



The **Homburg **C**ream and **S**ugar Study (HCS):
Prospective evaluation of postprandial triglycerides and
cardiovascular events in patients with coronary artery disease**

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Disclosures:

U. Laufs has received honoraria for lectures from AstraZeneca, Boehringer-Ingelheim, Daiichi-Sankyo, Essex, MSD Sharp & Dohme, Novartis, Roche, Sanofi, Servier, Trommsdorff

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ClinicalTrials.gov number: NCT00628524

The Homburg Cream and Sugar Study (HCS)

BACKGROUND

- Risk prediction by **fasting serum triglycerides** in patients at high cardiovascular risk remains uncertain.
- **Postprandial triglycerides** may be risk modifiers in secondary prevention.
- Postprandial triglycerides and **glucose tolerance** have not been assessed simultaneously in a prospective study in high risk patients.

Chapman MJ et al. Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management. *Eur Heart J* 2011;32:1345-61

Miller M et al. Triglycerides and cardiovascular disease: a scientific statement from the american heart association. *Circulation* 2011;123:2292-333

BACKGROUND

Postprandial increase of triglycerides



0h

3h

4h

5h

Time after meal

Factors affecting serum concentrations of TG-rich lipoproteins:

time of food intake

composition of food

glucose metabolism, insulin

lipid metabolism, HDL-C

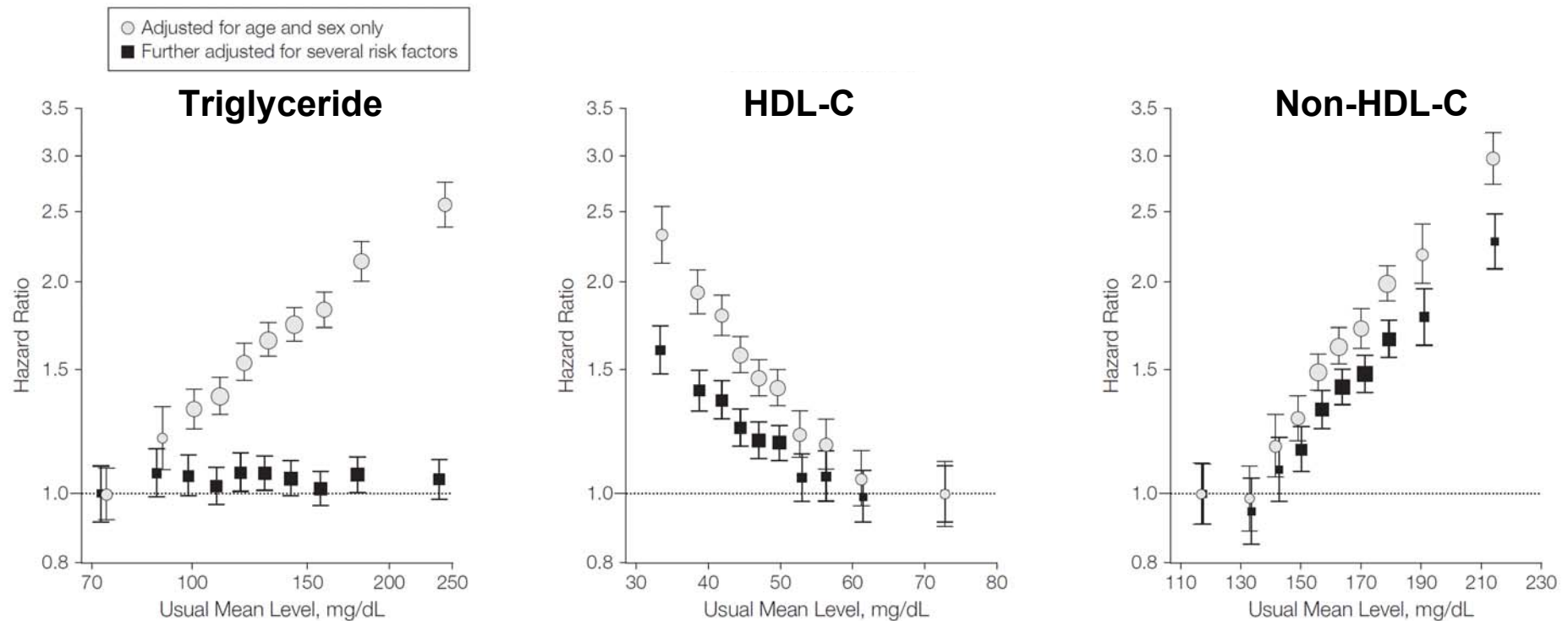
medication

comorbidities

genetic predisposition

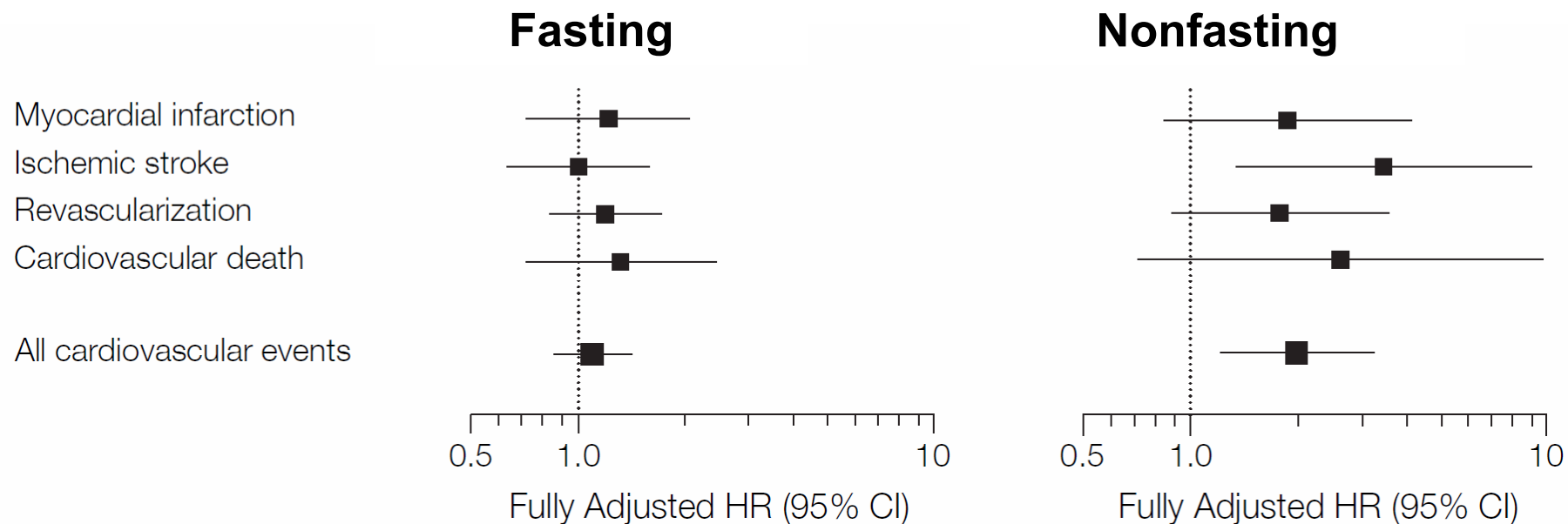
Fasting triglycerides, HDL-C, non-HDL-C and hazard ratios for coronary heart disease

