

# **WORLDWIDE MONITORING OF BLOOD PRESSURE**

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# Background

Only recently do guidelines start considering the circadian variation in blood pressure (BP). For a long time, fixed limits of 140/90 mmHg (systolic/diastolic BP) were used to diagnose hypertension in all adults 18 years and older.

The circadian rhythm in BP was thought to primarily reflect the rest-activity schedule rather than being partly endogenous.

While this is no longer the case, ambulatory BP monitoring is still restricted to “special cases”, often limited to 24 hours instead of being available continuously to everyone.

# AIM

Evidence is presented herein

- for the need to routinely screen for BP and heart rate (HR) variability, and
- -for continued monitoring in patients in need of treatment.

# Self-Measurements

Originally, chronobiologists relied on self-measurements taken a few times a day for 2 or more days to assess the circadian variation.

**Sampling requirements** were specified that include the **need for at least one nightly measurement**, preferably taken by another person in order not to disturb the subject's sleep.

Despite the obvious shortcomings of self-measurements, important findings were made that laid the **foundation for recognizing the importance of BP variability**.

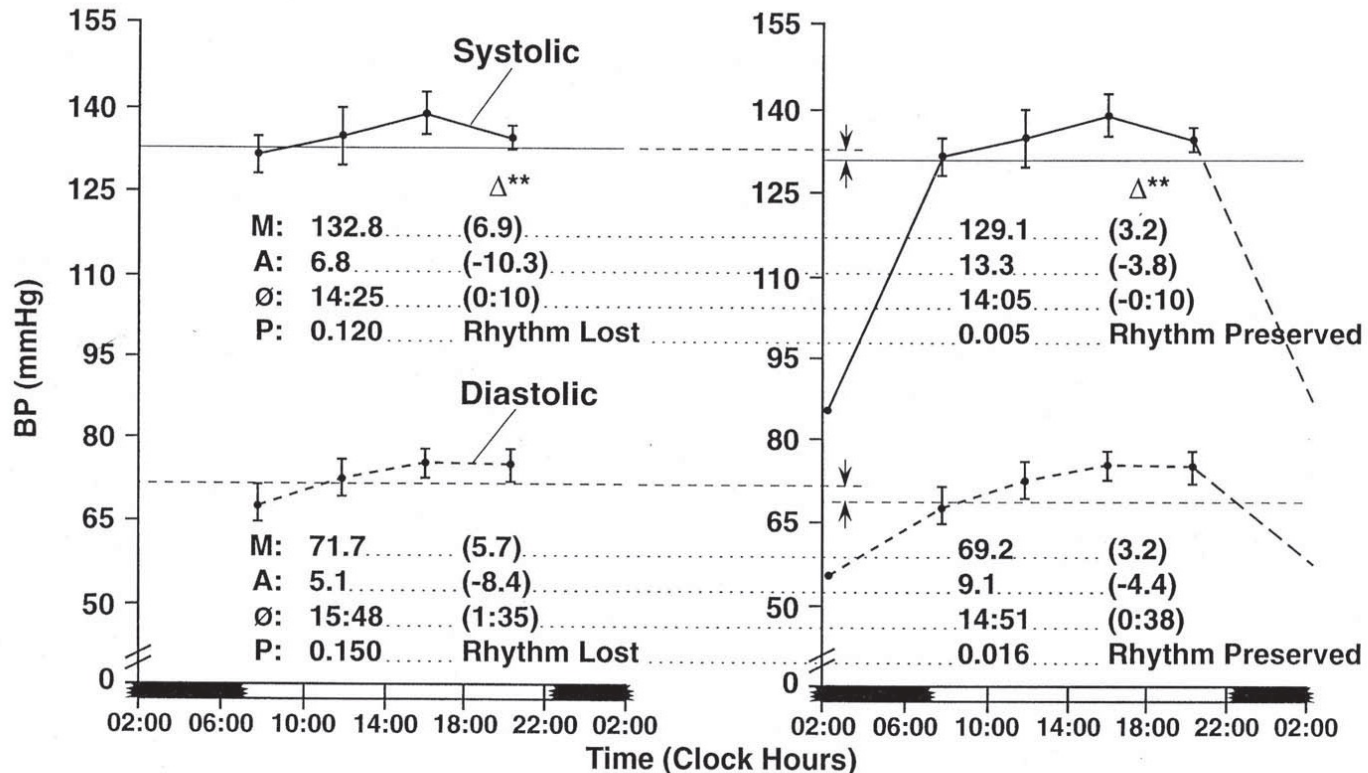
# Self-Measurements

SINGLE NIGHTLY MEASUREMENT ADDED TO 9 DAYS OF 4-HOURLY SAMPLING DURING WAKING GREATLY IMPROVES CIRCADIAN PARAMETER ESTIMATION OF BLOOD PRESSURE (BP)\*

N of Measurements:

