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SANTORINI AND HEYMANS REGISTRIES

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Treatment gaps in the implementation of LDL cholesterol control among high- and very high-risk patients in Europe between 2020 and 2021: the multinational observational SANTORINI study

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Santorini-Participating countries

- 9602 patients were enrolled between March 2020 and February 2021 at a total of 623 sites across 14 countries in Europe[1]
- Primary and secondary care settings[1,2]

Country	Overall (n=9044), n (%)
Austria	310 (3.43)
Belgium	489 (5.41)
Denmark	311 (3.44)
Finland	337 (3.73)
France	797 (8.81)
Germany	2086 (23.07)
Ireland	100 (1.11)
Italy	1977 (21.86)
Netherlands	523 (5.78)
Portugal	112 (1.24)
Spain	990 (10.95)
Sweden	190 (2.10)
Switzerland	149 (1.65)
United Kingdom	673 (7.44)

1. Ray KK, et al. Atherosclerosis Plus. 2021;43:24–30. 2. Ray KK, et al. Lancet Reg. Health Eur. 2023;29:100624. https://doi.org/10.1016/j.lanepe.2023.100624

Baseline CV risk factors by risk classification as reported by the physician

Risk factor	Overall (N=9044)	High risk (N=2637)	Very high risk (N=6401)
ASCVD, n (%)	6954 (76.9)	1094 (41.5)	5856 (91.5)
Diabetes with target organ damage, n (%)	610 (6.7)	125 (4.7)	485 (7.6)
Diabetes with no target organ damage, n (%)	2428 (26.9)	757 (28.7)	1669 (26.1)
HeFH with ASCVD	504 (5.6)	92 (3.5)	412 (6.4)
eGFR, mL/min/1.73 m^2, mean (SD)	78.2 (24.0)	81.4 (24.0)	76.9 (23.9)
Severe (eGFR <30 mL/min 1.73 m^2)	121 (1.3)	15 (0.6)	106 (1.7)
Moderate (eGFR 30–59 mL/min 1.73 m^2)	933 (10.3)	197 (7.5)	736 (11.5)
Primary prevention patients with SCORE reported, n (%)	2947 (32.6)	1840 (69.8)	1107 (17.3)
SCORE 5–9%	1026 (34.8)	573 (31.1)	453 (40.9)
SCORE ≥10%	240 (8.1)	123 (6.7)	117 (10.6)
Patients with elevated TC >8 mmol/L or LDL-C >4.9 mmol/L or SBP>180 mmHg or DBP>110 mmHg	559 (6.2)	222 (8.4)	334 (5.2)

Missing risk/not reported risk status, n=6

ASCVD, atherosclerotic cardiovascular disease; **CV**, cardiovascular; **DBP**, diastolic blood pressure; **eGFR**, estimated glomerular filtration rate; **HeFH**, heterozygous familial hypercholesterolaemia; **LDL-C**, low-density lipoprotein cholesterol; **SBP**, systolic blood pressure; **SCORE**, Systematic COronary Risk Evaluation; **SD**, standard deviation; **TC**, total cholesterol

