

A decorative graphic in the top-left corner consisting of a network of grey lines connecting small grey dots, forming a complex, web-like structure.

THE GOULD REGISTRY

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DISCLOSURES

- **Research grants to his institution from Amgen, Arrowhead, Eli Lilly, NIH, Novartis and Regeneron**
- **Consulting fees from Amgen, CRISPER Therapeutics Eli Lilly, Lipigon, Novartis, Precision Biosciences, Regeneron, UltraGenyx, Verve Therapeutics**
- **Non-promotional honoraria from Kowa**
- **Royalties from Wolters Kluwer (UpToDate)**
- **Stock holding in MediMergent, LLC.**
- **Patent applications on: Methods and systems for biocellular marker detection and diagnosis using a microfluidic profiling device. EFS ID: 32278349. Application No. (PCT/US2019/026364) (provisional); Compositions and methods relating to the identification and treatment of immunothrombotic conditions. New International Application No. PCT/US2021/63104926); and quantification of Lp(a) vs. non-Lp(a) apoB concentration: development of a novel validated equation. (PCT/US2021/63248837).**

Background



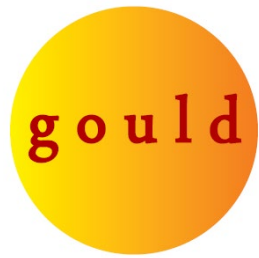
- The GOULD (Getting to an Improved Understanding of Low-Density Lipoprotein Cholesterol and Dyslipidemia Management) registry is prospective observational research study aiming to better understand cholesterol treatment among subjects with ASCVD in the United States.
- Since the inception of the study, the CV landscape has been evolving with
 1. Publication of new guidelines on lipid management for subjects with ASCVD
 2. Publication of new cardiovascular outcomes trials for innovative therapies
 3. Improvement in access to new lipid lowering therapies

Study Objectives



- **Primary Objective:**
 - Describe LDL-C treatment patterns over time in patients with clinical ASCVD
- **Secondary Objectives:**
 - Describe LDL-C levels and measurement patterns in patients with clinical ASCVD
 - Describe patient characteristics
 - Describe patient understanding of ASCVD risk, goals of lipid management, and attitudes towards lipid-lowering therapy (LLT)
- **Exploratory Objectives:**
 - Estimate the effect of patient, physician, and site factors on LLT patterns
 - Describe management of statin intolerance
 - Describe changes in LLT patterns after the release of updated lipid management guidelines and/or new clinical study data

Methods – *Key Patient Criteria*



- Inclusion Criteria
 - ≥ 18 years of age at signing of informed consent
 - At least one planned study visit in the next 12 months
 - Available for follow-up questionnaires
 - Established ASCVD (defined as meeting at least one of the following criteria):
 - Coronary artery disease
 - Prior history of myocardial infarction
 - Coronary or other arterial revascularization
 - Ischemic stroke or transient ischemic attack
 - Documented peripheral artery disease secondary to atherosclerosis (eg, aortic aneurysm, ankle brachial index < 0.9 , imaging evidence of $> 50\%$ stenosis in any peripheral artery, or intermittent claudication)
 - Carotid artery stenosis $> 50\%$

