HEART RATE MANAGEMENT

the Possible Role in Hypertension

Arieska Ann Soenarta
Cardiovascular Center Harapan Kita, Jakarta

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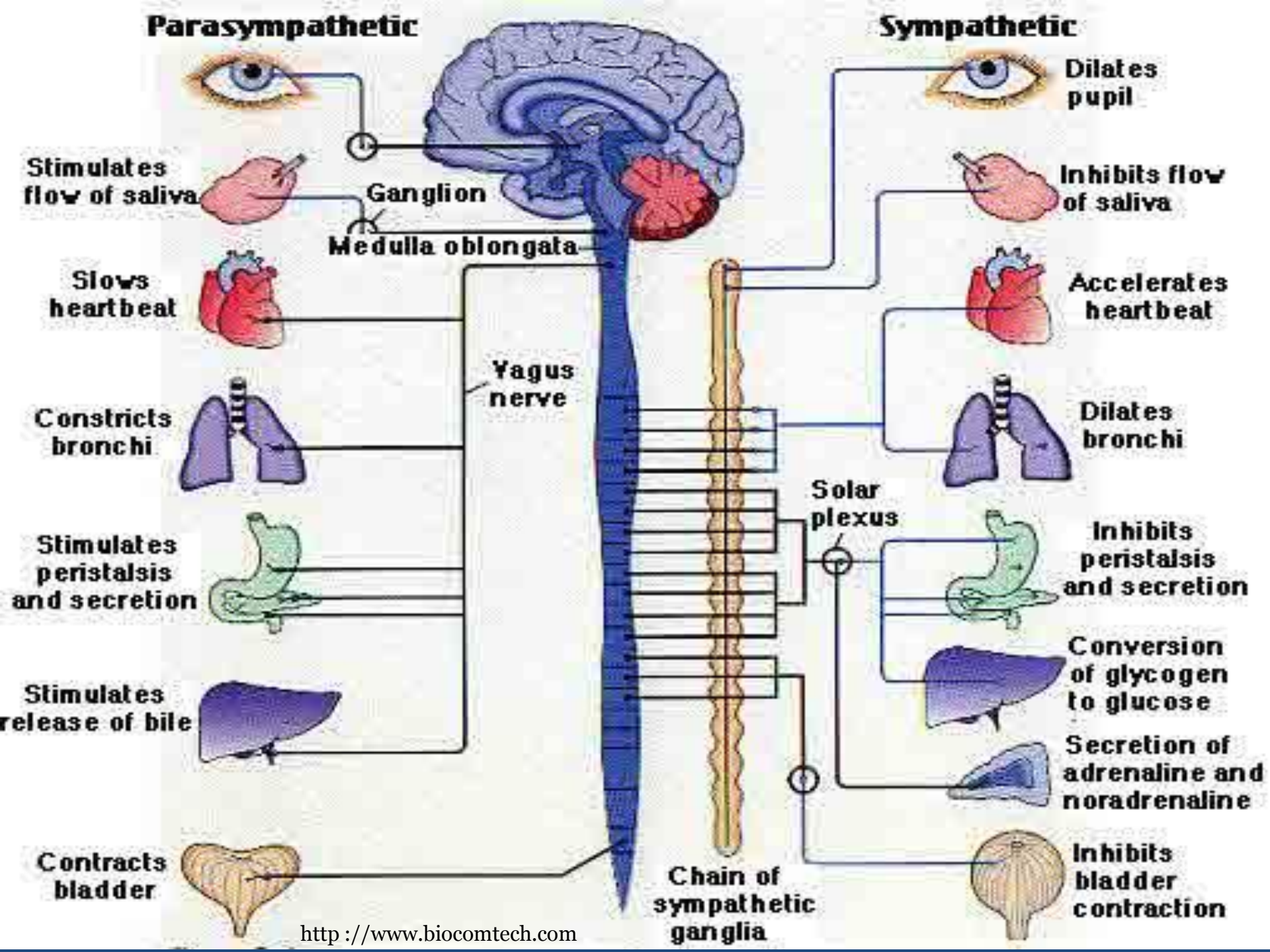
Factors involve in Heart Rate Management :

- INTRINSIC CONTROL :
  - Cardiac Tissue → self regulating
- EXTRINSIC CONTROLS :
  - Hormonal Responses
  - Commands From Nervous Systems


Parasympathetic
Sympathetic
Dilates pupil
Stimulates flow of saliva
Ganglion
Medulla oblongata
Inhibits flow of saliva
Slows heartbeat
Accelerates heartbeat
Vagus nerve
Constricts bronchi
Dilates bronchi
Solar plexus
Stimulates peristalsis and secretion
Inhibits peristalsis and secretion
Conversion of glycogen to glucose
Stimulates release of bile
Secretion of adrenaline and noradrenaline
Contracts bladder
Chain of sympathetic ganglia
Inhibits bladder contraction

ORIGIN of HEART BEAT :

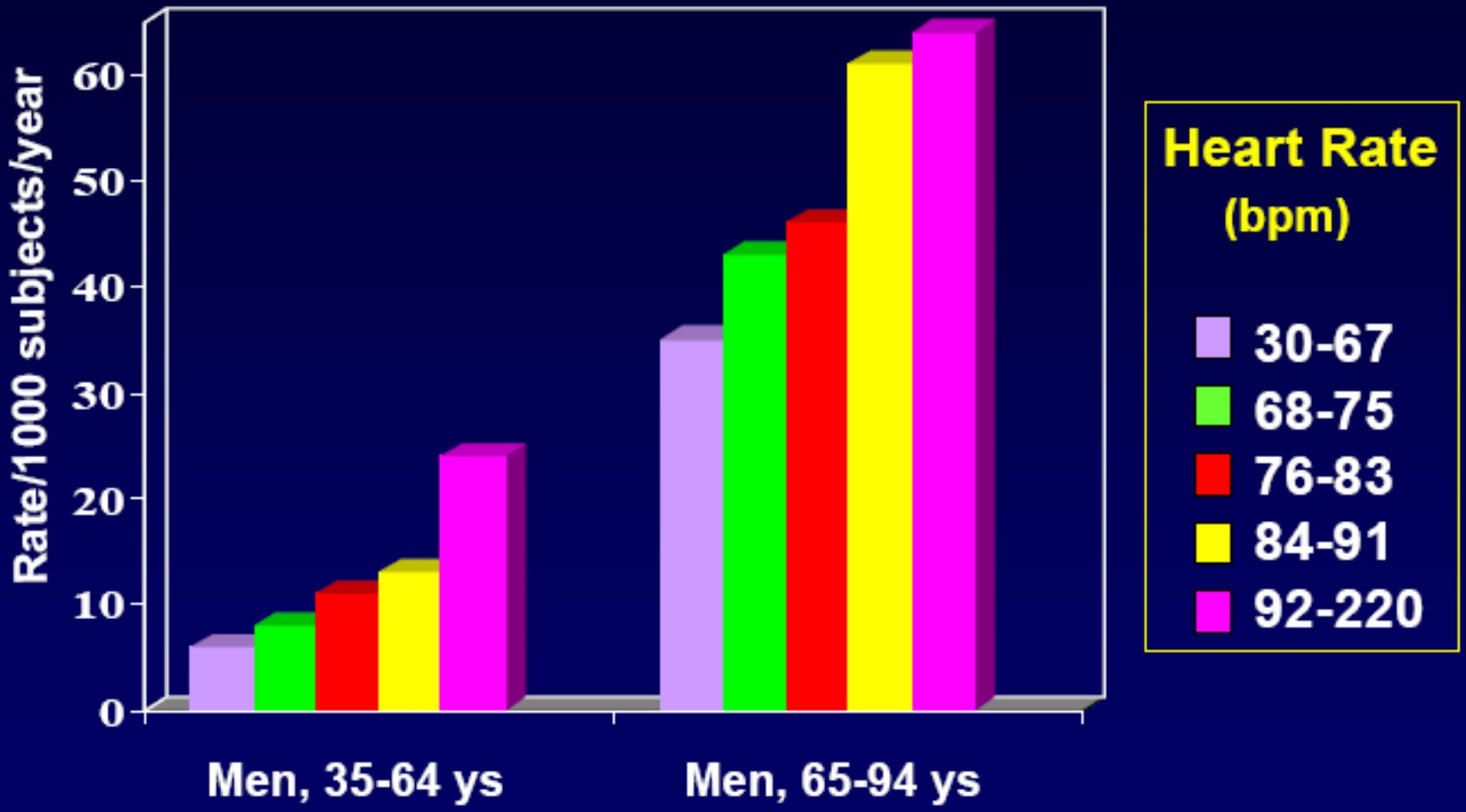
- Sino – Atrial (SA) Node of the Heart → impulses ± 100 – 120/min. at rest

