

Current Trend in Cardiovascular Research in China

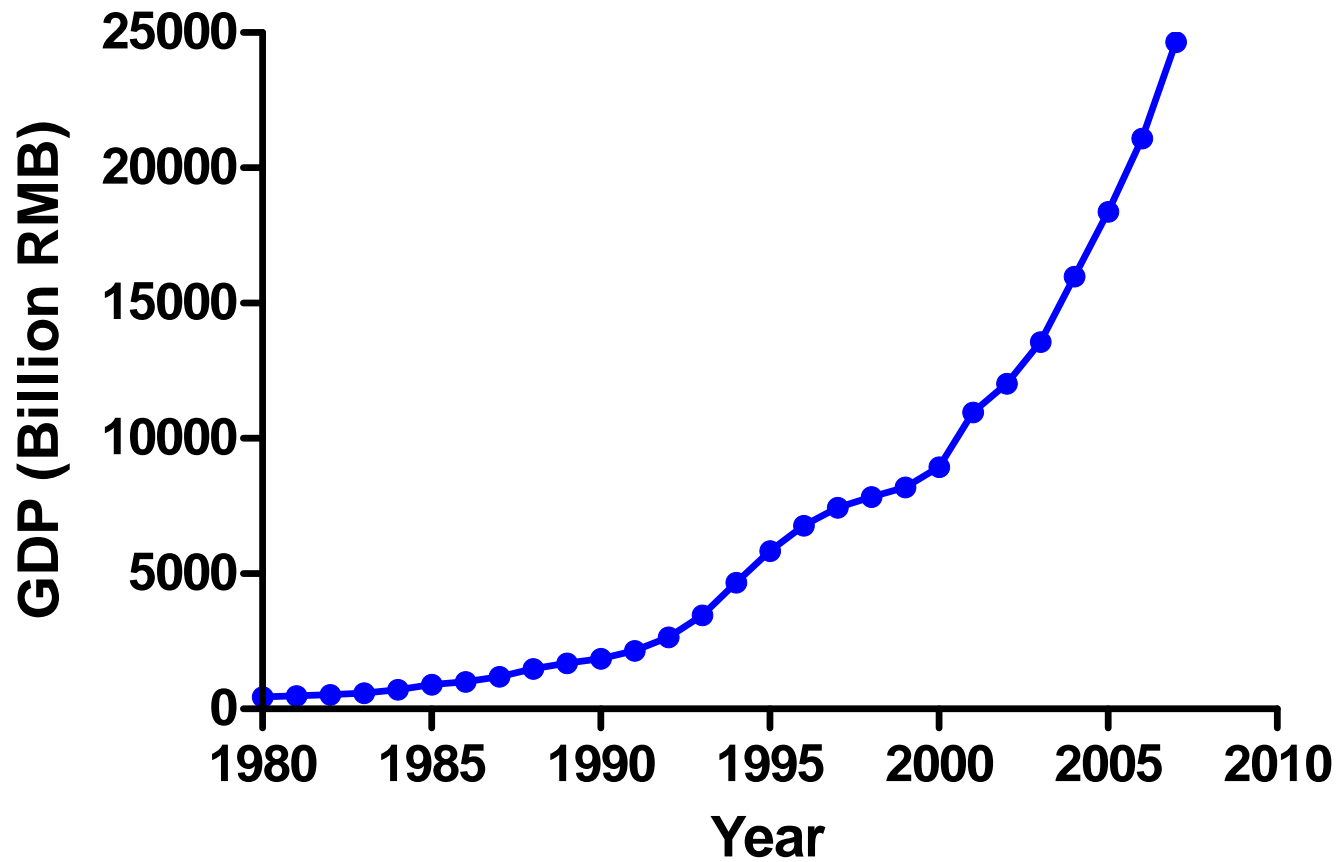
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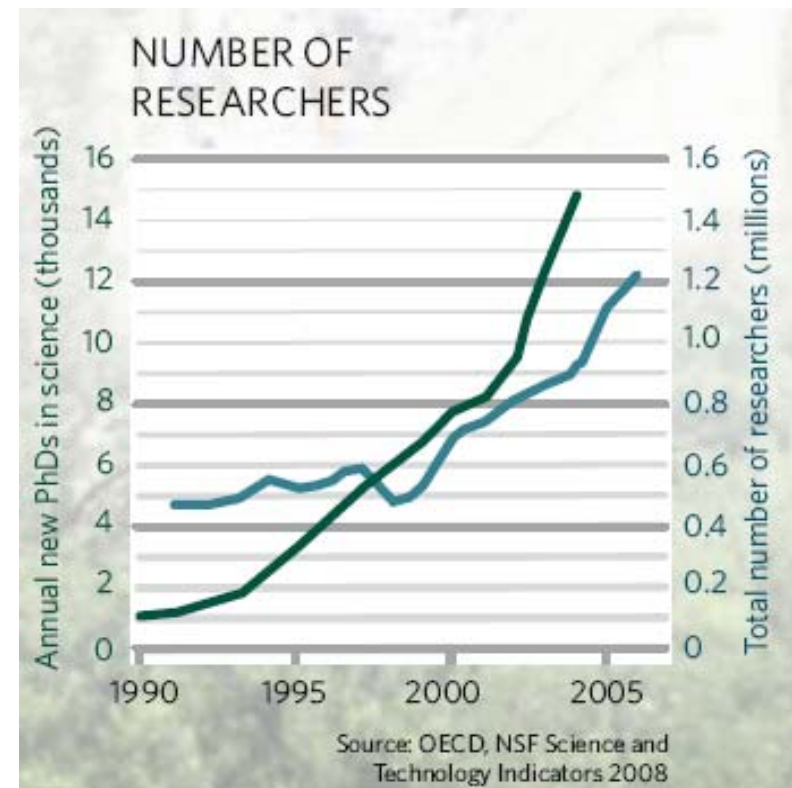
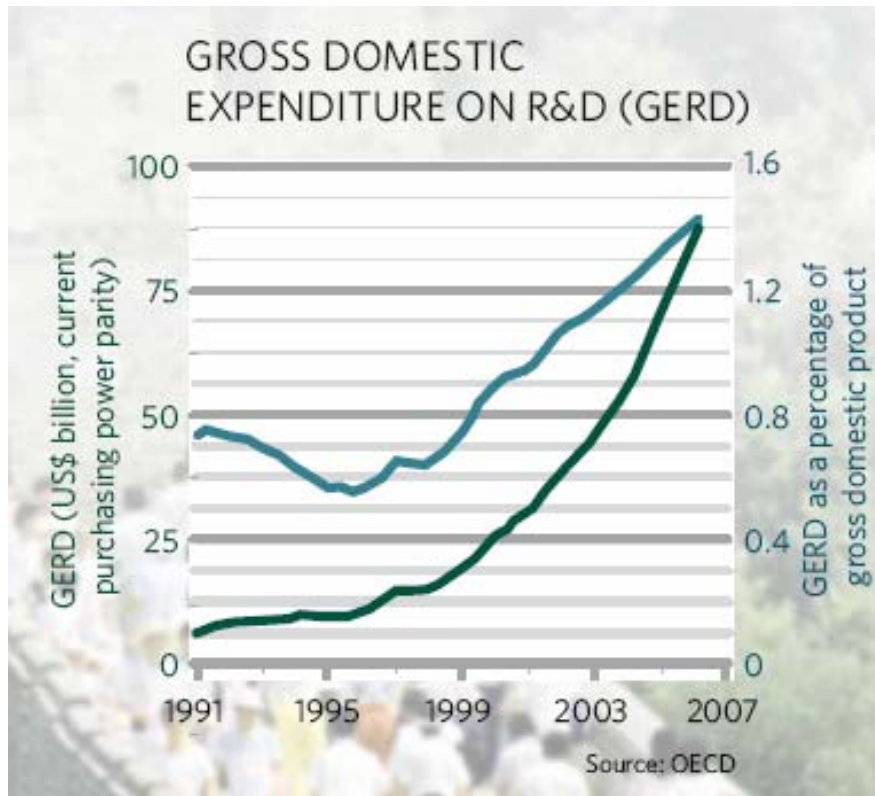
Overview

- Economic growth and scientific output
- Advances in cardiovascular research
- COMMIT trial
- Stem cell studies
- Prevention of cardiovascular disease
- Opportunities for research collaborations

GDP Growth (1980-2007)



Research spending and increasing number of scientists in China



Nature, July 2008

南亚TV 1

直播

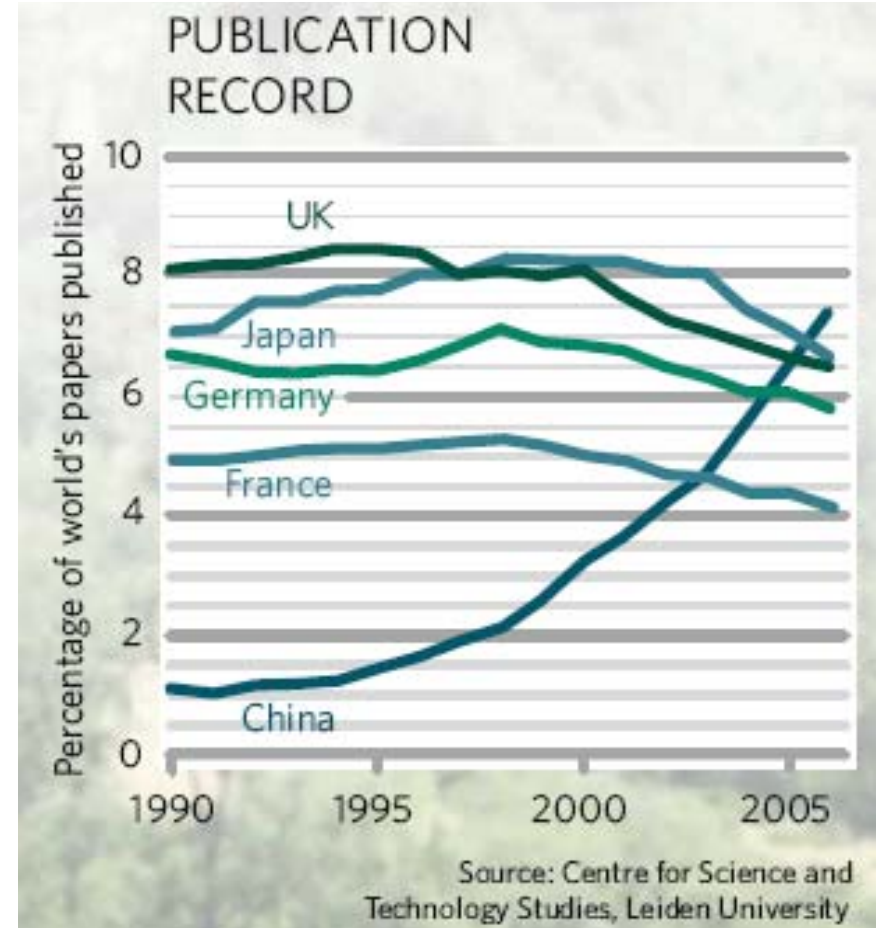
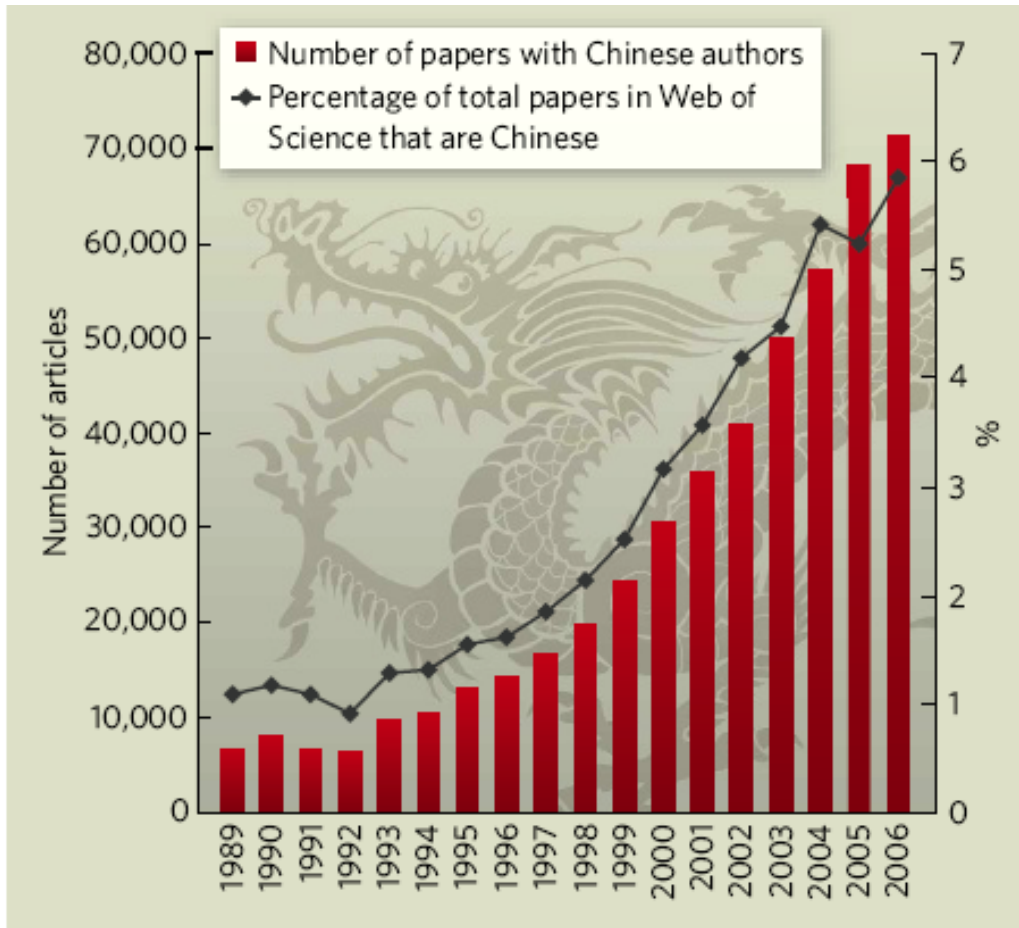
航天员出舱成功

