

Heart Failure in the Hospital

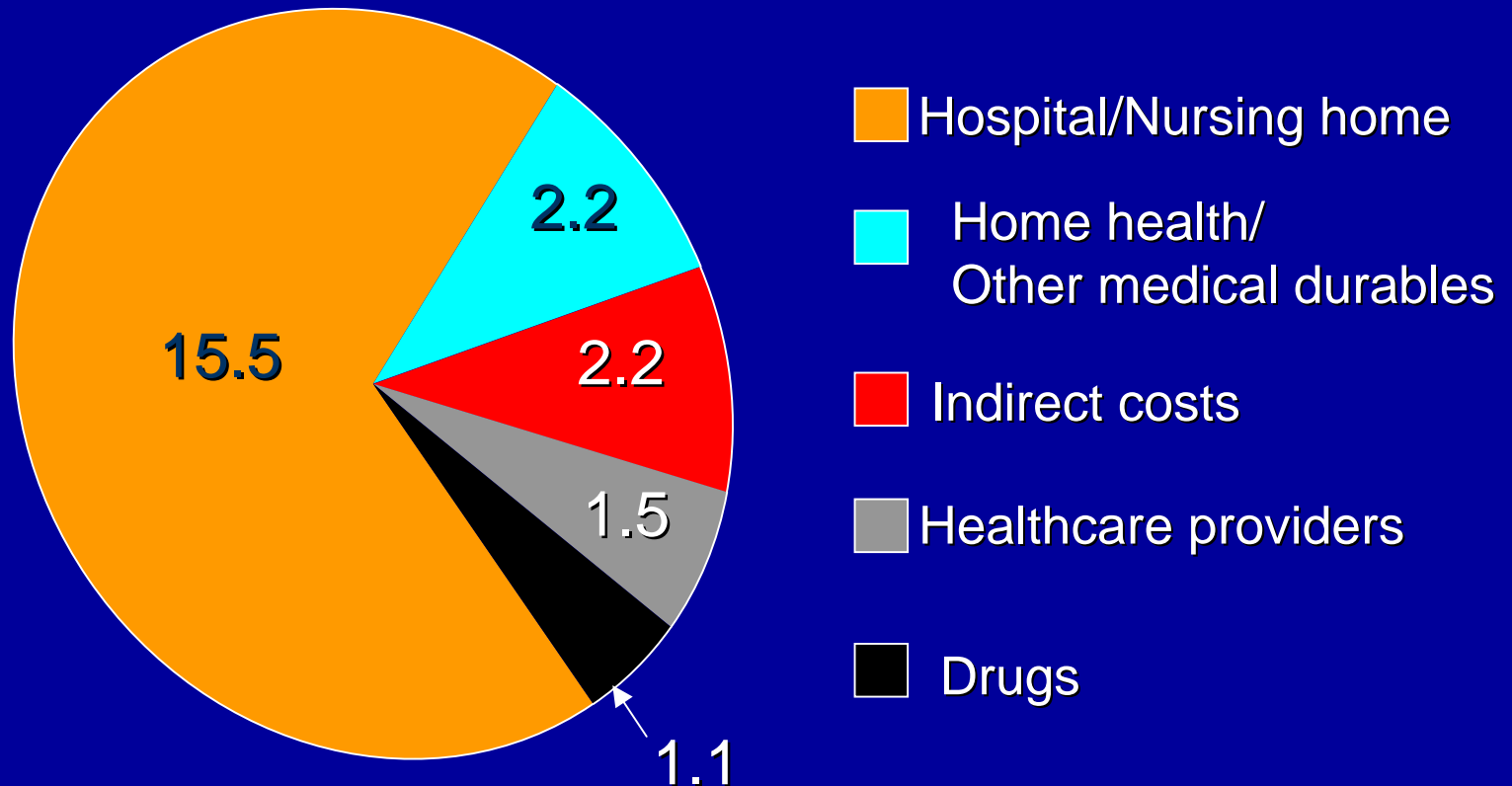
Meir Shinnar, MD PhD
Medical Director, Heart Failure
Service

