Disclosure

Simon Thom, UMPIRE Trial
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This work was funded by the European Commission.

Dr Reddy's Laboratories provided the trial medication.

Simon Thom has received funds towards travel costs from Dr Reddy's.

UMPIRE
Use of a Multidrug Pill In Reducing Cardiovascular Events

SEVENTH FRAMEWORK PROGRAMME

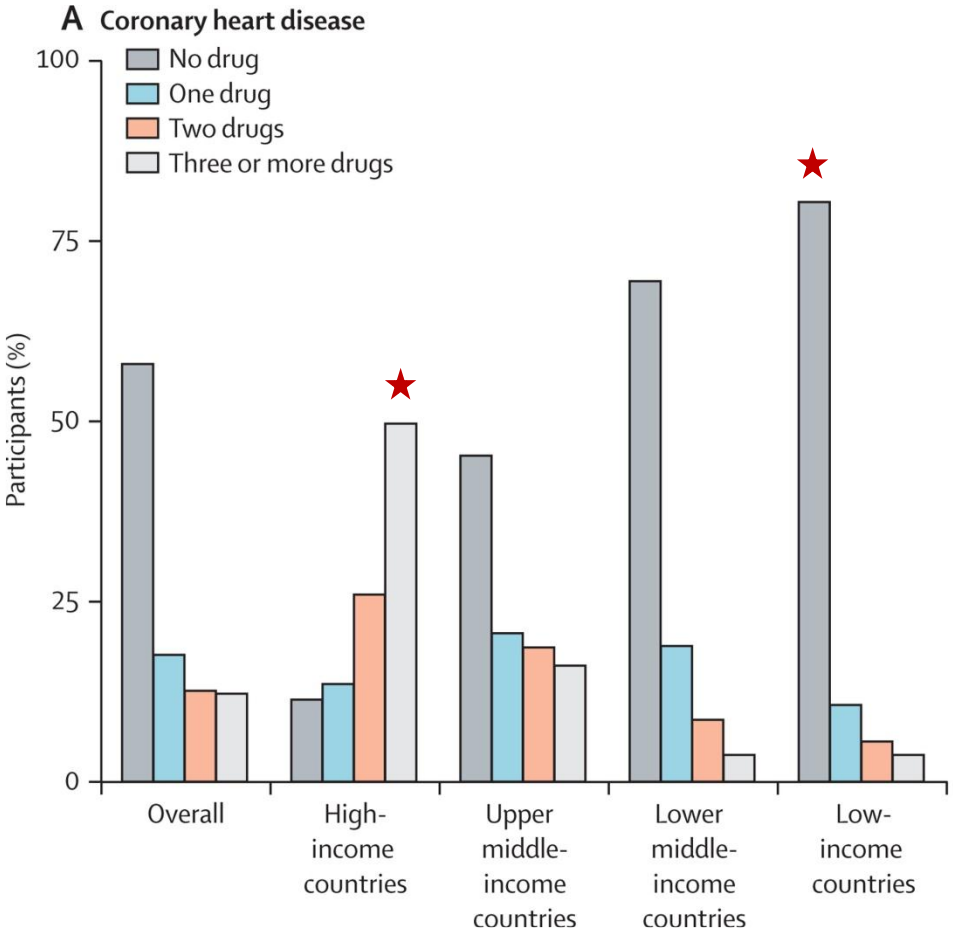
UMPIRE trial
Use of a Multidrug Pill In Reducing cardiovascular Events

