Evaluating the 10-year risk of recurrent cardiovascular events and potential effects of secondary prophylaxis in people with HIV

Rosa H. Elias, MD
PhD Candidate Infectious Diseases

University Medical Centre Utrecht,
the Netherlands

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Disclosure of speaker's interest

(Potential) conflict of interest	None

Rationale

- PWH have a higher risk of recurrent cardiovascular events[1]

- Main drivers are largely unknown

- Insight in recurrence risk and interventions

- Role of HIV-treating health care providers

- SMART2 tool[2]
  - 10-year recurrence risk
  - potential treatment effects

[1] Haji, M. *JAMA Netw Open* (2024), [2] Hageman, S. *Eur Heart J* (2022) 3

Objectives

- Assess the 10-year risk of recurrent atherosclerotic cardiovascular events in PWH

- Estimate the potential risk reduction

    And how this relates to the general population

Methods (1)

Population

- ATHENA cohort[1]
  - In follow-up between 2018 – 2021
  - Age 40 – 80 years
  - Established atherosclerotic cardiovascular disease (ASCVD)

<p style="text-align:center; color:#E8662D;">1:1 matched for non-modifiable SMART2 parameters*</p>

<p style="text-align:right; color:#E8662D;">* Age, sex, type of ASCVD, years since first event</p>

- UCC-SMART cohort[2]
  - Single centre with ~9000 participants with history of ASCVD
  - Collection of demographical, clinical and biochemical data
  - Yearly follow-up for the occurrence of new events

Methods (2)

SMART2 algorithm

1. 10-year risk of recurrent cardiovascular event
   - Hazard model with cardiovascular predictors *
   - Extensive external (international) validation[1]

   > * Gender, age, smoking status, years since first cardiovascular event, type of ASCVD, diabetes mellitus, systolic blood pressure, hs-CRP, eGFR, non-HDL-c, and use of antithrombotics

2. Estimate potential treatment effects
   - LDL-c reduction to < 1.4 mmol/L[2,3]
   - Treating systolic blood pressure when > 140 mmHg [4]
   - Smoking cessation [5]
   - Antithrombotics [6]

[1] Hageman, S. *Eur Heart J* (2022), [2] Baigent, C. *Lancet* (2010), [3] Mihaylova, B. *Lancet* (2012)
[4] Ettehad, D. *Lancet* (2016*),* [5] Mons, U. *BMJ* (2015), [6] Collins, R. *Lancet (*2009)

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Baseline characteristics (1)

	ATHENA cohort (HIV+)	UCC-SMART cohort (HIV-)	p-value
Matching criteria	N = 1,247	N = 1,247	
Age	62.4 (8.9)	62.5 (9.1)	0.670
Sex assigned at birth			0.444
Male	1,115 (89%)	1,103 (88%)	
Female	132 (11%)	144 (12%)	
Years since first cardiovascular event	7.3 (6.0)	7.5 (8.7)	0.487
Coronary artery disease	849 (68%)	843 (68%)	0.797
Cerebrovascular disease	457 (37%)	507 (41%)	0.040

Mean (SD) and median [Q1,Q3] accordingly.

Participants are generally well suppressed and have good immunological response

Baseline characteristics (2)

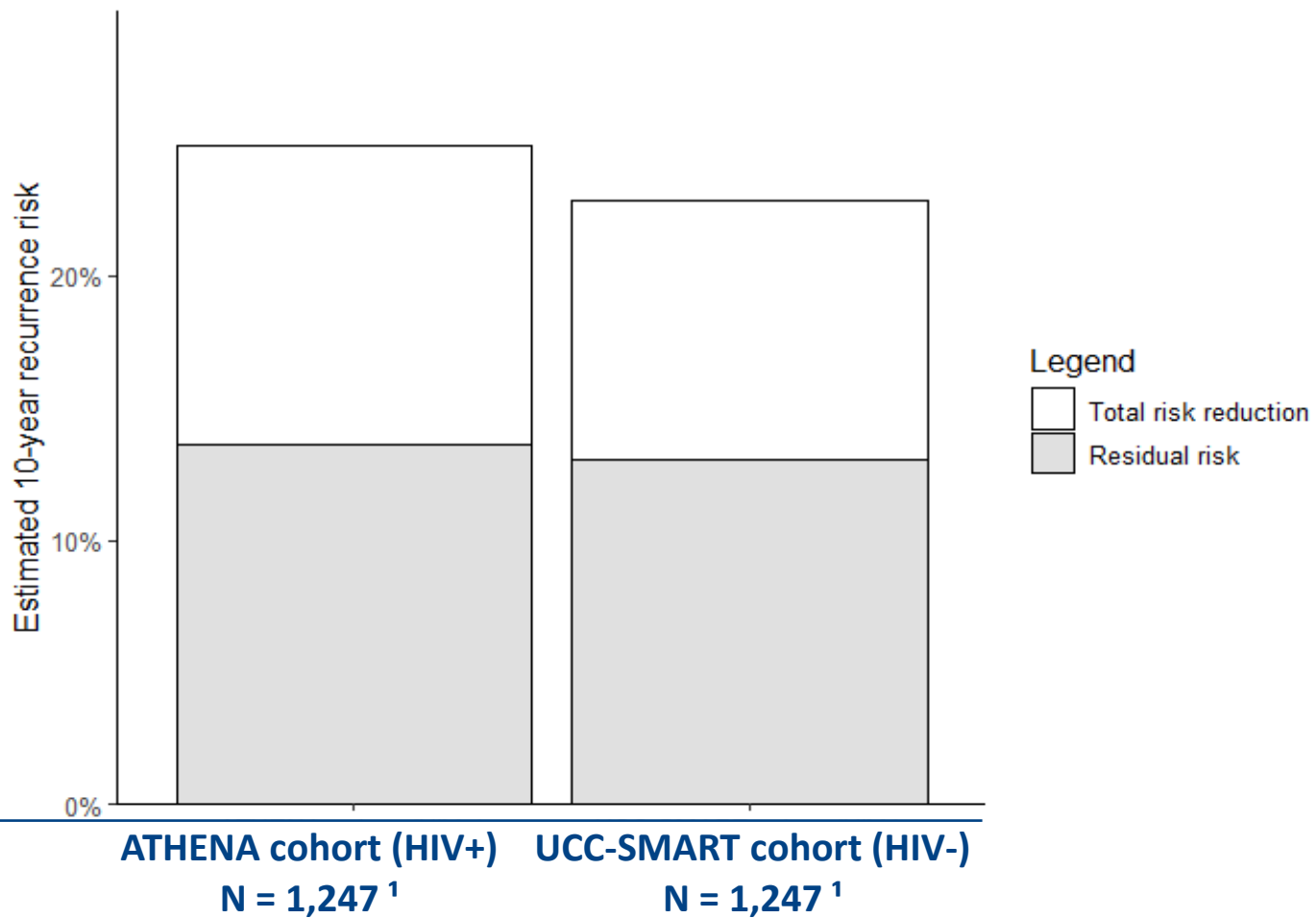|	ATHENA cohort (HIV+) N = 1,247	UCC-SMART cohort (HIV-) N = 1,247	p-value
Cardiovascular and metabolic parameters			
Current smoker	503 (40%)	237 (19%)	
Former smoker	410 (33%)	676 (54%)	
Systolic blood pressure (mmHg)	134 (19)	137 (19)	<0.001
Low-density lipoprotein (mmol/L)	2.30 (0.90)	2.50 (0.95)	<0.001
Antiretroviral therapy		NA	
Abacavir	132 (11%)		
Protease inhibitor	257 (21%)		

