

INTRODUCTION

- Hypercholesterolemia is a cardiovascular condition that is characterized by high blood levels of low-density lipoprotein cholesterol (LDL-C)^{1,2}
- Atherosclerotic cardiovascular disease (ASCVD) is a consequence of persistently high LDL-C, and is common in the US population, and especially in adults >60 years^{1,2}
- ASCVD risk factors include, hypercholesterolemia, metabolic syndrome, chronic kidney disease, and inflammatory conditions, along with certain races/ethnicities³
- Statins are recommended as first-line treatment for patients failing to control LDL-C, both in a primary prevention setting and secondary prevention setting^{1,2,4}
- Many patients struggle to reach LDL-C goals despite use of statins, and this residual cardiovascular risk potentially leads to poorer clinical and economic outcomes
- No comprehensive study of the extent of LDL-C goal attainment in the statin-treated US population with hypercholesterolemia has been conducted
- In particular, stratification of LDL-C goal attainment by primary and secondary prevention settings is an important evidence gap
- Finally, the clinical impact of LDL-C goal attainment among statin-treated patients with hypercholesterolemia has not been established with large-scale real-world US data

OBJECTIVES

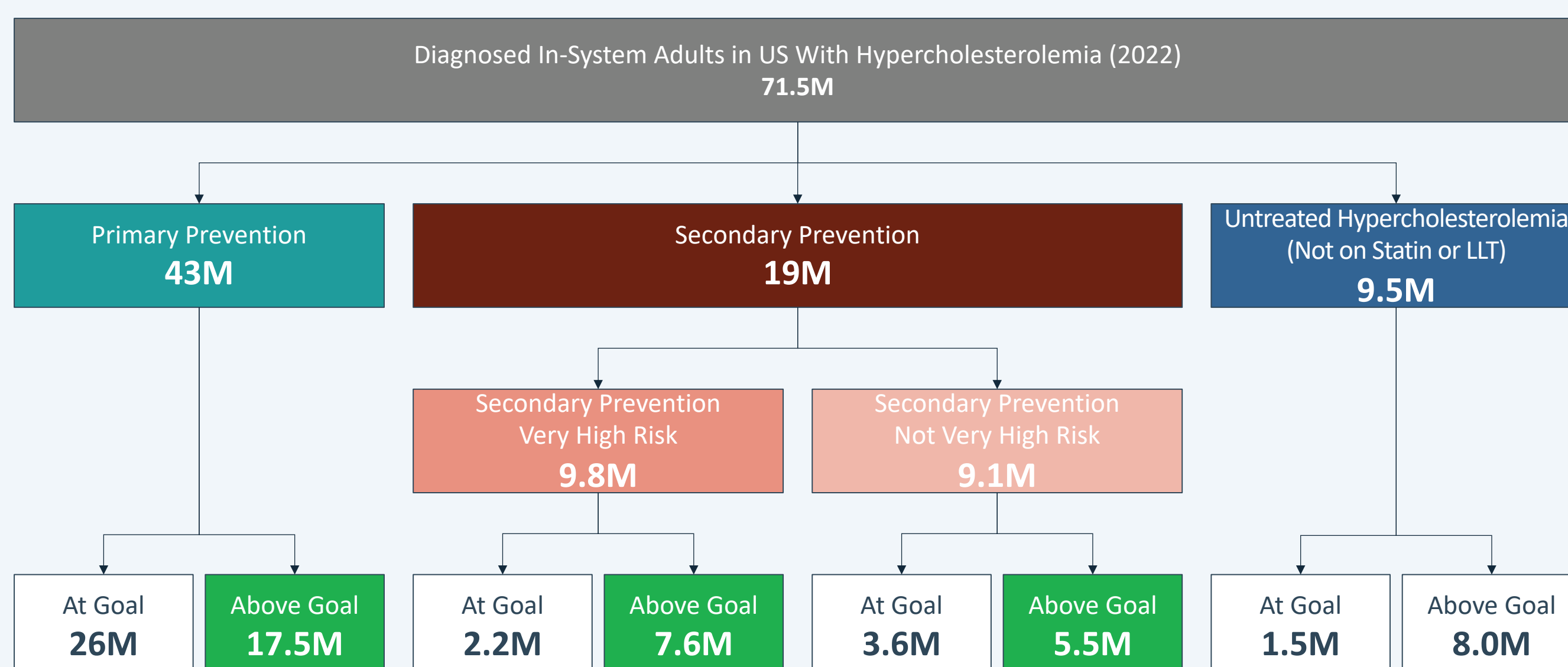
- The study objectives were to estimate the extent of LDL-C goal attainment in a representative US population, along with unmet clinical needs as a function of LDL-C goal attainment

