Does Evolocumab Use in Europe Match the 2019 ESC/EAS Lipid Guidelines? Results from the HEYMANS Study

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Does evolocumab use in Europe match the 2019 ESC/EAS lipid guidelines? Results from the HEYMANS study

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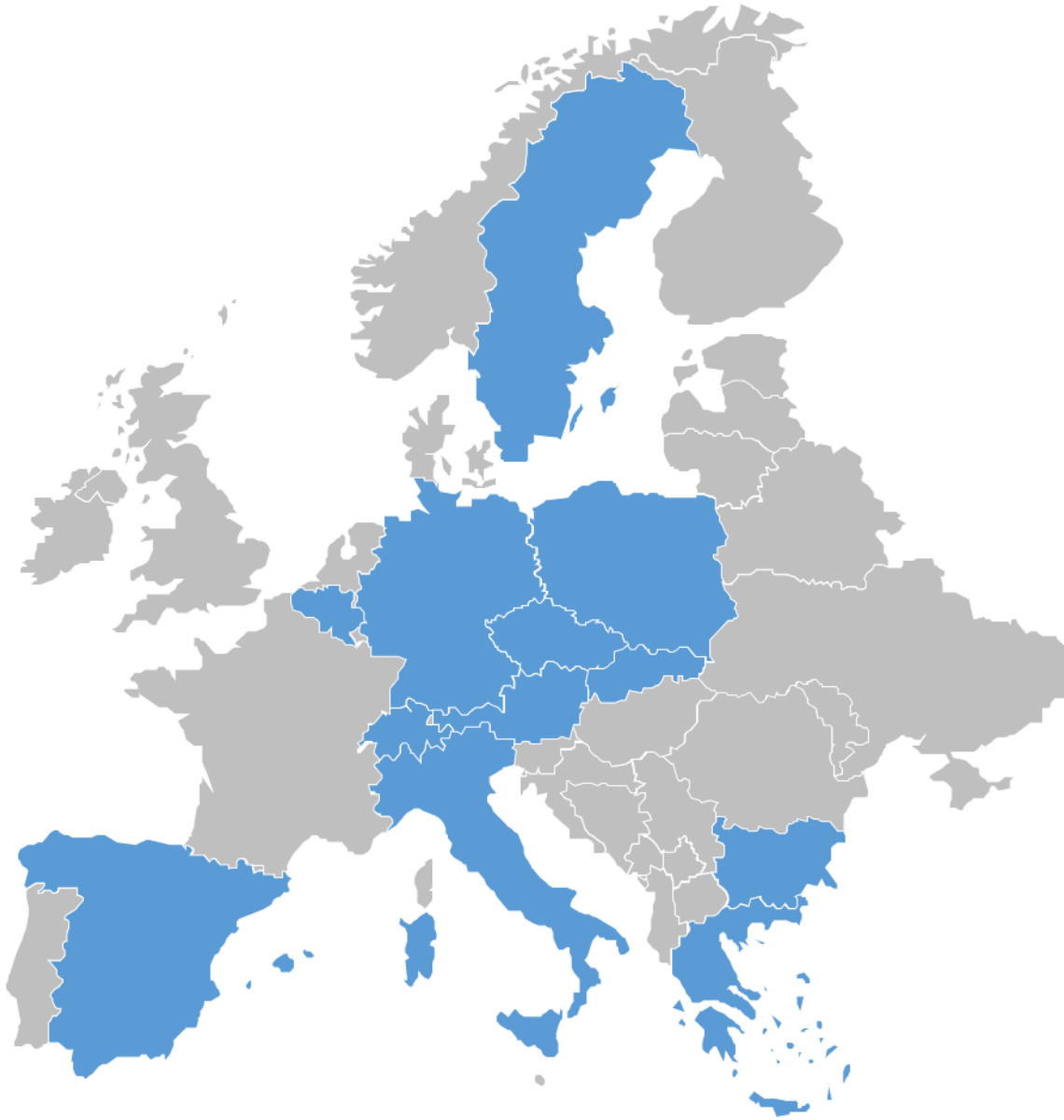
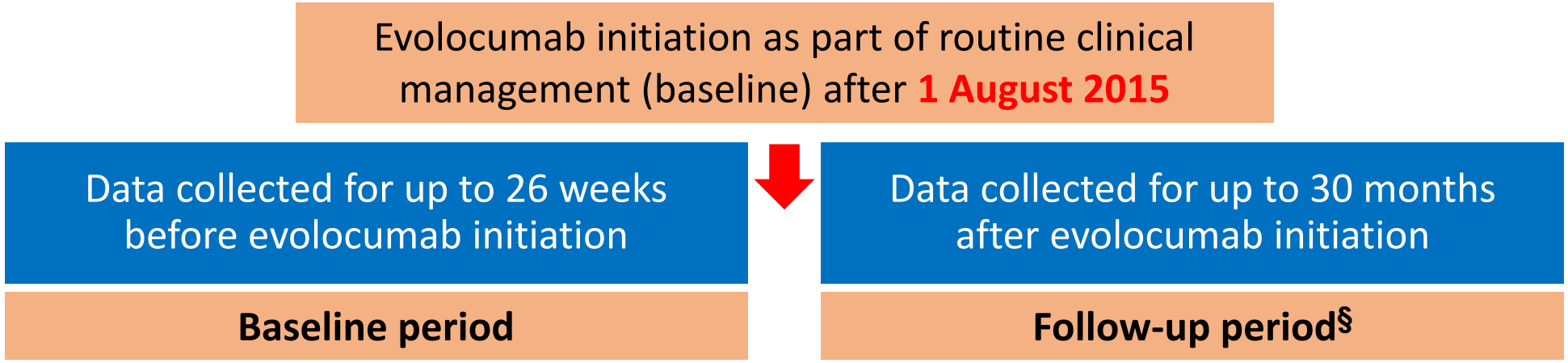


