Polypill strategy in secondary Cardiovascular prevention

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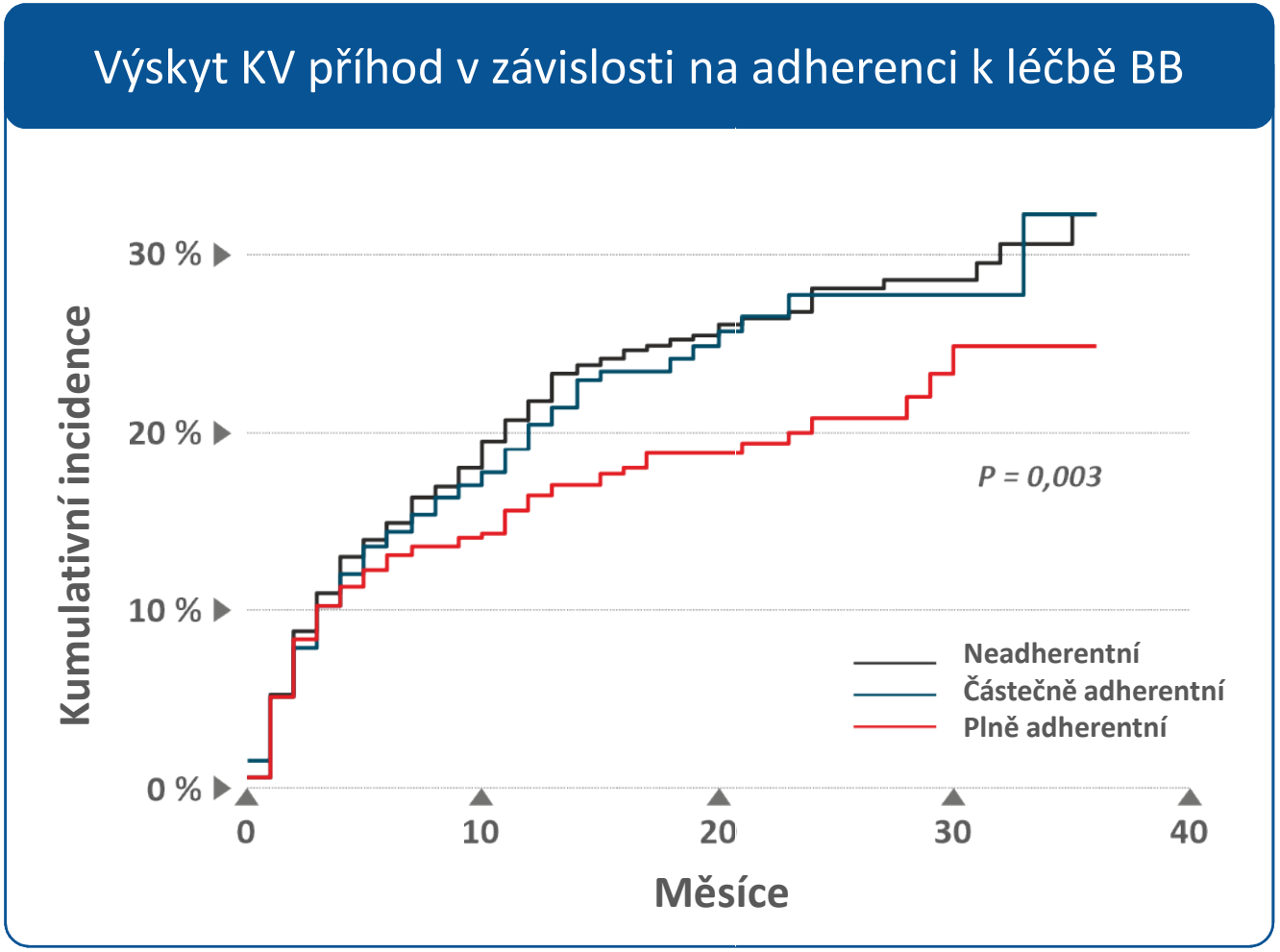
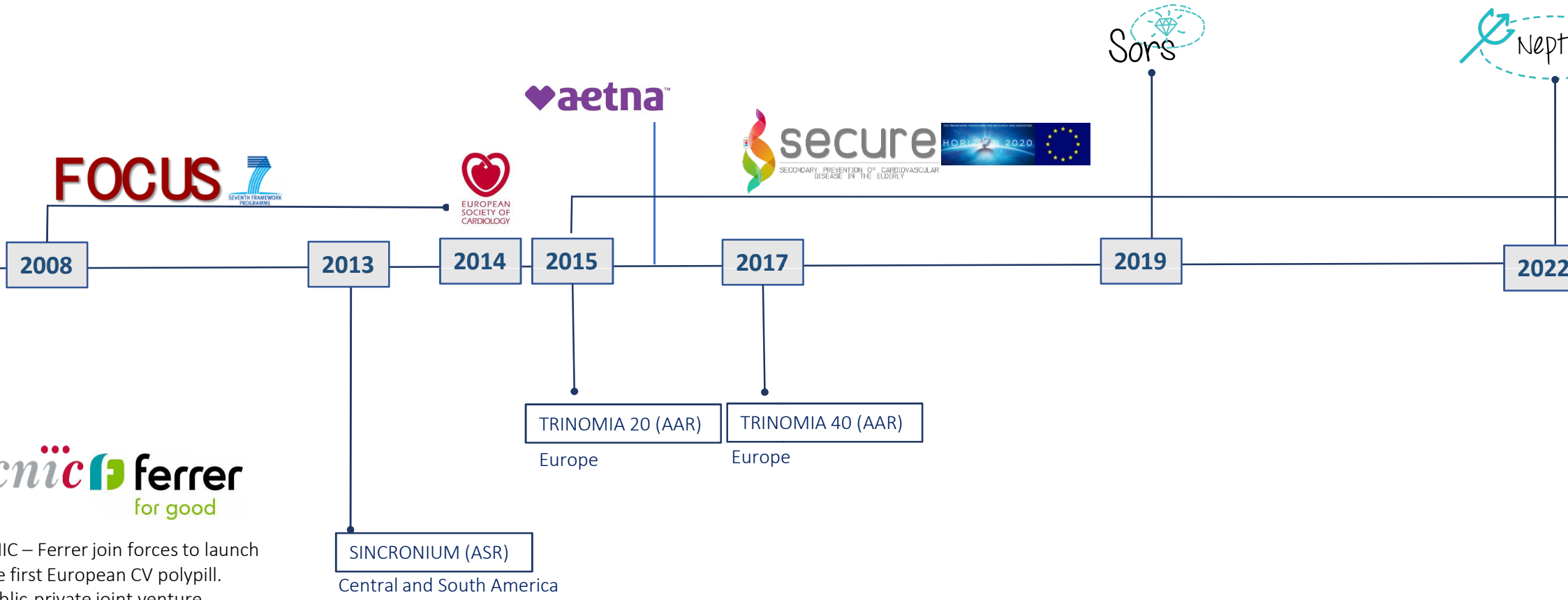
Horší prognóza až o 34 % u pacientů s nízkou nebo částečnou adherencí k léčbě beta-blokátorem



