

Navigating the complex relationship between statins, GLP-1, and glycemic control

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Figure 1: Changes in total cholesterol (TC), LDL-C, HbA1c, and fasting insulin in statin (red) and control (blue) groups over the 16-week study. From She *et al.* 2024.¹¹

Statins are the most common and cost-effective drugs for treating and preventing cardiovascular disease, the leading cause of death worldwide. But in recent years, the ubiquity and frontline status of these medications has led to increasing scrutiny. Every so often, concerns over potential adverse effects pop up in research literature and popular press and fuel a growing skepticism about whether statins are really leading to net improvements in health and longevity—despite ample evidence of their positive effect on all-cause mortality.

While most of the alleged concerns are just distractions with little evidentiary basis, some may reflect more legitimate drawbacks to these medications. So after the recent publication of a study indicating that statins can have a detrimental effect on GLP-1 secretion and insulin sensitivity, an important question quickly followed: should individuals on statins be concerned about these apparent effects on metabolic health?

Statins: a breakthrough for cardiovascular health

By 1980, physicians had a basic understanding of the pathogenic mechanisms behind atherosclerotic cardiovascular disease (ASCVD), which is defined by the presence of cholesterol in artery walls. This cholesterol is trafficked through circulation in lipoproteins—spherical particles with a hydrophobic core and a hydrophilic shell that are formed from lipids and proteins. While various classes of lipoproteins exist, only those containing the protein apoB (apolipoprotein B) are capable of entering artery walls and depositing cholesterol loads. The vast majority (~95%) of apoB-containing lipoproteins fall into the class of low-density lipoproteins, or LDLs, and thus, the more LDLs are present in circulation, the greater the rate at which cholesterol builds up in arteries. Over decades, this process gradually leads to the development of atherosclerotic plaques, which can cause artery blockages by narrowing the artery lumen or by rupturing and triggering clot formation. While additional details regarding the role of inflammation in this process had yet to be elucidated, for the most part, this core mechanism for ASCVD development was fairly clear by the Reagan administration.

But although we *knew* that high LDL drove atherosclerosis, there was unfortunately very little we could do to *intervene*. In the early '80s, the primary pharmacological option for lowering LDL cholesterol (LDL-C) was a class of medications known as bile acid sequestrants, which increase excretion of bile acids involved in the digestion of fats. Because bile acids are synthesized from cholesterol, greater depletion of bile acids through excretion prompts the liver to use up more cholesterol to replace them, and thus to take up more cholesterol (via LDL particles) from circulation. Indeed, these medications had demonstrated the ability to lower

LDL-C by around 10-20% from baseline—a modest but significant effect—but they came with severe gastrointestinal side effects that many found intolerable, in addition to interfering with the absorption and efficacy of other orally administered medications.^{1,2}

This was the backdrop against which statins emerged on the scene. These medications inhibit cholesterol synthesis in the liver and other tissues, which then stimulates the liver to increase uptake of LDL particles from circulation by enhancing expression of the LDL receptor (LDL-R). This proved to be a highly effective strategy for LDL reduction—trials with lovastatin, which in 1987 became the first statin to gain FDA approval, showed that the treatment was well-tolerated and lowered LDL-C by 25-40%, far exceeding the efficacy of bile acid sequestrants.^{3,4} In the decades that followed, other statin drugs were developed and approved, and dozens of clinical trials have proven that the LDL reductions elicited by this class of medication translates to significant reductions in risk of major adverse cardiovascular events such as heart attacks and strokes.⁵⁻⁷ (For further details on a handful of these trials, refer to our 2023 [premium article](#) on statin efficacy.) Indeed, few medications have ever been backed by such extensive, robust, and highly consistent supportive evidence. Thus, statins quickly became the standard therapy for ASCVD treatment and prevention, and seven statins are currently approved for this purpose: atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin.

