Secondary prevention (Post MI, Atrial fibrillation, Heart failure

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Post MI

• Secondary Prevention Benefit - 2-5 years •

RELATIVE BENEFIT	CVD RISK REDUCTION		MORTALITY
	Duration	CHD	CVA	
Beta-blockers	~2 years	?	?	~25%
ACEI/ARB - no HF	~4 years	~20%	~20%	~15%
Statins	~5 years	~25%	~20%	~15%
Fibrates	~5 years	~0% ~20% gemfibrozil	~0%	~0%
Niacin	~3 years	~ 0%	~ 0%	~0%
ASA	~2 years	~25%		~15%

ABSOLUTE BENEFIT	CVD RISK REDUCTION		MORTALITY
	Duration	CHD	CVA	
Beta-blockers	~2 years	1%	?	~2%
ACEI/ARB -no HF	~4 years	~1-1.5%	~0.5%	1% ~2% if heart failure
Statins	~5 years	~3-4% higher dose ~1.5% more	~1% higher dose ~0.5% more	~ 2% higher dose no additional benefit
Fibrates	~5 years	~0% ~3% gemfibrozil	~0%	~0%
Niacin	~3 years	~0%	~0%	~0%
ASA	~2 years	~3-4%		~1-2%

Atrial fibrillation

• Atrial Fibrillation Drugs Benefit - 1 year •

RELATIVE BENEFIT	ISCHEMIC STROKE
ASA	~20-25%
Warfarin	~65-70%
Dabigatran (150mg BID), apixaban, rivaroxaban	~75-80%

ABSOLUTE BENEFIT	ANNUAL ISCHEMIC STROKE RISK						ANNUAL BLEED RISK
CHADS2 score	0	1	2	3	4	5	
No therapy	~2%	~3%	~4%	~6%	~9%	~18%	
On ASA	~1.5%	~2%	~3%	~5%	~7%	~14%	~1%
On OAC	~0.5%	~1%	~1%	~2%	~3%	~6%	~2-3%
ASA minus OAC	~1%	~1%	~2%	~3%	~4%	~8%	

Heart failure

Diuretics for heart failure
(some withdrawal trials)
2-12 months

	Mortality (%)	HF worsening (%)
Placebo	12	15
Diuretics	3	0

Cochrane CD003838

Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction (36 months)

	Mortality (%)	Reinfarction (%)	Readmission for HF (%)	Overall (%)
Placebo	26.8	11	18.9	41
ACE inhibitor	23	8.9	13.7	33.8

Lancet 2000;355:1575-81

Beta-blockers in patients with heart failure or left-ventricular dysfunction (3-24 months)

	Mortality (%)	Admission for HF (%)
Placebo	12.8	15.6
Beta-blocker	8.4	10.3

Ann Intern Med 2001;134:550-60

ACE inhibitor issues

Dose issues

NETWORK trial – Eur H J 1998;19:481-9

1,532 patients with class II to IV heart failure randomised to receive either 5,10, or 20 mg of enalapril for 6 months

No difference in deaths, worsening of heart failure or hospitalization for heart failure

ACE inhibitor issues

Dose issues

ATLAS - Circ 1999;100:2312-8

3164 patients with class II to IV heart failure randomised to receive either 2.5 to 5.0 mg daily or 32.5 to 35 mg daily of lisinopril for approx 4 years

No difference in mortality

Mortality plus hospitalization for any cause reduced from 83.8% to 79.7%

Worsening heart failure reduced from 44 to 38%

Dizziness ARI by 7%, hypotension by 4% and worsening renal function by 3%

CHARM Overall – Candesartan in patients with CHF

Patients

7601 patients mean age 66 (32% women) with CHF (NYHA Class II 45%, Class III 52%), a history of MI (53%), stroke (9%), diabetes (29%), smoker (15%), HTN (55%), lipid lowering (42%), aspirin (56%)

Treatment

candesartan started at 4-8 mg PO daily, doubled approximately every 2 weeks up to a maximum of 32 mg PO daily (63% in candesartan group got to this dose) or placebo