SCIENTIFIC DEVELOPMENT & MILESTONES

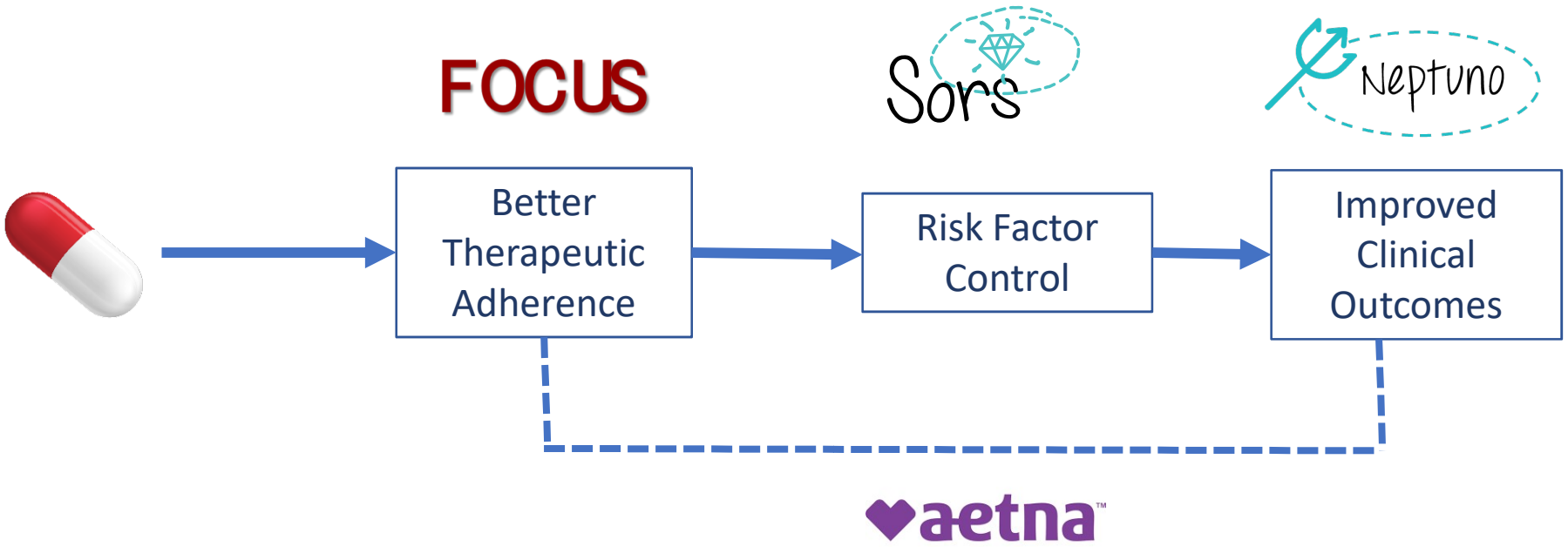
CNIC-Ferrer CV Polypill for Secondary Prevention



cnic ferrer for good

IC – Ferrer join forces to launch
e first European CV polypill.
blic-private joint venture.
. Valentin Fuster.

SECURE RATIONALE

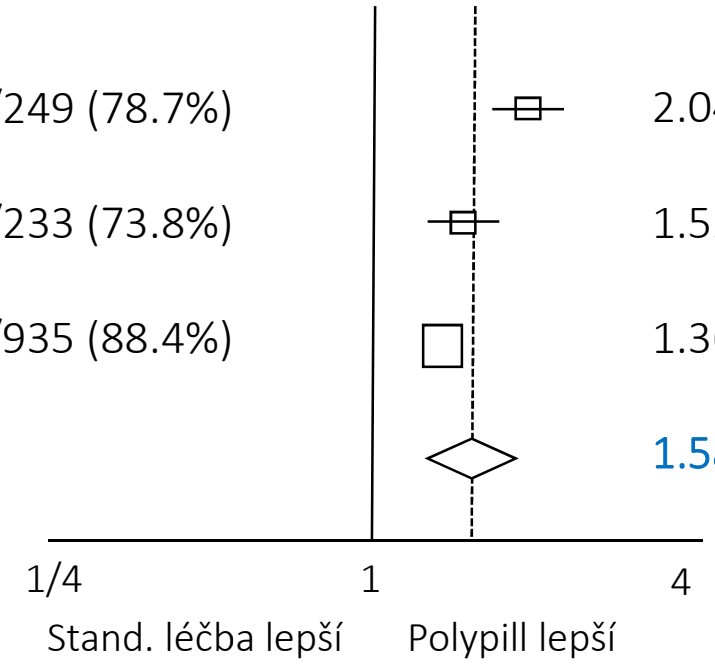


SPACE Program

Primary Outcomes – Adherence at 12 months

UMPIRE: n= 2002, India & W. Europe
Kanyini-GAP: n=623 in Australia, half indigenous
IMPACT: n=513 in NZ, half indigenous

	Usual Care	Polypill	Risk Ratio (95% CI)	P value
Kanyini-GAP	96/249 (38.6%)	196/249 (78.7%)	2.04 (1.72,2.42)	<0.01
IMPACT	106/218 (48.6%)	172/233 (73.8%)	1.52 (1.30,1.78)	<0.01
UMPIRE	602/925 (65.1%)	827/935 (88.4%)	1.36 (1.29, 1.43)	<0.01
Overall			1.58 (1.32, 1.90)	<0.01



Naderi SH et al.The American journal of medicine. 2012;125:882-887.

SECURE | Consortium

2499 patients recruited in 113 centers across 7 European Countries

Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC) |Valentin Fuster, MD, PhD (PI) Jose M. Castellano MD, PhD (Co-PI)

Istituto di Ricerche Farmacologiche "Mario Negri" (IRFMN) | **ITALY** |Maria Carla Roncaglioni, Biol Sci Dr

Charité, Universitätsmedizin Berlin | **GERMANY** |Wolfram Döhner, MD, Ph

University Hospital of Besançon| **FRANCE** |François Schiele, MD

Wroclaw Medical University |**POLAND** |Piotr Ponikowski, MD, PhD

Semmelweis University | **HUNGARY** |Matyas Keltai, MD, PhD

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Fundación Investigación Biomédica Hospital Clínico San Carlos | **SPAIN** |Antonio Fernandez Ortiz MD, PhD

London School of Hygiene and Tropical Medicine (LSHTM) | **UK** | Stuart Pocock, BSc MSc PhD

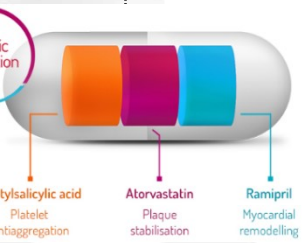
ferrer

Study Overview

n=2500
Post MI >65

+ at least one

a. Documented DM
b. Mild to moderate CKD
c. Prior MI
d. Prior coronary revascularization
e. Prior stroke
f. Age ≥ 75 years