Methods – *Study Cohorts*

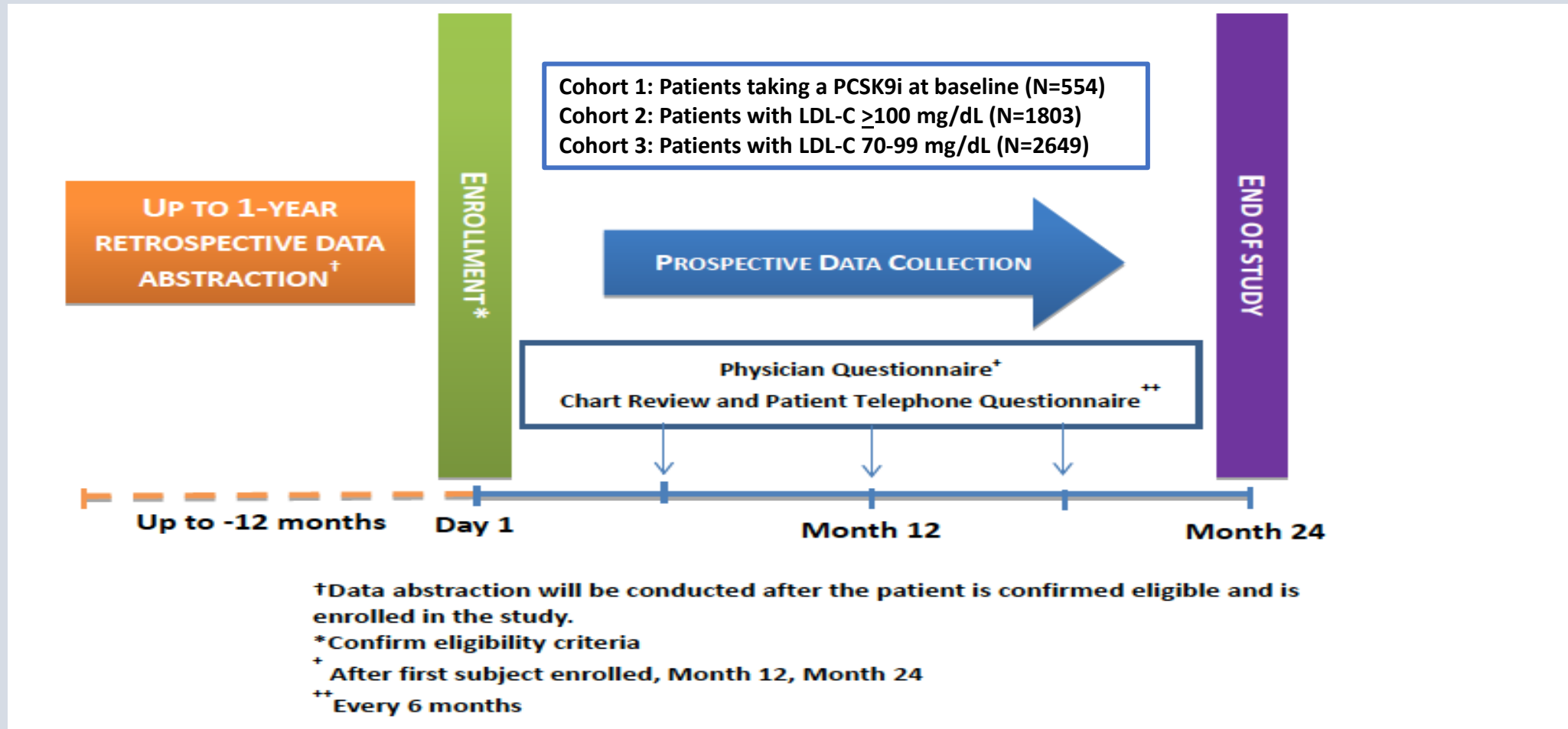


Up to 5000 patients will be enrolled at ~ 120 sites across the U.S., including cardiology, primary care, and multi-speciality practices, in rural and urban settings.

Patients will be categorized into 1 of 3 study cohorts:

- 1) Proprotein convertase subtilisin/kexin type 9 antibody inhibitor (PCSK9i) Cohort (Target sample size = 500 patients)
 - Evidence of a current prescription for an approved PCSK9i at baseline and patient confirmation that they have taken a PCSK9i within 30 days prior to enrollment
- 2) LDL-C \geq 100mg/dL Cohort (Target sample size = 2000 patients)
 - Confirmation of LDL-C \geq 100mg/dL at last measurement with no change in LLT for 4 weeks (statin and non-statin therapies)
- 3) LDL-C 70-99mg/dL Cohort (Target sample size = 2500 patients)
 - Confirmation of LDL-C 70-99 mg/dL at last measurement with no change in LLT for 4 weeks (statin and non-statin therapies)

Study Schema



Demographics and Site Characteristics



- N=5,006 subjects enrolled
- Mean age = 68yrs
- 60% Male
- 86% White, 10% African American
- 8% Hispanic

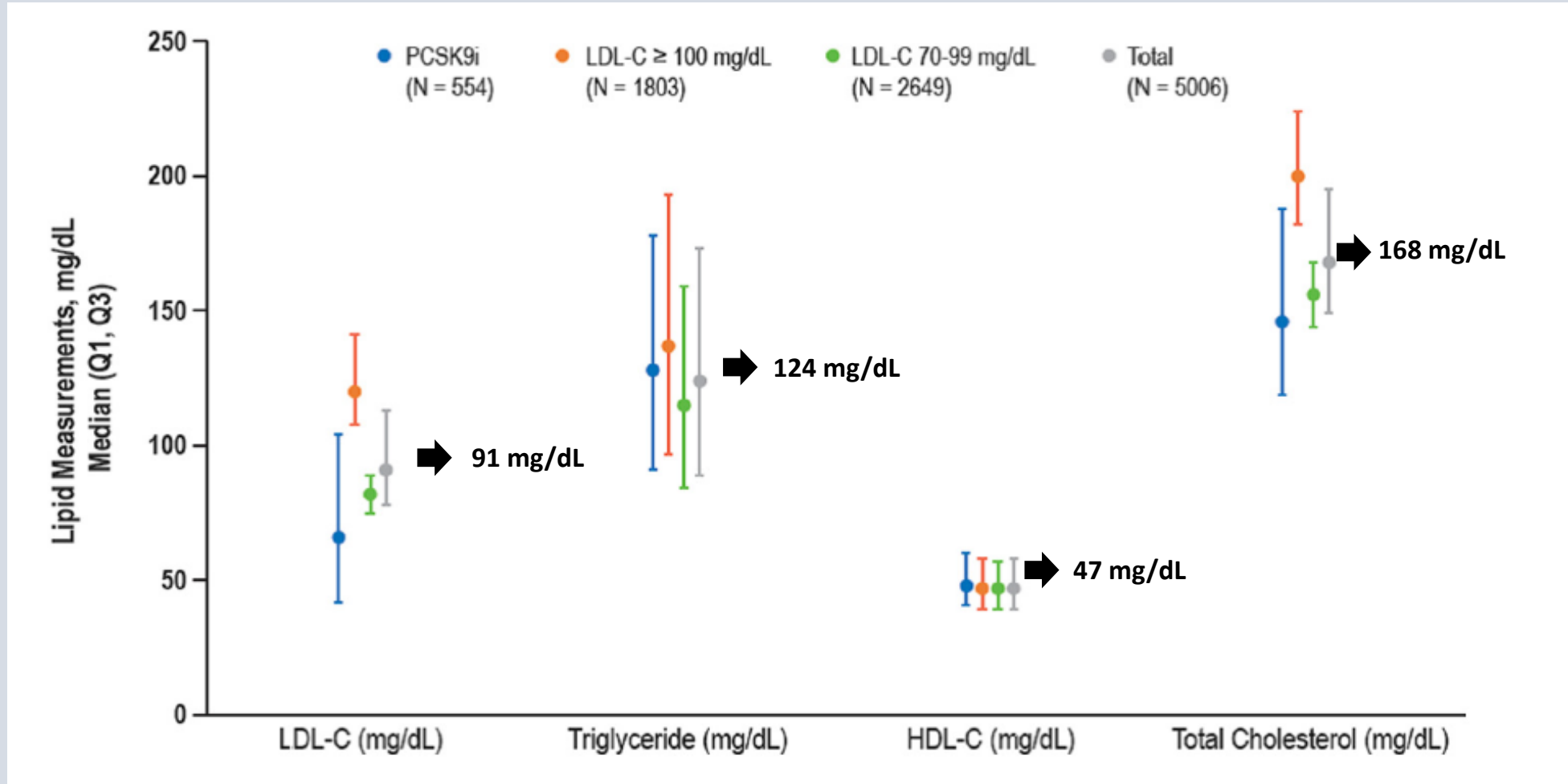
N=119 sites	%
Geographic Region	
Northeast	16.8%
Northwest	20.2%
South	44.5%
West	18.5%
Hospital or non-hospital site	
Hospital	14.3%
Non-hospital	85.7%
Type of practice	
Teaching	16.1%
Non-Teaching	83.9%
Location	
Rural	15.1%
Urban	84.9%