神七问天

中国载人航天工程



The rise of Chinese scientific publications



Nature, July 2008

The end of the science superpowers



Could the end of US world dominance over research mark the passing of national science giants?

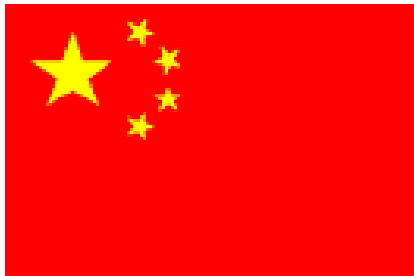
Hollingsworth et al. *Nature*, July 2008

Citation Ranking by Countries

COUNTRY PROFILES - 2008

September 2008

People's Republic of China
A featured country selection



According to *Essential Science Indicators* among 148 top-performing countries in all fields, **China ranked #12 for citations (2,294,868)**.

Source: *Essential Science Indicators* from the August 1, 2008 update covering 10-year + 4-month period, 1998-April 30, 2008

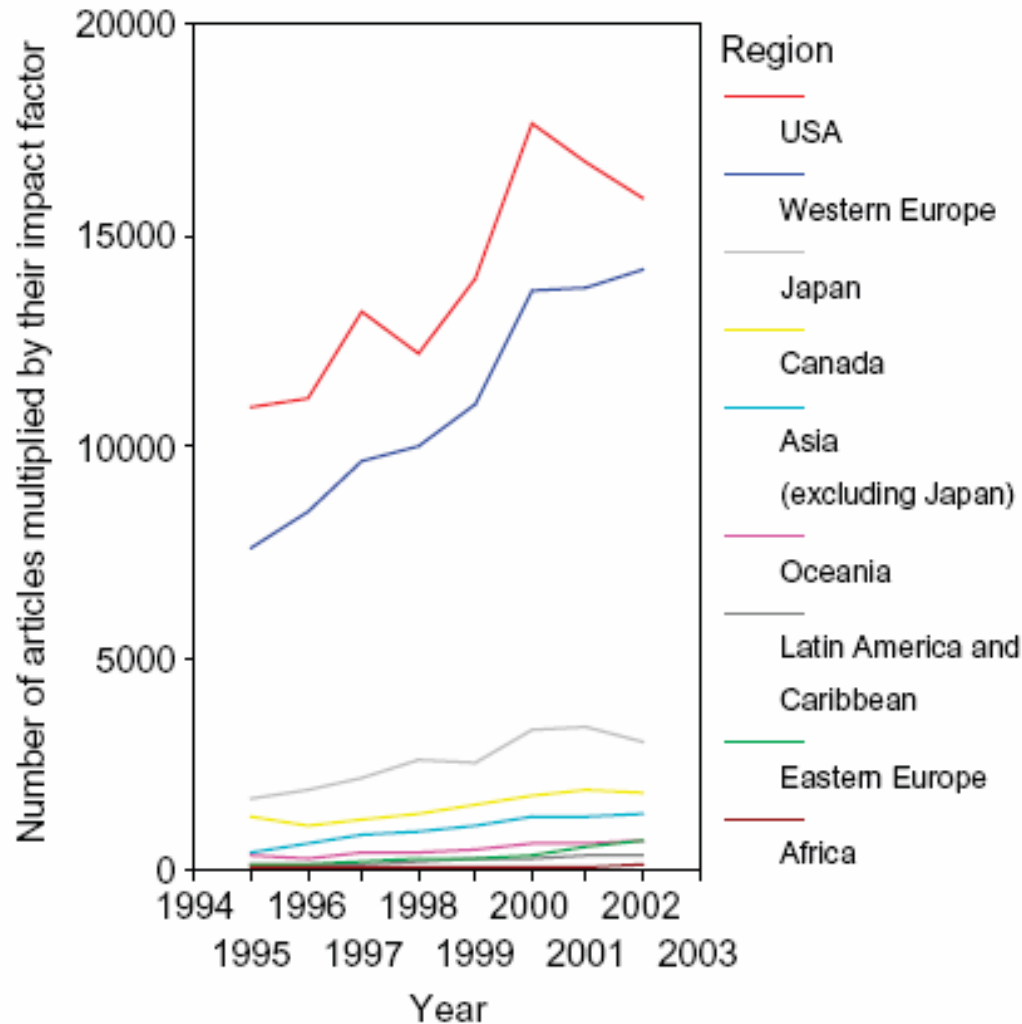
Top 20 Countries in Clinical Medicine

Ranked by Citations

Rank	Field	Papers	Citations	Citations Per Paper
1	USA	679,178	10,598,007	15.60
2	ENGLAND	161,257	2,223,465	13.79
3	GERMANY	166,413	1,869,962	11.24
4	JAPAN	159,194	1,493,009	9.38
5	CANADA	82,590	1,266,659	15.34
6	FRANCE	106,792	1,230,025	11.52
7	ITALY	93,577	1,184,239	12.66
8	NETHERLANDS	62,400	987,238	15.82
9	AUSTRALIA	56,527	710,752	12.57
10	SWEDEN	44,507	670,057	15.06
11	SWITZERLAND	38,745	586,313	15.13
12	SPAIN	49,831	520,892	10.45
13	BELGIUM	29,777	451,384	15.16
14	FINLAND	21,462	357,873	16.67
15	DENMARK	22,433	355,782	15.86
16	SCOTLAND	22,669	352,805	15.56
17	AUSTRIA	24,947	294,580	11.81
18	ISRAEL	25,267	267,052	10.57
19	PEOPLES R CHINA	36,737	259,523	7.06
20	NORWAY	14,871	221,609	14.9

SOURCE: *Essential Science Indicators* from the August 1, 2008 update covering a 10-year + 4-month period, 1998-April 30, 2008.

Worldwide trends of research productivity in the field of Cardiovascular System from different world regions in the period 1995–2002



Chinese scientists publish their work in top cardiovascular and other high impact journals

- Circulation
- Journal of American College of Cardiology
- Circulation Research
- European Heart Journal
- Cardiovascular Research
- Hypertension
- Heart
- Journal of Molecular and Cellular Cardiology

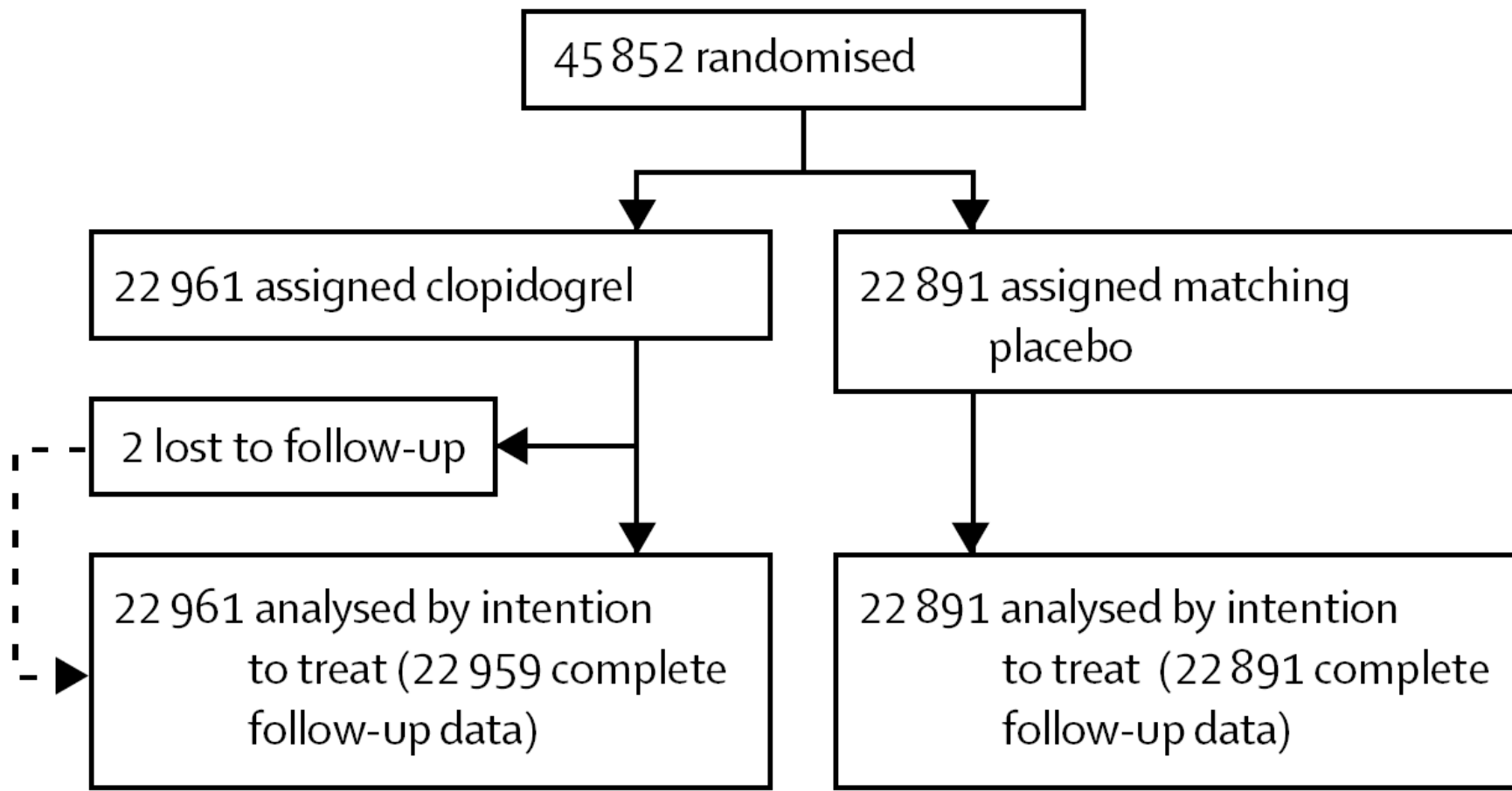
- New England Journal of Medicine
- Lancet

Recent advances in cardiovascular research in China

- Genetic basis of cardiovascular disease
- 3D echocardiography
- Radiofrequency catheter ablation for treatment of tachyarrhythmia
- Treatment of myocardial infarction
- Stem cell research

Addition of clopidogrel to aspirin in 45 852 patients with acute myocardial infarction: randomised placebo-controlled trial

COMMIT (CLOpidogrel and Metoprolol in Myocardial Infarction Trial)