- Activity of SA Node is controlled by the Autonomic Nervous System (ANS) → Resting Heart Rate in normals 50 – 70 Bpm

Epidemiologic Data of Elevated Heart Rate

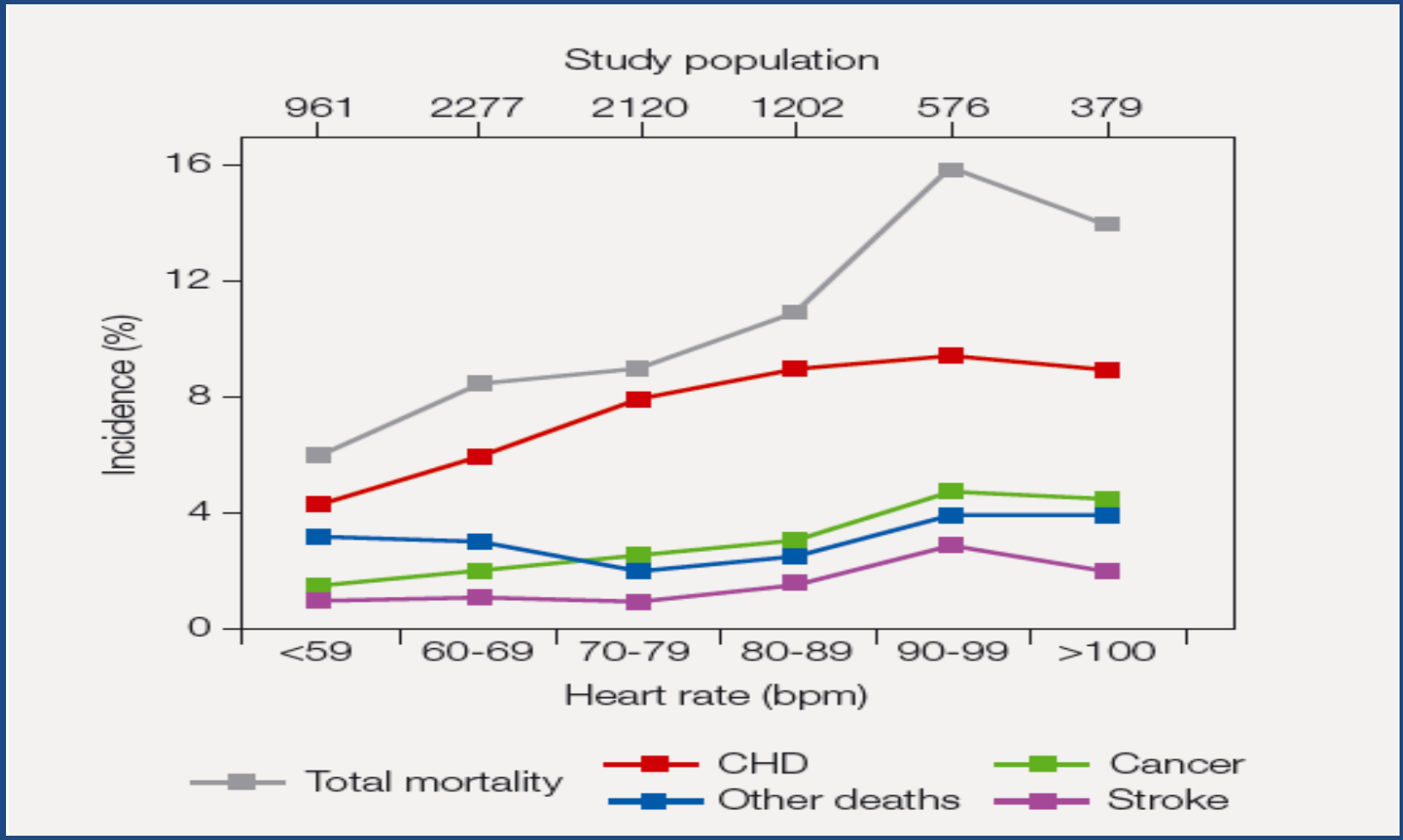
Heart Rate in General Population

Heart Rate and All-Cause Mortality
The Framingham Study



Kannel WB et al 1987;113:1489

All Cause and Cause Specific Mortality and Heart Rate in General Population

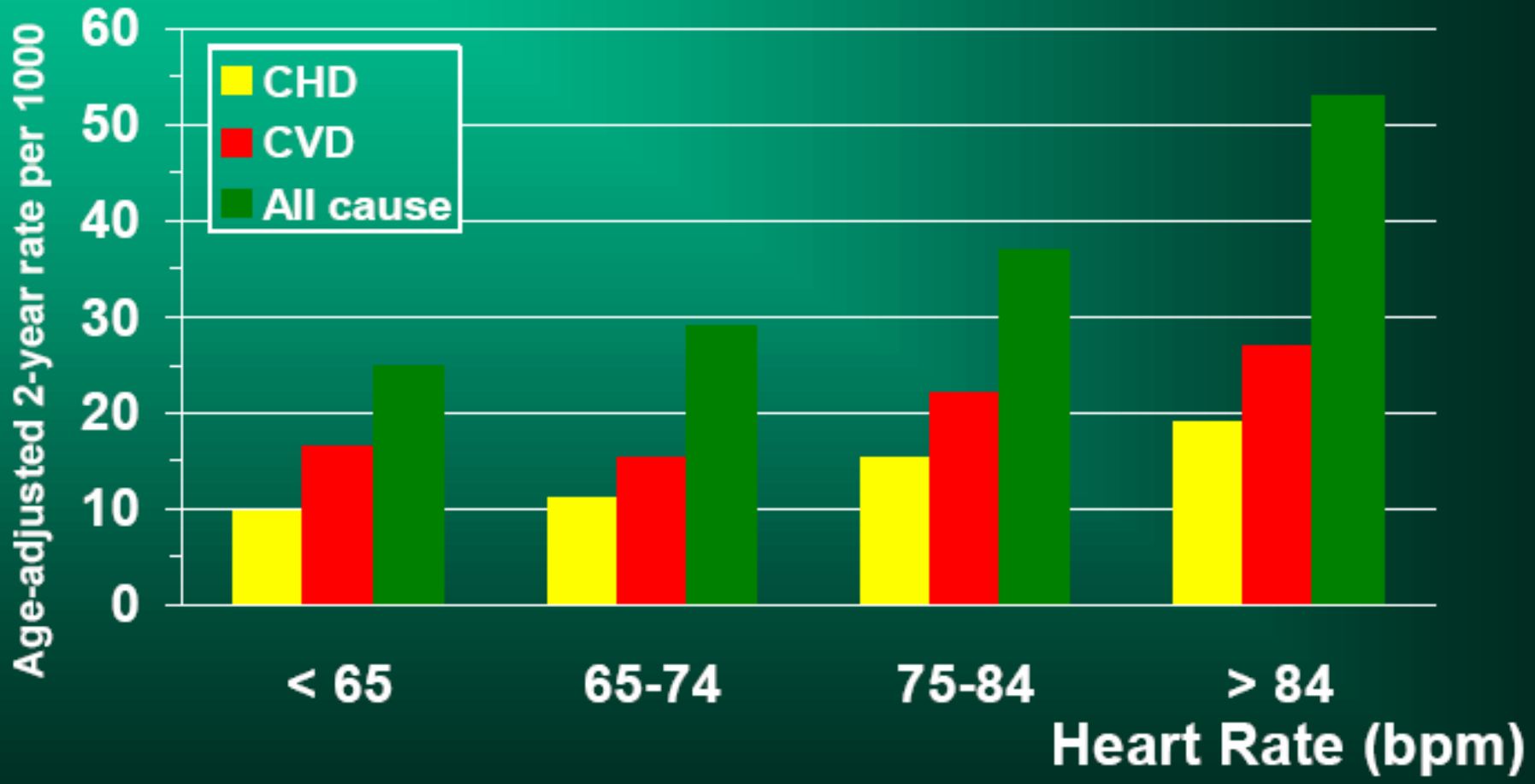