METHODS

- This retrospective cohort study leveraged 2017-2021 Merative MarketScan claims linked to laboratory data
- Two high-level cohorts were evaluated—patients aged 18 years or older in primary and secondary prevention settings with continuous enrollment during a 1-year washout period and 2 years of follow-up:
 - Primary Prevention: patients taking statins identified from January 1, 2018, through December 31, 2019
 - Secondary Prevention: patients taking statins and had at least 1 inpatient or 2 outpatient claims of ASCVD (at least 30 days apart) from January 1, 2018, through December 31, 2019
 - Two subsegments of the secondary prevention cohort were also evaluated—not very high-risk and very high-risk patients (evidence of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions)
- The data were evaluated for:
 - Prevalence of diagnosed hypercholesterolemia in the US and treated with statins in primary and secondary prevention settings, along with the proportion of these patients who met their risk-based LDL-C goals
 - Clinical implications of failure to attain LDL-C goals
 - Healthcare resource and direct healthcare costs among statin-treated patients

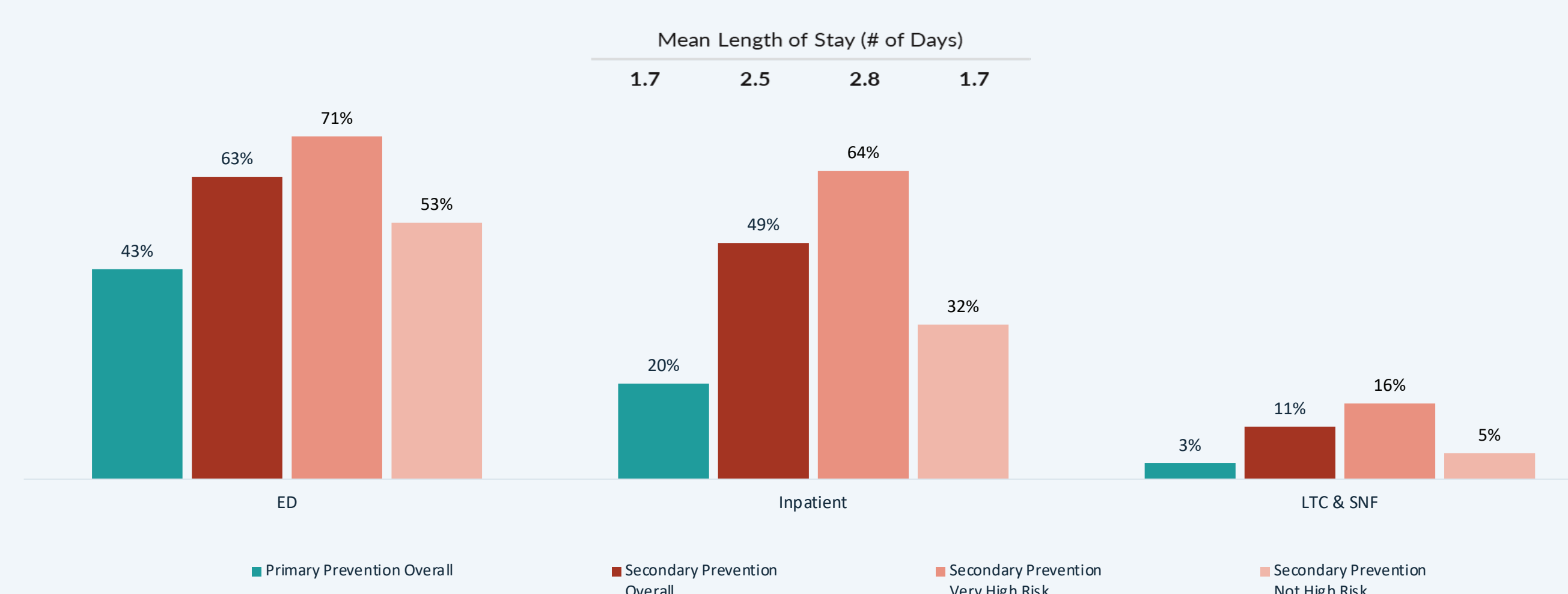
RESULTS

Figure 1 | Estimated US Prevalence of Hypercholesterolemia, Statin Treatment, and LDL-C Goal Attainment



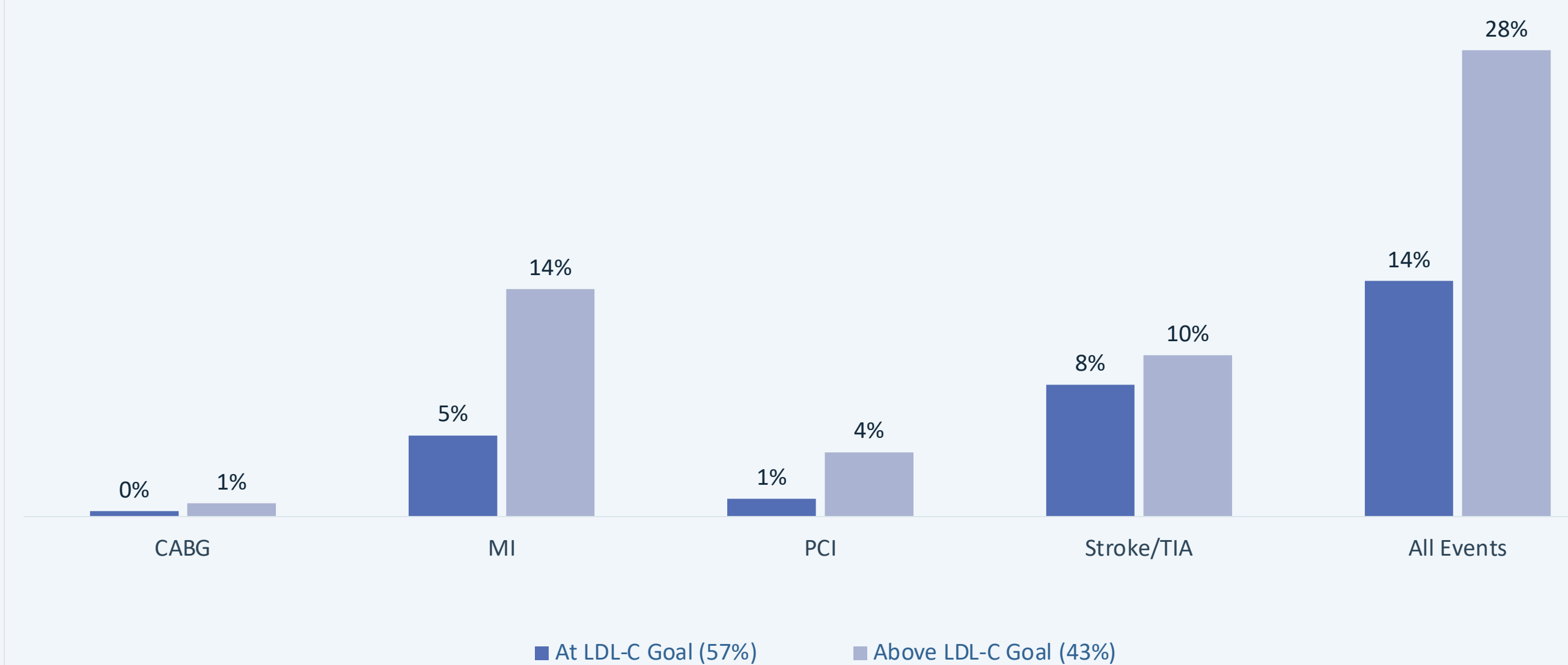
- ~72 million US patients with hypercholesterolemia were identified, with 62 million treated with statins (43 million in the primary prevention setting vs 19 million in secondary prevention)
 - Over half of patients in secondary prevention were characterized as very high risk
- In primary prevention, 17.5 million patients (~40%) were above goal and 13.1 million (~70%) were above goal in secondary prevention
 - Secondary prevention very high risk was comprised of 7.6 million patients (~78%) above goal; secondary prevention not at very high risk—5.5 million (~60%) above goal

