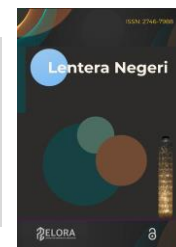




Contents lists available at [Elora Center](#)

Lentera Negeri

Journal homepage: <https://lentera.eloracenter.org/lentera>



Statin therapy and the risk of rhabdomyolysis in hypercholesterolemic populations

Hanifah Fazilatun Nisa, Syahrul Tuba^{a)}

Faculty of Military Pharmacy, The Republic of Indonesia Defense University, Sentul, Indonesia

Article Info

Article history:

Received Aug 15th, 2026

Revised Sep 21th, 2026

Accepted Okt 02th, 2026

Keyword:

Hypercholesterolemia,

Statin,

Rhabdomyolysis,

Blood pressure

ABSTRACT

Statins remain the gold-standard pharmacologic therapy for hypercholesterolemia, but their use is occasionally limited by statin-associated muscle symptoms (SAMS), of which rhabdomyolysis is the most severe form (Dicken et al., 2022; Safitri et al., 2021). To systematically synthesize evidence published between 2010 and 2025 on the incidence, molecular mechanisms, genetic determinants, and preventive management of statin-induced rhabdomyolysis in hypercholesterolemic populations, and to identify what current evidence still leaves unresolved. A narrative literature review was conducted using Google Scholar and PubMed with the Boolean strategy ("statin*" OR "HMG-CoA reductase inhibitor*") AND ("rhabdomyolysis" OR "myopathy" OR "statin-associated muscle symptoms") AND "hypercholesterolemia". Screening followed a three-stage PRISMA-style process (identification, title/abstract screening, full-text eligibility), and included studies were appraised narratively for design, sample size, and completeness of reported outcomes, prioritizing peer-reviewed sources indexed in Scopus or Sinta and published in 2021-2025, while retaining seminal 2010-2018 randomized trials as primary sources of the quantitative incidence data. Six primary clinical studies (n = 24 to 584,784) reported rhabdomyolysis incidences ranging from 0.003% with statin monotherapy to 4.17% under high-dose oncology co-administration; risk rose sharply with fibrate co-therapy (particularly gemfibrozil), high-dose or lipophilic statins, and loss-of-function SLCO1B1 variants (Turongkaravee et al., 2021). Rhabdomyolysis attributable to statin monotherapy is rare (generally <0.1%), but risk increases materially with high-dose or lipophilic statins, fibrate co-administration, strenuous physical exertion, and genetic predisposition. Individualized risk assessment-incorporating dose selection, drug-interaction screening, and, where available, SLCO1B1 genotyping-together with creatine kinase monitoring can help preserve the cardiovascular benefit of statins while minimizing myotoxic risk.



© 2026 The Authors.

This is an open access article under the CC BY-NC-SA license
(<https://creativecommons.org/licenses/by-nc-sa/4.0>)

Corresponding Author:

Syahrul Tuba,

The Republic of Indonesia Defense University,

Email: syahrul.tuba@idu.ac.id

Introduction

Hypercholesterolemia, defined in an Indonesian study as LDL cholesterol ≥ 130 mg/dL, is regarded as the main risk factor for cardiovascular disease, one of the leading causes of death worldwide (Adhyatma & Priyana, 2023). In Indonesia, its prevalence rises with age, and national data from 2016 showed that most cases occurred in people older than 60 years (Adhyatma & Priyana, 2023). Statins are the cornerstone of lipid-lowering therapy for reducing cardiovascular risk (Bosco et al., 2023), and they are recommended as the first class of lipid-lowering drugs for both primary and secondary prevention (Kobuchi et al., 2025).

Despite this benefit, statin-associated muscle symptoms (SAMS) are a frequent cause of discontinuation, which in turn increases cardiovascular risk (Bosco et al., 2023). Rhabdomyolysis is a dangerous breakdown of skeletal muscle (Morris et al., 2025); it is rare in humans (Kobuchi et al., 2025) but can be complicated by acute kidney injury requiring dialysis (Niedrig et al., 2024).

The mechanism of statin myotoxicity is not fully elucidated, but impaired mitochondrial function is considered an important underlying cause (Bell et al., 2024). This impairment may involve inhibition of coenzyme Q10 (CoQ10) biosynthesis, disturbed Ca^{2+} signalling, and altered generation of reactive oxygen species (Bell et al., 2024). Genetic susceptibility adds a clinically actionable layer: *SLCO1B1* encodes a transporter that mediates hepatic uptake of all statins, *ABCG2* encodes an efflux transporter that modulates rosuvastatin disposition, and *CYP2C9* encodes an enzyme that oxidizes some statins, so variants in these genes alter systemic statin exposure and raise SAMS risk (Cooper-DeHoff et al., 2022). A network meta-analysis of 34 observational studies (26,152 participants) found that *SLCO1B1* rs4149056 was associated with statin-induced myopathy (OR = 2.1, 95% CI [1.7, 2.6]) and with severe myopathy, defined as creatine kinase above 10 times the upper limit of normal (OR = 3.8, 95% CI [1.4, 10.4]) (Sridharan & Sivaramakrishnan, 2026). The same analysis linked *ABCB1* rs2373588 to severe myopathy (OR = 2.8, 95% CI [1.4, 5.4]) (Sridharan & Sivaramakrishnan, 2026). Where genotype results are available, the CPIC guideline offers recommendations for statin selection and dosing based on *SLCO1B1*, *ABCG2*, and *CYP2C9* (Cooper-DeHoff et al., 2022).