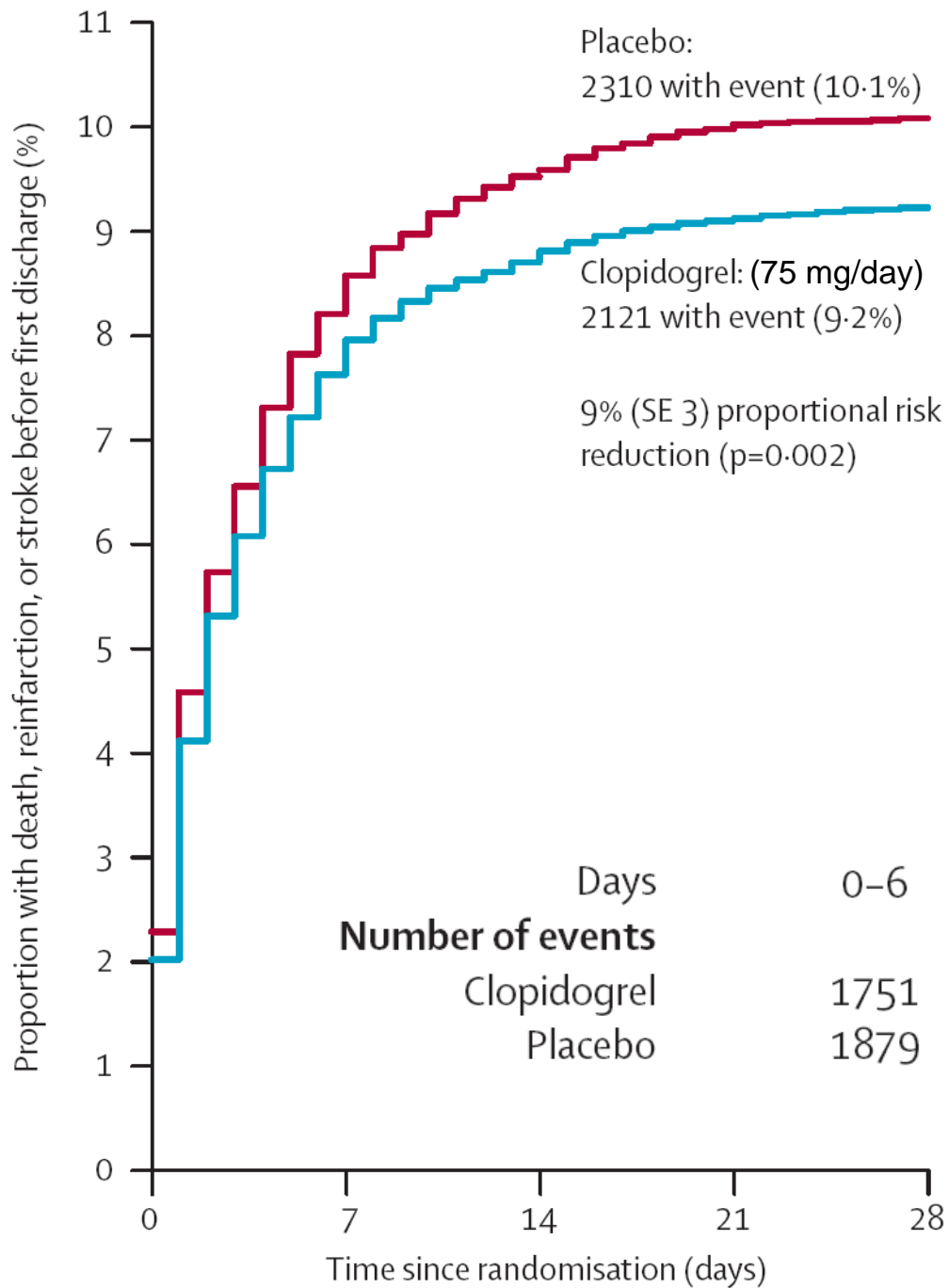
Lancet 2005; 366: 1607-21

Baseline characteristics and concomitant therapies in hospital

	Clopidogrel (n=22 961)	Placebo (n=22 891)
Age at entry (years)		
<60	9624 (41.9%)	9463 (41.3%)
60–69	7361 (32.1%)	7470 (32.6%)
≥70	5976 (26.0%)	5958 (26.0%)
Mean (SD)	61.3 (11.9)	61.4 (11.8)
Sex		
Female	6366 (27.7%)	6393 (27.9%)
Time since onset (h)		
<6	7745 (33.7%)	7707 (33.7%)
6 to <13	7567 (33.0%)	7505 (32.8%)
13–24	7649 (33.3%)	7679 (33.5%)
Mean (SD)	10.3 (6.7)	10.3 (6.7)
Systolic blood pressure (mm Hg)		
<120	7690 (33.5%)	7709 (33.7%)
120–139	8092 (35.2%)	8108 (35.4%)
140–159	4549 (19.8%)	4471 (19.5%)
≥160	2630 (11.5%)	2603 (11.4%)
Mean (SD)	128.2 (22.6)	128.2 (22.5)
Heart rate (bpm)		
<70	5094 (22.2%)	5043 (22.0%)
70–89	11 101 (48.3%)	11 161 (48.8%)
90–109	5140 (22.4%)	5069 (22.1%)
≥110	1626 (7.1%)	1618 (7.1%)
Mean (SD)	82.2 (17.2)	82.1 (17.2)

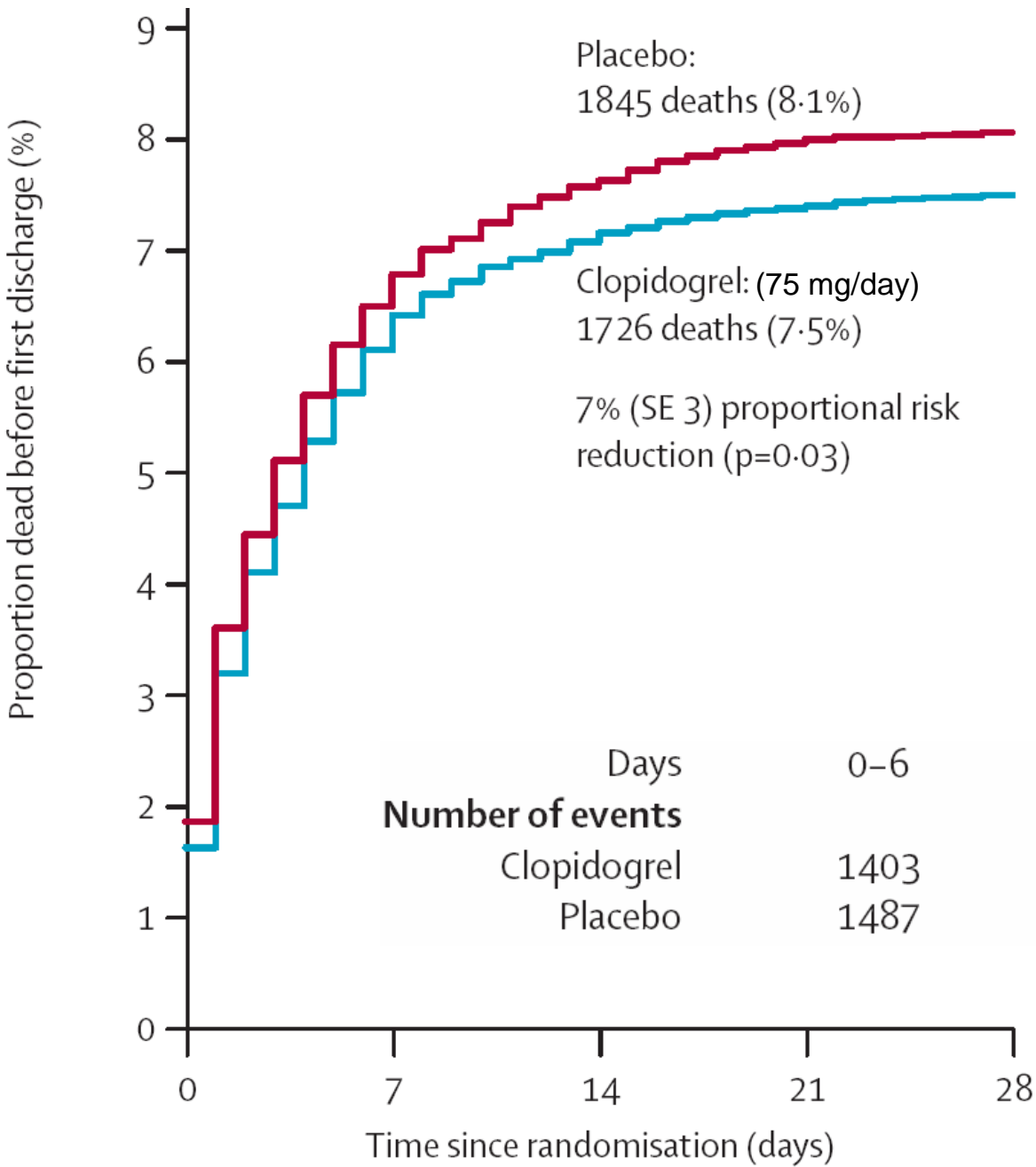
Baseline characteristics and concomitant therapies in hospital

	Clopidogrel (n=22 961)	Placebo (n=22 891)
ECG abnormality at entry		
ST elevation	19 877 (86.5%)	19 878 (86.9%)
Bundle branch block	1505 (6.6%)	1423 (6.2%)
ST depression (without ST elevation)	1579 (6.9%)	1590 (6.9%)
Killip class		
I	17 320 (75.4%)	17 283 (75.5%)
II or III	5641 (24.6%)	5608 (24.5%)
Previous disease and drug use		
Previous MI	1972 (8.6%)	1846 (8.1%)
Previous hypertension	9935 (43.3%)	9903 (43.3%)
Aspirin before admission	4214 (18.4%)	4230 (18.5%)
β blocker before admission	1457 (6.3%)	1533 (6.7%)
Fibrinolytic agent before randomisation	11 407 (49.7%)	11 387 (49.7%)
Non-trial treatment during hospital stay		
Non-trial antiplatelet	2305 (10.0%)	2280 (10.0%)
Fibrinolytic agents before or after entry	12 468 (54.3%)	12 499 (54.6%)
Anticoagulant	17 022 (74.1%)	17 157 (75.0%)
Antiarrhythmic	5150 (22.4%)	5093 (22.2%)
ACE inhibitor	15 649 (68.2%)	15 638 (68.3%)
Nitrate (oral or intravenous)	21 615 (94.1%)	21 590 (94.3%)
Diuretic	5344 (23.3%)	5344 (23.3%)
Calcium antagonist	2701 (11.8%)	2705 (11.8%)



Co-Primary Outcome:
Death, reinfarction, or stroke before first discharge

Lancet 2005; 366: 1607-21



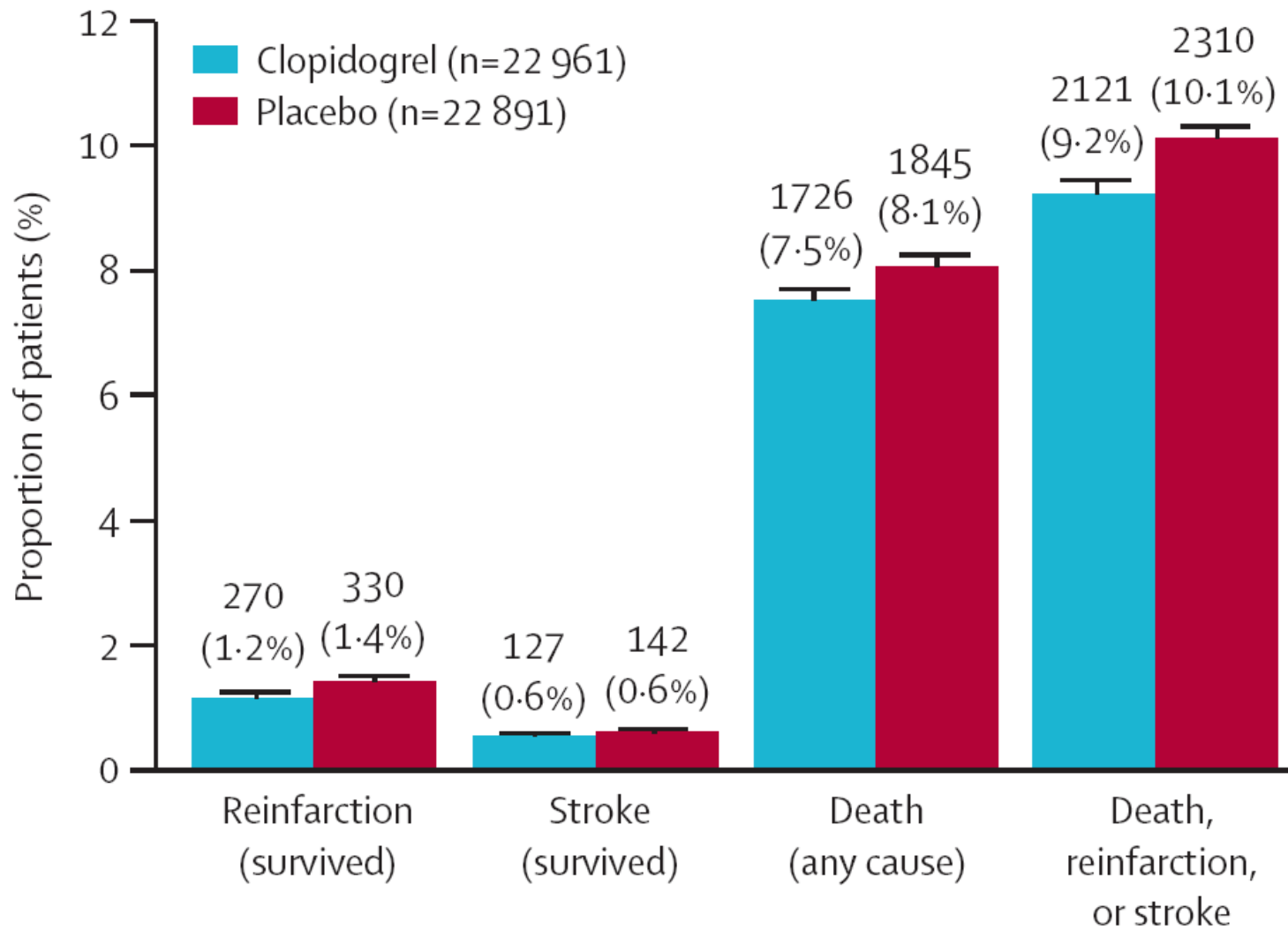
Co-Primary Outcome:
Death before first discharge