Mean (SD) and median [Q1,Q3] accordingly.

Baseline characteristics (2)

	ATHENA cohort (HIV+) N = 1,247	UCC-SMART cohort (HIV-) N = 1,247	p-value
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Antiretroviral therapy		NA	
Abacavir	132 (11%)		
Protease inhibitor	257 (21%)		

Mean (SD) and median [Q1,Q3] accordingly.

Baseline characteristics (3)

	ATHENA cohort (HIV+) N = 1,247	UCC-SMART cohort (HIV-) N = 1,247	p-value
Estimated 10-year risk	25% (12)	23% (12)	<0.001
Risk category			<0.001
<10%	37 (3.0%)	101 (8.1%)	
10-20%	479 (38%)	513 (41%)	
20-30%	396 (32%)	357 (29%)	
≥30%	335 (27%)	276 (22%)	

Mean (SD) and median [Q1,Q3] accordingly.

Risk reduction and Residual risk

	ATHENA cohort (HIV+) N = 1,247 [1]	UCC-SMART cohort (HIV-) N = 1,247 [1]
Residual risk (%)	**13.6 (7)**	**13.1 (8)**

[1] Mean (SD)

Risk reduction and Residual risk

Legend
- 🟩 LDL-c < 1.4 mmol/mL
- ⬜ Residual risk

Y-axis: Estimated 10-year recurrence risk (0% – 20%)
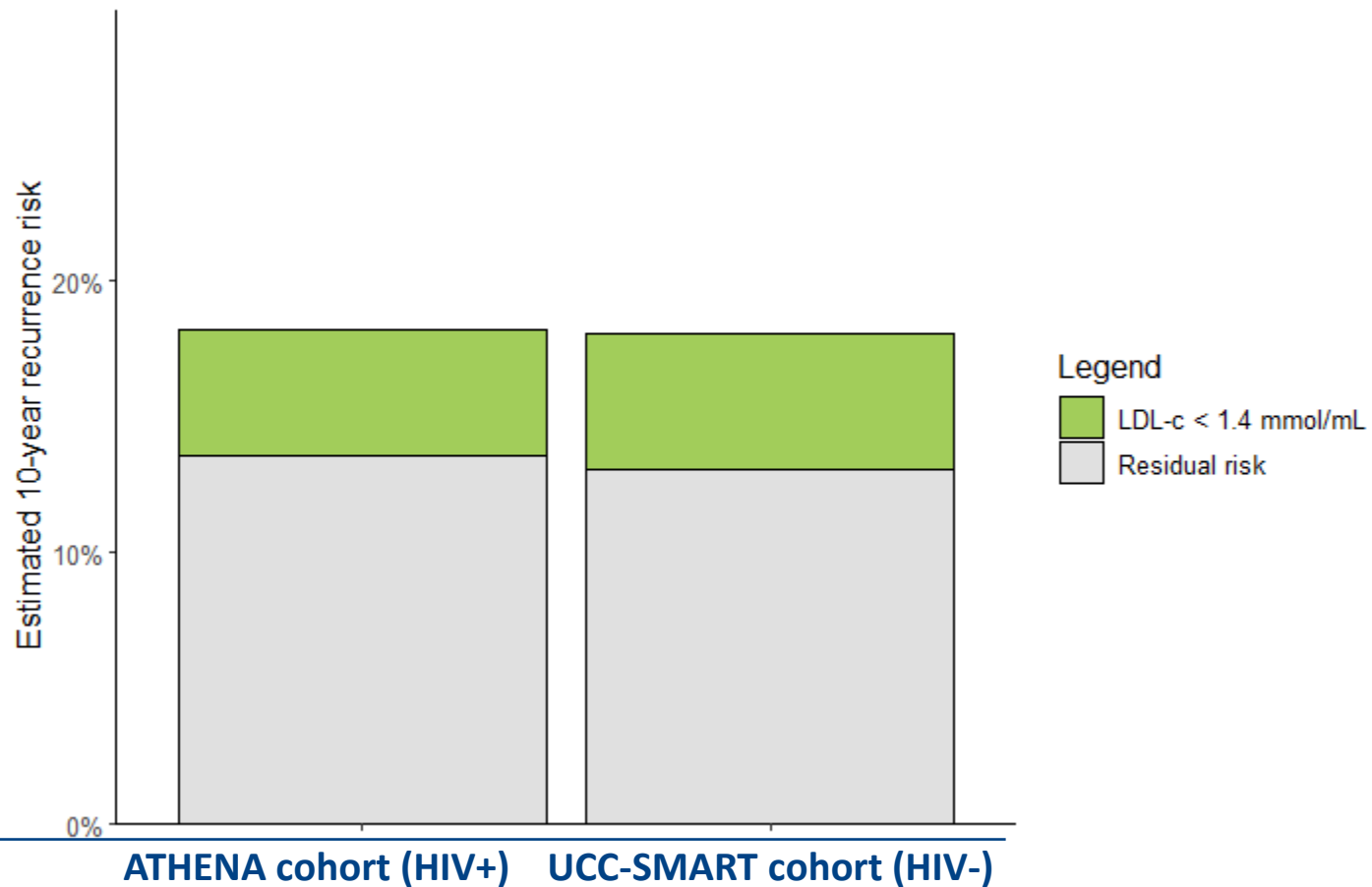
Treatment	ATHENA cohort (HIV+) N = 1,247 [1]	UCC-SMART cohort (HIV-) N = 1,247 [1]
LDL-c < 1.4 mmol/L (%)	4.6 (4.2)	5.0 (4.3)
Residual risk (%)	13.6 (7)	13.1 (8)