Beth Israel Medical Center

- No conflicts of interest to report

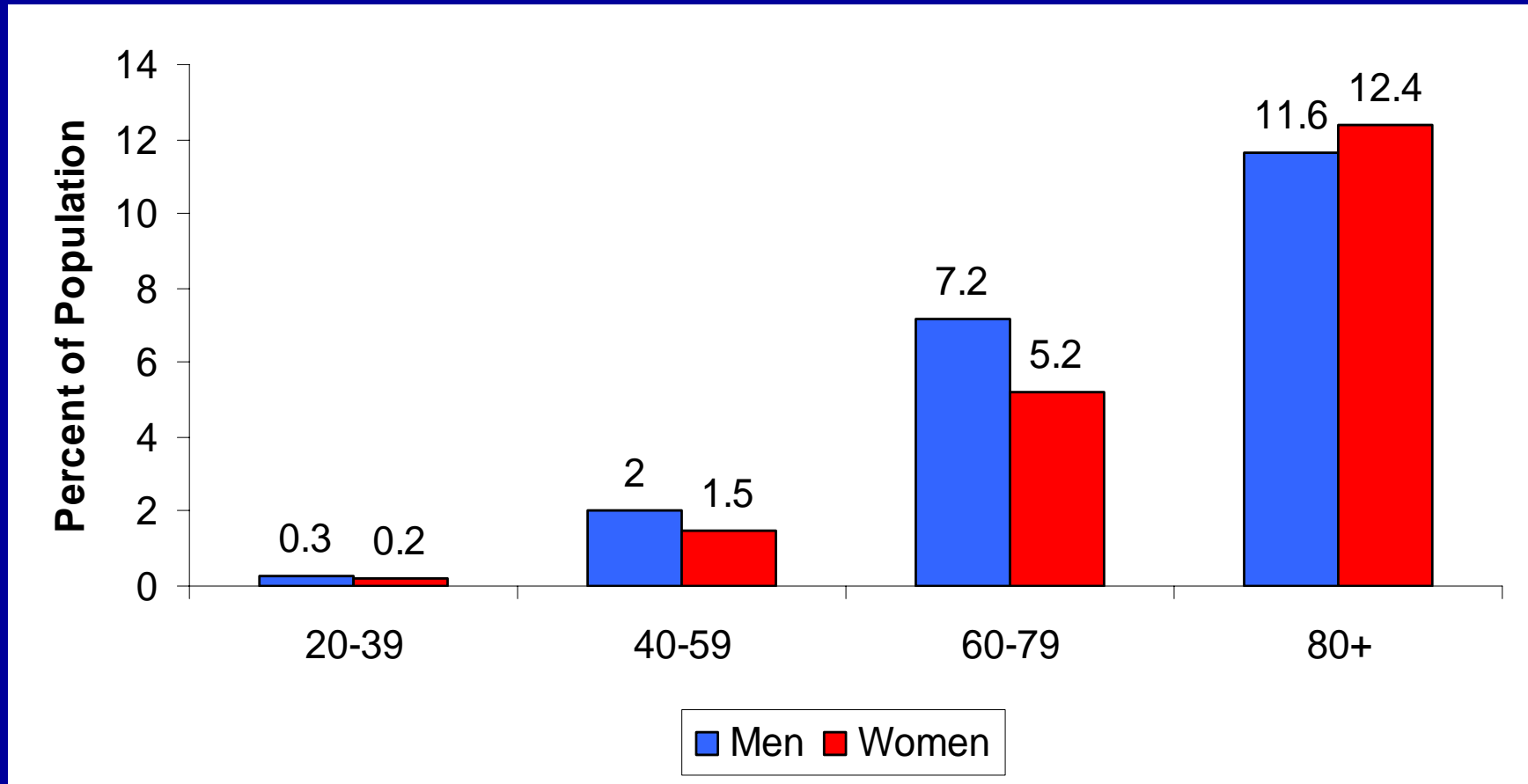
Cost* of Heart Failure to Society

\$22.5 billion



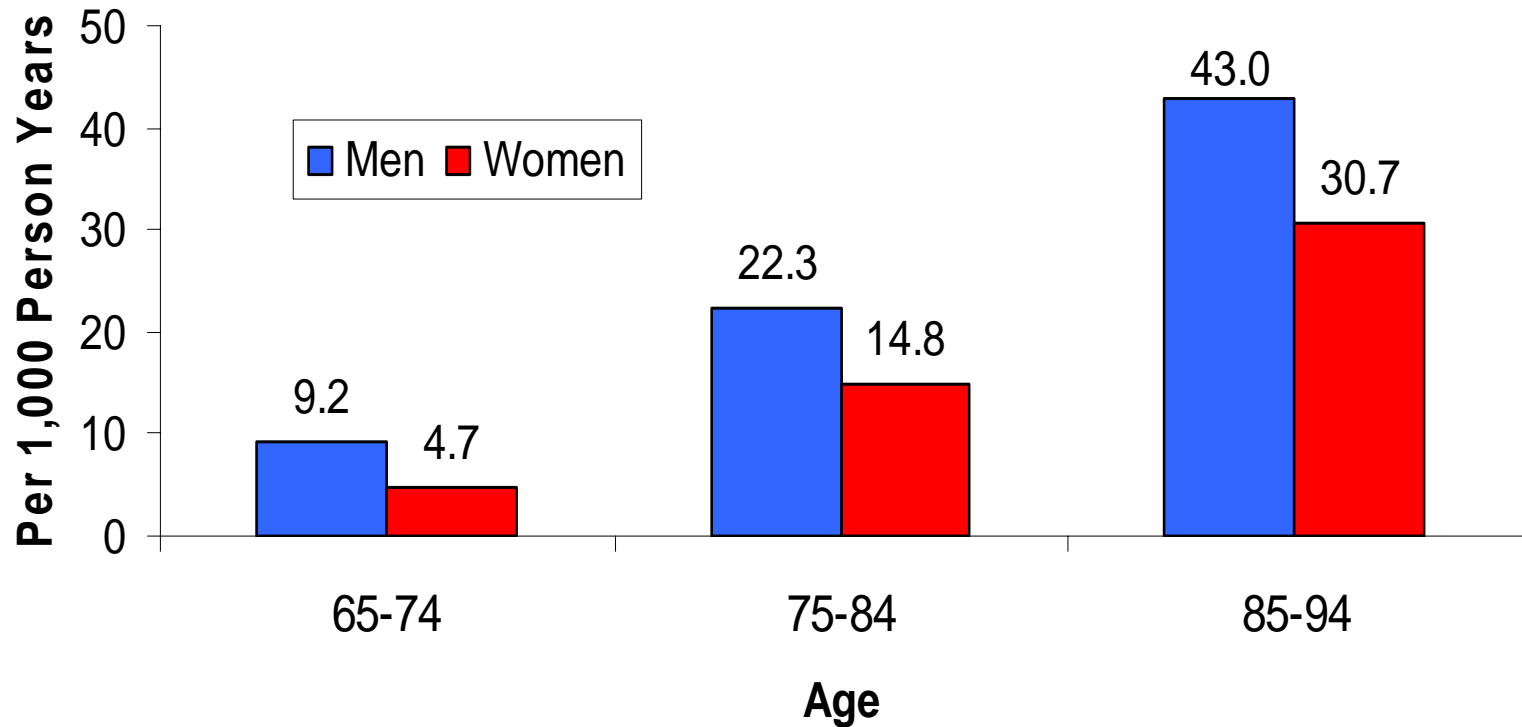
*Direct and indirect costs in billions of \$; estimated for year 2000