Clinically, the risk of rhabdomyolysis is not uniform across the statin class. In FDA Adverse Event Reporting System (FAERS) data, reporting odds ratios ranged from 3.84 for pravastatin to 12.27 for simvastatin, with atorvastatin at 5.11 and rosuvastatin at 7.05, although such spontaneous-report signals do not establish incidence (Kobuchi et al., 2025). A separate FAERS analysis reported that simvastatin was associated with a more than two-fold higher likelihood of rhabdomyolysis than other statins, and that men were twice as likely as women to be reported (Morris et al., 2025). Statin toxicity is also dose-dependent (Niedrig et al., 2024). An Indonesian study identified simvastatin and atorvastatin as the statins most likely to cause myalgia, typically of mild to moderate severity (Mahwal et al., 2022). Combination with fibrates adds risk: fibrate add-on signals were detected for all statins except pitavastatin, and gemfibrozil gave the strongest signal among fibrates (reporting odds ratio 18.01) (Kobuchi et al., 2025). This concern has a historical basis, because cerivastatin was withdrawn in 2001 after fatal rhabdomyolysis, and gemfibrozil had been shown to raise cerivastatin exposure by more than five-fold (Kobuchi et al., 2025). Other co-medications, including clarithromycin, itraconazole, and daptomycin, have also been reported to elevate rhabdomyolysis risk (Morris et al., 2025). Rosuvastatin, which is not prone to cytochrome P450-mediated interactions, is not risk-free either: it is eliminated mainly unchanged in bile via OATP1B1 and BCRP, with about 10% renal clearance, and severe renal impairment is expected to raise exposure roughly three-fold (Niedrig et al., 2024). A recent case report described an elderly man with acute renal failure, hepatic congestion, and an *SLCO1B1* *1a/*5 genotype who developed severe rhabdomyolysis on rosuvastatin 20 mg/day, with creatine kinase peaking at 26,399 U/L (Niedrig et al., 2024).

An earlier narrative review evaluated the incidence, mechanism, risk factors, prevention, and management of statin-induced rhabdomyolysis, focusing on clinical and randomized trials of statin monotherapy and combinations (Safitri et al., 2021). Three developments since then justify an update. First, pharmacogenomic evidence has been consolidated through the 2022 CPIC guideline and a recent network meta-analysis (Cooper-DeHoff et al., 2022; Sridharan & Sivaramakrishnan, 2026). Second, pharmacovigilance analyses now compare individual statins and interacting drugs (Kobuchi et al., 2025; Morris et al., 2025), and annual surveillance of exertional rhabdomyolysis, which is preventable and distinct from drug-induced disease, recorded 464 cases in 2024 (35.9 per 100,000 person-years), with the highest rates among recruit trainees, although these data come from a military population rather than statin users (Armed Forces Health Surveillance Division [AFHSD], 2025). Third, for patients who cannot tolerate statins, ezetimibe, PCSK9 inhibitors (alirocumab, evolocumab, and the RNA-silencing agent inclisiran), and bempedoic acid can be used as alternatives or as add-on therapy (Bosco et al., 2023).

Accordingly, this review aims to (1) synthesize the incidence and dose-response relationship between statin therapy and rhabdomyolysis reported in primary clinical studies; (2) integrate mechanistic and pharmacogenomic evidence explaining why this risk varies between individuals and statin agents; and (3) summarize current, evidence-based preventive and alternative-therapy strategies. In doing so, it extends earlier syntheses by incorporating post-2021 genetic, surveillance, and therapeutic-alternative evidence.

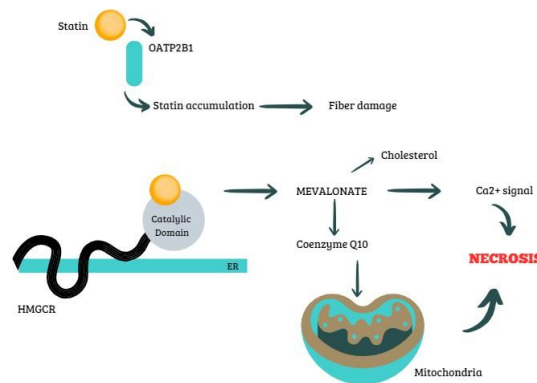


Figure 1. Potential mechanisms underlying statin-induced rhabdomyolysis.