Yet ironically, in an age in which shocking and contrarian views tend to attract more attention than tried and true knowledge, the very fact that statin use is so well-supported and ubiquitous has contributed to these drugs becoming a target for criticism and conspiracy theories. It's certainly true that statins have their share of side effects, including muscle pain and mild to moderate gastrointestinal distress, which occur in a minority of patients (around a 7% increase in muscle pain relative to placebo, or an absolute additional rate of 11 events per 1000 person-years, while GI distress affects around 2% of patients).^{8,9} Additionally, between 1-3% of patients on statins experience elevations in liver enzymes (ALT and AST), though this effect is usually regarded as mild and not of sufficient concern to cease medication.¹⁰

However, most of the more recent skepticism has revolved instead around the more fundamental question of whether statins truly have a net positive impact on health and longevity. Some of these arguments are based on the faulty notion that statins are ineffective in reducing ASCVD risk (again, our previous [article](#) examines this myth in depth), but others point to potential *negative* effects of statins—in particular, the possibility that they compromise metabolic health. Indeed, the use of statins has been known to slightly increase risk of type 2 diabetes, and recently, these concerns have intensified with the viral spread of a 2024 study published in *Cell Metabolism* linking statins to reductions in glycemic control on a *mechanistic* level. What can we make of this research, and how does it fit in the larger context of the risks and benefits of statin use?

About the study

As a first step, the investigators behind the 2024 study conducted a human trial involving 40 patients with diagnosed dyslipidemia or atherosclerosis.¹¹ These individuals fell into two groups: 1) the statin group, comprising 30 patients chose to take 20 mg/day of atorvastatin

(brand name Lipitor), and 2) the control group, comprising 10 control subjects who matched the statin group in baseline LDL-C and were offered statin treatment but refused. As expected, LDL-C levels in the statin group decreased significantly relative to the control group over the course of the 16-week study, from 3.41 mmol/L (132±0.94 mg/dL) at baseline down to 2.30±0.67 mmol/L (89 mg/dL) at week 16. Control participants, by contrast, experienced a non-significant reduction in LDL-C between baseline (3.28±0.84 mmol/L, or 127 mg/dL) and week 16 (2.98±0.65 mmol/L, or 115 mg/dL).

However, beyond the expected drop in LDL-C, researchers She *et al.* reported that patients on statins also experienced *other* metabolic shifts. After just four weeks, significant changes appeared in blood sugar metrics such as glycated hemoglobin (HbA1c) and fasting insulin (**Figure 1**). By the end of the study, mean HbA1c had risen from approximately 5.8% (slightly elevated above the “normal” cutoff of less than 5.7%) to 6.1%, indicating rising average blood glucose. Additionally, mean fasting insulin increased from 10 µU/mL (again, slightly elevated) to 13 µU/mL. Together, these results point to a clear drift toward higher insulin resistance with statin use, a trend that did *not* appear in the control group.

