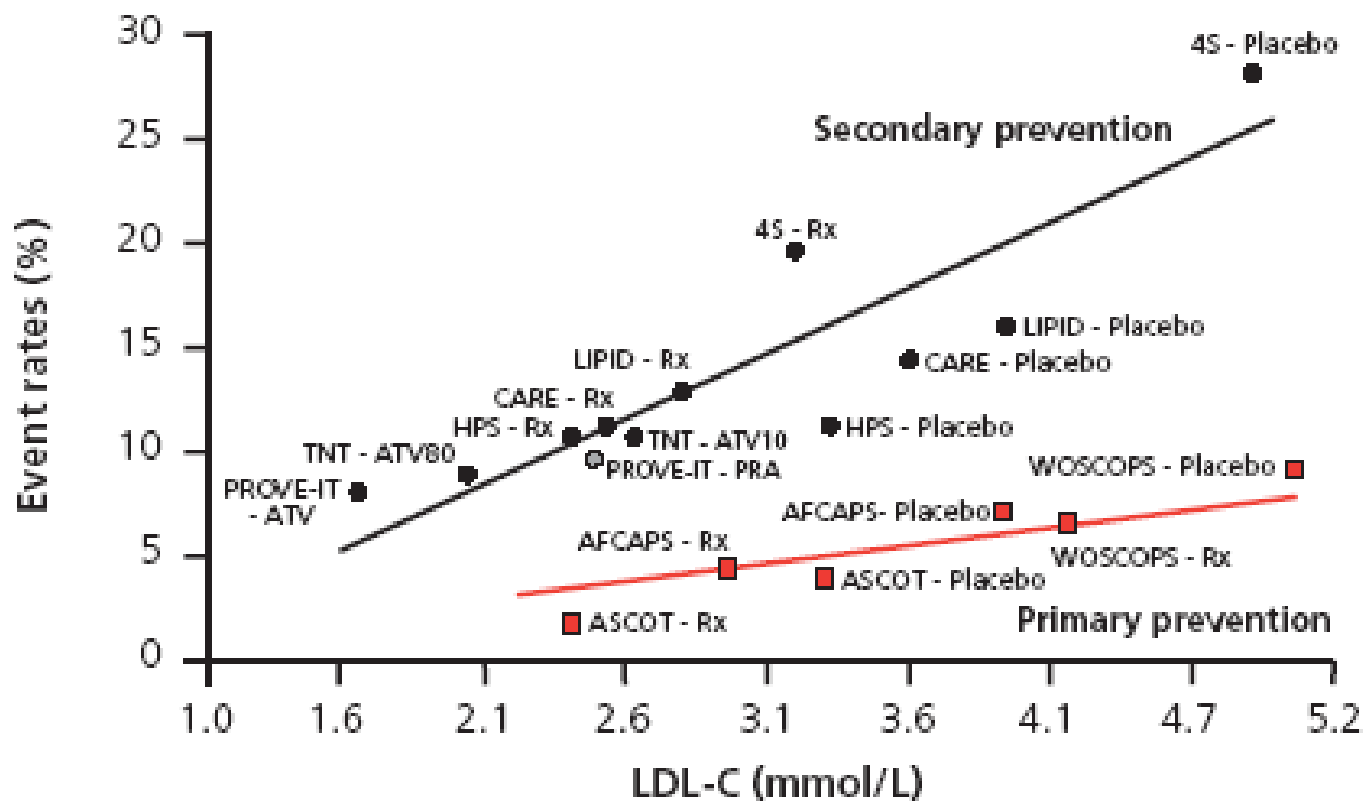


08:00 – 08:15

Cardiologie en LDL-c verlaging:
Wat hebben we en wat willen we?

