



FOCUS ON HEART RATE.

**NEW TREATMENT
POSSIBILITIES.**

**SHOULD IT BE A RISK
FACTOR?**

HEART RATE BASICS

$$\begin{array}{rcc} \text{STROKE VOLUME} & & \\ & \times & \\ & & = \text{CARDIAC OUTPUT} \\ & \text{HEART RATE} & \text{(C.O.)} \end{array}$$

Increasing C.O. – mostly due to increased H.R

**Increase in HR = LESS TIME SPENT IN DIASTOLE
CORONARY BLOOD FLOW MOSTLY OCCURS IN DIASTOLE**

YET:


**Increase in age, H.T., CHD – diastole takes longer
= MISMATCH**

**SO HR CONTROL ESPECIALLY IN AGE
AND DISEASE MAKES SENSE.**

HEART WORK
DEPENDS ON B.P. & H.R.

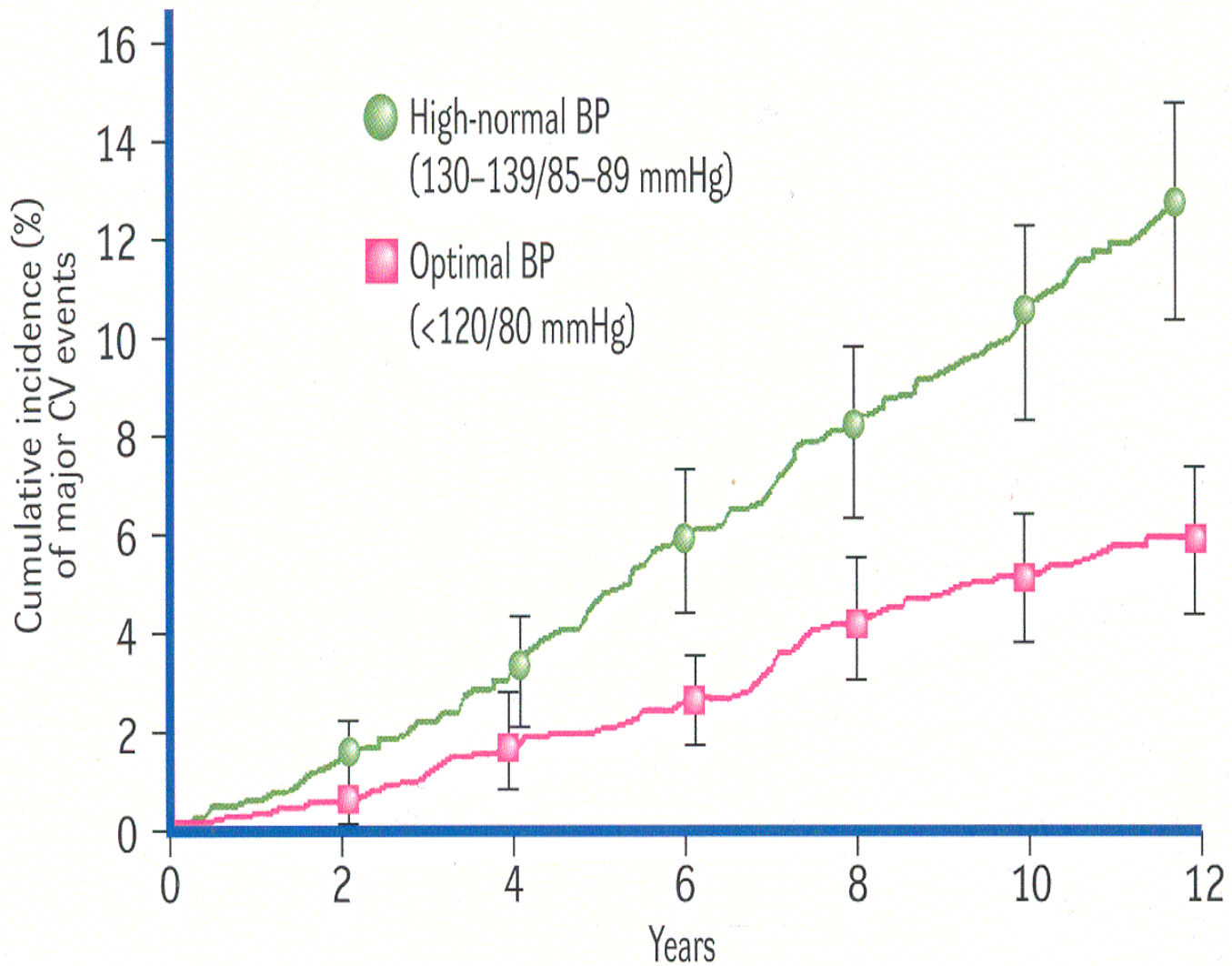
(RATE PRESSURE PRODUCT)

