSK9i-based treatment should be considered, especially if the LDL-C level is more than 50% above the target. Patients with FH should start PCSK9i-based therapy immediately.

If early MI occurred before the age of 55 and Lp(a) has not been previously measured, it should be assessed to evaluate the risk of thrombosis. An Lp(a) level of 50 mg/dL (125 nmol/L) indicates a high risk for atherosclerotic CV disease.<sup>23</sup>

The trained nurse should also address any gaps in education, information, or instructions provided to these patients.

## 3. Referral to Other Disciplines

**Dietitian Follow-up:** All patients who attend their first control visit at the Cardiology outpatient clinic should be referred to a dietitian within the clinic by the trained nurse. The dietitian will document any dietary recommendations on the patient's follow-up card.

**Physical Therapy and Rehabilitation Follow-up:** All patients visiting the Cardiology outpatient clinic for the first time should be referred by the trained nurse for cardiac rehabilitation, with their follow-up card accompanying them.

## 4. Collaboration with Primary Care (Family) Practitioner

A standardized short letter should be prepared for all patients post-visit to the Cardiology outpatient clinic, to inform their family practitioner about the consultation and any interventions. The letter aims to enhance the patient's adherence to the prescribed lipid-lowering therapy.

All patients are to be evaluated by their family practitioner 6 months after discharge. Subsequently, they should return to the Cardiology outpatient clinic at the 12-month mark. If the LDL-C target has not been achieved at the 6-month check, the family practitioner should immediately refer the patient back to the Cardiology clinic for further assessment.

The family practitioner is tasked with monitoring the lipid profile and assessing adherence for patients who meet their LDL-C

targets. Patients should be directed to revisit the Cardiology outpatient clinic as necessary. Optionally, the family practitioner may note any observations regarding patient compliance and other relevant risk factors on the patient's follow-up card to aid in ongoing treatment planning.

## 5. Tips for Managing Adherence to Lipid-Lowering Therapy

Poor adherence to lipid-lowering therapy is one of the biggest problems in the treatment of dyslipidemia. High rates of non-compliance are observed even among patients who have experienced a CV event.<sup>13,30</sup> In Türkiye, a study on ACS patients revealed that during the first year post-event, only 44.9% achieved an acceptable adherence level to statin therapy ( $\geq 9$  out of 12 prescription refills), with just 17.8% of fully adherent.<sup>31</sup> Non-compliance not only hinders the achievement of treatment goals but also results in suboptimal treatment outcomes. Moreover, poor adherence to statins, which are the cornerstone of lipid-lowering therapy, is associated with an increased risk of mortality.<sup>32</sup>

It is crucial to promote consistent adherence to prescribed lipid-lowering medications. If adherence rates are lower than expected, it is important to meticulously investigate the underlying reasons. Measures should be implemented to address and mitigate any preventable causes of non-compliance tailored to the individual patient's circumstances.

Common reasons patients stop taking statin medication include: intolerance to statins, the nocebo effect, side effects, doctor's recommendation, lack of knowledge about CHD and statins, insufficient follow-up, difficulties in obtaining statins, preference for traditional medicines, economic factors, not noticing benefits, doubts about the necessity and effectiveness of statins, poor doctor-patient relationships, complexity of treatment, and information from media/internet sources.<sup>33-37</sup>

Interventions that can improve adherence to lipid-lowering therapies are detailed in Table 1. The most important factor in enhancing statin adherence is improving communication with patients, particularly addressing their concerns and discussing potential side events. Engaging patients in shared decision-making can boost long-term adherence to statin therapy. Effective communication among healthcare providers (physicians, nurses, and pharmacists) and patients can also foster better adherence by educating patients about the benefits and risks of the therapy and involving them in treatment decisions.<sup>34,35</sup> Regarding adverse effects, myalgia is a frequent cause for stopping statins. It is important to assess causality and re-test the patient with a different statin to verify if the side effect is genuine.<sup>35</sup> If confirmed, the patient should be prescribed alternative non-statin therapies such as bempedoic acid, ezetimibe, or PCSK9i. Regarding practical measures that can aid adherence, providing reminders to take medication, distributing dose-dispensed medication packs that indicate the administration day/time, or simplifying the medication regimen, can be beneficial.<sup>34,35</sup>

## Discussion

In this paper, we propose a country-specific protocol for managing lipid-lowering therapy in patients with ACS in Türkiye, aimed at achieving optimal LDL-C levels.