Ron Peters

AMC



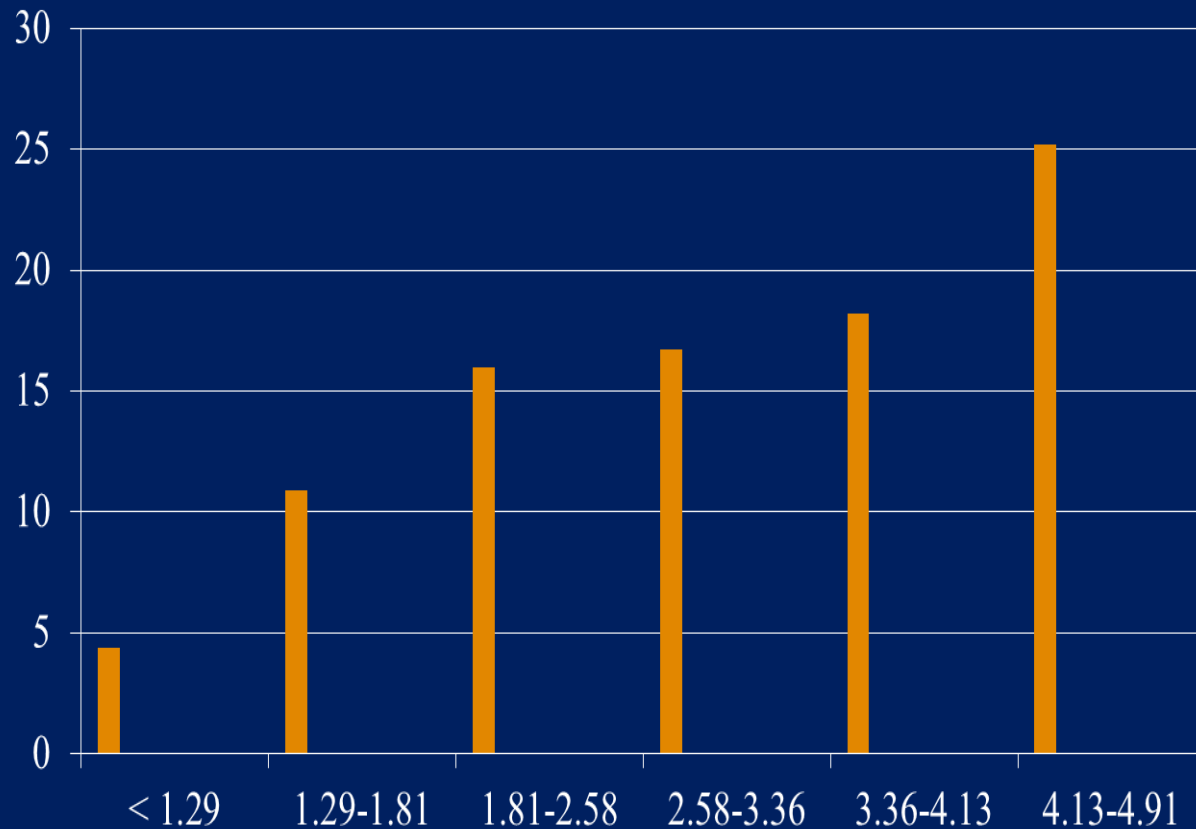
Key: LDL-C= low-density lipoprotein cholesterol; Rx= statin therapy;
 PRA = pravastatin; ATV = atorvastatin