28

29

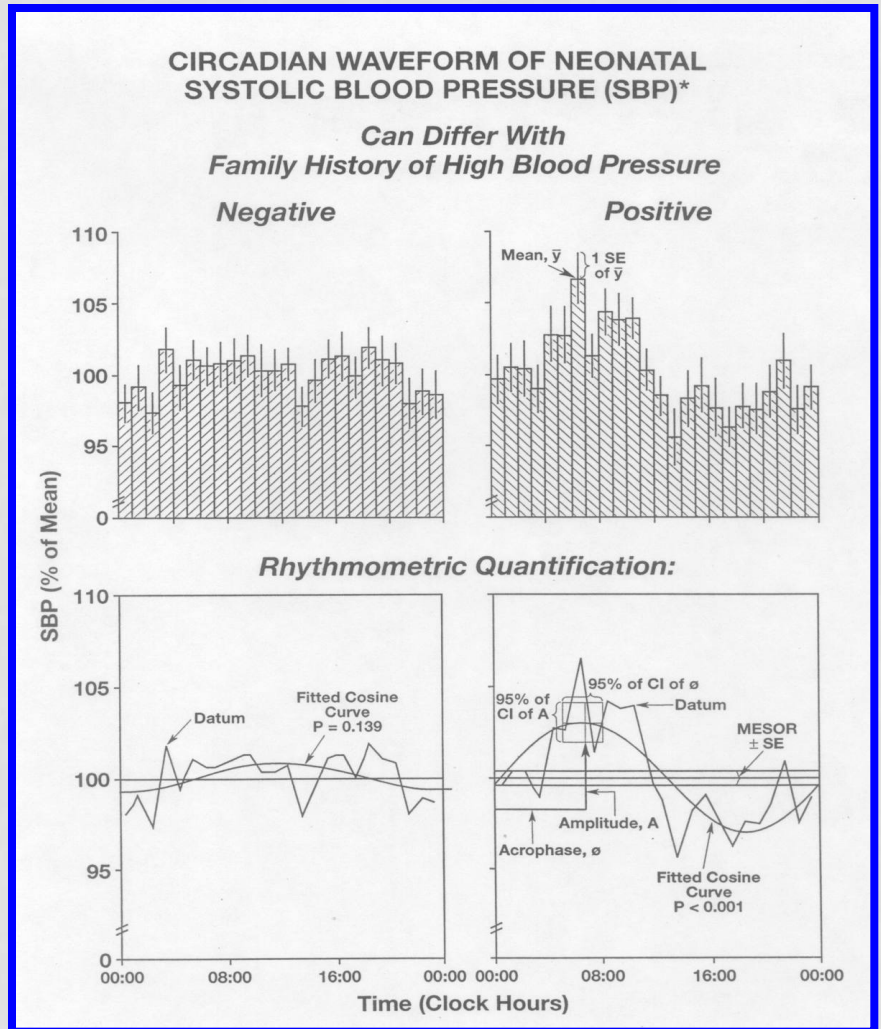


\* 64-year-old man (FH), 2 years after coronary bypass surgery automatically monitored his BP; data folded over idealized 24-hour day, decimated and rounded to nearest 5 mmHg (as practiced by some but not recommended). M = MESOR; A = circadian amplitude; Ø = circadian acrophase (referred to 00:00).

\*\* Deviation from all data-based estimates (93 hourly averages).

# Self-Measurements (school children) and Automatic BP Monitoring (neonates)

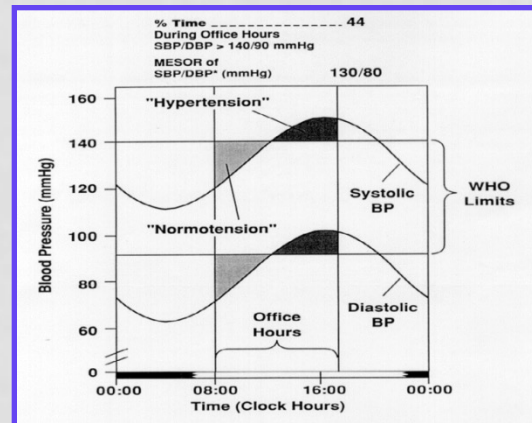
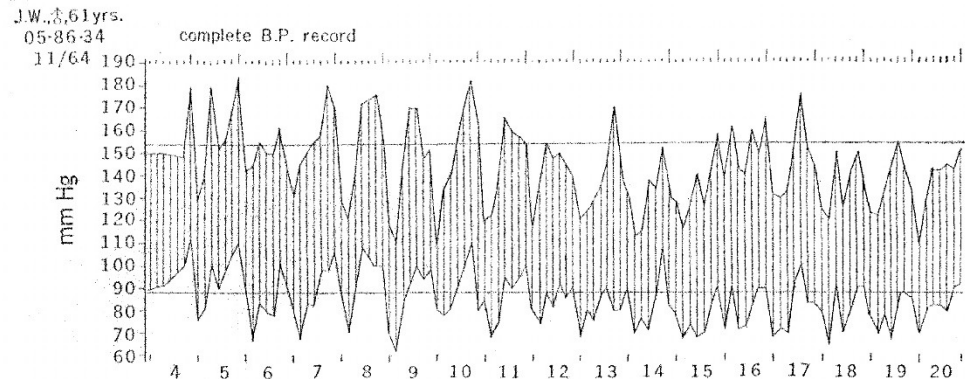
A positive family history of high BP and/or related cardiovascular diseases is associated with a larger circadian amplitude of BP: *school children* in Italy, Portugal, and USA (Arkansas, Connecticut, Minnesota); *neonates* in Minnesota, Italy, Japan, Russia, the Czech Republic, and Spain.