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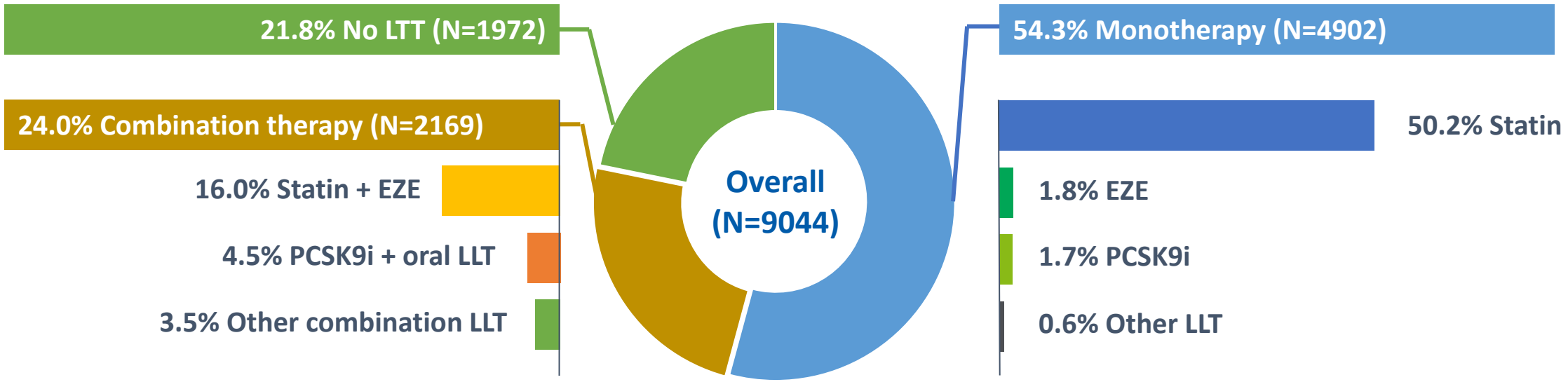
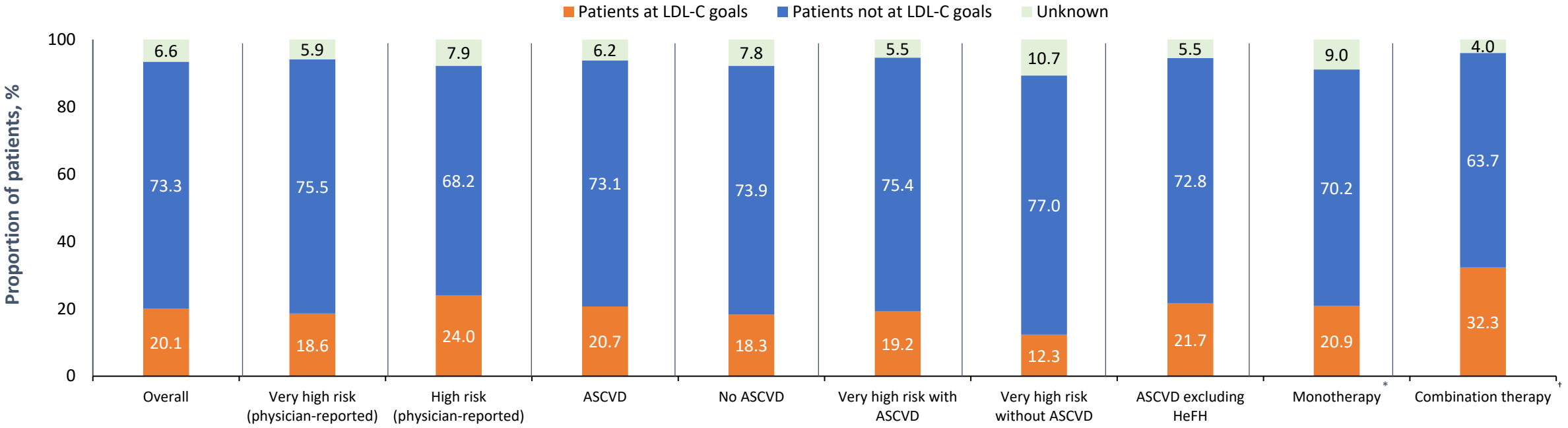
Lipid-lowering therapy in the overall population



Despite LDL-C levels above the recommended values, the majority of patients received monotherapy and 21.8% of patients had no documented LLT

- Data from one patient were missing
- **EZE**, ezetimibe; **LDL-C**, low-density lipoprotein cholesterol; **LLT**, lipid-lowering therapy; **PCSK9i**, proprotein convertase subtilisin kexin 9 inhibitor
- Ray KK, et al. Lancet Reg Health Eur. 2023;29:100624. https://doi.org/10.1016/j.lanepe.2023.100624