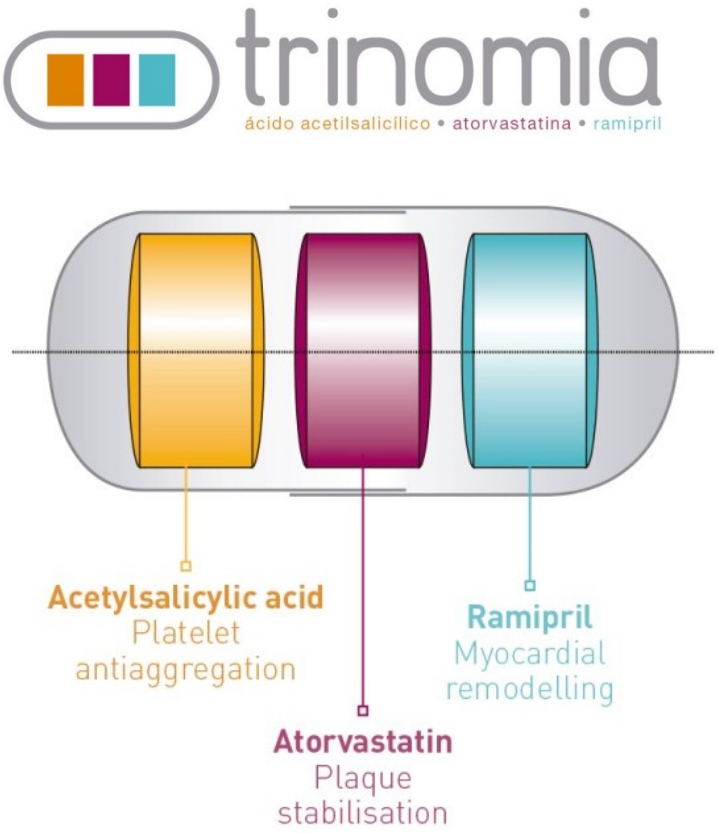
Median FU
3 years

MACE
Cardiovascular death
Nonfatal myocardial infarction
Nonfatal ischemic stroke
Urgent revascularization

The **primary composite endpoint** was cardiovascu
death, MI, stroke, or urgent revascularization.

The **key secondary endpoint** was the composite o
cardiovascular death, nonfatal MI, or stroke.

Přínosy strategie založené na polypill

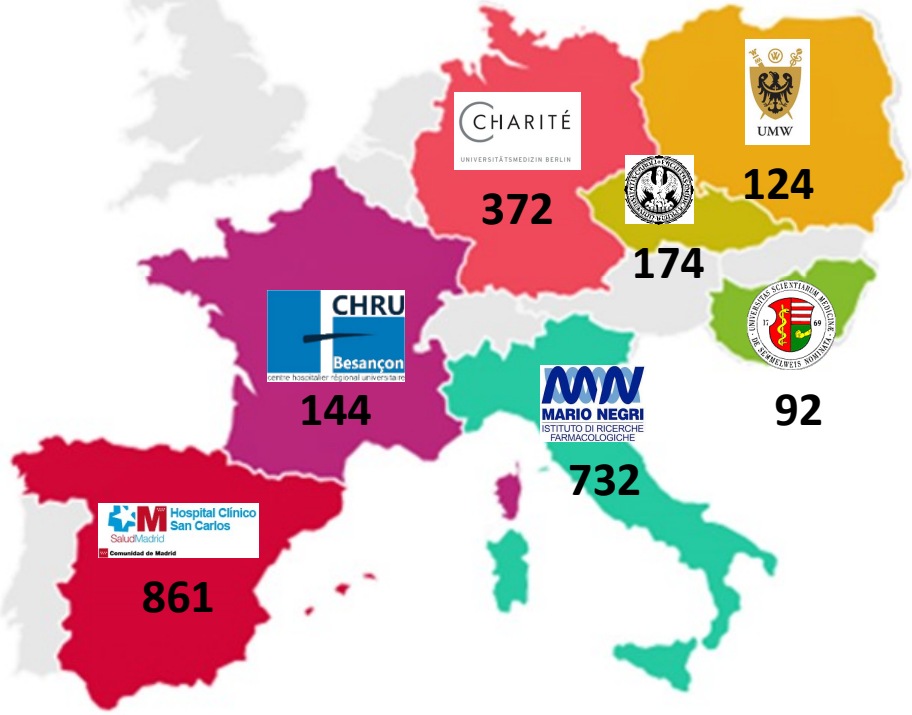


- Simplifikovat léčbu
- Zlepšit adherenci
- Snížit KV komplikace
- Zlepšit cost-efektivitu
- Zvýšit dostupnost
- Dosáhnout globálního efektu

Castellano JM et al., J Am Coll Cardiol. 2014;64:613-21.

Inclusion

Country, n (%)	Polypill	Usual Care
Spain	408 (16.3)	453 (18.1)
Italy	377 (15.1)	355 (14.2)
Germany	187 (7.5)	185 (7.4)
Czech Republic	87 (3.5)	87 (3.5)
France	80 (3.2)	64 (2.6)
Poland	58 (2.3)	66 (2.6)
Hungary	52 (2.1)	40 (1.6)



Baseline Demographics

	Polypill (n=1237)	Usual care (n=1229)
Age (years)		
Mean (SD)	75.8 (6.7)	76.1 (6.5)
<75	516 (41.7)	482 (39.2)
75+	721 (58.3)	747 (60.8)
Male	853 (69.0)	848 (69.0)
Female	384 (31.0)	381 (31.0)
Czech Republic	85 (6.9)	87 (7.1)
France	74 (6.0)	70 (5.7)
Germany	182 (14.7)	184 (15.0)
Hungary	45 (3.6)	45 (3.7)
Italy	366 (29.6)	365 (29.7)
Poland	63 (5.1)	60 (4.9)
Spain	422 (34.1)	418 (34.0)
Caucasian	1221 (99.2)	1211 (99.2)
Black	3 (0.2)	0 (0.0)
Other	7 (0.6)	10 (0.8)
Less than high school	580 (49.4)	576 (49.6)
Some high school	415 (35.3)	424 (36.5)
More than high school	179 (15.2)	162 (13.9)
Working full-time	37 (3.1)	27 (2.2)
Working part-time	17 (1.4)	13 (1.1)
Not working	39 (3.2)	34 (2.8)
Retired	1117 (92.3)	1132 (93.9)