Characteristics of patients initiating evolocumab and treatment patterns across 12 European countries: the HEYMANS* study

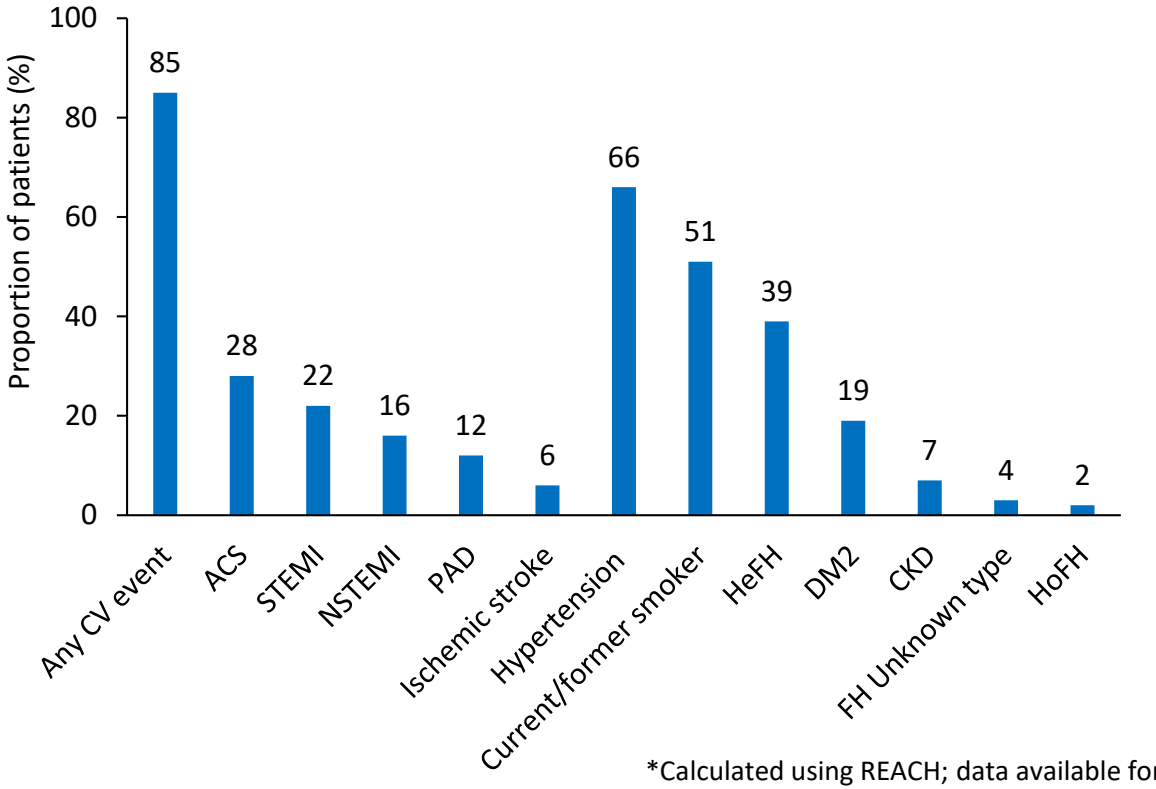
- Observational study in adults ≥ 18 years[†] **who received evolocumab as part of routine clinical management, and within local reimbursement criteria, after 1 August 2015** (in Austria, Belgium, Bulgaria, Czech Republic, Germany, Greece, Italy, Portugal[‡], Slovakia, Spain, Sweden and Switzerland)
- × Patients enrolled in a PCSK9i interventional study, or who received commercially available PCSK9i within 12 weeks before evolocumab initiation, were excluded
- Primary outcome: clinical characteristics of patients at evolocumab initiation
- Interim analysis reported here included data from **1896 patients across 11 countries**[‡] and **follow-up until October 2019**