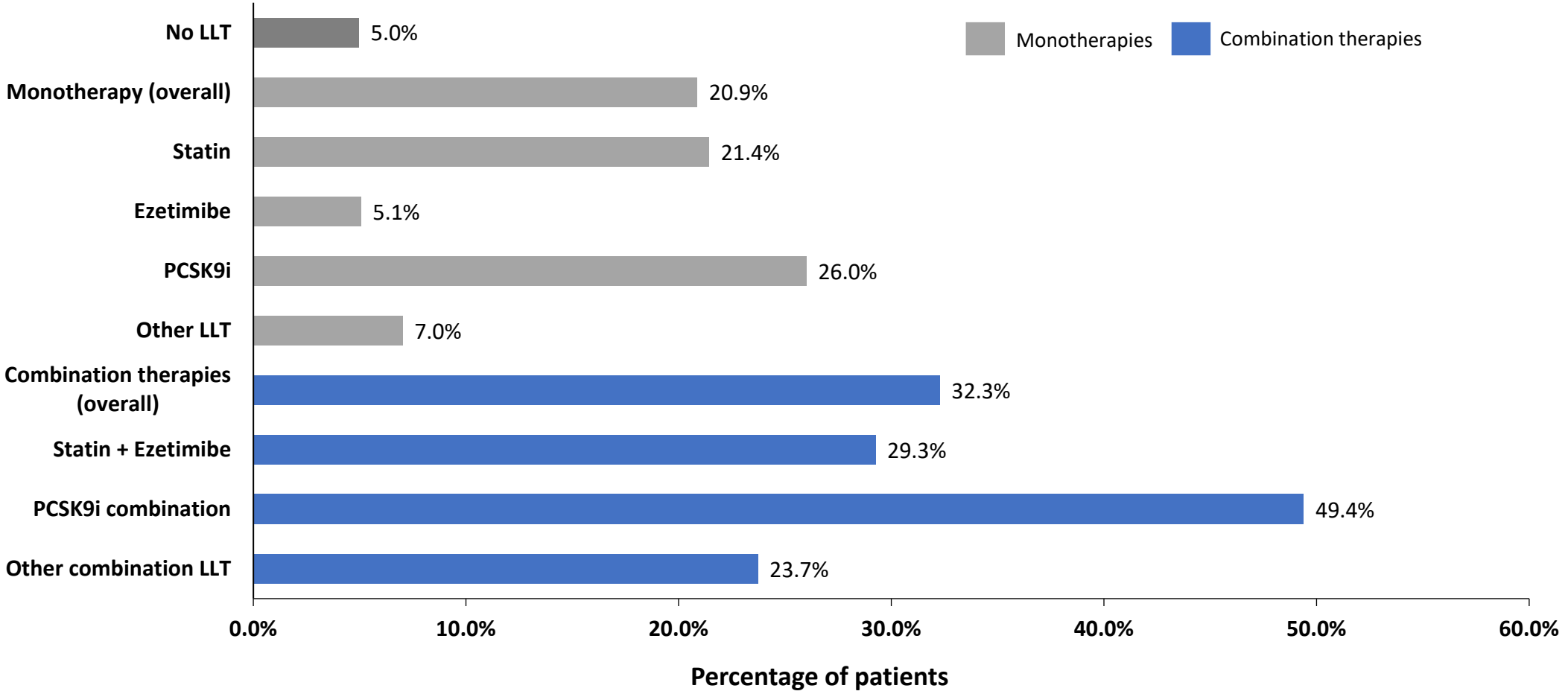
LDL-C goal attainment by CV risk, ASCVD status and lipid-lowering therapy



Median (IQR) LDL-C, mmol/L:									
2.1 (1.6, 3.0)	2.0 (1.5, 2.8)	2.4 (1.7, 3.4)	2.0 (1.5, 2.9)	2.6 (1.8, 3.5)	2.3 (1.1)‡	2.7 (1.5)‡	2.3 (1.1)‡	2.2 (1.0)†	1.9 (1.0)†