68 studies in 302 430 participants without prior history of CVD



Association of nonfasting triglyceride levels with cardiovascular events in healthy individuals

N=26.509 Women's Health Study (20.118 fasting, 6.391 nonfasting), 11.4 years

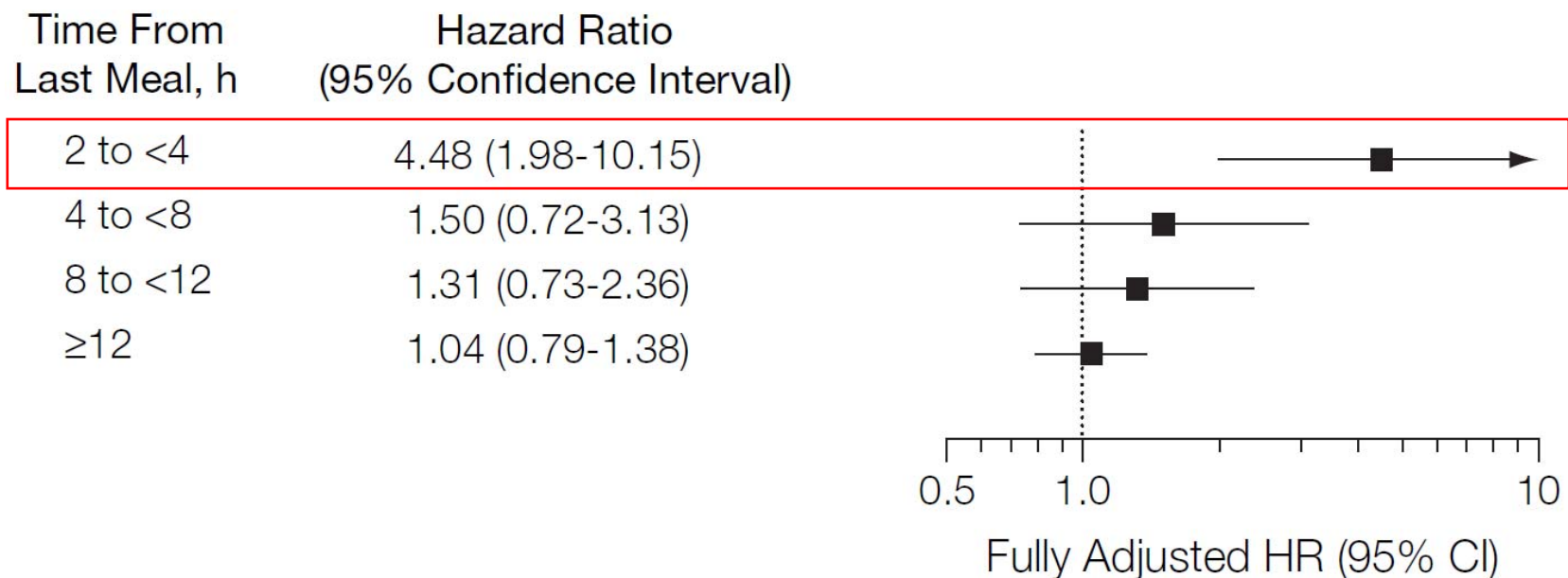


Bansal S et al., Women's Health Study, JAMA 2007;298(3):309-16

Nordestgaard BG et al., Copenhagen City Heart Study, JAMA 2007;298(3):299-308

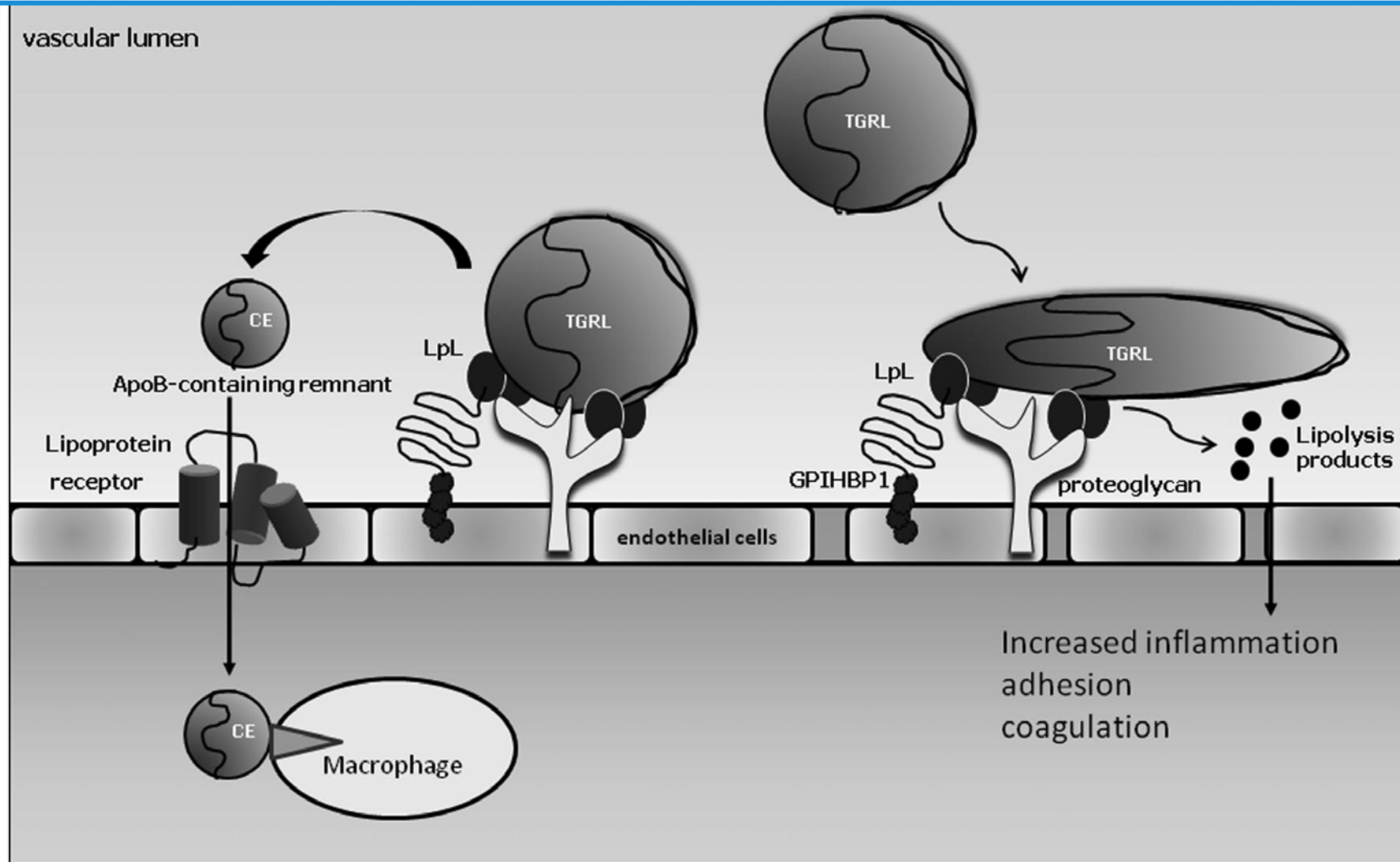
Association of nonfasting triglyceride levels with cardiovascular events in healthy individuals

