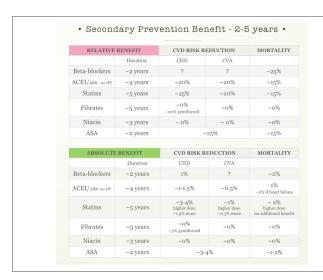
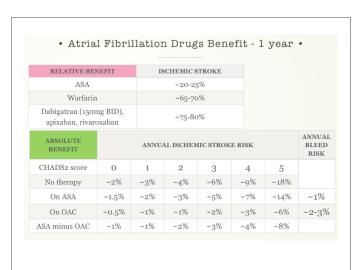
# Secondary prevention (Post MI, Atrial fibrillation, Heart failure

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Post MI



Atrial fibrillation



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 leftventricular 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		10	10
Absolute risk reduction	5	P=0.055	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		15	17	
Absolute risk reduction	NSS	6	6	NSS
Number needed to treat		17	17	

## Spironolactone and congestive heart failure

#### **Patients**

1663 patients with severe heart failure on diuretic and ACE inhibitor

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