[1] Mean (SD)

Risk reduction and Residual risk
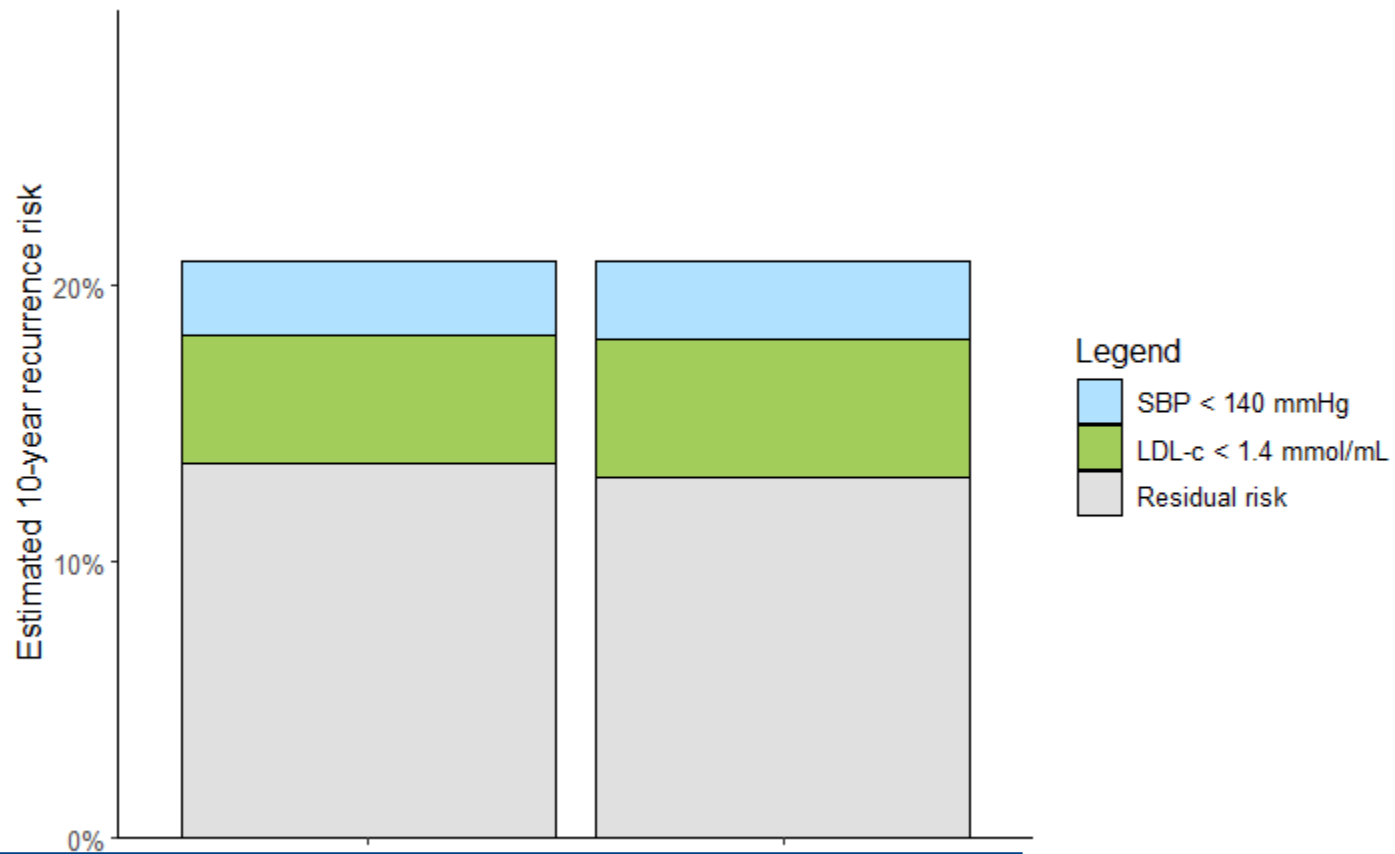
Treatment	ATHENA cohort (HIV+) N = 1,247 [1]	UCC-SMART cohort (HIV-) N = 1,247 [1]
SBP < 140 mmHg (%)	2.7 (4.8)	2.9 (4.7)
Residual risk (%)	13.6 (7)	13.1 (8)
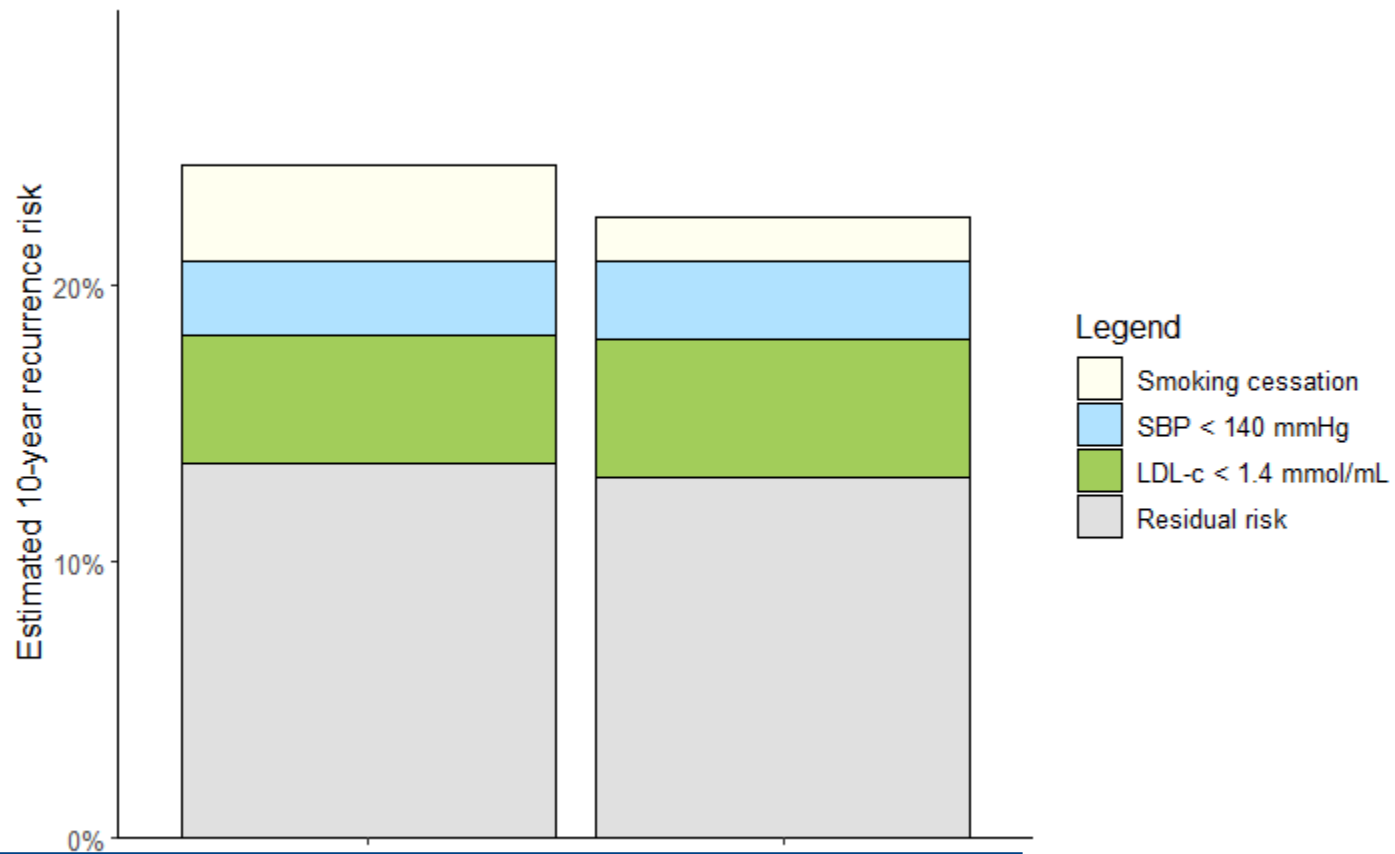
[1] Mean (SD)