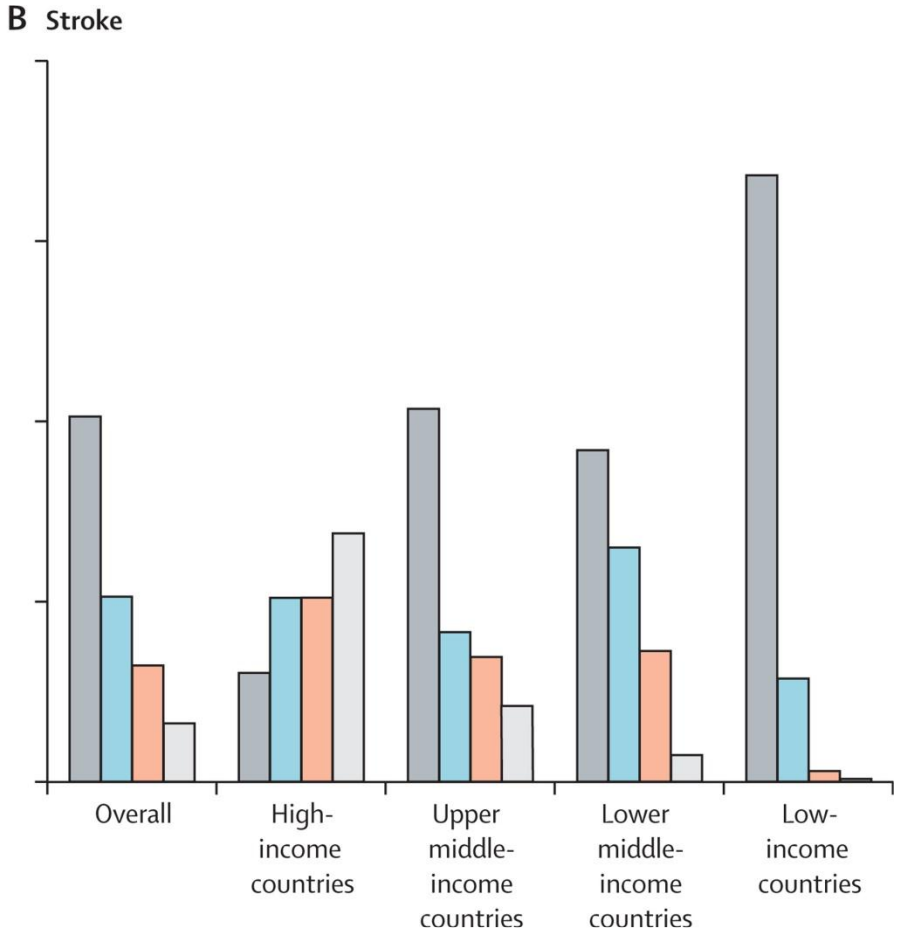
Simon Thom; UMPIRE Collaborative group

Universitair Medisch Centrum Utrecht
Imperial College London
The George Institute for International Health
phfi Public Health Foundation of India
Dr. Reddy's Life. Research. Hope
Centre for Chronic Disease Control
RCSI

Background

Use of secondary prevention drugs for CVD in the community in high-income, middle-income, & low-income countries (the PURE Study)