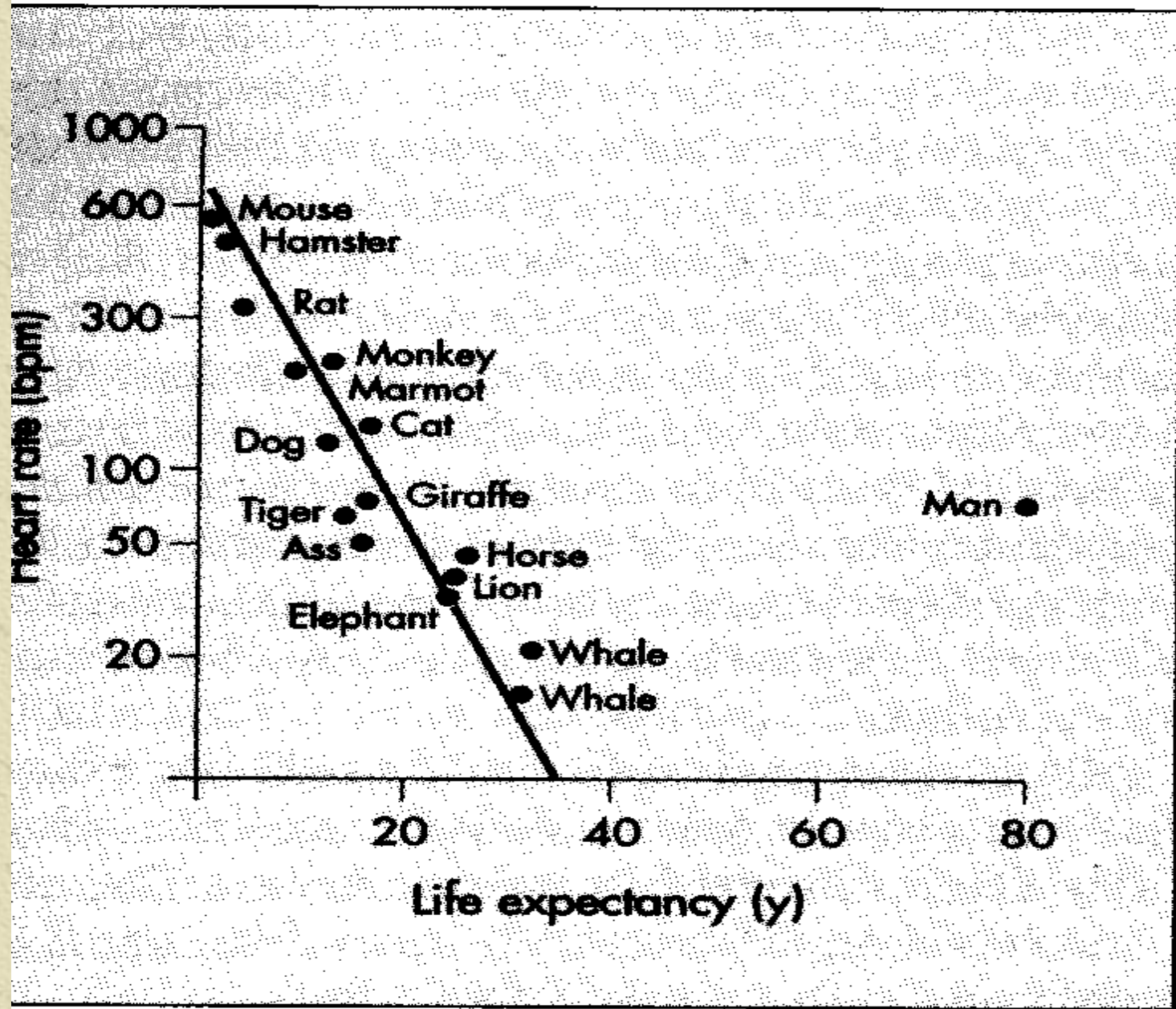
YET GENERALLY HEARTS PREFER VOLUME WORK
NOT
PRESSURE WORK

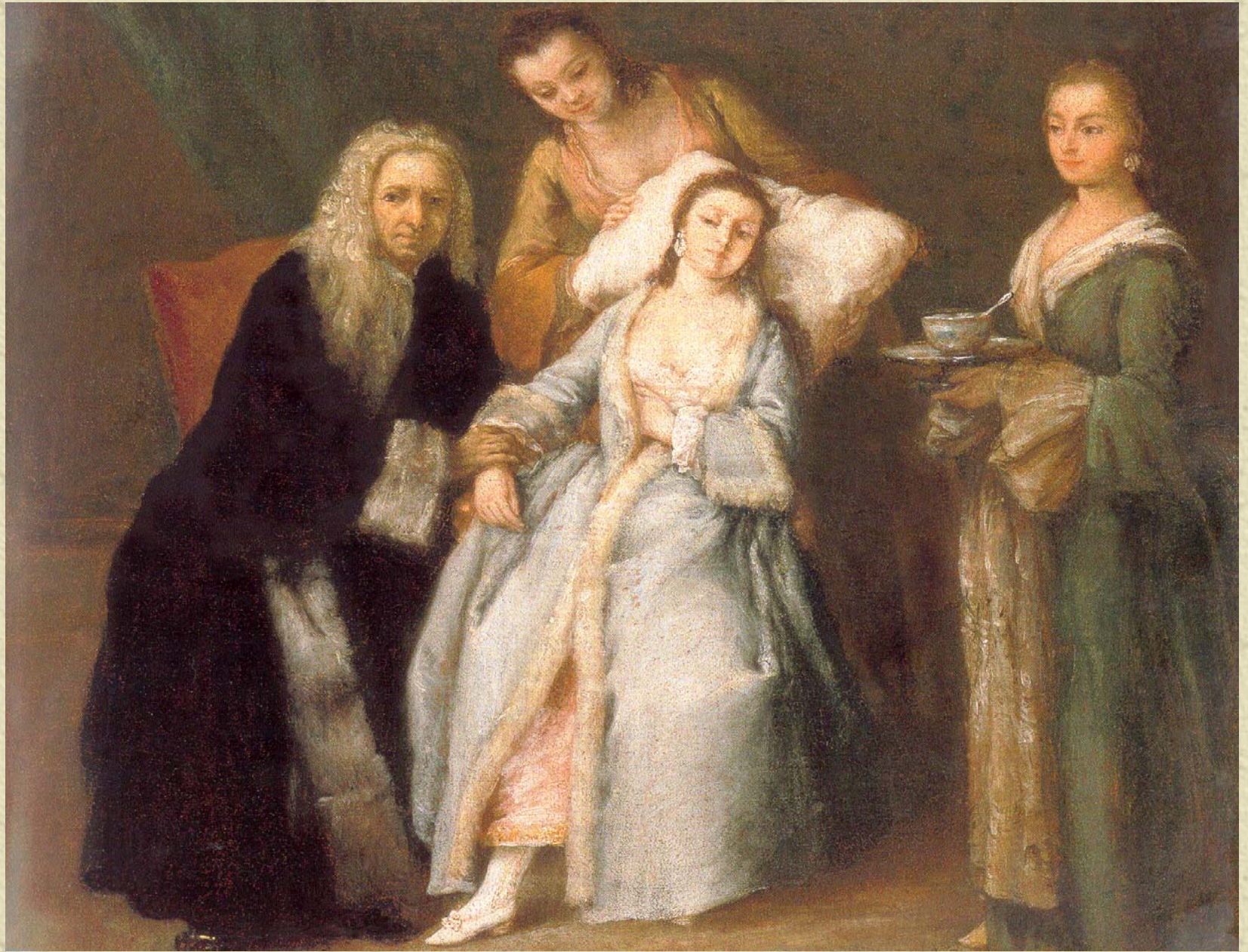