Baseline Medical History

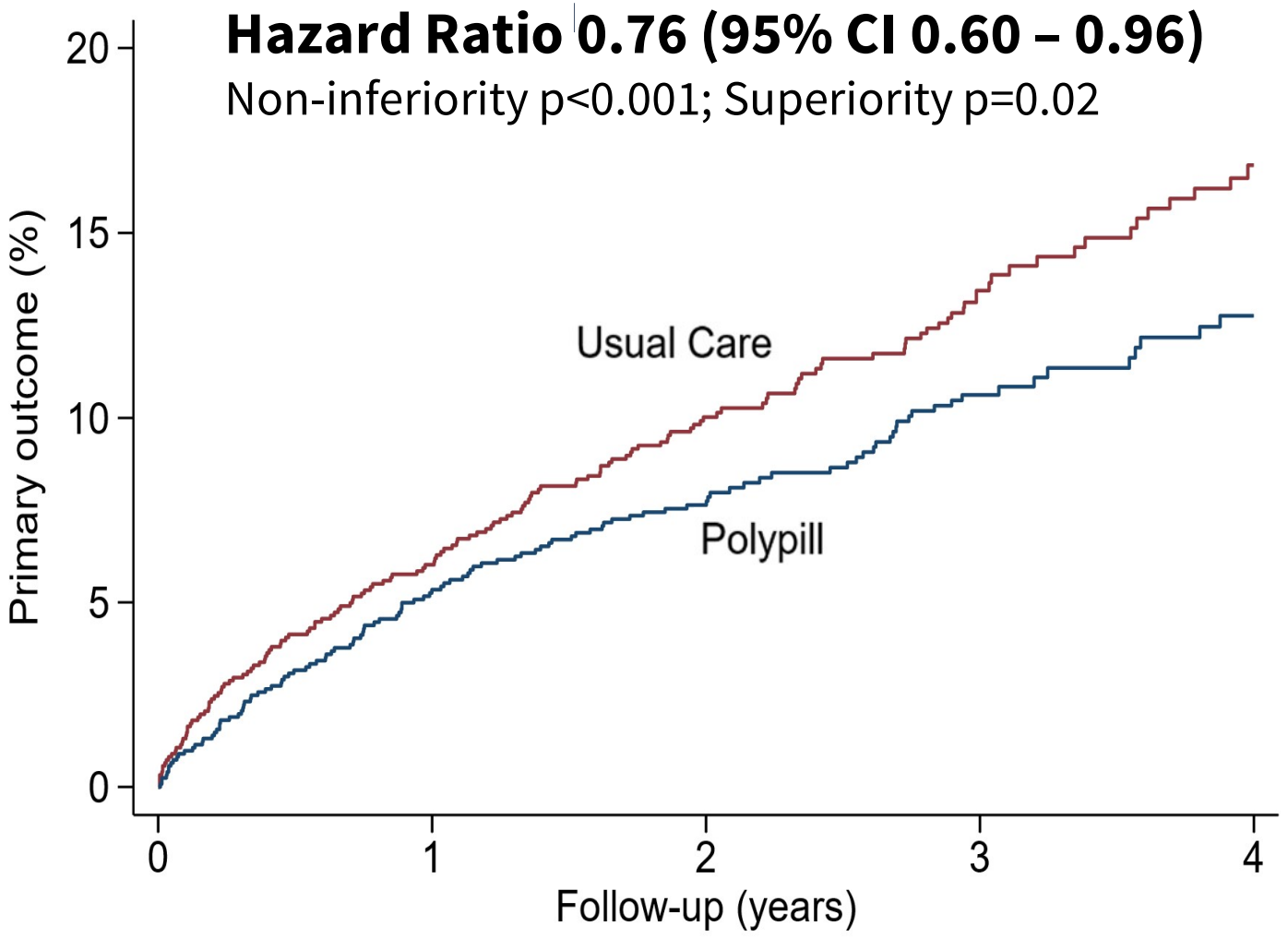
	Polypill (n=1237)	Usual care (n=1229)
Smoking status,		
Current	175 (15.0)	161 (13.8)
Former	459 (39.4)	471 (40.4)
Never	532 (45.6)	534 (45.8)
Diabetes mellitus,	520 (42.0)	531 (43.2)
Not insulin-dependent	370 (29.9)	412 (33.5)
Insulin-dependent	149 (12.1)	119 (9.7)
Hypertension,	952 (77.0)	966 (78.8)
Hyperlipidemia,	702 (57.4)	724 (59.6)
Angina pectoris,	280 (22.6)	317 (25.8)
Angina class,		
I	66 (28.2)	82 (29.3)
II	84 (35.9)	106 (37.9)
III	49 (20.9)	49 (17.5)
IV	35 (15.0)	43 (15.4)
Missing (%)	46 (16.4)	38 (12.0)
Previous MI,	260 (21.0)	276 (22.5)
Coronary artery disease,	373 (30.2)	389 (31.7)
Previous PCI,	273 (22.1)	274 (22.3)
Previous CABG,	71 (5.7)	92 (7.5)
Previous stroke,	88 (7.1)	79 (6.4)
Prior vascular event,	406 (32.8)	417 (33.9)
Previous heart failure,	25 (2.0)	25 (2.0)
CKD,	465 (37.6)	435 (35.4)
Peripheral arterial disease,	104 (8.4)	106 (8.6)
History of COPD/asthma,	123 (10.0)	116 (9.5)
History of cancer,	140 (11.3)	150 (12.2)

Primary Outcome

Composite of CV Death, MI, Stroke, and Urgent

Hazard Ratio 0.76 (95% CI 0.60 – 0.96)

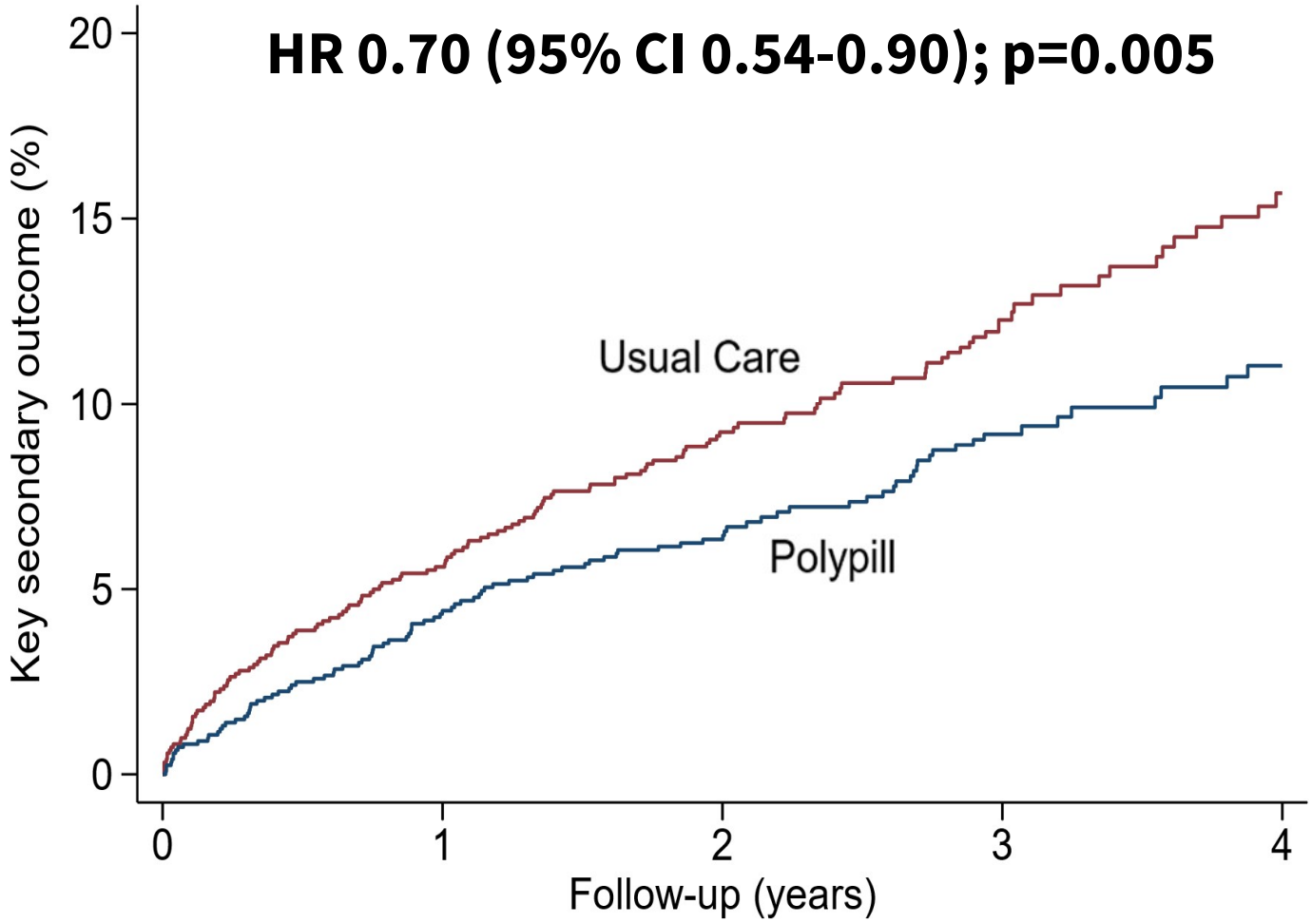
Non-inferiority p<0.001; Superiority p=0.02