Yusuf S et al. Lancet 2011; 378: 1231-43

UMPIRE trial, PROBE design

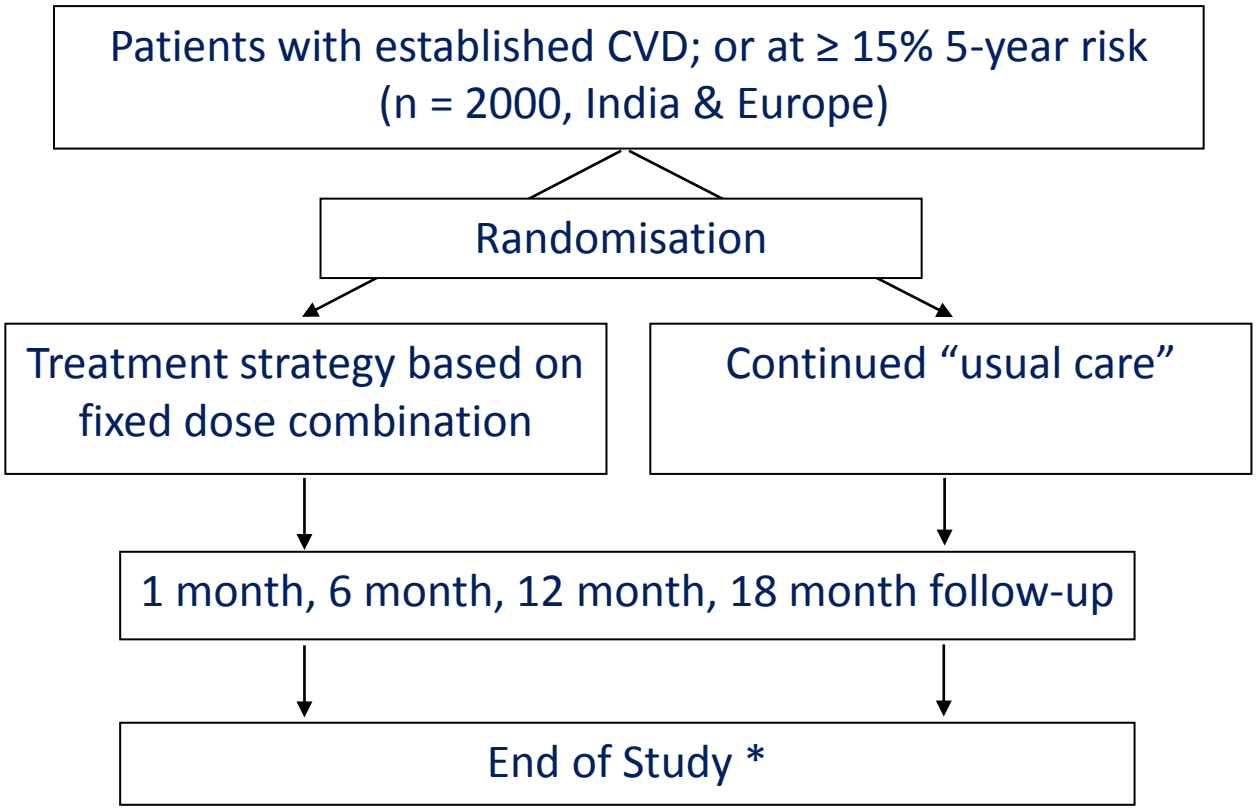
Primary objectives

- To test the hypothesis that a fixed dose combination-based strategy (a “polypill”) for delivery of preventive medications (aspirin, statin and two blood pressure lowering agents) compared with usual care might improve:
  - Adherence to indicated therapy
  - Systolic BP
  - LDL-cholesterol,

  at end of study,

  in people with (or at high risk of) cardiovascular disease.

PROBE design



← inclusion

exclusion: contraindications or known intolerance of FDC components

* 12 months after last randomisation

Methods

- Adherence: self-reported use of [antiplatelet, statin and ≥2 BP lowering therapy]