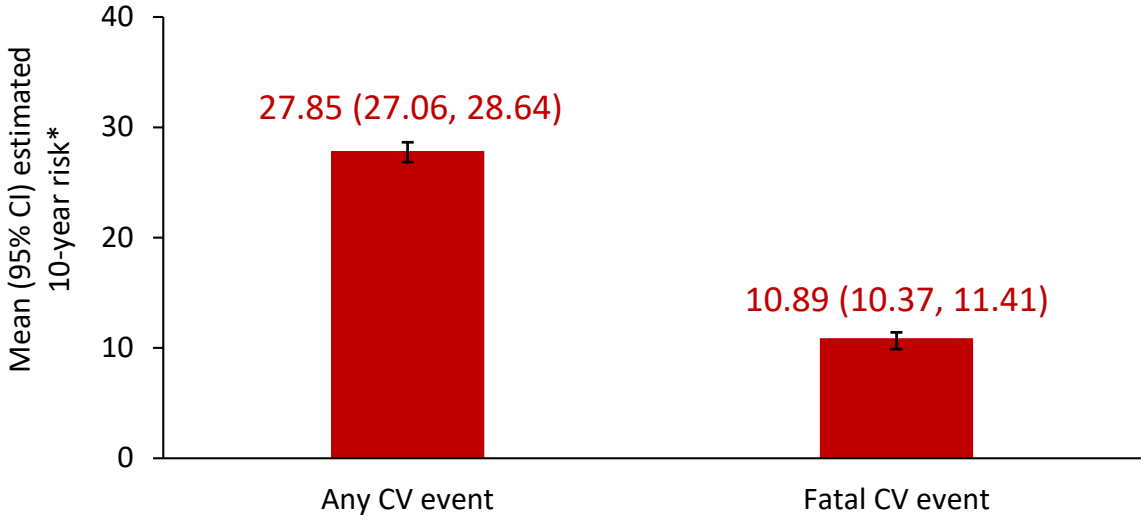
*CHaractEristics of hYperlipidaeMic pAtieNts at initiation of evolocumab and treatment patterns. [†]Providing informed consent, if applicable locally. [‡]Portugal had not enrolled any patients at the time of this interim analysis. [§]Where enrolment occurred after evolocumab initiation, follow-up data between initiation and enrolment was retrospective; patients were followed for up to 30 months irrespective of whether they continued to receive evolocumab. PCSK9i; proprotein convertase subtilisin/kexin type 9 inhibitor

Characteristics of patients initiating evolocumab (n = 1896)

- Mean (SD) age, 60.0 (10.8) years
- Most patients (88%) had 12 months follow-up; mean follow-up was 16.3 months
- The majority (60%) had a history of statin intolerance
- Most patients (85%) had a prior CV event