HEART FAILURE PREVALENCE



Prevalence of heart failure by age and sex
(NHANES: 1999-2004). **Source: NCHS and NHLBI.**

HEART FAILURE INCIDENCE

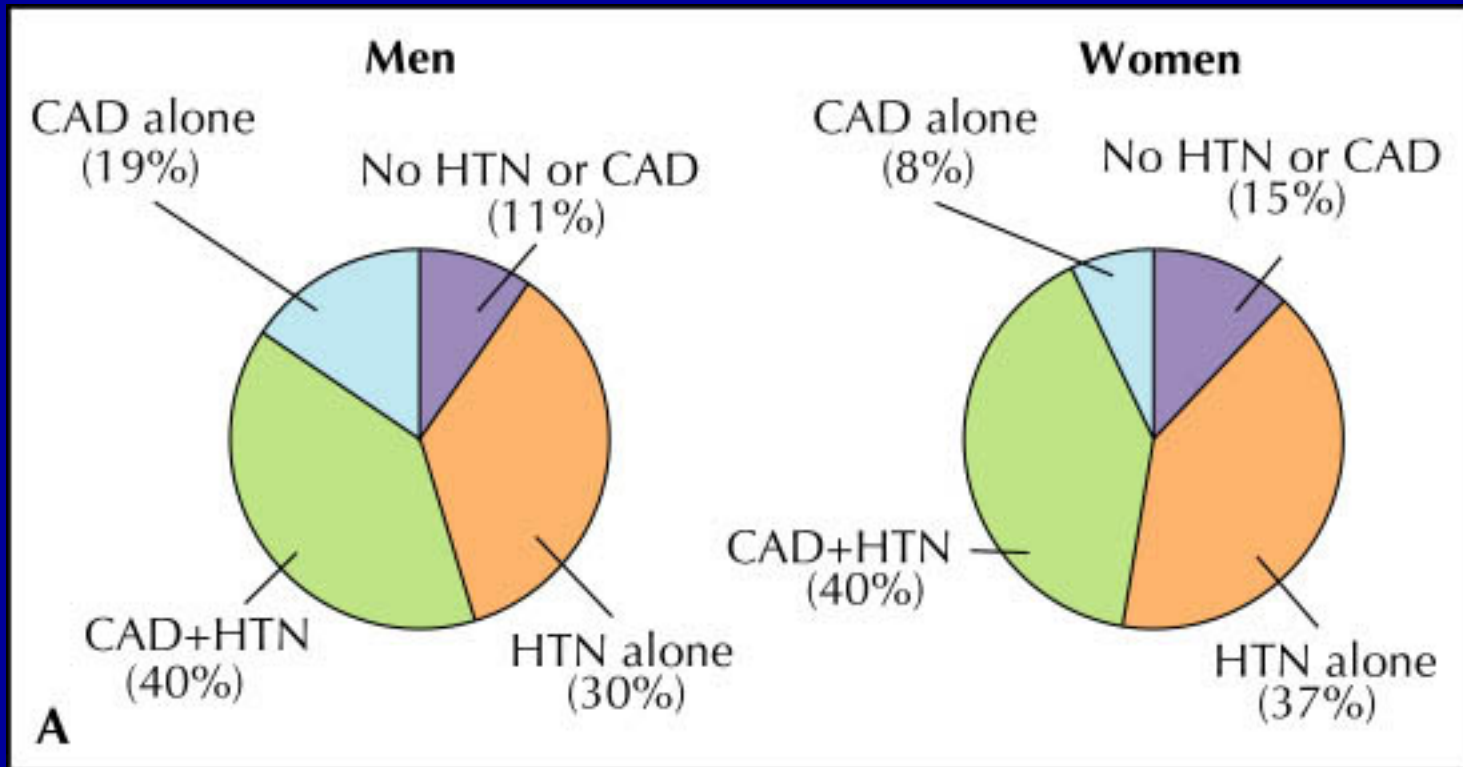


Incidence of Heart Failure* by age and sex. (FHS: 1980-2003).

Source: NHLBI.