- BP: electronic device (Omron 705CP II) + printer
- Cholesterol & all blood tests: local laboratories

Randomisation

- FDC : usual care, 1 : 1 (web-based)
- Stratified by presence or absence of established CVD

Trial sites

- 28 in India
- 3 in Europe (Dublin, London, Utrecht)

Recruitment

- June 2010 – July 2011

Study treatments

Fixed dose combinations, x 2

Version 1	Version 2
aspirin 75mg	aspirin 75mg
simvastatin 40mg	simvastatin 40mg
lisinopril 10mg	lisinopril 10mg
atenolol 50mg	hydrochlorothiazide 12.5mg

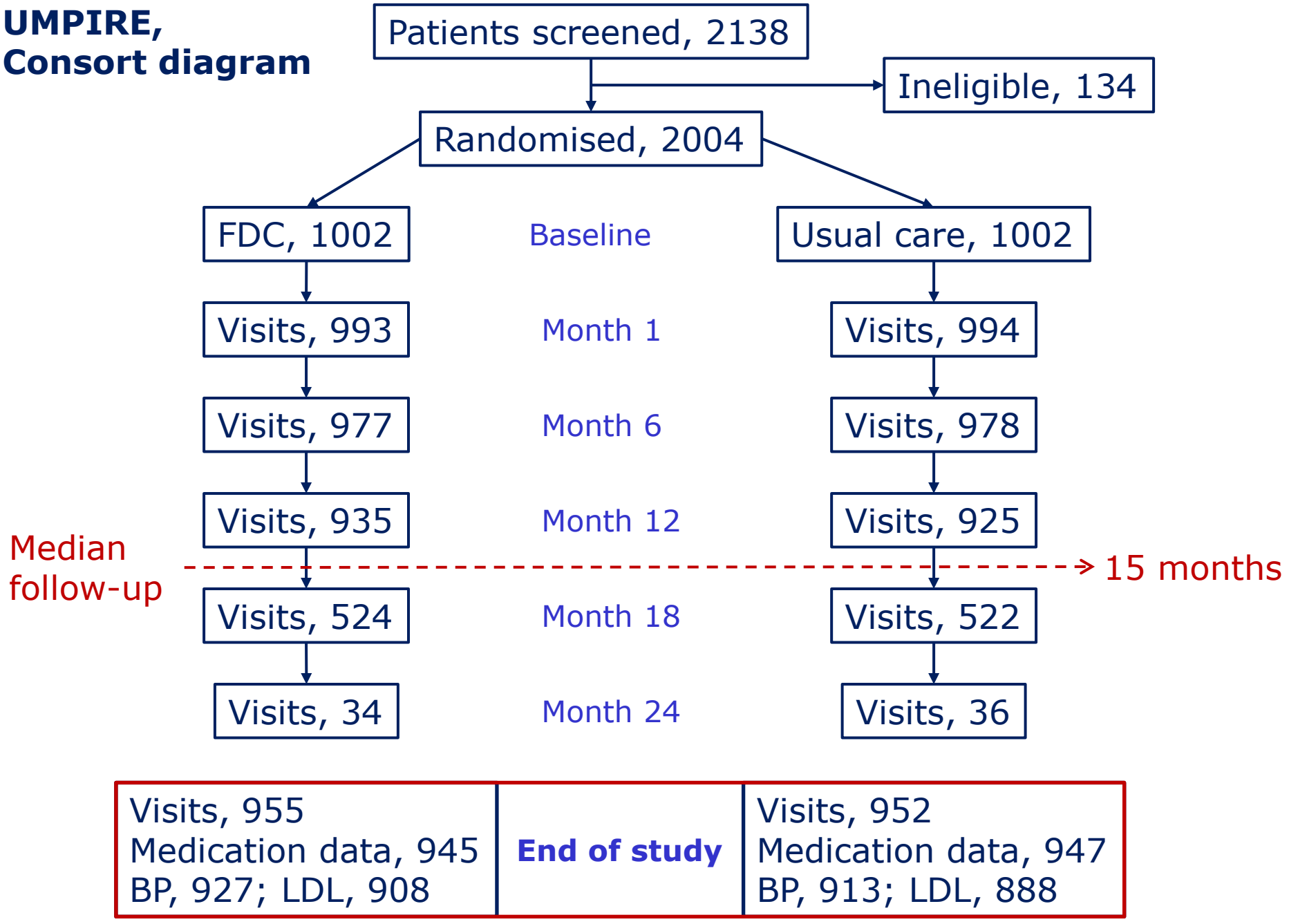
Physicians could add additional medications, stop the FDC & begin treatment with separate medications, or switch FDC version.