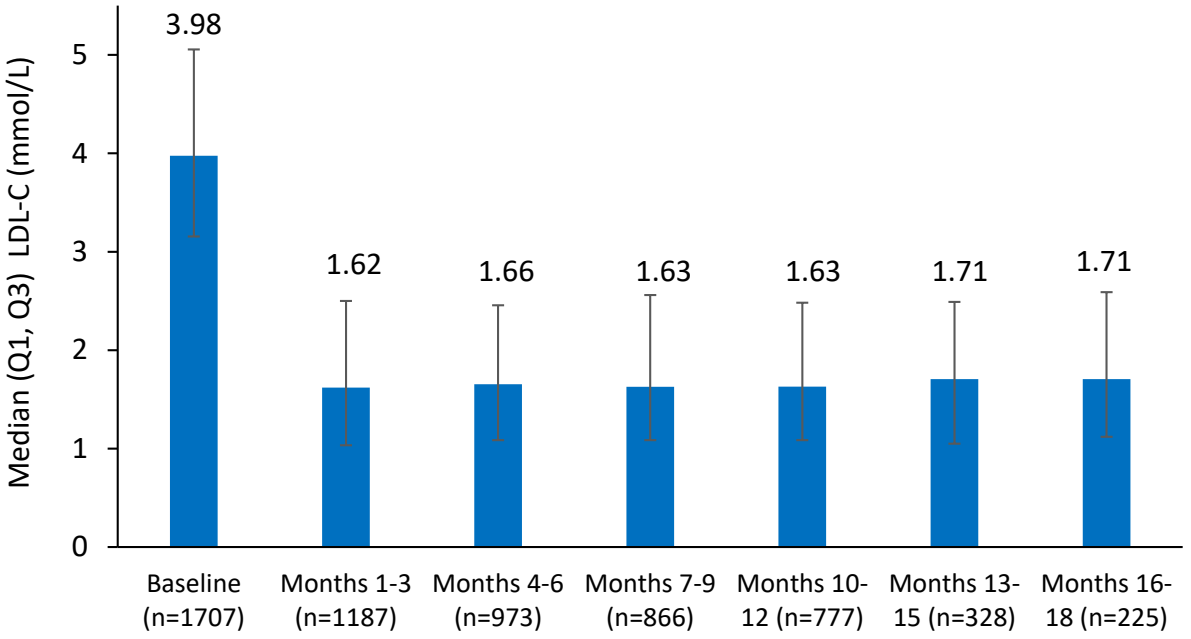
- Based on estimated 10-year risk, over one-quarter of subjects with established ASCVD (excluding FH) were likely to experience a fatal or non-fatal CV event in the next 10 years*
- Similarly, one in 10 patients with established ASCVD (excluding FH) were likely to experience a fatal CV event in the next 10 years*



*Calculated using REACH; data available for n = 990 patients with established ASCVD, excluding FH. ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; CI, confidence interval; CKD, chronic kidney disease; CV, cardiovascular; DM2, type 2 diabetes; FH, familial hypercholesterolemia; HeFH, heterozygous FH; HoFH, homozygous FH; NSTEMI, non-STEMI; PAD, peripheral arterial disease; REACH, REduction of Atherothrombosis for Continued Health (Wilson et al, 2012); SD, standard deviation; STEMI, ST-segment elevation myocardial infarction

LLT use and LDL-C target achievement

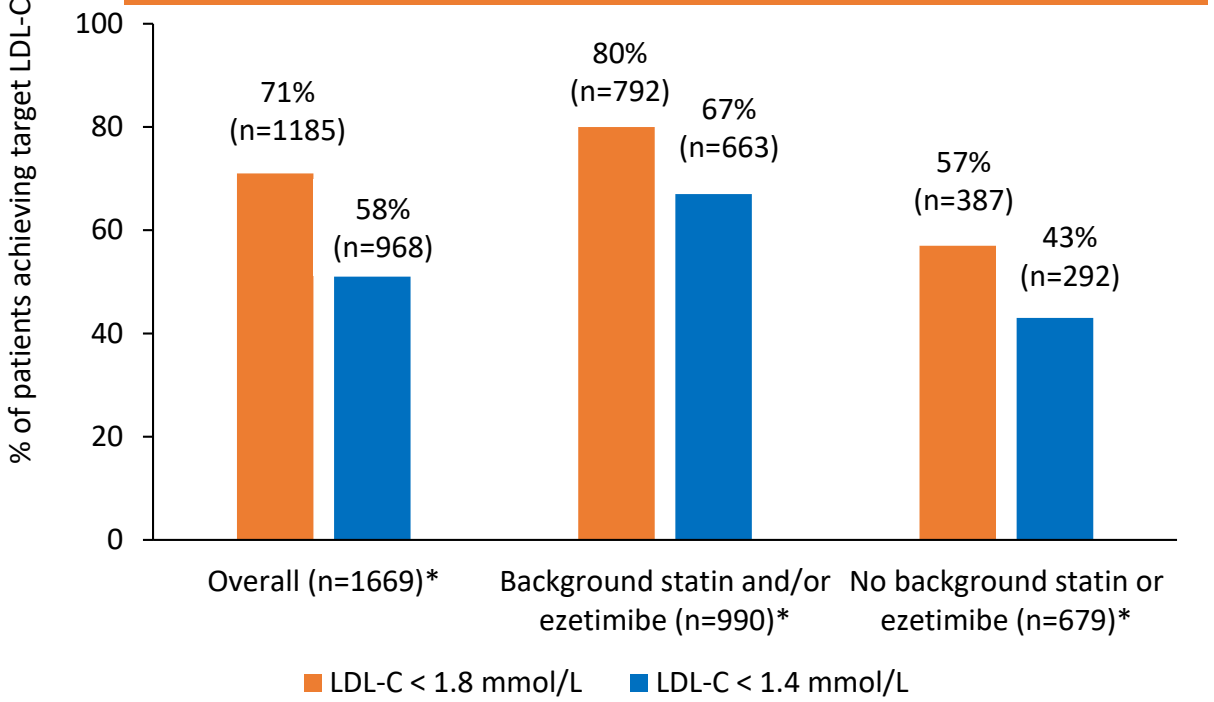
- **LDL-C levels decreased by 58% within three months of evolocumab initiation**
- **This reduction was maintained over 12-18 months**