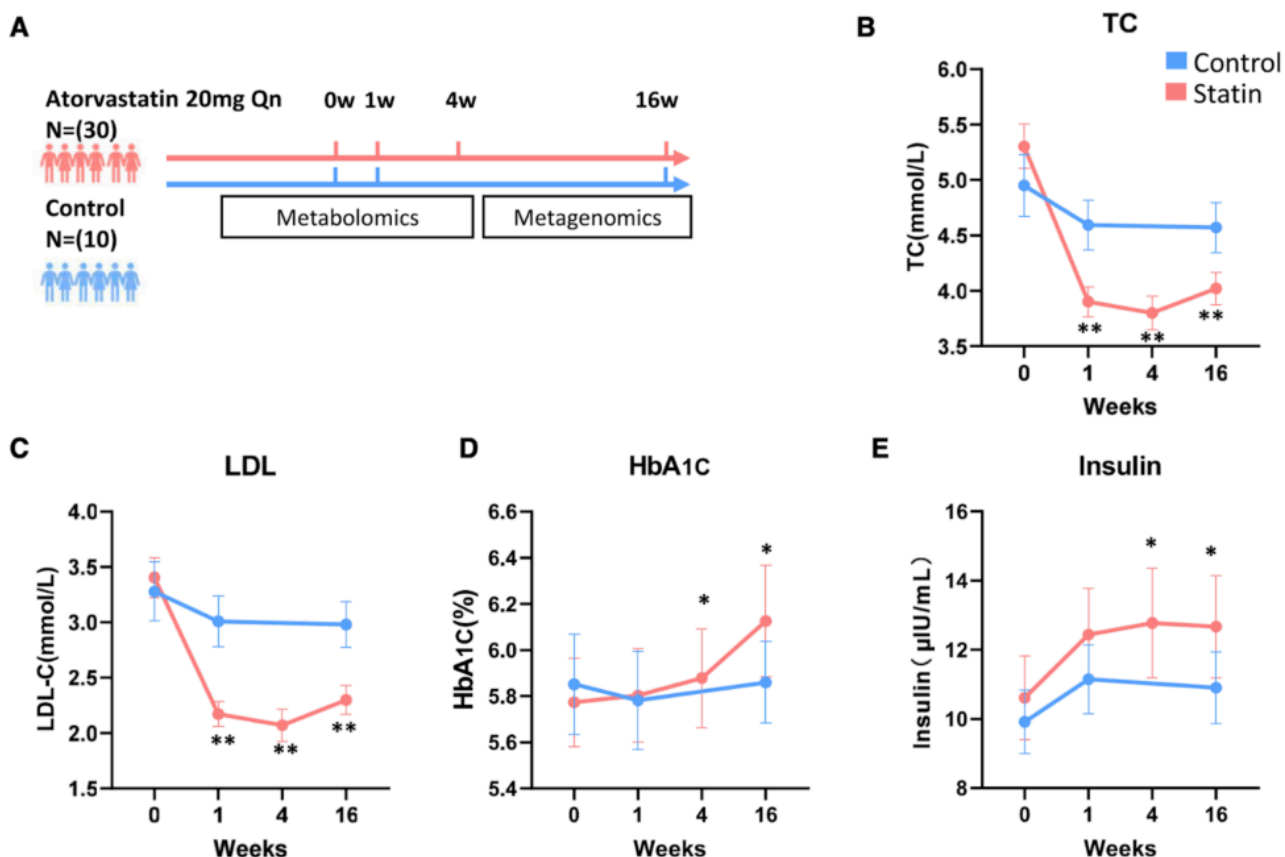


Figure 1: Changes in total cholesterol (TC), LDL-C, HbA1c, and fasting insulin in statin (red) and control (blue) groups over the 16-week study. From She *et al.* 2024.¹¹

How do statins raise HbA1c?

The researchers then sought to understand *why* these metabolic changes were occurring by performing a series of mechanistic experiments. Indeed, this part of the study provided the most novel results and has drawn most of the recent attention from health influencers and statin skeptics.

She *et al.* began by measuring GLP-1 among study participants over the course of the trial. This hormone, which has become a household name thanks to drugs like Ozempic and Mounjuro, is of interest in this context because it plays a key role in stimulating insulin secretion and improving insulin sensitivity. The investigators found that active GLP-1 levels in serum fell by approximately 50% in the statin group: from 5 picomolar down to about 2.5 picomolar. These results represented another deviation from the control group, which showed no significant reduction in GLP-1, and thus, the authors hypothesized that this drop in GLP-1 might explain the worsening glycemic control on statins.

But how exactly was atorvastatin causing a drop in GLP-1? GLP-1 is produced by enteroendocrine L-cells in the intestine, which can be stimulated by various signals including certain bile acids. Though bile acids are synthesized in the liver, they are subject to conversion and modification by bacteria in the gastrointestinal tract, such that overall bile acid composition is dictated in part by the gut microbiome. Thus, the researchers turned their attention to the gut microbiome as a possible pathway of interest, as orally administered statins may interact with GI bacteria.

Indeed, they found that those in the statin group had decreases in *Clostridium* species of bacteria that normally convert one bile acid, CDCA (chenodeoxycholic acid), into another, UDCA (ursodeoxycholic acid). The researchers now had a potential mechanistic pathway: statin therapy was altering gut microbial composition, causing a reduction in conversion of CDCA to UDCA, and this bile acid disruption appeared to be associated with decreased GLP-1 secretion and increased insulin resistance. As further evidence, She *et al.* reported an inverse correlation between *Clostridium* species and blood glucose, indicating that fewer *Clostridium* bacteria corresponded to poorer glycemic control.

This mechanistic framework suggested an intervention target. If UDCA *depletion* was contributing to the negative metabolic effects, could UDCA *supplementation* reverse them? To test this hypothesis, the authors conducted a pilot study in five statin users whose HbA1c had drifted above 6.0%, administering 500 mg of UDCA daily for two months. The preliminary results were promising. Median HbA1c decreased from an average of ~6.8% to 6.4%, and median GLP-1 levels rose from ~2 to 4 picomolar—all while maintaining the LDL-lowering efficacy of the statin.