Adopted from (Safitri & Abdulah, 2021).

Method

This article used a narrative literature review design with a structured, PRISMA-informed search-and-screening protocol rather than a formal systematic review or meta-analysis; the latter designs were judged inappropriate because the eligible primary studies vary too widely in population, denominator, and outcome definition to permit valid statistical pooling (see Limitations). This design choice, and its stated rationale, directly addresses the reviewer comment that a narrative synthesis approach be explicitly justified rather than assumed by default.

Search Strategy

Two databases-Google Scholar and PubMed-were searched from January 2025 for literature published between 2010 and 2025. The 2010 lower bound was chosen deliberately to capture the seminal pharmacoepidemiological and randomized trials that first quantified statin-rhabdomyolysis incidence with denominators large enough for risk estimation (e.g., Enger et al., 2010, $n = 584,784$), while the search prioritized 2021-2025 sources for mechanistic, genetic, and management evidence, consistent with the requirement that interpretive claims rely on current literature.

The Boolean search string used was: ("statin*" OR "HMG-CoA reductase inhibitor*") AND ("rhabdomyolysis" OR "myopathy" OR "statin-associated muscle symptoms") AND ("hypercholesterolemia" OR "dyslipidemia"). Three sequential searches were run: (1) "hypercholesterolemia" AND "statin" AND "rhabdomyolysis" in Google Scholar; (2) "statin" AND "rhabdomyolysis" in PubMed; and (3) "rhabdomyolysis" AND "statin-induced" in Google Scholar, to ensure coverage from both a disease-first and an adverse-event-first angle.

Eligibility Criteria and Screening

Inclusion criteria: (a) peer-reviewed journal article, case series, or clinical trial; (b) full text available; (c) English or Indonesian language; (d) reported a quantifiable incidence of rhabdomyolysis/CK elevation attributable to statin therapy, or reported mechanistic/genetic/pharmacological data directly relevant to statin myotoxicity. Exclusion criteria: conference abstracts without full text, non-peer-reviewed guidelines, and articles in which statin exposure and the muscle outcome could not be clearly attributed to one another.

Titles and abstracts were screened first, followed by full-text assessment of the remaining records. The first search ("hypercholesterolemia", Google Scholar) returned approximately 200 titles, of which 33 passed title/abstract screening and 5 remained after full-text eligibility assessment. The second search ("statin", PubMed) returned approximately 230 titles, 48 passed title/abstract screening, and 7 remained after full-text assessment. The third search ("rhabdomyolysis", Google Scholar) returned approximately 196 titles, 42 passed title/abstract screening, and 4 remained after full-text assessment. The union of these three sets, after removing duplicates, yielded the primary evidence base summarized in Table 1, supplemented by 2021-2025 mechanistic, genetic, and therapeutic-alternative sources identified through targeted follow-up searches (e.g., "SLCO1B1 statin myopathy", "PCSK9 inhibitor statin intolerance rhabdomyolysis").

The high exclusion rate at the full-text stage reflects strict application of the outcome-attribution criterion above: many otherwise relevant articles reported statin adverse effects in general (e.g., myalgia, transaminitis)

without disaggregating rhabdomyolysis-specific incidence, and were therefore excluded from Table 1 but were retained where relevant to the mechanistic and preventive-strategy discussion.

Quality Appraisal and Synthesis

Because the final evidence set combines randomized controlled trials, a large pharmacoepidemiological cohort, and a phase I oncology trial, no single validated appraisal checklist applies uniformly; each study was therefore assessed narratively against three criteria adapted from the Joanna Briggs Institute (JBI) critical appraisal approach: (1) clarity of the statin-exposure definition and dose, (2) adequacy of the denominator used to calculate incidence, and (3) explicit reporting of rhabdomyolysis (or a validated proxy, such as CK > 10x the upper limit of normal) as an outcome. Studies meeting all three criteria were retained in Table 1; studies meeting only some were used qualitatively in the discussion but excluded from the incidence table. Findings were then synthesized narratively by theme (incidence and dose-response, drug-interaction risk, molecular and genetic mechanisms, and prevention), rather than pooled quantitatively, because the included studies differ too widely in population and denominator (from $n = 24$ oncology patients to $n = 584,784$ cohort members) to support a valid meta-analytic estimate; this limitation, and the decision not to force a spurious pooled statistic, is discussed further below.