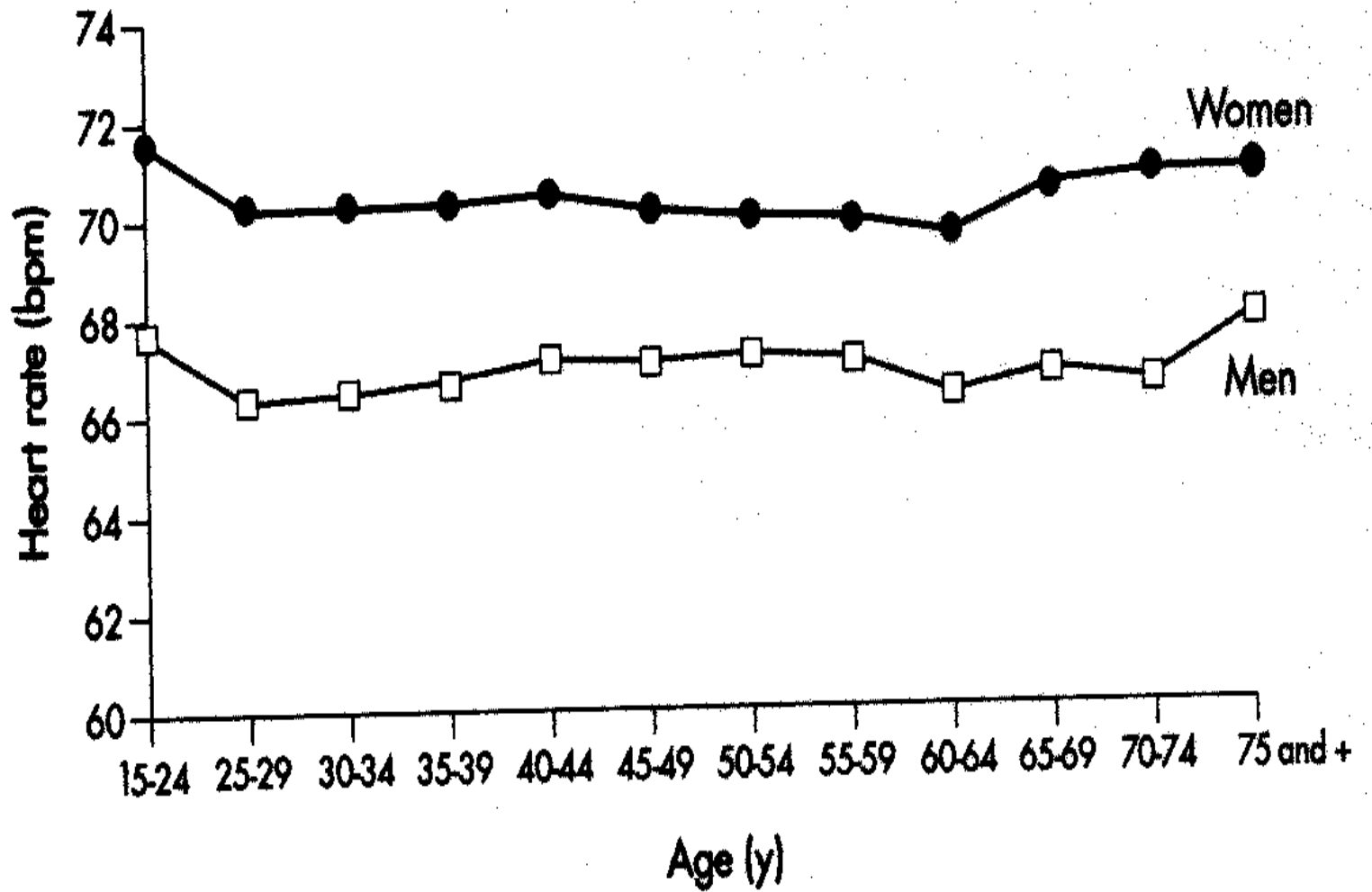
**WHY HAVE WE FOCUSSED
ON BLOOD PRESSURE
AND NOT
HEART RATE?**