# Staff Measurements

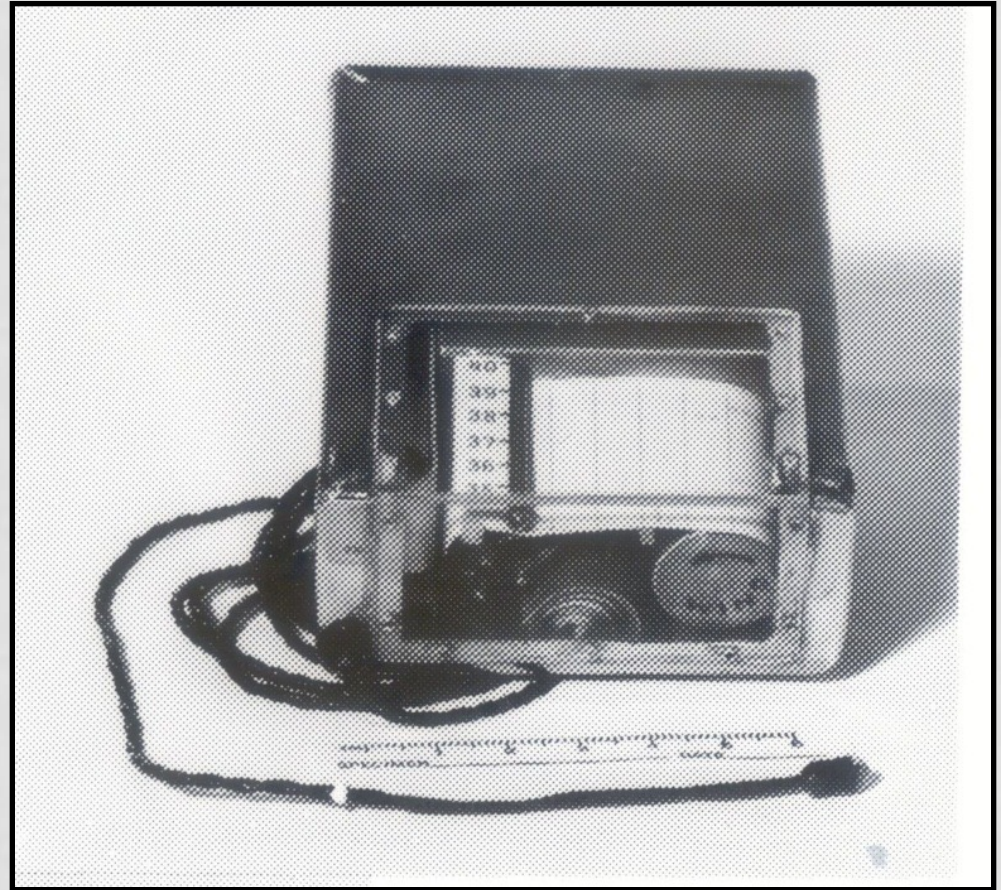
By 1974, Frederic C Bartter (NIH Clinical Director) wrote: "By conventional standards, this patient is clearly **normotensive every morning**. Yet the blood pressure determined each **day at 6 in the afternoon** provides especially convincing evidence **that this patient is a hypertensive**. ... My plea today is that information contained in such curves [cosinor fits] become a routine minimal amount of information accepted for the description of a patient's blood pressure. **The analysis of this information by cosinor should become a routine.** ..."