Figure 3 | Percentage of Patients Utilizing High-Cost Healthcare Services



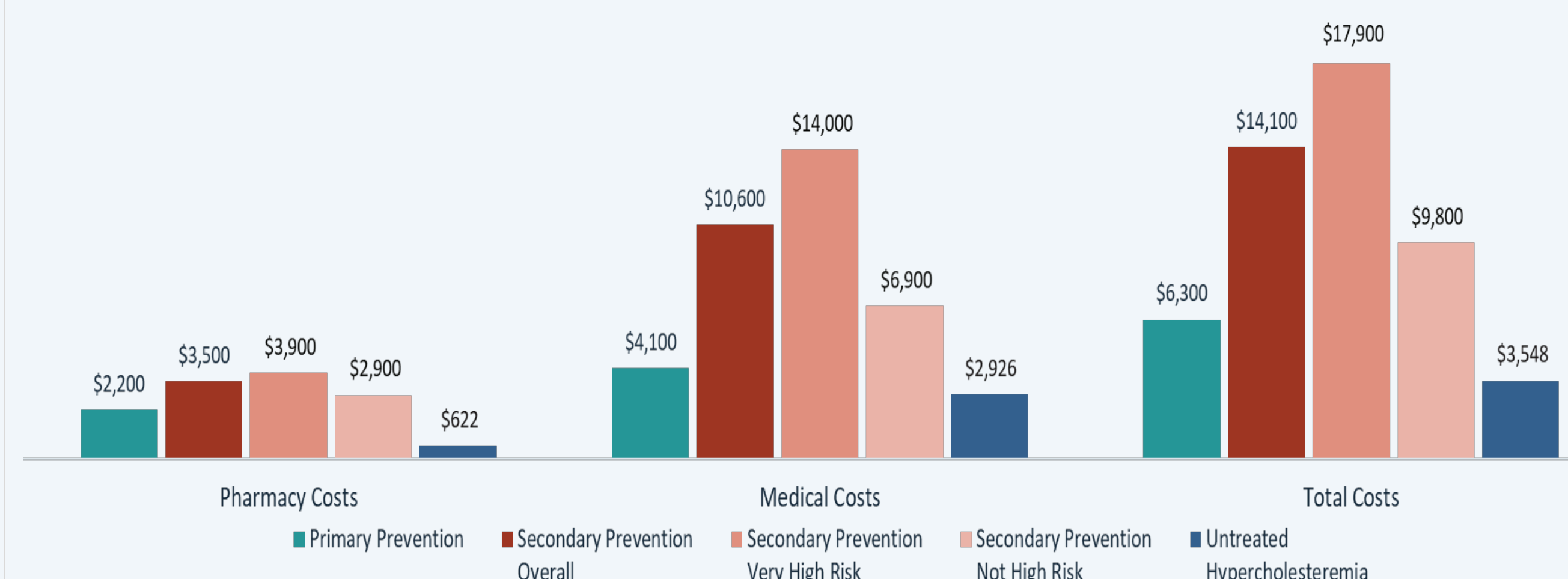
- % of statin-treated patients visiting high-cost care settings increases as patients progress from primary to secondary prevention, and again from not very high risk to very high risk among patients in secondary prevention
 - % of annual secondary prevention patients with visits to the emergency department was over 45% higher than patients in primary prevention (63% vs 43%); 150% more patients with inpatient visits (49% vs 20%); and 267% more patients utilizing long-term care (11% vs 3%)
 - The % of very high-risk patients in secondary prevention was also considerably higher than those not at very high risk
 - The % of high-risk patients visiting the emergency department, inpatient ward, and long-term care was 34% (71% vs 53%), 100% (64% vs 32%), and 220% (16% vs 5%) higher than patients not at very high risk, respectively