Risk reduction and Residual risk

Treatment	ATHENA cohort (HIV+) N = 1,247 [1]	UCC-SMART cohort (HIV-) N = 1,247 [1]
Smoking cessation (%)	3.5 (4.8)	1.6 (3.5)
Residual risk (%)	**13.6 (7)**	**13.1 (8)**
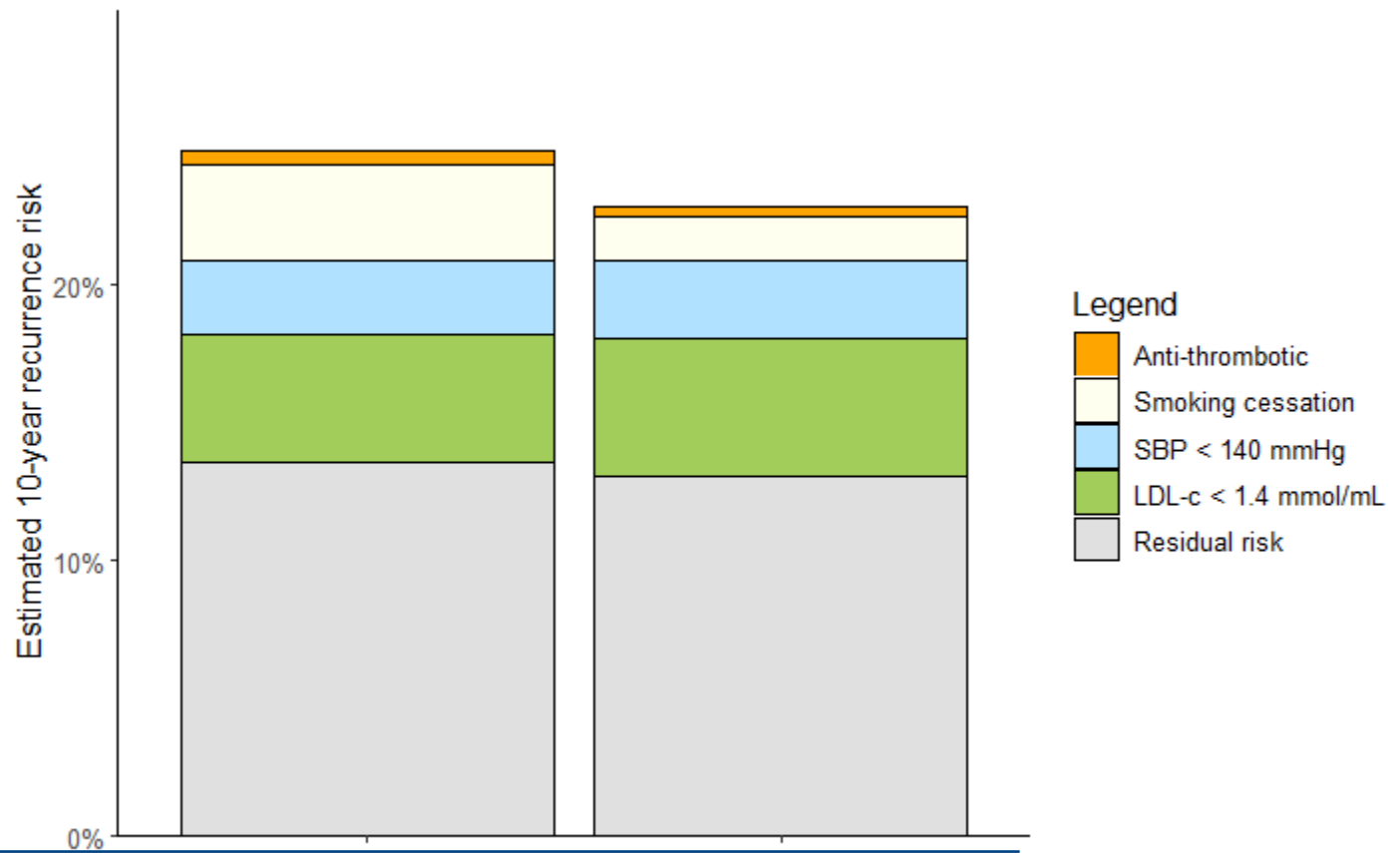
[1] Mean (SD)

Risk reduction and Residual risk

Treatment	ATHENA cohort (HIV+) N = 1,247 [1]	UCC-SMART cohort (HIV-) N = 1,247 [1]
Anti-thrombotic (%)	0.51 (1.46)	0.37 (1.15)
Residual risk (%)	**13.6 (7)**	**13.1 (8)**

