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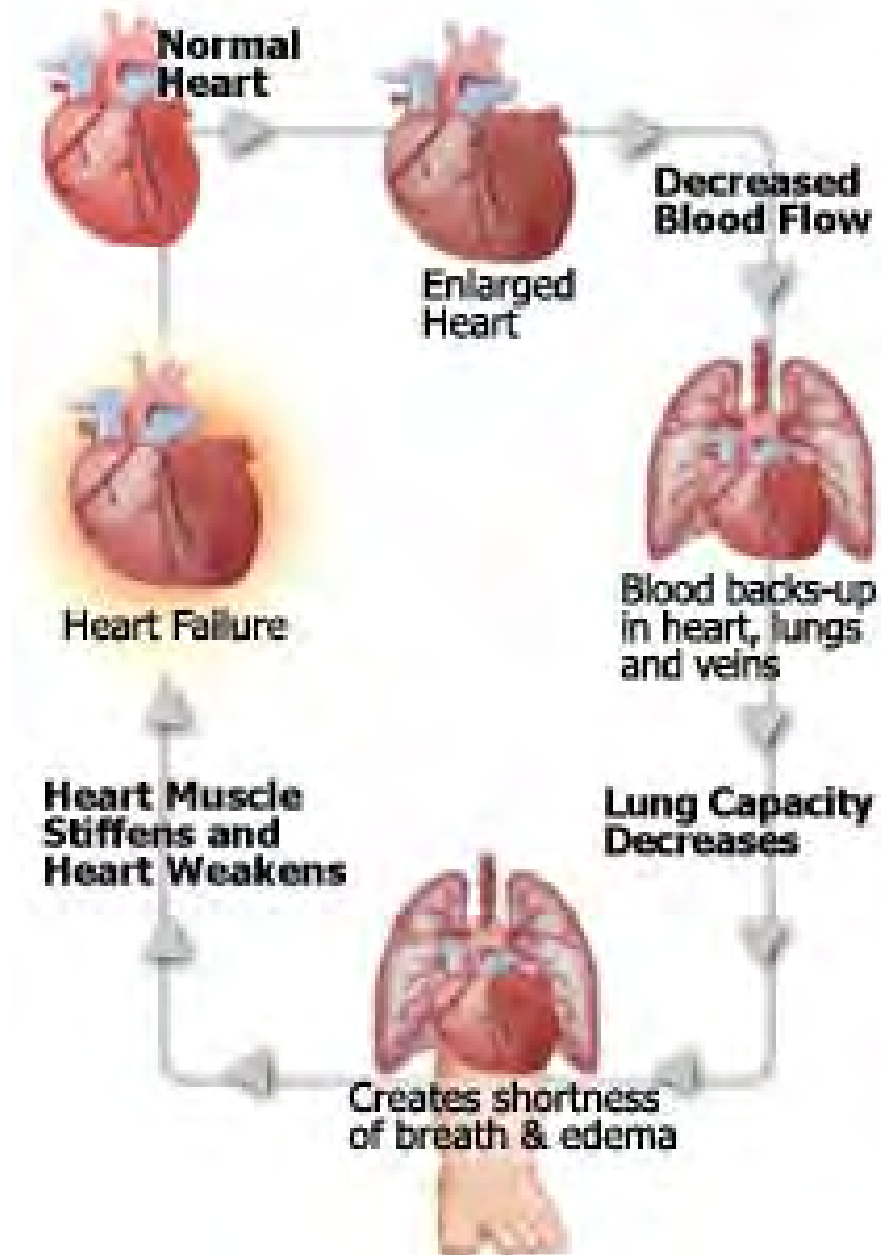
ST. MICHAEL'S HOSPITAL

A teaching hospital affiliated with the University of Toronto

PREVALENCE OF THIAMIN DEFICIENCY IN HOSPITALIZED PATIENTS WITH CONGESTIVE HEART FAILURE

Divisions of Cardiology, Cardiovascular Surgery and Nutrition, St. Michael's Hospital, The University Health Network, and Department of Nutritional Sciences, University of Toronto, Toronto, Ontario

Congestive Heart Failure



What are the Main Causes of Heart Failure?

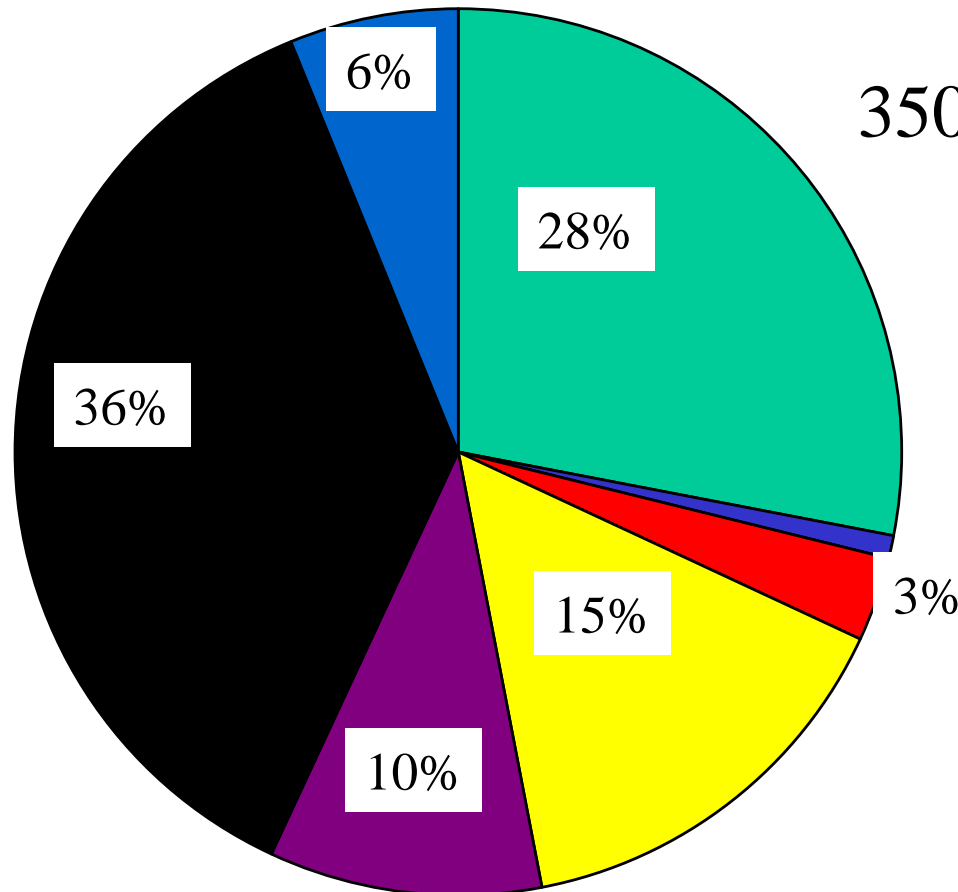
- A viral infection of the heart
- Myocardial infarction (heart attack)
- Chronic high blood pressure
- A heart valve that is not working properly
- Alcohol abuse or other drugs
- Congenital defects

Symptoms of Heart Failure

- Salt and water retention
- Shortness of breath – reduced capacity
- Swelling of the ankles
- Weight gain
- Fatigue
- Loss of appetite – bloated feeling
- Nausea/ vomiting

Health Burden of Heart Failure

350,000 Canadians



 cancer

 diabetes

 respiratory

 accidents/violence

 infectious disease

 other

 cardiovascular

Heart and Stroke Foundation of Canada, 2003

Management of Heart Failure

- Pharmacologic

Beta blockade, ACE inhibitors, inotropes, calcium channel blockers, statins and DIURETICS

