Integrating icosapent ethyl in CV risk reduction strategies: practical experience and guidance

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Conflicts of interest

I have received consulting and/or lecture fees from:

- Amarin, Amgen, Sanofi, Pfizer, Daiichi-Sankyo, Novartis, Boehringer, NAPP, Bayer

Essentials for incorporation of new treatments

- evidence based
- supporting national (and international) guidelines
- disseminating information locally
- establishing a specialist clinic

NICE has recommended icosapent ethyl for the secondary prevention of CV risk (TA805)

Icosapent ethyl is recommended as an option for reducing risk of CV events in adults

1. with raised **fasting TGs (≥1.7 mmol/L) and taking statins**, but only if they have:[1]

2. **established CV disease** (**secondary prevention**) defined as history of any of:
   - acute coronary syndrome
   - coronary or other arterial revascularisation
   - coronary heart disease
   - ischaemic stroke
   - peripheral arterial disease, **and**

3. LDL-C levels above 1.04 mmol/L and below or equal to 2.60 mmol/L

National Institute for Health and Care Excellence, TA805. Published: 13th July 2022.

International guidelines

European Society of Cardiology/European Atherosclerosis Society (ESC/EAS)

- CV disease with
- TG levels 135 mg/dL to 499 mg/dL *despite statin treatment*

American College of Cardiology (ACC) Consensus Statement 2021

- clinical ASCVD and
- LDL-C <70 mg/dL and
- persistent fasting TG ≥150 and
- <500 mg/dL on maximally tolerated statin therapy[1]

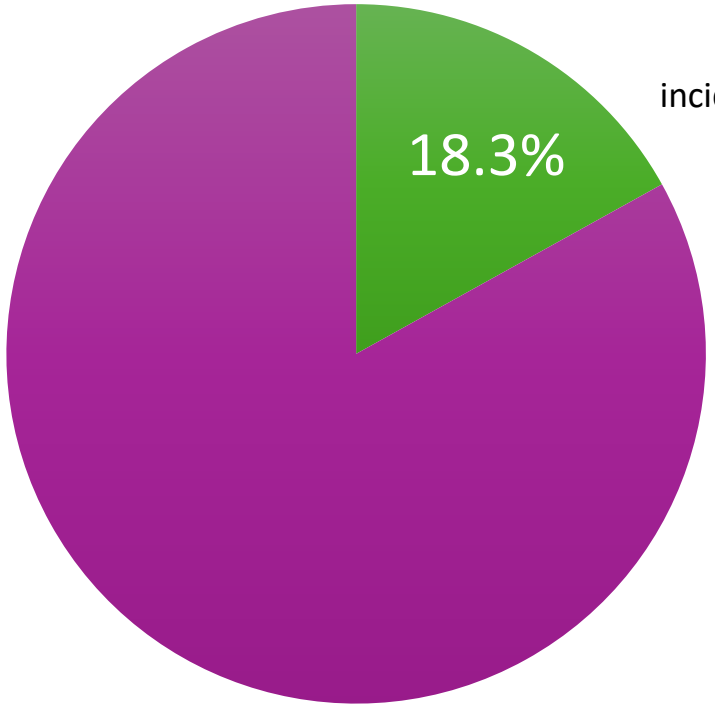
Eur Heart J. 2020;41(1):111-188

J Am Coll Cardiol. 2021;78(9):960-993

APOLLO HELICON analysis

~1 in 5 patients will suffer a MI, stroke or CV death within the first year after a MI