Usual care

As per local clinical guidelines.

Participants in the FDC group were dispensed study FDC free of charge from their trial centre.
Participants in the usual care group acquired their medications subject to local payments or exemptions.

UMPIRE, Consort diagram



Baseline characteristics

	FDC (N = 1002)	Usual care (N = 1002)
Age	62.1 (10.4)	61.6 (10.8)
Male	81 %	82 %
SBP (mmHg)	137.0 (21.3)	137.7 (21.1)
LDL-cholesterol (mmol/L)	2.3 (0.8)	2.4 (0.9)
Medical history		
Established CVD	88 %	88 %
Diabetes mellitus	28 %	28 %
Current drug treatment		
Antihypertensive treatment		
None	7.6 %	6.6 %
1 BP drug	26.5 %	22.5 %
≥2 BP drugs	65.9 %	71.0 %
Statin	88.0 %	87.6 %
Anti-platelet drug	91.8 %	91.0 %
All indicated medications	59.7 %	63.4 %

Indicated medications =
statin +
anti-platelet +
≥2 anti-hypertensive drugs

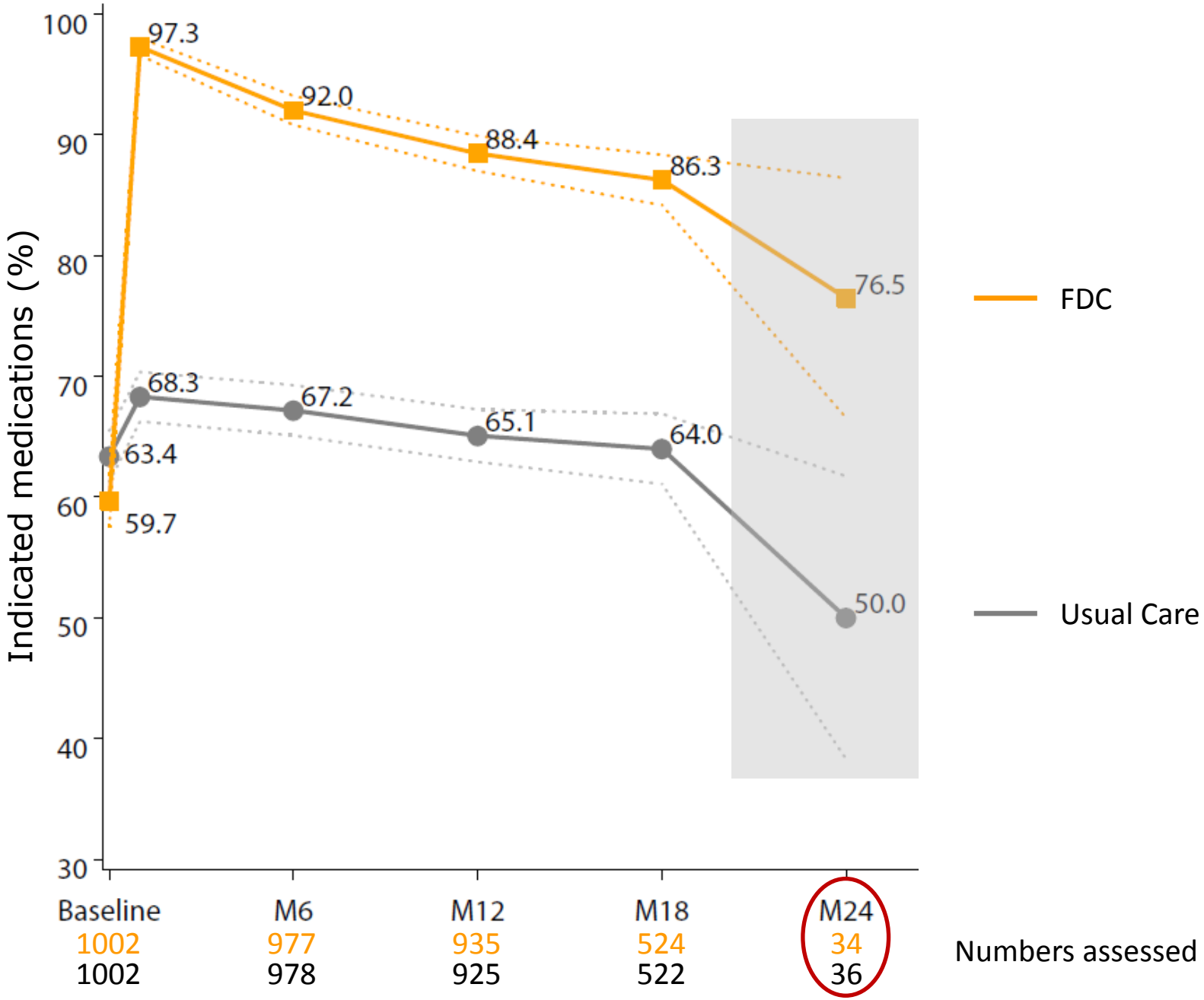
Primary outcomes

Effects of treatment on adherence to indicated medications, systolic BP & LDL-cholesterol at end of study