Number at risk				
Usual Care 1229	1075	852	518	196
Polypill 1237	1064	848	511	192

Key Secondary Outcome

Composite of CV Death, MI, Stroke



Number at risk

Usual Care	1229	1079	857	522	196
Polypill	1237	1074	859	521	201

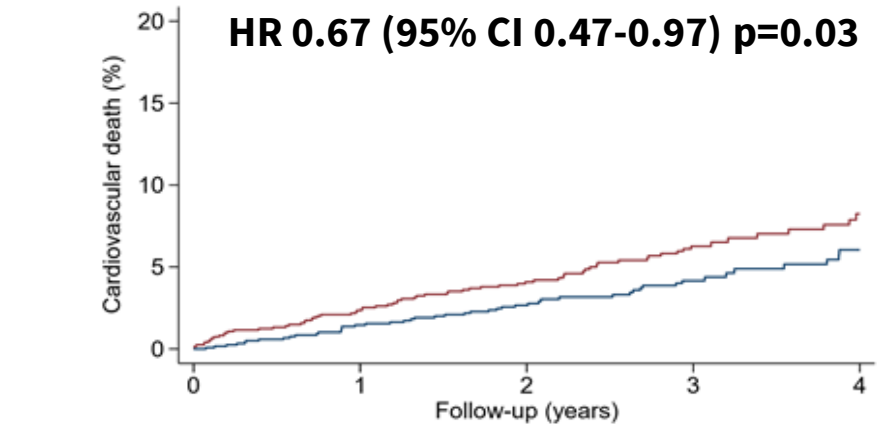
Primary and Secondary Outcomes ITT Analysis

	Polypill (n=1258)		Usual Care (n=1241)		HR (95% CI)	P
	N	%	N	%		
Primary outcome	118	9.5	156	12.7	0.76 (0.60, 0.96)	Non-inferiority p<0.001 Superiority p=0.02
Key secondary outcome						
Composite of CV death, type 1 MI or ischemic stroke	101	8.2	144	11.7	0.70 (0.54, 0.90)	0.005
Components of primary outcome						
CV death	48	3.9	71	5.8	0.67 (0.47, 0.97)	0.03
Type 1 MI	44	3.6	62	5.0	0.71 (0.48, 1.05)	0.09
Ischemic stroke	19	1.5	27	2.2	0.70 (0.39, 1.26)	0.24
Urgent revascularization	27	2.2	28	2.3	0.96 (0.57, 1.63)	0.88
Safety						
All-cause death	115	9.3	117	9.5	0.97 (0.75, 1.25)	0.79
Non-CV death	67	5.4	46	3.7	1.42 (0.97, 2.07)	0.07

Individual Components of the Primary Outcome

Cardiovascular Death

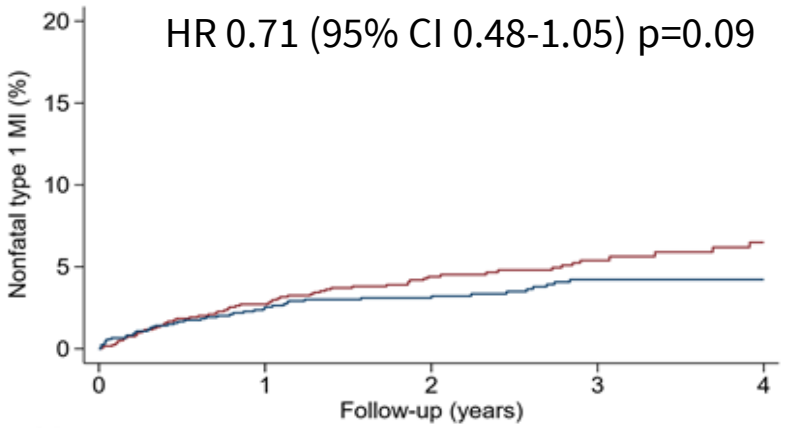
HR 0.67 (95% CI 0.47-0.97) p=0.03



Number at risk				
Usual Care 1229	1115	908	557	210
Polypill 1237	1108	890	550	209

Nonfatal type 1 MI

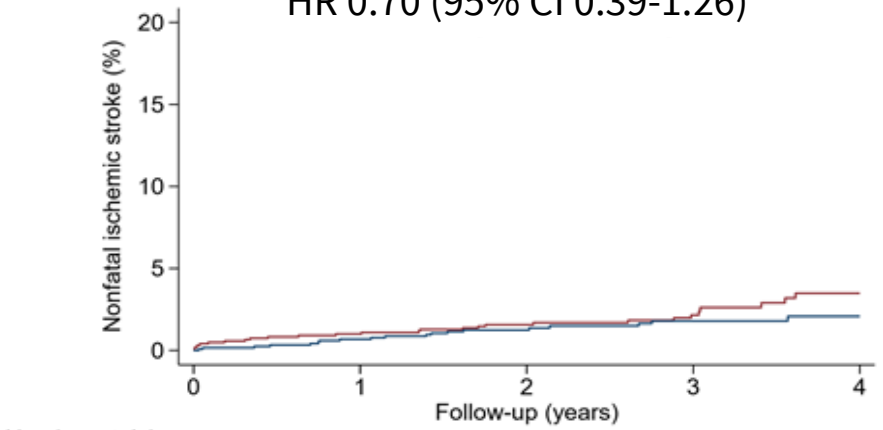
HR 0.71 (95% CI 0.48-1.05) p=0.09



Number at risk				
Usual Care 1229	1090	873	533	204
Polypill 1237	1079	867	530	204