Days	0-6	7-13	14-20	21-28
Number of events				
Clopidogrel	1403	223	69	31
Placebo	1487	246	89	23

Lancet 2005; 366: 1607-21

Absolute effects of clopidogrel on death, reinfarction, or stroke

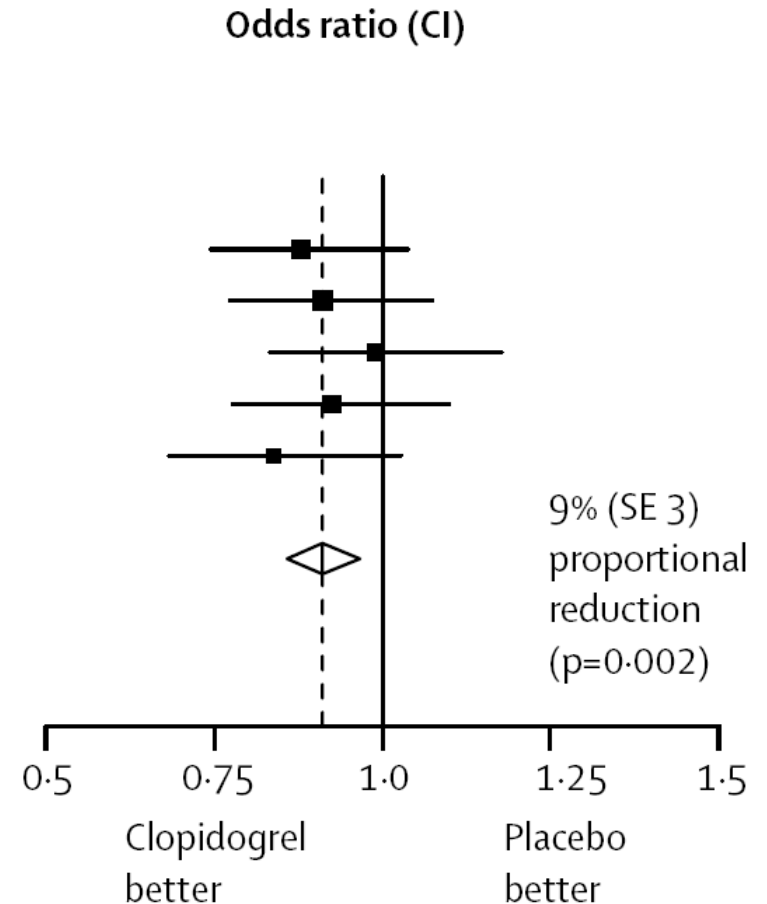
Benefit (SE), 1000,	3 (1)	1 (1)	5 (2)	9 (3)
p	0.01	0.3	0.03	0.002



Effects of clopidogrel allocation on death, reinfarction, or stroke by day of event

Days of event	Events (%)	
	Clopidogrel (22 961)	Placebo (22 891)
0	463 (2.0%)	524 (2.3%)
1	482 (2.1%)	525 (2.3%)
2-3	450 (2.0%)	451 (2.0%)
4-7	432 (1.9%)	463 (2.0%)
8-28	294 (1.3%)	347 (1.5%)
Total	2121 (9.2%)	2310 (10.1%)

Heterogeneity test: $\chi^2_4=3.0$; $p=0.6$



Conclusions

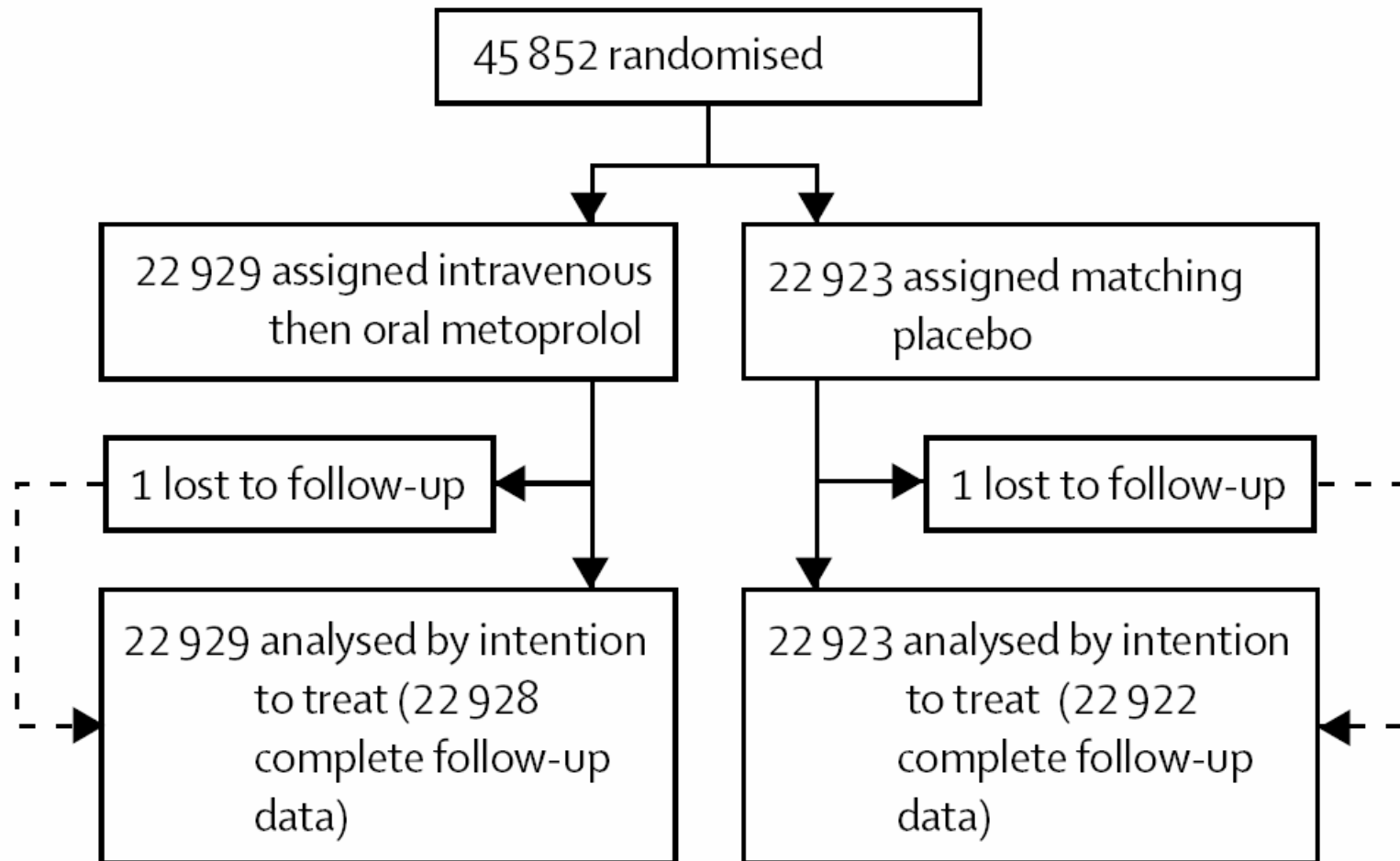
In a wide range of patients with acute MI, adding clopidogrel 75 mg daily to aspirin (162 mg) and other standard treatments (such as fibrinolytic therapy) safely reduces mortality and major vascular events in hospital, and should be considered routinely.

Times Cited: 247 (Web of Science ®)

Lancet 2005; 366: 1607-21

Early intravenous then oral metoprolol in 45 852 patients with acute myocardial infarction: randomised placebo-controlled trial

COMMIT (CLOpidogrel and Metoprolol in Myocardial Infarction Trial)



Lancet 2005; 366: 1622-32

Baseline characteristics and concomitant therapies in hospital

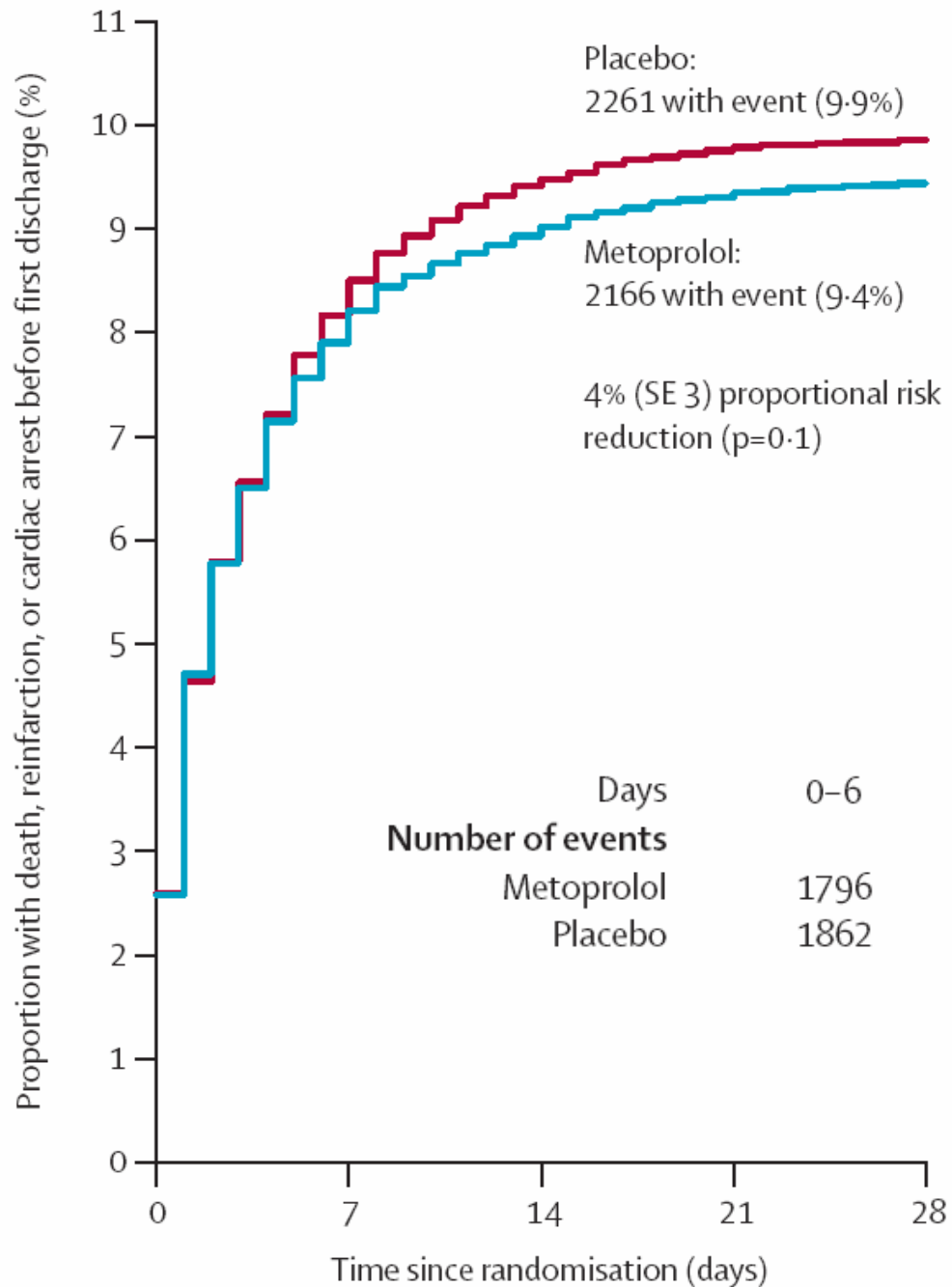
	Metoprolol (n=22 929)	Placebo (n=22 923)
Age at entry (years)		
<60	9459 (41.3%)	9628 (42.0%)
60–69	7489 (32.7%)	7342 (32.0%)
≥70	5981 (26.1%)	5953 (26.0%)
Mean (SD)	61.4 (11.8)	61.3 (11.8)
Sex		
Female	6431 (28.0%)	6328 (27.6%)
Time since onset (h)		
<6	7771 (33.9%)	7681 (33.5%)
6 to <13	7500 (32.7%)	7572 (33.0%)
13–24	7658 (33.4%)	7670 (33.5%)
Mean (SD)	10.3 (6.7)	10.3 (6.7)
Systolic blood pressure (mm Hg)		
<120	7724 (33.7%)	7675 (33.5%)
120–139	8111 (35.4%)	8089 (35.3%)
140–159	4443 (19.4%)	4577 (20.0%)
≥160	2651 (11.6%)	2582 (11.3%)
Mean (SD)	128.2 (22.6)	128.2 (22.5)
Heart rate (bpm)		
<70	5179 (22.6%)	4958 (21.6%)
70–89	11 076 (48.3%)	11 186 (48.8%)
90–109	5080 (22.2%)	5129 (22.4%)
≥110	1594 (7.0%)	1650 (7.2%)
Mean (SD)	82.0 (17.3)	82.3 (17.1)