Adapted from: Rosensen RS. *Exp Opin Emerg Drugs* 2004;9:269-79 and La Rosa JC⁴

absence of lower threshold for LDL lowering

Boekholdt et al.
JACC 5 August 2014, p. 485–494

% major cardiovascular events



38,153 study participants
155,573 person-years of follow-up

LDL mmol/L

Online Table 1. Study characteristics

Trial	Patients	Treatment	N	Follow-up
4S	Stable CAD	Placebo	2223	Median 5.4 years
	TC 213-310 mg/dL	Simvastatin 20-40 mg	2221	
AFCAPS-TexCAPS	No cardiovascular disease	Placebo	3301	Mean 5.2 years
	HDL-C < 45 mg/dL	Lovastatin 20-40 mg	3304	
LIPID	Stable CAD	Placebo	4502	Mean 6.1 years
	LDL-C 155-271 mg/dL	Pravastatin 40 mg	4512	
CARDS	T2D without documented CVD	Placebo	1410	Median 3.9 years
	LDL-C < 160 mg/dL	Atorvastatin 10 mg	1428	
TNT	Stable CAD	Atorvastatin 10 mg	5006	Median 4.9 years
	LDL-C < 130 mg/dL	Atorvastatin 80 mg	4995	
IDEAL	Post myocardial infarction	Simvastatin 20-40 mg	4449	Median 4.8 years
	Qualifying for lipid-lowering therapy	Atorvastatin 80 mg	4439	
SPARCL	Recent stroke or TIA	Placebo	2365	Median 4.9 years
	LDL-C 100-190 mg/dL	Atorvastatin 80 mg	2366	
JUPITER	No cardiovascular disease	Placebo	8901	Median 1.9 years
	LDL-C < 130 mg/dL and CRP \geq 2 mg/L	Rosuvastatin 20 mg	8901	

Data are based on all participants of the respective trials, irrespective of availability of lipid or apolipoprotein data. CAD = coronary artery disease, T2D = type 2 diabetes, CVD = cardiovascular disease, TIA = transient ischemic attack, TC = total cholesterol, LDL-C = low-density lipoprotein cholesterol, HDL-C = high-density lipoprotein cholesterol, CRP = C-reactive protein.

CVRM Herziening 2011



Tabel 2. Risicotabel. 10-jaarskans op ziekte en sterfte door HVZ voor patiënten zonder HVZ.

SBD	Vrouwen					Leeftijd	Mannen													
	Niet-rookster						Niet roker													
180	35	38	41	43	44	47	50	>50	>50	>50	>50	>50	>50	>50	>50					
160	28	31	33	35	36	38	41	44	46	48	45	48	>50	>50	>50	>50	>50	>50	>50	>50
140	22	24	26	28	29	31	33	36	38	39	37	40	42	44	46	49	>50	>50	>50	>50
120	18	19	21	22	23	25	27	29	30	32	30	32	34	36	38	40	43	45	48	50
180	14	17	20	24	30	27	32	37	45	>50	25	30	36	44	>50	45	>50	>50	>50	>50
160	10	12	14	17	21	19	22	27	32	39	18	21	26	32	40	33	39	47	>50	>50
140	7	8	10	12	15	14	16	19	23	28	12	15	18	23	29	23	28	34	42	>50
120	5	6	7	9	11	10	11	14	17	20	9	11	13	16	21	17	20	24	30	38
180	10	12	15	18	23	20	23	28	34	42	22	26	32	40	50	40	48	>50	>50	>50
160	7	8	11	13	16	14	17	20	24	30	15	19	23	29	36	29	35	42	>50	>50
140	5	6	7	9	12	10	12	14	17	21	11	13	16	20	26	20	25	30	38	47
120	4	4	5	7	8	7	8	10	12	15	8	9	12	15	19	14	18	22	27	34
180	5	6	8	10	12	10	12	15	18	22	13	16	20	26	32	25	31	38	47	>50
160	4	4	5	7	9	7	8	10	13	16	10	12	15	18	23	18	22	27	34	43
140	3	3	4	5	6	5	6	7	9	11	7	8	10	13	17	13	16	19	24	31
120	2	2	3	3	4	4	4	5	6	8	5	6	7	9	12	9	11	14	17	22
180	2	3	4	5	6	5	6	7	9	11	8	10	12	15	20	15	18	23	28	36
160	2	3	3	3	4	3	4	5	6	8	6	7	9	11	14	11	13	16	20	26
140	1	1	2	2	3	2	3	3	4	6	4	5	6	8	10	7	9	12	15	19
120	1	1	1	2	2	2	2	2	3	4	3	3	4	6	7	5	7	8	10	13
180	1	1	1	1	1	1	1	1	2	2	3	3	4	6	7	5	6	8	10	13
160	<1	<1	1	1	1	1	1	1	1	2	2	2	3	4	5	4	4	6	7	9
140	<1	<1	<1	1	1	<1	<1	1	1	1	1	2	2	3	4	3	3	4	5	7
120	<1	<1	<1	<1	<1	<1	<1	1	1	1	1	1	2	2	3	2	2	3	4	5
	4	5	6	7	8	4	5	6	7	8	4	5	6	7	8	4	5	6	7	8

SBD: systolische bloeddruk.