Non Fatal Ischemic Stroke

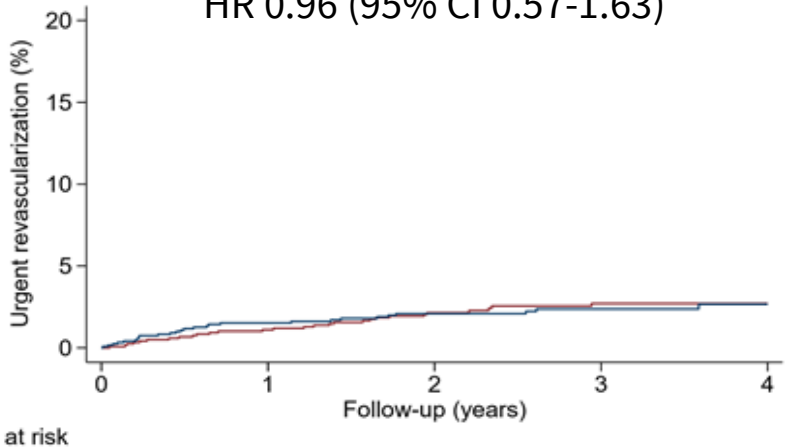
HR 0.70 (95% CI 0.39-1.26)



Number at risk				
Usual Care 1229	1104	892	546	201
Polypill 1237	1102	881	540	206

Urgent Revascularization

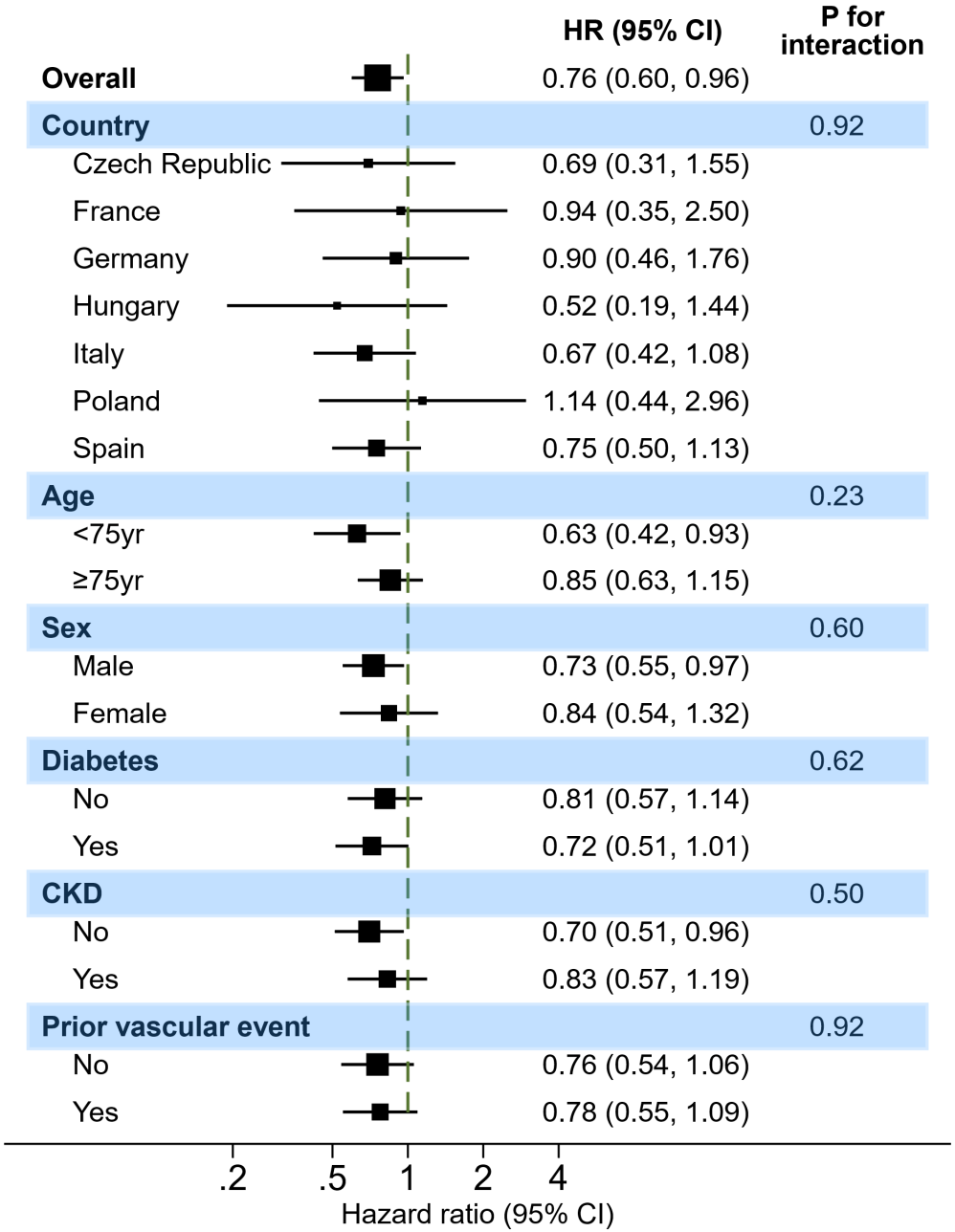
HR 0.96 (95% CI 0.57-1.63)



Number at risk				
Usual Care 1229	1106	895	547	210
Polypill 1237	1091	872	535	200

Usual Care Polypill

Primary Outcome in Prespecified Subgroups



Secondary Endpoints | SBP, DBP, LDL

	Polypill			Usual Care		
	N	Mean (SD)	Change from baseline, mean (SD)	N	Mean (SD)	Change from baseline, mean (SD)
SBP, mmHg						
Baseline	1235	129.1 (17.6)		1226	129.1 (17.9)	
6 months	1067		5.2 (21.3)	1053		5.7 (22.1)
12 months	986		7.5 (22.5)	972		5.7 (22.4)
24 months	882		6.3 (21.9)	830		6.3 (22.1)
DBP, mmHg						
Baseline	1235	71.1 (11.0)		1226	71.4 (11.4)	0.0 (0.0)
6 months	1067		3.0 (12.7)	1052		2.7 (13.0)
12 months	986		3.5 (12.7)	972		2.3 (13.1)
24 months	882		3.6 (12.6)	829		3.1 (13.3)
LDL cholesterol, mg/dL						
Baseline	1144	90.3 (37.9)		1144	88.3 (36.3)	
12 months	874		-20.3 (35.6)	871		-20.5 (36.9)
24 months	781		-22.3 (36.7)	715		-20.7 (38.4)