Modified from Wilhelmsem I. et al EHJ 1996;7 : 279-288

Heart Rate as a Risk Factor in Subjects with Hypertension or Diabetes (6 Studies)

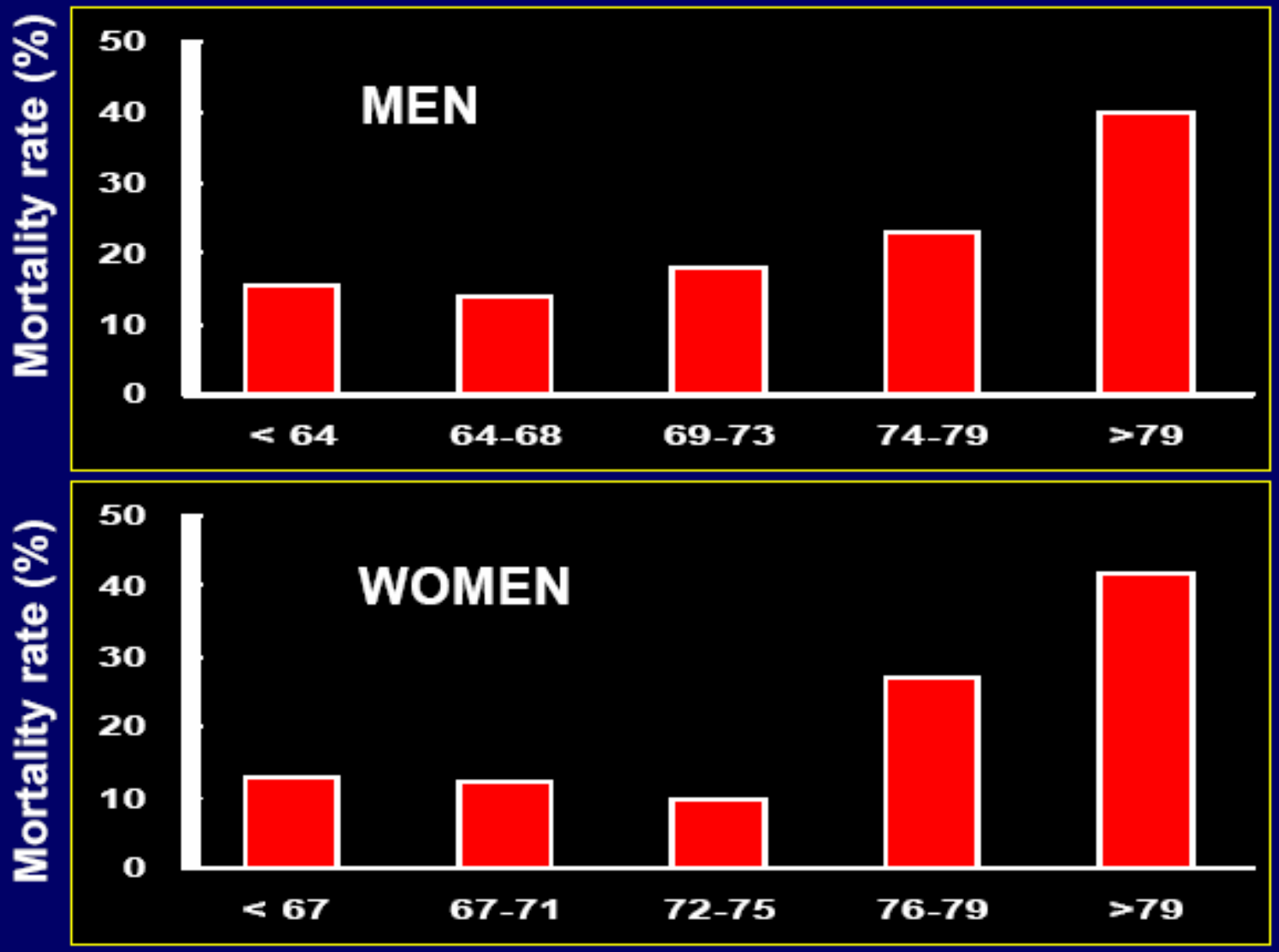
Negative studies:
Total mortality = 0
CV mortality = 0

ASSOCIATION OF HEART RATE WITH MORTALITY RATE AMONG MEN WITH HYPERTENSION
(The Framingham Study)



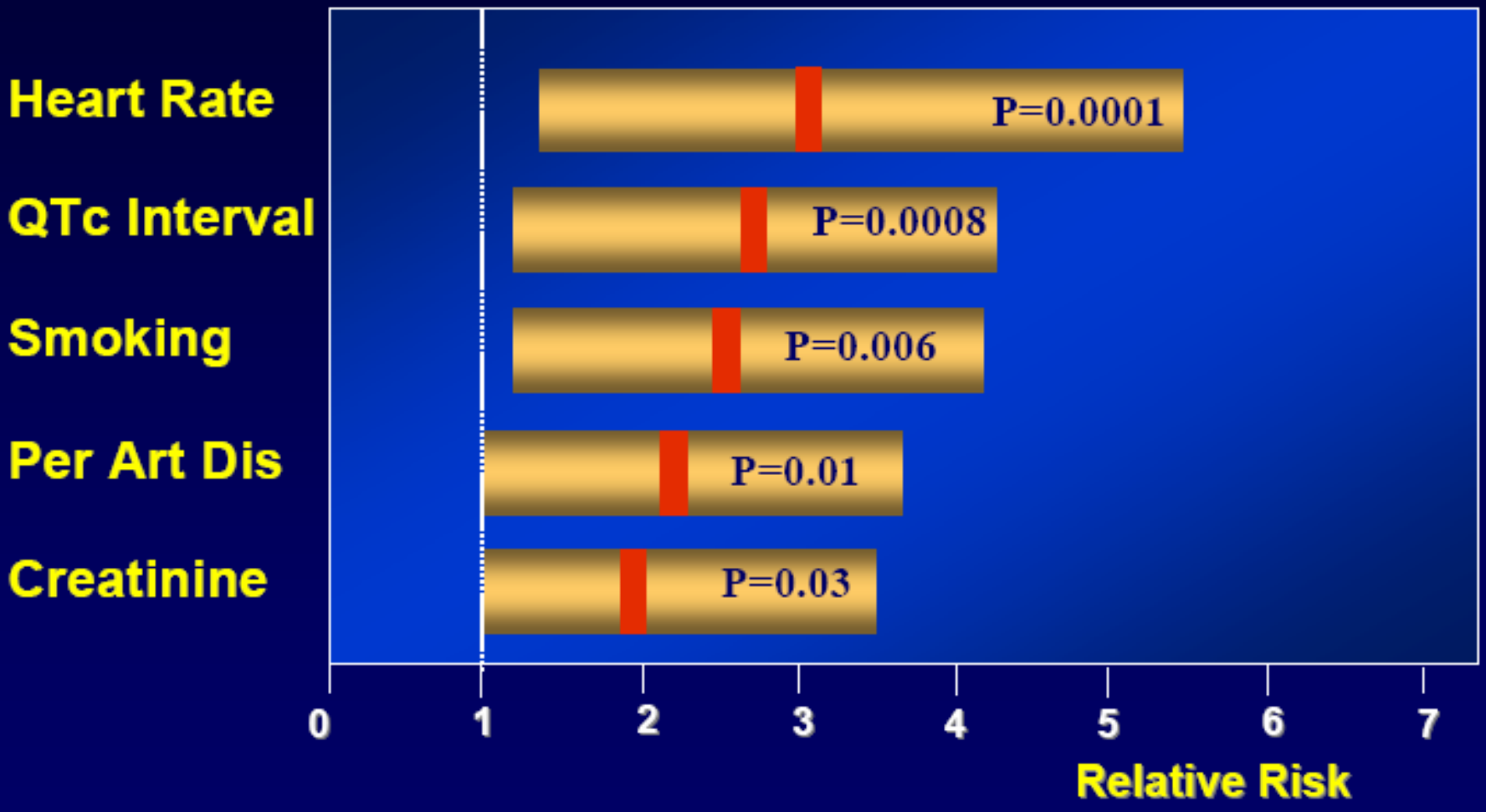
Gillman et al., Am Heart J 1993; 125: 1148