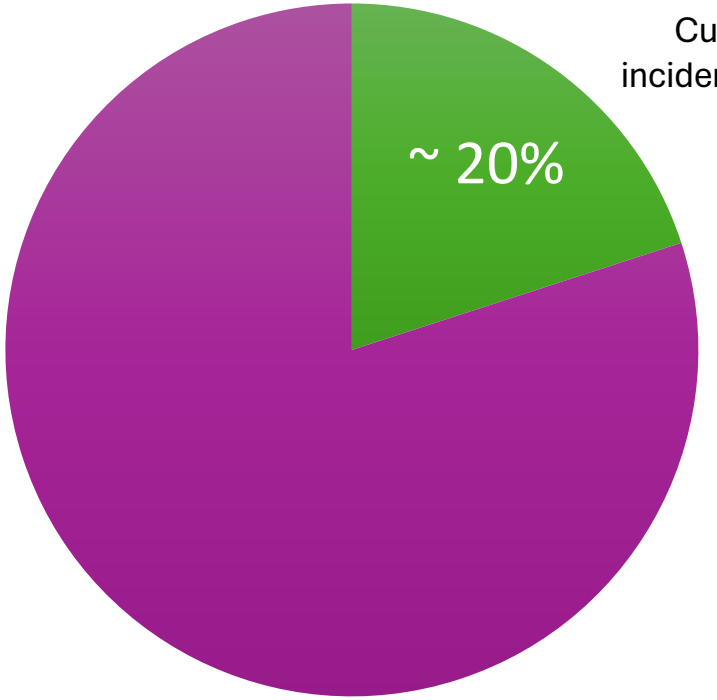
Immediate post-MI survivors (n=97,254)[1]
1-year follow-up



Cumulative 1-year incidence of CV death, MI or stroke.

~1 in 5 patients, event-free for 1-year post-MI, suffered an MI, stroke or CV death within 3 years

1-year event-free MI survivors (n=76,687)[1]
3-year follow-up

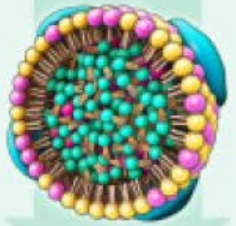
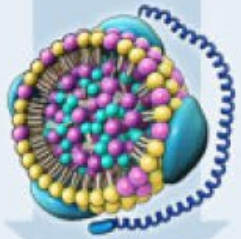
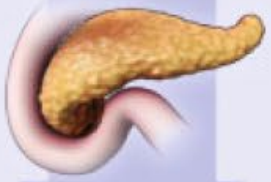


Cumulative 3-year incidence of CV death, MI or stroke

CV=cardiovascular; MI=myocardial infarction

Jernberg T et al. *Eur Heart J* 2015: doi:10.1093/eurheartj/ehu505

KNOWN PATHOPHYSIOLOGICAL MECHANISMS OF CARDIOVASCULAR RISK

Biological Issue	Residual Cholesterol Risk	Residual Inflammatory Risk	Residual Thrombotic Risk	Residual Triglyceride Risk	Residual Lp(a) Risk	Residual Diabetes Risk
						
Critical Biomarker	LDL-C ≥100 mg/dL	hsCRP ≥2mg/L	No simple biomarker	TG ≥150mg/dL	Lp(a) ≥50mg/dL	HbA1c Fasting glucose
Potential Intervention	Targeted LDL/Apo B Reduction	Targeted Inflammation Reduction	Targeted Antithrombotic Reduction	Targeted Triglyceride Reduction	Targeted Lp(a) Reduction	SGLT2 Inhibitors GLP-1 Agonists

Reference:
1. Adapted from: Lawler, PR et al. Targeting cardiovascular inflammation: next steps in clinical translation European Heart Journal (2021) 42, 113–131;

Subgroup analysis: CV benefit of IPE independent of baseline LDL-C levels

LDL-C by tertiles

Primary endpoint in subgroups[1]	Icosapent ethyl n/N (%)	Placebo n/N (%)	HR (95%CI)	Int P value
Baseline LDL-C				
• ≤1.73 mmol/L (67 mg/dL)	244/1481 (16.5%)	302/1386 (21.8%)	0.72 (0.61–0.85)	0.62
• >1.73 and ≤2.17 mmol/L (>67 and ≤84 mg/dL)	248/1347 (18.4%)	307/1364 (22.5%)	0.81 (0.68–0.96)	
• >2.17 mmol/L (> 84 mg/dL)	213/1258 (16.9%)	292/1339 (21.8%)	0.74 (0.62–0.89)	

LDL-C < or ≥ 1.4 mmol/L (55 mg/dL)