*** HF based on physicians review of medical records and strict diagnostic criteria.**

EPIDEMIOLOGY OF HEART FAILURE IN USA



WHAT IS HEART FAILURE?

- HF is a syndrome caused by cardiac dysfunction, generally resulting from myocardial muscle dysfunction or loss and characterized by left ventricular dilation or hypertrophy. Whether the dysfunction is primarily systolic or diastolic or mixed, it leads to neurohormonal and circulatory abnormalities, usually resulting in characteristic symptoms such as fluid retention, shortness of breath, and fatigue, especially on exertion.

WHAT IS HEART FAILURE? (cont)

- In the absence of appropriate therapeutic intervention, HF is usually progressive at the levels of cardiac function and clinical symptoms. The severity of clinical symptoms may vary substantially during the course of the disease process and may not correlate with changes in underlying cardiac function. Although HF is progressive and often fatal, patients can be stabilized and myocardial dysfunction and remodeling may improve, either spontaneously or as a consequence of therapy.

What is acute decompensated heart failure?

- Patients with heart failure of sufficient severity to require hospitalization
- Most common Medicare diagnosis for hospital admission

THERAPY OF ADHF

- In the context of ADHF, these are noteworthy findings. To date, no other therapeutic intervention has been demonstrated in large-scale randomized, placebo-controlled studies to positively influence symptoms in ADHF without generating a question of harm.

WHAT IS ADHF?

- Who gets ADHF?
- How do they differ from chronic heart failure?
- What causes decompensation?
- How is it treated?

ADHF (old)

- 1. Population is similar to chronic heart failure, skewed towards more severe
- 2. Decompensation - cause can be readily identified
- 3. Treatment - treat cause, volume overload, and chronic heart failure

What is acute decompensated
heart failure?

Several different syndromes

- Decompensated chronic heart failure
- Acute vascular failure
- Acute ischemia
- Arrhythmias
- Valvular disease

Decompensated chronic heart failure

- Progression of chronic heart failure
- Frequently due to
 - Dietary noncompliance
 - Pharmacologic noncompliance
 - Disease progression

Acute vascular failure

- Rapidly progressive
- Active inflammation
- Neurohormonal activation
- Vasoconstriction
- Reduction in cardiac output

EPIDEMIOLOGY OF ADHF

- Registry from hospitals
- Population based studied

ADHERE TRIAL

- Registry of Acute decompensated heart failure
- >105,000 patients
- Average age 72.4
- 52% female
- Significantly older and more female than most studies of chronic heart failure

ADHERE TRIAL LVEF

- Average LVEF 34.4%
- 46% with normal or mildly impaired systolic function during or just prior to hospitalization

ADHERE TRIAL SYMPTOMS

- NYHA Class I 4
- NYHA Class II 20
- NYHA Class III 44
- NYHA Class IV 32
- Average of 1 hospitalization in prior 6 months

ADHERE TRIAL ETIOLOGY

- CAD 57%
- Hypertension 73%
- Diabetes Mellitus 44%
- Renal Insufficiency 30%

ADHERE TRIAL OUTCOMES

- Death in hospital 4%

OPTIMIZE-HF

- Number of patients 48612
- Average age 73
- 52% female
- 49 % systolic dysfunction
- 51% diastolic dysfunction
- Average LVEF 39%
- Inpatient mortality 3.8%

OPTIMIZE-HF

Precipitating factors, No. (%)	18888 (38.7)
Arrhythmia	7155 (13.5)
Uncontrolled hypertension	5220 (10.7)
Ischemia/acute coronary syndromes	6552 (14.7)
Worsening renal function	3304 (6.8)
Pneumonia/respiratory process	7426 (15.3)
Nonadherence to medications	4309 (8.9)
Nonadherence to diet	2504 (5.2)
Other	6171 (12.7)
No. of precipitating factors	
0	18798 (38.7)
1	20504 (42.2)
2	6599 (13.6)
3	2050 (4.2)
≥ 4	661 (1.4)

OPTIMIZE-HF

- 39% of time no cause found
- Noncompliance only 14%
- Arrhythmias, worsening renal function might be secondary rather than primary
- Most common cause - pulmonary
- Ischemia - 15%

Canada Heart Failure

- Studied: All Ontario residents admitted in an Ontario hospital 1994-1997
- Admitting Diagnosis: Heart Failure
- First admission for heart failure

Canada HF Trial

Age	Men	Mortality		Women	Mortality	
		30 day	1 year		30 day	1 year
20-49	655	4.6	15.0	375	4.3	10.9
50-64	3048	5.5	20.5	1892	5.4	19.5
65-74	5923	8.6	28.8	4412	6.8	23.0
≥75	9310	15.6	43.1	13087	14.7	37.9
All ages	18936	11.4	34.0	19766	11.8	32.3

Arch Int Med 162: 1689-1694 (2002)

Worcester HF Trial

- All patients admitted with Heart failure to any of 11 Worcester, MA hospitals in 2000
- 2445 patients
- Average age: 76
- 43% Men
- LVEF not available

Worcester Heart Failure Trial

- 5.5% died during hospitalization
- 37.3% of remainder died during first year
- 78.5% died during next five years
- Newly diagnosed heart failure – 27.8%
1 year, 62.5 5 year mortality