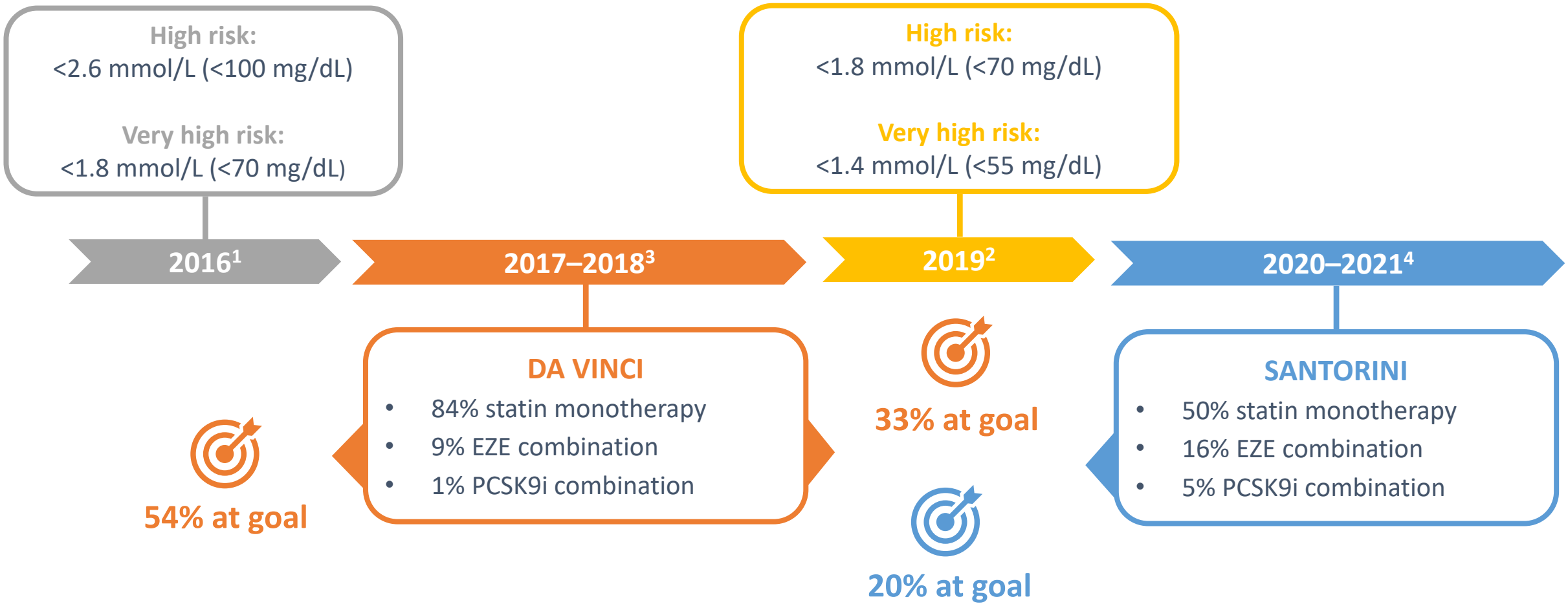
- LLT record was missing for patients n=1. Patients receiving monotherapy, n=1023/4902. Patients receiving combination therapy, n=2169. *Monotherapy including: statin alone; EZE alone; PCSK9i alone; bempedoic acid alone; any other oral LLT alone; †Combination therapy including: statin + EZE; PCSK9i combination; bempedoic acid FDC; any other oral combination therapy; ‡Data are presented as mean ± SD
- **ASCVD**, atherosclerotic cardiovascular disease; **CV**, cardiovascular; **EZE**, ezetimibe; **FDC**, fixed-dose combination; **HeFH**, familial hypercholesterolaemia **IQR**, interquartile range; **LLT**, lipid-lowering therapy; **PCSK9i**, proprotein convertase subtilisin/kexin type 9 inhibitor; **SD**, standard deviation.
- Ray KK, et al. Lancet Reg Health Eur. 2023;29:100624. https://doi.org/10.1016/j.lanepe.2023.100624

Goal Attainment by Type of LLT Regimen Used



- **LDL-C,** low-density lipoprotein cholesterol; **LLT,** lipid-lowering therapy; **PCSK9i,** proprotein convertase subtilisin/kexin type 9 inhibitor

2016–2019 ESC/EAS LDL-C goals and lipid management in clinical practice



- **EAS**, European Atherosclerosis Society; **ESC**, European Society of Cardiology; **EZE**, ezetimibe; **LDL-C**, low-density lipoprotein cholesterol; **PCSK9i**, proprotein convertase subtilisin/kexin type 9 inhibitor
- 1. Catapano AL, et al.Eur Heart J. 2016;37:2999–3058; 2. Mach F, et al. Eur Heart J. 2020;41:111–188; 3. Ray KK, et al. Eur J Prev Cardiol. 2021;28:1279–1289; 4. Ray KK, et al. Lancet Reg Health Eur. 2023;29:100624. https://doi.org/10.1016/j.lanepe.2023.100624