[1] Mean (SD)

Risk reduction and Residual risk

Treatment	ATHENA cohort (HIV+) N = 1,247 [1]	UCC-SMART cohort (HIV-) N = 1,247 [1]
LDL-c < 1.4 mmol/L (%)	4.6 (4.2)	5.0 (4.3)
SBP < 140 mmHg (%)	2.7 (4.8)	2.9 (4.7)
Smoking cessation (%)	3.5 (4.8)	1.6 (3.5)
Anti-thrombotic (%)	0.51 (1.46)	0.37 (1.15)
Total risk reduction (%)	**11.3 (9)**	**9.8 (8)**
Residual risk (%)	**13.6 (7)**	**13.1 (8)**

[1] Mean (SD)

Risk reduction and Residual risk

Treatment	ATHENA cohort (HIV+) N = 1,247 [1]	UCC-SMART cohort (HIV-) N = 1,247 [1]
LDL-c < 1.4 mmol/L (%)	4.6 (4.2)	5.0 (4.3)
SBP < 140 mmHg (%)	2.7 (4.8)	2.9 (4.7)
Smoking cessation (%)	3.5 (4.8)	1.6 (3.5)
Anti-thrombotic (%)	0.51 (1.46)	0.37 (1.15)
Total risk reduction (%)	11.3 (9)	9.8 (8)
Residual risk (%)	13.6 (7)	13.1 (8)

[1] Mean (SD)

Results

People with HIV

Combined intervention

- *Total group (N = 1,247)*   113 events per 1000 PY averted

- *≥ 30 % risk group (N = 335)*   207 events per 1000 PY averted

Individual interventions

- *Smoking cessation (N = 503)*   87 events per 1000 PY averted

- *LDL-c reduction (N = 1096)*   52 events per 1000 PY averted

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Discussion

10-year recurrence risk of 25% versus 23%

- Main drivers in PWH: smoking and LDL-c
- Similar treatment effects in both groups
    - Smoking cessation major impact

Considerations

SMART2 not primarily validated for HIV population but:
- Insight in traditional risk factors and interventions
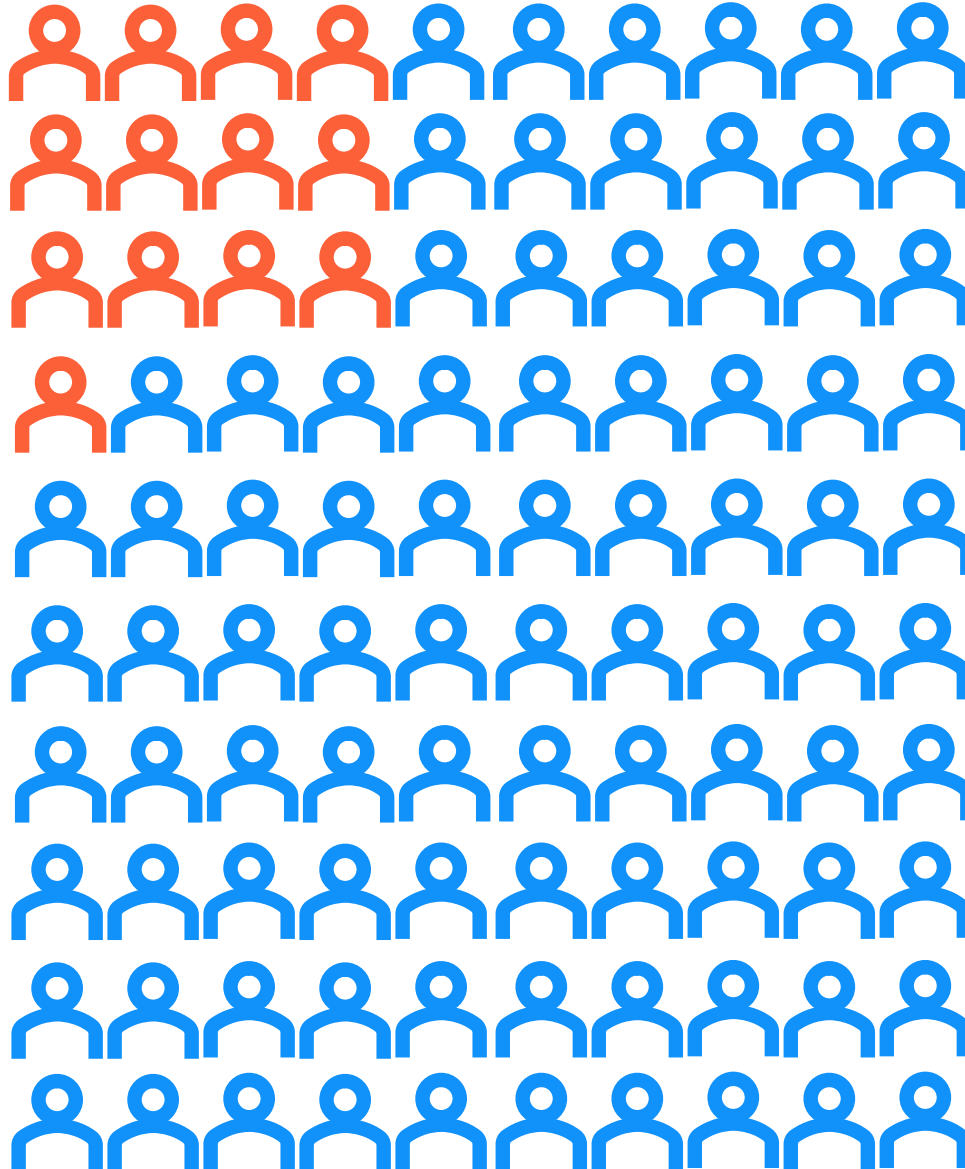- Possibly underestimating statin effect [1]

- Follow-up: validating in prospective cohort

Effect of weight reduction?