- Nutritional

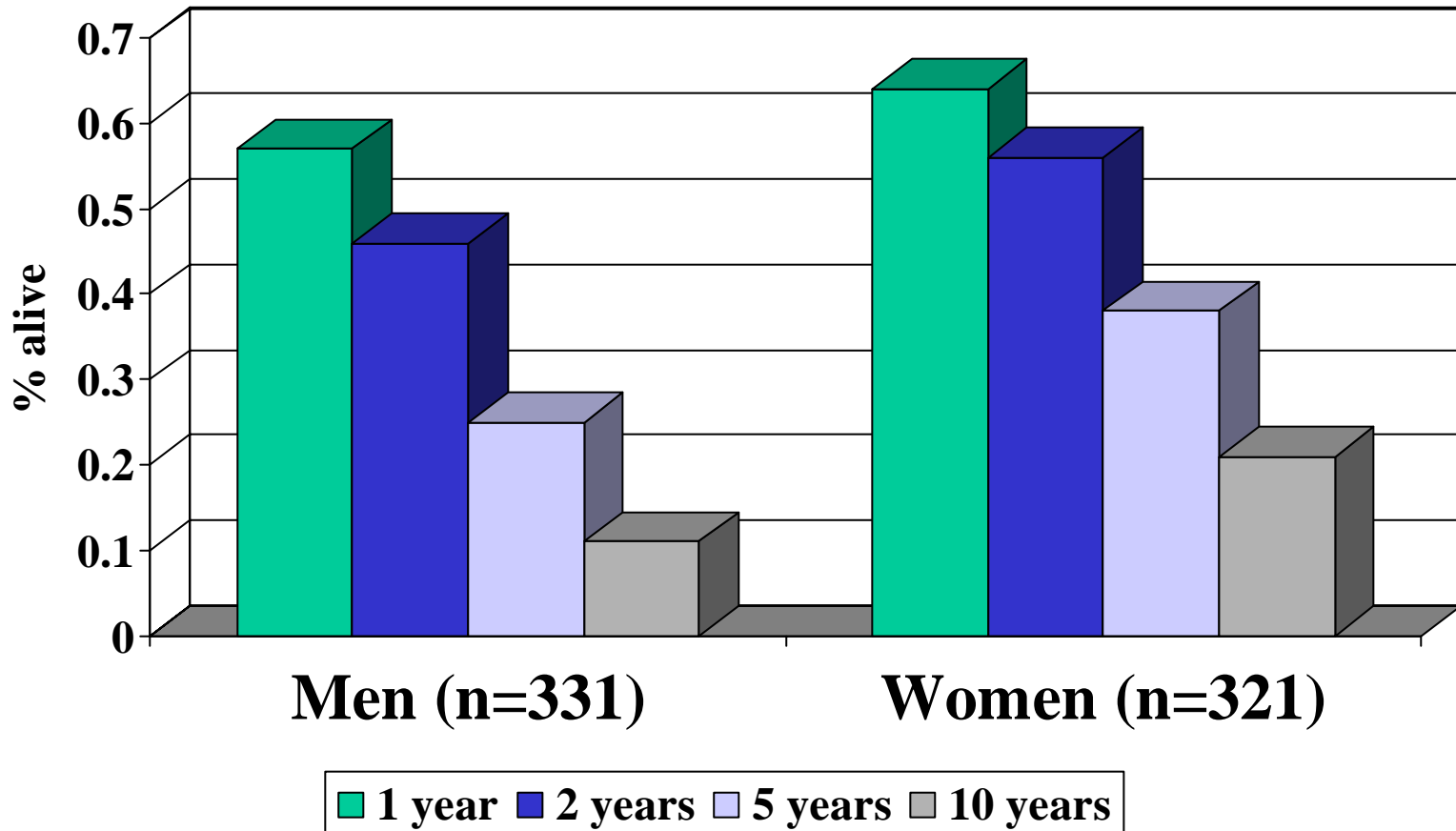
Sodium and fluid restriction, potassium balance, cholesterol reduction and heart healthy eating

- Lifestyle

Smoking and exercise

- Dismal Prognosis

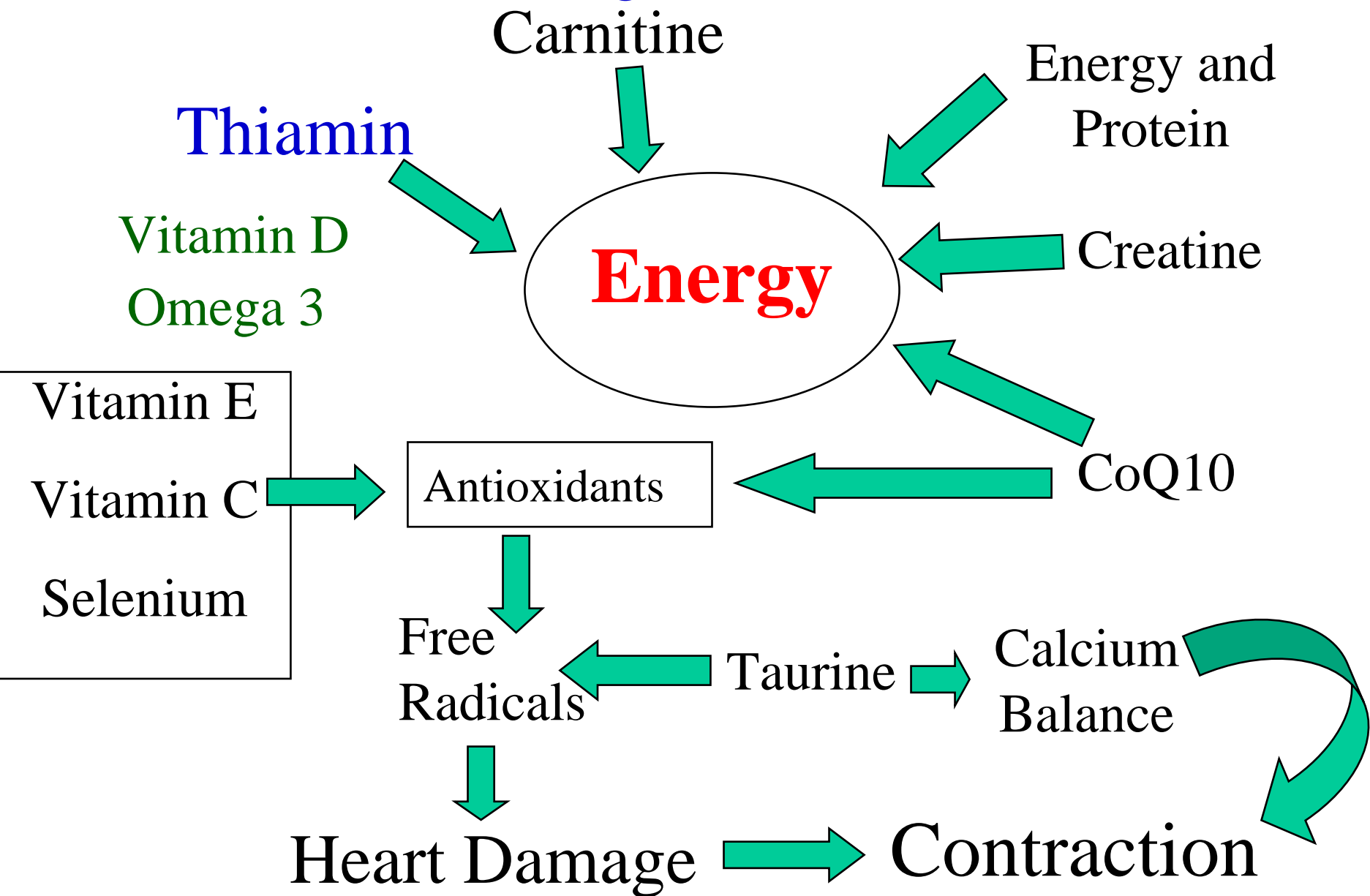
Overall Survival after CHF as Estimated using Kaplan-Meier Methods