**Table 1. Strategies to Enhance Patient Adherence to Lipid-Lowering Medications<sup>34,35</sup>**

<b>General Communication</b>
Facilitate shared decision-making to involve patients in their treatment decisions.
Educate patients about coronary heart disease and dyslipidemia.
Provide information and education about the benefits and risks associated with lipid-lowering treatments, including potential side effects.
Address any concerns patients may have about their lipid-lowering medications.
Tailor advice to meet each patient's specific needs.
Use various communication methods including face-to-face meetings, telephone calls, booklets, online videos, and smartphone apps.
Provide ongoing follow-up counseling and support.
<b>Medication Management</b>
Implement reminders to take medication using methods like telephone calls, text messages, smartphone apps, or online calendars.
Utilize dose-dispensed medication that provides clear reminders of the days and times doses should be taken.
Simplify the medication regimen by opting for single-pill and once-daily formulations when feasible.
Identify and address any statin intolerance, and adjust the treatment plan as necessary.
Employ digital tools such as electronic reminders and medication reconciliation to enhance adherence monitoring and support.
<b>Healthcare Staff</b>
Involve a multidisciplinary team including physicians, nurses, and pharmacists to provide a comprehensive approach to various elements of the adherence strategy.

Currently, only 18% of secondary prevention patients at cardiology clinics in Türkiye meet their LDL-C targets.<sup>37,38</sup> The EPHEBUS study (Evaluation of perceptions, knowledge and compliance with guidelines in real-life practice: A survey on the under-treatment of hypercholesterolemia) reported that only 70% of patients requiring secondary prevention (for any reason) were prescribed statins, with about half receiving high-intensity statin therapy.<sup>37</sup> Conversely, the TURKMI study (Turkish Myocardial Infarction Registry) noted that among patients specifically with an acute myocardial infarction, 96.3% were prescribed anti-lipid medications upon hospital discharge.<sup>39</sup>

Physicians often do not treat dyslipidemia in accordance with major guideline recommendations.<sup>14,40</sup> A Delphi panel evaluation of common practice among expert cardiologists in Türkiye revealed that approximately one-third of treatment-naïve patients with LDL-C  $\geq$  190 mg/dL requiring secondary prevention were either left untreated or given only low to moderate statin therapy.<sup>41</sup> Furthermore, only a quarter of treatment-naïve patients with LDL-C < 55 mg/dL, who require secondary prevention, were considered for lipid-lowering therapy, despite guidelines suggesting that a 50% reduction in LDL-C from baseline should be achieved, in addition to reaching LDL-C levels below 55 mg/dL.<sup>41</sup> Moreover, target attainment among those who do receive lipid-lowering therapy is often poor. A study in Türkiye found that among patients undergoing lipid-lowering therapy for secondary prevention, only 21% achieved an LDL-C level of < 55 mg/dL, and 18.2% achieved both LDL-C < 55 mg/dL and a 50% reduction from baseline.<sup>42</sup>

Additionally, despite experiencing an ACS, many patients demonstrate poor adherence to lipid-lowering therapy in the year following the event.<sup>13,31</sup> Among patients in Türkiye, common reasons for discontinuing lipid-lowering drugs include misinformation from media sources, inadequate information from physicians, drug access issues, and a preference for non-pharmaceutical alternatives.<sup>36,37</sup> Notably, less than 7% of statin discontinuations in Türkiye are due to side effects. Thus, the minimal role of side effects in medication discontinuation and the misleading impact of social media should be highlighted in patient education.

To lower mortality from cardiovascular diseases (CVD), the WHO has established a global target: by 2025, at least 50% of eligible individuals should receive drug therapy and counseling to prevent heart attacks and strokes.<sup>43</sup> The Turkish Cardiovascular Diseases Prevention and Control Program Action Plan (2021-2026) was recently updated.<sup>44</sup> It aims to reduce the risk of vascular diseases by enhancing awareness of CV diseases and risk factors and includes multiple initiative for the prevention, early diagnosis, and regular follow-up of patients with CV conditions.<sup>45</sup> It is projected that effective LDL-C reduction in high-risk individuals requiring secondary prevention could prevent approximately 980,000 acute CV events requiring hospitalization over 20 years in Türkiye, potentially saving around US\$8.1 billion.<sup>45</sup>

Therefore, enhancing the management of dyslipidemia in secondary prevention in Türkiye is important. Several countries have launched initiatives to improve in-hospital and/or post-discharge management of dyslipidemia in ACS patients, yielding promising results.<sup>12,46</sup> These strategies include in-hospital protocols and algorithms focused on optimal drug therapy, standardized processes for identifying FH patients, achieving targets within 3 months, nurse-led cardiac rehabilitation programs, provision of standardized discharge letters to family practitioners, and the implementation of virtual follow-up visits. Each approach is specifically designed to address the identified gaps within that country.