Medical History

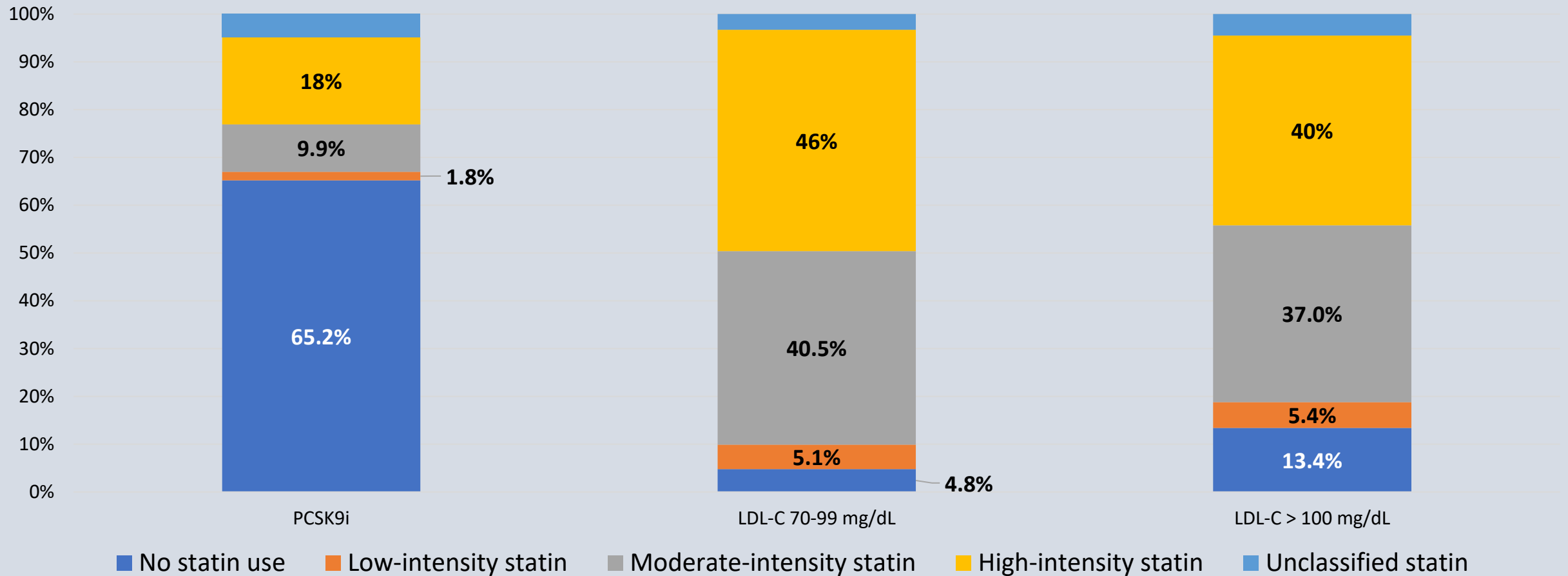


- Coronary artery disease: 80%
- Cerebrovascular accident: 10%
- Peripheral arterial disease: 13%
- Prior MI: 31%
- Type 2 Diabetes: 33%
- Family history of premature ASCVD: 35%