**Barter's patient diagnosed as normotensive in the morning and hypertensive in the evening**



# Arteriosonde: an analog BP monitor (1970s)

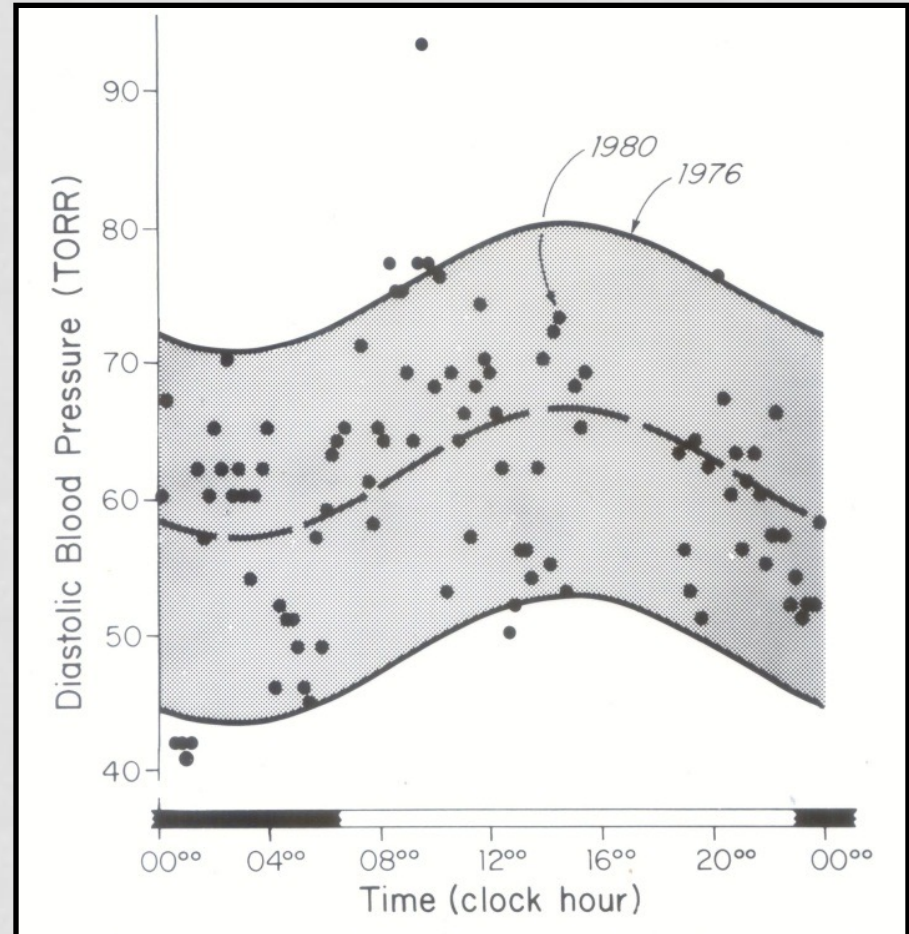
In adults, the first automatic around-the-clock measurements of BP were obtained with the Arteriosonde, within the scope of the Minnesota-Kyushu study of breast cancer risk. This analog device necessitated the **manual taking off of data from graphic recordings.**





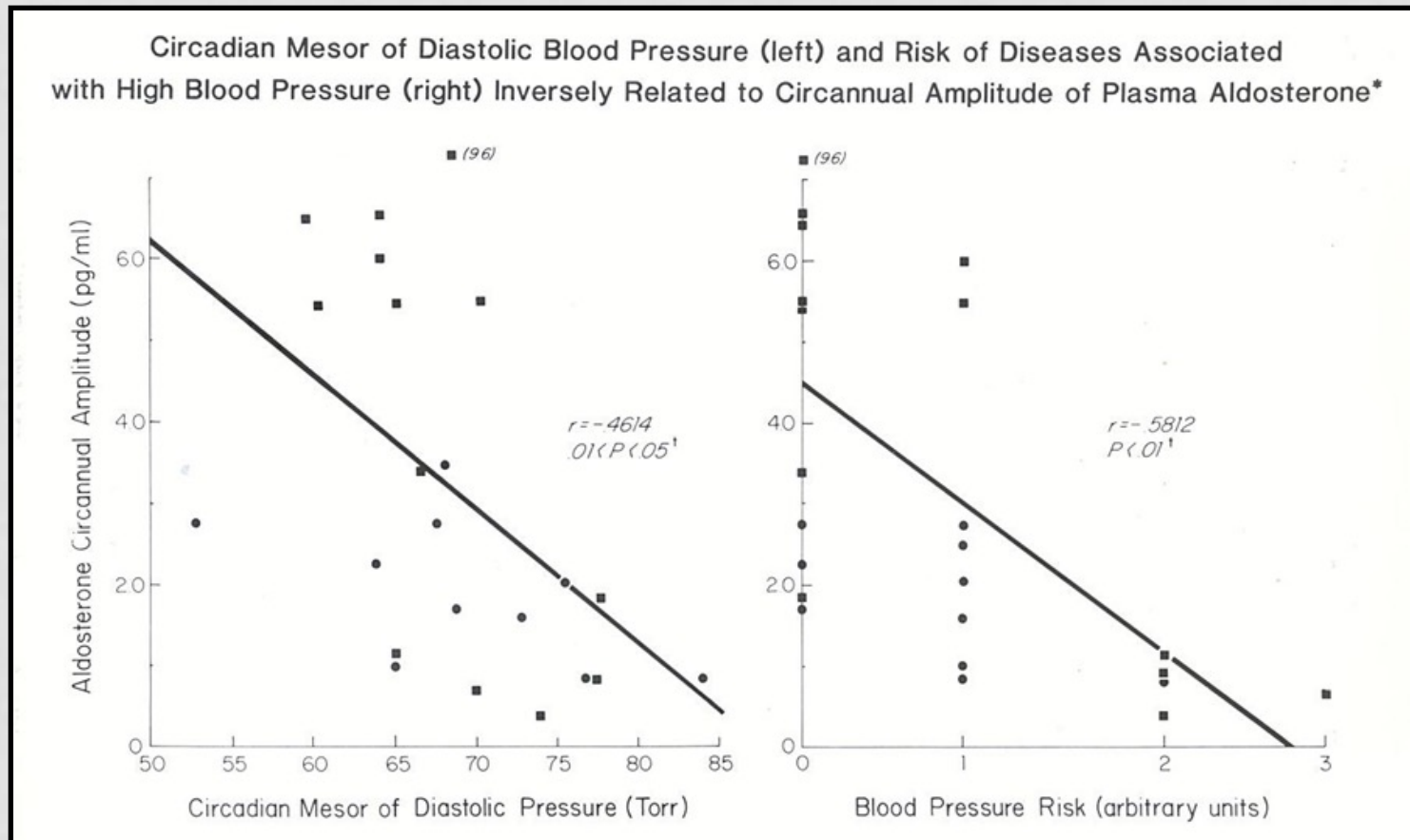
# Arteriosonde: an analog BP monitor (1970s)

The Arteriosonde was first used at the Clinical Research Center of the University of Minnesota to compare **healthy women in three age groups** who were either at a **low or high risk of developing breast cancer**. They were monitored once in each season. Concomitant **hormonal determinations** were obtained.