The race continues for new, alternative and complementary strategies

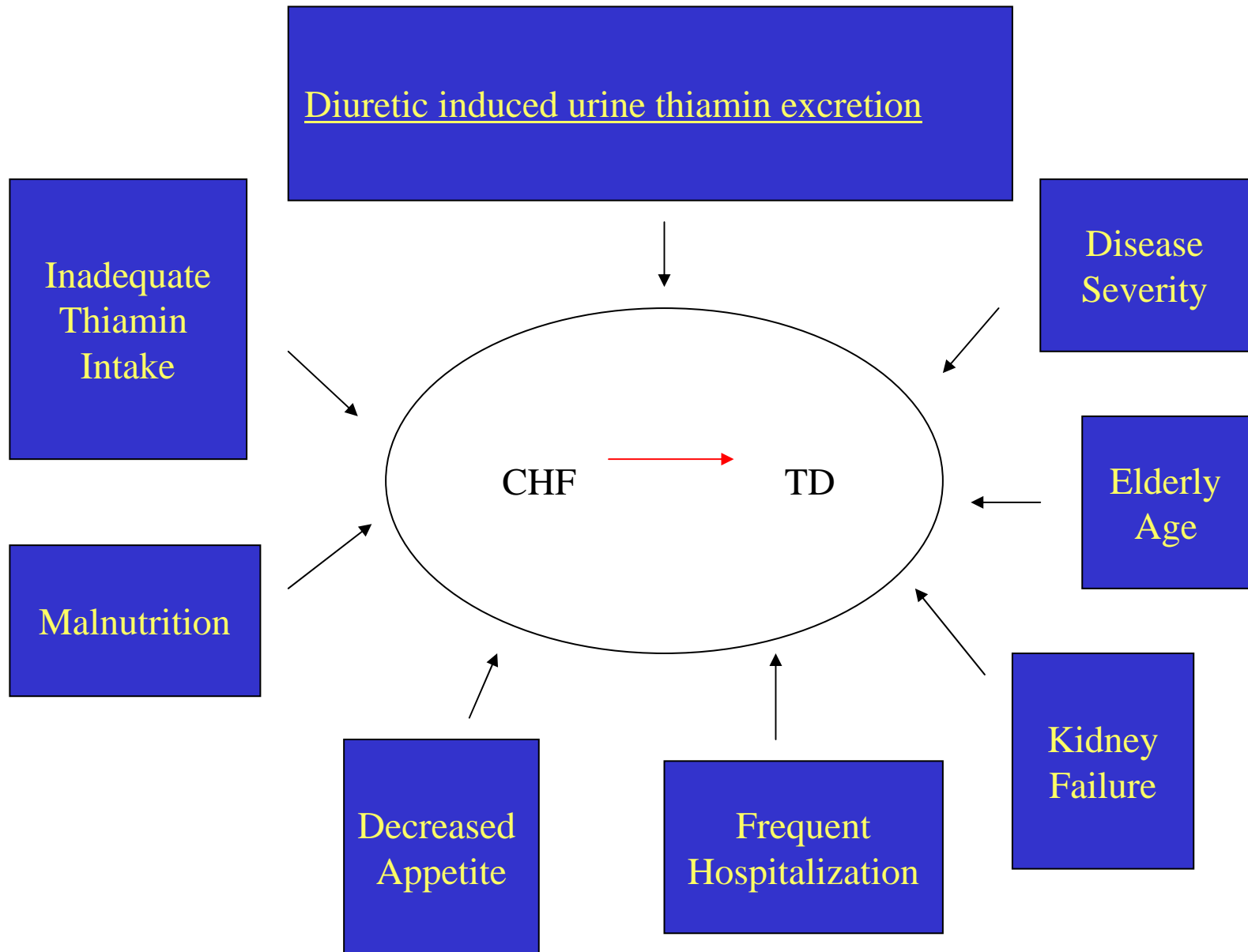
New Paradigm of Nutritional Care



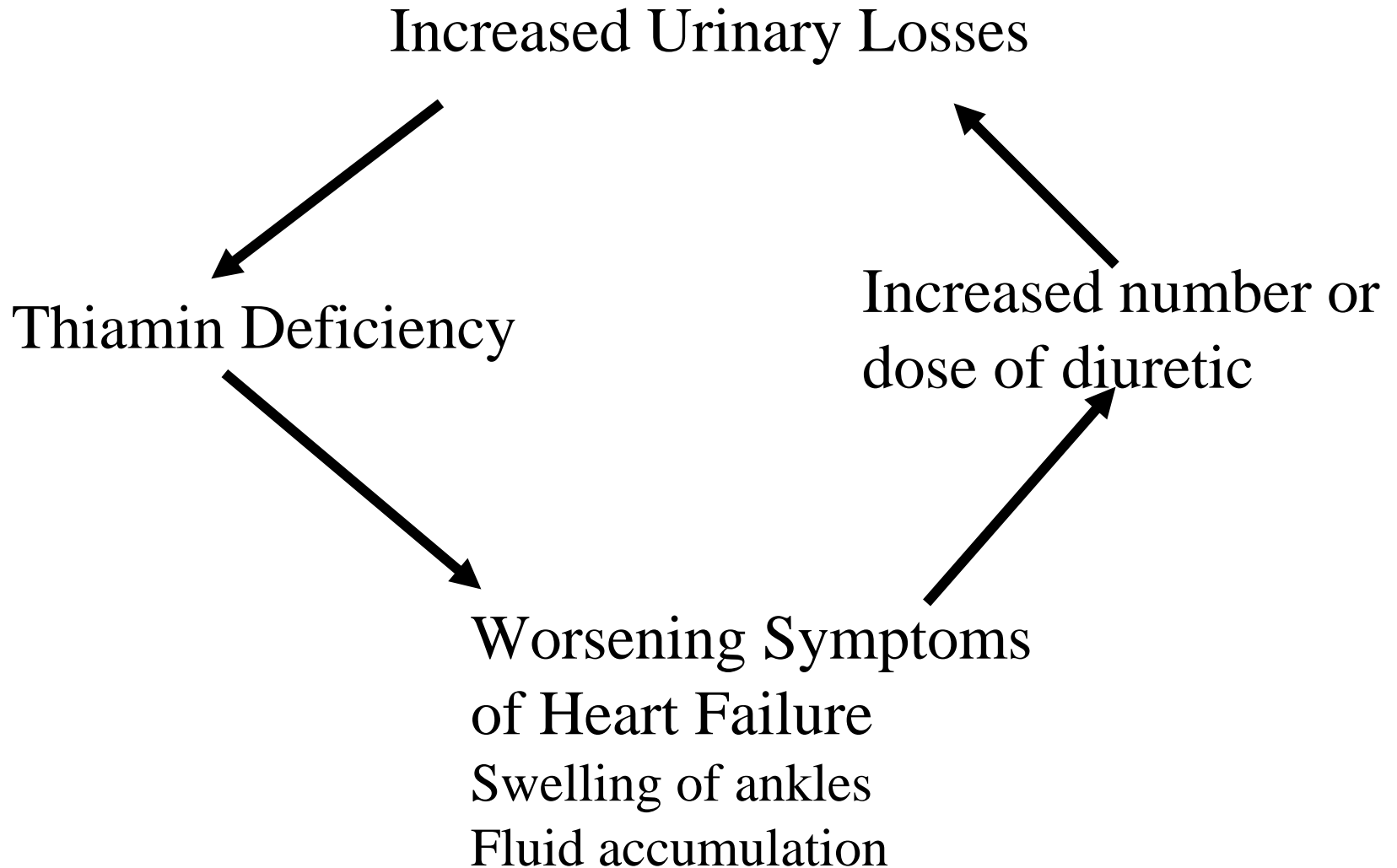
Thiamin Background

- Thiamin is a water soluble vitamin – B vitamin.
It is not stored in the body and is excreted in the urine.
- Thiamin (TPP) is a coenzyme in carbohydrate metabolism - production of ATP for cellular energy.
- Thiamin deficiency manifests as symptoms of CHF (wet beri-beri).