Median (Q1, Q3) reduction from baseline (%)

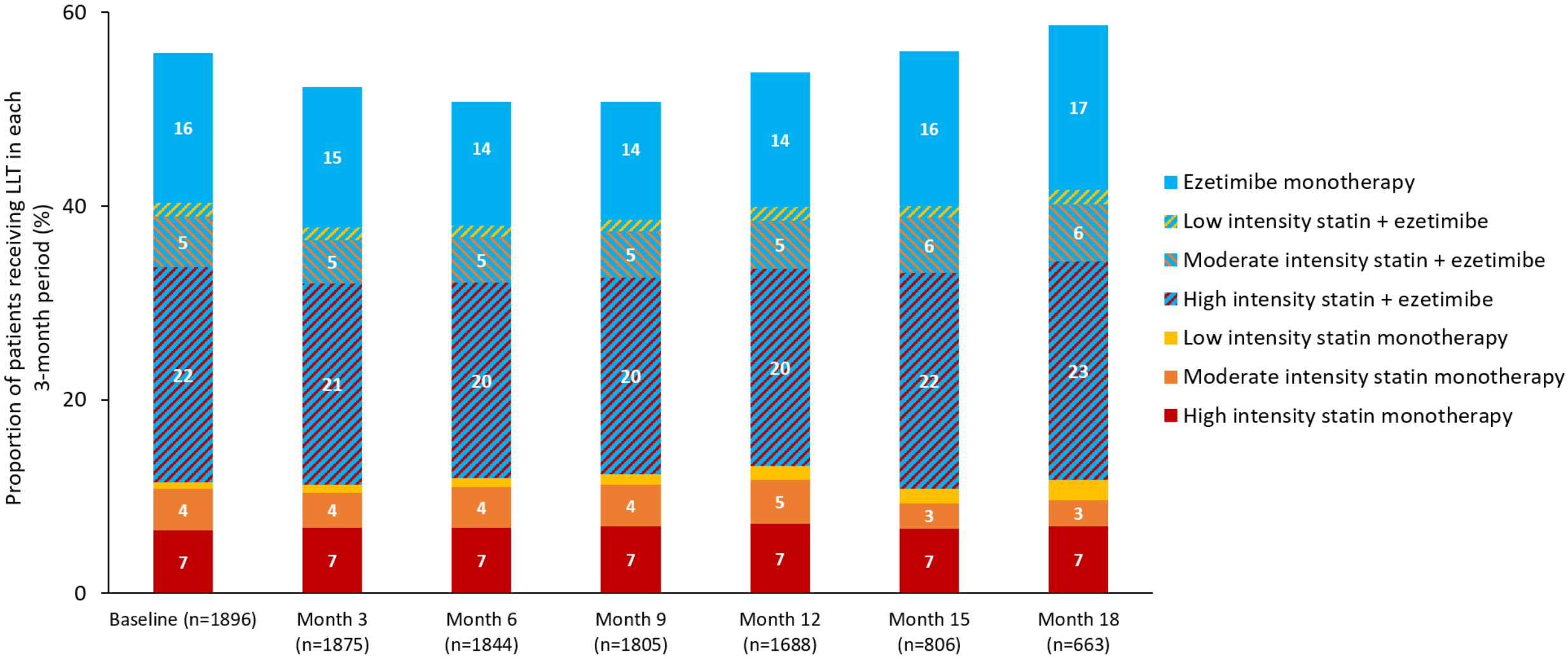
Months 1–3	Months 4–6	Months 7–9	Months 10–12	Months 13–15	Months 16–18
↓ 58.10%	↓ 57.39%	↓ 56.95%	↓ 57.59%	↓ 56.00%	↓ 57.76%
(−70.98, −40.92)	(−69.91, −41.38)	(−70.70, −42.00)	(−68.90 −40.55)	(−69.78, −39.83)	(−71.43, −39.53)

- **Most patients achieved an LDL-C level of < 1.8 mmol/L; 58% achieved an LDL-C level of < 1.4 mmol/L**
- **Patients receiving evolocumab in combination with statins ± ezetimibe were more likely to achieve goal†**