In aggregate, the findings from this study suggest that statins may modestly increase insulin resistance through a pathway involving gut microbiome alterations, bile acid dysregulation, and impaired GLP-1 signaling—a detailed mechanistic hypothesis generated from a relatively small study. But do these results mean that we should stop prescribing statins for fear of altered gut microbiome and diabetes risk? Or that everyone on statins should be taking UDCA supplements?

A critical lens

To answer these questions, we can start by evaluating this study and its results in isolation before assessing how they fit within the broader research literature. This study reported a 0.3% increase in HbA1c over just 16 weeks, and this is indeed a significant effect. However, several

factors suggest this number doesn't reflect the *true* risk of atorvastatin.

First, this wasn't a randomized, let alone blinded, study. Everyone was offered a statin, and those who accepted became the intervention group while those who declined became the controls. Who's more likely to refuse a statin even when their lipid levels suggest they need one? Probably people who are healthier overall, and indeed, this is exactly what we see in the baseline characteristics. In the statin group, one-third were smokers, one in five were drinkers, half had hypertension, and one in five already had diabetes. In the control group, *all of those numbers were zero*.

Further, the data indicate that the effects of statins on glycemic control are not uniform across the population. The statin group showed much higher variability in HbA1c at the final timepoint than the control group, suggesting that particular individuals—such as those at higher baseline risk for diabetes due to other factors, like hypertension or high BMI—may be more susceptible than others to the HbA1c elevation on these medications. Specifically, the statin group had a standard error over twice as large as the control group: $\pm 1.26\%$ for HbA1c at 16 weeks compared with $\pm 0.56\%$ in controls. This tells us the response wasn't consistent—some patients likely saw no change in HbA1c, while a smaller subset drove the average (and the variability) upward.

Taken together, these results look less like a reliable 0.3% HbA1c effect of atorvastatin in everyone, and more like what you'd expect when higher-risk patients are treated and a few of them worsen over time.

Still, as we noted earlier, She *et al.* were neither the first nor the only investigators to report detrimental effects of statins on glycemic control. The fact that statins—especially at higher intensities—can modestly increase risk of insulin resistance had already been well documented,¹² particularly in people who carry metabolic risk factors like those seen in the statin group: hypertension, elevated fasting glucose, and higher BMI (though BMI was similar in the two groups in this study).¹³

What we *hadn't* known prior to She *et al.*'s study was the role that GLP-1 and the microbiome might play in mediating this effect on glycemic control. As we noted earlier, these results have become a particular area of focus for statin naysayers on social media, and they've helped fuel the viral spread of this study due to the widespread familiarity with GLP-1 and its association with weight loss medications (more on this in a moment). But how much faith can we have in the mechanism proposed by this study? And what does it really imply for those taking statins?

Is GLP-1 really driving this effect?

She *et al.* presented a fairly tidy mechanism for HbA1c elevation: statins decrease *Clostridium* bacteria, which convert the bile acid CDCA to the bile acid UDCA. Without less UDCA, intestinal L-cells secrete less GLP-1, and the reduction in GLP-1 causes decreases in insulin sensitivity. But how strong was their evidence for this chain of events?

The investigators attempted to bolster their case by testing the mechanism in mice. They treated mice with atorvastatin or placebo and observed significant deficits in glucose tolerance in the statin-treated animals only, along with reduced *Clostridium* bacteria and a moderate decrease in GLP-1 levels. The authors reported that colonizing these animals with *Clostridium* bacteria or treating them with UDCA reversed these metabolic derangements, though in actuality, this “reversal” was far from complete. While these interventions improved GLP-1 levels, insulin sensitivity barely improved at all, and it certainly didn’t come anywhere close to levels seen in animals without statin treatment. (Unfortunately we cannot make precise statistical comparisons, as the researchers failed to include a no-statin control in the UDCA or *Clostridium* replenishment experiments). In other words, what these experiments really show is that statins reduce *Clostridium* bacteria, and that these bacteria can, via UDCA, stimulate GLP-1 release (which we’d already known). What they **do not** show is that any of that has anything to do with changes in blood glucose or insulin sensitivity on statins. If anything, the results show just the opposite—these manipulations are ineffective in reversing statin-associated insulin resistance.