Highlight

- Currently: 10-year risk of 25%

- Aim: 45% relative risk reduction

  - Effective individual interventions

- Identifying high-risk individuals is key

  → Still a lot to achieve
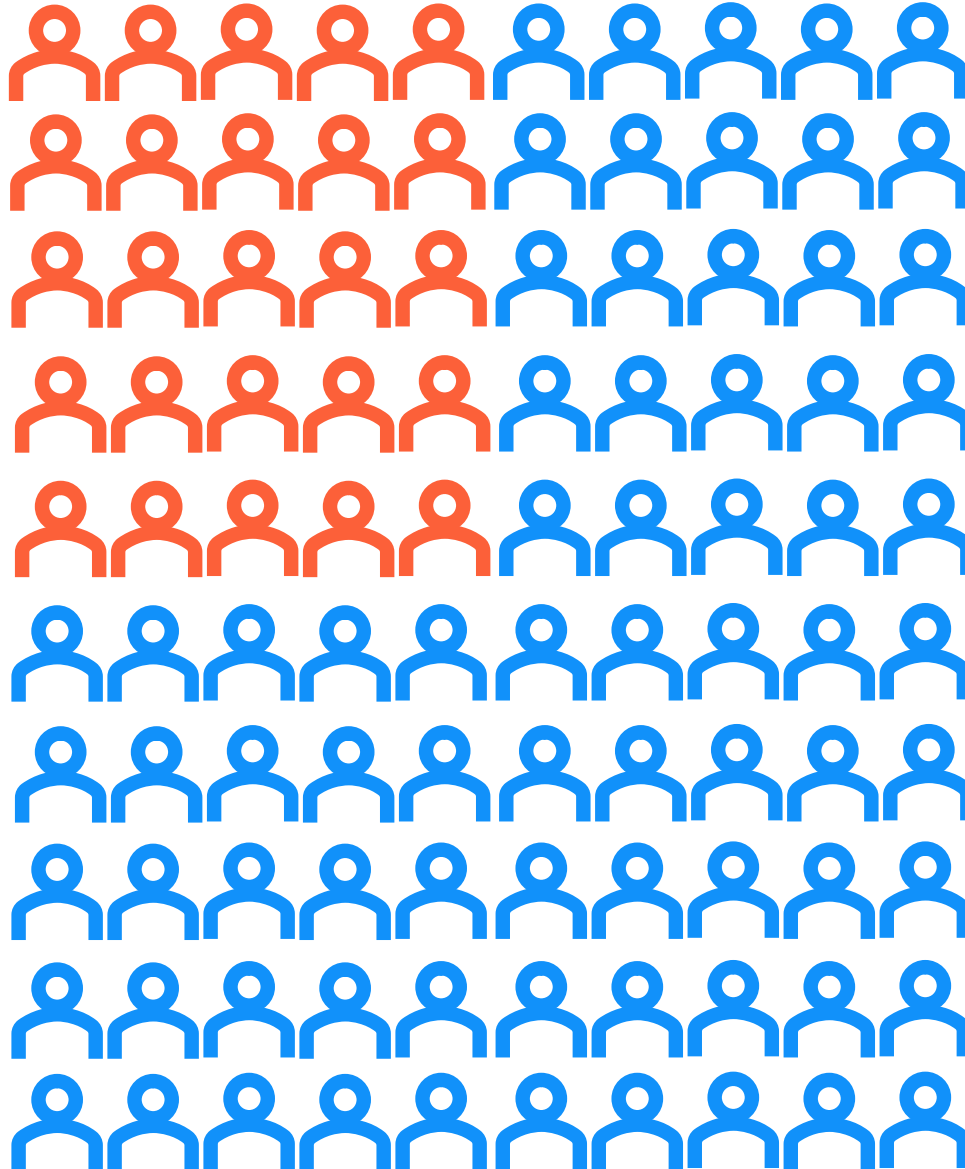
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Colette Smit, PhD

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	ATHENA cohort (HIV+)	UCC-SMART cohort (HIV-)	p-value[2]
Demographics	N = 1,247	N = 1,247	
Age	62.4 (8.9)	62.5 (9.1)	0.670
Sex assigned at birth			0.444
Male	1,115 (89%)	1,103 (88%)	
Female	132 (11%)	144 (12%)	
Region of origin			<0.001
Western Europe	947 (76%)	1,192 (96%)	
Central and South America	142 (11%)	17 (1.4%)	
Sub-Saharan Africa	71 (5.7%)	3 (0.2%)	
Other	87 (7.0%)	35 (2.8%)	
Body Mass Index	25.7 (4.6)	27.6 (4.5)	<0.001
Cardiovascular and metabolic parameters			
Smoking status			<0.001
Current smoker	503 (40%)	237 (19%)	
Former smoker	410 (33%)	676 (54%)	
Never smoker	334 (27%)	334 (27%)	
Systolic blood pressure (mmHg)	134 (19)	137 (19)	<0.001
Systolic blood pressure < 140 mmHg	853 (68%)	785 (63%)	0.004
Using antihypertensives	909 (73%)	1,032 (83%)	<0.001
Years since first cardiovascular event	7.3 (6.0)	7.5 (8.7)	0.487
Coronary artery disease	849 (68%)	843 (68%)	0.797
Cerebrovascular disease	457 (37%)	507 (41%)	0.040
Peripheral artery disease	NA	80 (6.4%)	
Aortic aneurysm	NA	93 (7.5%)	

	ATHENA cohort (HIV+)	UCC-SMART cohort (HIV-)	p-value[2]
	N = 1,247	N = 1,247	
Using antithrombotics	1,089 (87%)	1,116 (89%)	0.091
Thrombocyte agreggation inhibitor	708 (57%)	893 (72%)	<0.001
P2Y12 inhibitor	387 (31%)	416 (33%)	0.214
Oral anticoagulants	150 (12%)	198 (16%)	0.006
Diabetes Mellitus	275 (22%)	244 (20%)	0.126
HbA1c (mmol/mol)	54 (17) n = 239	53 (12) n = 244	0.371
High sensitive C-reactive protein	NA	1.90 [1.00, 4.00]	
Estimated GFR *	80.1 (22.2)	82.4 (19.7)	0.005
Total cholesterol (mmol/L)	4.26 (1.05)	4.39 (1.12)	0.003
High-density lipoprotein (mmol/L)	1.24 (0.40)	1.19 (0.30)	0.004
Non high-density lipoprotein (mmol/L)	3.03 (1.02)	3.19 (1.05)	<0.001
Low-density lipoprotein (mmol/L)	2.30 (0.90)	2.50 (0.95)	<0.001
Low-density lipoprotein < 1.4 mmol/L	175 (14%)	103 (8.3%)	<0.001
Lipid-lowering therapy	924 (74%)	1,049 (84%)	<0.001
Statin	924 (74%)	1,007 (81%)	<0.001
Ezetimibe	8 (0.6%)	178 (14%)	<0.001