The recommendations in this paper for lipid management protocols for ACS patients treated in Türkiye were developed by local experts, who carefully considered the unique issues and healthcare structures within the country. The proposed algorithms aim to guide healthcare practitioners in reducing therapeutic inertia, enhancing patient adherence, and improving coordination among different healthcare providers. This approach is designed to help achieve the guideline-recommended LDL-C targets for this high-risk patient group.

Efforts to optimize lipid management for ACS patients in other countries have demonstrated notable successes. In France, an expert group formulated an algorithm for managing lipid levels

in ACS patients during hospitalization and post-discharge, targeting an LDL-C level below 55 mg/dL. This comprehensive approach includes patient education, dietary advice, high-intensity lipid-lowering therapy, and systematic LDL-C checks after 4–6 weeks.<sup>47</sup> An evaluation of the algorithm in a Cardiology department revealed a decrease in mean LDL-C from 120 mg/dL at admission to 57 mg/dL after 2 months, with 50% of the patients achieving LDL-C levels below 55 mg/dL. In the UK, the introduction of a lipid-management pathway in a hospital that focused on LDL-C targets for patients after myocardial infarction (MI) led to improved target attainment within 6 months of its introduction. Specifically, 26% of patients achieved a reduction in LDL-C levels below 50% and reached LDL-C levels below 1.4 mmol/L, compared to 17% before the pathway was implemented.<sup>48</sup> In the Netherlands, the introduction of an ESC-guideline-based algorithm, which included a stepwise intensification of lipid-lowering therapy at 22 hospitals, resulted in 99% of very high-risk ACS patients meeting their LDL-C targets within 3 months post-event.<sup>12</sup>

Initiatives where nurses play a coordinating role have proven successful. For instance, in Sweden, the implementation of a nurse-led multidisciplinary lipid protocol at a hospital led to an increase in the proportion of MI patients with LDL-C levels below 70 mg/dL one year post-MI to 82%, up from 54% prior to the protocol, with 55% achieving LDL-C levels below 55 mg/dL.<sup>12</sup> Similarly, in Spain, a nurse-coordinated multidisciplinary cardiac rehabilitation program for ACS patients demonstrated significant improvements after 6 months. Specifically, 62% of patients in the intervention group achieved LDL-C levels of  $\leq 70$  mg/dL compared to 37% in the usual-care group ( $P = 0.047$ ) and 25.6% of the intervention group achieved an LDL-C reduction of  $\geq 50\%$ , versus only 2.6% in the usual-care group ( $P = 0.007$ ).<sup>25</sup> In Sweden, a nurse-led, telephone-based intervention provided post-ACS patients with lifestyle advice, blood lipid measurements, and treatment adjustments overseen by physicians, with reassessment every 4 weeks until targets were met.<sup>27</sup> After 12 months, 77.7% of the intervention group reached target LDL-C values, compared to 63.2% of the control group ( $P < 0.05$ ).<sup>27</sup> This significant difference between the groups was maintained at 36 months, with 65.6% of the intervention group versus 53.1% of the control group achieving target levels ( $P < 0.001$ ).<sup>26</sup>

Currently, Türkiye has a limited number of nurses specialized in CV prevention,<sup>49</sup> highlighting the need for strategies to recruit and train nurses to act as coordinators and facilitators of lipid management pathways. Additionally, further work is required to clearly define certain aspects, such as the optimal content of the proposed patient information booklet and the patient's follow-up card. Research is also necessary to evaluate the practical effectiveness of these strategies.

The proposed algorithms call for the distribution of tasks among various healthcare practitioners and departments, necessitating enhanced coordination and cooperation. Multidisciplinary initiatives have proven effective in the context of post-ACS lipid management.<sup>12, 25</sup> If successfully implemented, these strategies could improve patient outcomes and confer broader societal benefits.