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BACKGROUND - PATHOPHYSIOLOGY

Atherogenicity of triglyceride-rich lipoproteins



Remnant hypothesis

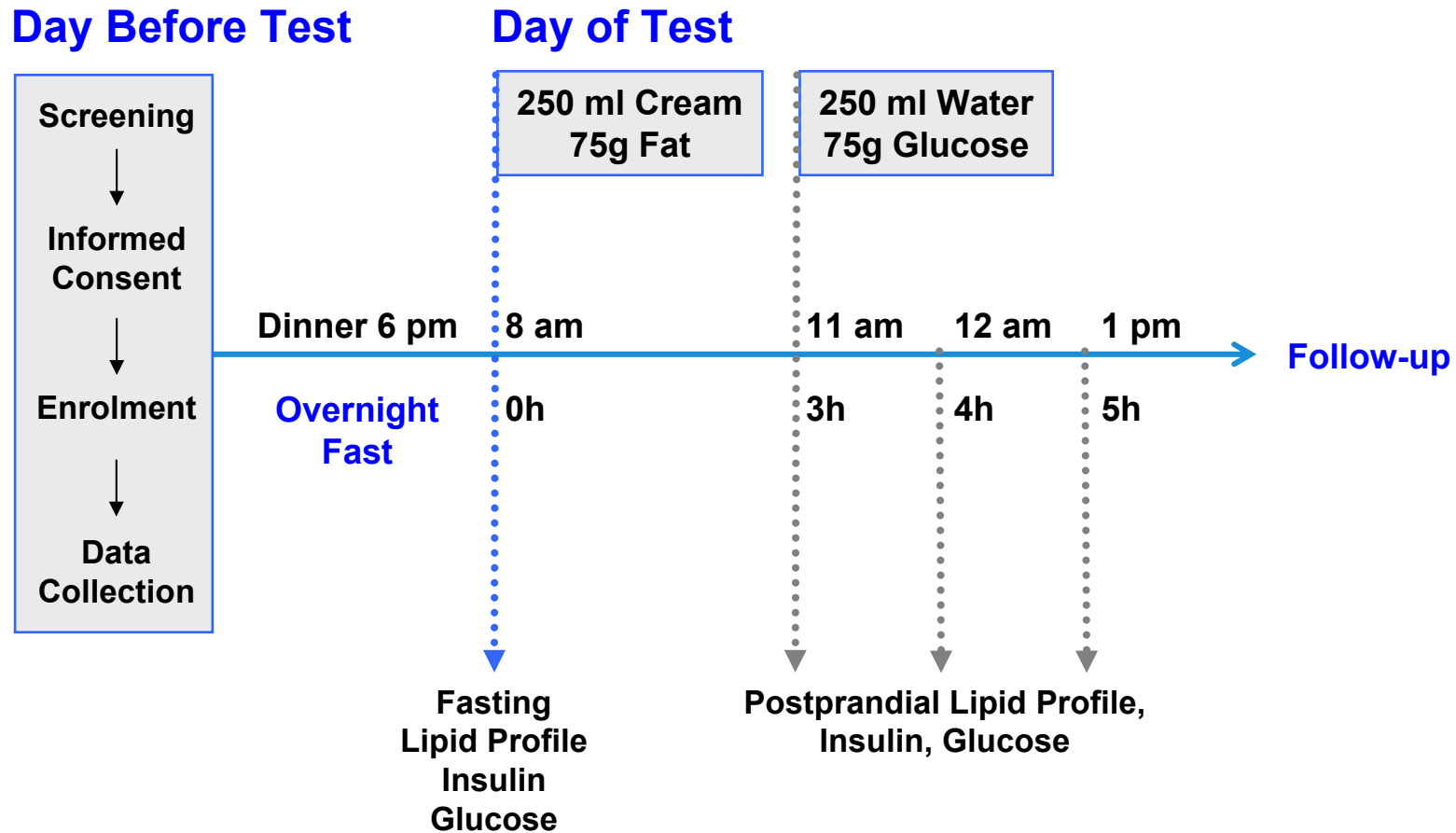
Lipolytic toxin hypothesis

The Homburg Cream and Sugar Study (HCS) AIMS

To determine whether characterization of postprandial triglyceride kinetics may

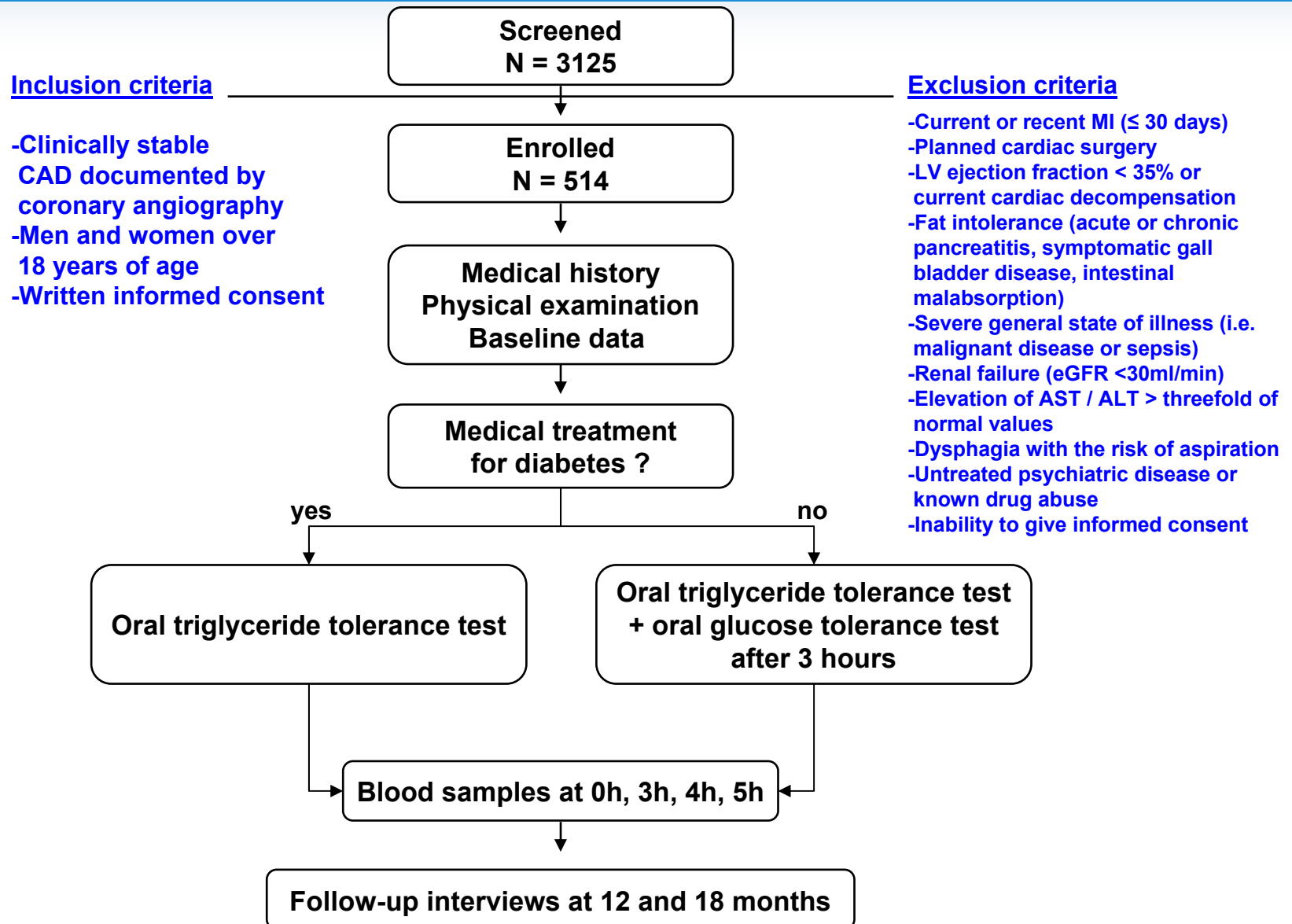
- improve the prediction of cardiovascular events**
- in addition to the assessment of glucose tolerance and traditional risk factors**
- in patients with coronary artery disease.**

The Homburg Cream and Sugar Study (HCS) SEQUENTIAL METABOLIC TEST PROTOCOL



Patients with known diabetes received fat only

The Homburg Cream and Sugar Study (HCS) DESIGN



The Homburg Cream and Sugar Study (HCS) OUTCOME

18 months follow-up

Primary outcome:

composite of cardiovascular death and cardiovascular hospitalization

Definition of cardiovascular hospitalization:

unstable angina and myocardial infarction, **unplanned symptom-induced coronary angiography**, heart failure, ischemic stroke, transitory ischemic attack, vascular disease requiring revascularization, cardiac arrhythmia requiring cardiopulmonary resuscitation, unplanned cardiac device implantation

The Homburg Cream and Sugar Study (HCS)

PATIENT CHARACTERISTICS

N 514
 Age (years) 66.4±10.1
 Male 82.9 %

Clinical characteristics

Smoking (active) (%) 18.9
 Alcohol >3x / week (%) 23.9
 Positive family history (%) 31.7
 Arterial hypertension (%) 92.9
 Systolic BP (mmHg) 126.7±15.8
 Diastolic BP (mmHg) 74.6±9.2
 LV ejection fraction (%) 64.0±12.9
 Heart rate (min⁻¹) 66.7±9.1
 Body mass index (kg/m²) 28.9±4.2
 Waist circumference (cm) 103.6±11.4
 Waist-to-hip-ratio 1.00±0.1

Metabolic characterisation

Normal glucose tolerance (%) 24.5
 Impaired glucose tolerance (%) 29.2
 Diabetes mellitus (%) 46.3
 Metabolic syndrome (%) 53.7
 Fasting glucose (mg/dl) 120.7±27.4
 HOMA index (mg/dl*µIU/ml) 3.54±5.2
 HbA1c (%) 6.17±1.1
 Total cholesterol (mg/dl) 173.0±38.8
 HDL cholesterol (mg/dl) 44.8±13.8
 LDL cholesterol (mg/dl) 105.1±33.9

Medication (%)

Platelet inhibitors 97.3
 ACE-I / ARB 95.5
 Beta-blockers 93.5
 Diuretics 43.9
 Statins 94.6