Impact of high-normal BP on risk of major CV events* in men.^{†1}

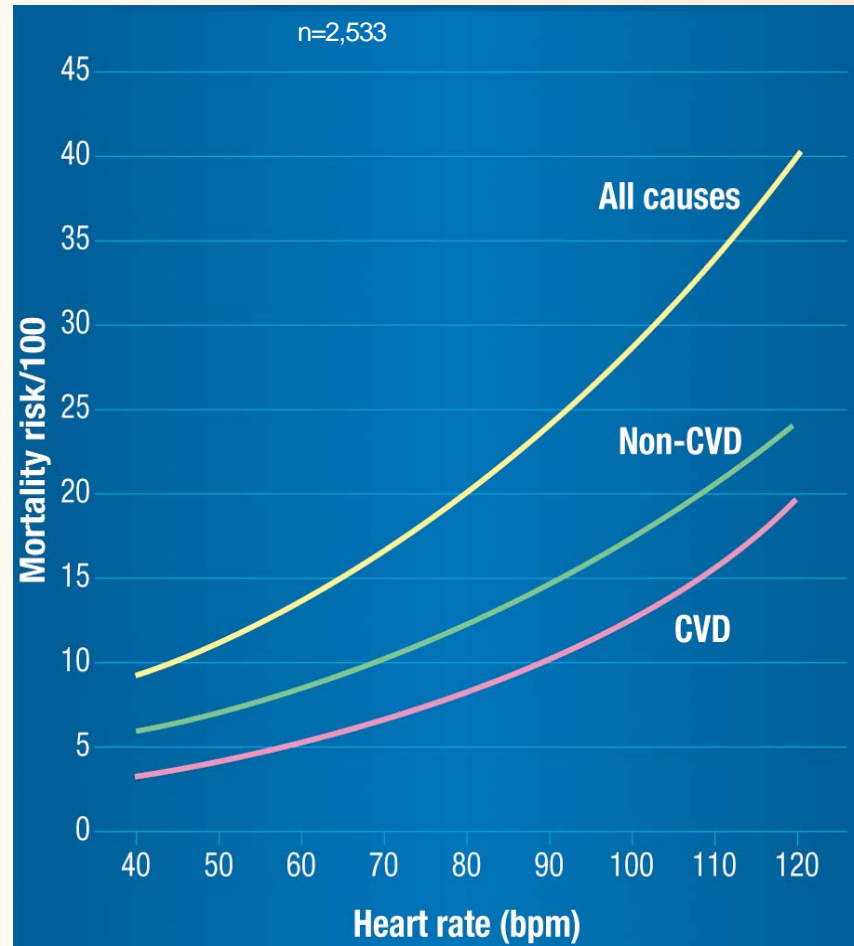




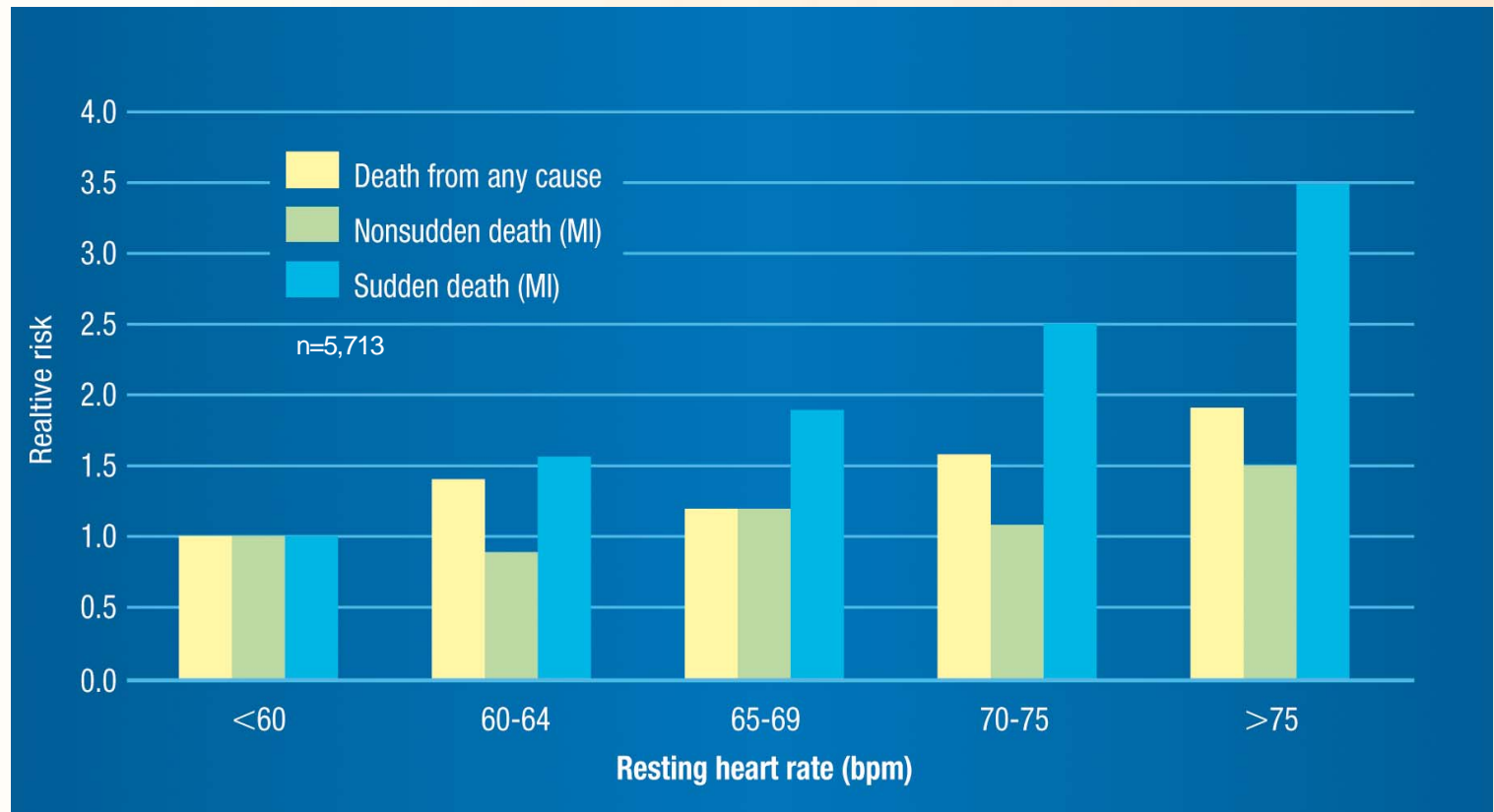




High resting heart rate: an independent predictor of mortality in the Italian men.



High resting heart rate is associated with an increase in sudden death in asymptomatic men