Baseline characteristics and concomitant therapies in hospital

	Metoprolol (n=22 929)	Placebo (n=22 923)
ECG abnormality at entry		
ST elevation	19 868 (86.7%)	19 887 (86.8%)
Bundle branch block	1431 (6.2%)	1497 (6.5%)
ST depression (without ST elevation)	1630 (7.1%)	1539 (6.7%)
Killip class		
I	17 276 (75.3%)	17 327 (75.6%)
II	4573 (19.9%)	4532 (19.8%)
III	1080 (4.7%)	1064 (4.6%)
Previous disease and drug use		
Previous MI	1925 (8.4%)	1893 (8.3%)
Previous hypertension	9948 (43.4%)	9890 (43.1%)
Aspirin before admission	4219 (18.4%)	4225 (18.4%)
β blocker before admission	1484 (6.5%)	1506 (6.6%)
Fibrinolytic agent before randomisation	11 407 (49.7%)	11 387 (49.7%)
Non-trial treatment during hospital stay		
Non-trial β blocker	1395 (6.1%)	3607 (15.7%)
Fibrinolytic agents before or after entry	12 458 (54.3%)	12 509 (54.6%)
Anticoagulant	17 051 (74.4%)	17 128 (74.7%)
Antiarrhythmic	5034 (22.0%)	5209 (22.7%)
ACE inhibitor	15 397 (67.2%)	15 890 (69.3%)
Nitrate (oral or intravenous)	21 584 (94.1%)	21 621 (94.3%)
Diuretic	5553 (24.2%)	5135 (22.4%)
Calcium antagonist	2508 (10.9%)	2898 (12.6%)

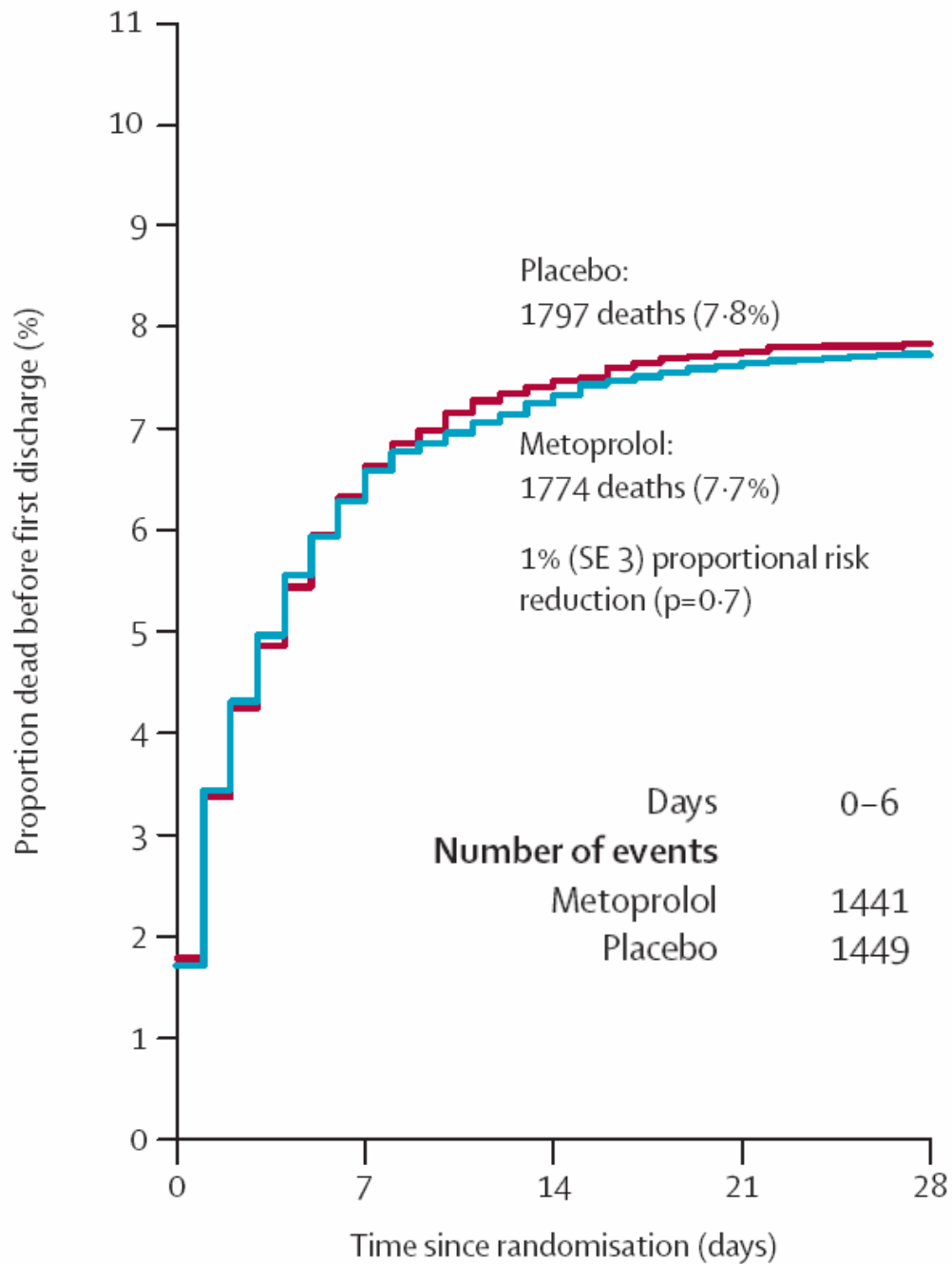
Effects of metoprolol on main clinical events during scheduled treatment period in hospital

	Metoprolol (n=22 929)	Placebo (n=22 923)	Odds ratio (95% CI)	Absolute difference per 1000 (SE)	p
Co-primary outcomes					
Composite*	2166 (9.4%)	2261 (9.9%)	0.96 (0.90–1.01)	–4.2 (2.8)	0.10
Death	1774 (7.7%)	1797 (7.8%)	0.99 (0.92–1.05)	–1.0 (2.6)	0.69
Death, by recorded cause					
Arrhythmia	388 (1.7%)	498 (2.2%)	0.78 (0.68–0.89)	–4.8 (1.3)	0.0002
Shock†	496 (2.2%)	384 (1.7%)	1.29 (1.13–1.47)	4.9 (1.3)	0.0002
Neither	890 (3.9%)	915 (4.0%)	0.97 (0.89–1.07)	–1.1 (1.8)	0.55
Reinfarction					
Any	464 (2.0%)	568 (2.5%)	0.82 (0.72–0.92)	–4.5 (1.4)	0.001
Died, any cause	206 (0.9%)	226 (1.0%)	0.91 (0.75–1.10)	–0.9 (0.9)	0.33
Survived	258 (1.1%)	342 (1.5%)	0.75 (0.64–0.88)	–3.7 (1.1)	0.0005
Ventricular fibrillation‡					
Any	581 (2.5%)	698 (3.0%)	0.83 (0.75–0.93)	–5.1 (1.6)	0.001
Died, any cause	492 (2.1%)	600 (2.6%)	0.82 (0.73–0.92)	–4.7 (1.4)	0.001
Survived	89 (0.4%)	98 (0.4%)	0.91 (0.68–1.21)	–0.4 (0.6)	0.51
Other cardiac arrest§					
Any	685 (3.0%)	632 (2.8%)	1.08 (0.97–1.21)	2.3 (1.6)	0.14
Died, any cause	624 (2.7%)	593 (2.6%)	1.05 (0.94–1.18)	1.3 (1.5)	0.38
Survived	61 (0.3%)	39 (0.2%)	1.55 (1.05–2.30)	1.0 (0.4)	0.03
Cardiogenic shock¶					
Any	1141 (5.0%)	885 (3.9%)	1.30 (1.19–1.41)	11.2 (1.9)	<0.0001
Died, any cause	755 (3.3%)	628 (2.7%)	1.20 (1.08–1.34)	5.5 (1.6)	0.0006
Survived	386 (1.7%)	257 (1.1%)	1.50 (1.28–1.75)	5.6 (1.1)	<0.0001
Death, reinfarction, cardiac arrest, or shock	2501 (10.9%)	2465 (10.8%)	1.02 (0.96–1.08)	1.5 (2.5)	0.54



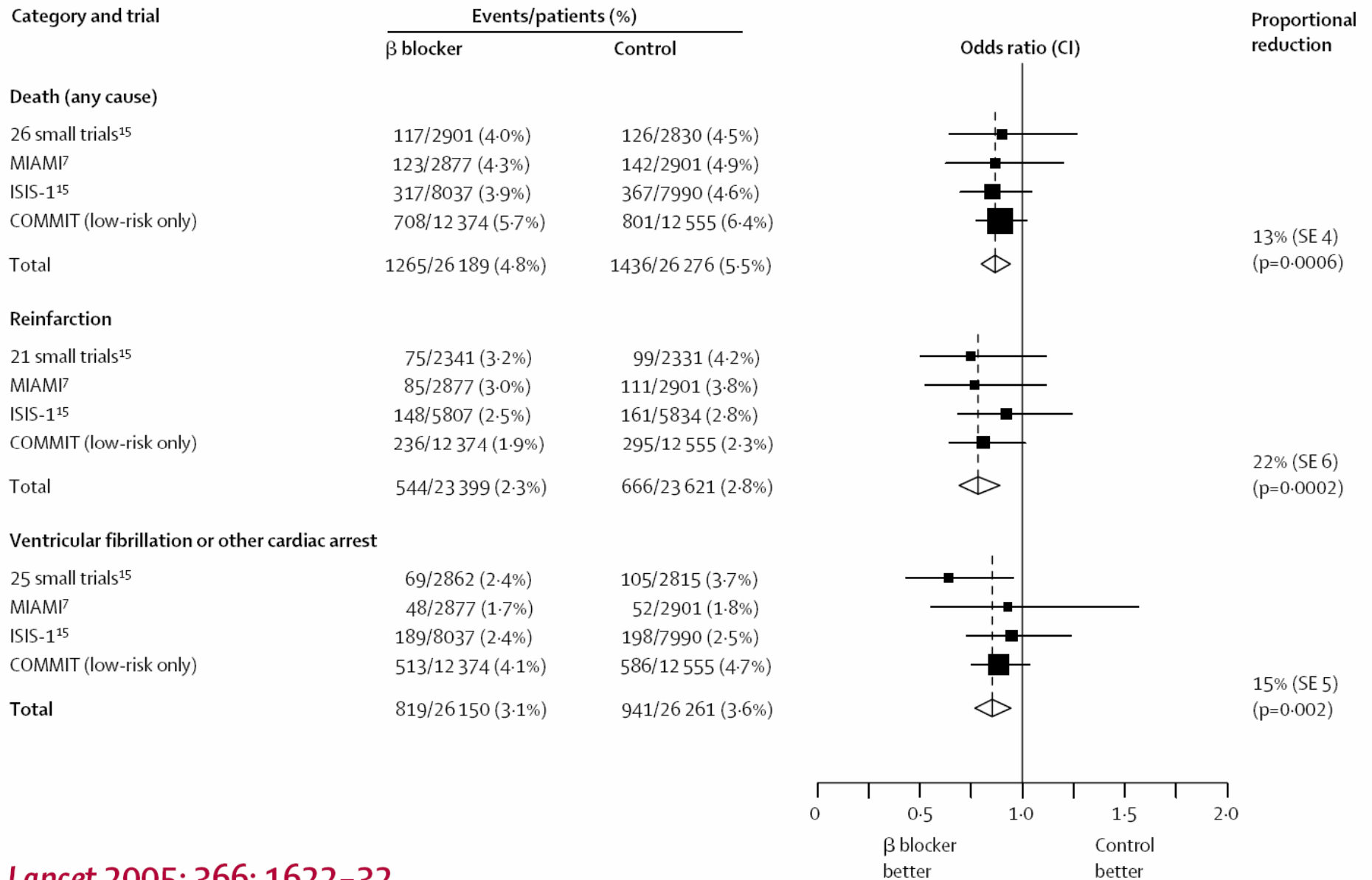
Co-Primary Outcome:
Death, reinfarction, or cardiac arrest