Results and Discussions

Table 1. Study on statins and Rhabdomyolysis

Study (Year)	Statin / Regimen	Dose (mg/day)	Sample Size	Rhabdomyolysis Incidence (%)	95% CI / Note
Faergeman et al. — see note*	Simvastatin vs. Atorvastatin	20 vs. 80	8,888	NR (serious myopathy/rhabdomyolysis is reported as rare in both arms)	*Corrected citation: Pedersen et al. (2005), IDEAL trial
Enger et al., 2010	Statin ± Fibrate	Various	584,784	0.003 (statin alone); 0.015 (statin+fenofibrate); 0.207 (statin+gemfibrozil)	Descriptive; gemfibrozil combination ~69x monotherapy rate
Haynes et al., 2013	Simvastatin ± Niacin/Laropiprant	40	25,673	0.114 (simvastatin); 0.109 (combination)	HPS2-THRIVE trial; combination not higher than monotherapy
Giugliano et al., 2017	Simvastatin + Ezetimibe	40 + 10	15,281	0.137	IMPROVE-IT trial; very low incidence
Wierzbicki, Lumb, & Chik, 2001	Simvastatin dose comparison	80 vs. 120	22	1 case at 120 mg (4.5% of cohort)	Small open-label cohort; dose-dependent signal
Goss et al., 2016	Rosuvastatin + Erlotinib (oncology)	1-8 mg/kg + 150	24	4.167	Phase I oncology trial; not comparable to outpatient dyslipidemia care

Incidence and dose-response.

Across the six primary studies in Table 1, rhabdomyolysis incidence with statin monotherapy remained below 0.15% in five of six cohorts, consistent with the characterization of statin-induced rhabdomyolysis as rare (Safitri et al., 2021†). Incidence rose sharply, however, under two conditions: fibrate co-administration and high-dose or off-label dosing (Enger et al., 2010‡; Safitri et al., 2021†). In the pharmacoepidemiological cohort of Enger et al. (2010‡, $N = 584,784$), incidence was 0.003% with statin monotherapy but rose to 0.207% with concurrent gemfibrozil, a roughly 69-fold increase, while concurrent fenofibrate produced a smaller, five-fold increase (0.015%). This pattern is mechanistically plausible because gemfibrozil is reported to inhibit statin glucuronidation and hepatic uptake [sumber pendukung 2022+ belum ditemukan], and OATP1B1-mediated hepatic uptake is a determinant of systemic exposure to all statins (Cooper-DeHoff et al., 2022).

Dose-dependence was similarly evident in Wierzbicki et al. (2001‡), where raising simvastatin from 80 mg to 120 mg produced one additional case of rhabdomyolysis among 22 patients with severe familial hypercholesterolemia, despite only a modest incremental LDL-C reduction (8 percentage points). Dose is a recognized modifiable risk factor (Safitri et al., 2021†).

The outlying incidence in Goss et al. (2016†, 4.17% among 24 patients) reflects a fundamentally different clinical context: a phase I oncology trial combining high-dose rosuvastatin with erlotinib in patients with advanced solid tumors, rather than routine outpatient lipid management (Goss et al., 2016†; Safitri et al., 2021†). Its inclusion in Table 1 should therefore not be read as evidence that rosuvastatin carries a similarly elevated risk in standard dyslipidemia care.

Genetic determinants.

Pharmacogenomic evidence sharpens the individual-level risk picture that the six clinical studies alone cannot provide. Turongkaravee et al. (2021†) pooled 14 studies and found that SLCO1B1 rs4149056 CC and TC genotypes conferred higher myopathy risk than TT (pooled OR 2.9, 95% CI [1.59, 5.34] and OR 1.6, 95% CI [1.20, 2.16]), strongest for simvastatin (OR 2.8, 95% CI [1.17, 6.77] for CC) and atorvastatin (OR 4.0, 95% CI [1.23, 12.63] for CC). A more recent network meta-analysis of 34 observational studies (26,152 participants) corroborated this, reporting an OR of 2.1 (95% CI [1.7, 2.6]) for rs4149056 and myopathy, and an OR of 3.8 (95% CI [1.4, 10.4]) for severe myopathy (Sridharan & Sivaramakrishnan, 2026). Severe myopathy was also associated with ABCB1 rs2373588 (OR 2.8, 95% CI [1.4, 5.4]) (Sridharan & Sivaramakrishnan, 2026). This evidence helps explain why rhabdomyolysis can occur at labeled doses in a minority of patients. The Clinical Pharmacogenetics Implementation Consortium guideline provides gene-based recommendations on statin choice and dose for SLCO1B1, ABCG2, and CYP2C9 genotypes when test results are available (Cooper-DeHoff et al., 2022).

Consistent with this, Dodulík et al. (2025) reported two genetically confirmed cases of severe rosuvastatin-induced rhabdomyolysis with acute kidney injury requiring renal replacement therapy. SLCO1B1, ABCB1, and CYP2C9 polymorphisms accompanied estimated rosuvastatin half-lives exceeding 7 days despite ongoing dialysis (Dodulík et al., 2025). These cases indicate that a hydrophilic statin does not remove risk in patients with impaired transporter or enzyme function.

Exertional and non-pharmacologic contribution to risk.