No evidence of treatment differences over time

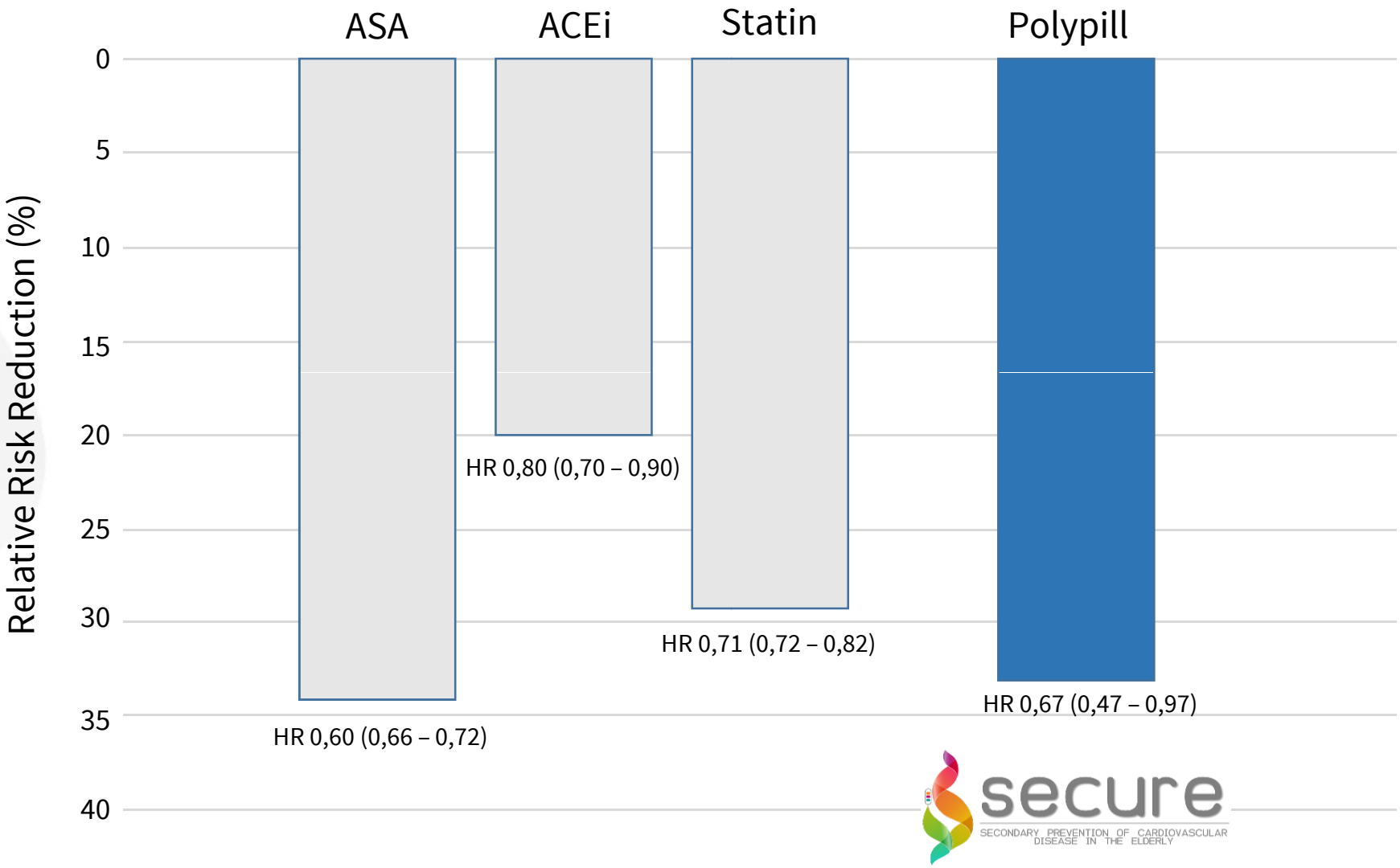
Adverse Events

	Polypill (n=1237)	Usual Care (n=1229)
Total AEs, n	704	688
Patients experiencing an AE, n (%)	404 (32.7)	388 (31.6)
Total non-fatal SAEs, n	339	346
Experiencing a non-fatal SAE, n (%)	237 (19.2)	224 (18.2)
Specific AEs of interest		
BARC Bleeding	57 (4.6)	49 (4.0)
Refractory cough*	40 (3.2)	35 (2.8)
Renal†	24 (1.9)	22 (1.8)
Drug allergy	14 (1.1)	7 (0.6)

AE – Adverse Event; SAE – Serious Adverse Events; BARC - Bleeding Academic Research Consortium
***Leading to drug discontinuation**
†Leading to drug discontinuation

Results in Context | Reductions in CV Death

Estimated Efficacy of Pharmacotherapy in Secondary Prevention



secure
SECONDARY PREVENTION OF CARDIOVASCULAR DISEASE IN THE ELDERLY

Strengths

- Kaplan meyer curves for primary endpoint and key secondary endopoint for polypill vs. usual care diverge early and differences increase over time.
- Control group probably displayed better adherence than real world patients who are not enrolled on a RCT where adherence is measured at 6 and 24 months.
- It is reasonable to infer differences may be larger in the real world in similar settings and even larger in LMICs.

Contribution from the Czech republic

Nemocnice Slaný
Prim. MUDr. Ondřej Čermák

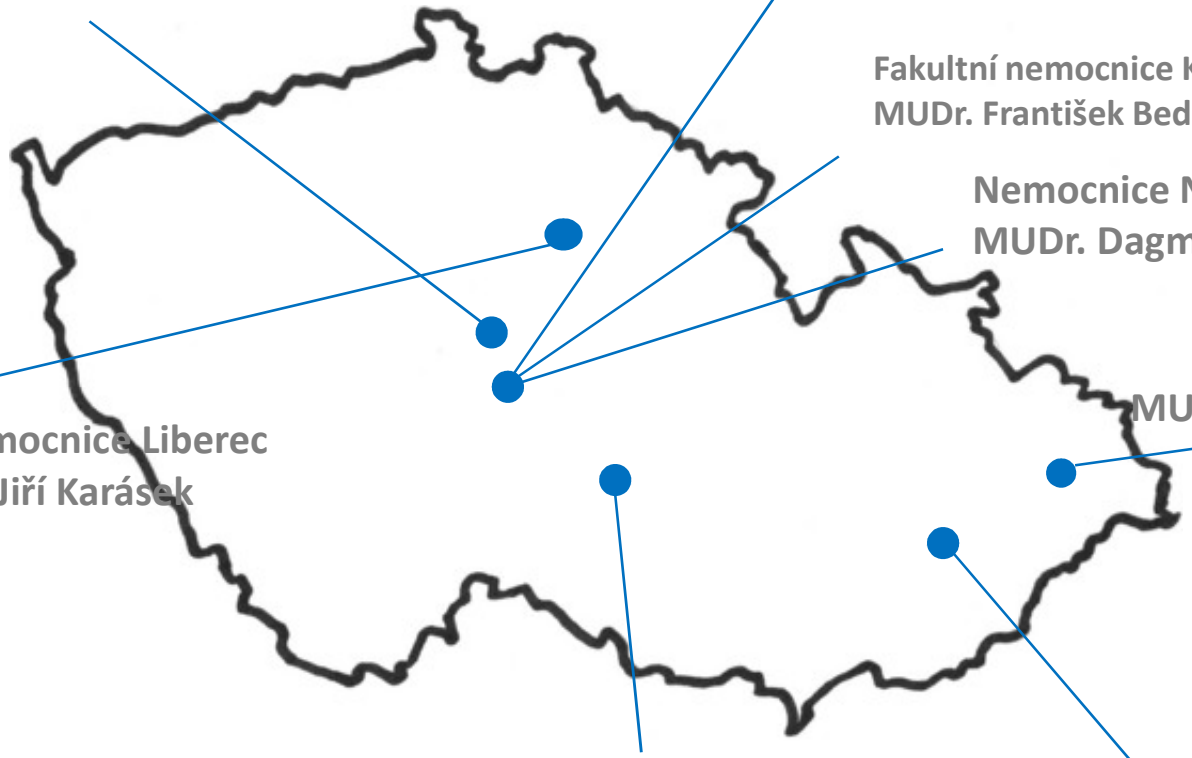
Všeobecná fakultní nemocnice v Praze
Doc. MUDr. Jean-Claude Lubanda, PhD
Prof. MUDr. Aleš Linhart, DrSc.