Even the test of UDCA supplementation in five human subjects cannot be interpreted as proof of She *et al.*’s mechanism. The authors provide no data on how HbA1c levels changed in these particular patients with the initiation of statins—we only know their HbA1c before and after UDCA treatment. They also did not include a control group for comparison to UDCA, so we can’t rule out the possibility of a placebo effect or behavioral changes that might underlie the effect. Therefore, we have no idea whether UDCA truly offset any impact of statins on glycemic control (and if so, to what extent), so between these experiments and those in mice, we can, at best, only conclude that the mechanism proposed by this study represents a fairly minor pathway by which statins affect metabolic health.

Perhaps at this point you are asking yourself how it could be possible that a significant change in GLP-1 *wouldn’t* have a major impact on insulin sensitivity. After all, GLP-1 receptor agonist medications like Ozempic are highly effective in treating diabetes by replicating the natural actions of GLP-1. But the apparent paradox is resolved when we look more closely at the size of the GLP-1 changes observed in this study. While a 50% *relative* drop in GLP-1 may sound dramatic, the *absolute* magnitude of this change is quite small—from 5 picomolar down to 2.5 picomolar. To put this in perspective, a single meal can raise GLP-1 levels up to around 50 picomolar. So while the relative decrease is notable and may contribute slightly to HbA1c effects, it is unlikely to be a primary driver, and a number of other mechanisms are thought to be at play.¹⁴

This miniscule absolute change in GLP-1 should also allay any concerns over statins and weight gain. As mentioned earlier, GLP-1 has become famous for its association with GLP-1 receptor agonist medications, which have shown remarkable efficacy in promoting weight loss by mimicking the effects of GLP-1 itself. But clinical trials to date do not indicate that statins have the inverse effect of causing increases in fat mass or body weight due to a *reduction* in GLP-1.¹⁵ (However, weight gain has been reported with statins among patients who experience significant muscle pain on these drugs and, as a result, reduce their physical activity level.¹⁶)

How do we balance statin risks and benefits?

Regardless of the mechanism (or more likely, mechanisms) involved, we know that statins can raise blood glucose levels and reduce insulin sensitivity in some individuals. So despite the limitations of She *et al.*'s study itself, we are nevertheless left with the same questions: should individuals on statins be concerned about negative effects on metabolic health, and how do those risks balance against the cardiovascular benefits of these medications?

HbA1c increases on statins aren't universal

To start, we must reiterate that metabolic responses to statins are not uniform. Some patients experience increases in HbA1c, while others see no effect or even the *opposite* effect. Thus, the possibility of an increase in HbA1c may be a reason to *stop* a statin, but it isn't a reason not to *start* a statin. You won't know how you as an individual will respond until you start the medication and monitor changes in metabolic metrics.

We do know that those who are in poorer metabolic health at baseline tend to be at higher risk of incident diabetes after starting a statin than those who are metabolically healthier,¹⁴ but it's important to understand that this doesn't necessarily mean that these individuals are more likely to experience increases in HbA1c or are experiencing *greater* increases in HbA1c. Instead, the higher rate of new-onset diabetes with statins among those with other risk factors (e.g., high BMI, hypertension, higher baseline HbA1c) is probably due to the fact they are closer to the threshold for diabetes in the first place, such that any incremental decrement in metabolic health might be enough to meet diagnostic criteria. Some studies have indicated that those in *better* metabolic health at baseline are more likely to experience increases in HbA1c,^{17,18} though results have not been consistent. Indeed, the unpredictability of metabolic effects of statins underscores the need for careful monitoring across all patients, regardless of metabolic health.

A population-level perspective

Of course, to estimate individual risk, it's helpful to understand how common adverse metabolic effects occur with statins across the population, and from there, we can weigh that risk against cardiovascular benefits. To do this, we can evaluate population-level data on the incidence of new-onset diabetes with statin use versus reductions in risk for cardiovascular events such as heart attacks or strokes.

For instance, a large meta-analysis of randomized statin trials comprising over 91,000 individuals showed that statin treatment increased relative risk for new-onset diabetes by 9%, or approximately one case per 1000 patients per year of medication use. However, the same analysis reported that statin treatment also *prevented* 5.4 first-time coronary events per 1000 patients per year.¹⁹ (The total number of prevented coronary events would likely be significantly higher, as the analysis did not count *recurrent* events.) This study, which has been corroborated by a number of other analyses,^{20,21} therefore demonstrates a significant asymmetry between diabetes risk and cardiovascular benefits with statins, with the latter far outweighing the former.