Lancet 2005; 366: 1622-32



Co-Primary Outcome:
Death

Meta-analysis of effects of β -blockers on death, reinfarction, and cardiac arrest during the scheduled treatment periods in 26 small randomized trials, MIAMI, ISIS-1 and low-risk subset of COMMIT



Lancet 2005; 366: 1622-32

Conclusions

- The use of early β -blocker therapy in acute MI reduces the risks of reinfarction and ventricular fibrillation, but increases the risk of cardiogenic shock, especially during the first day or so after admission.
- Consequently, it might generally be prudent to consider starting β -blocker therapy in hospital only when the haemodynamic condition after MI has stabilized.

Times Cited: 100 (Web of Science ®)

Lancet 2005; 366: 1622-32

Effect on left ventricular function of intracoronary transplantation of autologous bone marrow mesenchymal stem cell in patients with acute myocardial infarction

Chen SL et al. *Am J Cardiol* 2004;94:92-95

Times cited: 190 (Web of Science ®)

Baseline characteristics of 69 patients

Parameters	BMSC Group (n = 34)	PCI Group (n = 35)
Age (yrs)	58 ± 7	57 ± 5
Men/women	32/2	34/1
Creatinine kinase-MB (U/L)	98 ± 54	92 ± 49
Time		
Onset to PCI (h)	8.3 ± 3.8	8.5 ± 3.9
PCI to injection* (d)	18.4 ± 0.5	18.2 ± 0.3
Coronary angiography		
No. of diseased coronary arteries	1.6 ± 0.5	1.7 ± 0.4
AMI-related vessel: LAD/LC*/ right	20/6/8	21/7/7
Stents deployed (n=)	36	38
<p>*Intracoronary injection of BMSC or saline. AMI = acute myocardial infarction; LAD = left anterior descending; LC = left circumflex.</p>		

Comparison of LV hemodynamics in two groups of patients

Variables	BMSC Group	Control Group	p Value
Patients (n)	34	35	0.20
Functional defect (%)			
Just before BMSC implantation	32 ± 11	33 ± 10	0.20
At 3-mo follow-up	13 ± 5	28 ± 10	0.001
Infarcted area movement velocity (cm/s)			
Just before BMSC implantation	2.17 ± 1.3	2.19 ± 1.5	0.20
At 3-mo follow-up	4.2 ± 2.5	2.7 ± 1.7	0.01
Left ventricular ejection fraction (%)			
Just before BMSC implantation	49 ± 9	48 ± 10	0.20
At 3-mo follow-up	67 ± 11	53 ± 18	0.01
At 6-mo follow-up	67 ± 3	54 ± 5	0.01

Cardiac function at 3-month follow-up in two groups of patients

Variables	Control Group	BMSC Group	p Value
Patients (n)	35	34	0.20
LV ESV (ml)	162 ± 27	136 ± 31	0.001
LV ESV (ml)	88 ± 19	63 ± 20	0.01
Circumferential shorting (mm/s)	21.7 ± 5.9	24.8 ± 4.2	0.10
P _{syst} /ESV (mm Hg/ml)	2.84 ± 1.30	1.72 ± 1.23	0.01
Perfusion defect by PET (cm ²)	185 ± 87	134 ± 66	0.001

ESV = end-systolic volume; LV = left ventricular; PET = positron emission tomography; P_{syst} = left ventricular end-systolic pressure.

Administration of intracoronary bone marrow mononuclear cells on chronic myocardial infarction improves diastolic function

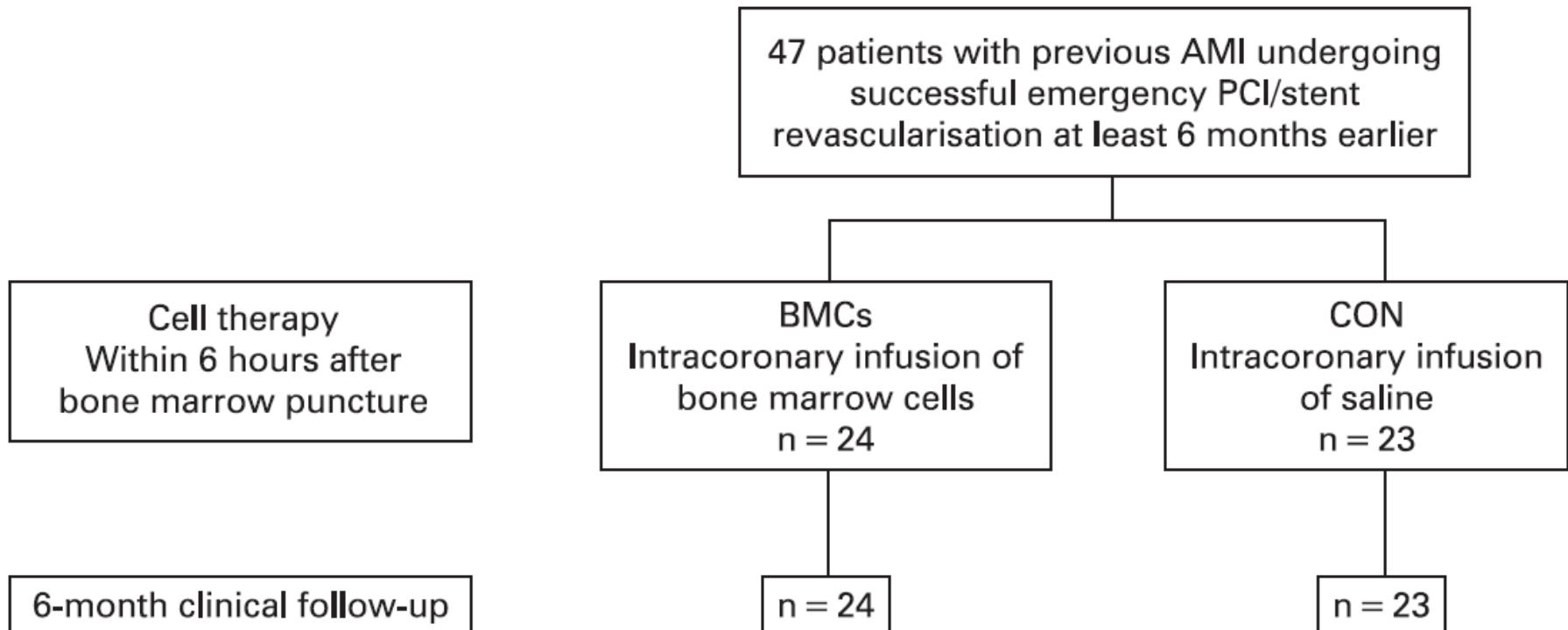


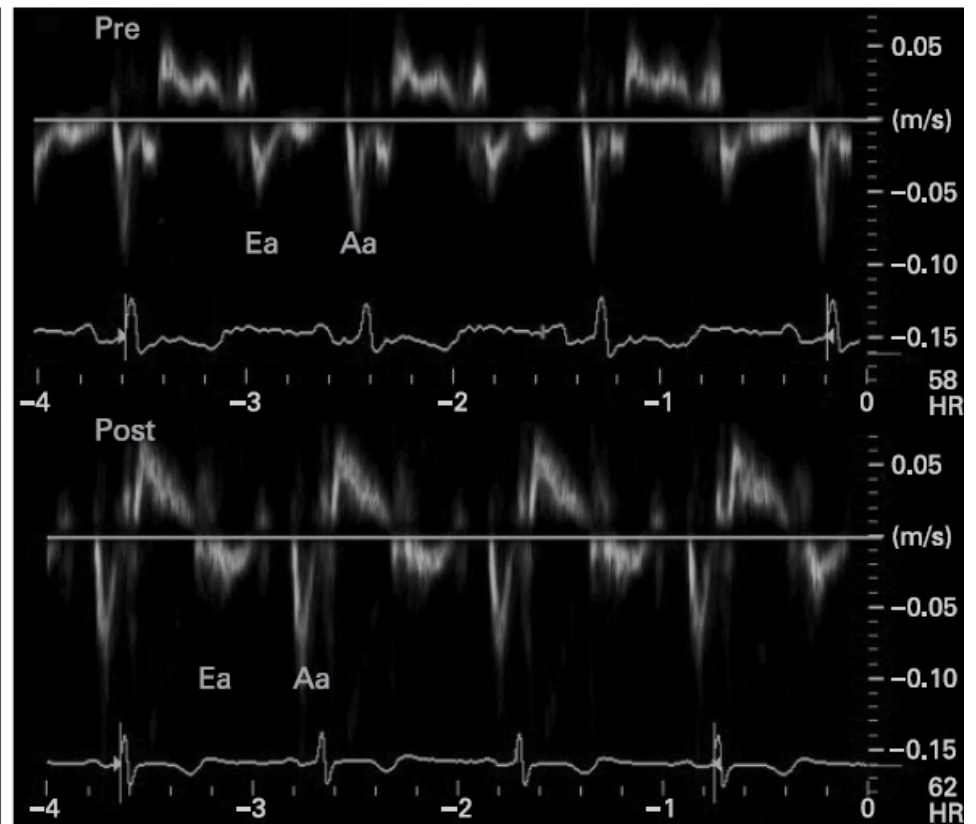
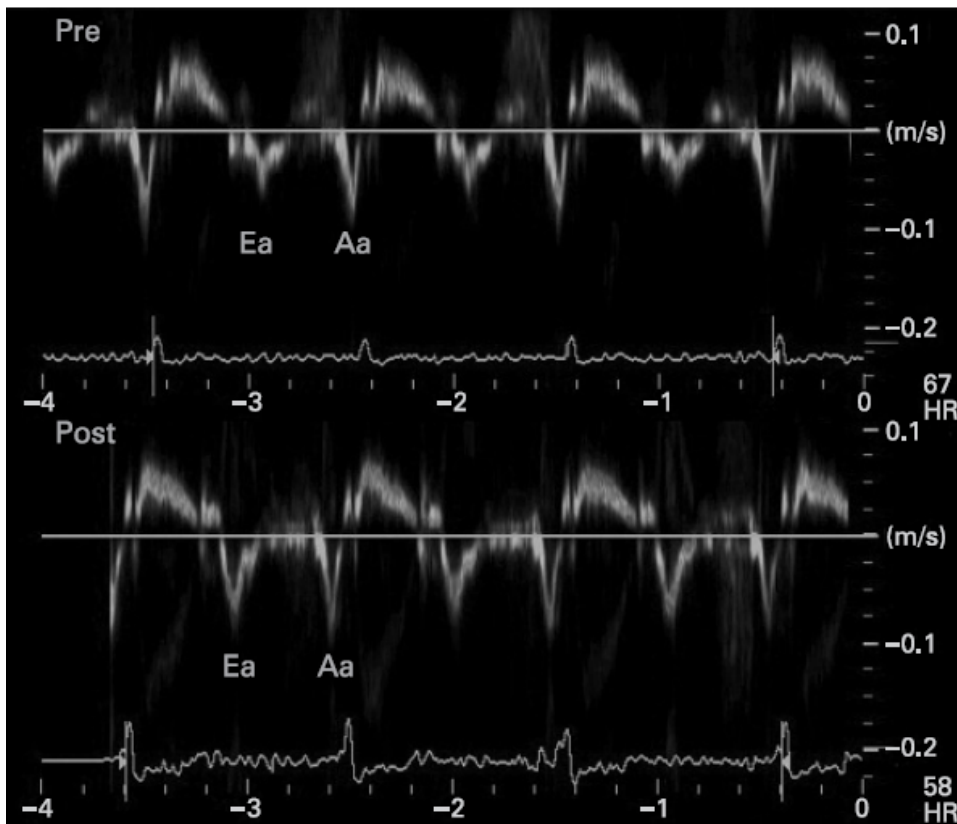
Table 2 Quantitative data from echocardiography, magnetic resonance imaging (MRI) and ²⁰¹Tl-SPECT imaging