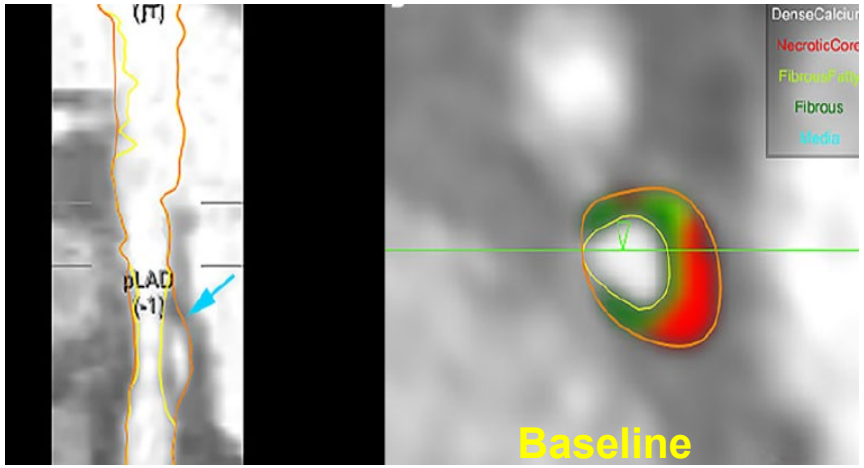
Primary endpoint in subgroups[2]	Icosapent ethyl n/N (%)	Placebo n/N (%)	HR (95%CI)	Int P value
Baseline LDL-C				
• <1.4 mmol/L (< 55 mg/dL)	89/549 (16.2%)	116/509 (22.8%)	0.66 (0.50–0.87)	0.40
• ≥1.4 mmol/L (≥ 55 mg/dL)	616/3537 (17.4%)	785/3580 (21.9%)	0.76 (0.69–0.85)	

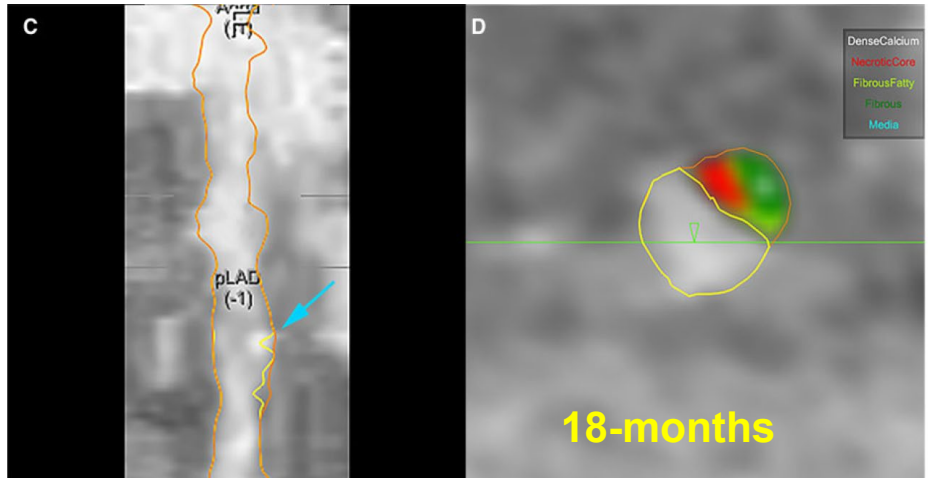
CV benefit for IPE reported irrespectively of baseline LDL-C, even among patients with lowest baseline LDL-C, controlled as per current guidelines. This indicates that CV benefit associated with IPE was independent of LDL-C levels.

1. Bhatt DL et al. *N Engl J Med.* 2019;380(1), prespecified subgroups; 2. Aggarwal et al. ACC 2024 Abstract; *JACC* 83(13), Suppl A., post-hoc analysis

Elucidating the MOA of icosapent ethyl[1]- **EVAPORATE** study

CTCA in a 54-year-old male with diabetes, hypertension, and hyperlipidemia on optimal statin therapy