This asymmetry is reflected in data on statin use and all-cause mortality (ACM). Several of the clinical trials investigating statin efficacy have monitored ACM and have shown that statins are effective not only in reducing cardiovascular events over the follow-up period but in lowering *overall* mortality as well.^{22–25} These trials were generally conducted in patients at high baseline cardiovascular risk, so we might assume that reductions in cardiovascular events likely played an outsized role in determining overall mortality rates, but a 2022 meta-analysis reported that reductions in ACM with statin use persist even in randomized trials for conditions other than ASCVD, such as kidney disease, cancer, and inflammatory diseases.²⁶ Specifically, this analysis shows statins reduce the risk of mortality from any cause by 28%, with no significant differences in risk reduction between trials on cardiovascular disease and trials for other health conditions.

Together, these data point to a clear imbalance between small risks for metabolic health and large benefits for cardiovascular health. In other words, statins save lives, *even accounting for the increased risk of type 2 diabetes*.

Our clinical approach

By now, we have demonstrated that impairments in glycemic control are certainly not a universal response to statins and that, on a population scale, any excess risk for insulin resistance is more than offset by decreased risk of cardiovascular events. Still, it's undeniable that some patients *do* experience increases in HbA1c when starting these drugs, potentially to a level that meets the threshold for diabetes or prediabetes. For those individuals, this change absolutely warrants concern, regardless of population trends—but it *doesn't* necessarily mean that statins need to be avoided altogether.

Not all statins are equal

Throughout this piece, we've largely been referring to all statin medications collectively, but recall that this is not a homogenous group. The seven statins currently on the market vary in chemical structure, potency, half-life, and effects on glycemic control. This means that a patient who experiences an elevation in HbA1c on one statin might see a reversal of this effect simply by changing to another.

Although we have very limited data from clinical trials making direct, head-to-head comparisons of different statins and diabetes incidence, we can still make out certain trends by turning to observational studies, mechanistic experiments, and meta-analyses of trials comparing individual statins against placebo. Across these sources, atorvastatin, rosuvastatin, and, to a slightly lesser extent, simvastatin are frequently reported to be associated with a higher likelihood of insulin resistance and new-onset diabetes than others at comparable doses.^{27,28} Pravastatin and pitavastatin, by contrast, are considered the least diabetogenic, with some evidence indicating that these statins significantly *decrease* diabetes risk relative to placebo.^{29,30}

Dose matters

Beyond the type of statin, the *dose* of statin also has a substantial impact on the risk for insulin resistance and other side effects, such as muscle pain and GI distress. In our practice, we always try to get patients on the lowest dose possible, as this approach significantly reduces risk *without* a commensurate compromise on efficacy. Increases in HbA1c are much more likely with *high* statin doses and are rarely observed with low or mid-range doses, but most of the benefits for cardiovascular health can be achieved at relatively *low* doses.

The reason for this is that, in terms of LDL-C reduction, statins exhibit a non-linear, *logarithmic* dose-response relationship, in which the difference in LDL-C reduction per dose increment is largest at the *lower* end of dose ranges (**Figure 2**). In other words, you get the most benefit from the lowest dose of a statin, with each doubling of dose generally showing only an additional 6% reduction in LDL-C. For example, if atorvastatin at 10 mg reduced LDL-C by 35%, then doubling to 20 mg would lower it by 41%, and doubling that to 40 mg would lower it by 47%. This diminishing return underscores the value of starting low, and indeed, our view is that no one should ever be on more than a 50% maximal dose of a statin.