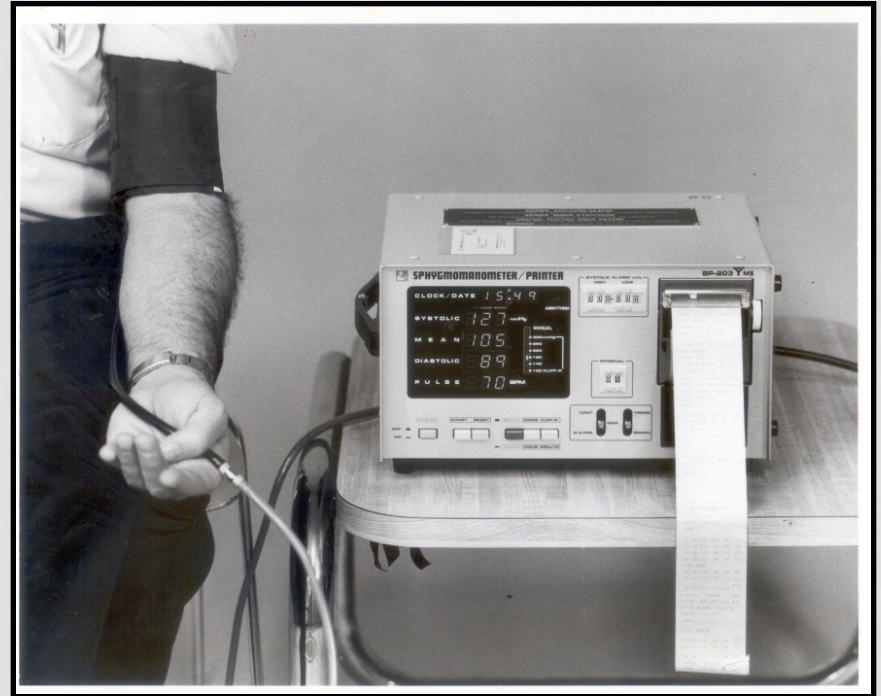
# Arteriosonde: an analog BP monitor (1970s)

Despite this limitation, cardiovascular disease risk and diastolic BP were both related to the circannual amplitude of aldosterone.



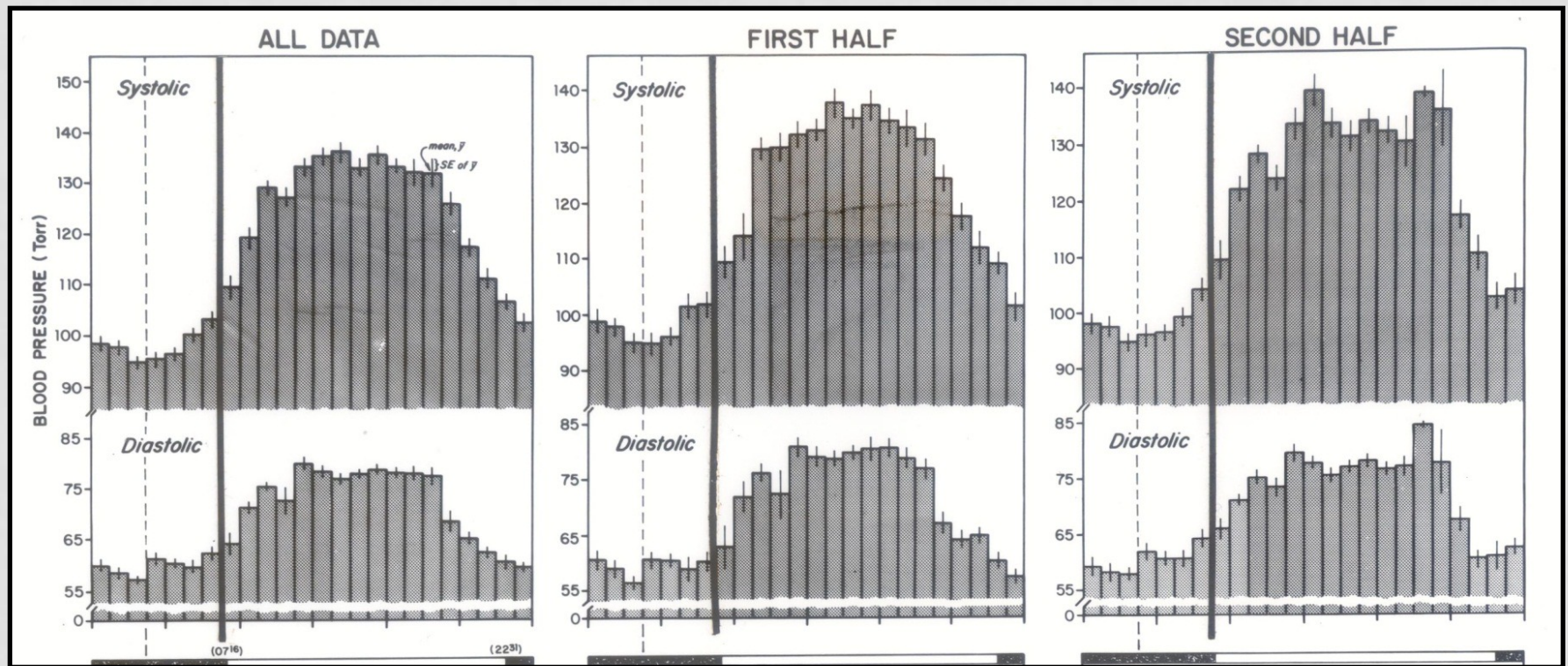
# Portable Nippon-Colin BP monitor (1980s)