	CON (n = 23)	BMC (n = 24)	p Value
LVEF (%) (echocardiography)			
Baseline	45.4 (7.2) (44.0)	46.3 (7.2) (46.0)	0.665
6 months	47.6 (7.4) (47.0)	49.8 (6.7) (51.0)	0.284
Change from baseline	2.3 (2.7) (2.0)	3.5 (3.3) (4.0)	0.136
LVEDd (mm)			
Baseline	55.8 (6.0) (54.0)	54.1 (6.7) (53.5)	0.522
6 months	56.8 (6.2) (54.0)	54.8 (6.6) (54.5)	0.441
Change from baseline	1.0 (1.3) (1.0)	0.6 (1.3) (1.0)	0.504
LVESd (mm)			
Baseline	36.8 (5.7) (36.0)	36.6 (7.3) (36.0)	0.927
6 months	36.7 (7.3) (36.0)	36.3 (8.5) (35.5)	0.892
Change from baseline	-0.1 (2.7) (0.0)	-0.3 (3.5) (-0.5)	0.881
LVEF (%) (MRI)			
Baseline	42.5 (7.3) (40.5)	44.3 (5.5) (42.5)	0.500
6 months	44.1 (8.4) (43.0)	46.6 (5.6) (45.0)	0.383
Change from baseline	1.6 (2.1) (2.0)	2.4 (3.1) (2.0)	0.515
Myocardial infarct area (%) (MRI)			
Baseline	24.3 (4.5) (25.5)	23.6 (4.1) (25.5)	0.714
6 months	22.7 (5.8) (24.0)	21.4 (4.3) (22.5)	0.519
Change from baseline	-1.6 (1.8) (2.0)	-2.3 (1.7) (2.0)	0.354
Myocardial perfusion defect (%) (SPECT)			
Baseline	29.0 (7.7) (31.0)	28.2 (7.2) (27.0)	0.700
6 months	28.0 (7.8) (30.5)	26.0 (6.0) (26.0)	0.332
Change from baseline	-1.0 (1.8) (-1.5)	-2.2 (2.4) (-3.0)	0.073

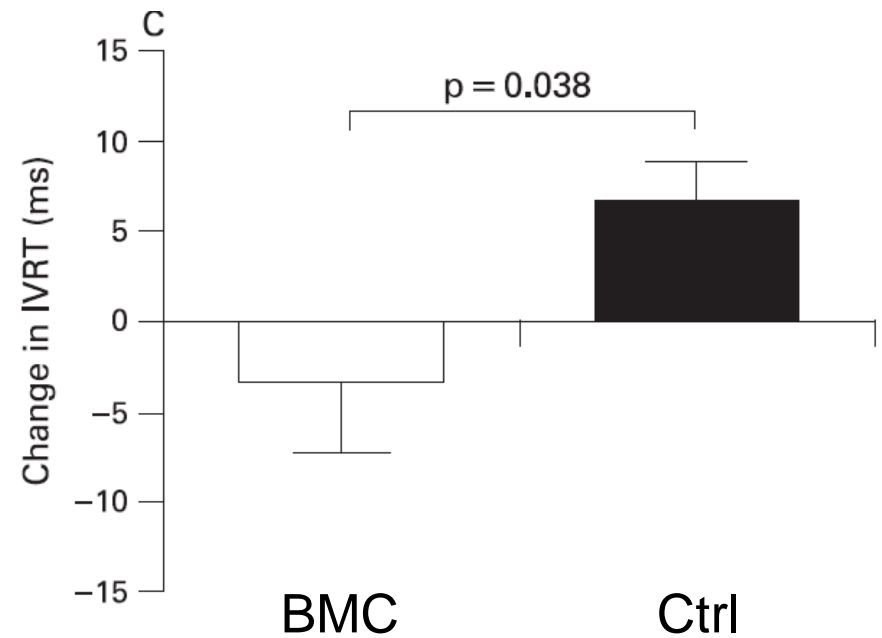
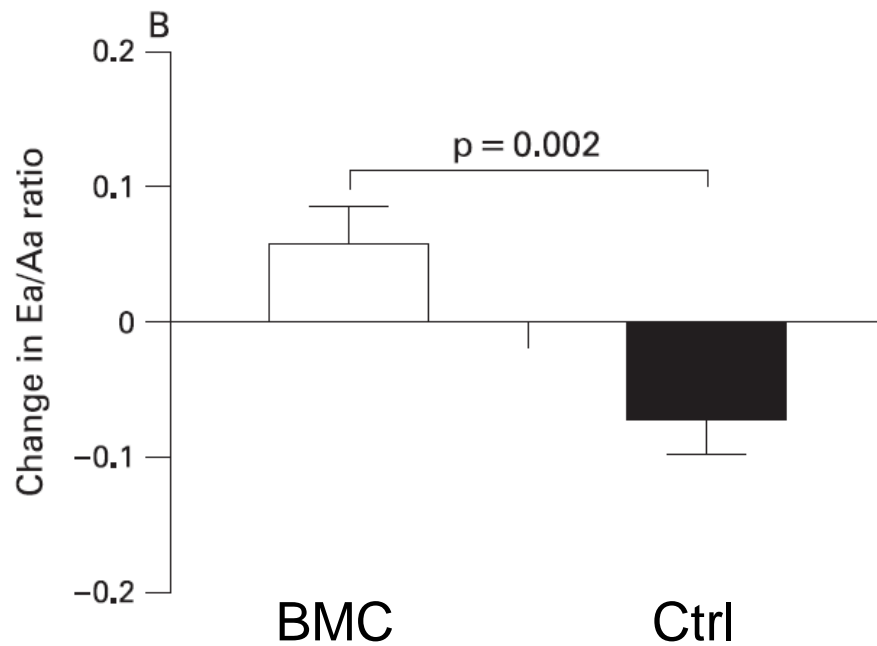
Doppler recordings of transmitral early diastolic (Ea) and late diastolic (Aa) velocities

BMC

Saline



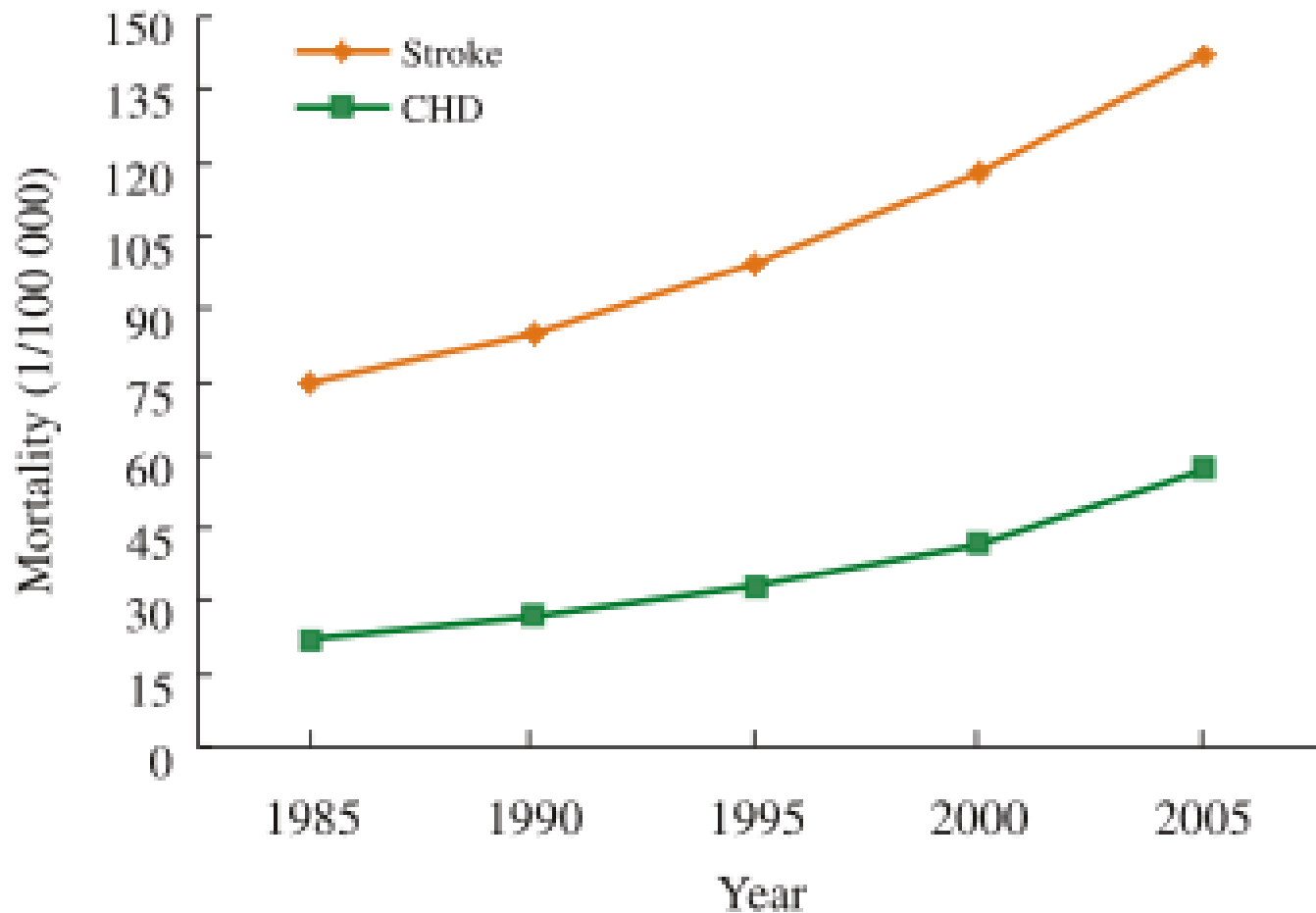
Improvement in diastolic function by BMC treatment from baseline to 6-month follow-up



Conclusions

Intracoronary transfer of autologous BMC in patients with healed MI did not significantly improve cardiac systolic function, infarct size or myocardial perfusion, but did improve diastolic function.