- Leefstijladviezen, doorgaans geen medicamenteuze behandeling
- Leefstijladviezen, overweeg medicamenteuze behandeling bij aanvullende risicofactoren
- Leefstijladviezen, meestal medicamenteuze behandeling

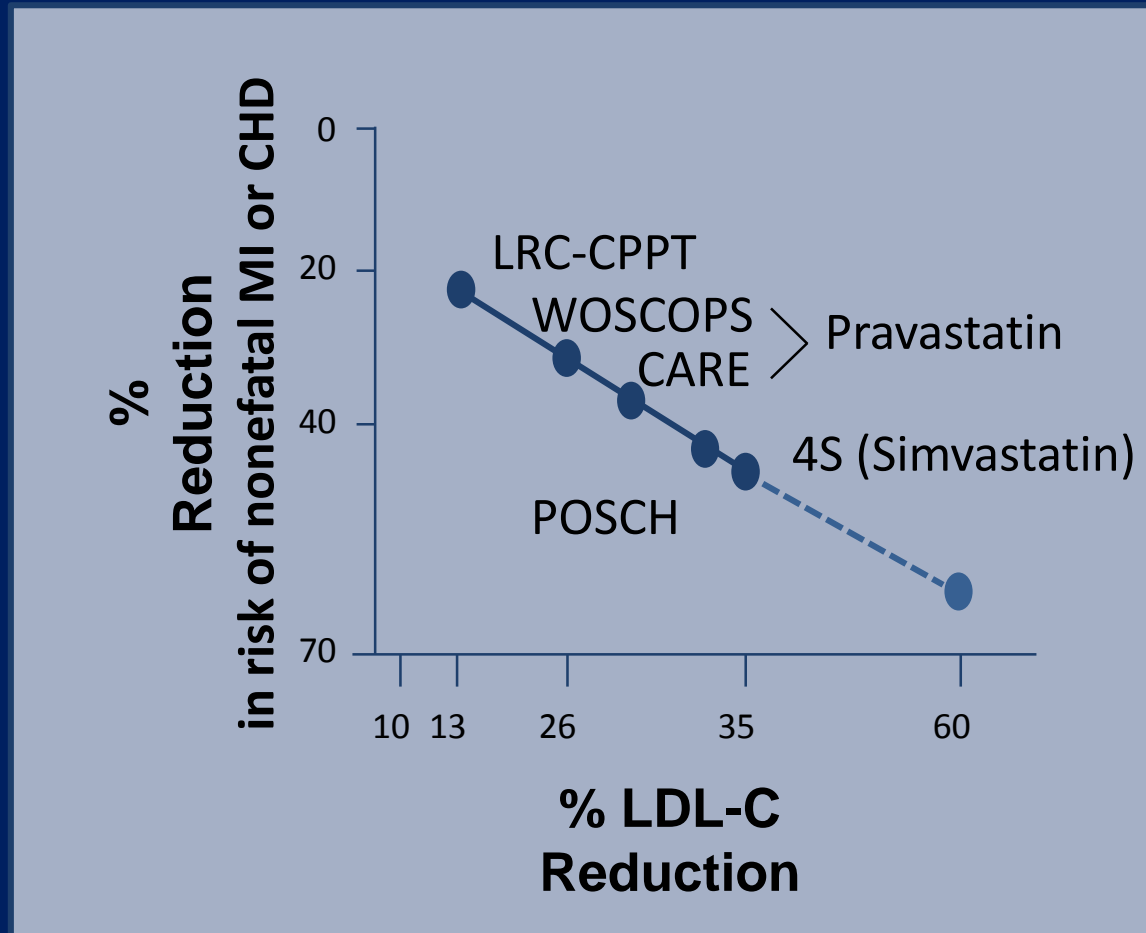
Het risico bij patiënten met DM of RA kan worden geschat door bij de actuele leeftijd van de patiënt 15