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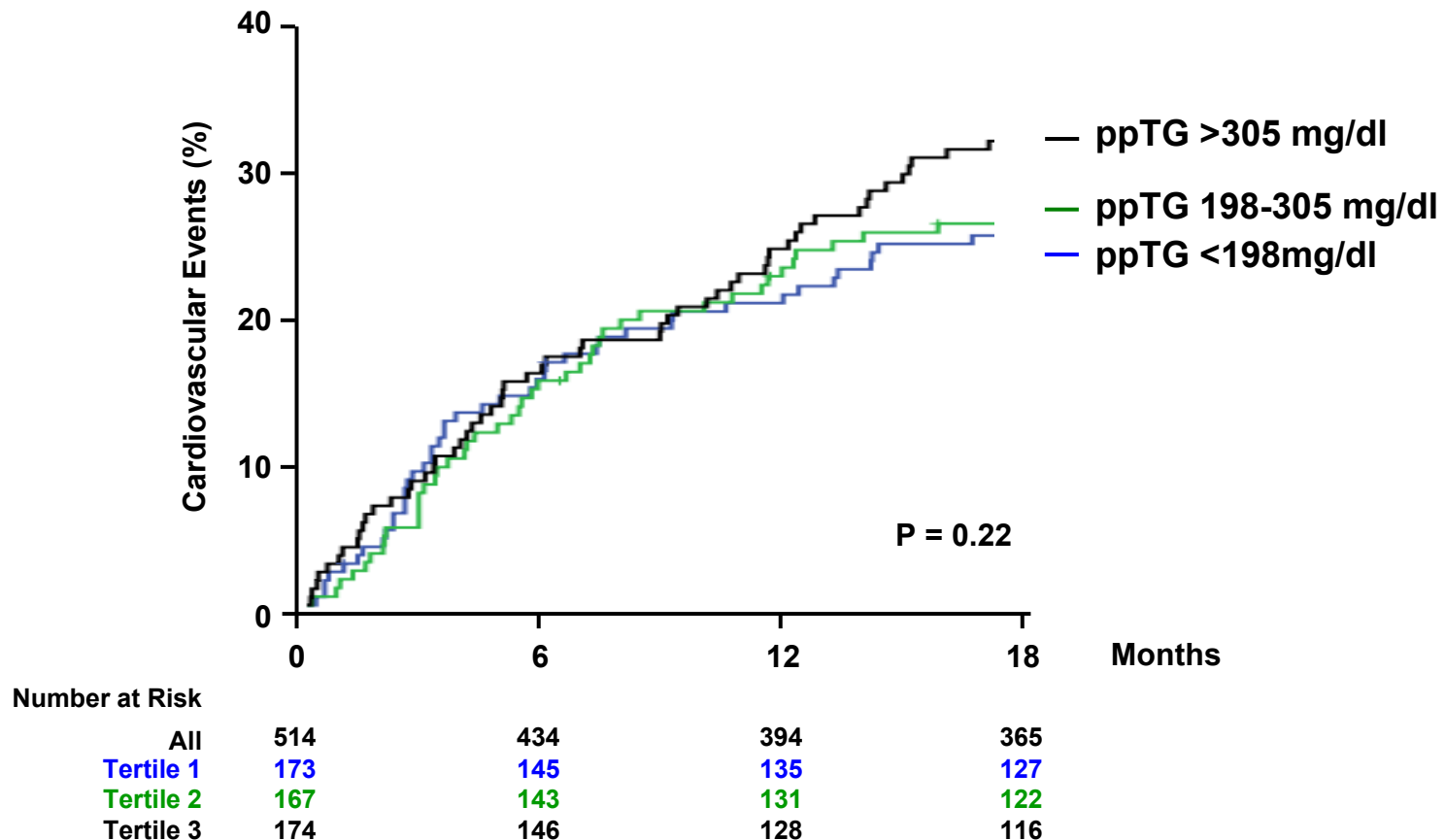
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HCS - OUTCOMES

Postprandial triglycerides do not predict outcome

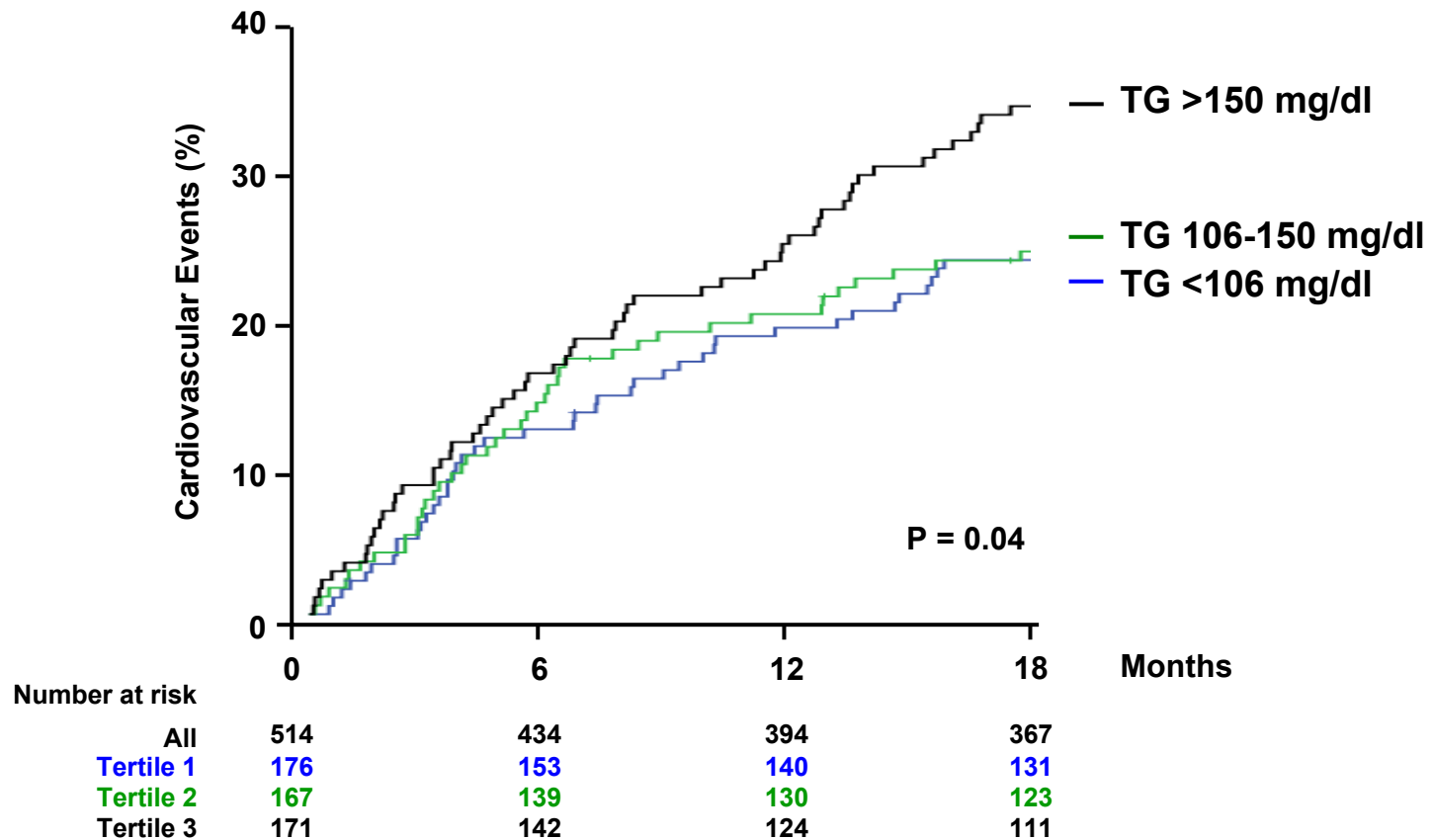
Kaplan-Meier plots of primary outcome events (cardiovascular death and cardiovascular hospitalization) in the total cohort up to 18 months stratified by tertiles of maximal postprandial triglyceride serum concentrations