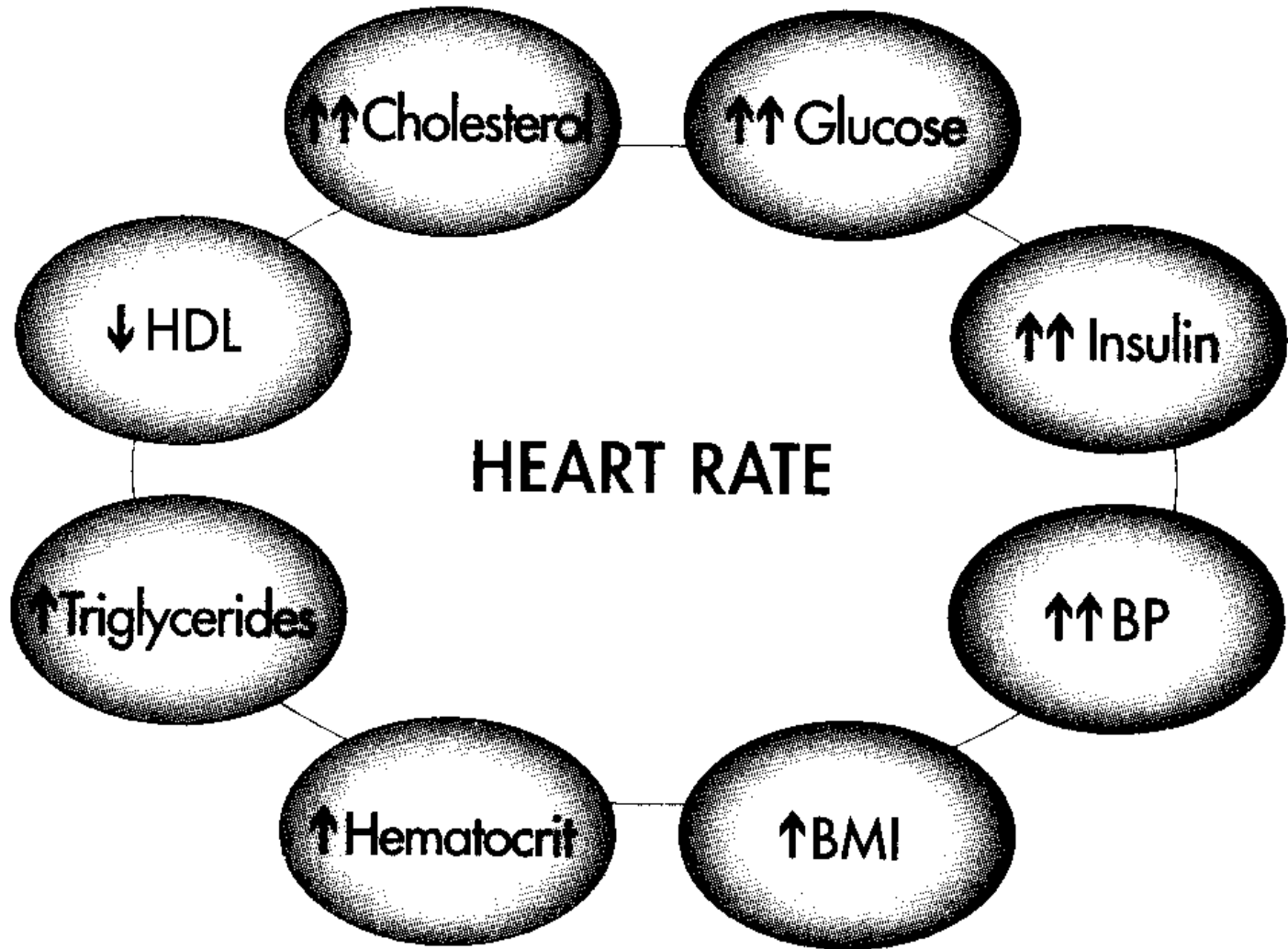
RESTING HEART RATE (RHR) & RISK

- 50 LONGITUDINAL STUDIES

- CONFIRM LINK BETWEEN RHR & RISK
- BOTH TOTAL AND CV MORTALITY AND MORBIDITY
- ALL AGES, VARIETY OF CLINICAL SETTINGS AND CO-MORBIDITIES

- STUDIES CONFIRMING PATHOGENETIC MECHANISMS FOR LINKS WITH:

- ATHEROSCLEROSIS
- PLAQUE RUPTURE
- C.V. MORBIDITY



HEART RATE

↑↑ Cholesterol

↑↑ Glucose

↑↑ Insulin

↑↑ BP

↑ BMI

↑ Hematocrit

↑ Triglycerides

↓ HDL

RESTING HEART RATE (RHR)
AND RISK

STANDS UP AS AN INDEPENDENT RISK
(after controlling for a variety of C.V. risk factor)

RISK IS GRADED ACROSS THE HEART RATE
RANGE
(dose related effect)

SO WHEN SHOULD WE SLOW HEART RATE? 2.

FLANNERY 2008

CHRONIC SYSTOLIC HEART FAILURE & B-BLOCKERS

- 35 TRIALS, 23,000 PATIENTS
- ASSOCIATION BETWEEN RHR REDUCTION, EF & MORTALITY
- CLOSE RELATIONSHIP CONFIRMED WITH RHR REDUCTION A MAJOR CONTRIBUTOR TO BENEFIT SEEN.

Resting Heart Rate as a risk factor

- Yes in cardiac patients
 - treatment benefit clearcut
- Yes in hypertensives
 - treatment benefit probable
- Yes in the normal subjects
 - but no evidence that pharmacologic lowering gives benefit.

SLOWING HEART RATE

LIFESTYLE

- EXERCISE TRAINING – increased vagal tone
- REDUCE CENTRAL ADIPOSITY – reduced sympathetic drive
- AVOID STIMULANTS
- MEDITATION – YOGA