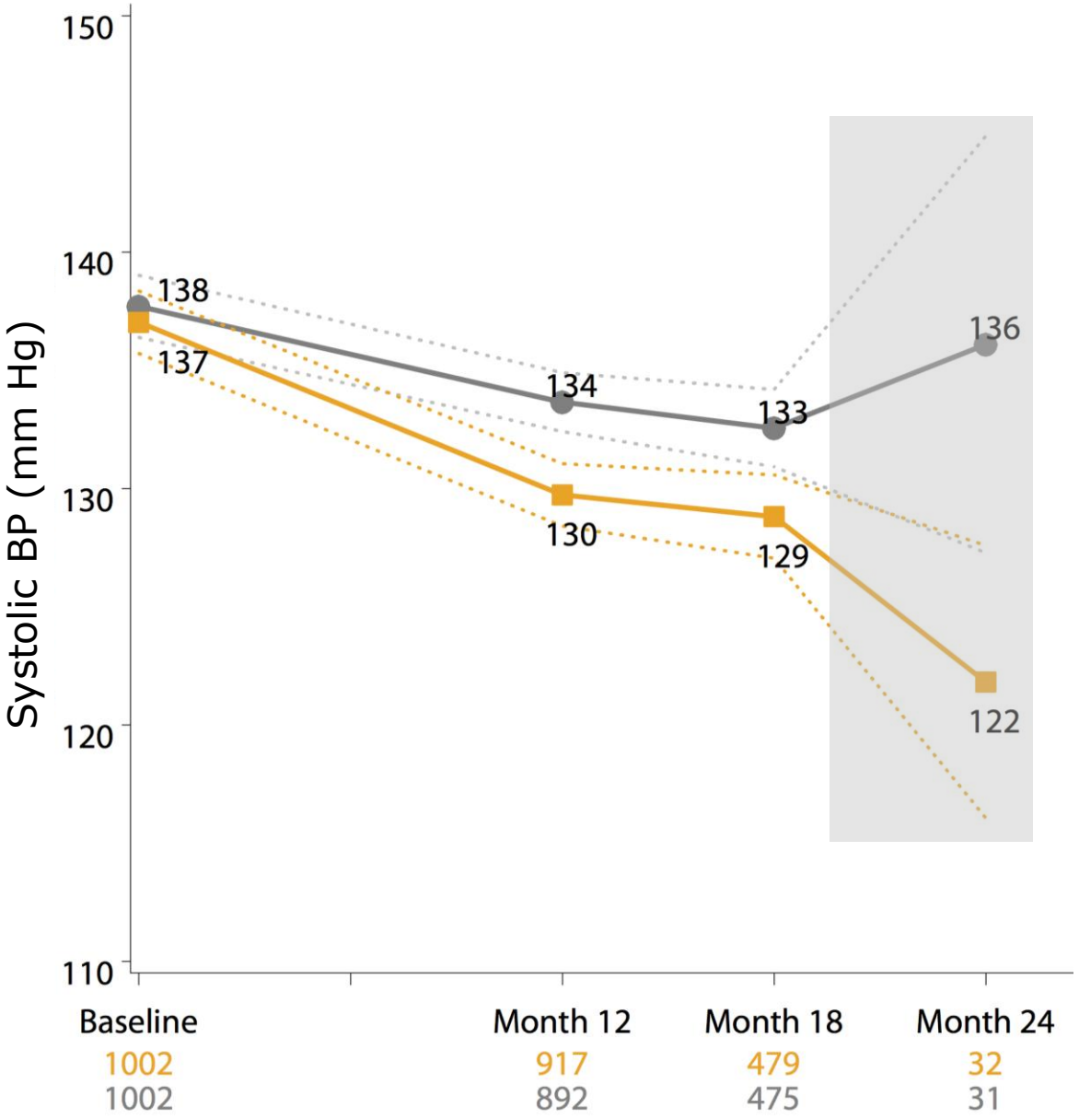
Outcome	FDC (N = 1002)	Usual care (N = 1002)	Treatment Effect (95% CI)	P-value
Adherence (%)	86% (1%)	65% (2%)	1.33 (1.26; 1.41)	<.0001
Systolic BP (mmHg)	129.2 (0.5)	131.7 (0.5)	-2.6 (-4.0; -1.1)	0.0005
LDL-cholesterol (mmol/L)	2.18 (0.02)	2.29 (0.02)	-0.11 (-0.17; -0.05)	0.0005