Baseline Lipid Levels by Study Cohort



Statin use at Enrollment Varied by Study Cohort

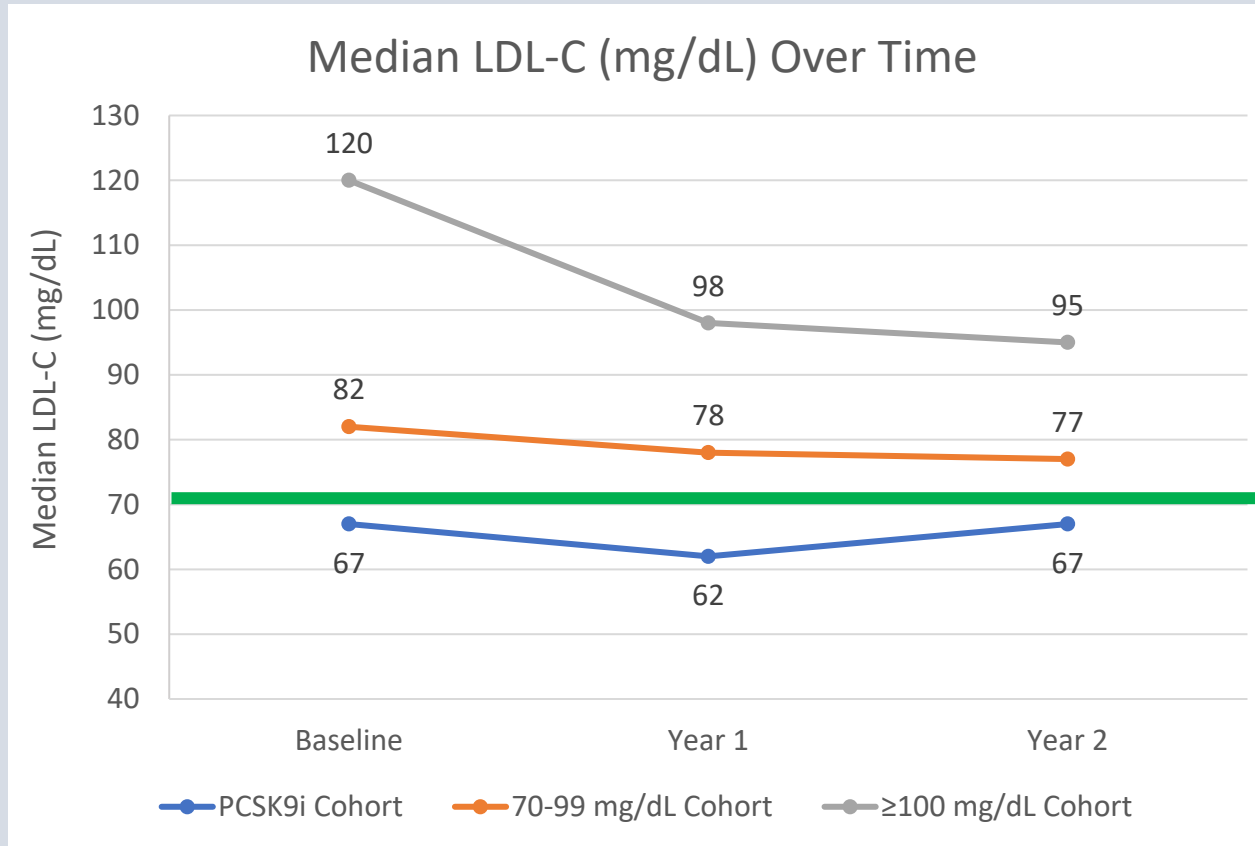


Summary of Baseline Patient Chart Reviews



- High intensity statins and ezetimibe are underutilized in high risk patients outside of clinical trials
- Use of high-intensity statins varies by sex and geographic region
- Among patients on a PCSK9i, approximately 1/3 were receiving a statin, suggesting statin intolerance is a driver of PCSK9i use at time of baseline
- Clear opportunities to improve lipid management in this population