HCS - OUTCOMES

Increased number of events in patients with fasting TG >150mg/dl

Kaplan-Meier plots of primary outcome events (cardiovascular death and cardiovascular hospitalization) in the total cohort up to 18 months stratified by fasting triglyceride tertiles



HCS - OUTCOMES

Fasting, but not postprandial TG predict outcome in total cohort

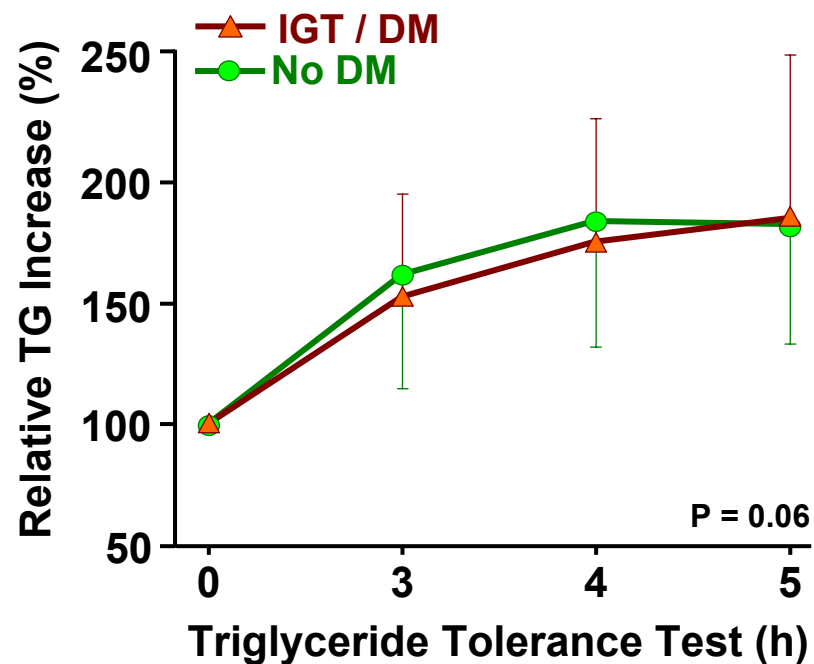
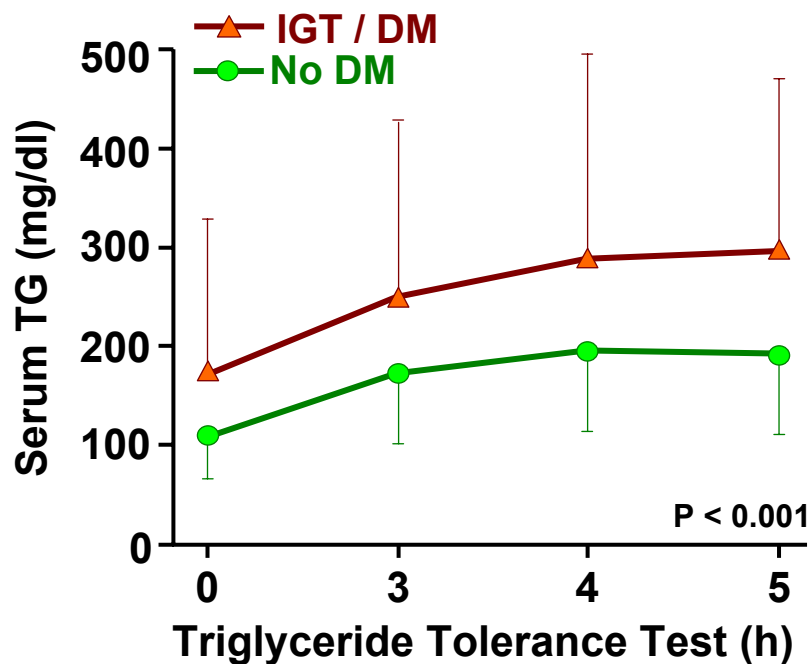
cumulative primary endpoints and TG tertiles in total cohort, n=514

	Tertile 1	Tertile 2	Tertile 3	P-value
	<i>number (rate)</i>	<i>number (rate)</i>	<i>number (rate)</i>	
Fasting triglycerides	58 (33.0)	56 (33.5)	93 (54.4)	0.01*
Postprandial TG maximum	68 (39.3)	57 (34.1)	82 (47.1)	0.30
Absolute triglyceride increase	66 (38.2)	75 (44.4)	66 (38.4)	0.70
Area under the curve	53 (31.0)	71 (41.8)	83 (48.0)	0.12
Incremental area under the curve	69 (40.8)	69 (40.8)	69 (39.2)	0.98
Relative triglyceride increase	64 (37.4)	67 (40.6)	76 (42.7)	0.80

*significance is lost in multivariable analysis, e.g. by including age and gender or HDL-C