1 mmol/L = 38.67 mg/dl cholesterol

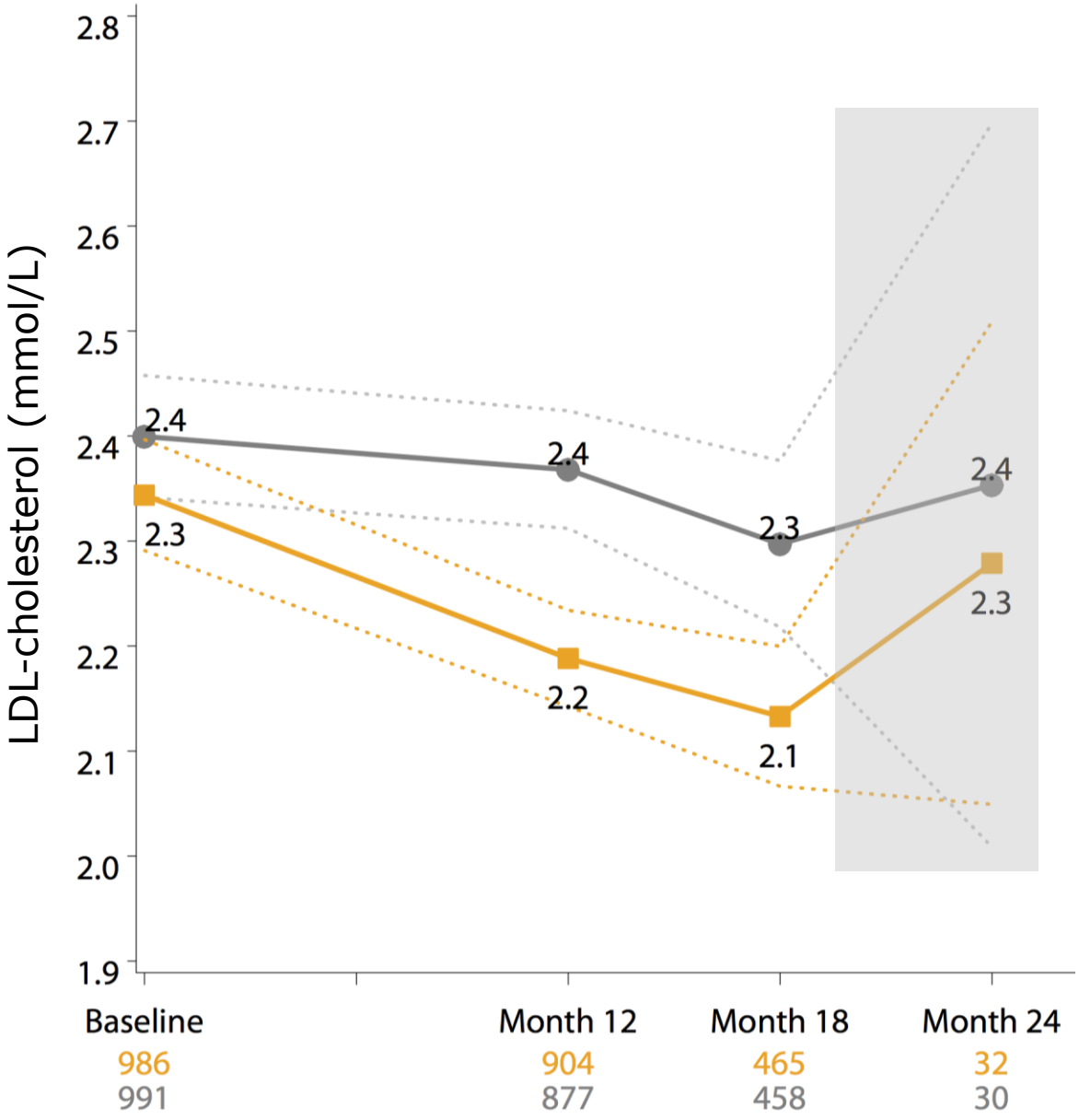
Adherence to indicated medications by treatment group



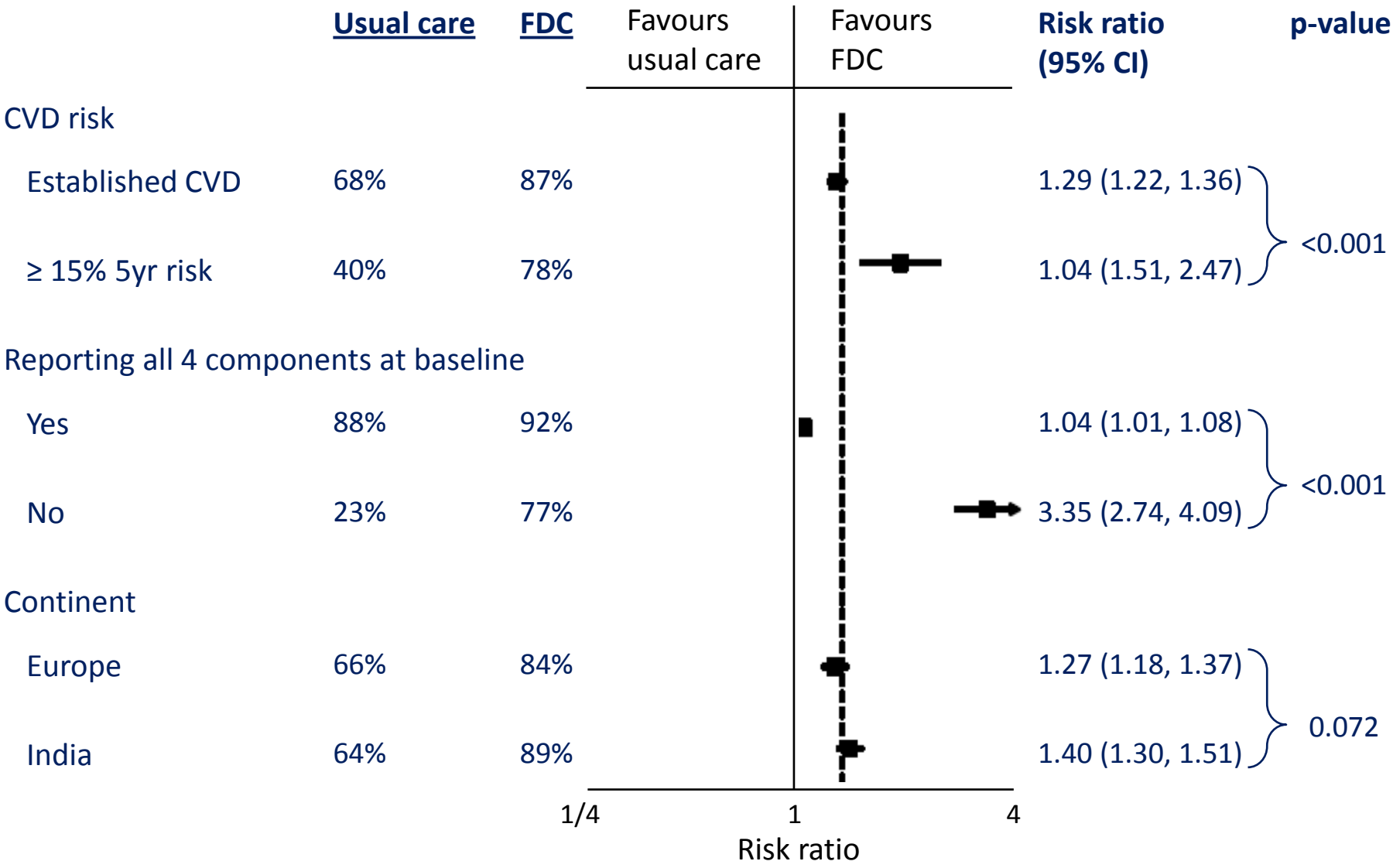
Systolic blood pressure by treatment group