*n=number of patients with at least one LDL-C value post evolocumab initiation. †Compared with patients receiving evolocumab monotherapy. LDL-C, low-density lipoprotein cholesterol; LLT, lipid lowering therapy; Q, quartile

Background LLT use remained stable during evolocumab treatment



LLT, lipid lowering therapy

Conclusions

- Median LDL-C at evolocumab initiation was 3.98 mg/dL, far above the ESC/EAS recommended thresholds of 1.8 mmol/L and 1.4 mmol/L for PCSK9i initiation in high and very high-risk patients, respectively[1], reflecting local reimbursement criteria
- In this study of clinical practice, evolocumab reduced LDL-C by approximately 58% and this reduction was sustained over 12–18 months
- Approximately 40% of these very high-risk patients were receiving evolocumab monotherapy and 58% achieved the 2019 ESC/EAS LDL-C goal of less than 1.4 mmol/L[1]
- 2019 ESC/EAS goal attainment was higher among patients receiving evolocumab with background statin ± ezetimibe
- Our data suggest a large gap between patients eligible for PCSK9i and those who receive them in clinical practice, and that achievement of ESC/EAS LDL-C goals is improved with combination therapy and a lower threshold for PCSK9i initiation

EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; LDL-C, low-density lipoprotein cholesterol; LLT, lipid lowering therapy; PCSK9i; proprotein convertase subtilisin/kexin type 9 inhibitor. 1. Mach F, et al. *Eur Heart J* 2019; 41: 111-188

What Potential Risk Reduction Could Be Achieved with Evolocumab Treatment? A Simulation Based on Observational Data from a Cohort of Users in 10 European Countries

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What Potential Risk Reduction Could Be Achieved with Evolocumab Treatment? A Simulation Based on Observational Data from a Cohort of Users in 10 European Countries

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[1]Imperial College London, London, UK; [2]Amgen Ltd, Uxbridge, UK; [3]Hôpital Pitié Salpêtrière, Paris, France; [4]University of Sheffield, Sheffield, UK; [5]Amgen (Europe) GmbH, Rotkreuz, Switzerland

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Introduction and Purpose

- The FOURIER[a] trial enrolled patients at very high cardiovascular (CV) risk with a mean low-density lipoprotein cholesterol (LDL-C) of 2.5 mmol/L, and demonstrated that evolocumab reduced major CV events by 1.5% in absolute terms over 2.2 years.[1]
- More research is necessary to further understand the potential benefits of evolocumab in a real-world setting.
- Simulate baseline CV risk and assess potential CV risk reduction among a large European cohort of evolocumab users.

a.FOURIER: Further cardiovascular OUtcomes Research with PCSK9 Inhibition in subjects with Elevated Risk

1. Sabatine MS et al. *Am Heart J* 2016;173:94–101.

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Methods

- We used interim data from HEYMANS,[a] an observational study of patients initiating evolocumab across 10 European countries.
- Data analysed were from August 2015, with follow-up until October 2019.[2]
- For each included patient, we:
  - estimated baseline 10-year CV risk, using three different methods
    1. prediction using REduction of Atherothrombosis for Continued Health (REACH) equation[3]
    2. simulation based on FOURIER trial[1]
    3. simulation based on FOURIER-like observational data[4]
  - calculated the absolute LDL-C reduction with evolocumab treatment
  - simulated the relative risk reduction (RRR), using random sampling from the probability distribution of the rate ratio per 1 mmol/L (from the key secondary endpoint in FOURIER)[1]
  - calculated the absolute risk reduction (ARR).

a.HEYMANS: cHaractEristics of hYperlipidaeMic pAtieNts at initiation of evolocumab and treatment patterns.

1. Sabatine MS et al. *Am Heart J* 2016;173:94–101. 2. Ray KK et al. Oral presentation presented at the ESC Congress 2020, 29 August–1 September 2020, online. 3. Wilson PWF et al. *Am J Med* 2012;125:695–703.e1.
4. Lindh M et al. *Eur Heart J Qual Care Clin Outcomes* 2019;5:225–32.
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Results

- Our analysis included 799 patients initiating evolocumab in clinical practice as per local reimbursement criteria, with up to 18 months of follow-up.
- Mean (standard deviation [SD]) baseline LDL-C was 3.8 (1.4) mmol/L, with a mean (SD) absolute reduction of 2.1 (1.2) mmol/L during evolocumab treatment.