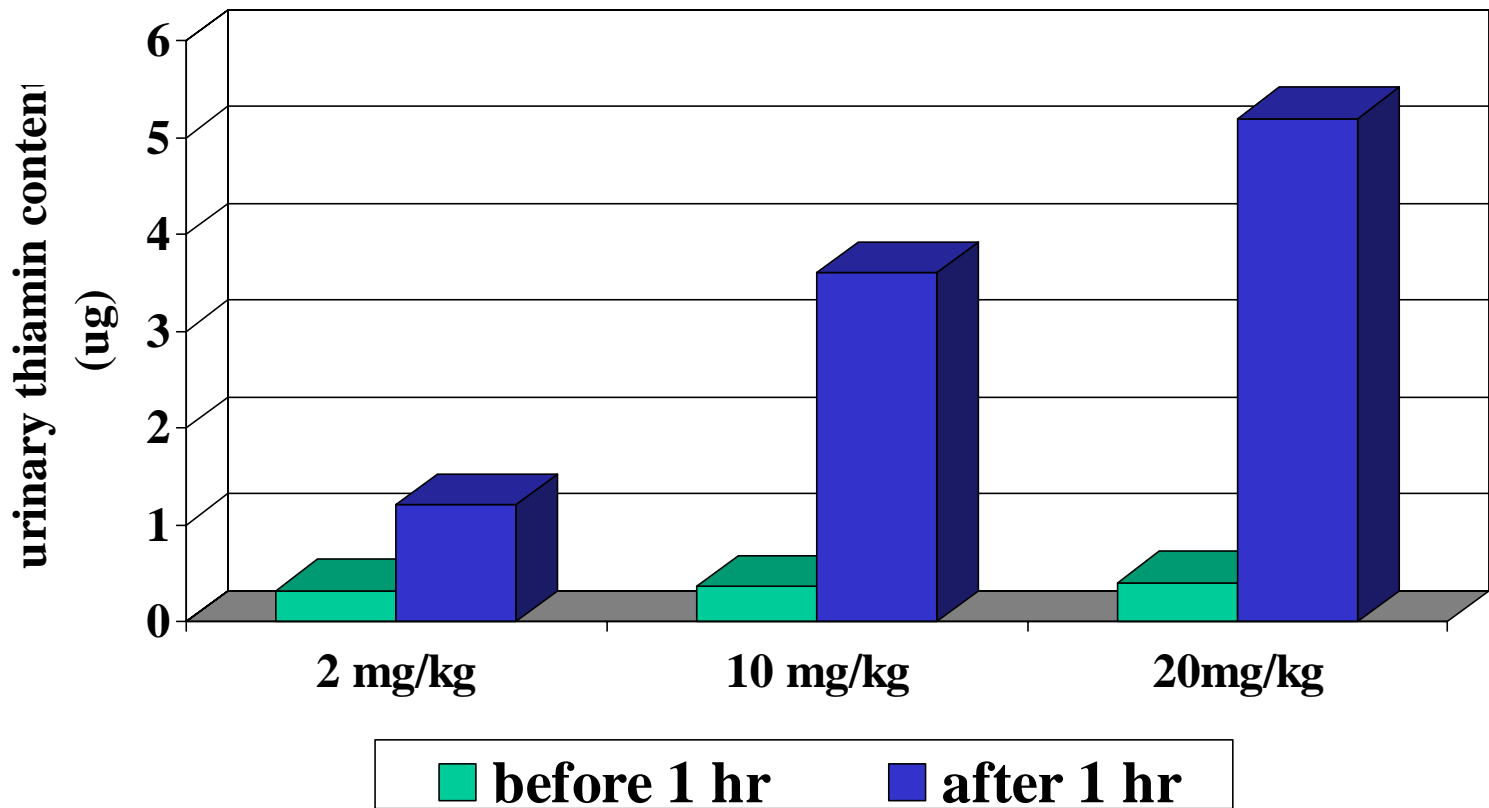
Thiamin Deficiency in Heart Failure



Proposed Vicious Cycle of Deficiency

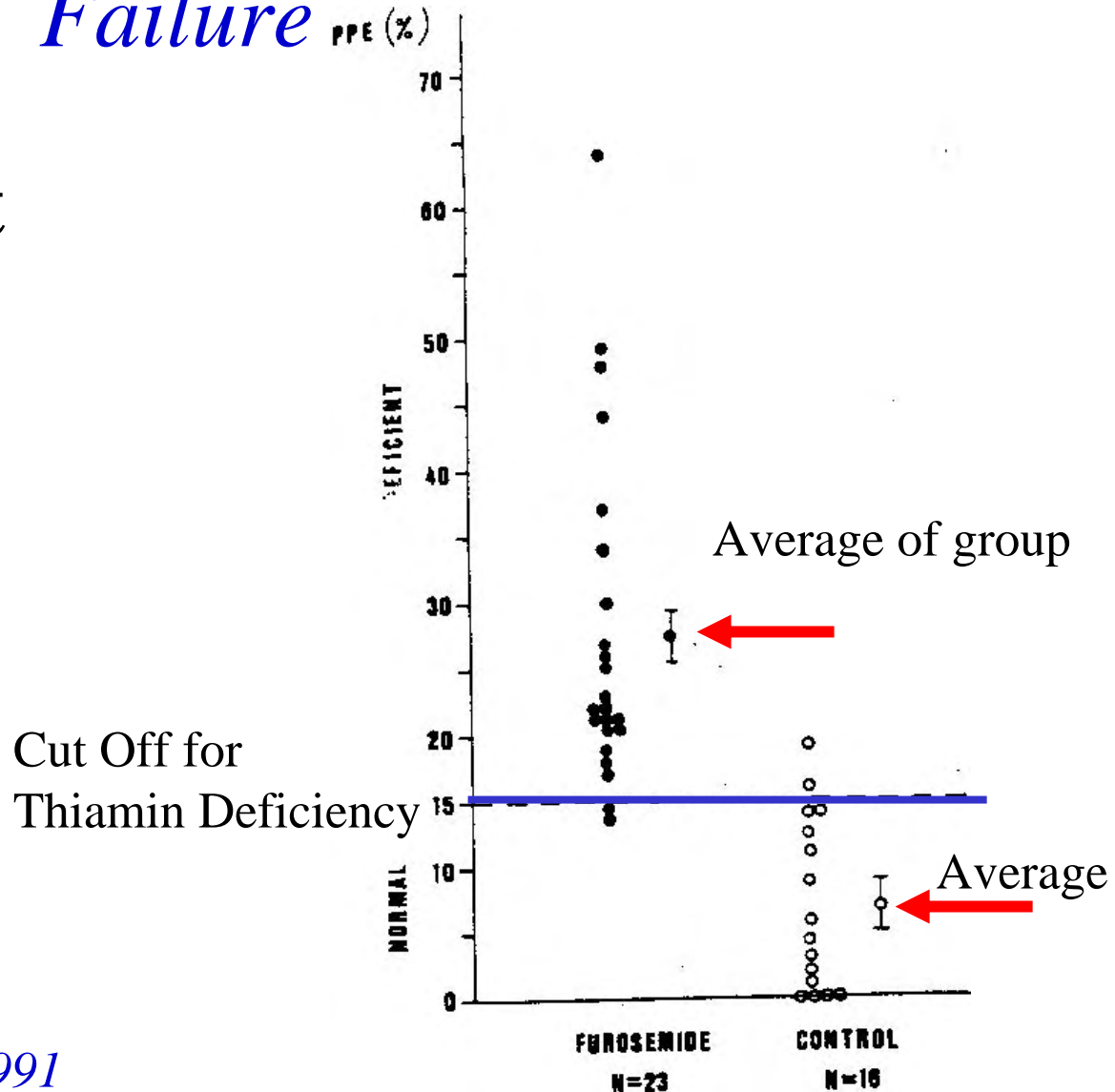


Changes in Urinary Thiamin Content before and after treatment with Furosemide

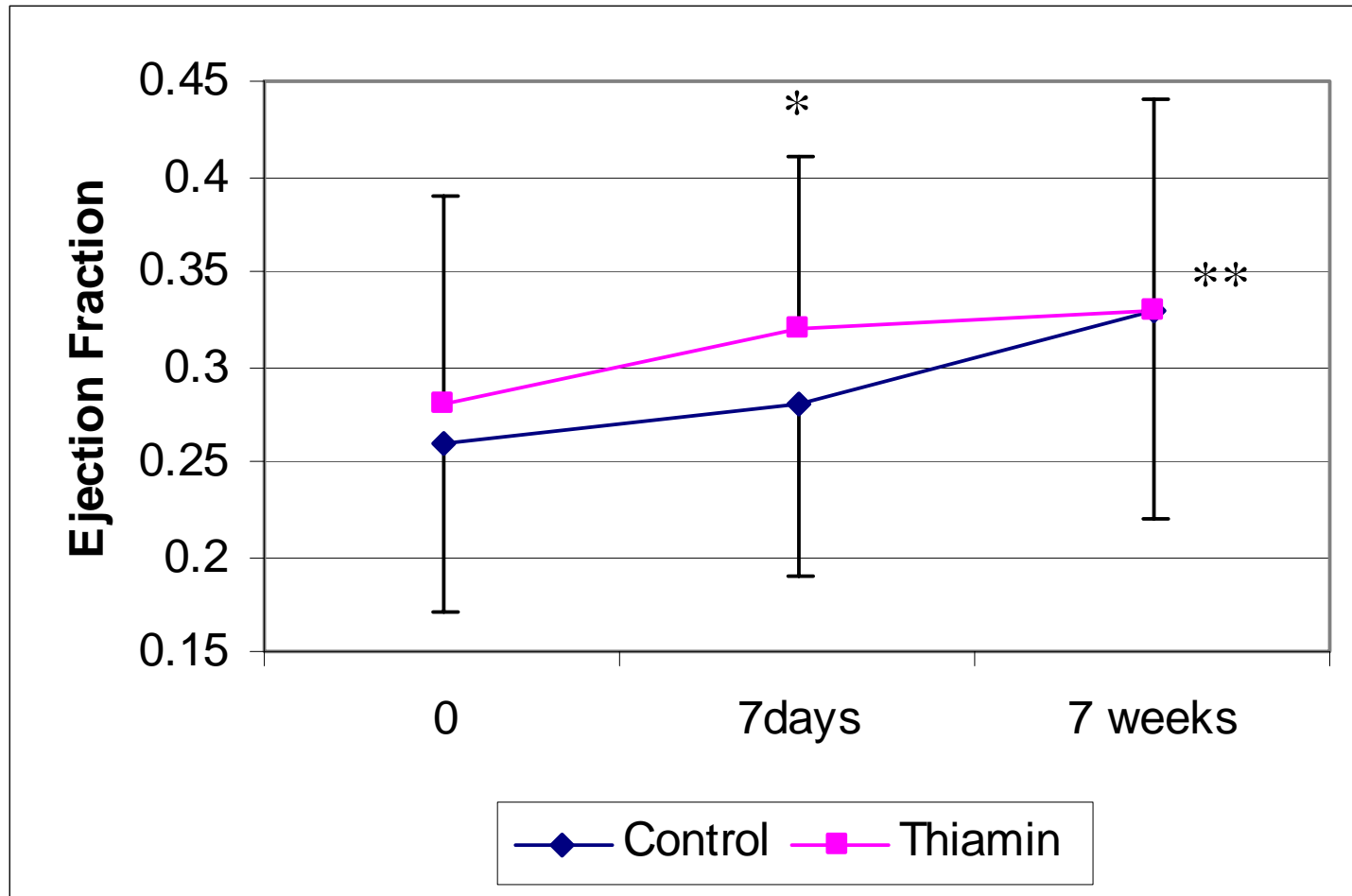


Thiamine Status of Patients with Heart Failure

21/23 deficient



The Effect of Thiamin Supplementation on Heart Function



* $p < 0.05$ vs baseline

** $p < 0.01$ vs baseline

Shimon et al 1994 Am J Med

OBJECTIVES

1. To determine the prevalence of TD in a large cross-section of hospitalized CHF patients.
2. To investigate the influence of age, sex, diuretics, urinary thiamin excretion, CHF disease severity, hospitalization, thiamin intake, appetite, malnutrition, decreased renal function, and diabetes on the development of TD.

METHODS: CHF PATIENTS

- 100 CHF patients admitted to St. Michael's Hospital (April 2001-June 2002).
- 50 age and sex matched healthy control subjects.
- TD was defined as erythrocyte TPP < 78 ng/mL packed cells.
- Approval for this study was obtained from SMH Research Ethics Board.

Patients—Selection Criteria

Inclusion Criteria:

Patients admitted to the cardiology ward or coronary care unit at SMH with a primary diagnosis of CHF