Streefwaarde LDL bij secundaire preventie: <2,5 mmol/L

Therapies to Lower LDL-C

Class	Drug(s)
3-Hydroxy-3-Methylglutaryl Coenzyme A (HMG-CoA) reductase inhibitors [Statins]	Atorvastatin (Lipitor) Fluvastatin (Lescol XL) Lovastatin (generic and Mevacor) Pravastatin (Pravachol) Rosuvastatin (Crestor) Simvastatin (Zocor)
Bile acid sequestrants	Cholestyramine (generic and Questran) Colesevelam (Welchol) Colestipol (Colestid)
Cholesterol absorption inhibitor	Ezetimibe (Zetia)
Nicotinic acid	Niacin
Dietary Adjuncts	Soluble fiber Soy protein Stanol esters

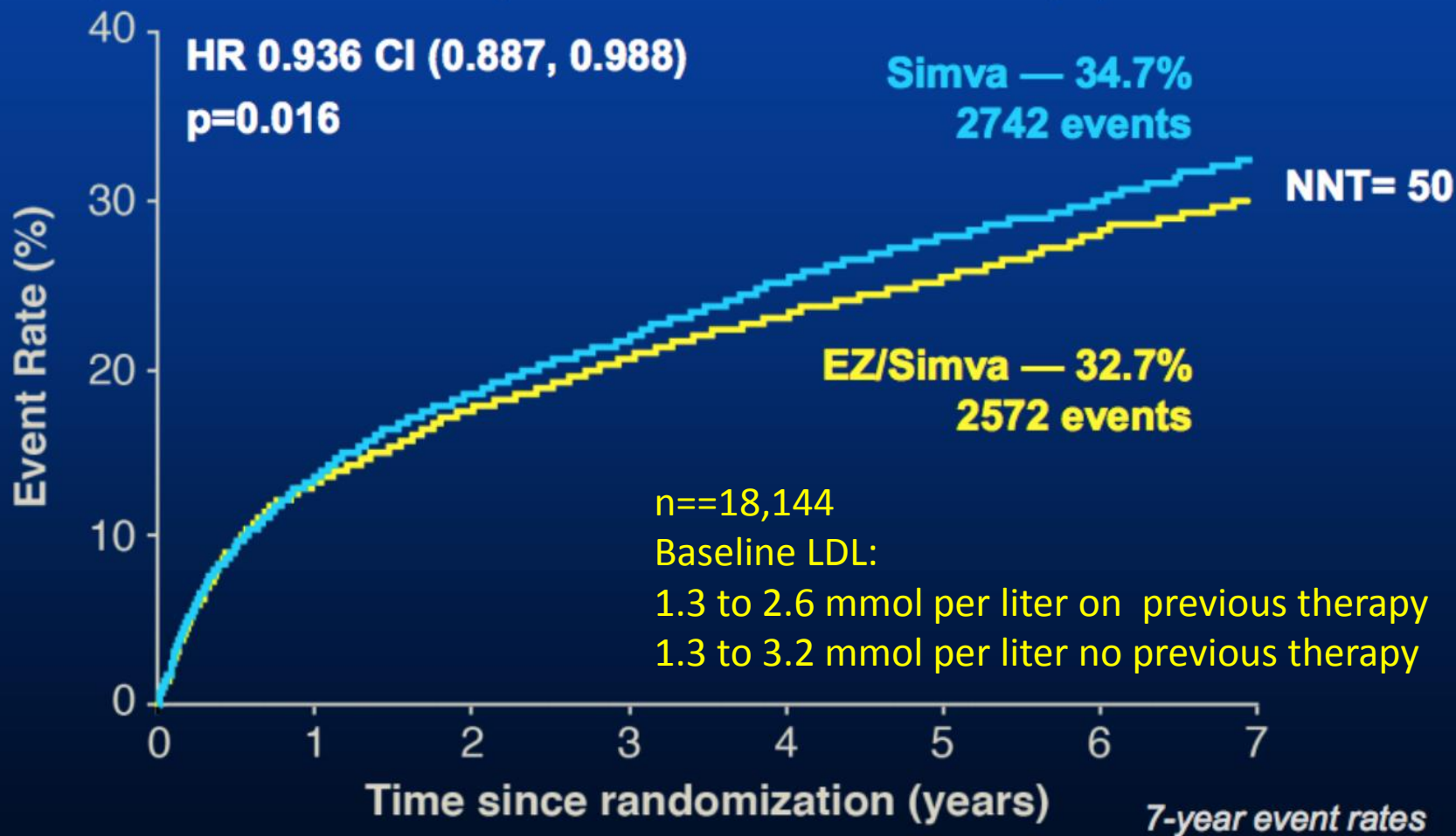
Statin vs Non Statin Trials



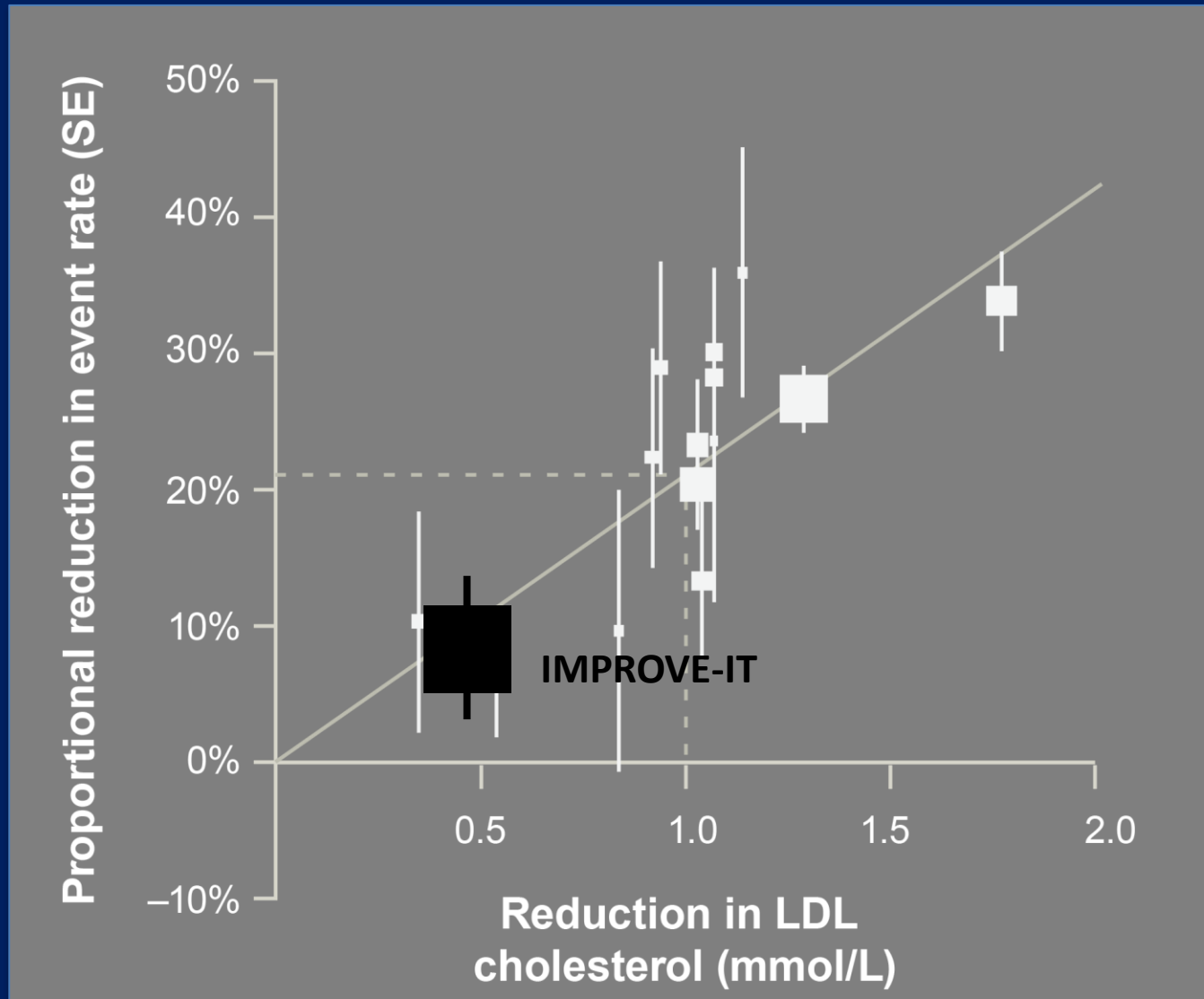
Primary Endpoint — ITT

IMPROVE-IT

Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization (≥ 30 days), or stroke