It is important to note that the existence of guidelines and recommendations does not guarantee their implementation in practice. In this context, there is a growing interest in implementation science as a means to enhance the adoption and practical application of lipid management guidelines in daily clinical settings.<sup>50,51</sup> Implementation science seeks to bridge the gap between established guidelines and routine clinical practice, enhancing the quality, dissemination, and effectiveness of health services. This field plays a crucial role in developing tools that help bridge the gap between lipid management guidelines and actual clinical practice. For instance, it aims to facilitate behavioral changes in both physicians and patients to enhance adherence to lipid-lowering therapies. Additionally, the WHO has emphasized the importance of utilizing digital technologies, such as remote monitoring and artificial intelligence, to improve health outcomes.<sup>52</sup>

A systematic review focusing on statin use implementation strategies found evidence that these approaches can enhance statin prescribing and adherence, and reduce LDL-C levels. However, the components of these strategies are often not clearly defined, and no single strategy or combination of strategies has demonstrated clear superiority.<sup>50</sup> There is a need to refine how implementation strategies are described and to develop standard terminology, definitions, and core outcome sets that facilitate the evaluation and comparison of different approaches.<sup>50</sup> Creating evidence-based implementation strategies could enable healthcare systems and practitioners to more effectively translate guidelines into practice.<sup>51</sup> The detailed strategy we have outlined serves as a foundational step for enhancing lipid management in ACS patients in Türkiye.

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## References

1. World Health Organization. Non-communicable diseases. Accessed April 26, 2024. <https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases>
2. World Health Organization. Global health estimates: Life expectancy and leading causes of death and disability. Accessed April 26, 2024. <https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates>
3. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe: Epidemiological update. *Eur Heart J*. 2013;34(39):3028–3034. [CrossRef]