Mortality Rate by Quintile of Clinic Heart Rate in the ISH Patients from the Syst-Eur Study



Palatini P et al, Arch Int Med 2002;162:2313

Significant Predictors of CV Death in 475 Type 2 Diabetics. The Bremen Diabetes Study.

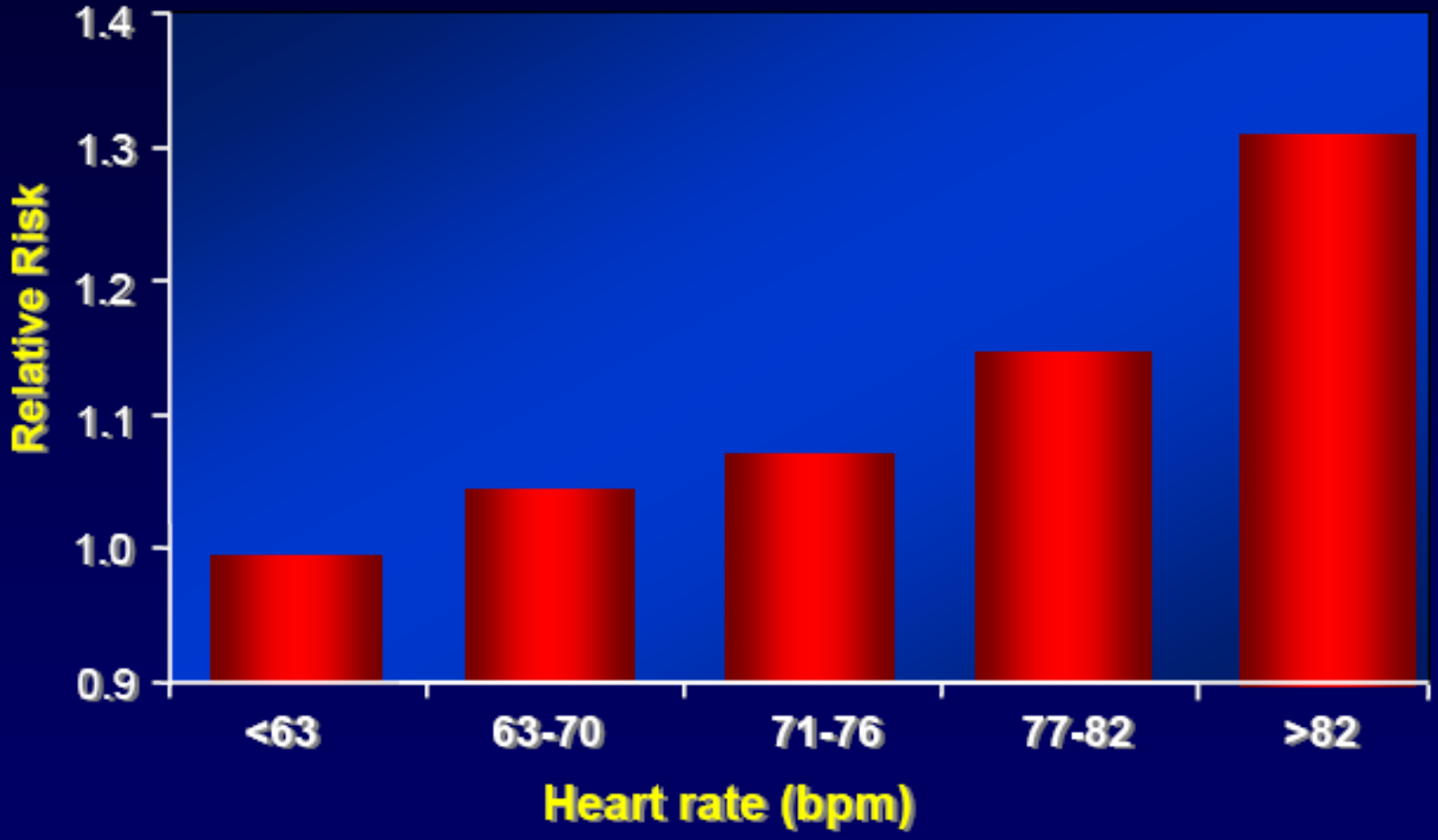


Adapted from Linnemann B, Janka BU, Exp Clin Endocrinol Diabetes 2003;111:215

Heart Rate as a Risk Factor in Acute or Chronic Coronary Syndromes

14 Studies

Heart rate and CV mortality in 24,913 patients with chronic ischemic heart disease (CASS Study)



Adapted from Diaz A et al., Eur Heart J 2005;26:967

Association: increased heart rate as a cardiovascular risk factor

General population	Hypertensive individuals	Coronary artery disease
Dyer et al.1980 [10]	Gillman et al. 1993 [120]	Kjekshus et al. 1986 [124]
Kannel et al. 1987 [9]	Benetos et al. 1999 [12]	Wong et al. 1989 [125]
Gillum et al.1991 [119]	Thomas et al. 2001 [121]	Hjalmarson et al. 1990 [14]
Benetos et al. 1999 [12]	Farinaro et al. 1999 [122]	Copie et al. 1996 [15]
Kristal-Boneh et al. 2000 [13]	Palatini et al. 2002 [123]	Heidland et al. 2001 [106]
Jouven et al. 2005 [11]		Diaz et al. 2005 [16]
		Fox et al. 2008 [17]

JACC 2010;56(24) :1973-1983

Heart Rate and Sympathetic Activity

- High heart rate → altered balance of the autonomic nervous system tone characterised by high sympathetic and/or reduced vagal activity
- Sympathetic overactivity → may cause insulin resistance syndrome through acute and chronic stimulation of both alfa and beta adrenergic receptors
- Patient with hypertention → increased sympathetic activity → develop obesity
- By promoting the development of left ventricular and vascular hypertrophy → the occurance of coronary thrombosis through increased blood viscosity, platelet activation, procoagulant state developed by high sympathetic activity explaine the precipitation of CV event in individual with high heart rate