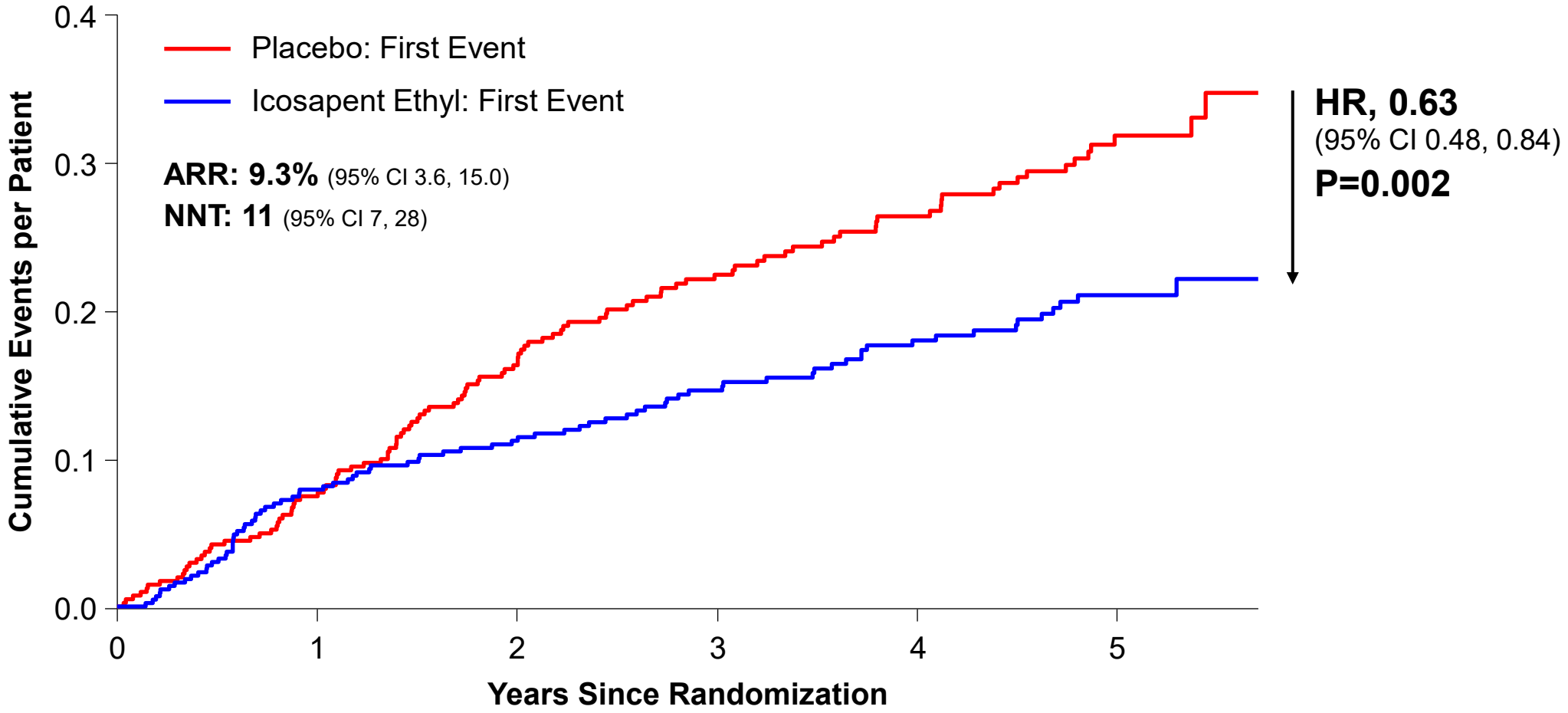




CTCA, Coronary computed tomography angiogram; MOA, Mode of action.

1. Budoff MJ, *et al. Eur Heart J.* 2020;41:3925–3932

Time to First Event, Primary Composite Endpoint in Patients with Recent ACS <12 Months



No. at Risk:						
Placebo	407	395	373	311	253	150
Icosapent Ethyl	433	425	402	338	284	142

Steg PG, Bhatt DL, Miller M, et al. ACC 2023.