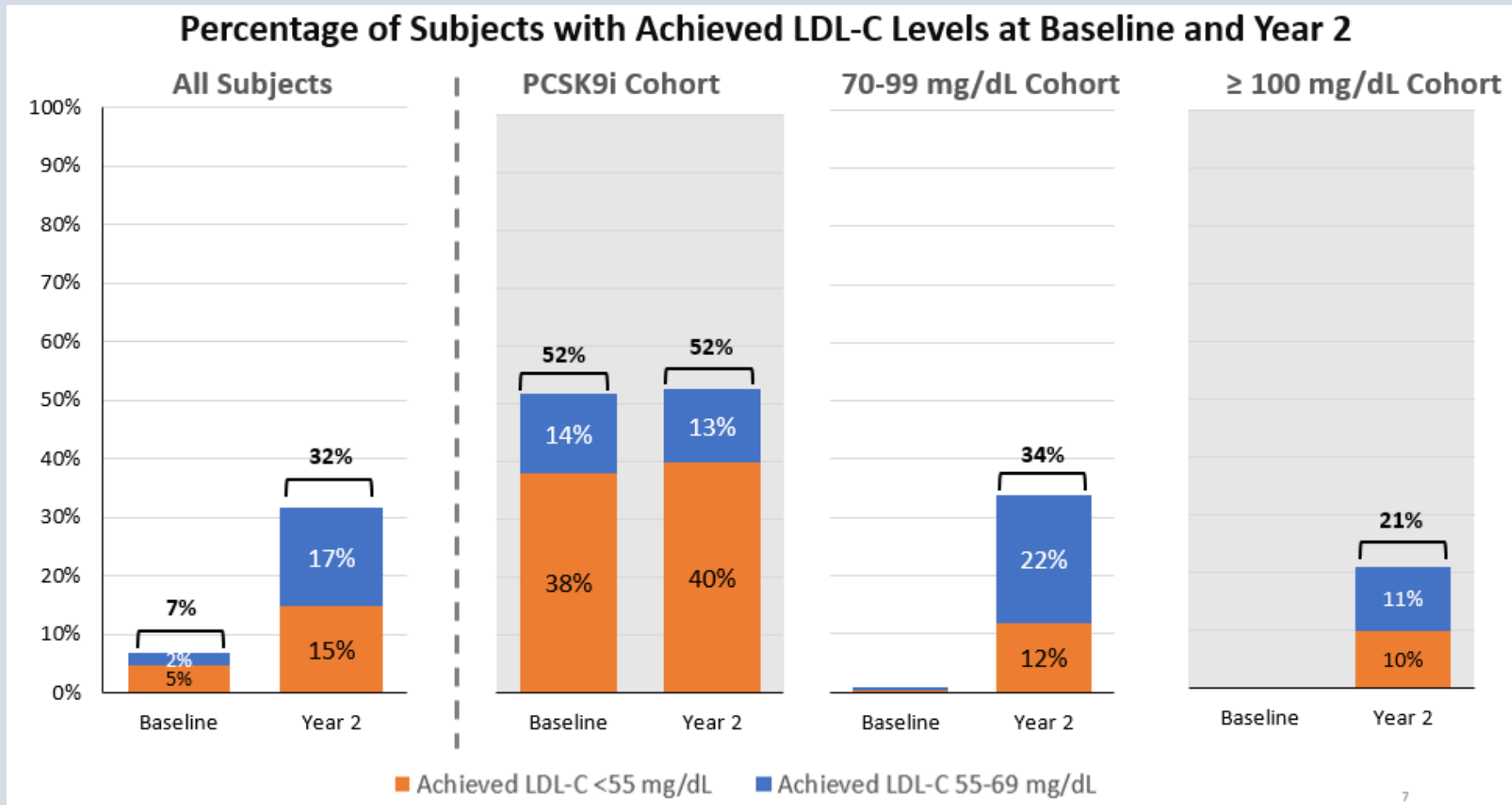
Change in LDL-C from Baseline to Year 2



**Recommended
ACC/AHA threshold**

The majority of patients in non-PCSK9i cohorts did not achieve ACC/AHA recommended LDL-C level of < 70 mg/dL by Year 2 and there was little change between Year 1 and Year 2

At 2 Years, 32% of Subjects Achieved an LDL-C <70 mg/dL



Over 2 Years of Follow-up, Intensification of LLT Occurred in Only 17% of Subjects



	All Subjects N=5,006
Lipid treatment intensification	17%
Statin up-titrated	6%
Statin added	3%
Ezetimibe added	5%
PCSK9i added	4%
Lipid treatment de-escalation*	9%
Statin down titrated	2%
Statin discontinued	5%
Ezetimibe discontinued	2%
PCSK9i discontinued	1%

*Out of the subjects on a specific medication, statins were discontinued in 6%, ezetimibe in 15%, and PCSK9i in 9%

	All Subjects N=5,006	PCSK9i Cohort N=554	LDL-C 70-99 mg/dL Cohort N=2,651	LDL-C ≥ 100 mg/dL Cohort N=1,801
Lipid treatment intensification	17%	13%	14%	22%
Lipid treatment de-escalation	9%	19%	8%	9%

LLT intensification rate was low in the LDL-C ≥ 100 and 70-99 mg/dL cohorts, 22% and 14% respectively

Factors related to LLT Intensification and LDL-C Achievement



- Intensification of LLT was more common among
 - Baseline LDL-C \geq 100 mg/dL (yet this group achieved LDL-C goal less often)
 - Younger patients (\leq 65 yrs); Married; Income \geq \$75,000
 - Sites in the Northwest, Urban practices, Affiliation with teaching hospital
 - Cardiology sites
 - Sites with lipid protocols in place
 - If physician's ideal goal for ASCVD patients is 'Less than 70 m/dL' or lower
 - If physician frequently prescribes non-statin LLT when LDL-C remains high despite HI statin
- Achievement of LDL-C <70 mg/dL was more common among
 - Baseline LDL-C 70-99 mg/dL
 - Males, College educated, Married, Income \geq \$75,000, Diabetes
 - Sites affiliated with teaching hospitals
 - Sites with lipid protocols in place
 - Cardiology sites
 - If physician's ideal goal for ASCVD patients is 'Less than 70 m/dL' or lower

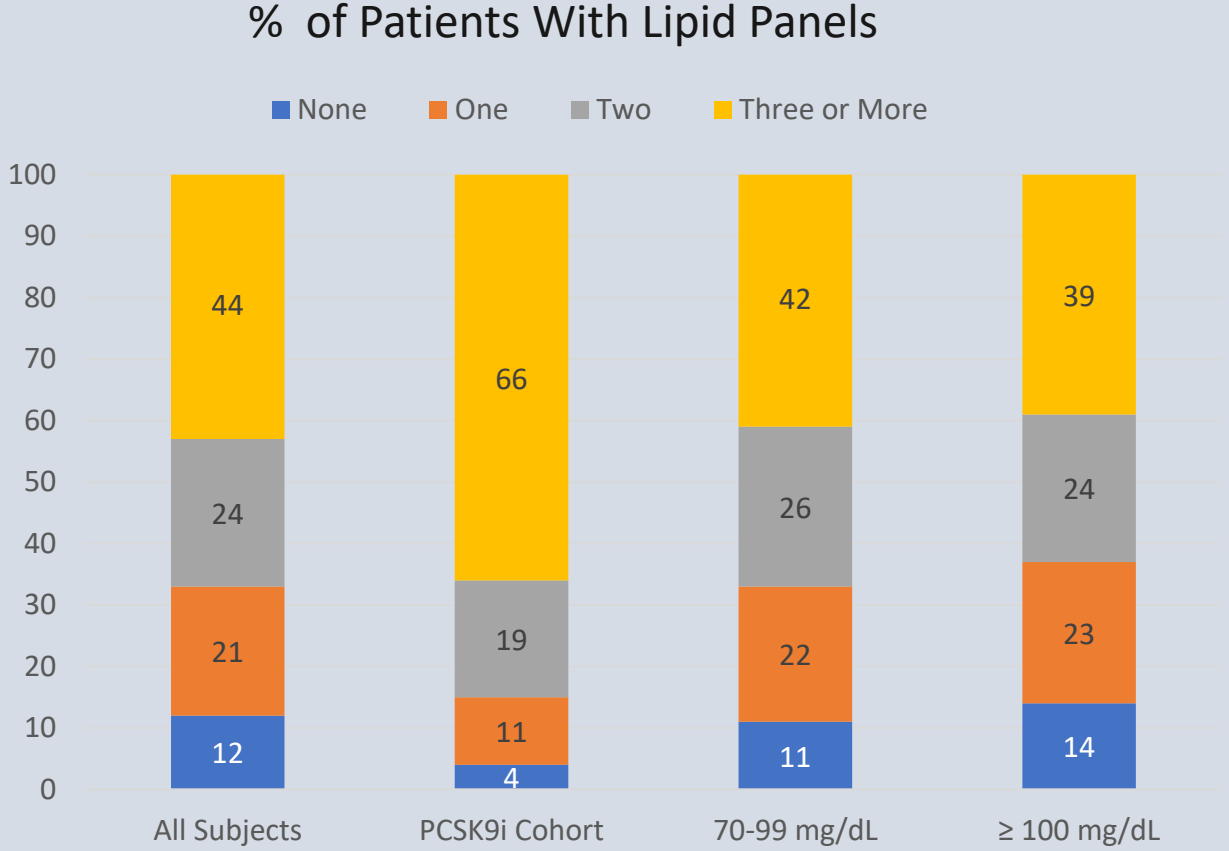
Physician Reporting of Lipid Measurement and the Frequency of Lipid Panels Observed in Clinical Care