HIV specific characteristics

HIV transmission risk category	
Men who have sex with men	823 (66%)
Heterosexual	307 (25%)
Other/Unknown	117 (9.4%)
Years living with HIV	19 [13, 25]
Nadir CD4+ T-cell count (cells/mm^3)	160 [60, 280]
Most recent CD4+ T-cell count (cells/mm^3)	660 [475, 911]
Undetectable viral load (< 50 copies/mL)	1,103 (88%)
Antiretroviral therapy	
NRTI	1,107 (89%)
Emtricitabine	763 (61%)
Tenofovir alafenamide	546 (44%)
Tenofovir disoproxil fumarate	305 (24%)
Lamivudine	260 (21%)
Abacavir	132 (11%)
Zidovudine	14 (1.1%)
NNRTI	440 (35%)
Integrase strand transfer inhibitor	710 (57%)
Protease inhibitor	257 (21%)
Entry inhibitor	8 (0.6%)

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Risk reduction and Residual risk

Estimated 10-year recurrence risk
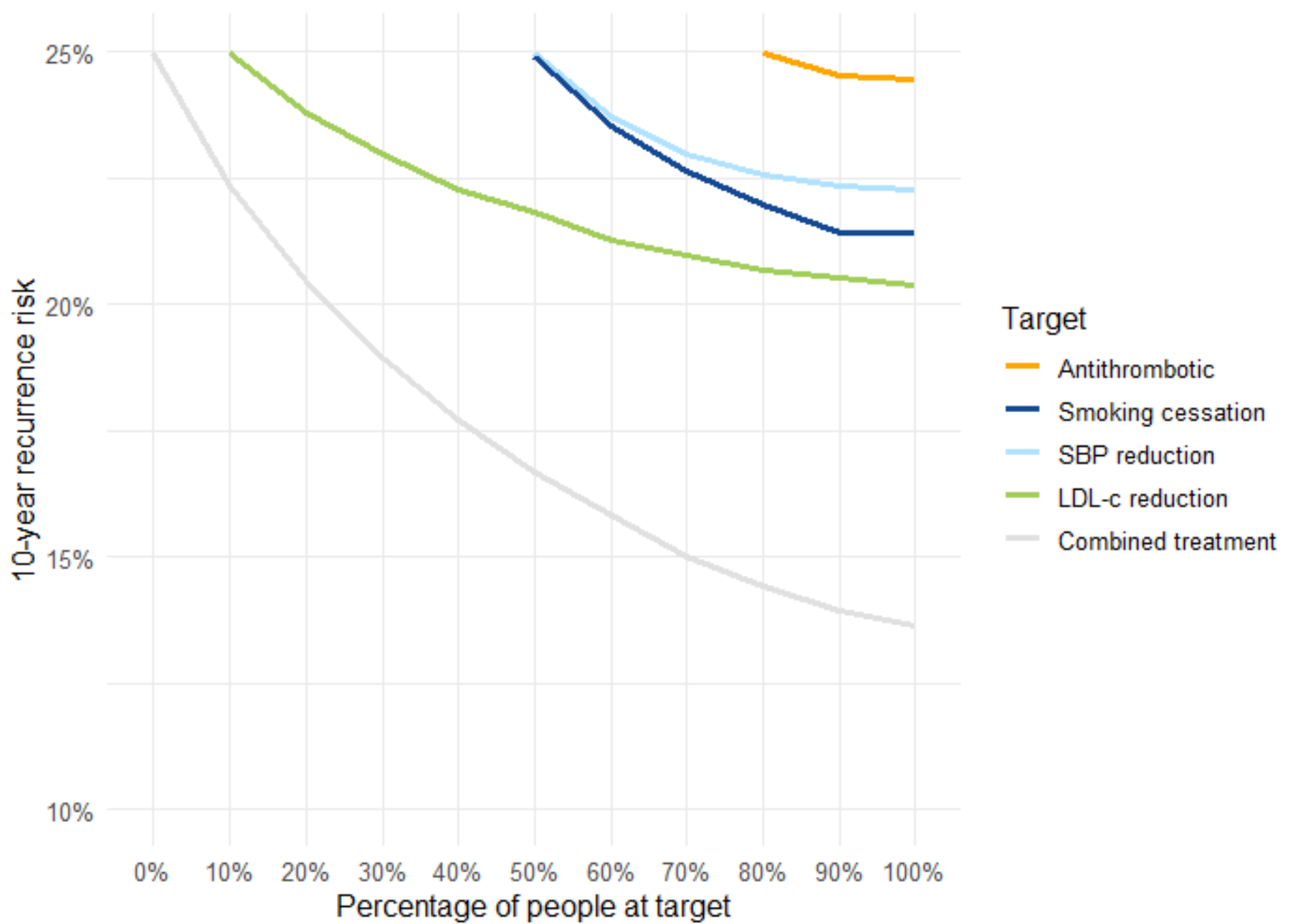
Legend
- Anti-thrombotic
- Smoking cessation
- SBP < 140 mmHg
- LDL-c < 1.4 mmol/mL
- Residual risk
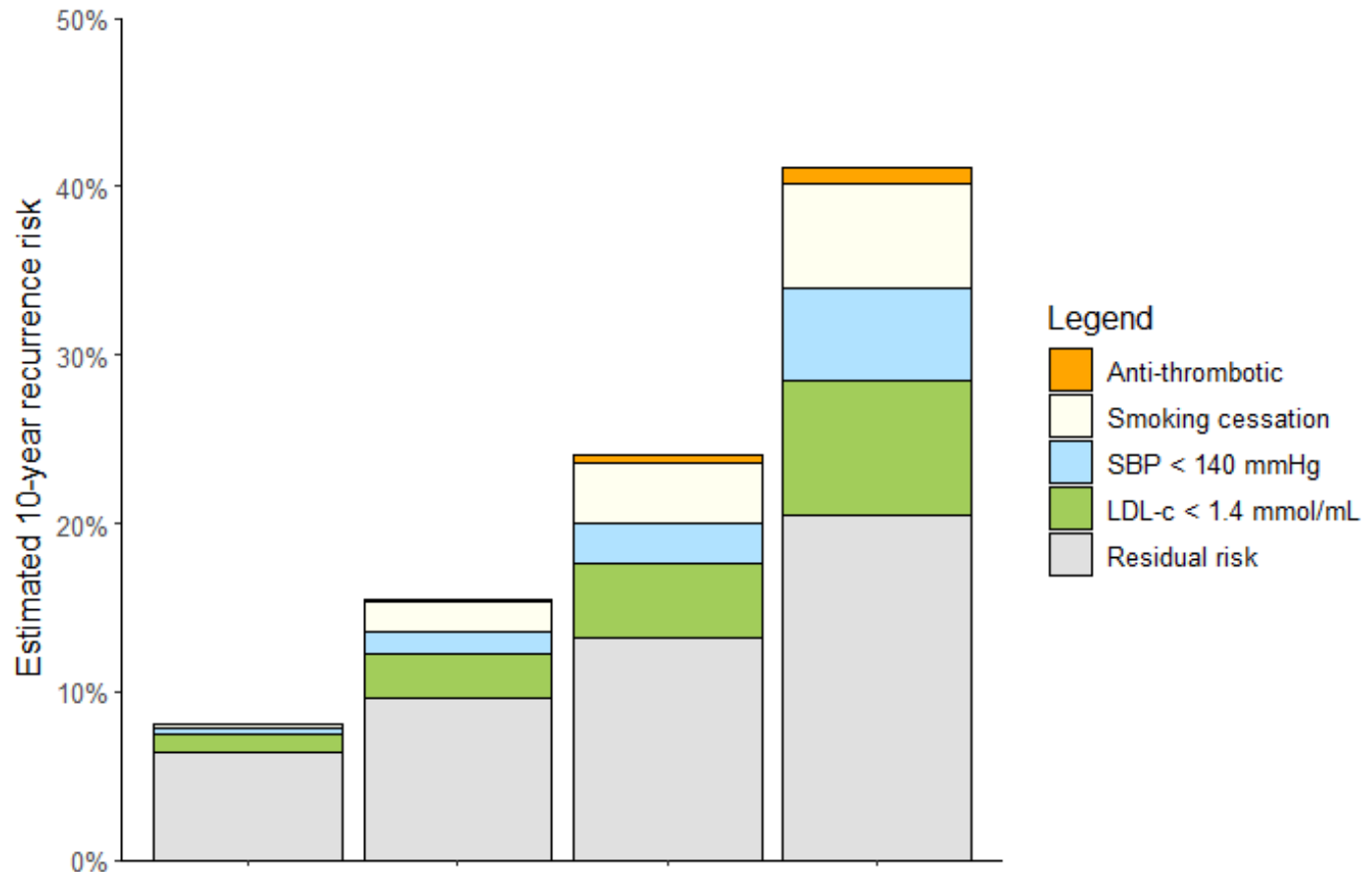
	<10% N = 37[1]	10-20% N = 478[1]	20-30% N = 397[1]	≥30% N = 335[1]
Anti-thrombotic (%)	0.05 (0.29)	0.20 (0.67)	0.49 (1.24)	1.03 (2.24)
Smoking cessation (%)	0.2 (0.8)	1.7 (2.7)	3.6 (4.0)	6.2 (6.6)
SBP < 140 mmHg (%)	0.3 (0.9)	1.3 (2.2)	2.4 (3.5)	5.4 (7.4)
LDL-c < 1.4 mmol/L (%)	1.1 (1.0)	2.6 (2.0)	4.4 (3.1)	8.1 (5.5)
Total risk reduction (%)	2 (1)	6 (3)	11 (5)	21 (10)
Residual risk (%)	6 (2)	10 (3)	13 (5)	20 (9)