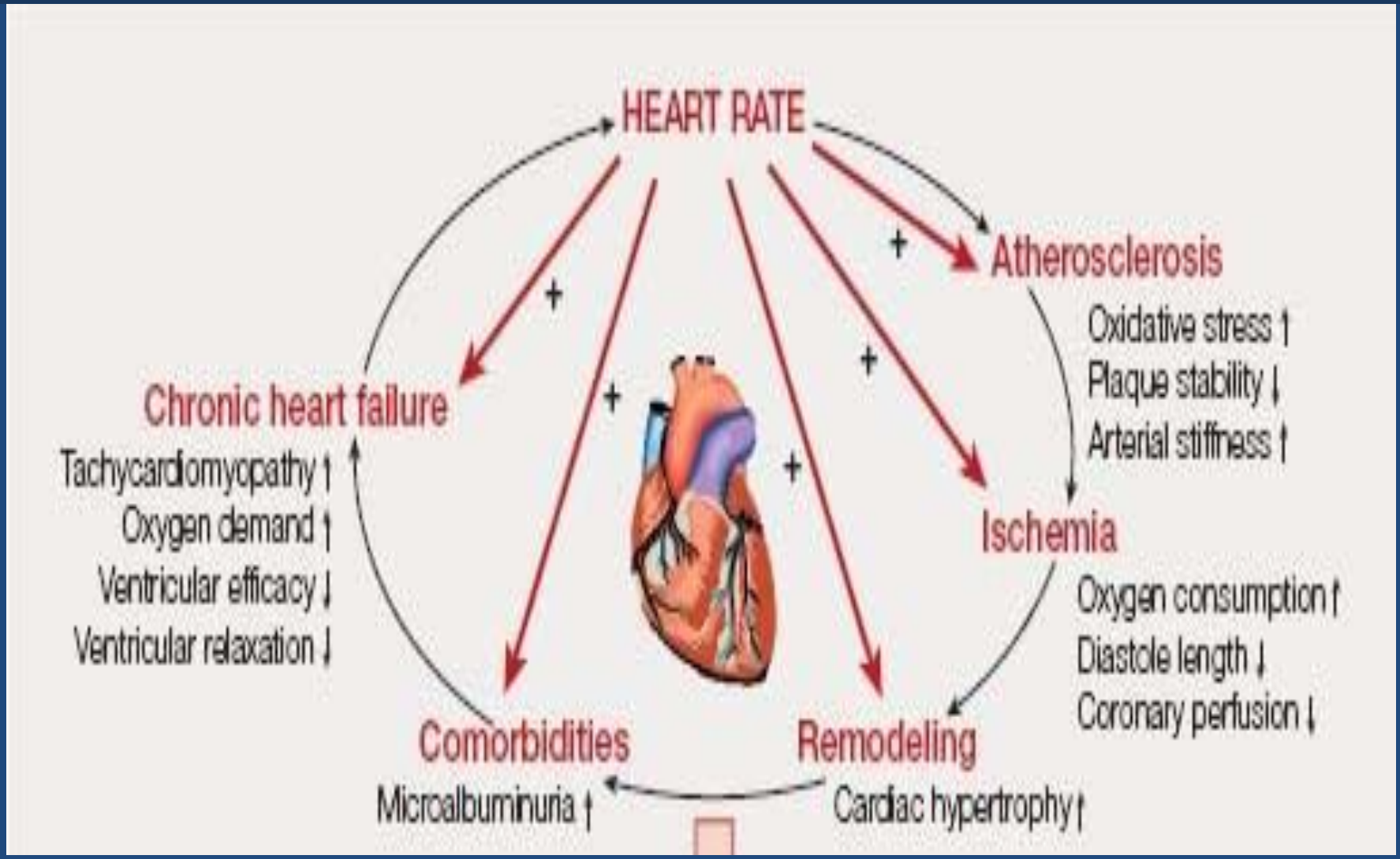
Palatini et. Al, Drugs 2006, 66 (2) : 133-144

Heart Rate Determine Metabolic Demand

- Increased heart rate is associated with high blood pressure and metabolic disturbances that lead to hypertension, atherosclerosis and increased cardiovascular morbidity and mortality
- Whole body temperature and energy needs are controlled by heart activity → via its rate
- The heart rate's intensity and frequency of shear stress → is used to regulate endothelial function and vascular tone.
- A close link between body temperature, metabolism and heart rate has been observed, and so heart rate may determine metabolic demand and 'control' the duration of life.

Ferrari et.al, EHJ (suppl G) , 2003 :G10- G14

Clinical and Experimental Evidence for the Potential Role of Heart Rate along the Cardiovascular Continuum



Medicographia 2009, 31(4) : 362

Heart Rate,Atherosclerosis and CV Events

The additive effect of high heart rate and high BP was also observed for the increase in pulse wave velocity over time and, interestingly enough, the influence of heart rate on the acceleration of arterial stiffness was mainly observed in hypertensive patients

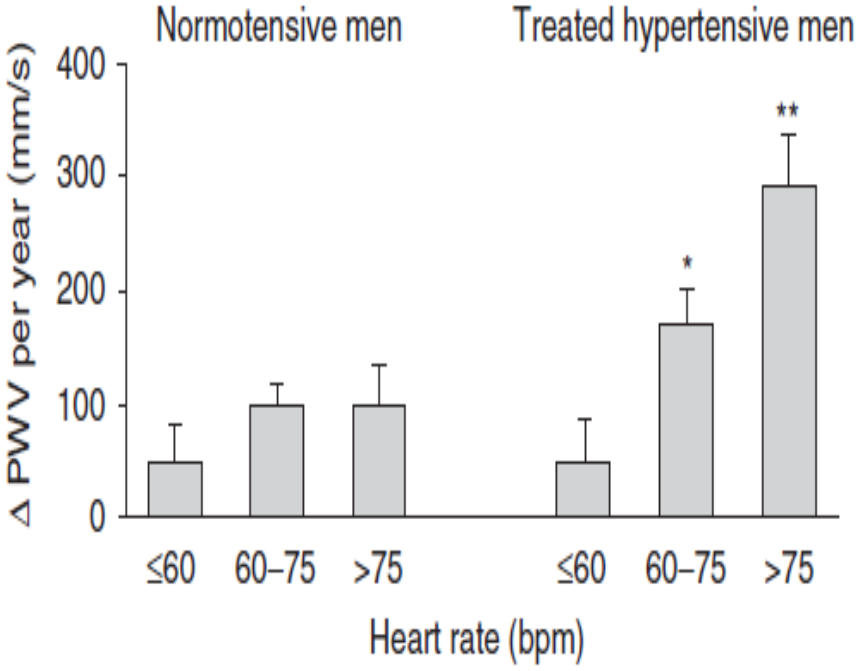
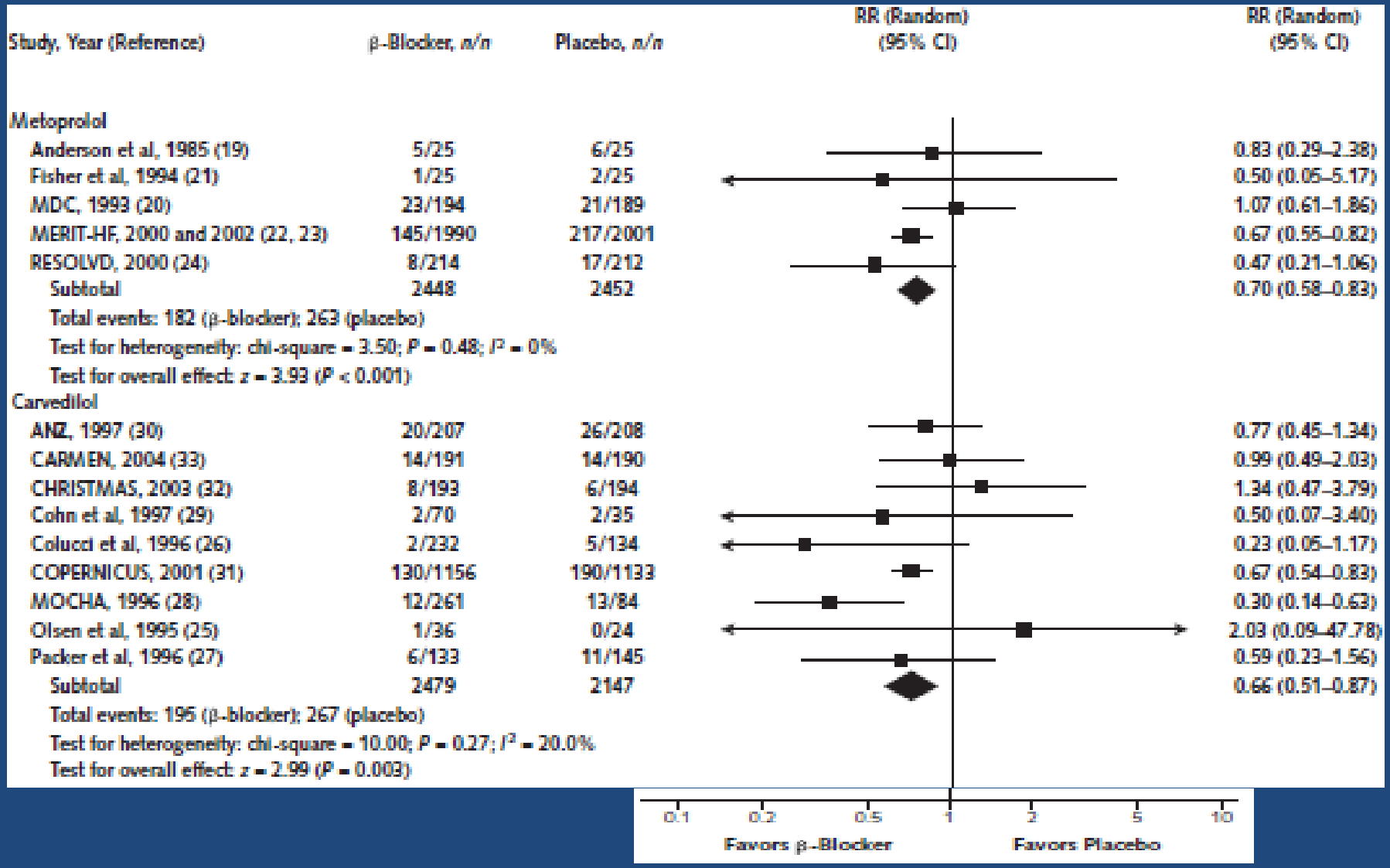