Lipid panels were measured less frequently in the LDL-C cohorts

Table 1. Physician Responses Related to Lipid Measurement and Statin Adherence

Time to first reassessment after initiation of statins	
< 3 months	39.1%
3-6 months	0.9%
> 6 months	0.9%
Never	59.1%
Frequency of lipid-level measurements after 1 year of statins	
At least every 6 months	56.4%
Every 6 months to 1 year	3.6%
Never	40.0%



Cannon CP, et al. What Do US Physicians Think About Lipid-Lowering Therapy and the Guidelines? Results From a National Survey in the Getting to an ImprOved Understanding of Low-Density Lipoprotein Cholesterol and Dyslipidemia Management (GOULD) Registry. AHA 2018. Chicago, IL.
 Cannon CP, De Lemos JA, Rosenson RS, Ballantyne CM, Liu Y, Gao Q, Palagashvilli T, Alam S, Mues KE, Bhatt DL, Kosiborod MN, Gould Investigators. JAMA Cardiol 2021;6:1060-1068

Baseline Questionnaires Reveal 73% of Physicians believe in Lowering LDL-C to <70 mg/dL or Lower

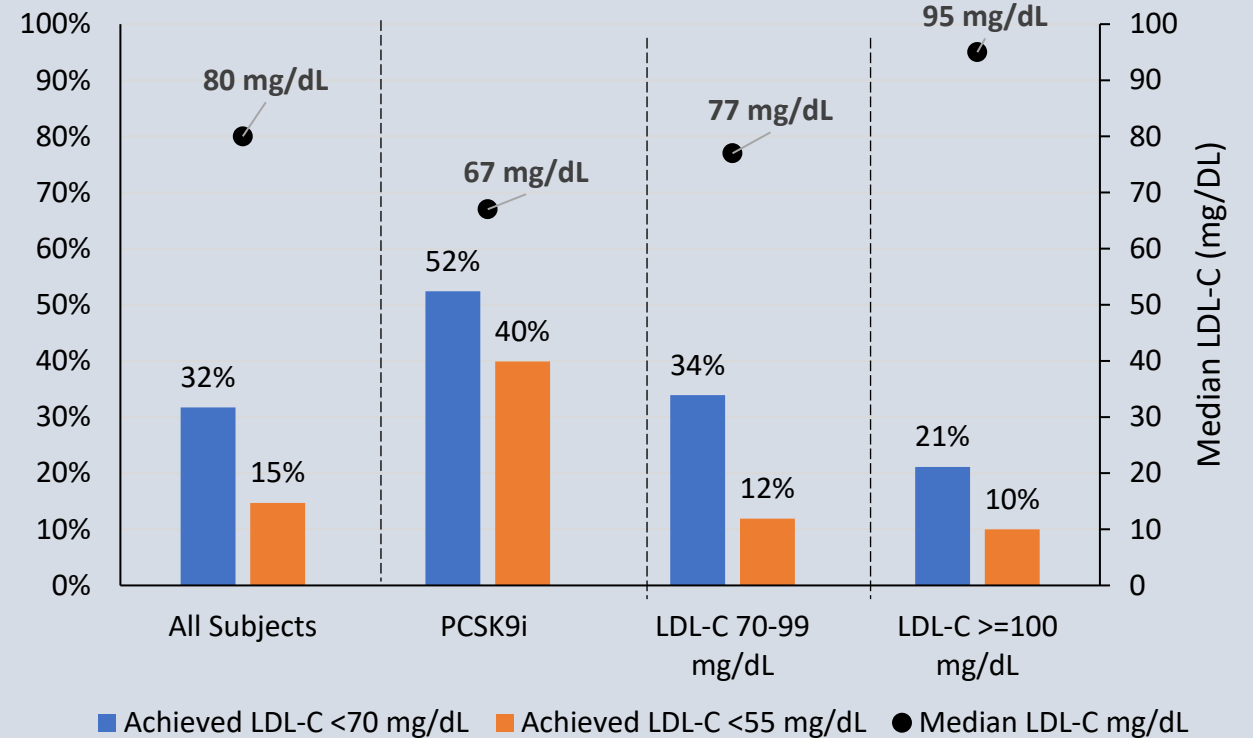


LDL-C goal to achieve with cholesterol lowering therapy	N=113
<50 mg/dL	4.5%
<70 mg/dL	68.8%
Other	26.8%