With a portable – albeit not ambulatory – monitor from Masayuki Shinoda (Nippon Colin, Komaki, Japan), our first truly automatic BP measurements were collected.



# Portable Nippon-Colin BP monitor (1980s)

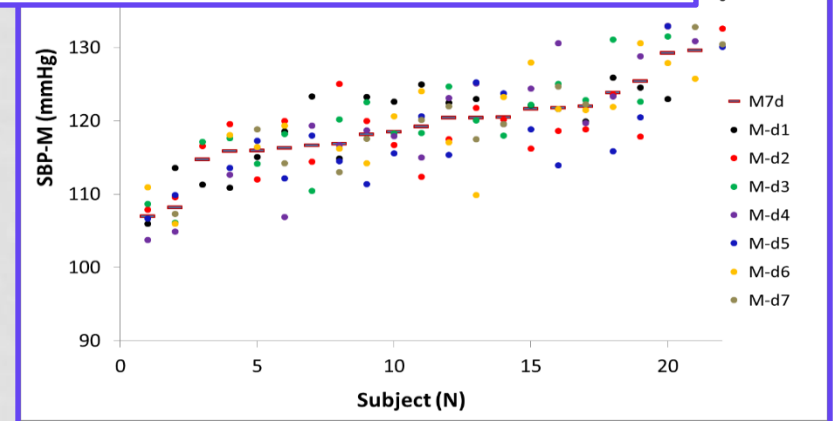
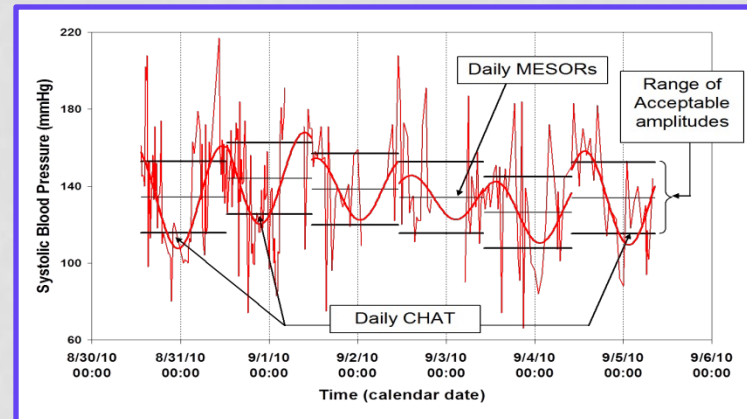
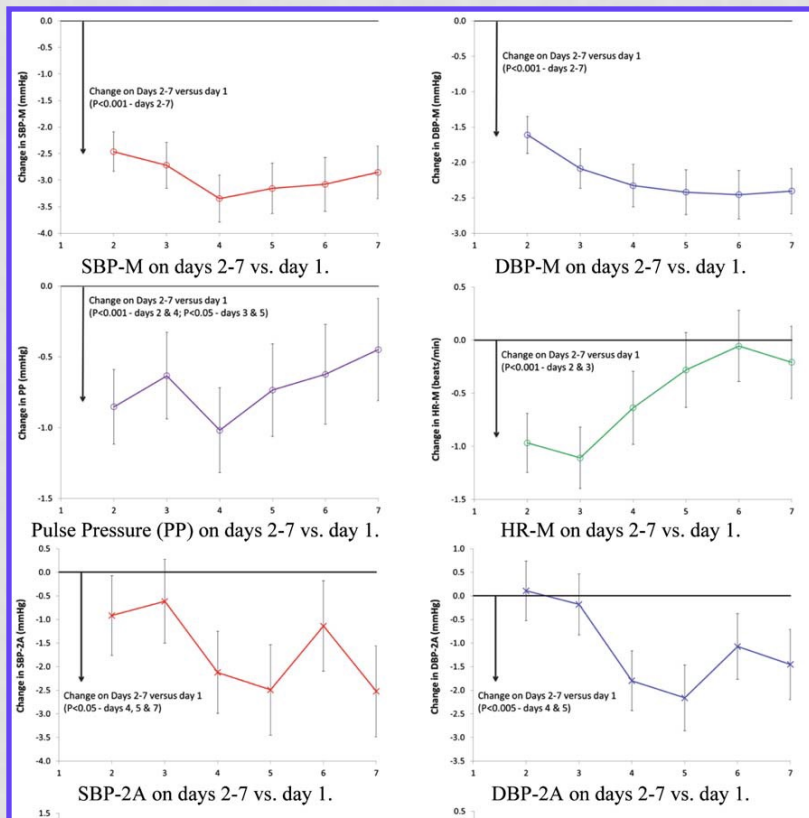
It was instrumental in demonstrating that **BP increases toward mid-sleep**, well before awakening, the latter associated with a larger and faster increase in BP. It confirmed that **circadian rhythms remain demonstrable during bedrest**.