Duration

3 years

Results

blood pressure was 5/3 mmHg lower in the candesartan group at 6 months

Lancet 2003;362:759-66

Candesartan results

	CV death or hospitalization for CHF (%)	All deaths (%)	CV deaths (%)	CV death, hospitalizations for CHF, MI, stroke, revascularization (%)
Candesartan	30	23	18	37
Placebo	35	25	20	41
Relative risk reduction	14	P =0.055	10	10
Absolute risk reduction	5		2	4
Number needed to treat	20		50	25

Combined ACEI and ARBs

Admissions for heart failure - RR 0.81 (0.72-0.91)

Overall hospitalizations - RR 0.92 (0.82-1.05)

Mortality - RR 0.97 (0.92-1.03)

Fatal MI - RR 0.97 (0.76-1.22)

Non fatal Mis - RR 0.91 (0.78-1.07)

Worsening renal function RR 1.91 (1.40-2.6)

Symptomatic hypotension RR 1.57 (1.44-1.71)

Hyperkalemia RR 1.95 (0.85-4.48)

ONTARGET trial showed similar results

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0009946

COMET - carvedilol vs metoprolol in CHF

Patients

3029 patients mean age 62 (20% women) with CHF (NYHA Class II 48%, Class III 48%), a history of IHD (53%), cardiomyopathy (44%), diabetes (24%), HTN (36%), ACEI (92%), digoxin (60%), spironolactone (11%), lipid lowering (21%), aspirin (36%)

Treatment

carvedilol started at 3.125 mg PO BID up to 25 mg PO BID (75% got to this dose) or metoprolol started at 5 mg PO BID up to 50 mg PO BID (78% got to this dose)

Duration

5 years

Results

Heart rate was 1.6 BPM lower and systolic blood pressure was 1.8 mmHg lower at 4 months in carvedilol group

Lancet 2003;362:7-13

COMET results

	Mortality and all cause admission (%)	All deaths (%)	CV deaths (%)	Serious adverse events (%)
Carvedilol	74	34	29	75
Metoprolol	76	40	35	77
Relative risk reduction	NSS	15	17	NSS
Absolute risk reduction		6	6	
Number needed to treat		17	17	

Spironolactone and congestive heart failure

Patients

1663 patients with severe heart failure on diuretic and ACE inhibitor

Treatment

placebo or spironolactone 25-50 mg PO daily

Duration

24 months

Results

no differences in side effects overall but 9% (spironolactone) versus 1% (placebo) incidence of gynecomastia

3% more patients withdrew because of side effects in the spironolactone group

no difference in serious hyperkalemia

New Engl J Med 1999;Sept 2

Spironolactone Results

	Hospitalizations due to cardiac causes (%)	Death from cardiac causes (%)	Death from any cause (%)
Placebo	40	37	46
Spironolactone	32	28	35
Relative risk reduction	20	24	24
Absolute risk reduction	8	9	11
Number needed to treat	13	11	9

Nitrates

Stable Angina

Increased exercise duration by 30-50 sec

Attacks/per week - reduced by 2.45 episodes - baseline 5-15 episodes

52% headaches - dizziness, hypotension, skin rashes

Heart failure Int JCard 2011;146:3-12

10 MONTHS	ISDN/hydralazine	Placebo
HF exacerb (%)	8.7	12.8
Mortality (%)	6.2	10.2
HF hosp (%)	16.4	24.4
Dizziness (%)	29.3	12.2
Headache (%)	47.5	19.2

NEJM 2004;351:2049-57

Nitrates (treatment/prevention)

Lingual spray: 1 to 2 sprays (0.4 to 0.8 mg) onto or under the tongue every 3-5 min as needed, up to 3 sprays in 15 minutes

Sublingual tablet: 0.3 to 0.6 mg dissolved under the tongue or in the buccal pouch every 5 minutes as needed, up to 3 doses in 15 minutes

Headache, hypotension, tolerance