HCS - Metabolism

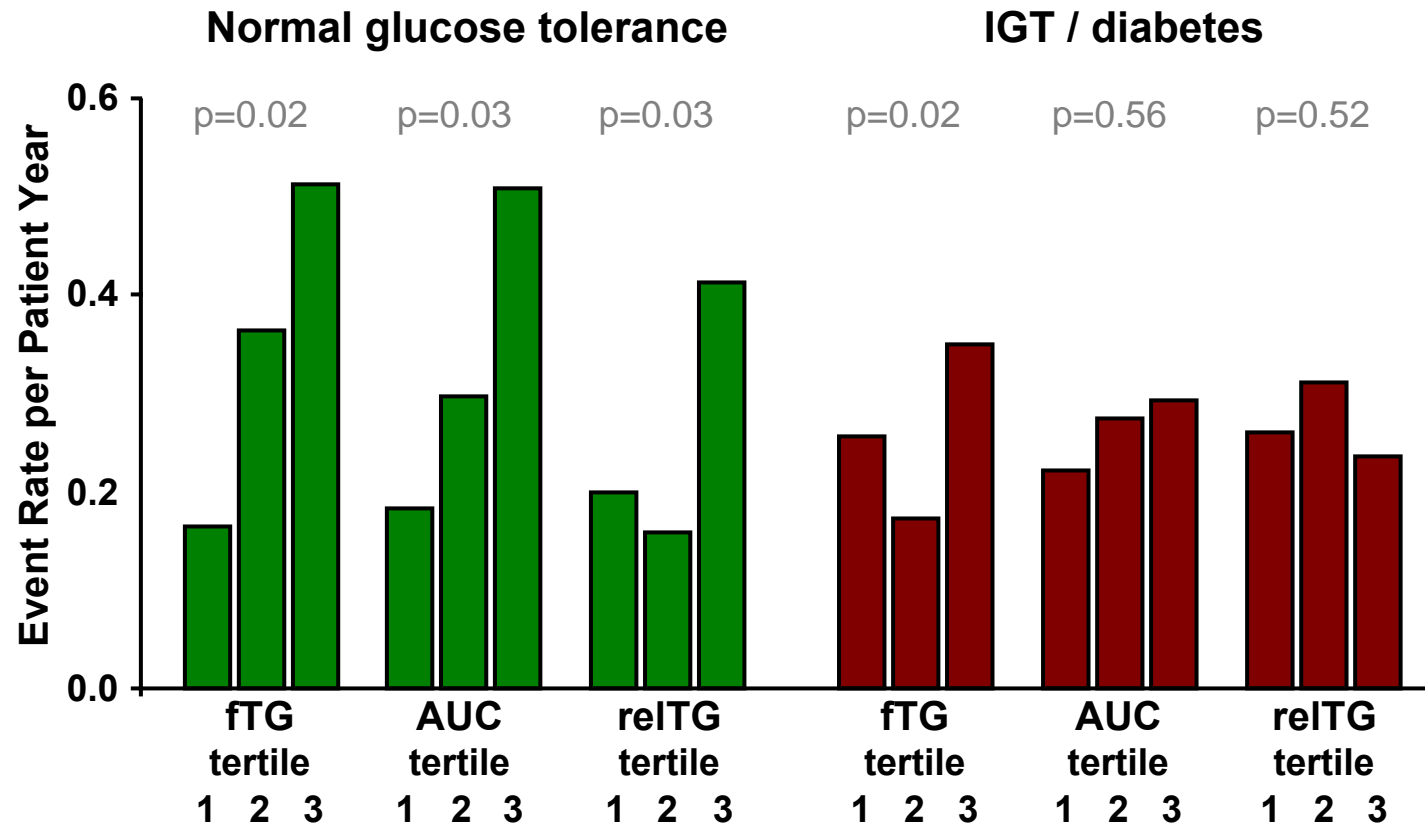
Postprandial triglyceride kinetics and glucose tolerance



	All	No DM	IGT / DM	<i>P-Value</i>
Fasting Triglycerides (mg/dl)	156.1±140.7	108.1±42.0	171.8±157.1	<0.001
Absolute TG increase (mg/dl)	134.2±99.5	103.6±62.7	144.1±107.0	<0.001
Area Under the Curve (mg/dl)	1082±722.1	788.3±306.5	1177±789.7	<0.001
Relative TG Increase (%)	195.4±58.2	200.3±55.5	194.4±59.0	0.15

HCS: Postprandial TG predict outcomes only in patients with normal glucose tolerance

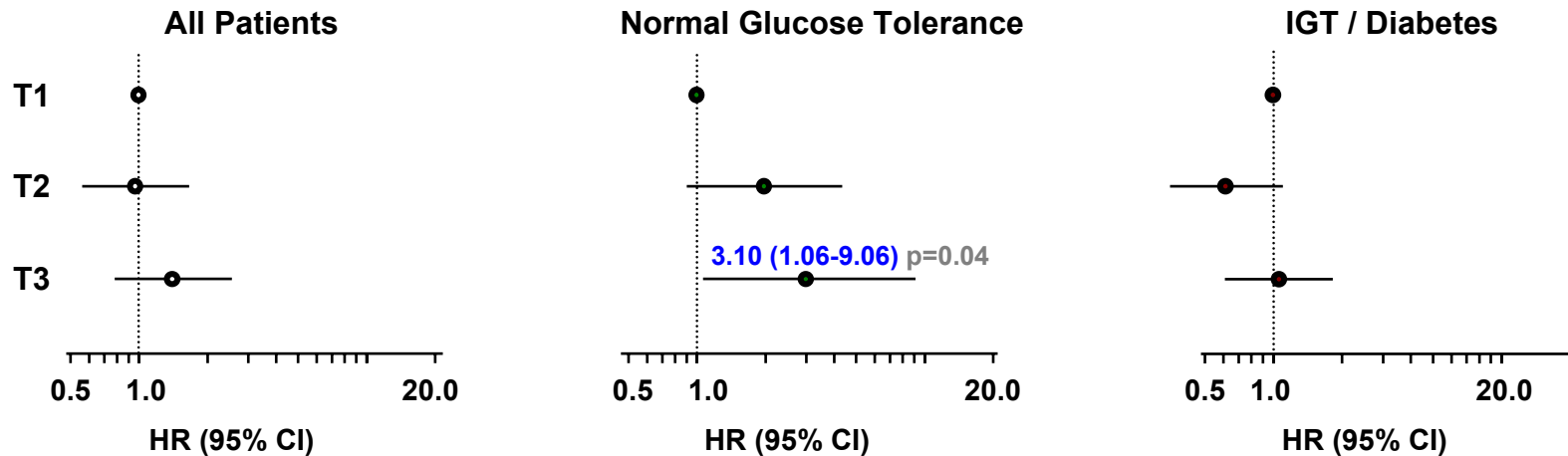
cumulative primary endpoints and TG tertiles



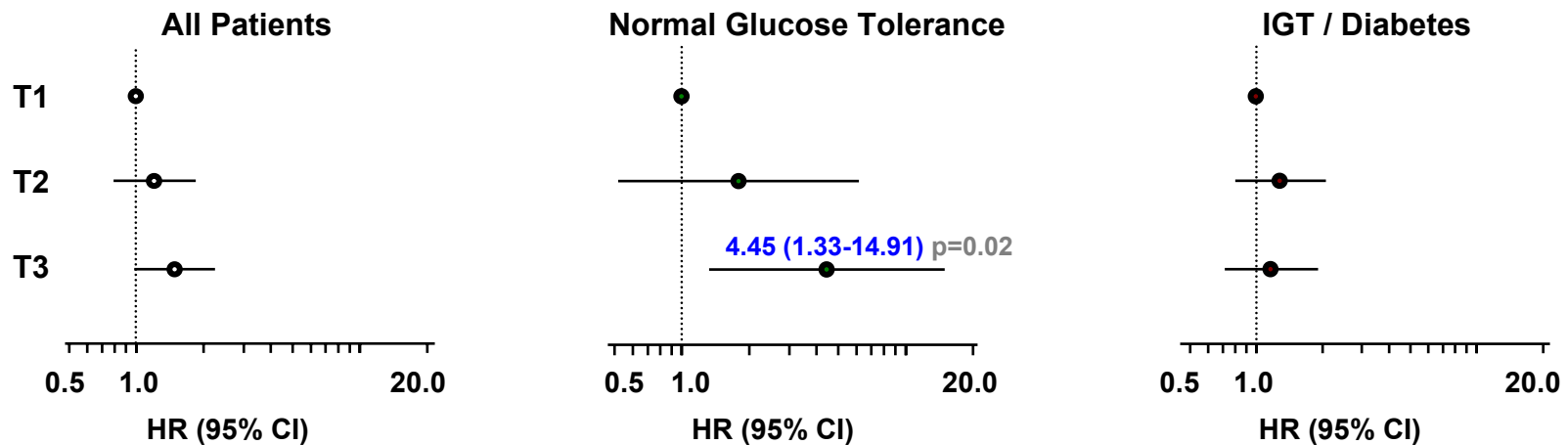
fTG, fasting triglyceride concentrations; AUC, area under the curve; reITG, relative TG increase (% vs. fasting); statistical test: ANOVA