4. Mannsverk J, Wilsgaard T, Mathiesen EB, et al. Trends in modifiable risk factors are associated with declining incidence of hospitalized and nonhospitalized acute coronary heart disease in a population. *Circulation*. 2016;133(1):74-81. [CrossRef]
5. Ference BA, Ginsberg HN, Graham I, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J*. 2017;38(32):2459-2472. [CrossRef]
6. Pencina KM, Thanassoulis G, Wilkins JT, et al. Trajectories of non-HDL cholesterol across midlife: Implications for cardiovascular prevention. *J Am Coll Cardiol*. 2019;74(1):70-79. [CrossRef]
7. Raja V, Aguiar C, Alsayed N, et al. Non-HDL-cholesterol in dyslipidemia: Review of the state-of-the-art literature and outlook. *Atherosclerosis*. 2023;383:117312. [CrossRef]
8. Johannessen CDL, Mortensen MB, Langsted A, Nordestgaard BG. Apolipoprotein B and Non-HDL cholesterol better reflect residual risk than LDL cholesterol in statin-treated patients. *J Am Coll Cardiol*. 2021;77(11):1439-1450. [CrossRef]
9. Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J*. 2021;42(34):3227-3337. [CrossRef]
10. Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk. *Eur Heart J*. 2020;41(1):111-188. [CrossRef]
11. Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J*. 2023;44(38):3720-3826. [CrossRef]
12. Alings M, Descamps O, Guillon B, et al. Implementation of clinical practices and pathways optimizing ACS patients lipid management: Focus on eight European initiatives. *Atheroscler Suppl*. 2020;42:e59-e64. [CrossRef]
13. Bruckert E, Desameriq G, Khachatryan A, Ngo P, Gusto G, Sorio-Vilela F. Patient characteristics, treatment patterns, and adherence to lipid-lowering therapies following an acute coronary syndrome. *Rev Cardiovasc Med*. 2020;21(4):643-650. [CrossRef]
14. De Backer G, Jankowski P, Kotseva K, et al. Management of dyslipidaemia in patients with coronary heart disease: Results from the ESC-EORP EUROASPIRE V survey in 27 countries. *Atherosclerosis*. 2019;285:135-146. [CrossRef]
15. Tokgözoğlu L, Kaya EB, Erol C, Ergene O. EUROASPIRE III: A comparison between Turkey and Europe. *Turk Kardiyol Dern Ars*. 2010;38(3):164-172. Turkish
16. Kotseva K, Wood D, De Bacquer D, et al. EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. *Eur J Prev Cardiol*. 2016;23(6):636-648. [CrossRef]
17. Gencer B, Auer R, Nanchen D, et al. Expected impact of applying new 2013 AHA/ACC cholesterol guidelines criteria on the recommended lipid target achievement after acute coronary syndromes. *Atherosclerosis*. 2015;239(1):118-124. [CrossRef]
18. Gencer B, Koskinas KC, Räber L, et al. Eligibility for PCSK9 inhibitors according to American College of Cardiology (ACC) and European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) Guidelines after acute coronary syndromes. *J Am Heart Assoc*. 2017;6(11):e006537. [CrossRef]
19. Koskinas KC, Gencer B, Nanchen D, et al. Eligibility for PCSK9 inhibitors based on the 2019 ESC/EAS and 2018 ACC/AHA guidelines. *Eur J Prev Cardiol*. 2021;28(1):59-65. [CrossRef]
20. Vallejo-Vaz AJ, Kondapally Seshasai SR, Cole D, et al. Familial hypercholesterolaemia: A global call to arms. *Atherosclerosis*. 2015;243(1):257-259. [CrossRef]
21. Kayıkçioğlu M, Alan B, Payzin S, Can LH. Lipid profile, familial hypercholesterolemia prevalence, and 2-year cardiovascular outcome assessment in acute coronary syndrome: Real-life data of a retrospective cohort. *Turk Kardiyol Dern Ars*. 2019;47(6):476-486. [CrossRef]
22. Sabouret P, Puymirat E, Kownator S, et al. Lipid-lowering treatment up to one year after acute coronary syndrome: guidance from a French expert panel for the implementation of guidelines in practice. *Panminerva Med*. 2023;65(2):244-249. [CrossRef]
23. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: Executive summary: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *J Am Coll Cardiol*. 2019;73(24):3168-3209. [CrossRef]
24. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med*. 2015;372(25):2387-2397. [CrossRef]
25. Ruiz-Bustillo S, Ivern C, Badosa N, et al. Efficacy of a nurse-led lipid-lowering secondary prevention intervention in patients hospitalized for ischemic heart disease: A pilot randomized controlled trial. *Eur J Cardiovasc Nurs*. 2019;18(5):366-374. [CrossRef]
26. Henriksson R, Huber D, Moos T. Nurse-led, telephone-based follow-up after acute coronary syndrome yields improved risk factors after 36 months: The randomized controlled NAILED-ACS trial. *Sci Rep*. 2021;11(1):17693. [CrossRef]
27. Huber D, Henriksson R, Jakobsson S, Moos T. Nurse-led telephone-based follow-up of secondary prevention after acute coronary syndrome: One-year results from the randomized controlled NAILED-ACS trial. *PLoS One*. 2017;12(9):e0183963. [CrossRef]
28. Özdoğan O, Gungor B, Kayıkçioğlu M, et al. First diagnosis and follow up features of patients with dyslipidemia in Turkey. *Atherosclerosis*. 2022;355:114. [CrossRef]
29. Fitchett DH, Hegele RA, Verma S. Cardiology patient page. Statin intolerance. *Circulation*. 2015;131(13):e389-e391. [CrossRef]
30. Lin I, Sung J, Sanchez RJ, et al. Patterns of statin use in a real-world population of patients at high cardiovascular risk. *J Manag Care Spec Pharm*. 2016;22(6):685-698. [CrossRef]
31. Şimşek B, Çınar T, Tanık VO, İnan D, Avcı İİ, Zeren G, et al. In-hospital statin initiation characteristics and one-year statin adherence rates in patients hospitalized for acute coronary syndrome. *Acta Cardiol*. 2021;76(8):852-858. [CrossRef]
32. De Vera MA, Bhole V, Burns LC, Lacaille D. Impact of statin adherence on cardiovascular disease and mortality outcomes: A systematic review. *Br J Clin Pharmacol*. 2014;78(4):684-698. [CrossRef]
33. Ingersgaard MV, Helms Andersen T, Norgaard O, Grabowski D, Olesen K. Reasons for nonadherence to statins - A systematic review of reviews. *Patient Prefer Adherence*. 2020;14:675-691. [CrossRef]
34. Lansberg P, Lee A, Lee ZV, Subramaniam K, Setia S. Nonadherence to statins: Individualized intervention strategies outside the pill box. *Vasc Health Risk Manag*. 2018;14:91-102. [CrossRef]
35. Drexel H, Coats AJS, Spoletini I, et al. An expert opinion paper on statin adherence and implementation of new lipid-lowering medications by the ESC Working Group on Cardiovascular Pharmacotherapy: Barriers to be overcome. *Eur Heart J Cardiovasc Pharmacother*. 2020;6(2):115-121. [CrossRef]
36. Tokgözoğlu L, Özdemir R, Altındağ R, et al. Patient characteristics and statin discontinuation-related factors during treatment of hypercholesterolemia: an observational non-interventional study in patients with statin discontinuation (STAY study). *Turk Kardiyol Dern Ars*. 2016;44(1):53-64. [CrossRef]
37. Doğan V, Başaran Ö, Özlek B, et al. Evaluation of perceptions, knowledge and compliance with guidelines in real-life practice: A survey on the under-treatment of hypercholesterolemia. *Turk Kardiyol Dern Ars*. 2019;47(7):599-608. [CrossRef]
38. Mert GÖ, Başaran Ö, Mert KU, et al. The reasons of poor lipid target attainment for secondary prevention in real life practice: Results from EPHEUS. *Int J Clin Pract*. 2019;73(9):1-9. [CrossRef]
39. Erol MK, Kayıkçioğlu M, Kılıçkap M, et al. Baseline clinical characteristics and patient profile of the TURKMI registry: Results of a nation-wide acute myocardial infarction registry in Turkey. *Anatol J Cardiol*. 2020;24(1):43-53. [CrossRef]
40. Landmesser U, Pirillo A, Farnier M, et al. Lipid-lowering therapy and low-density lipoprotein cholesterol goal achievement in patients with acute coronary syndromes: The ACS patient pathway project. *Atheroscler Suppl*. 2020;42:e49-e58. [CrossRef]
41. Kayıkçioğlu M, Yuksel UC, Yılmaz MB, et al. Management of patients with LDL-cholesterol levels >190mg/dL (4.9mmol/L) in Turkey: an analysis based on Delphi Panel Approach. Poster presented at 90th Annual Scientific Session EAS 2022 (European Atherosclerosis Society), 22-25 May 2022, Milan, Italy. [CrossRef]