Fig. 2. Progression in pulse wave velocity (ΔPWV) over a period of 6 years according to the heart rate in a study of normotensive and hypertensive men (reproduced from Benetos et al.,[50] with permission). **bpm** = beats per minute; * $p < 0.05$ vs heart rate <60 bpm; ** $p < 0.001$ vs heart rate <60 bpm.

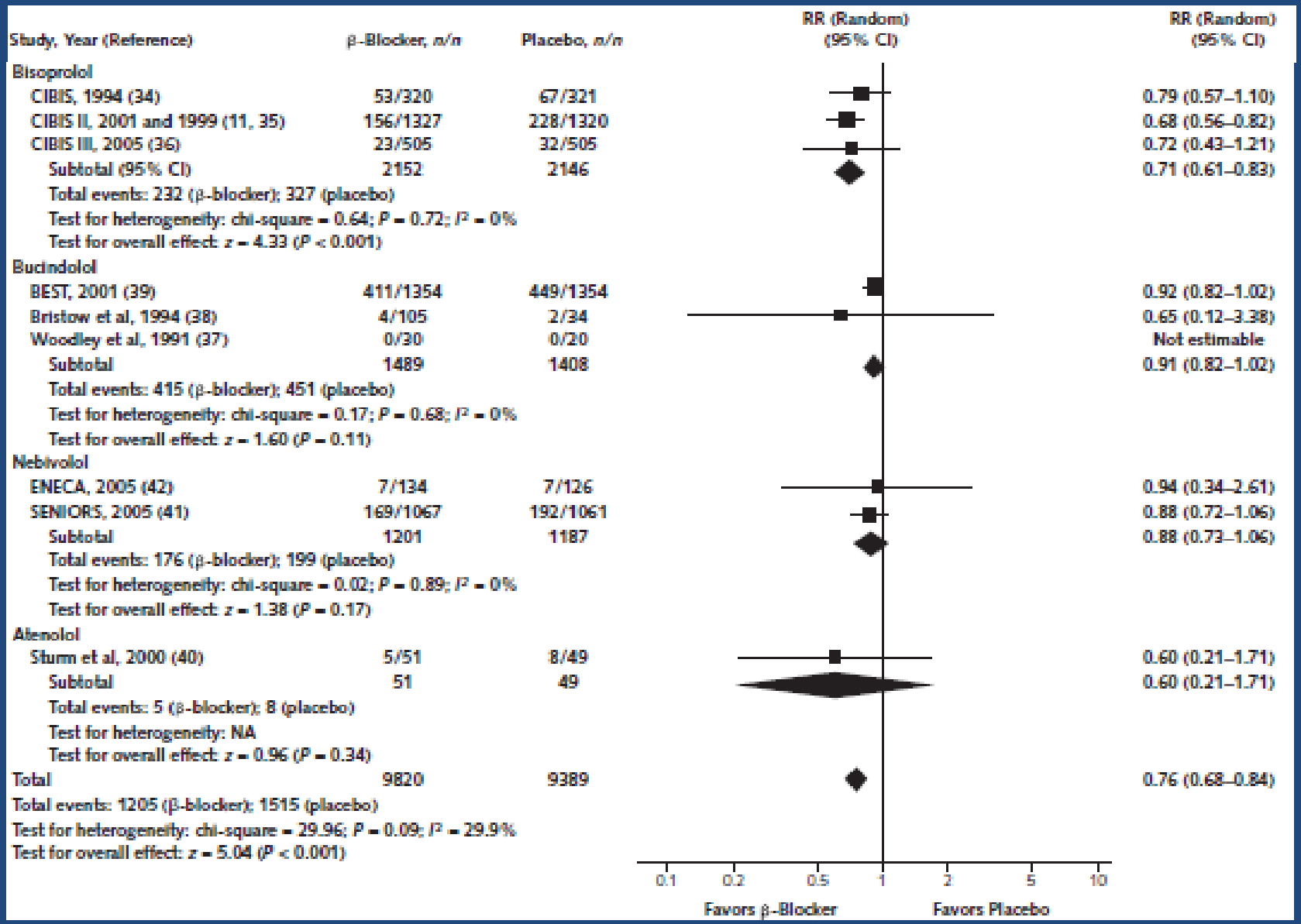
Palatini et.al , Drugs 2006 : 66(2) ; 133-144

Mortality Rate in BB Trials with HF Patients (1)



Mac Alliter . Ann Intern Med 2009 ; 150 : 784-794

Mortality Rate in BB Trials with HF Patients (2)