[1] Mean (SD)

Risk reduction and Residual risk
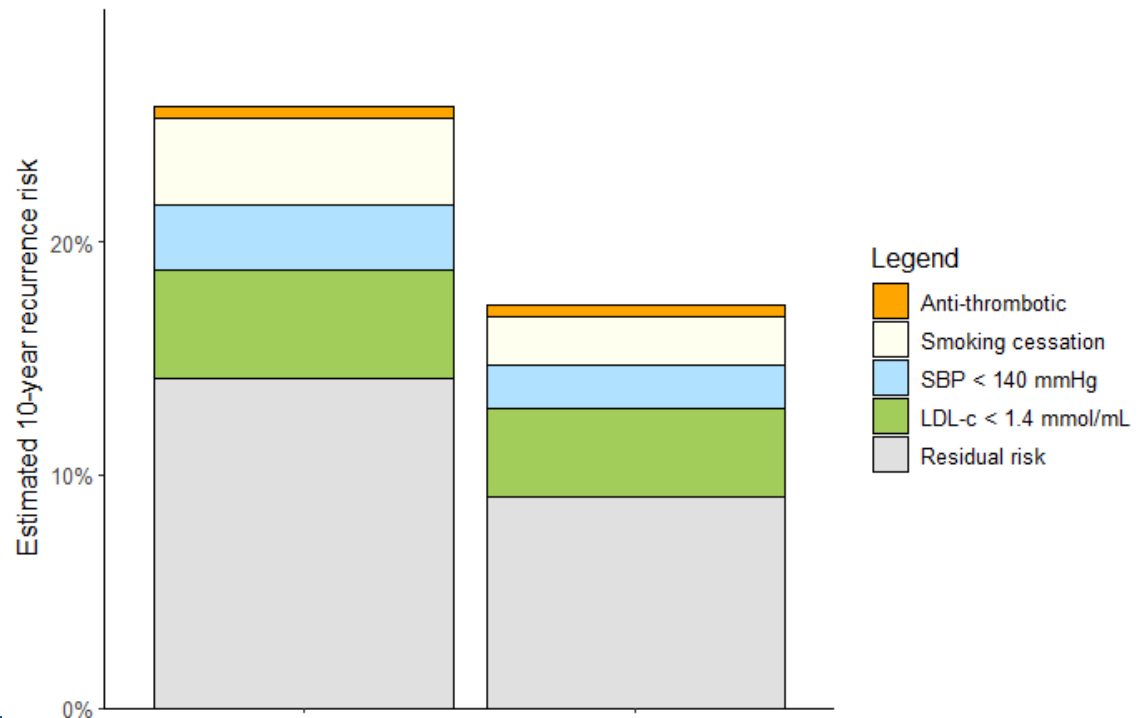
	Male	Female
	N = 1,115[1]	N = 132[1]
Anti-thrombotic (%)	0.51 (1.49)	0.50 (1.21)
Smoking cessation (%)	3.7 (4.9)	2.0 (3.2)
SBP < 140 mmHg (%)	2.8 (4.9)	1.9 (4.2)
LDL-c < 1.4 mmol/L (%)	4.7 (4.3)	3.8 (3.6)
Total risk reduction (%)	12 (9)	8 (7)
Residual risk (%)	14 (7)	9 (4)

[1] Mean (SD)

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Flow of Population Across Risk Categories