ESC European Society of Cardiology

European Heart Journal - Quality of Care and Clinical Outcomes (2022) **8**, 447–460
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ORIGINAL ARTICLE

Low-density lipoprotein cholesterol levels exceed the recommended European threshold for PCSK9i initiation: lessons from the HEYMANS study

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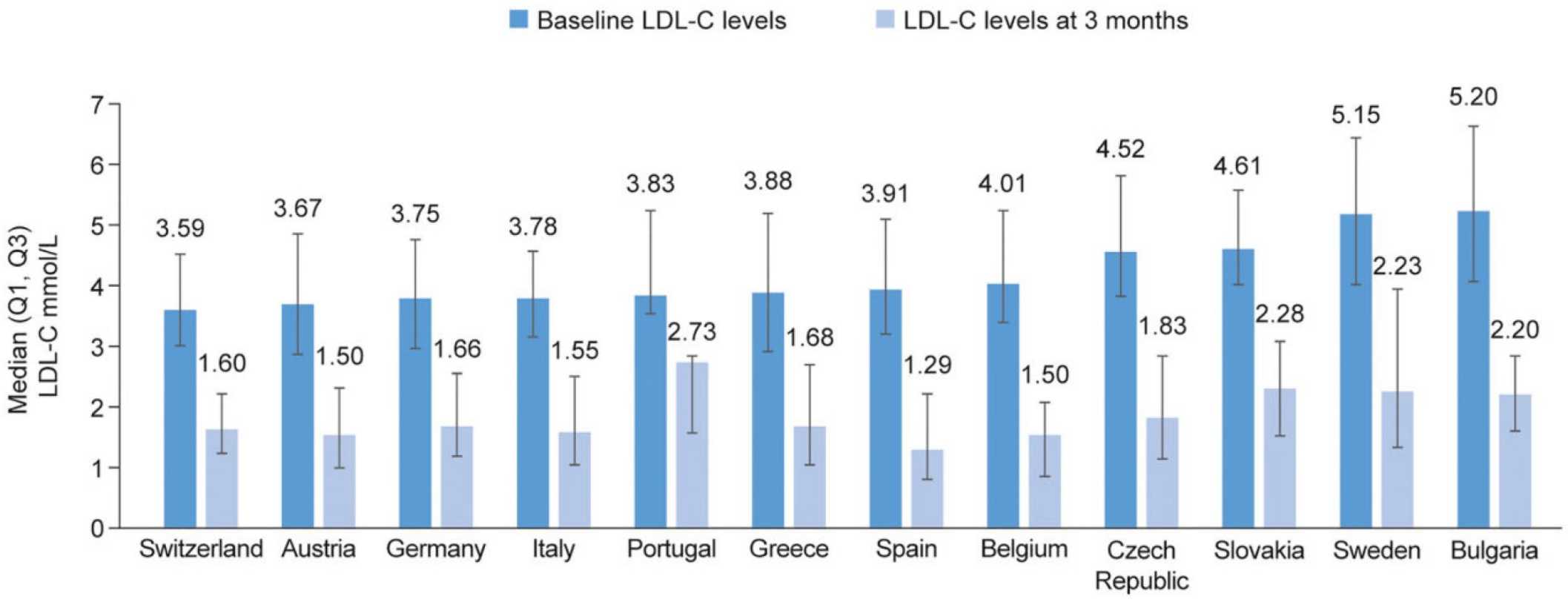
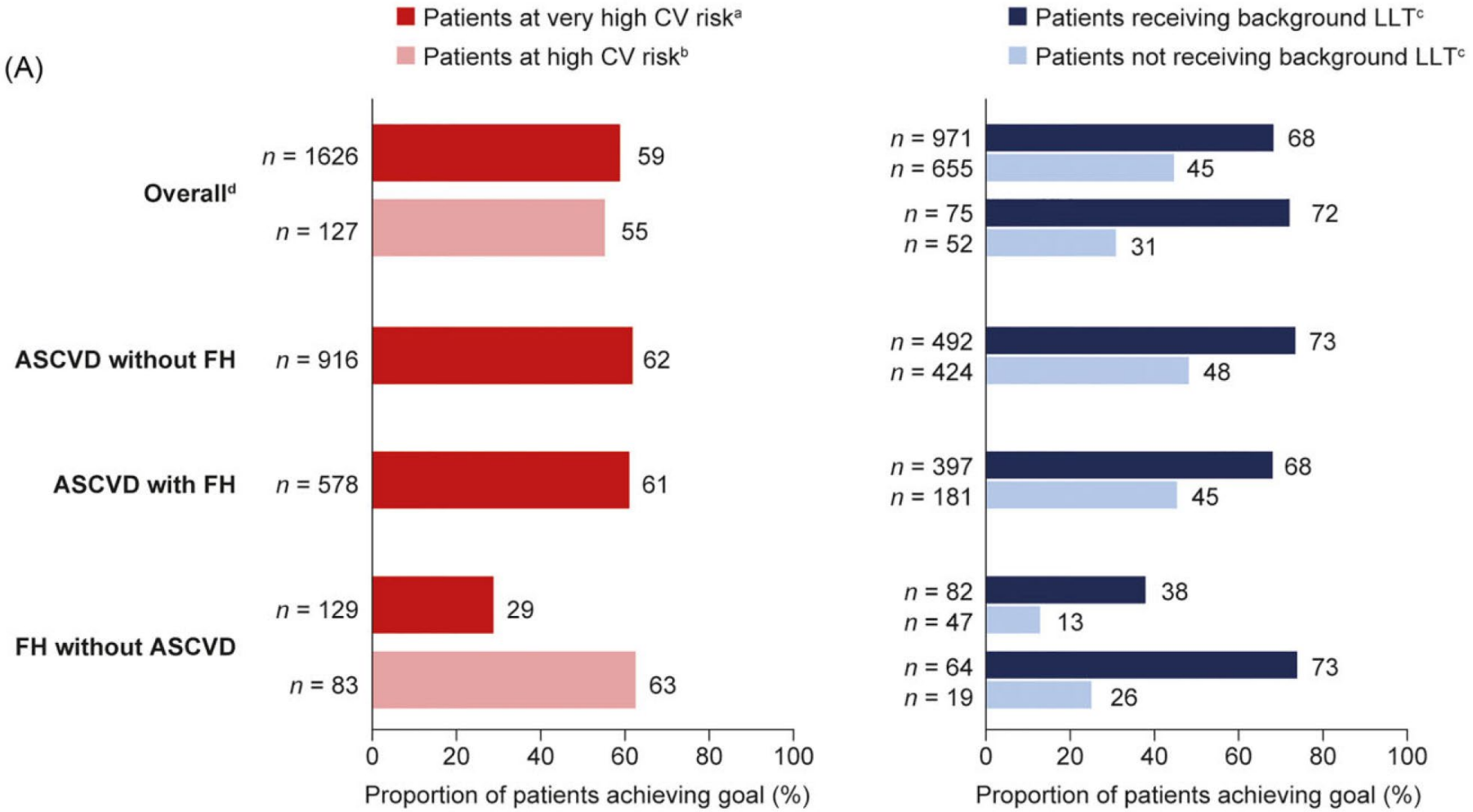
Main determinant of starting LDL-C levels and between country variation are reimbursement thresholds