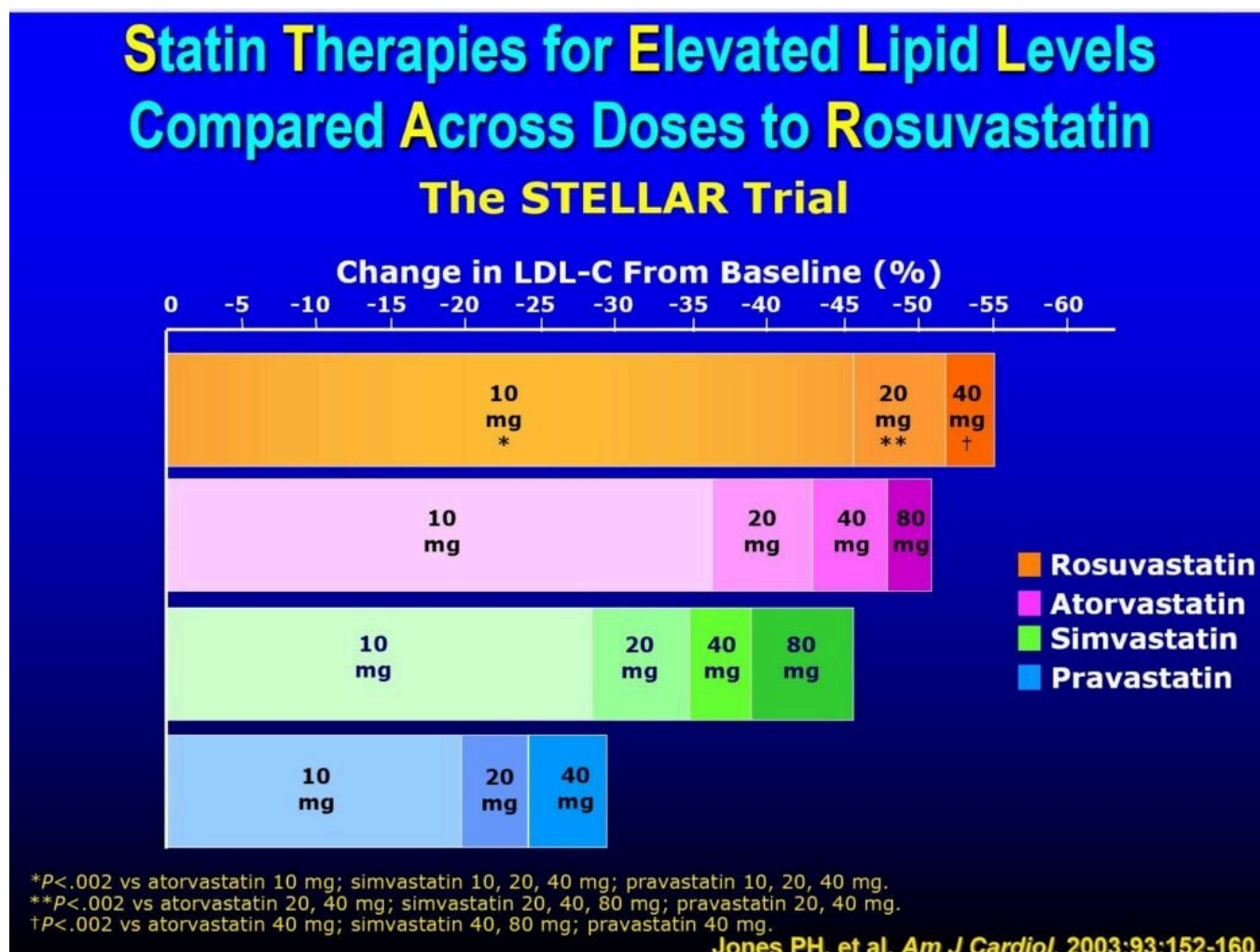


Figure 2: Reduction in LDL-C by dose of different statins. From the STELLAR trial.³¹

Supplementing with statin alternatives

Not all patients reach target LDL-C ranges on lower-dose statins, but even in such cases, we can avoid high statin doses thanks to the existence of *other* classes of lipid-lowering medications, including ezetimibe and PCSK9 inhibitors. These drugs are typically used in combination with statins to achieve additive reductions in LDL-C, and analyses have shown that this combined approach results in significantly greater LDL-C lowering than is seen with simple upward titration of dosage on statin monotherapy.³²

Ezetimibe and PCSK9 inhibitors may also be used alone and in place of statins, though this is mostly reserved for certain instances where statins are poorly tolerated or contraindicated. One reason for this is cost. PCSK9 inhibitors (i.e., evolocumab, alirocumab, and inclisiran) are capable of achieving LDL-C reduction on par with or even exceeding that of statins,^{33,34} but they are also significantly more expensive. Typical costs are around \$6000–8000 annually, whereas generic statins often fall below \$100 for a year's worth of treatment. Ezetimibe can have similar affordability as statins, but it produces significantly smaller LDL-C reductions as a stand-alone therapy than either statins or PCSK9 inhibitors.^{34,35}

Thus, statins remain our first-line therapy because they are the most cost-effective: they achieve profound LDL-C reduction at a low price. When further reduction is needed, we have the option to *moderately* increase statin dose and/or bring in additional medication classes if costs are not prohibitive. Between these options, we can almost always reach target LDL-C and apoB ranges while maintaining low risk for insulin resistance.