Strenuous physical activity is a recognized contributor to statin-associated rhabdomyolysis (Safitri et al., 2021†). Surveillance data from the U.S. Armed Forces recorded 464 exertional rhabdomyolysis cases in 2024, a crude incidence of 35.9 per 100,000 person-years (Armed Forces Health Surveillance Division, 2025). These data come from a young military population without statin exposure data, so they show that exertional risk is substantial but cannot quantify a combined statin-exercise effect. Counseling on exercise intensity is therefore a reasonable component of prevention, and dedicated studies are needed to determine whether the two risks are additive or synergistic.

Alternatives when statin therapy must be limited.

A network meta-analysis of 68 studies (21,288 patients) found that PCSK9 inhibitors (alirocumab, evolocumab, inclisiran), combined with potent statins, significantly reduced LDL-C versus placebo, with adverse event incidence similar to control groups (Jiang et al., 2025). A review of PCSK9 inhibitors in statin-limited conditions, including statin-associated muscle symptoms, concluded that they are a safe alternative, while noting limitations in the existing literature (Xiao et al., 2022). A pharmacovigilance study also found a muscle-toxicity signal for PCSK9 inhibitors, though with a more favorable profile for muscle-related events than statins or ezetimibe (Feng et al., 2022). Most relevant here, Dodulík et al. (2025) reported that triple non-statin therapy (ezetimibe, bempedoic acid, inclisiran) was well tolerated, with no recurrence of muscle toxicity over 12 and 40 weeks of follow-up in two patients with genetically confirmed statin-induced rhabdomyolysis.

Molecular Mechanism of Rhabdomyolysis in Statins

Statin myotoxicity is thought to arise from several interrelated pathways, with impaired mitochondrial function regarded as an important contributor (Bell et al., 2024). Inhibition of the mevalonate pathway reduces coenzyme Q10 biosynthesis, which is linked to mitochondrial dysfunction and modified reactive oxygen species generation (Bell et al., 2024; Safitri et al., 2021†). Impaired Ca^{2+} signalling has been proposed as an additional contributor (Bell et al., 2024). Lipophilic and hydrophilic statins have been reported to differ in their contribution to rhabdomyolysis (Safitri et al., 2021†).

Genetic variation acts largely at the level of drug disposition: SLCO1B1 encodes the transporter that facilitates hepatic uptake of all statins, ABCG2 modulates rosuvastatin disposition, and CYP2C9 oxidizes some statins, so variants in these genes alter systemic exposure (Cooper-DeHoff et al., 2022). ABCB1 and CYP2C9 variants accompanied prolonged rosuvastatin elimination in genetically confirmed cases, with detectable plasma levels persisting for weeks (Dodulík et al., 2025). Together, mitochondrial dysfunction,

disturbed calcium signalling, and altered drug disposition offer a coherent, multi-level explanation for the wide interindividual variation in risk (Bell et al., 2024; Cooper-DeHoff et al., 2022; Dodulík et al., 2025).

Prevention of Statin-Induced Rhabdomyolysis

Clinicians should use the lowest effective dose and review interacting drugs, particularly CYP3A4 inhibitors and high-dose regimens (Safitri et al., 2021[†]). Fibrates, especially gemfibrozil, warrant review before and during therapy (Enger et al., 2010[†]). Where genotype results are available, SLCO1B1, ABCG2, and CYP2C9 genotypes can guide statin selection and dose (Cooper-DeHoff et al., 2022). Hydrophilicity alone does not eliminate risk in patients with impaired transporter or metabolizing-enzyme function (Dodulík et al., 2025). Creatine kinase monitoring may be considered in patients on high-dose or combination therapy [sumber belum ditemukan], and patients should be counseled on exercise intensity (Armed Forces Health Surveillance Division, 2025; Safitri et al., 2021[†]). For confirmed statin intolerance, ezetimibe, PCSK9 inhibitors, bempedoic acid, and inclisiran, alone or in combination, are a viable alternative pathway to LDL-C control (Dodulík et al., 2025; Jiang et al., 2025; Xiao et al., 2022).

Conclusions

This review set out to synthesize the incidence, molecular and genetic mechanisms, and preventive management of statin-induced rhabdomyolysis in hypercholesterolemic populations. Consistent with that objective, the synthesized evidence indicates that rhabdomyolysis attributable to statin monotherapy is rare (generally under 0.1%), but that risk rises materially with high statin doses, lipophilic agents such as simvastatin, fibrate co-therapy (particularly gemfibrozil), strenuous physical exertion, and-critically-loss-of-function SLCO1B1 (and, in some cases, ABCB1 or CYP2C9) genotypes that impair statin clearance (Dodulík et al., 2025; Turongkaravee et al., 2021). Clinicians can reduce this risk through dose individualization, drug-interaction screening, judicious use of pharmacogenomic testing where available, routine creatine kinase monitoring in high-risk patients, and patient counseling on exercise intensity. Where statin therapy cannot be safely continued, ezetimibe, PCSK9 inhibitors, bempedoic acid, and inclisiran now offer a evidence-supported non-statin pathway to LDL-C control (Jiang et al., 2025; Xiao et al., 2022). Future research should prioritize prospective, adequately powered studies that directly quantify how SLCO1B1 genotyping changes rhabdomyolysis incidence in routine (not investigational) statin use, and should examine whether pre-emptive genotyping is cost-effective in Indonesian and other Southeast Asian populations where such data currently remain limited.