ACS Medicines Optimisation Clinic

- run by senior pharmacist and consultant
- high risk ACS patients identified using PEGASUS criteria (any 2 of: second ACS, age >65yo, MVD, T2DM, CKD>3, PAD) at discharge
- letter sent for appointment at 3 months
- lipid profile repeated on standard discharge medication (atorvastatin 80mg od)

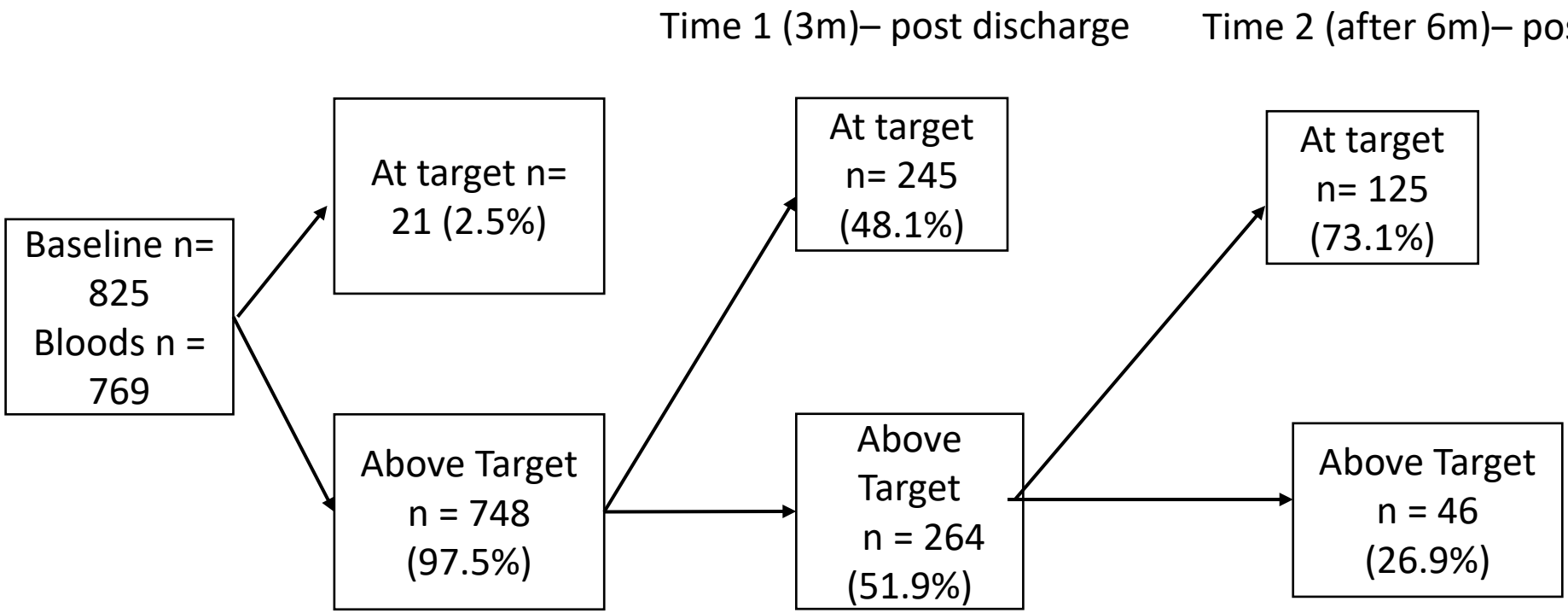
Establishing criteria for prescribing and to comply with NICE Guidelines

- secondary prevention of CV disease already on maximally tolerated statins and TG ≥ 1.7mmol/L (even though substudy analysis……..)