Lowering LDLc reduces CV-risk *independent of 'pathway'*

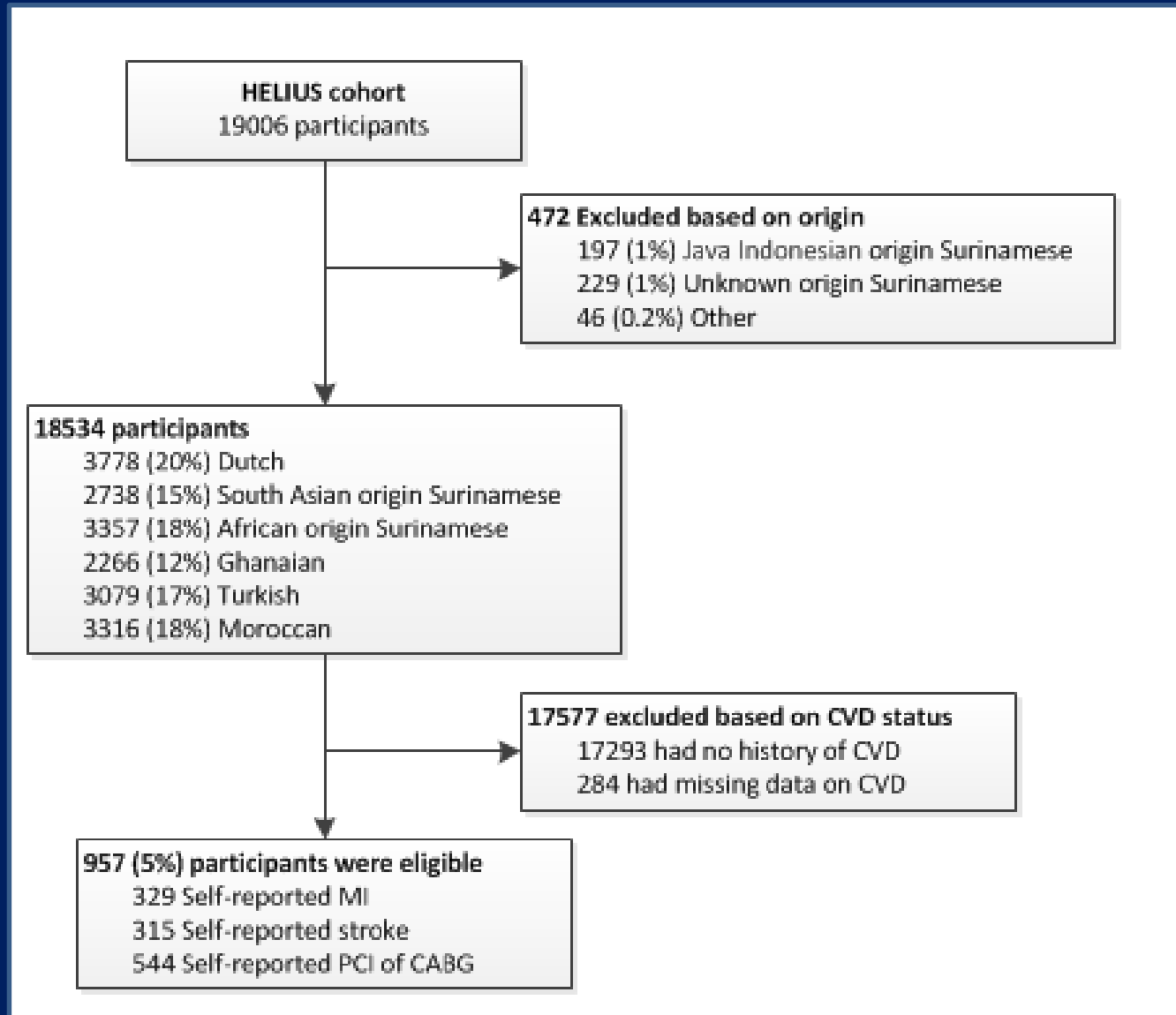


Secondary prevention in EUROASPIRE

- Nederlandse deelnemers (n=700)
- meting 1,5 jaar na ontslag wegens ACS
- 82% van patienten nog bij cardioloog