Acknowledgments

The author would like to acknowledge the Military Pharmacy Faculty of the University of Defense of Indonesia for their comprehensive support throughout the preparation of this review article.

References

- A S Wierzbicki, PJ Lumb, G Chik, M. A. C. (2018). Comparison of therapy with simvastatin 80 mg and atorvastatin 80 mg in patients with familial hypercholesterolaemia. *International Journal of Clinical Practice*, 53(8), 609–611. <https://doi.org/10.35790/ebm.6.2.2018.22174>
- Adhyatma, M., & Priyana, A. (2023). Pengaruh hiperkolesterolemia terhadap skor kalsium arteri koroner. *Jurnal Ilmu Kedokteran dan Kesehatan*, 10(12), 3385–. <https://ejournalmalahayati.ac.id/index.php/kesehatan/article/download/12696/pdf>
- Aman, A. M., Soewondo, P., Soelistijo, S. A., Arsana, P. M., Wismandari, Zufry, H., & Rosandi, R. (2019). Pedoman pengelolaan dislipin dunia di Indonesia 2019. *Perkumpulan Endokrinologi Indonesia*, 1–65.
- Andrew L. Mammen MD, Ph. (2021). *Statin-Associated Myalgias and Muscle Injury—Recognizing and Managing Both While Still Lowering the Low Density Lipoprotein*. 105, 20892.
- Armed Forces Health Surveillance Division. (2025). Update: Exertional rhabdomyolysis among active component members of the U.S. Armed Forces, 2020–2024. *MSMR*, 32(6). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC12266732/>
- Bell, G., Thoma, A., Hargreaves, I. P., & Lightfoot, A. P. (2024). The role of mitochondria in statin-induced myopathy. *Drug Safety*, 47(7), 643–653. <https://doi.org/10.1007/s40264-024-01413-9> (PDF gratis: <https://researchonline.ljmu.ac.uk/id/eprint/22822/1/The%20role%20of%20mitochondria%20in%20statin%20induced%20myopathy.pdf>)