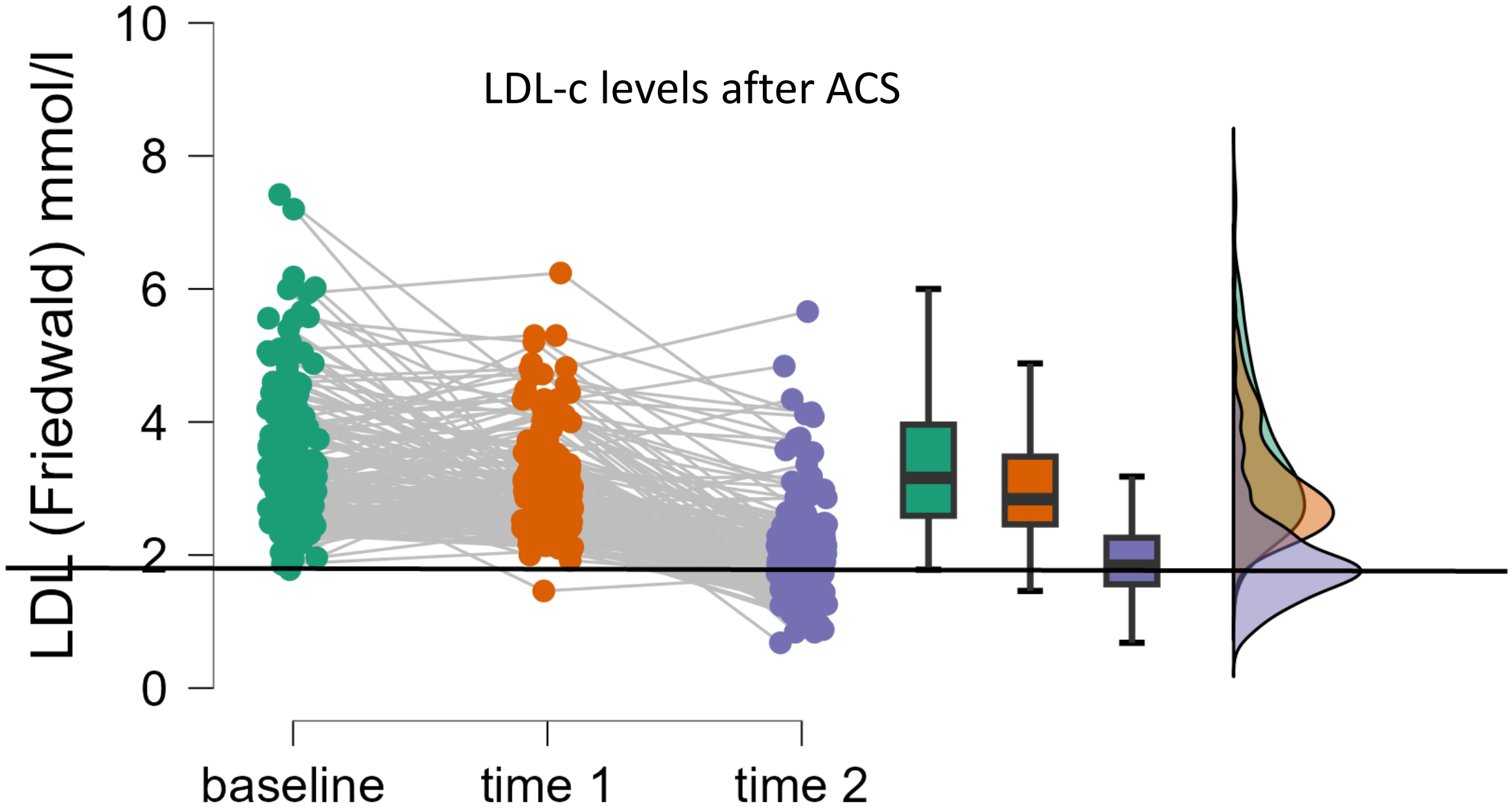
- patients with diabetes mellitus and ASCVD and TG ≥ 1.7mmol/L