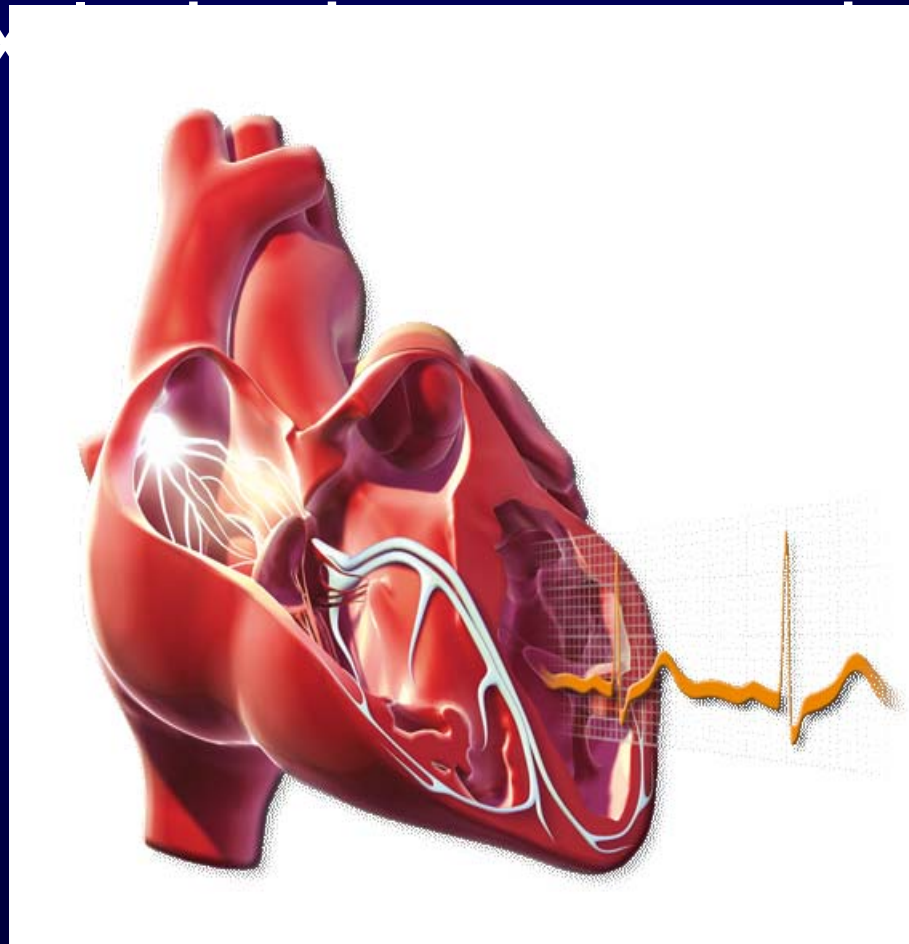
PHARMACOLOGIC

- BETA BLOCKERS
- CENTRALLY ACTING CALCIUM CHANNEL BLOCKERS
 - VERAPAMIL
 - DILTIAZEM
- IVABRADINE – SPECIFIC TO THE SINUS NODE.

Ivabradine

A selective I_f inhibitor

providing extra-systolic contraction