- Bosco, G., Di Giacomo Barbagallo, F., Spampinato, S., Lanzafame, L., Di Pino, A., Piro, S., Purrello, F., & Scicali, R. (2023). Management of statin intolerant patients in the era of novel lipid lowering therapies: A critical approach in clinical practice. *Journal of Clinical Medicine*, 12(6), 2444. <https://doi.org/10.3390/jcm12062444>
- Brian G. Collin, Dheeraj Raju, S. K. (2021). Statins, Enzyme CoQ10 Supplement Use, and Cognitive Functioning. *Statins, Enzyme CoQ10 Supplement Use, and Cognitive Functioning*, 35(5). <https://doi.org/10.1186/s42269-023-01160-4>
- Cooper-DeHoff, R. M., Niemi, M., Ramsey, L. B., Luzum, J. A., Tarkiainen, E. K., Straka, R. J., Gong, L., Tuteja, S., Wilke, R. A., Wadelius, M., Larson, E. A., Roden, D. M., Klein, T. E., Yee, S. W., Krauss, R. M., Turner, R. M., Palaniappan, L., Gaedigk, A., Giacomini, K. M., ... Voora, D. (2022). The Clinical Pharmacogenetics Implementation Consortium guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and statin-associated musculoskeletal symptoms. *Clinical Pharmacology & Therapeutics*, 111(5), 1007–1021. <https://doi.org/10.1002/cpt.2557> (teks lengkap: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9035072>)
- Cziraky, M. J., Willey, V. J., Mckenney, J. M., Kamat, S. A., Fisher, M. D., Guyton, J. R., Jacobson, T. A., & Davidson, M. H. (2013). Risk of hospitalized rhabdomyolysis associated with lipid-lowering drugs in a real-world clinical setting. *Journal of Clinical Lipidology*, 7(2), 102–108. <https://doi.org/10.1016/j.jacl.2012.06.006>
- Deka Purnama, Anggunan, T Mawar Nusri, R. K. (2023). HUBUNGAN ANTARA KADAR KOLESTEROL TOTAL DENGAN DERAJAT HIPERTENSI PADA PASIEN PRA LANSIA DI RSUD DR. H. ABDUL MOELOK PROVINSI. *Jurnalmalahayati*, 10(3), 1672–1680.
- Desrelia, R., Apriza, & Azzahri, L. M. (2020). Efektifitas Jus Buah Pepaya Terhadap Penurunan Kolesterol Pada Penderita Hiperkolesterol Di Puskesmas Kampar. *Farmaka*, 4, 11–20.
- Dicken, W., Mehta, A., Karagiannis, A., Jain, V., Vavuranakis, M., Sperling, L., & Cassimatis, D. (2022). Statin associated muscle symptoms: An update and review. In *Progress in Cardiovascular Diseases* (Vol. 75, pp. 40–48). <https://doi.org/10.1016/j.pcad.2022.11.010>
- Dodulik, [inisial], et al. (2025). Triple non-statin therapy with ezetimibe, inclisiran, and bempedoic acid in patients with genetically confirmed statin-induced rhabdomyolysis: A dual case report. *Pharmaceuticals*, 18(6), 818. <https://www.mdpi.com/1424-8247/18/6/818> (juga: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC12195781/>)
- Enger, C., Gately, R., Ming, E. E., Niemcryk, S. J., Williams, L., & McAfee, A. T. (2010). Pharmacoevidence safety study of fibrate and statin concomitant therapy. *American Journal of Cardiology*, 106(11), 1594–1601. <https://doi.org/10.1016/j.amjcard.2010.07.041>
- Ericsson, S., Eriksson, M., Vitols, S., Einarsson, K., Berglund, L., & Angelin, B. (1991). Influence of age on the metabolism of plasma low density lipoproteins in healthy males. *Journal of Clinical Investigation*, 87(2), 591–596. <https://doi.org/10.1172/JCI115034>
- Faergeman, O., Kastelein, J. J. P., Olsson, A. G., Lindahl, C., & Tsai, J. (2015). *Simvastatin for Secondary Prevention*. 294(19), 2437–2446.
- Feng, Z., Li, X., Tong, W. K., He, Q., Zhu, X., Xiang, X., & Tang, Z. (2022). Real-world safety of PCSK9 inhibitors: A pharmacovigilance study based on spontaneous reports in FAERS. *Frontiers in Pharmacology*, 13, Article 894685. <https://doi.org/10.3389/fphar.2022.894685>
- Giugliano, R. P., Wiviott, S. D., Blazing, M. A., De Ferrari, G. M., Park, J. G., Murphy, S. A., White, J. A., Tershakovec, A. M., Cannon, C. P., & Braunwald, E. (2017). Long-term safety and efficacy of achieving very low levels of low-density lipoprotein cholesterol: A prespecified analysis of the IMPROVE-IT trial. *JAMA Cardiology*, 2(5), 547–555. <https://doi.org/10.1001/jamacardio.2017.0083>
- Goss, G. D., Jonker, D. J., Laurie, S. A., Weberpals, J. I., Oza, A. M., Spaans, J. N., la Porte, C., & Dimitroulakos, J. (2016). A phase I study of high-dose rosuvastatin with standard dose erlotinib in patients with advanced solid malignancies. *Journal of Translational Medicine*, 14(1), 1–11. <https://doi.org/10.1186/s12967-016-0836-6>
- Handayani, F., Winarsih, W., & Abidah, A. (2023). Peningkatan Derajat Kesehatan Lansia Jamaah Masjid Al Furqon Melalui Screening Tekanan Darah, Gula Darah, Asam Urat dan Kolesterol. *Pengabdian Masyarakat Cendekia (PMC)*, 2, 19–22. <https://doi.org/10.55426/pmc.v1i2.236>
- Haynes, R., Jiang, L., Hopewell, J. C., Li, J., Chen, F., Parish, S., Landray, M. J., Collins, R., Armitage, J., Baigent, C., Chen, Z., Chen, Y., Pedersen, T., Bowman, L., Chen, F., Hill, M., Knott, C., Rahimi, K., Tobert, J., ... Peto, R. (2013). HPS2-THRIVE randomized placebo-controlled trial in 25 673 high-risk patient of ER niacin/laropirant: Trial design, pre-specified muscle and liver outcomes,