Patients seen since June 2023

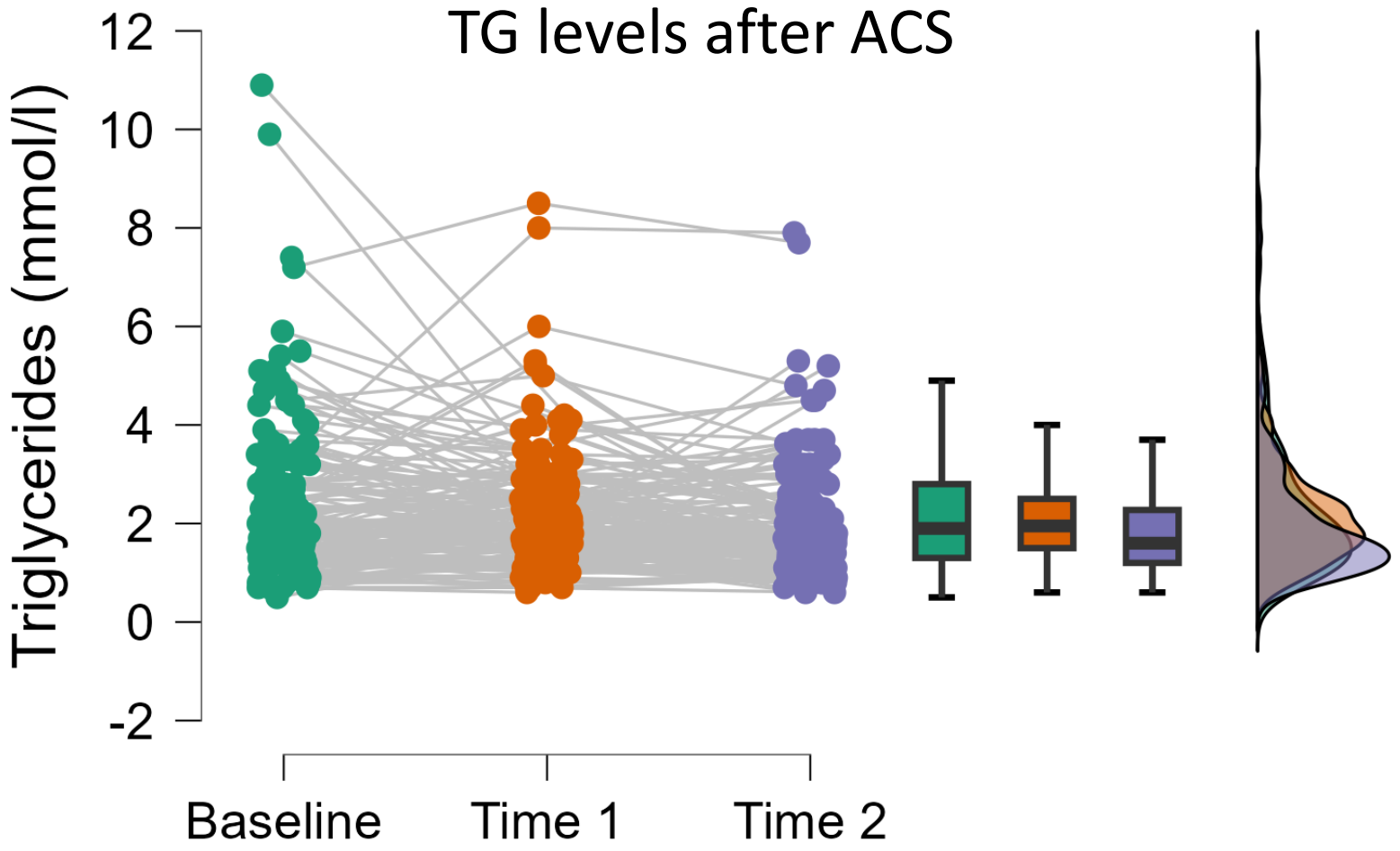
- "high risk" ACS patients – any 2 or more of: *second ACS, MVD, PVD, T2DM, CKD>3, age>65yo*
  - Post cardiology appointment (time1) – 476 with paired data
  - Post pharmacy intervention (time2) – 166 with all three time points