COPERNICUS TRIAL

- 2289 patients randomized to placebo or carvedilol
- Symptoms at rest or minimal exertion
- LVEF \leq 25%

COPERNICUS TRIAL

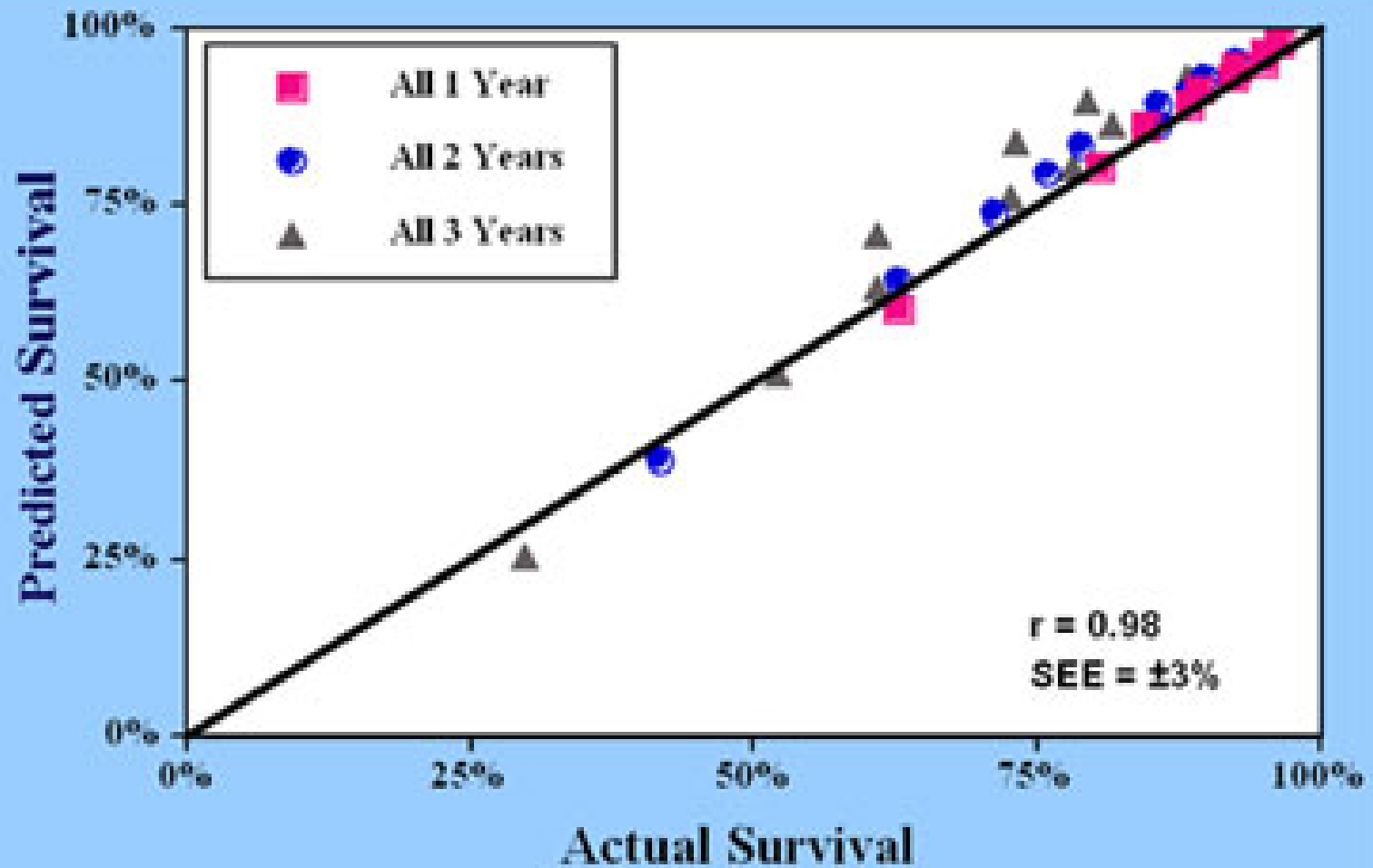
- High risk subgroup
 - Wet despite diuresis
 - ≥ 3 hospitalizations last year
 - Hospitalized when randomized
 - Treatment with intravenous vasodilators or inotropes within 2 weeks of randomization
 - LVEF ≤ 15

COPERNICUS TRIAL

- In placebo group
 - 1 year mortality 19.7 %
- In placebo high risk group
 - 1 year mortality 28.5%

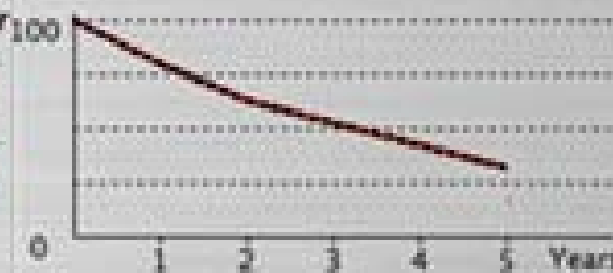
Seattle Heart Failure Model

Circulation 2006;113:1424-33



11,067 Patients - 1 Year ROC - 0.729

	Baseline			Post-intervention		
	1 year	2 year	5 year	1 year	2 year	5 year
Survival	80%	63%	32%	80%	63%	32%
Mortality	20%	37%	68%	20%	37%	68%
Mean life expectancy	4.0 years			4.0 years		