In the rare cases in which we *have* seen modest elevations in HbA1c in patients after starting a statin, we have typically responded by decreasing the dose and adding another lipid-lowering therapy or by switching to statin alternatives altogether, especially for patients experiencing other intolerable side effects like muscle pain. Patients in our practice are less cost-sensitive, which allows us to make these large, quick pivots. However, for those whose lipids are well managed with statins but who experience mild increases in HbA1c, drastic changes in lipid-lowering medications aren't the only way to offset or reverse this side effect. Modifications to diet and exercise can be effective in improving insulin sensitivity, and if needed, impaired glycemic control can also be managed through pharmacologic interventions such as metformin and GLP-1 receptor agonists.

The overarching point here is that we have options for reducing risk of insulin resistance and for addressing insulin resistance should it arise. These options, in turn, mean that preventing cardiovascular disease through apoB reduction doesn't need to come at the expense of compromising metabolic health.

Real medical practice doesn't exist in the same sort of vacuum as an isolated research study like She *et al.* Many variables are at play—including the magnitude of risk, factors that modulate risk, and how that risk weighs against benefits. And just as we would never shy away from communicating the potential downsides of statins (or any other medications) with patients, we are also careful to put these downsides into that broader context, such that patients and their providers can make decisions based on the full picture, rather than a solitary detail.

What we cantake away from this study

This study by She *et al.* confirms something we've known for years—that statins can, in a minority of patients, increase the risk of insulin resistance and diabetes. The novelty was in the investigations into possible mechanisms behind this effect, as the authors propose a previously unidentified role for the microbiome, bile acid signaling, and GLP-1. These experiments are genuinely interesting, and though the proposed mechanism is unlikely to be the sole or even primary pathway linking statins to increases in HbA1c, they may open the door to future co-therapies that might allow us to obtain the full cardiovascular benefit while minimizing or eliminating the small penalty to glycemic control seen in certain patients.

According to the study results, UDCA supplementation might be one such option for ameliorating insulin resistance without compromising LDL reduction, though it was tested in only five patients and without a control group. UDCA is FDA-approved and commonly prescribed in liver and gallbladder disease, with side effects usually being minor, such as diarrhea and itchy skin.³⁶ However, it has not been thoroughly investigated for the potential new indication discussed here, so this deserves investigation in larger, randomized trials before we start prescribing UDCA to patients on statins.

The bottom line

Few concepts in medicine are so deeply grounded in highly consistent research as the idea that statins are remarkably effective in treating and preventing atherosclerotic cardiovascular disease—and even reducing risk of all-cause mortality in certain populations. Like any medication, statins carry side effects for some [small] percentage of individuals who take them, but these side effects—including possible elevation in HbA1c—have likewise been rigorously characterized and analyzed by many independent groups, and they have been found to pale in comparison to the far greater benefits to cardiovascular health for most individuals.

It is easy to forget this context when we see highlights from a single study flash across our social media feed. Indeed, evidence that appears to upend long-established beliefs can appeal to our innate human interest in the new and unexpected, and this interest can drive the viral spread of such isolated contrarian perspectives. But while it may be true that scientific knowledge is ever-evolving and subject to revision with new evidence, keeping in mind the *existing* body of evidence is critical to evaluating how the new findings fit within our overall understanding of health and clinical decision-making. The more firmly validated the existing belief, the higher the bar for overthrowing it, and in the case of statins, the burden of proof required to frame them as “net harmful” is practically in the stratosphere. As we've seen, the study by She *et al.* doesn't come close to hitting that bar.

However, it does remind us that decisions about health are rarely black and white. Interventions can impact different individuals in different ways, and they often have tradeoffs that must be balanced against benefits in a patient-specific manner. With statins, we have many options for mitigating the downsides without compromising the upsides, and the balance

clearly tips in favor of benefit in the vast majority of cases. With dose modulation, alternative medications, and other strategies, the apparent need to choose between cardiovascular and metabolic health is nothing more than an illusion. We can—and should—pursue both..

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