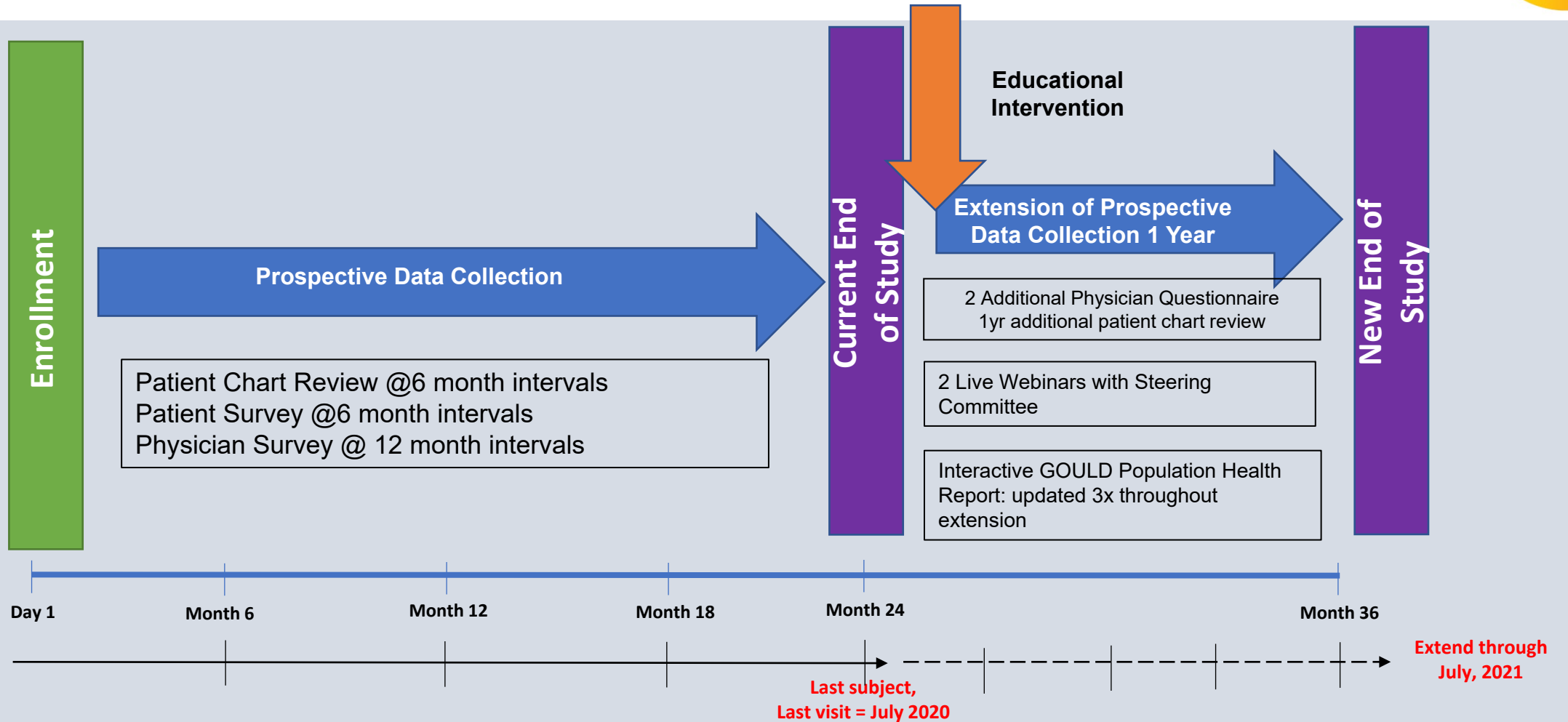
However, this belief does not appear to align with the observed clinical care of patients.



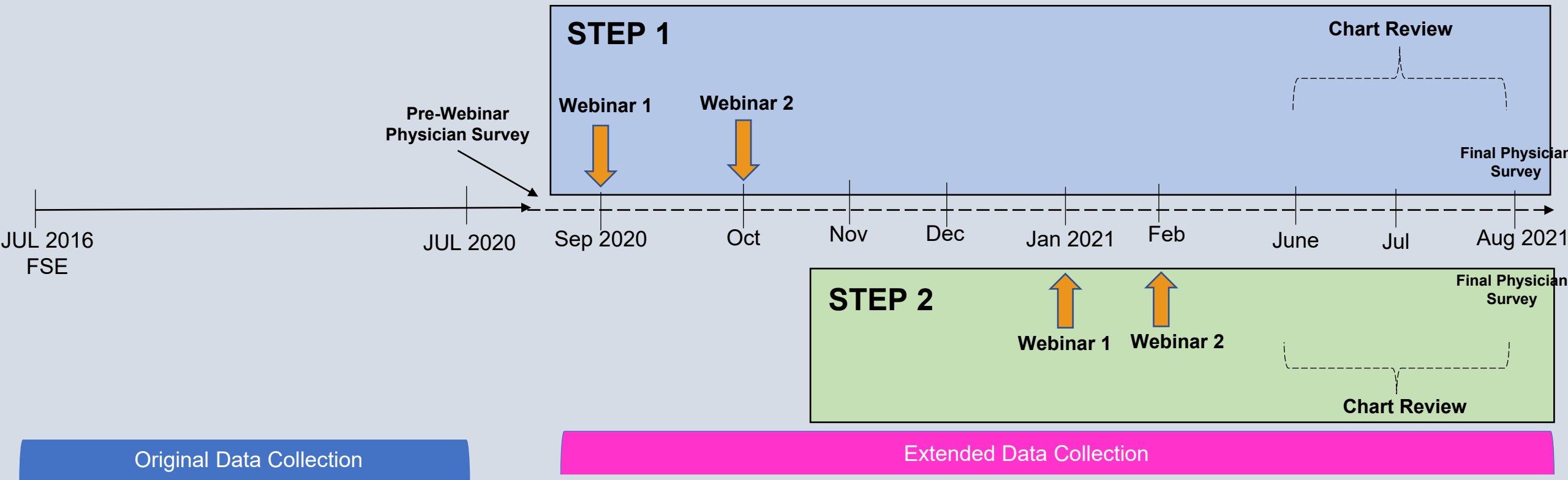
Median LDL-C and Percentage of Subjects with Achieved LDL-C Levels at 2-Years of Follow-Up in the GOULD Registry