Baseline Characteristics

Clinical

Age: 65
 Gender: Male
 NYHA Class: 3
 Weight (kg): 80
 EF: 20
 Syst BP: 120

Ischemic

Medications

ACE-I
 Beta-blocker
 ARB
 Statin
 Allopurinol
 Aldosterone blocker

Diuretics

Furosemide: 80
 Bumetanide: 0
 Torsemide: 0
 Metolazone: 0
 HCTZ: 0

Lab Data

Hgb: 13.7
 Lymphocyte%: 25
 Uric Acid: 8
 Total Chol: 195
 Sodium: 138

QRS >120 msec

Devices

None
 BIV Pacer
 ICD
 BIV ICD

Defaults

Interventions

ACE-I ARB Beta-blocker
 Statin Aldosterone Blocker

Devices

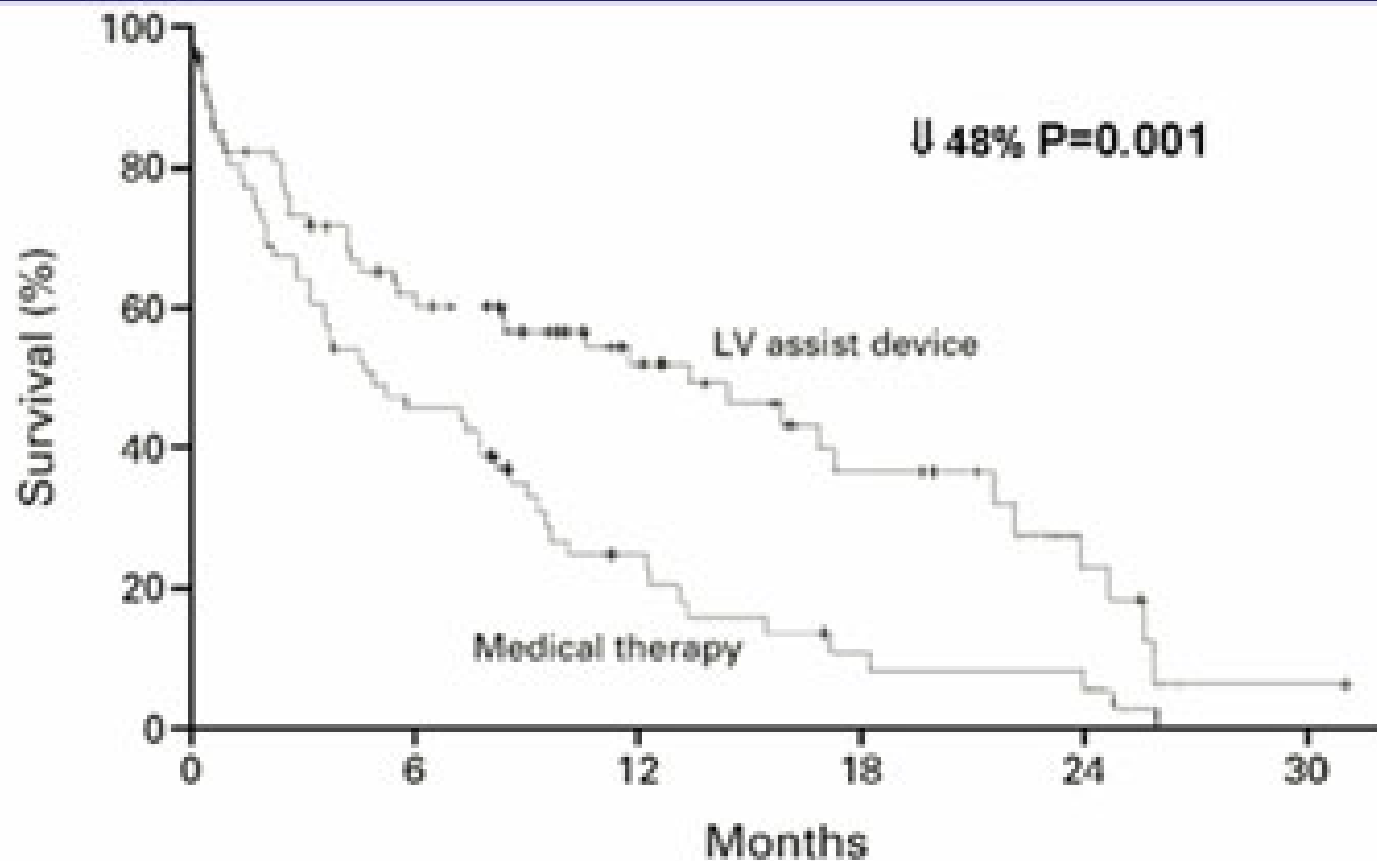
None
 BIV Pacer BIV ICD
 ICD LVAD

Note: Some devices may be disabled if CMS clinical criteria are not met. See below.