LDL-cholesterol by treatment group



Adherence by pre-specified subgroups



Secondary outcomes

Outcome	FDC (N = 1002)	Usual care (N = 1002)	Treatment Effect (95% CI)	P-value
Adherence at 12 months (%)	88% (1%)	65% (2%)	1.36 (1.29; 1.43)	<.0001
Diastolic BP (mmHg)	72.8 (0.3)	75.2 (0.3)	-2.5 (-3.3; -1.6)	<.0001
Total cholesterol (mmol/L)	4.06 (0.03)	4.12 (0.03)	-0.07 (-0.14; 0.01)	0.08
HDL-cholesterol (mmol/L)	1.14 (0.01)	1.13 (0.01)	0.01 (0.00; 0.03)	0.1
Triglycerides (mmol/L)	1.61 (0.03)	1.57 (0.03)	0.04 (-0.03; 0.11)	0.3
Creatinine (µmol/L)	94.6 (0.6)	91.9 (0.6)	2.7 (1.0; 4.4)	0.002
Quality of life (EQ5D; VAS)	76.1 (0.56)	73.7 (0.57)	2.43 (0.87; 3.99)	0.002
Cardiovascular events (n)	50 (5%)	35 (3.5%)	1.45 (0.94; 2.24)	0.09

Cholesterol 1 mmol/L = 38.67 mg/dl; Triglyceride 1 mmol/L = 88.6 mg/dl; Creatinine I µmol/L = 0.0113 mg/dl.

Serious adverse events

SAE category	FDC (N = 1002)	Usual care (N = 1002)
Total	154	142
Patients with at least one SAE	118 (11.8%)	102 (10.2%)
Cardiac disorders	42 (4.2%)	27 (2.7%)
Infections & infestations	16 (1.6%)	10 (1.0%)
Neoplasms benign & malignant	13 (1.3%)	11 (1.1%)
Vascular disorders	11 (1.1%)	12 (1.2%)
Nervous system disorders	9 (0.9%)	13 (1.3%)
Gastrointestinal disorders	10 (1.0%)	11 (1.1%)
Other	36 (3.6%)	40 (4%)

Conclusions

- A fixed dose combination strategy including aspirin, statin & 2 BP lowering drugs improves adherence, blood pressure and cholesterol in patients with established cardiovascular disease and those at high risk.
- The effect, a 33% increase in adherence over a 15 month interval, was evident in a trial population with an unusually high reported use of indicated medication at the outset.

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Thanks for your attention

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http://www.spacecollaboration.org

SPACE (Single Pill Against Cardiovascular Events)

http://clinicaltrials.gov/ct2/show/NCT01057537?term=umpire&rank=1

http://www.ctri.in/Clinicaltrials/index.jsp

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