# Portable Nippon-Colin BP monitor (1980s)

It also served to demonstrate the **novelty effect** and

to assess the **extent of day-to-day variability**.



# Portable Nippon-Colin BP monitor (1980s)

We showed that by extending the monitoring span from 24 to 48 hours, the uncertainty on the estimation of circadian parameters was reduced by 30%, with another 10% gain by prolonging the record to 7 days.

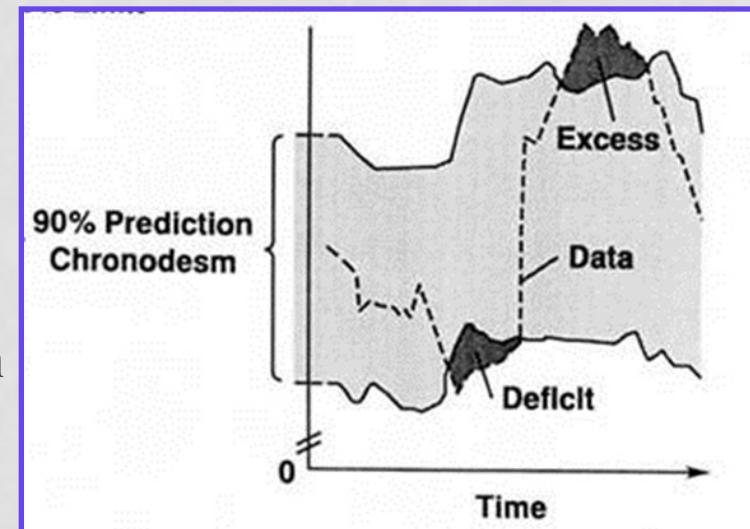
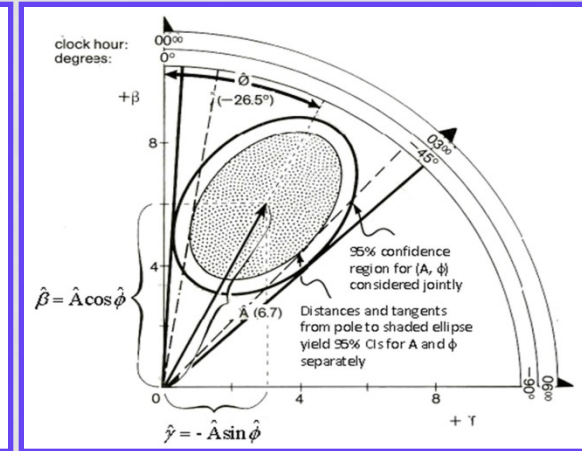
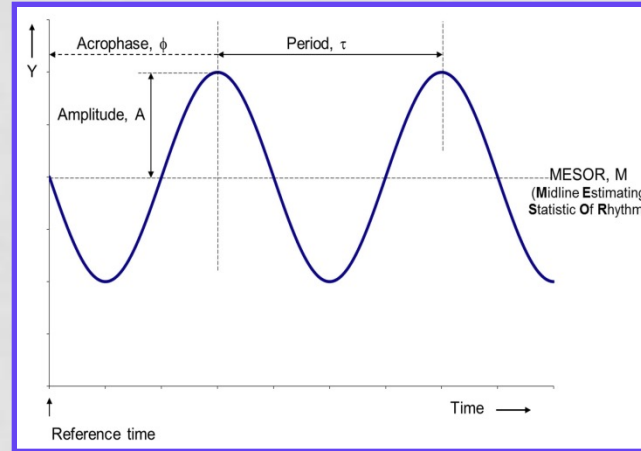
**Monitoring for 7 days** at the outset has been recommended in several consensus meetings

- To obtain more **reliable estimates of the circadian rhythm**, and
- To obtain a rough **estimation of the weekly variation**.

# Ambulatory BP monitoring: ABPM-630

The ABPM-630 operated on gas cartridges, allowing collection of around-the-clock data in **clinically healthy individuals** on 3 continents from neonates to centenarians, and during pregnancy.