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REMATCH - LVAD vs Medical Therapy

NEJM 2001;345:1434-43



No. AT Risk

LV assist device	68	38	22	11	5	1
Medical therapy	61	27	11	4	3	0

ADHF

- Older
- More diastolic dysfunction
- Cause unknown in 40%
- Very high mortality

Pathophysiology

- Symptoms related to high filling pressure
- High Left ventricular end diastolic pressure -> high pulmonary capillary wedge -> pulmonary congestion

Pathophysiology

- Do high filling pressures reflect significant volume overload or more of a volume redistribution?

Weight Change and ADHF

- 77 patients
- 34 clinically stable
- 43 clinically decompensated

Weight Change and ADHF

- Average weight gain over baseline for decompensated patients - 0.7 kg
- Average weight gain for compensated patients - 0.7 kg
- Sensitivity of acute 2 kg weight gain - 9%

Wedge versus weight

- Wedge pressure rises before Acute heart failure hospitalizations, not associated with weight changes.

Am Heart J 2008; 155:9-18, citing personal communication

VOLUME GAIN

- Symptoms are consistent with volume gain
- Wedge and impedance consistent with volume gains
- Weight does not correlate

Wedge versus weight

- Weight loss above mean associated with less orthopnea, less dyspnea on exertion
- Not associated with fewer hospitalizations or death at 60 days

Am Heart J 2008; 155:9-18, citing personal communication

Novel Mechanisms

- Vascular resistance and afterload mismatch
- Diastolic dysfunction
- Cardiorenal
- Neurohormonal and inflammatory activation

Novel Mechanisms

- Vascular resistance and afterload mismatch
 - Acute rise in Systemic vascular resistance
 - Etiology unclear - ? Inflammatory
 - Documented in some patient populations

Novel Mechanisms

- Diastolic Dysfunction
 - 38 patients with acute pulmonary edema
 - Blood pressure > 160
 - LVEF did not change from presentation to discharge

Novel Mechanisms

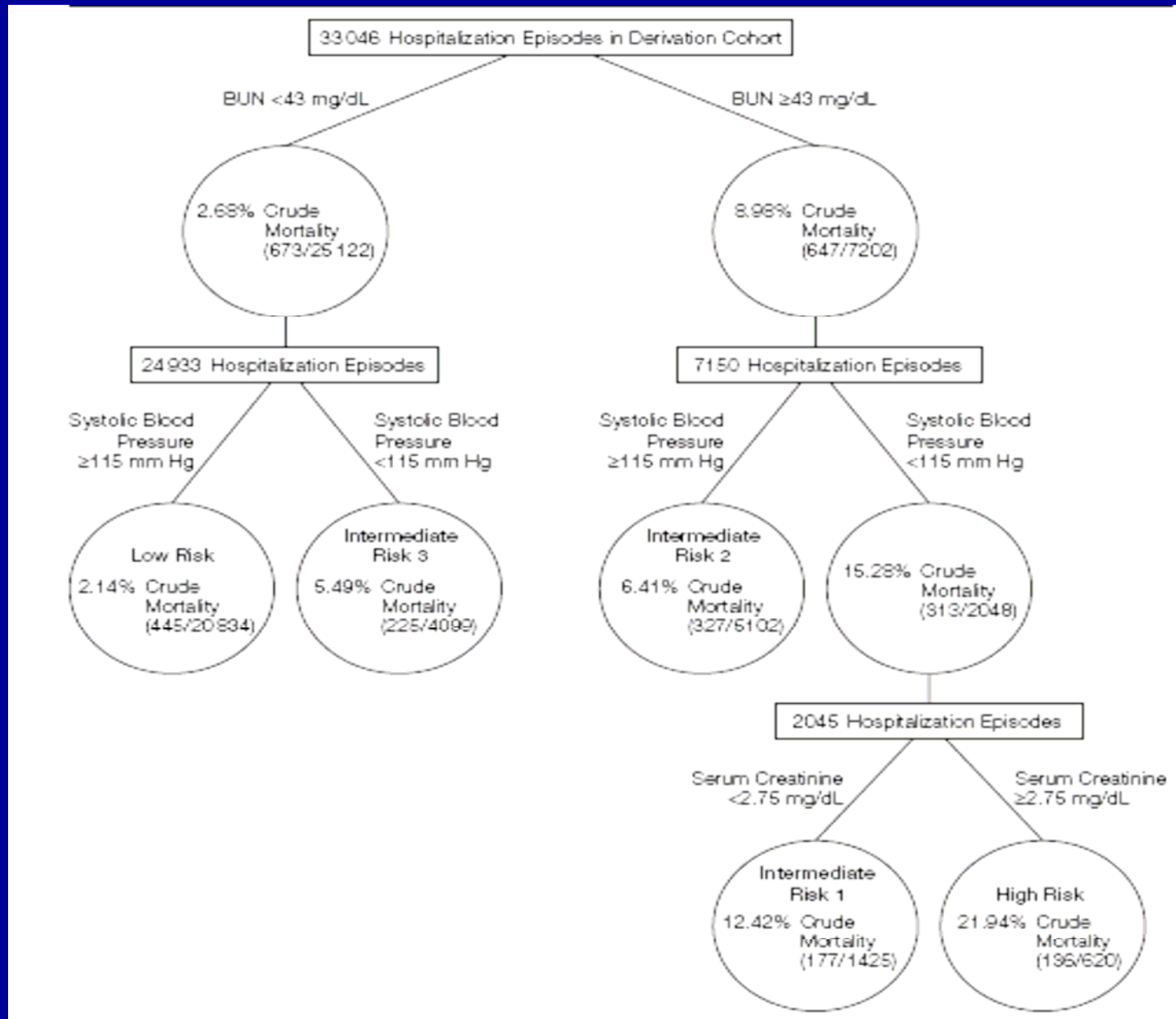
- Diastolic dysfunction
 - Two consecutive series of ADHF patients
 - (114 and 109 patients)
 - Variables predictive of death or readmission within 6 months:
 - BNP
 - Doppler measures of diastolic dysfunction
 - LVEF, clinical variables not predictive