Patients– Exclusion Criteria

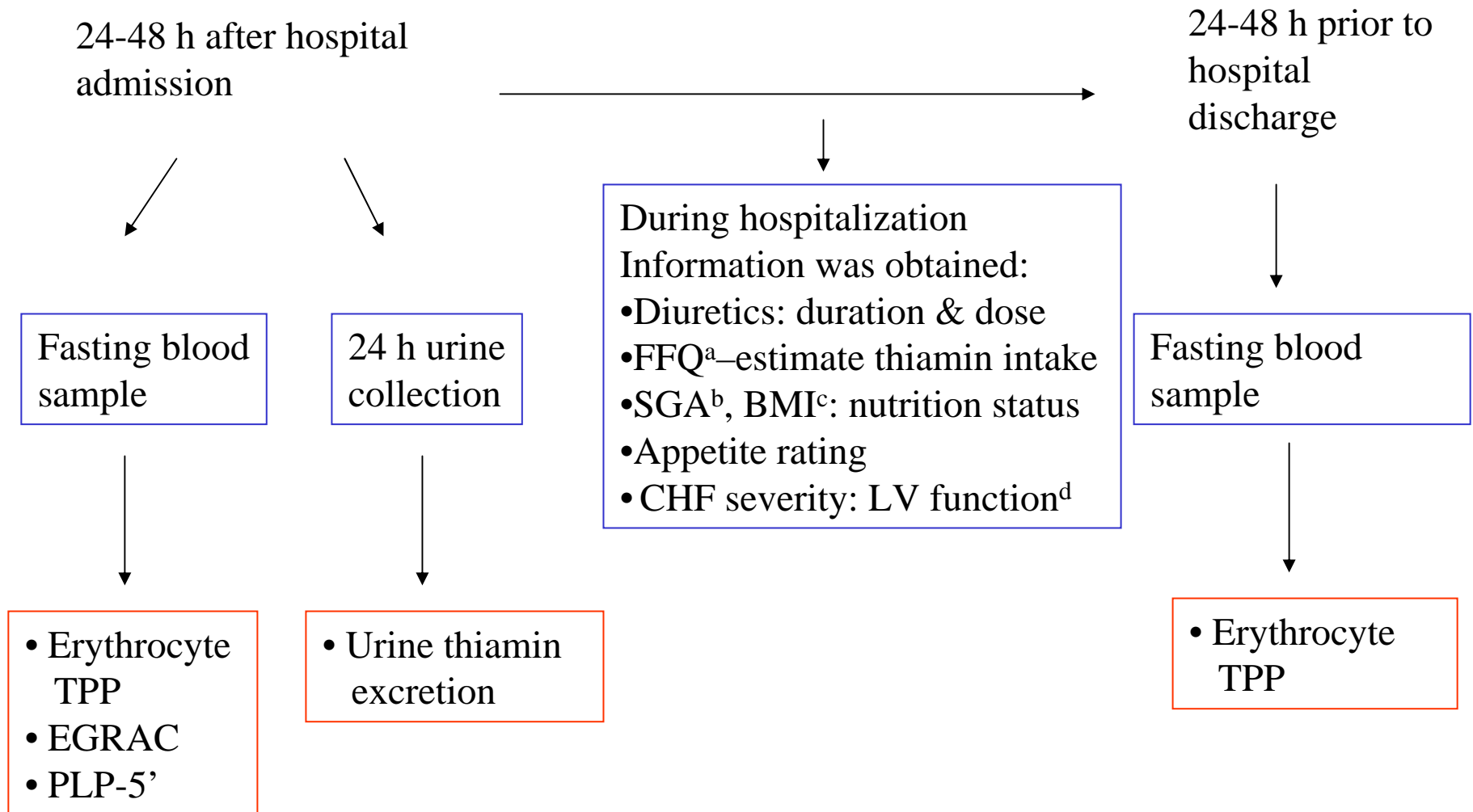
- Exclusion Criteria:
 - High-dose thiamin supplementation (200mg/day) for alcohol abuse
 - Experimental medication
 - Inability to give informed consent (because of dementia or inability to speak English)
 - Short anticipated hospital stay

Healthy Controls

- Inclusion Criteria:
 - Age-matched to patients within 5 years
- Exclusion Criteria:
 - Any known conditions affecting thiamin status
 - Use of thiamin-containing supplements.

Spouses, staff members, patients undergoing elective cardiac procedures, cardiac rehab patients

STUDY PROCEDURES FOR CHF PATIENTS



^aFFQ, food frequency questionnaire. ^bSGA, subjective global assessment. ^cBMI, body mass index.

^dLV, left ventricle function.

Study procedures for control subjects included age and sex matching to CHF patients and obtaining a fasting blood sample for determination of erythrocyte TPP concentration.

Characteristics of CHF patients and control subjects

Characteristics	CHF (n = 100)	Control (n = 50)	P Value
Gender Male/Female	58 (58%) / 42 (42%)	24 (48%) / 26 (52%)	0.246 ^a
Age [mean(SD)]	67.1 (10.1) y	61.1 (11.1) y	0.001^b
BMI [mean(SD)]	27.3 (5.5) kg/m ²	27.2 (4.7) kg/m ²	0.762 ^b
Thiamin-containing Supplement use	21 (21%)	NA	
Other supplement use	41 (41%)	9 (18%)	0.001^c

^a Pearson Chi-Square, ^b Mann-Whitney, ^c Fisher's Exact

Cardiac disease characteristics of CHF patients

Characteristics	n	Characteristics	n
CHF Etiology		NYHA Classification	
Coronary artery disease	40	Class I	6
Valve disease	18	Class II	18
Hypertension	3	Class III	43
CAD & Valve	11	Class IV	32
Cardiomyopathy	28		
Left Ventricle Function		Diuretic Use at Admission	
Grade I	21	Furosemide	80
Grade II	26	Spironolactone	16
Grade III	27	Metolazone	7
Grade IV	26	Multiple Diuretics	26

Prevalence of TD in CHF patients and control subjects

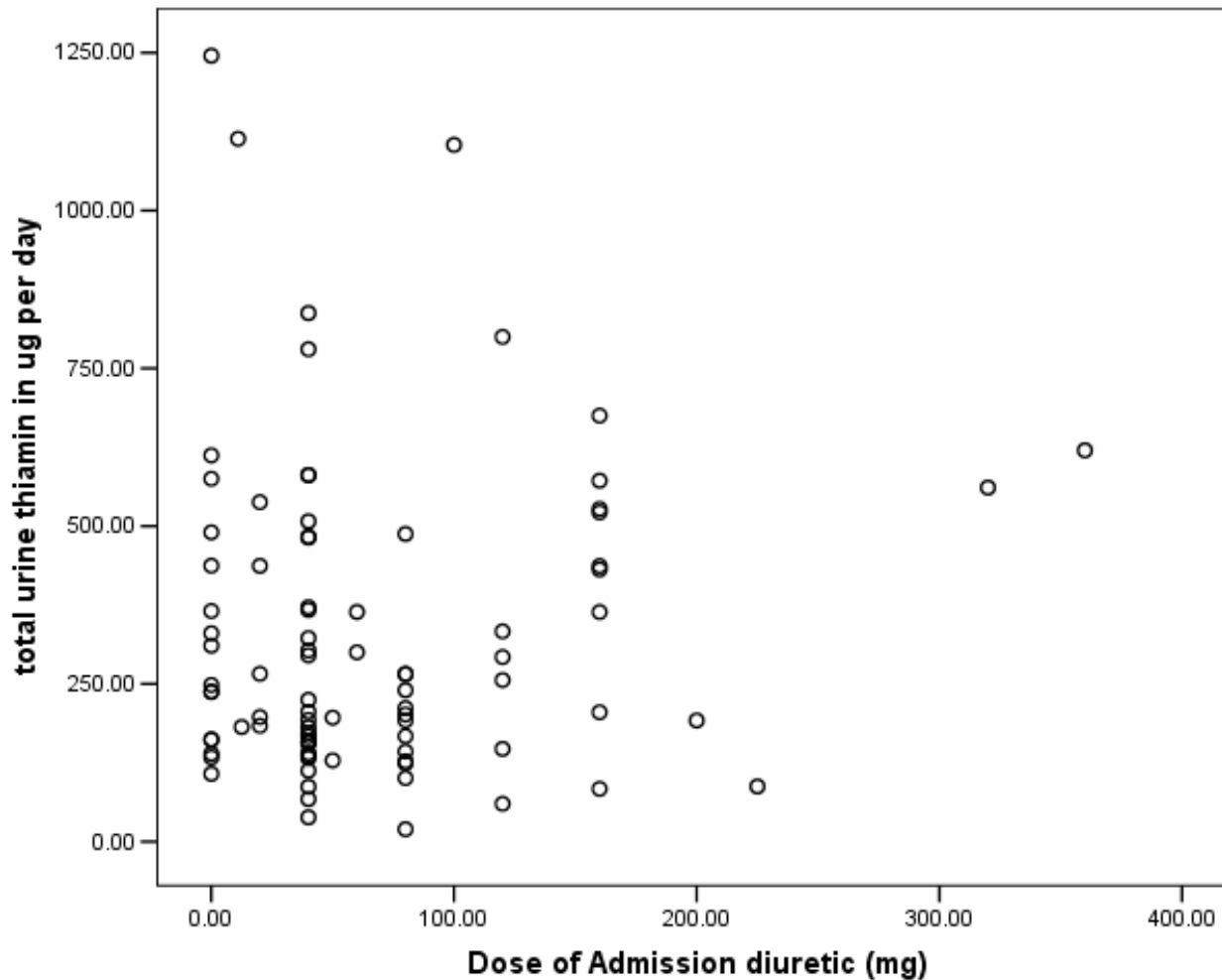
CHF (n = 100)	Control (n = 49)	P^a
33.0 %	12.2 %	0.007*