Mac Alliter . Ann Intern Med 2009 ; 150 : 784-794

Clinical Consequences of High Rate and Implications of Reducing Heart Rate

Heart rate	Impact	Population
>84 beats/min at rest	Elevated risk for CHD	White men aged 65–74 years; white women aged 45–74 years
Increase of 40 beats/min	>Twofold higher all-cause mortality	Hypertensive persons
50–69 beats/min on admission	15% total mortality at 1 year post-MI	AMI patients
≥90 beats/min on admission	41% total mortality at 1 year post-MI	AMI patients
>110 beats/min on admission	48% total mortality at 1 year post-MI	AMI patients
<90 beats/min	5–7% severe heart failure	AMI patients
≥90 beats/min on admission	24% severe heart failure	AMI patients
14 beats/min decrement within 12 h of symptom onset	25–30% decreased infarct size	AMI patients
5 beats/min increment in heart rate	1.14 higher probability of coronary events	Men and women, mean age 81 years

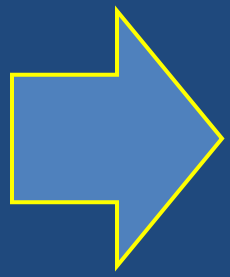
AMI=acute myocardial infarction; CHD=coronary heart disease; MI=myocardial infarction. Adapted from Habib.[25]

Singh BN. EHJ 2003; 5 (Suppl G) : G3-9

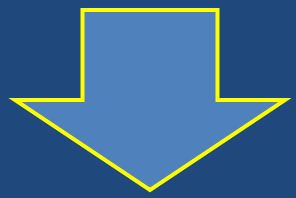
Therapeutic Consideration in Hypertensives

Non Pharmacologically :

- Sedentary habits
- Overweight
- Smoking
- Excessive Alcohol Consumption
- Coffee



↑ Sympathetic Activity



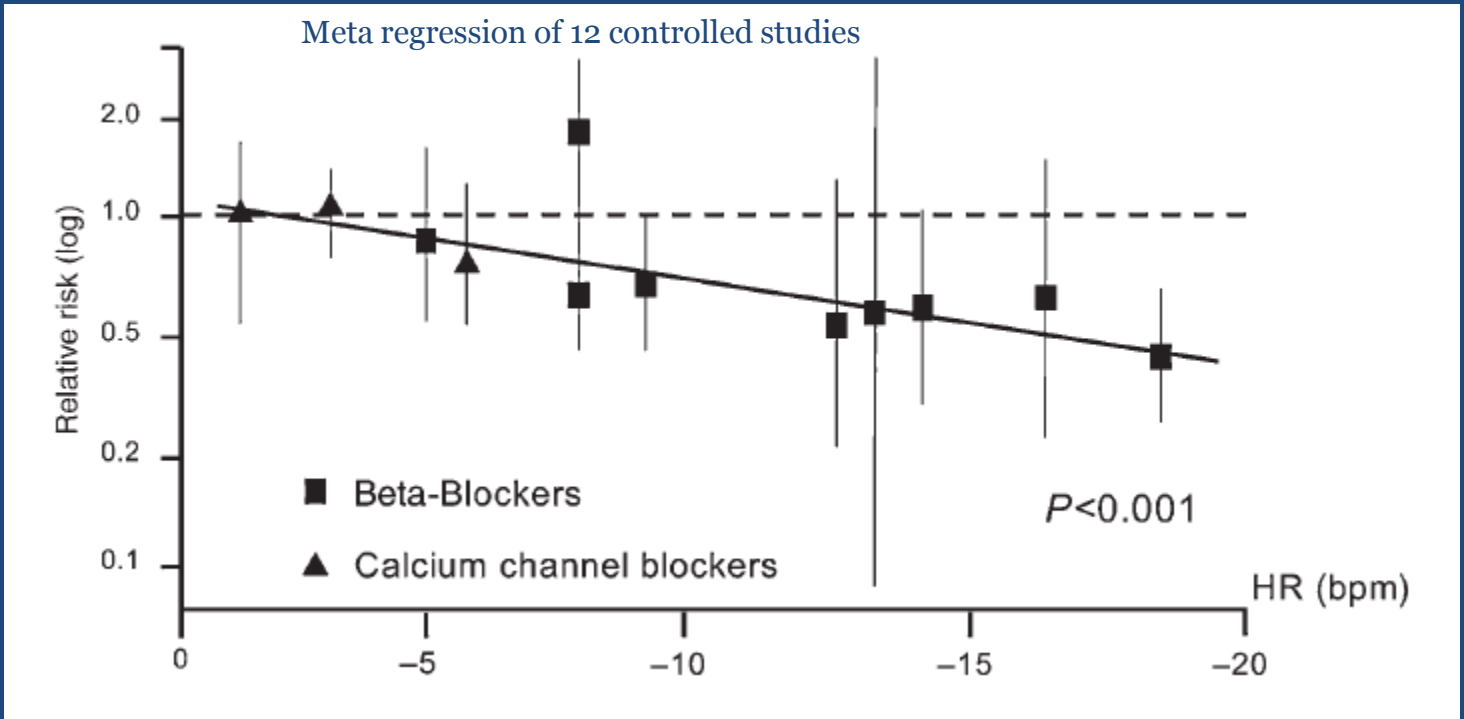
↑ Heart Rate

Pharmacologically

- Beta Blockers :
  - In pts with MCI :
    - Benefit is clear when heart rate was reduced by > 14 bpm
    - Only 3rd generation beta blockers
- Calcium Channel Blockers
  - Non Dehydropyridine CCB (Phenylalkiylamines & Benzothiazepines)
- Angiotensin Receptor Blockers :
  - AII has an effect on CNS (↑ Sympathetic Outflow)
- Heart Rate Lowering with no effect on BP
  - Ivabradine / Cilobradine / Zatebradine
  - Inhibits the current (I_f) in the Sinoatrial Node

Palatini P. et.al Drugs 2006 : 66(2); 133-144

Heart rate lowering is associated with reduction in cardiac deaths in post – MI patients



Each 10 bpm heart rate reduction = 26 % cardiac death reduction

Cucherat M. EHJ 2007; 28 :3012-19

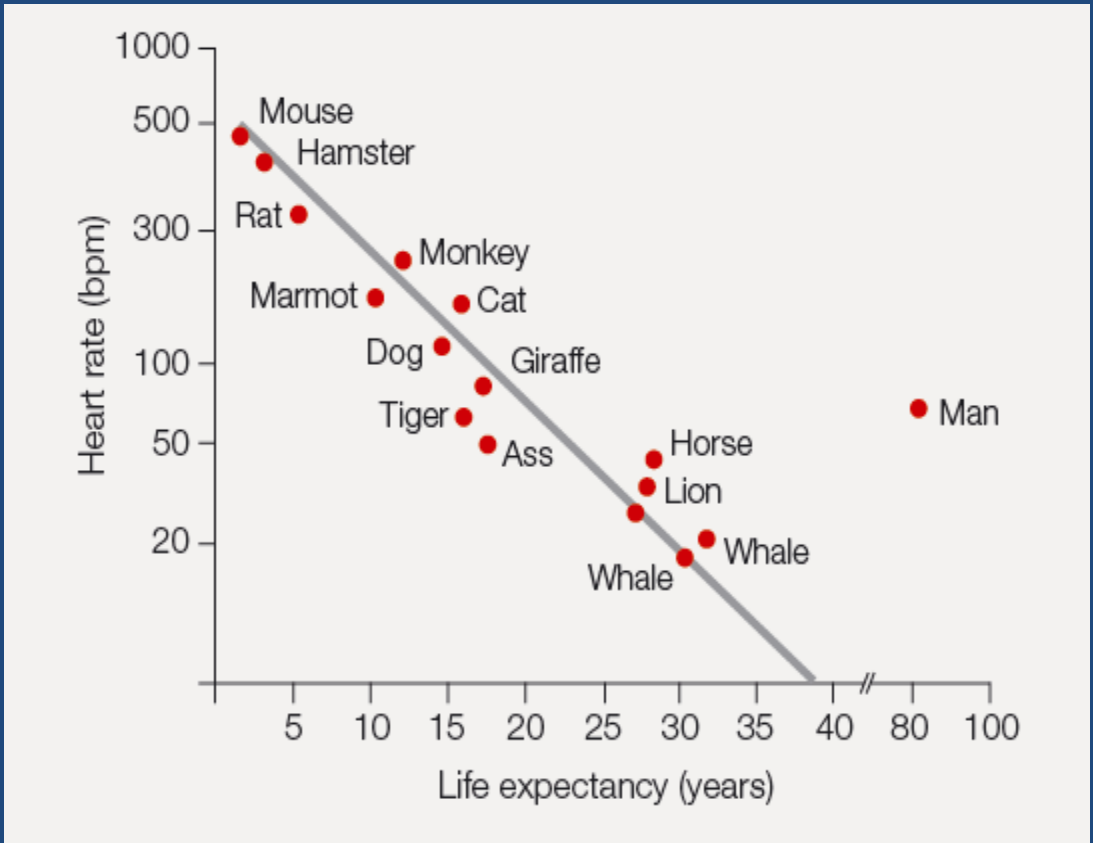
An Optimal Heart Rate ; Is There Any ?