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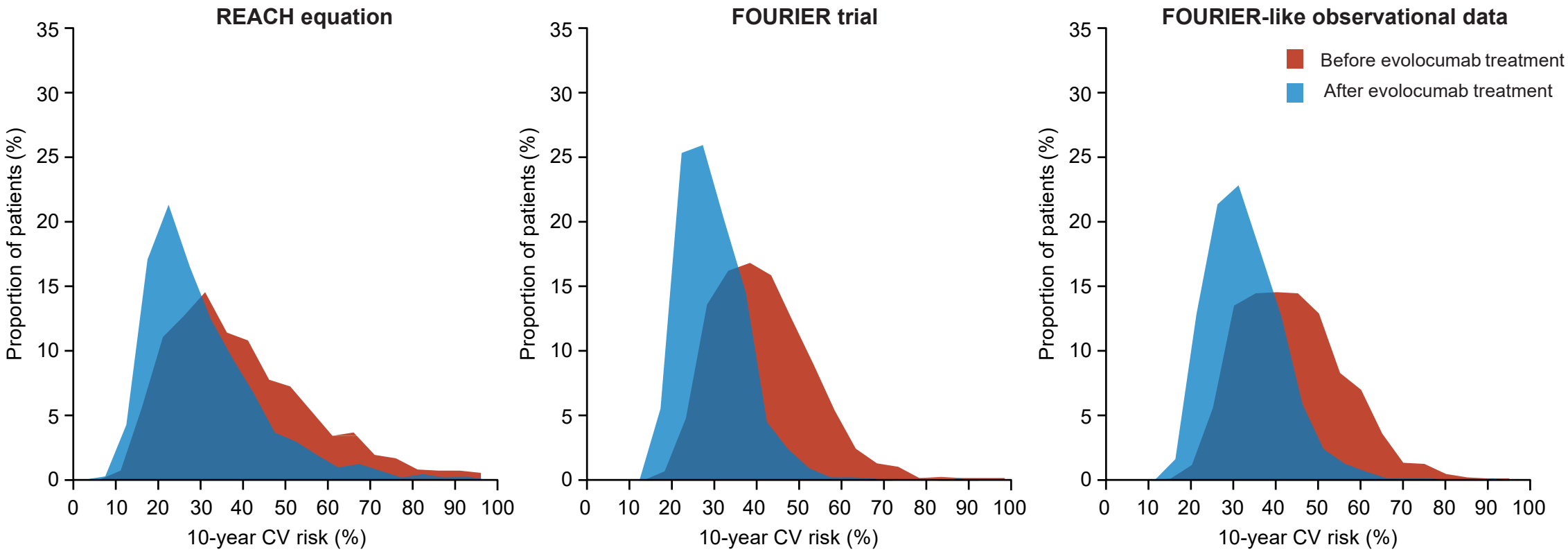
Simulated Probability Distributions for 10-year CV Risk Before and After Evolocumab Treatment (Figure 1)

- Probability distributions using the three different methods for simulating 10-year CV risk before and after evolocumab treatment



CV, cardiovascular; REACH, REduction of Atherothrombosis for Continued Health.

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Predicted 10-year CV Risk Before and After Evolocumab Treatment (Table 1)

- Predicted 10-year CV risk, RRR and ARR

	REACH equation[2]	FOURIER trial[1]	FOURIER-like observational data[3]
Before evolocumab treatment, %, mean (SD)	35.7 (16.7)	35.9 (12.1)	41.4 (13.0)
After evolocumab treatment, %, mean (SD)	25.3 (13.4)	24.9 (8.2)	29.3 (9.2)
RRR, %, mean (SD)	33.3 (17.3)	33.3 (17.3)	33.3 (17.3)
ARR, %, mean (SD)	10.4 (8.0)	11.0 (8.1)	12.1 (8.6)
NNT	10	9	8

ARR, absolute risk reduction; CV, cardiovascular; NNT, number needed to treat; REACH, REduction of Atherothrombosis for Continued Health; RRR, relative risk reduction; SD, standard deviation.

1. Sabatine MS et al. *Am Heart J* 2016;173:94–101. 2. Wilson PWF et al. *Am J Med* 2012;125:695–703.e1. 3. Lindh M et al. *Eur Heart J Qual Care Clin Outcomes* 2019;5:225–32.