^a Pearson Chi-Square, * Significant at $P < 0.05$

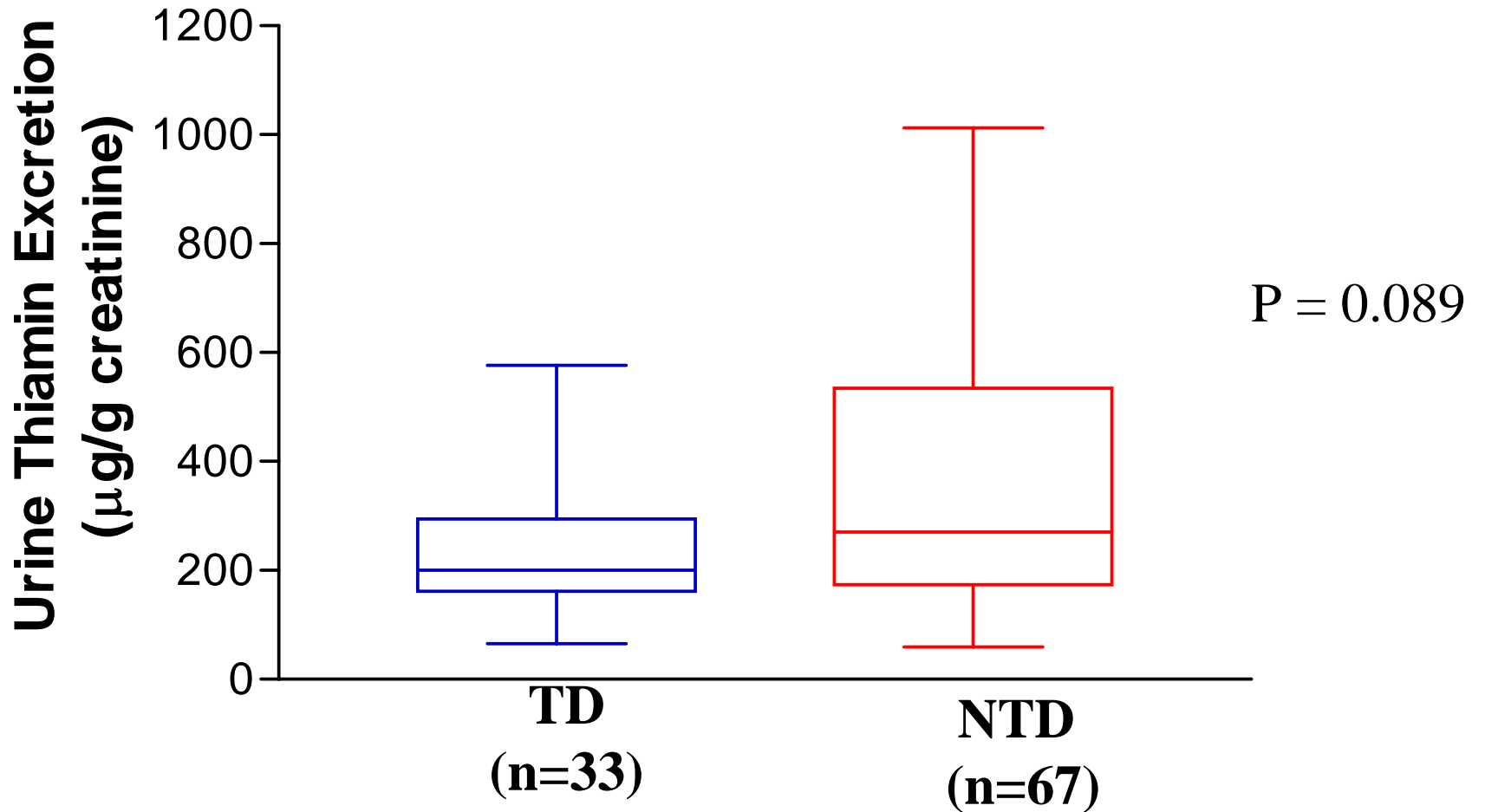
Factors Related to the Presence of Thiamin Deficiency

Which are predictive of those at risk?

Relationship Between Diuretic Dose and Urine Thiamin Loss

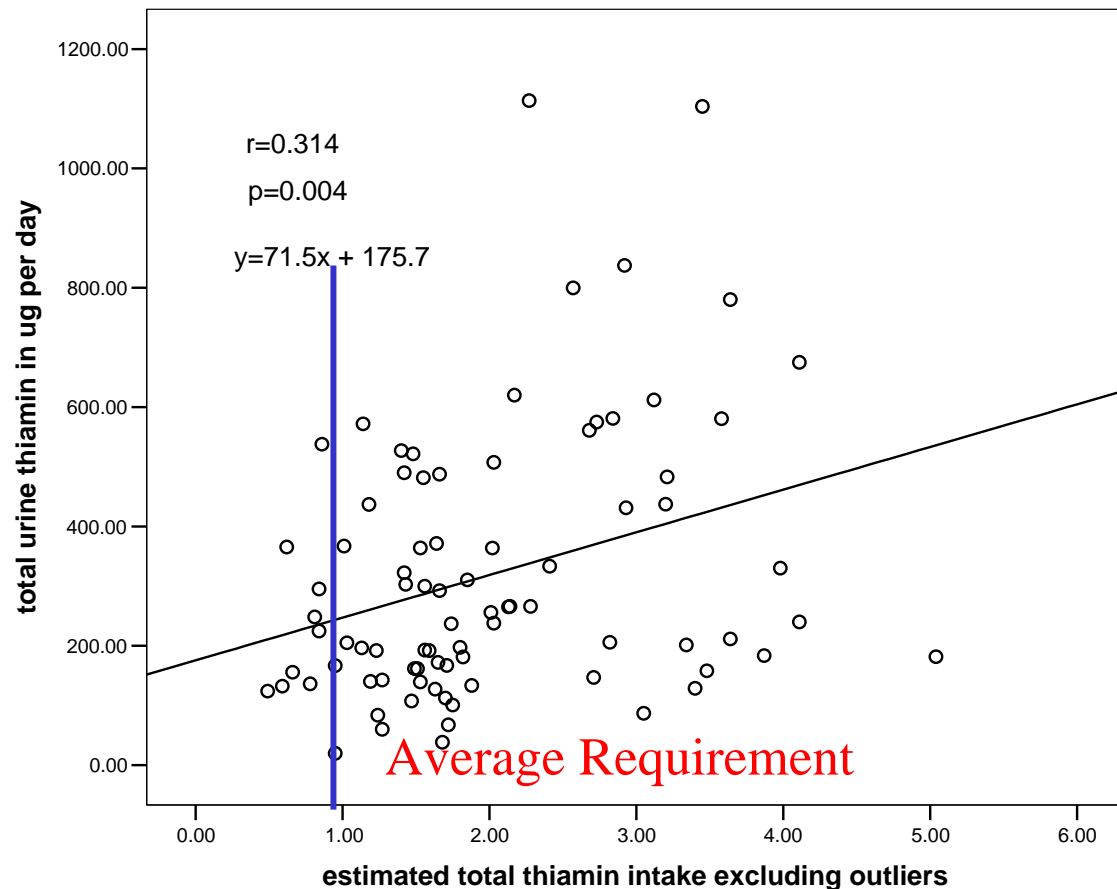


Relationship between TD and urine thiamin excretion in CHF patients

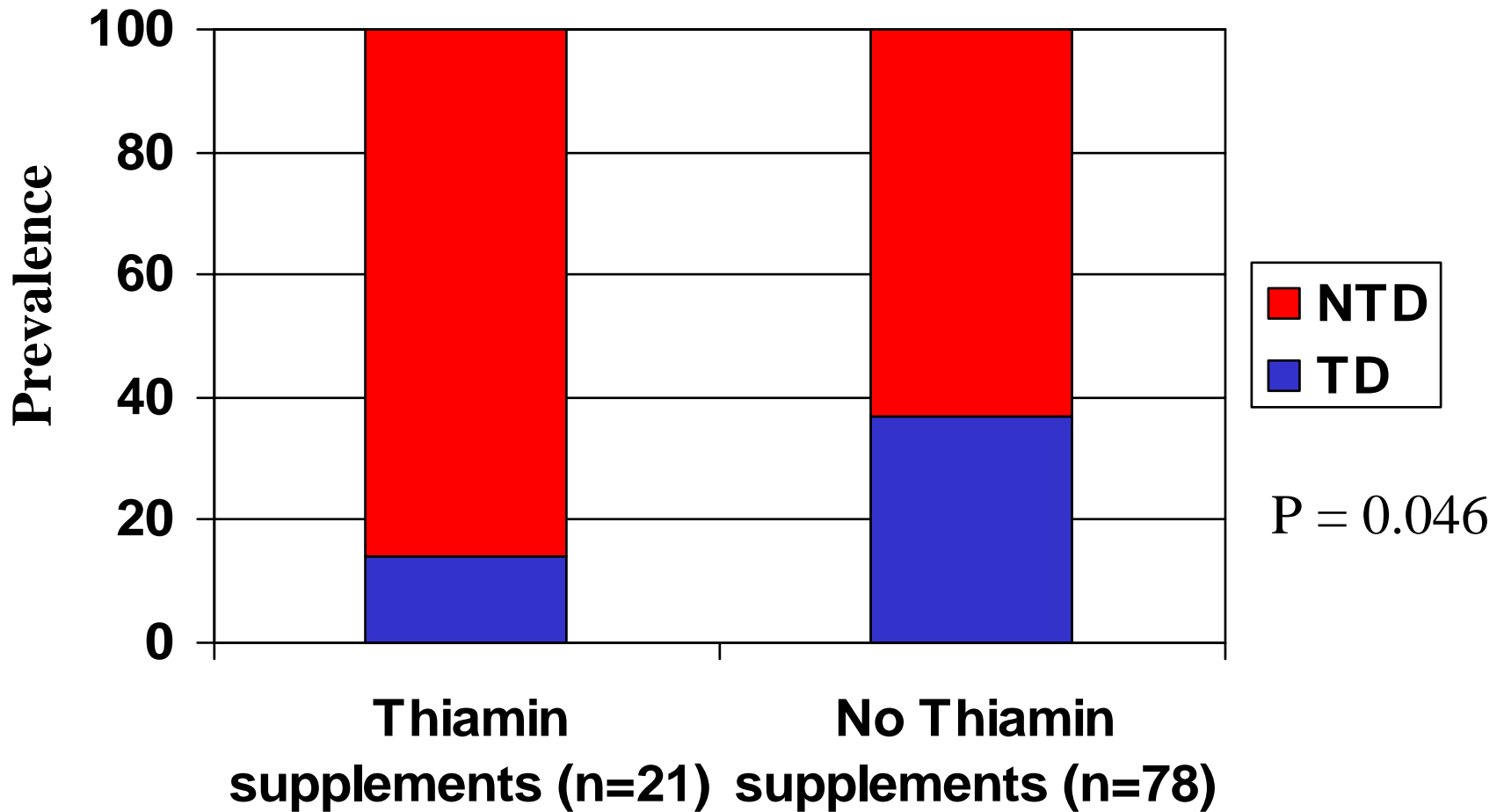


Mann-Whitney Test

Relationship between Thiamin Intake and Loss



Relationship between TD and thiamin supplement use in CHF patients



Pearson Chi-Square Test

Factors not associated with Thiamin Deficiency in CHF patients

- Age
- Gender
- Hospitalization
- Diabetes
- Furosemide use
- Metolazone use
- multiple diuretics