Fakultní nemocnice Královské Vinohrady
MUDr. František Bednář, PhD.

Nemocnice Na Homolce
MUDr. Dagmar Vondráková

Nemocnice Podlesí
MUDr. Libor Škňouřil, PhD.

Krajská Nemocnice Liberec
MUDr. Jiří Karásek



Nemocnice Jihlava
Prim. MUDr. Zdeněk Klimsa

Fakultní nemocnice Olomouc
Prof. MUDr. Miloš Táborský, CSc., MBA

THE FRAMEWORK PROGRAMME FOR RESEARCH AND INNOVATION
HORIZON 2020

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SECONDARY PREVENTION OF CARDIOVASCULAR DISEASE IN THE ELDERLY

Number of subject breakdown in the Czech republic

number	center	n
101	VFN	71
102	NNH	10
103	FNKV	11
104	FN Olomouc	6
105	Nemocnice RS Benešov	2
106	Nemocnice Slaný	12
107	Nemocnice Jihlava	20
108	Nemocnice Podlesí	35
109	Krajská nemocnice Liberec	7
	total	**174**

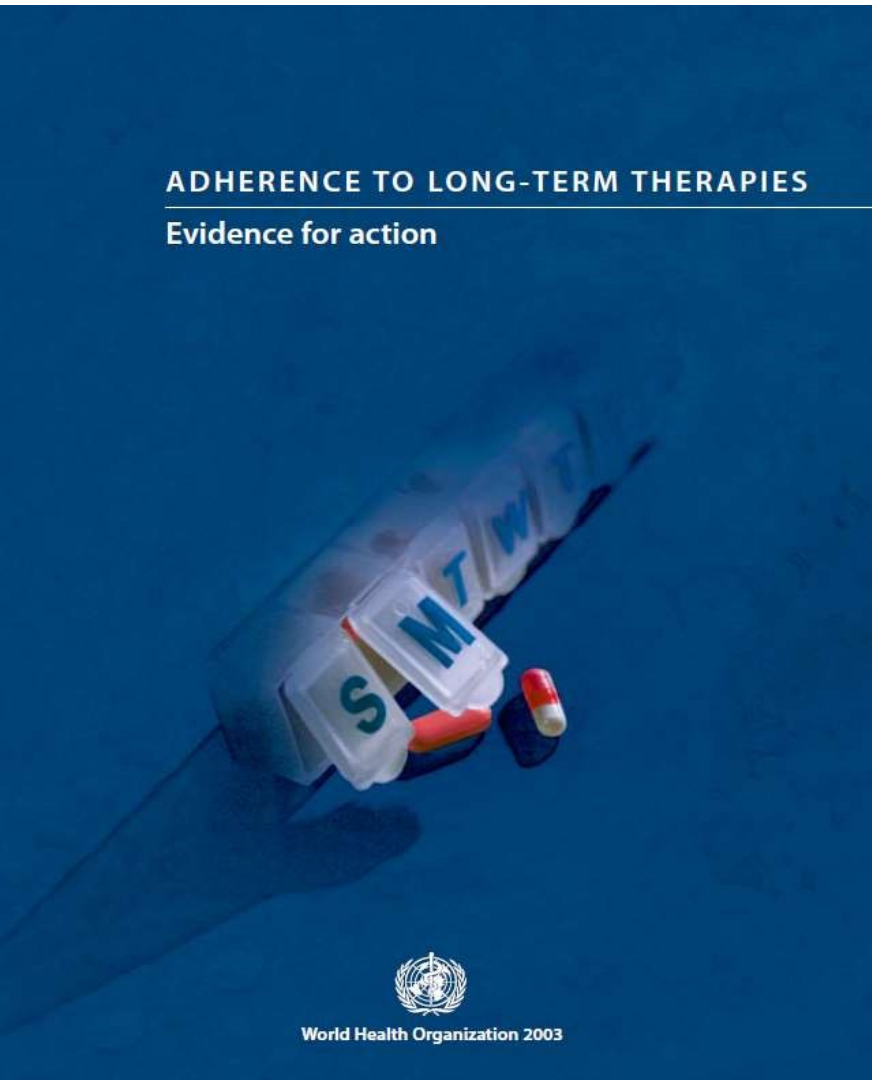
Conclusions

A treatment strategy based on **a polypill containing aspirin, atorvastatin, and ramipril**, led to **reductions in recurrent cardiovascular** events following MI in elderly patients.

- 24% RRR composite MACE
- 30% RRR in key secondary endpoint
- 33% RRR in CV death

The **use of a polypill strategy is safe**, there were no significant differences in adverse events between groups.

The use of a cardiovascular polypill as a substitution approach could be an integra part of a **global strategy to improve secondary prevention**.



"Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments"

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Polypill Strategy in Secondary Cardiovascular Prevention

J.M. Castellano, S.J. Pocock, D.L. Bhatt, A.J. Quesada, R. Owen, A. Fernandez-Ortiz, P.L. Sanchez, F. Marin Ortuño, J.M. Vazquez Rodriguez, A. Domingo-Fernández, I. Lozano, M.C. Roncaglioni, M. Baviera, A. Foresta, L. Ojeda-Fernandez, F. Colivicchi, S.A. Di Fusco, W. Doehner, A. Meyer, F. Schiele, F. Ecarnot, A. Linhart, J.-C. Lubanda, G. Barczi, B. Merkely, P. Ponikowski, M. Kasprzak, J.M. Fernandez Alvira, V. Andres, H. Bueno, T. Collier, F. Van de Werf, P. Perel, M. Rodriguez-Manero, A.A. Garcia, M. Proietti, M.M. Schoos, T. Simon, J. Fernandez Ferro, N. Lopez, E. Beghi, Y. Bejot, D. Vivas, A. Cordero, B. Ibañez, and V. Fuster, for the SECURE Investigators*

Cor et Vasa

REPRINT

Fixní kombinace a adherence u pacientů po infarktu myokardu nebo s kardiovaskulárním onemocněním – zkušenosti v rámci studie SECURE

Jean-Claude Lubanda, Hana Lubanda

Cor Vasa 2024;66:99–102.