43. Şimşek B, İnan D, Çınar T, et al. Evaluation of low-density lipoprotein cholesterol target attainment rates according to the 2016 and 2019 European Society of Cardiology/European Atherosclerosis Society Dyslipidemia Guidelines for secondary prevention in patients with acute myocardial infarction. *Rev Invest Clin*. 2021;73(3):371–378.
44. World Health Organization. Global action plan for the prevention and control of noncommunicable diseases 2013–2020. Accessed April 26, 2024. <https://iris.who.int/handle/10665/94384>
45. Republic of Turkey Ministry of Health. Prevention and control program for cardiovascular diseases. Accessed April 26, 2024. <https://tkd.org.tr/TKDDData/Uploads/files/prevention-action-plan-for-cardiovascular-diseases.pdf>
46. Balbay Y, Gagnon-Arpin I, Malhan S, et al. The impact of addressing modifiable risk factors to reduce the burden of cardiovascular disease in Turkey. *Turk Kardiyol Dern Ars*. 2019;47(6):487–497. [CrossRef]
47. Nakao S, Ishihara T, Tsujimura T, et al. Effectiveness of hospital lipid-lowering protocol of intensive lipid-lowering therapy for patients with acute coronary syndrome. *J Cardiol*. 2022;79(3):391–399. [CrossRef]
48. Buonvino C, Chopard R, Guillon B, et al. An innovative lipid-lowering approach to enhance attainment of low-density lipoprotein cholesterol goals. *Eur Heart J Acute Cardiovasc Care*. 2020;9(8):879–887. [CrossRef]
49. Jones C. Evaluation of a lipid management pathway within a local cardiac rehabilitation service. *Br J Cardiol*. 2022;29(4):34.
50. Kayıkciolu M, Oto A. Control and management of cardiovascular disease in Turkey. *Circulation*. 2020;141(1):7–9. [CrossRef]
51. Jones LK, Tilberry S, Gregor C, et al. Implementation strategies to improve statin utilization in individuals with hypercholesterolemia: A systematic review and meta-analysis. *Implement Sci*. 2021;16(1):40. [CrossRef]
52. Jones LK, Sturm AC, Gionfriddo MR. Translating guidelines into practice via implementation science: an update in lipidology. *Curr Opin Lipidol*. 2022;33(6):336–341. [CrossRef]
53. World Health Organization. Global strategy on digital health 2020–2025. Accessed April 26, 2024. <https://www.who.int/publications/i/item/9789240020924>