Factors associated with thiamin deficiency

- Having low urinary thiamin losses
- Not using thiamin containing supplements
- Having good kidney function
- Worsening heart failure
- Having a poor appetite
- Having a thiamin intake that is less than the average requirement
- Having mild or moderate malnutrition

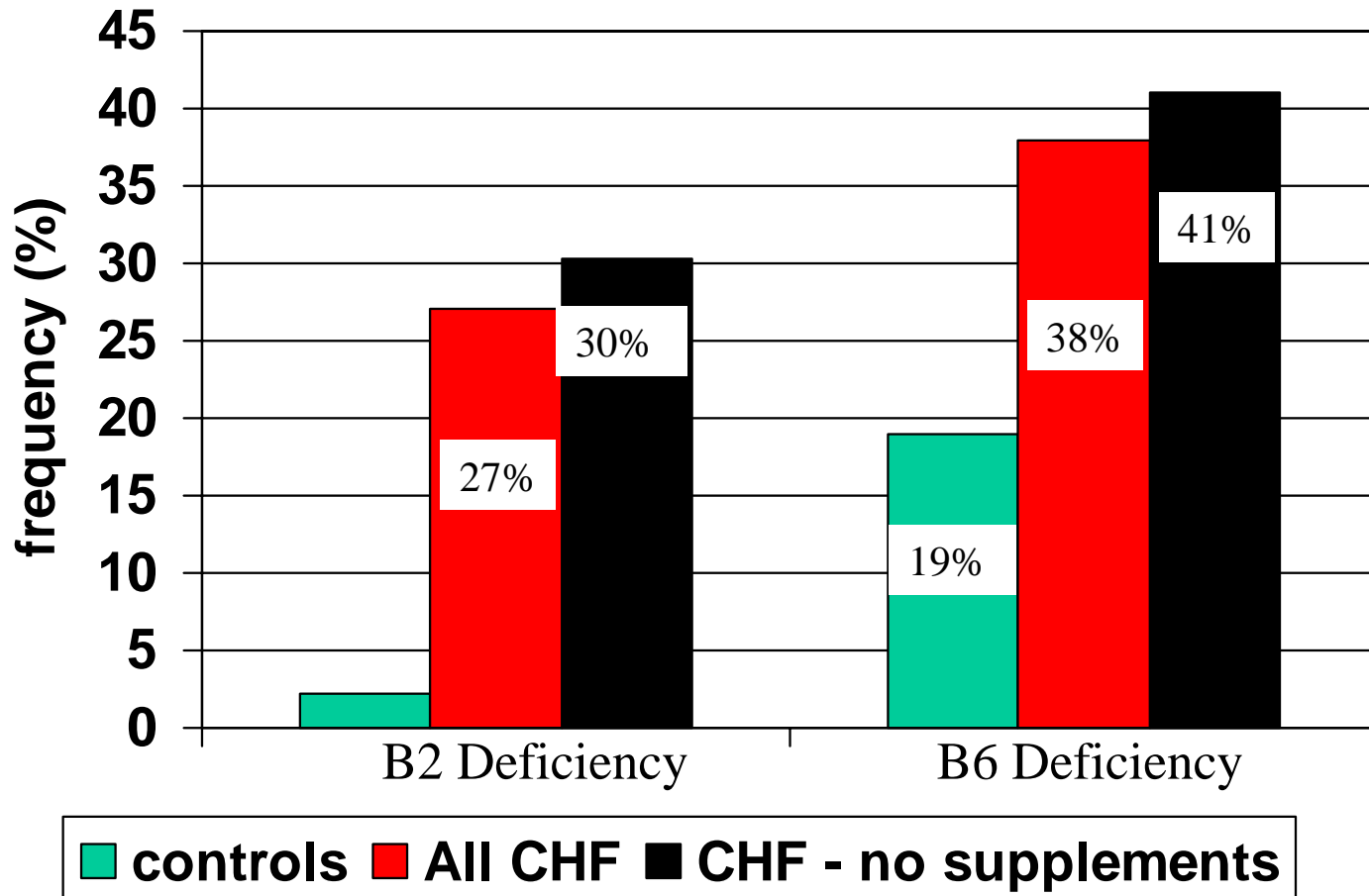
CHF and B Vitamins

- We have demonstrated that 33% of CHF patients at SMH were thiamin deficient (*Hanninen et al, 2005*).
- Riboflavin and vitamin B6 are water-soluble with no appreciable tissue storage.
- Therefore, as an adjunct study, we investigated the status of riboflavin and vitamin B6 in the same CHF patients

Role of Riboflavin (B2) and B6 in Metabolism

- Important factor in fatty acid oxidation and glucose metabolism.
- B2 and B6 participate in the production of energy
- B2 required to form active B6
- B6 is needed for red blood cell formation (heme) and plays a role in homocysteine metabolism

The Prevalence of B6 and B2 Deficiency in CHF Patients and Controls



Discussion: Inter-relationships Between B Vitamin Deficiencies

- B6 deficiency significantly related to riboflavin deficiency

- plasma B6 significantly correlated with total riboflavin intake

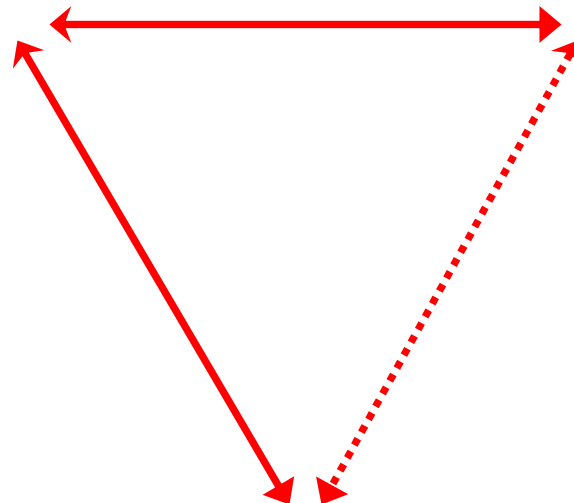
Riboflavin

Vitamin B6

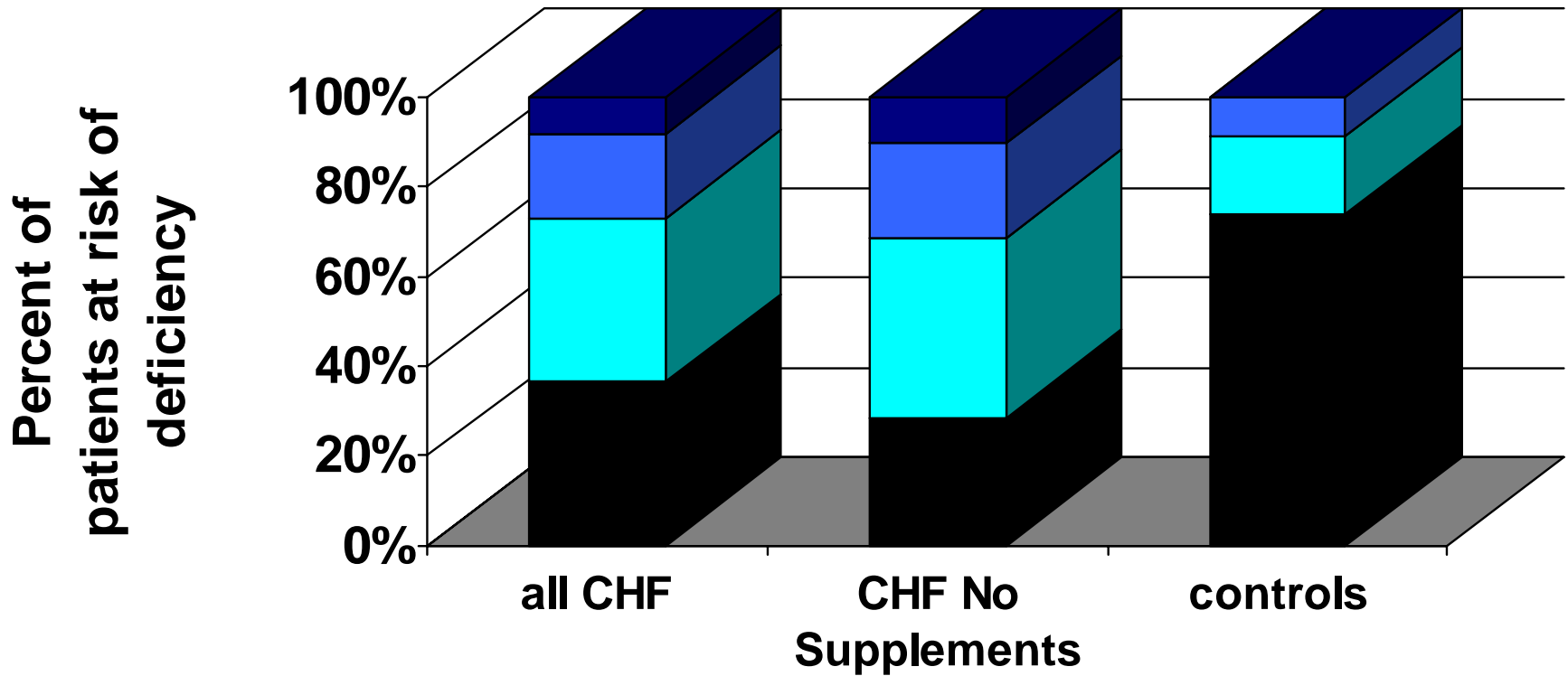
- riboflavin deficiency was significantly related to thiamin deficiency
- EGRAC correlated significantly with thiamin intake even when supplement users excluded

- no relationship between B6 deficiency and thiamin deficiency

Thiamin



The Overall Prevalence of B vitamin Deficiency in CHF Patients



- no vitamin deficiency
- 1 vitamin at risk
- 2 vitamins at risk
- 3 vitamins at risk

CONCLUSIONS

- The prevalence of B vitamin deficiency in our hospitalized CHF patients is high (71%).
- Development of deficiency is complex – not simply related to the dose or duration of furosemide (diuretic) use
- Dietary intake meeting requirement for healthy population yet deficient - Conditional Nutrient Deficiency? Paucity of data – NIH call

Our Research Team

Stacy Douglas-Hanninen

Mary Keith

Pauline Darling

Michael Sole

Aiala Barr

CFDR funds allowed the completion of the
biochemical analysis of B vitamin status

Study Methodology

- Same population as B1 study
- Plasma riboflavin was assessed by enzymatic activity assay (*Sauberlich, 1999*)
- Deficiency was defined as erythrocyte glutathione reductase activity coefficient (EGRAC) > 1.2
- Vitamin B6 concentrations were determined by radioimmunoassay (RIA) measures PLP-5'
- Deficiency was defined as < 20 nmol/L plasma

Implications for Practice

What about routine supplementation?