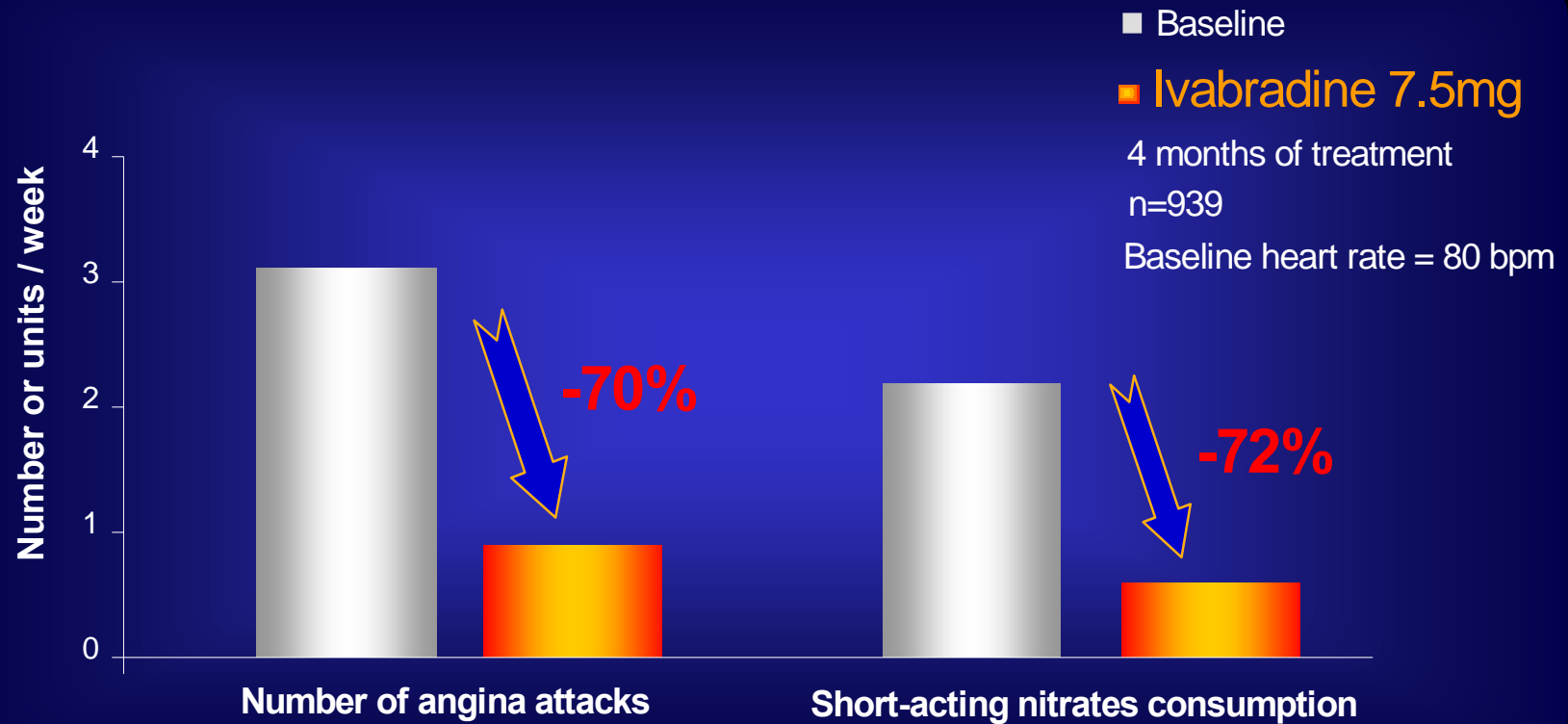
Ivabradine

- Selective inhibition of the I_f current by binding to the sinus node f-channel
- No adverse effects on the other ion currents in the sinus node
- Reduces the diastolic depolarization slope of the action potential