Trends of standardized cardiovascular disease mortality rate between 1985 and 2005



Increasing prevalence of cardiovascular risk factors in China

- Obesity
- Diabetes
- Hypertension
- Metabolic syndrome
- Smoking
- Aging

上 医 医 未 病 之 病

中 医 医 将 病 之 病

下 医 医 已 病 之 病

— 黄 帝 内 经

Prevention and control of cardiovascular disease

- Beijing health #7 project
 - Community mobilization, policy development, creation of supportive environments, development of health education and services
- Beijing #143 project
 - Health promotion study to improve health life style in Beijing inhabitants and immigrants
- Zhejiang Hypertension Prevention study
 - Community-based treatment and control of hypertension in urban and rural areas

KCNQ1 Gain-of-Function Mutation in Familial Atrial Fibrillation

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Hao Sun,² Xiao-Yan Su,¹ Qi-Nan Zhuang,² Yi-Qing Yang,¹
Yue-Bin Li,² Yi Liu,¹ Hong-Ju Xu,¹ Xiao-Fei Li,¹ Ning Ma,¹
Chun-Ping Mou,¹ Zhu Chen,^{2,6} Jacques Barhanin,⁴ Wei Huang^{2,3,6}

Science 2003; 299:251-254

Times cited: 193 (Web of Science ®)

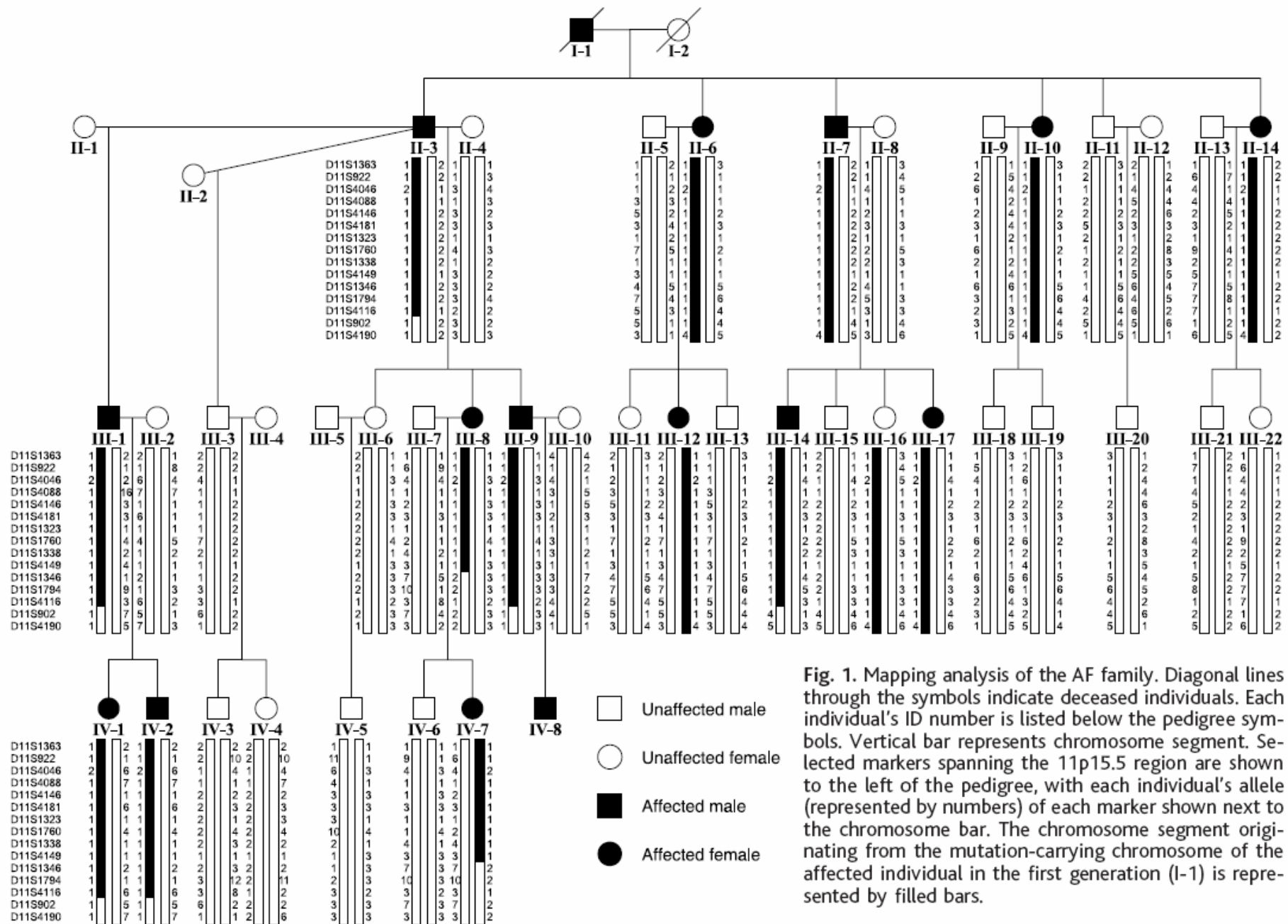
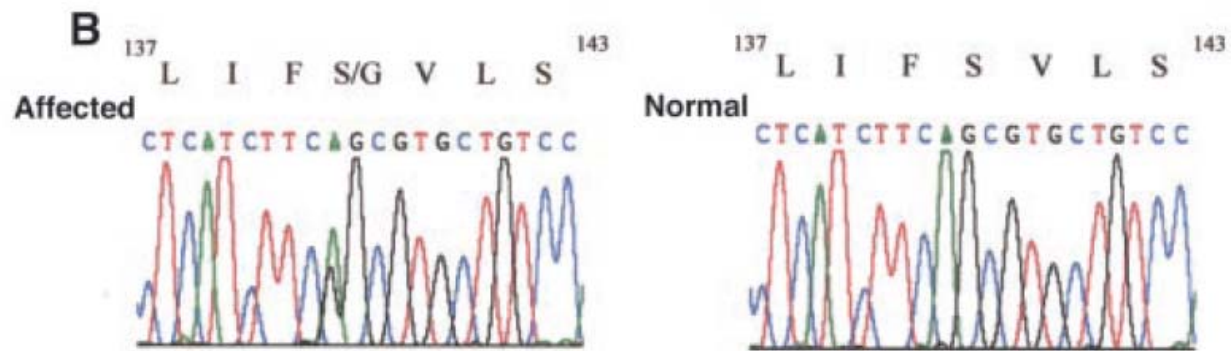
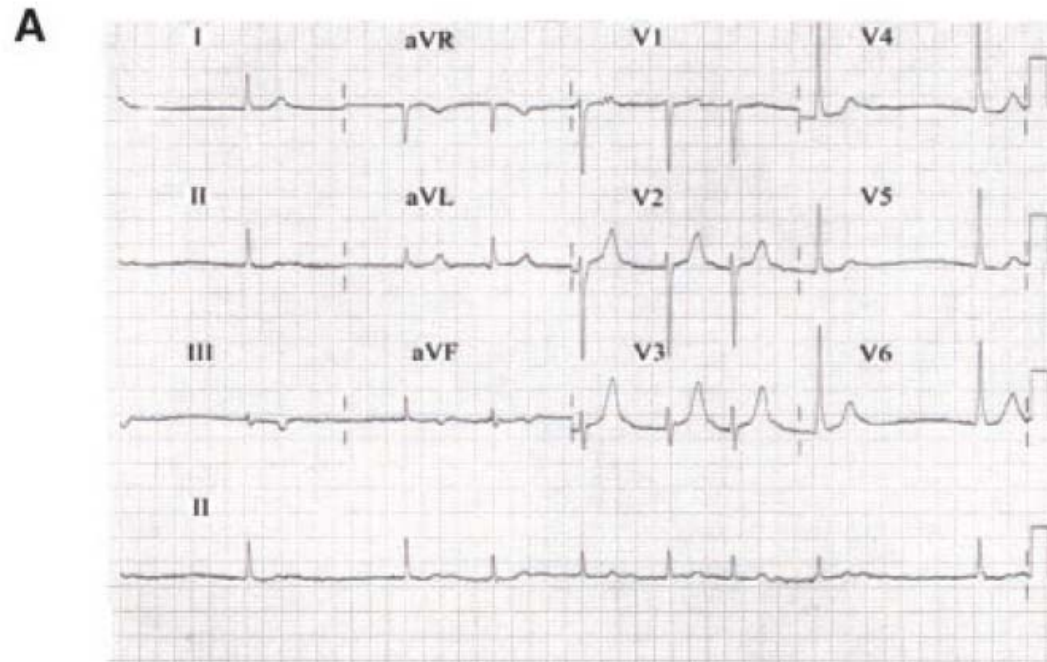
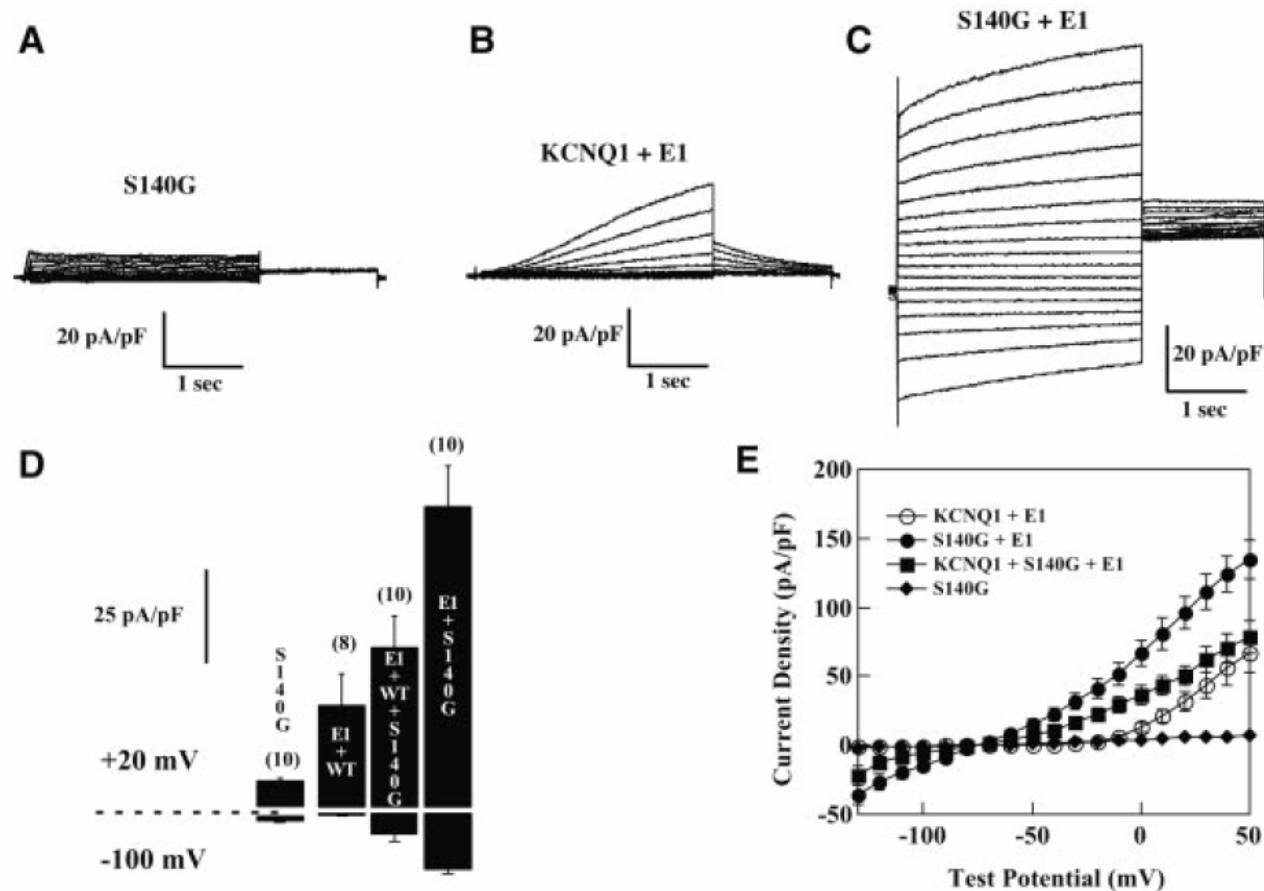


Fig. 1. Mapping analysis of the AF family. Diagonal lines through the symbols indicate deceased individuals. Each individual's ID number is listed below the pedigree symbols. Vertical bars represent chromosome segment. Selected markers spanning the 11p15.5 region are shown to the left of the pedigree, with each individual's allele (represented by numbers) of each marker shown next to the chromosome bar. The chromosome segment originating from the mutation-carrying chromosome of the affected individual in the first generation (I-1) is represented by filled bars.

S140G mutation in *KCNQ1* is associated with atrial fibrillation



S140G mutation alters the KCNQ1-KCNE1 current



The S140S mutation is likely to initiate and maintain AF by reducing action potential duration and effective refractory period in atrial myocytes.

Opportunities for research collaboration in China

- Project 211: The biggest investment in higher education in China
 - To build about 100 key universities in priority disciplines in the 21 century
- 863 program: High tech program
 - To develop advanced technologies in a wide range of fields
- 973 program: The national basic research program
 - To organize and implement basic research to meet the nation's major strategic needs
- Opportunities for guest professors, visiting professors
- China-Canada Joint Health Research Initiative - Grants Program

Clinical Trials in China

- 1.3 billion population with a huge number of subjects
- Ethnic, demographic and cultural diversities
- Excellent compliance
- Geographically stable with less migration – easier to follow-up
- Costs are much cheaper

ClinicalTrials.gov

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Locations: China

447 Studies

Search terms: Cardiovascular

Recruitment: Open Studies

Locations: China

94 Studies

Thank You!