- Thiamin status was significantly improved in those taking a multi-vitamin (low dose B1 – 1.5 mg/day) or B complex supplement
- B6 status was also improved ($p=0.09$) in those taking a multi-vitamin or B complex supplement
- Evidence of benefit difficult to obtain – do the potentials benefit outweigh the risks?
- How can we measure success?

Micronutrient Supplementation in Elderly Patients with CHF

- 32 patients with age >70 years
- Stable – reduced heart function
- Quality of Life, cytokines, six minute walk test and cardiac magnetic resonance imaging
- Randomized, double blind study
- Multi-micronutrients – 9 months

Witte et al. European Heart Journal, 2005

Multi-Nutrient Supplement for Heart Failure

Table 1 Doses of micronutrients, RDI, and upper safe daily intakes

Nutrient	Daily dose (four capsules)	RDI	Upper safe limit for total daily intake
Calcium	250 mg	800 mg	2500 mg
Magnesium	150 mg ^a	300 mg	700 mg
Zinc	15 mg	15 mg	30 mg
Copper	1.2 mg	1.2 mg	9 mg
Selenium	50 µg	65 µg	450 µg
Vitamin A	800 µg	800 µg	3300 µg
Thiamine	200 mg ^a	1.4 mg	No limit
Riboflavin	2 mg	1.5 mg	No limit
Vitamin B ₆	200 mg ^a	2 mg	300 mg
Folate	5 mg ^a	200 µg	No limit
Vitamin B ₁₂	200 µg	1 µg	No limit
Vitamin C	500 mg ^a	60 mg	2000 mg
Vitamin E	400 mg ^a	10 mg	900 mg
Vitamin D	10 µg ^a	5 µg	25 µg
Co-enzyme Q10	150 mg ^a	15 mg	No limit

^aDoses taken from previous work⁸ or RDI.

Clinical Outcomes Following Micro-Nutrient Supplementation

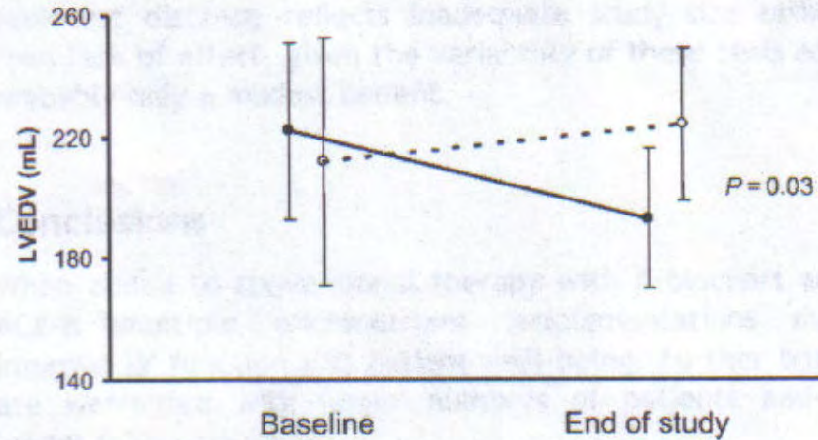


Figure 1 Change in left ventricular end-diastolic volume with placebo (unfilled circles and dashed line) and micronutrient supplementation (filled circles and solid line), (error bars are SD).

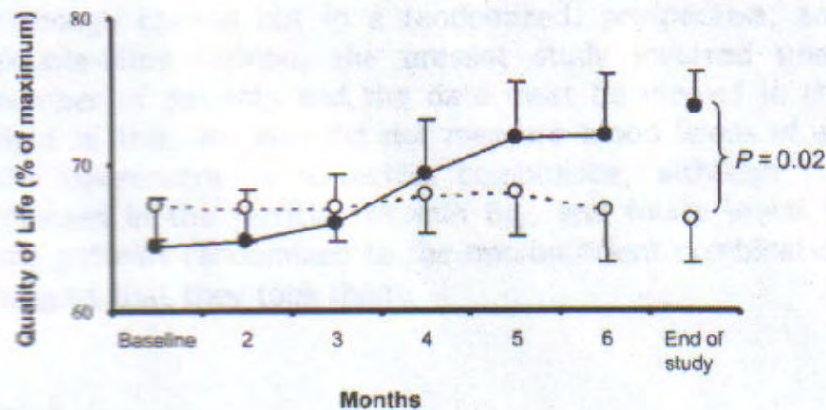
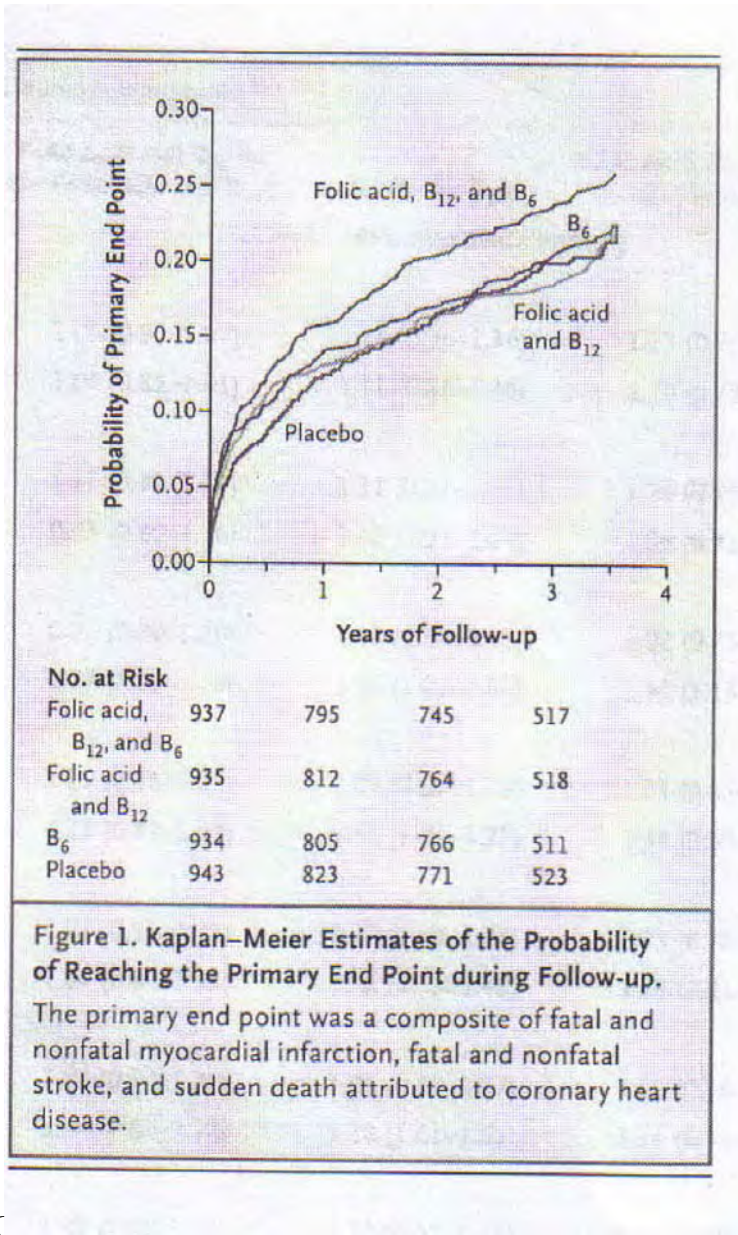


Figure 2 Quality of life score (percentage of maximum) during study period for patients taking placebo (unfilled circles and dashed line) or micronutrient supplementation (filled circles and solid line), (error bars are SD).

NORVIT Study

- Large trial post MI - 3749 patients
- Gave 0.8mg folic acid, 0.4 mg B12, 40mg B6
- Looked at homocysteine lowering and cardiovascular risk over 4 years
- Composite endpoint – fatal MI and non-fatal MI, stroke and sudden death due to heart disease.



N=3749

0.8 mg folic acid
 0.4 mg B12
 40 mg B6

Implications for Practice

- NIH call recognizing paucity of data
- Routine supplementation of B1 appears safe and justifiable
- Supplementation with B6 requires additional investigation to determine:

the impact of deficiency status

the impact of dose (high or low)

Continue to investigate the impact of specific disease states on nutritional requirements