- When considering a desirable or optimal HR for an individual patient, demographic and measurement factors also must be taken into account ;
  - The HR has been reported to decrease with age
  - HR is higher in women than in men
  - The HR shows a clear circadian rhythm, being substantially higher during waking hours, but the variations are relatively small between 10 AM and 6 PM
  - HR also changes with posture, being some 3 beats/min higher in the sitting compared with the supine position

- A recent consensus meeting recommended measurement of HR by pulse palpation during two 30-s periods, performed in a sitting position, after 5 min sitting in a quiet room.

Fox et.al JACC 2007; 50 : 823-30

Inverse linear relationship between heart rate and life expectancy in different species. Bpm, beats per minute.



Modified from Levine JH. JACC 1997; 30:1104-1106

Tortoise
– 6 bmp
– Life Exp 177 yrs
Rat
– 240 pm
– 5 yrs

EHJ 2003; 5 (Suppl G) : 10-14

"Can human life be extended by cardiac slowing ?"

Identification and management of the hypertensive patient with elevated heart rate: statement of a European Society of Hypertension Consensus Meeting

Paolo Palatini, Athanase Benetos, Guido Grassi, Stevo Julius, Sverre E. Kjeldsen, Giuseppe Mancia, Krzystof Narkiewicz, Gianfranco Parati, Achille C. Pessina, Luis M. Ruilope and Alberto Zanchetti

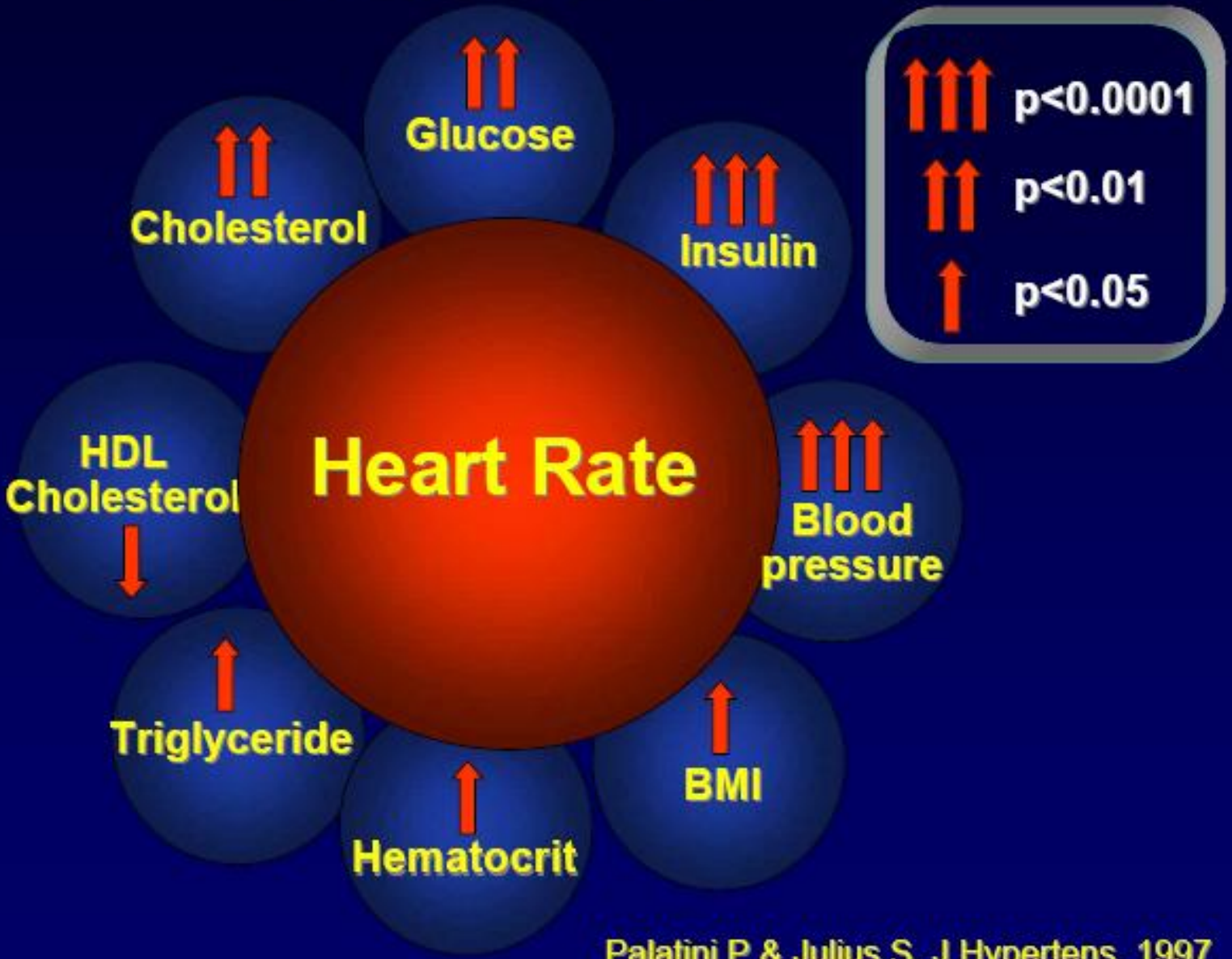
Journal of Hypertension 2006, 24:603-610

Association Between Heart Rate and Mortality Conclusions

- Positive association with total and/or cardiovascular mortality in 49 out of 51 Studies
- Association independent of other risk factors
- Consistency similar to that for smoking
- Association present in different clinical settings
- Association still present after exclusion of first years after baseline evaluation
- Association with mortality less consistent for women

Modified from J Hypertens 2006;24:603

Association Between Heart Rate and Other Risk Factors for Atherosclerosis



Palatini P & Julius S, J Hypertens, 1997

Heart Rate as Independent Risk Factor

- Increased arterial wall stress
- Higher mean blood pressure
- Decreased arterial compliance
- Facilitation to coronary plaque disruption
- Increased cardiac work and oxygen consumption
- Trigger of ventricular arrhythmias

CV Risk Factors and 10-yr Mortality in Elderly Men Living in Finland, Italy, and The Netherland

The FINE Study

10-year mortality

Age (+)	p=0.0001
Smoking (+)	p=0.0001
Heart rate (+)	p=0.0001
BMI (-)	p=0.0006
HDL-chol. (-)	p=0.002

6-to-10-year mortality

Age (+)	p=0.0001
Smoking (+)	p=0.0001
Heart rate (+)	p=0.0001
Systolic BP (+)	p=0.01

Menotti A et al, Eur Heart J 2001;22:573

Resting Heart Rate

- **Is Important !!**
- **Time to put As Risk Factor in Current Guidelines ????**

Thank You

Bunaken, 2010