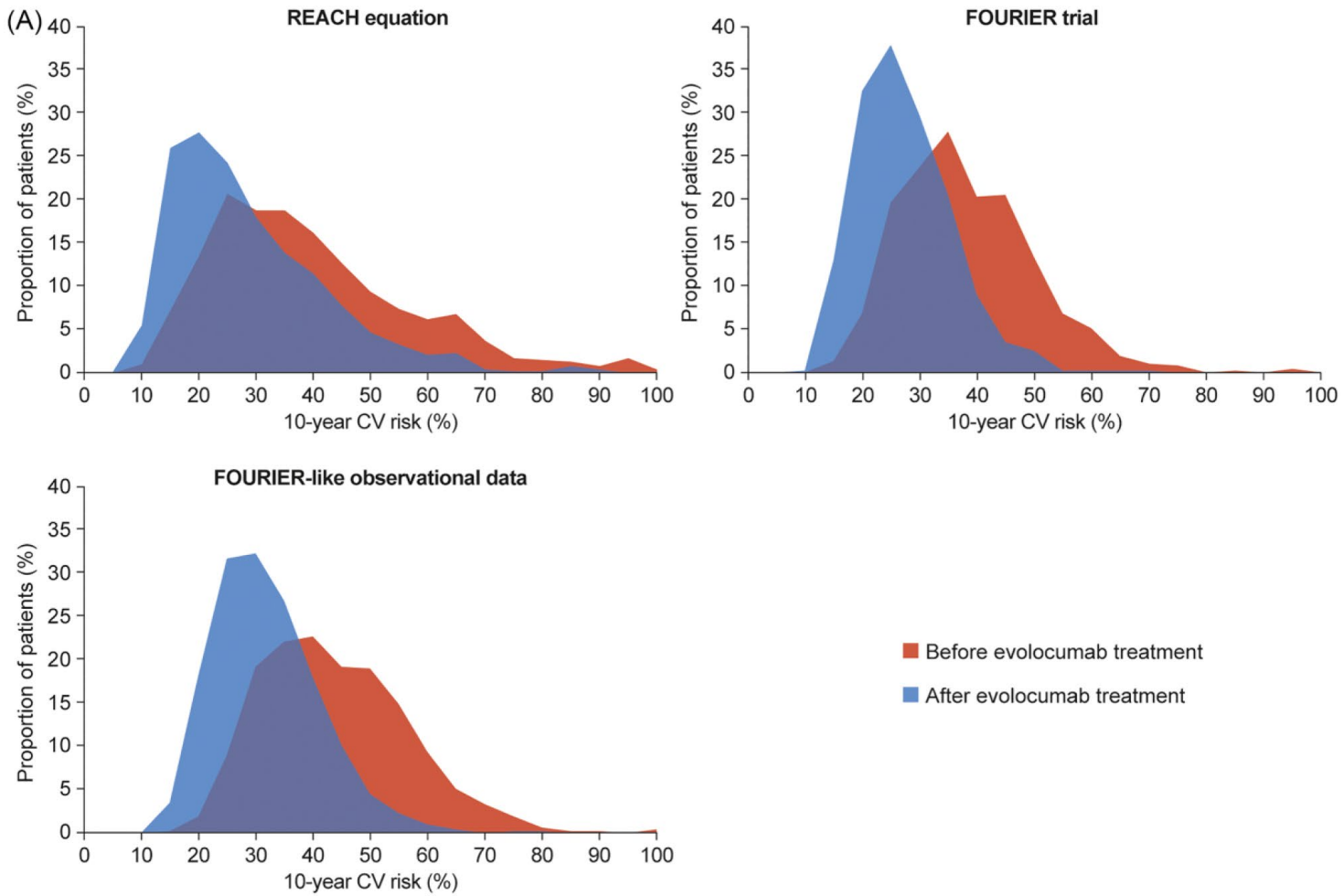


	Switzerland	Austria	Germany	Italy	Portugal	Greece	Spain	Belgium	Czech Republic	Slovakia	Sweden	Bulgaria
n =	75	364	380	311	21	132	201	91	120	125	44	88
Change from baseline (%)												
Median (Q1, Q3)	↓−54.17 (−67.16, −42.48)	↓−58.75 (−70.83, −42.62)	↓−52.81 (−67.83, −37.03)	↓−61.23 (−73.54, −49.23)	↓−62.86 (−77.78, −47.95)	↓−55.90 (−68.86, −32.18)	↓−65.92 (−76.19, −49.25)	↓−68.31 (−78.21, −54.19)	↓−63.98 (−73.11, −45.55)	↓−53.18 (−64.79, −38.67)	↓−56.12 (−66.67, −34.86)	↓−60.82 (−71.89, −43.63)

Goal attainment more likely when there is background oral LLT- i.e. we need combination therapy



Among those in whom Evolocumab was added, large predicted shifts in population risk predicted



Conclusion

- Registries over 5years show increase in use of combination therapies essential to achieve lower LDL-C goals
- Implementation lags behind the goals with respect to use of combination therapies
- Even monoclonals as monotherapy will not the entire population to goal
- Lowering LDL-C threshold for reimbursement will mean more patients become eligible for monoclonals on a background of oral LLT
- Time to discard statin monotherapy for those at highest risk and start to talk about combination therapies as a minimum with statins and ezetimibe but then perhaps a third agent whether that is an oral agent like bemepedoic acid or a PCSK9 directed injectable therapy