GOULD-EDU



Timing of GOULD EDU Webinars and Additional Data Collection

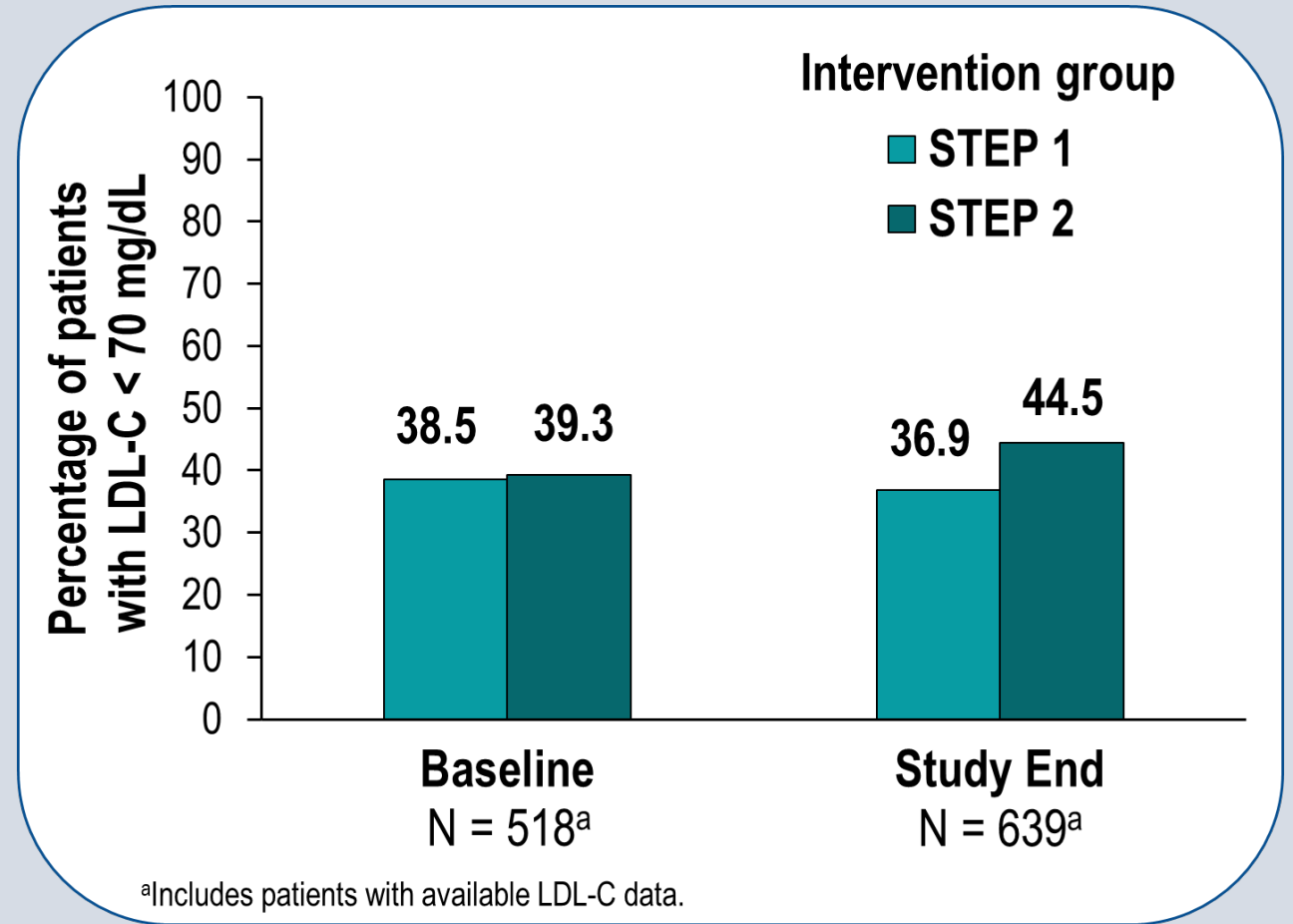


Stepped-wedge approach deals with secular trends

Percentage of Patients who Achieved the Goal of LDL-C < 70 mg/dL



- Overall, 46.8% of patients had an LDL-C measurement in the last half of the study.
- Minimal change in LDL-C occurred from baseline to study end. **Figure** shows the percentage of patients meeting the goal of LDL-C < 70 mg/dL at baseline and end of study (36.9% and 44.5% in STEPs 1 and 2, respectively).



Summary of GOULD Follow-up Results



- A small percentage of patients (17%) had their therapy intensified over 2 years of follow-up
- There was variability in who was intensified, with variation in different patient groups and by physician practice type and approach to LLT at baseline
- Over time, only modest changes in the use of high-intensity statins, ezetimibe, and PCSK9i's were seen, despite new large CV outcomes trials as well as the 2018 ACC/AHA cholesterol guidelines
- These results highlight the need for new approaches to improving adherence to clinical guidelines