LDL-c levels after ACS



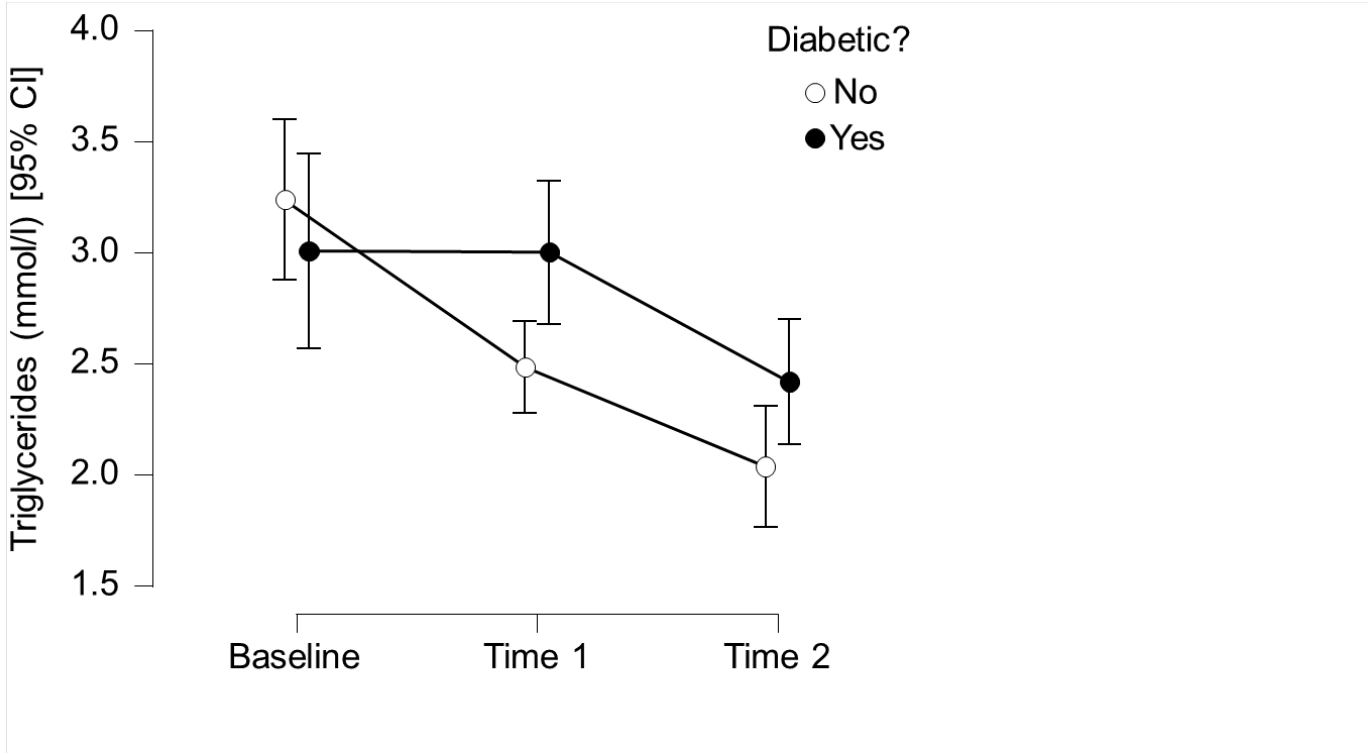
Mean drop (mmol/l)	**0.35**	**1.07**
SD	1.13	0.85
d (95% C.I.)	0.31 [0.15 – 0.46]	1.25 [1.05 – 1.45]



- Time 2 is significantly different to baseline (p=.001) and Time 1 (p=.009)
- Time 1 is not significantly different to baseline (p=.50)

Clinic data: Of 166 patients with TG measurements at all 3 timepoints, 89 patients had TG >1.7

	Baseline	Time 1	Time 2	Totals (95% CI]
Non-Diabetic (n=52)	3.29 (1.86)	2.49 (1.19)	2.04 (1.23)	2.57 [2.23 - 2.91]
Diabetic (n=37)	3.01 (1.26)	3.00 (1.34)	2.42 (1.35)	2.79 [2.46 - 3.13]
Totals (95% CI]	3.10 [2.81 - 3.40]	2.73 [2.42 - 3.02]	2.21 [1.92 - 2.51]	



Clinic data

- High risk ACS patients have elevated LDL-c and TGs
- Both respond to maximally tolerated lipid lowering therapy
- After treatment over 53% of patients remain with TG level above NICE recommended levels >1.7mmol/L
- ACS focused clinic facilitates guideline recommended treatment of LDL-c
- And allows identification of patients with elevated TG suitable for treatment

Summary

- CV disease has multiple pathophysiological mechanisms
- “Optimally” treated ACS patients have 18% recurrent ischaemia event within one year
- Known risk factors should be optimised to guideline levels
- Trial data shows that even if LDL-c optimised, integrating icosapent ethyl in CV risk reduction strategies may help to further reduce recurrent ischaemic events after ACS
- Dedicated ACS clinic facilitates identification and treatment of high-risk patients