HCS: Fasting and postprandial TG independently predict outcomes in patients with normal glucose tolerance

Fasting Triglycerides



Relative Increase of Postprandial Triglycerides

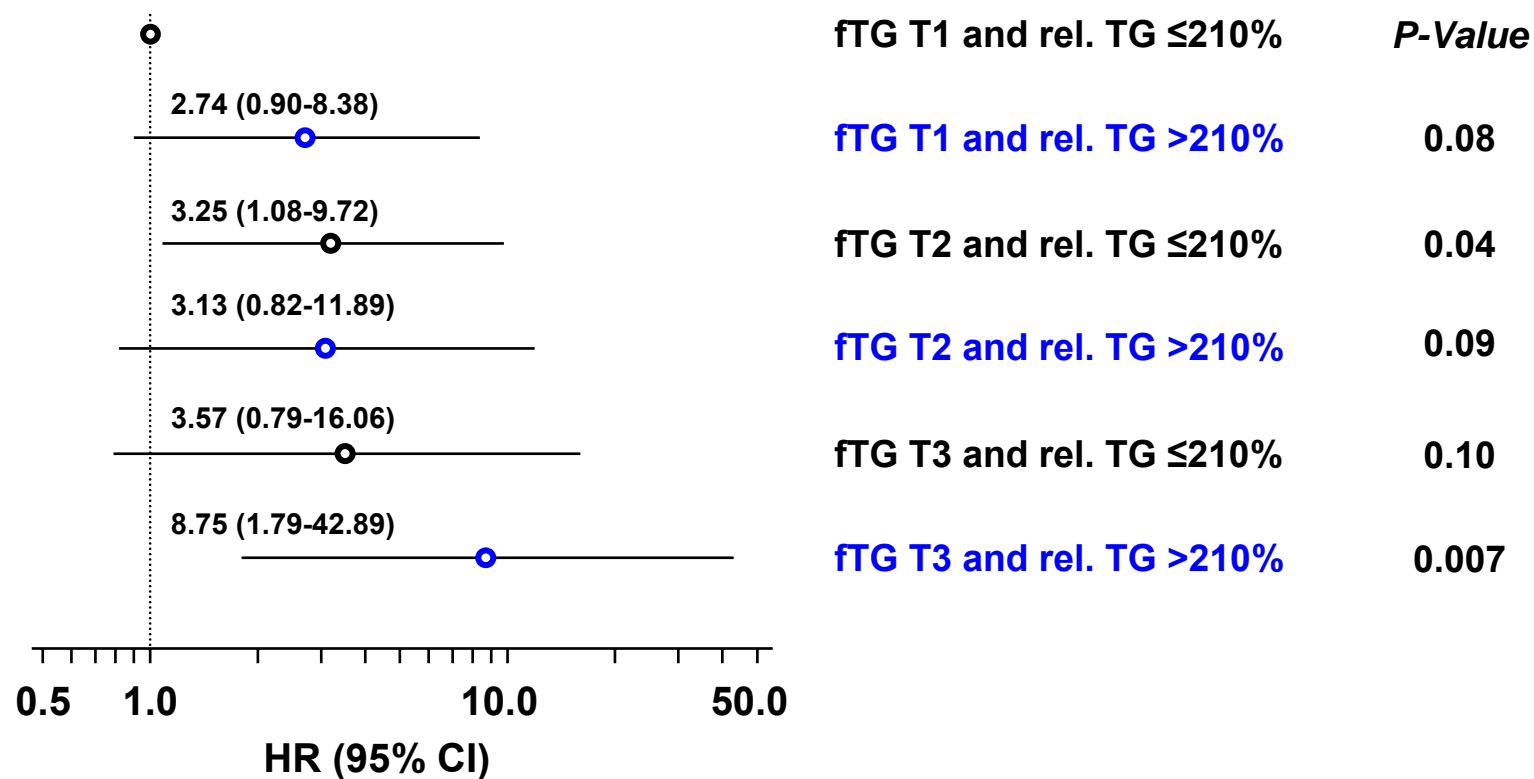


Multivariable Cox regression model adjusted for age, gender, waist-to-hip ratio, blood pressure, smoking, diabetes, metabolic syndrome, HOMA index, HDL-C, LDL-C, regular alcohol intake, statins, beta-blockers.

Laufs et al., ESC Hotline Abstract 28. 08. 2011

HCS: Triglycerides predict CV events in CAD patients with normal glucose tolerance

– discrimination by postprandial TG kinetics



Multivariable Cox regression model adjusted for age, gender, waist-to-hip ratio, blood pressure, smoking, diabetes, metabolic syndrome, HOMA index, HDL-C, LDL-C, regular alcohol intake, statins, beta-blockers.

The Homburg Cream and Sugar Study (HCS)

LIMITATIONS

- **5 h test protocol**
- **95% on statin**
- **no genetic testing**
- **predominantly caucasian ethnicity**

The Homburg Cream and Sugar Study (HCS) SUMMARY

- **Combined testing of postprandial glucose and triglyceride tolerance is feasible in clinical practice.**
- **Postprandial TG do not predict CV outcomes in the total cohort of patients with CAD on statin treatment.**
- **Subgroup analyses:**

Patients with CAD + IGT / diabetes:

Fasting and postprandial TG are elevated but do not independently predict CV outcomes.

Patients with CAD + normal glucose metabolism:

Both fasting and - with superior risk prediction - postprandial TG are independent markers for CV outcomes.

The Homburg Cream and Sugar Study (HCS)

CONCLUSION

Fasting and postprandial triglyceride concentrations independently predict cardiovascular events in patients with coronary artery disease and normal glucose tolerance.



Thank you

The **Homburg **C**ream and **S**ugar Study (HCS):
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