Figure 2 | Percent of Patients Who Experienced Select Cardiac Events According to LDL-C Goal Attainment



- Clinical outcomes among US statin-treated patients with hypercholesterolemia are highly dependent on achieving their LDL-C goals
- Patients at goal were less likely to experience the following clinical events:
 - Coronary artery bypass graft [CABG] (<1% at goal vs >1% above goal)
 - Myocardial infarction [MI] (5% at goal vs 14% above goal)
 - Percutaneous coronary intervention [PCI] (1% at goal vs 4% above goal)
 - Stroke/transient ischemic attack [TIA] (8% at goal vs 10% above goal)
- Ultimately, managing LDL-C to goal leads to a 50% decrease in the proportion of patients with 1 of the 4 cardiovascular events (14% at goal vs 28% above goal)

Figure 4 | Annualized Healthcare Costs Among Patients in Primary and Secondary Prevention Settings (USD)



- Patients treated in primary prevention accrue far fewer pharmacy and medical costs per year vs patients treated in a secondary prevention setting
 - Pharmacy costs are approximately 60% higher in secondary prevention vs primary prevention (\$3,500 vs \$2,200), though the difference is much more pronounced among medical costs (\$10,600 vs \$4,100; 158% higher), culminating in 124% higher total costs in secondary prevention vs primary prevention (\$14,100 vs \$6,300)
- The trends were similar when comparing very high-risk vs not very high-risk patients within secondary prevention: 34% higher pharmacy costs (\$3,900 vs \$2,900), 101% higher medical costs (\$14,000 vs \$6,900), and 83% higher total costs (\$17,900 vs \$9,800)

DISCUSSION & CONCLUSION

Discussion

- In this real-world data analysis, a vast majority of patients with hypercholesterolemia are treated with statins; however, statins alone are not leading to optimal cardiovascular risk reduction with approximately 40%-80% not meeting their LDL-C goals
 - This trend is present in both primary and secondary prevention populations, along with secondary prevention risk-based subgroups
- The impact of the lack of LDL-C control may manifest in higher rates of select cardiovascular events, and in particular myocardial infarction
- The increased morbidity among secondary prevention patients vs. those in primary prevention, as well as secondary very high risk vs. secondary not very high risk, may drive increased use of emergency department visits, inpatient hospitalizations, and long-term care, which in turn may contribute to the higher annual medical, pharmacy, and total direct medical costs among these population segments
- Consequently, as patients move up the risk continuum, they face greater exposure to negative cardiovascular outcomes, indicating the importance of controlling LDL-C to manage these transitions

Conclusions

- Elevated LDL-C is highly prevalent within the US population, with over 30 million patients across primary ASCVD prevention and secondary prevention contexts
- Among patients with ASCVD, most are considered at high risk for a secondary cardiac event and accrue higher healthcare resource utilization and costs compared to ASCVD patients not at very high risk and primary prevention patients
- Despite taking statins, residual cardiovascular risk remains, and patients above their LDL-C goals are exposed to more frequent healthcare utilization and high direct medical costs
- Consequently, providers and patients need additional therapeutic options to close this treatment gap

REFERENCES

- Faxon DP, Fuster V, Libby P, et al. Atherosclerotic vascular disease conference: writing group III: pathophysiology, *Circulation*. 2004;109:2617-2625.
- Libby P, Ridker PM, Hansson GK. Progress and challenges in translating the biology of atherosclerosis. *Nature*. 2011;473:317-325.
- 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease
- Virani SS, Smith SC Jr, Stone NJ, Grundy SM. Secondary prevention for atherosclerotic cardiovascular disease comparing recent US and European guidelines on dyslipidemia. *Circulation*. 2020;141:1121-1123.