ADHERE Inpatient mortality predictors

- Three best predictors of inpatient mortality
 - BUN \geq 43
 - BP \leq 115
 - Cr \geq 2.75

JAMA. 2005;293:572-580

ADHERE Database



ADHERE

Preserved versus low LVEF

- Preserved – LVEF \geq 40%
- Inpatient mortality 2.8 vs 3.9
- Predictors of mortality:
 - BUN \geq 37
 - SBP \leq 125

ADHERE

Troponins

- Positive troponins in ADHF identify patients with a high inpatient mortality (8.0 vs 2.7 %)
- Troponins did not correlate with whether there was an ischemic etiology to the heart failure

THERAPY IN ADHF

- Diuretics
- Vasodilators
 - Nitroglycerin
 - Nitroprusside
 - Nesiritide
- Inotators
 - Dobutamine
 - Milrinone
- Inotropes
 - Dopamine
- Others
 - Vasopressin antagonists
 - Ultrafiltration

THERAPY OF ADHF

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DIURETICS

- No randomized clinical trial
- Some retrospective data suggest harm
- Remain mainstay of treatment

VASODILATORS

- Nitroprusside - requires CCU
- Nitroglycerin - underutilized.
- Nesiritide - highly controversial.
Currently, only approved for rapid symptom relief

INOLATORS

- Dobutamine and milrinone
 - Both inotropes and vasodilators
 - Dobutamine stronger inotrope versus vasodilator
 - Milrinone may be used with beta blockers

OPTIME IN CHF

951 patients with exacerbation of systolic CHF

Average LVEF 23%

Average age 66

Male 66%

Not requiring intravenous inotropes

Randomized to placebo or 48 hrs of IV milrinone (0.5 mcg/kg/min)

OPTIME IN CHF

- Routine milrinone of no benefit and possible harm
- Hemodynamic benefit may not be of clinical benefit

ADHERE Temporal trends

Table IV. Inhospital outcomes over 12 quarters, 2002 to 2004

	Q1	Q12	P
Outcomes			
Inhospital mortality, n (%)	372 (4.5)	303 (3.2)	<.0001
Mechanical ventilation, n (%)	439 (5.3)	325 (3.4)	<.0001
ICU admissions, n (%)	1555 (18.9)	1460 (15.2)	<.0001
ICU/CCU, Q1 (median) Q3	1.4 (2.8) 5.0	1.3 (2.3) 4.1	.0002
Total LOS, Q1 (median) Q3	2.9 (4.7) 7.7	2.8 (4.1) 6.7	<.0001

CCU, Cardiac care unit.

ADHERE Temporal trends

IV medications during hospitalization, n (%)

Inotrope	1208 (14.7)	763 (7.9)	<.0001
Dobutamine	626 (7.6)	350 (3.6)	<.0001
Milrinone	340 (4.1)	151 (1.6)	<.0001
Dopamine	545 (6.6)	404 (4.2)	<.0001
Nitroglycerin	751 (9.1)	840 (8.7)	.36
Nesiritide	418 (5.1)	2054 (21.4)	<.0001
Diuretics	7237 (88.0)	8393 (87.3)	.16

Oral medications during hospitalization in patients with LVSD*, n (%)

ACEI/ARB	2612 (81.8)	2794 (81.0)	.41
β -blockers	2130 (63.4)	3244 (82.6)	<.0001
Aldosterone receptor antagonists	916 (29.1)	1046 (34.6)	<.0001
Diuretics	2981 (81.4)	3303 (79.6)	.05
Digoxin	1942 (53.0)	1660 (40.0)	<.0001

CHRONIC HEART FAILURE

3 Phases in understanding

- Phase 1 (through mid 1980s) - hemodynamics
- Phase 2 1980s - now - neurohormonal
- Phase 3 last 10 years - remodeling

Acute Decompensated Heart Failure

- Phase 1 Hemodynamics and volume
- Phase 2. ??

SUMMARY

- Epidemiology of ADHF patients is different than chronic heart failure
- Admission for ADHF means patient is at high risk for death in next year
- Markers of risk are only imperfectly understood

Summary

- Hemodynamics and volume status are only part of problem
- Issue of role of inflammation, neurohormonal activation, and other acute decompensation still being investigated

Summary

- Implications for therapy are still being evaluated
- No therapy has been shown to decrease mortality
- Vasodilator therapy perhaps should be more widely used
- Inotropes and inolators to be used only when evidence of hypoperfusion

Summary

- Recommendations are rapidly evolving
- Models are being developed to help estimate prognosis to guide therapy