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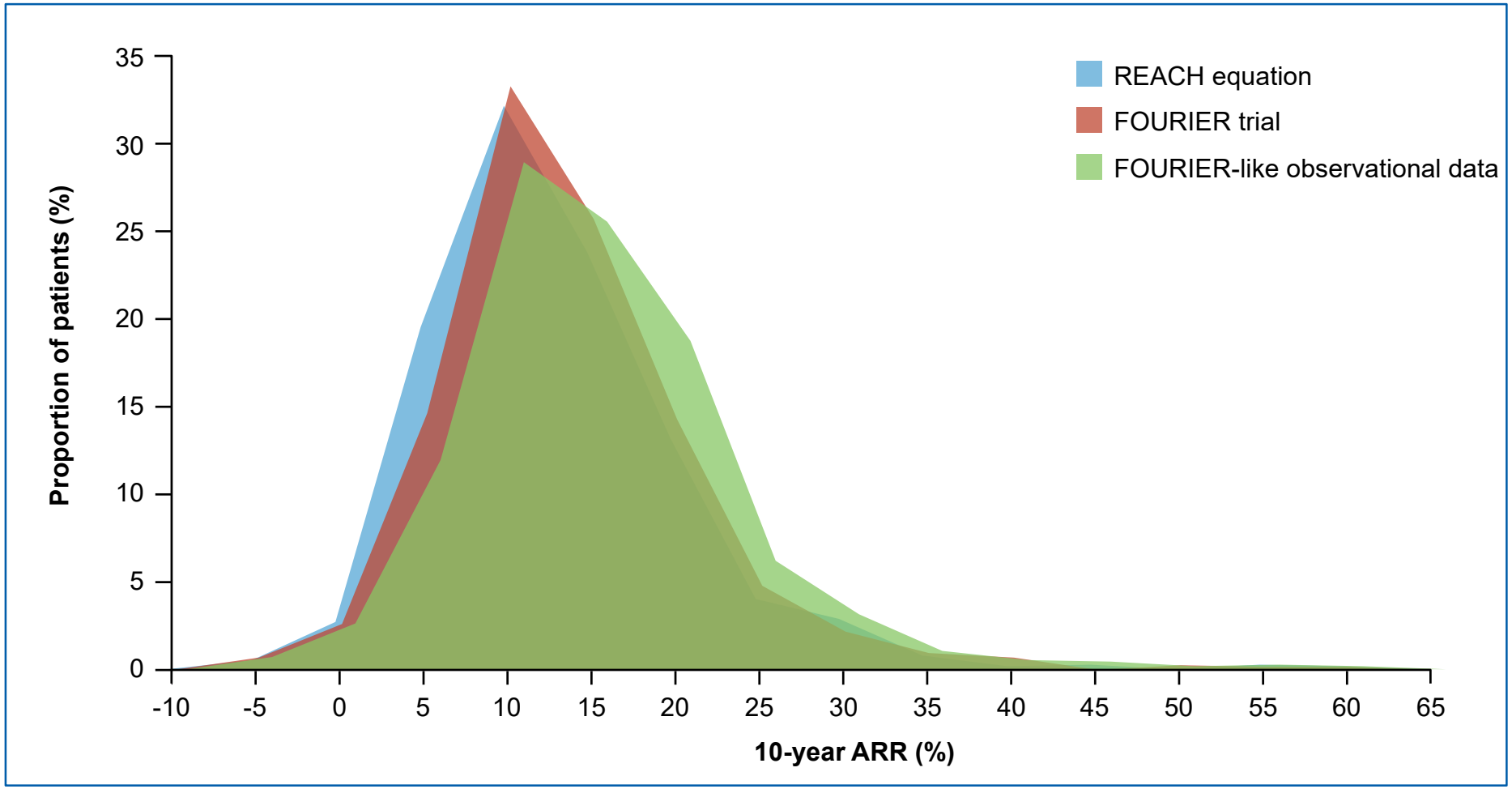
Simulated Probability Distributions for 10-year ARR (Figure 2)

- Probability distributions for 10-year ARR using the three different methods for simulating 10-year CV risk



ARR, absolute risk reduction; REACH, REduction of Atherothrombosis for Continued Health.

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Key Results and Conclusions

- This European cohort of 799 evolocumab users had an almost two-fold higher baseline LDL-C (3.8 mmol/L) than patients enrolled in the FOURIER trial, which translated to higher baseline 10-year CV risk, ranging from 35.7% to 41.4%.
- Consequently, the estimated 10-year ARR, based on efficacy results from FOURIER, was larger than observed in the trial, ranging from 10.4% to 12.1%.

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Disclosures

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- **IB** is an employee of Amgen Ltd.
- **EB** reports personal fees from Aegerion, Akcea, Amgen, Danone, MSD, Mylan, Sanofi/Regeneron and Servier.
- **BVH** receives consulting fees from Amgen.
- **MS** and **GV** are employees of Amgen Europe (GmbH).

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