- **77% overgewicht BMI >25**
- **29% obesitas BMI > 30**
- **78% abdominaal overgewicht (94 en 80 cm)**
- **43% diabetes volgens WHO**
- **20% bekend met diabetes**
- **16% rookt**
- **50% RR > 140 mmHg**
- **40% LDL > 2,5 mmol/L (richtlijn CVRM 2011)**
- **79% LDL > 1,8 mmol/l (richtlijn ESC 2012)**

HELIUS: secondary prevention



HELIUS secondary prevention: ESC prevention goals

	Total Population
Blood pressure	
SBP < 140 mmHg	646/953 (68%)
SBP < 140 mmHg with medication	325/646 (50%)
SBP > 140 mmHg without medication	105/306 (34%)
SBP > 140 mmHg with medication	201/306 (66%)
Cholesterol	
LDL cholesterol < 2.5 mmol/L	405/938 (44%)
LDL cholesterol < 2.5 mmol/L with medication	295/408 (72%)
LDL cholesterol > 2.5 mmol/L without medication	365/529 (69%)
LDL cholesterol > 2.5 mmol/L with medication	164/529 (31%)
Antithrombotic therapy	(+/- 50%)
Non smoking	638/950 (67%)
Healthy weight (BMI<25 kg/m ²)	233/955 (24%)
Physical activity (>30 min/5days/week)	520/957 (54%)
Diabetes Mellitus regulation	
Self-reported DM	281/943 (30%)
Glucose lowering medication	219/280 (78%)
Glucose < 7 mmol/mol	119/277 (43%)
HbA1c < 48mmol/mol	85/275 (31%)
Glucose regulation (in patients without selfreported DM)	
Glucose < 7 mmol/mol	624/652 (96%)

Tabel 1			
LDL-streefwaarde na ACS in AMC			
		N=103	(%)
LDL \leq 2,5 mmol/L		79/103	(77%)
LDL \leq 1,8 mmol/L		36/103	(35%)

Tabel 1					
LDL-streefwaarde na ACS per behandelaar					
		Cardioloog		Cardioloog i.o.	
		n=54	(%)	n=48	(%)
LDL \leq 2,5 mmol/L		36/54	(67%)	43/48	(90%)
LDL \leq 1,8 mmol/L		16/54	(30%)	20/48	(42%)

Prevalance of SAMS in Observational study Risk of Muscle Symptoms with High Dose Statins (PRIMO)

Statin	Dosage	% patients with muscle sympt	Odds Ratio [†] [95% CI]	P value [‡]
<i>Pravastatin</i>	40 mg/day	10.9%		
<i>Atorvastatin</i>	40–80 mg/day	14.9%	1.28 [1.02–1.60]	0.035
<i>Simvastatin</i>	40–80 mg/day	18.2%	1.78 [1.39–2.29]	<0.0001
<i>Fluvastatin</i>	80 mg/day	5.1%	0.33 [0.26–0.42]	<0.0001

*% values relative to the total number of patients with or without muscular symptoms.

†

Odds ratios were calculated using pravastatin as the reference.

conclusies

- LDL cholesterol is een centrale factor in atherosclerose
- Verlaging van LDL verbetert de prognose, ongeacht het mechanisme
- Statines zijn de belangrijkste middelen
- In de praktijk is implementatie van secundaire preventie het grootste probleem
- Voor een deel van de patienten zouden sterkere middelen welkom zijn:
 - Zeer hoog risico ondanks huidige behandeling (bv FH, recidivisten)
 - Intolerantie voor statines