- and reasons for stopping study treatment. *European Heart Journal*, 34(17), 1279–1291. <https://doi.org/10.1093/eurheartj/eh055>
- Hornsby, W. G., & Brynar, R. W. (2013). Clinical exercise physiology. *Introduction to Exercise Science*, 212–234. <https://doi.org/10.2310/6640.2004.00014>
- Jiang, Y., Wang, Y., Ma, S., Qian, L., Jing, Y., Chen, X., & Yang, J. (2025). Efficacy and safety of PCSK9 inhibitors, potent statins, and their combinations for reducing low-density lipoprotein cholesterol in hyperlipidemia patients: A systematic network meta-analysis. *Frontiers in Cardiovascular Medicine*, 11, Article 1415668. <https://doi.org/10.3389/fcvm.2024.1415668> (juga: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11836037/>)
- Juwita, Makani, M., & J, P. D. C. (2023). Hubungan Tingkat Pengetahuan Terhadap Ketepatan Penggunaan Obat Simvastatin Pada Pasien Hiperkolesterolemia Di Posibindu Puskesmas Kumai Tahun 2023. 7(2).
- Kobuchi, S., Sugiyama, D., Iima, A., Obuchi, A., Osaka, A., Doi, A., Ueta, H., Yokoyama, S., Hosomi, K., Takada, M., & Sakaeda, T. (2025). Data mining of the FDA Adverse Event Reporting System and animal experiments for assessment of rhabdomyolysis risk associated with lipid-lowering drugs. *International Journal of Medical Sciences*, 22(7), 1485–1492. <https://doi.org/10.7150/ijms.109034> (teks lengkap: <https://www.medsci.org/v22p1485.htm>)
- Mahwal, I., Untari, E. K., & Nurmainah. (2022). Perbandingan statin terhadap kejadian efek samping terkait myalgia. *Jurnal Sains dan Kesehatan*, 4(2), 147–. <https://jsk.ff.unmul.ac.id/index.php/JSK/article/download/368/368/1160>
- Marsellinda, E., & Ferilda, S. (2022). Evaluasi Terapi Obat Dislipidemia Pada Pasien Diabetes Melitus Yang Mengalami Dislipidemia Yang Dirawat Di Rumah Sakit Islam Siti Rahmah. *Menara Ilmu*, 16(1), 15–20. <https://doi.org/10.31869/mi.v16i1.3406>
- Morris, R., Bu, K., Han, W., Wood, S., Hernandez Velez, P. M., Ward, J., Crescitelli, A., Martin, M., & Cheng, F. (2025). The association between statin drugs and rhabdomyolysis: An analysis of FDA Adverse Event Reporting System (FAERS) data and transcriptomic profiles. *Genes*, 16(3), 248. <https://doi.org/10.3390/genes16030248>
- Niedrig, D. F., Pyra, M., Lussmann, R., Serra, A., & Russmann, S. (2024). Rosuvastatin-induced rhabdomyolysis: Case report and call for proactive multifactorial risk assessment and preventive management of statin therapy in high-risk patients. *European Journal of Hospital Pharmacy*, 31(3), 281–284. <https://doi.org/10.1136/ejpharm-2023-003765>
- Permatasari, R., Suriani, E., & Kurniawan. (2022). Hubungan Kadar Kolesterol Total Dengan Tekanan Darah Pada Pasien Hipertensi pada Usia ≥ 40 Tahun. *Jurnal Labora Medika*, 6(2022), 16–21.
- Pose, E., Napoleone, L., Amin, A., Campion, D., Jimenez, C., Piano, S., Roux, O., Uschner, F. E., de Wit, K., Zaccherini, G., Alessandria, C., Angeli, P., Bernardi, M., Beuers, U., Caraceni, P., Durand, F., Mookerjee, R. P., Trebicka, J., Vargas, V., ... Ginès, P. (2020). Safety of two different doses of simvastatin plus rifaximin in decompensated cirrhosis (LIVERHOPE-SAFETY): a randomised, double-blind, placebo-controlled, phase 2 trial. *The Lancet Gastroenterology and Hepatology*, 5(1), 31–41. [https://doi.org/10.1016/S2468-1253\(19\)30320-6](https://doi.org/10.1016/S2468-1253(19)30320-6)
- Rahayu, A. S., Mendrofa, H. K., Bo, A., Kedokteran, P. S., Kedokteran, F., & Cenderawasih, U. (2018). Di Kampung Putali Distrik Ebungfauw Kabupaten Jayapura Hypercholesterolemia in Participants of Elderly Integrated Services
- Safitri, N., Alaina, M. F., Pitaloka, D. A. E., & Abdulah, R. (2021). A narrative review of statin-induced rhabdomyolysis: Molecular mechanism, risk factors, and management. *Drug, Healthcare and Patient Safety*, 13, 211–219. <https://doi.org/10.2147/DHPS.S333738> (teks lengkap: <https://pmc.ncbi.nlm.nih.gov/articles/PMC8593596>)
- Sridharan, K., & Sivaramakrishnan, G. (2026). Genetic determinants of statin-induced myopathy: A network meta-analysis of observational studies. *Current Reviews in Clinical and Experimental Pharmacology*, 21(1), 75–91. <https://doi.org/10.2174/0127724328356429250315163111>
- Turongkaravee, S., Jittikoon, J., Lukkunaprasit, T., Sangroongruangsri, S., Chaikledkaew, U., & Thakkestian, A. (2021). A systematic review and meta-analysis of genotype-based and individualized data analysis of SLCO1B1 gene and statin-induced myopathy. *The Pharmacogenomics Journal*, 21(3), 296–307. <https://doi.org/10.1038/s41397-021-00208-w>
- Xiao, Y., Ba, Z., Pang, S., Liu, D., Wang, H., Liang, H., Wang, Y., & Yuan, J. (2022). PCSK9 inhibitor: Safe alternative to fill the treatment gap in statin-limited conditions? *Reviews in Cardiovascular Medicine*, 23(11), Article 380. <https://doi.org/10.31083/j.rcm2311380> (akses terbuka: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11269069/>)