Ivabradine provides exclusive heart rate reduction

Ivabradine reduces angina attacks and consumption of nitrates



Ivabradine contributes to the improvement of the quality of life of CAD patients

Tolerability vs heart rate lowering agents

	β -Blockers	Verapamil Diltiazem	Ivabradine
Lipid/ glucose metabolism disturbances	+		
Depression/ mood disorders/ nightmares	+		
Bronchoconstriction	+		
Rebound phenomena	+		
Masked symptoms of hypoglycemia	+	+	
Impotence	+		
Cold extremities	+		
Hypotension	+	+	
Vasoconstriction	+		
Fatigue	+		
Edema/flushing	+	+	
Visual effects	+		+
Bradycardia	++	+	+
Constipation		++	

Ivabradine

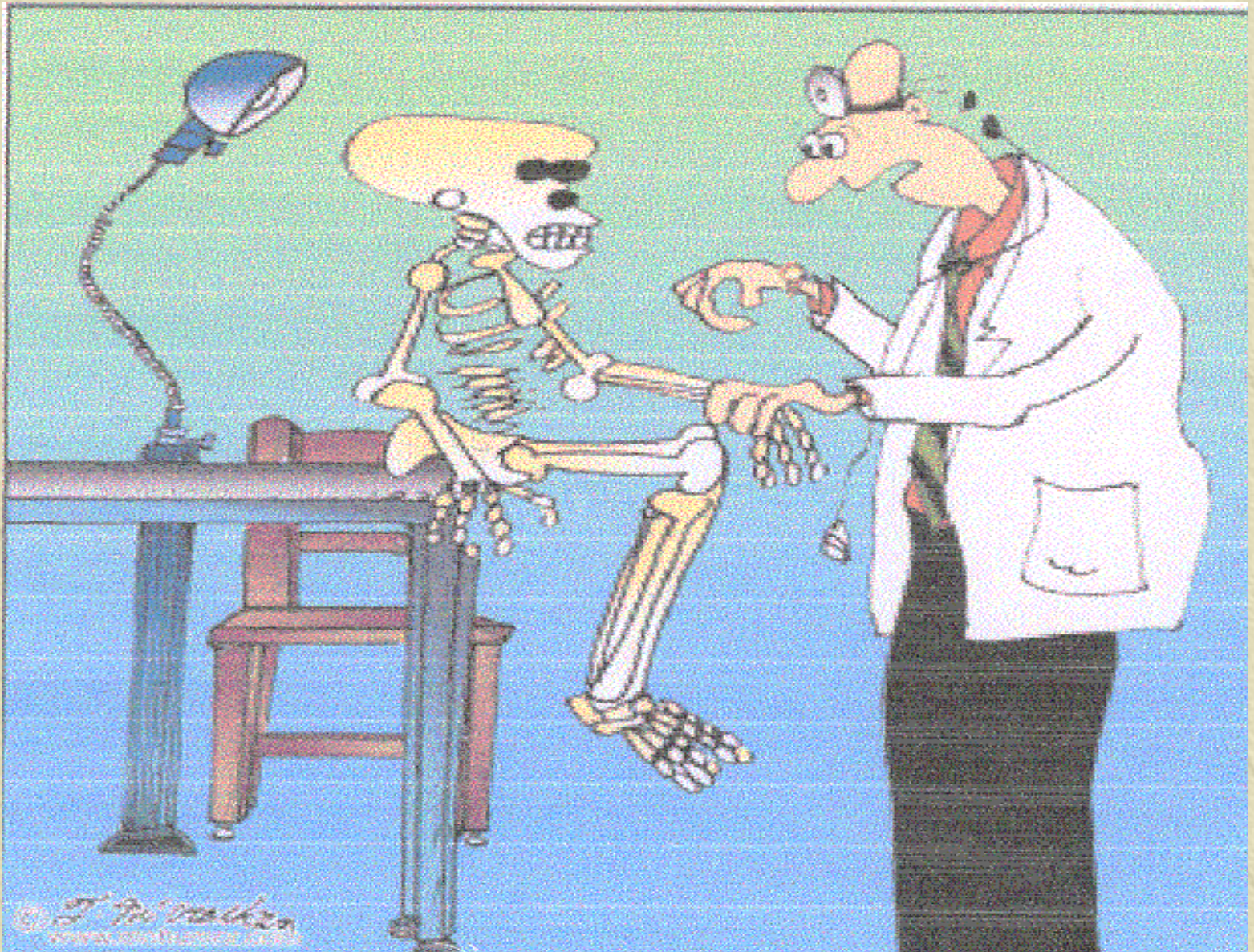
Future perspectives

➤ Heart Failure

SH/**f**T

➤ CAD and Left Ventricular
Dysfunction

BEAUT/**f**UL



“YOU SHOULD HAVE TAKEN MY PULSE
EARLIER DOC”