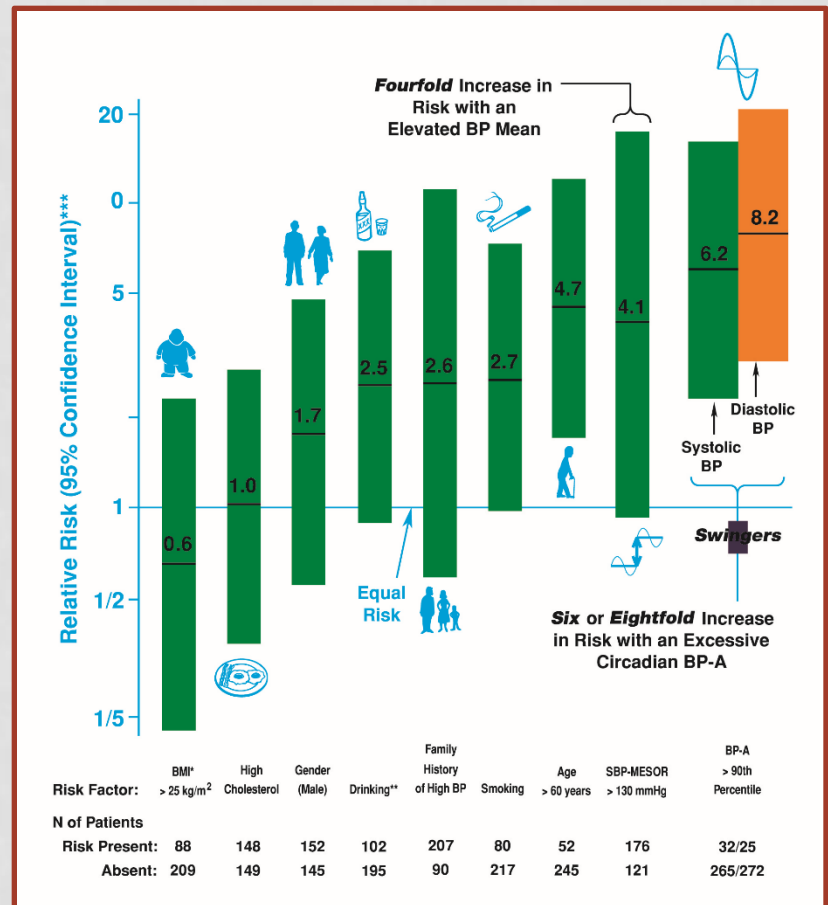
These data were essential to derive **time-specified reference values** qualified by **gender and age**, on which our **sphygmochron** analysis is based.



# Ambulatory BP monitoring

The ABPM-630 and later the TM-2421 and TM-2430 (A&D, Tokyo, Japan) were critical for the assessment of **outcomes from prospective as well as retrospective clinical trials.**

Outcome studies corroborated the **risk associated with an excessive circadian amplitude of BP (CHAT, brief for Circadian Hyper-Amplitude-Tension).**

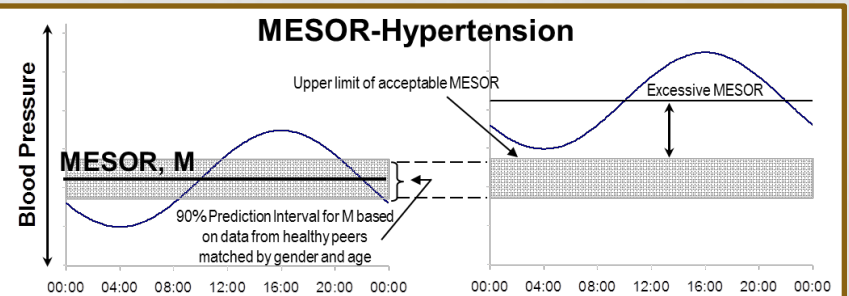


**CHAT carries a higher risk of morbidity than high BP**

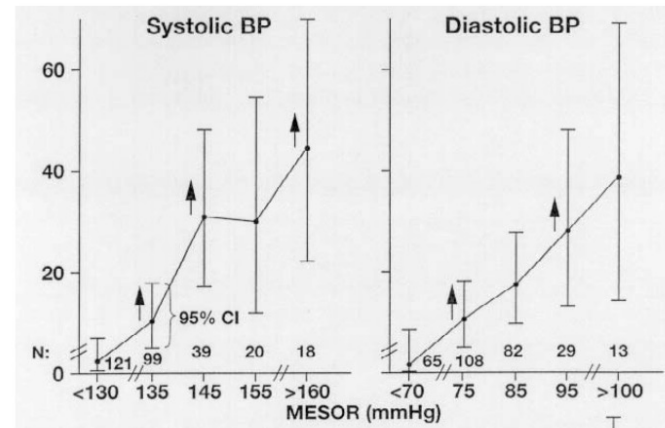


# Ambulatory BP monitoring

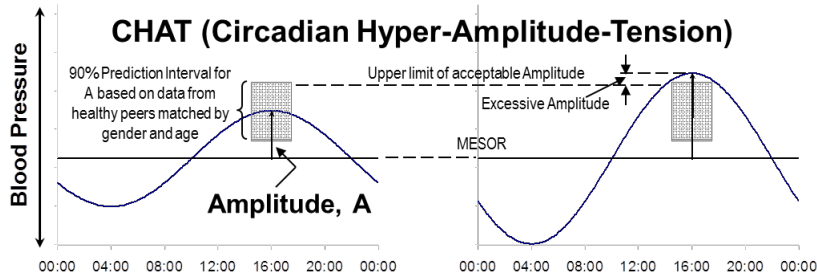
**Outcome studies** in Japan, Taiwan, Minnesota, the Czech Republic, and Germany further identified other abnormalities in the variability of BP and heart rate, which we named **Vascular Variability Disorders (VVDs)**.



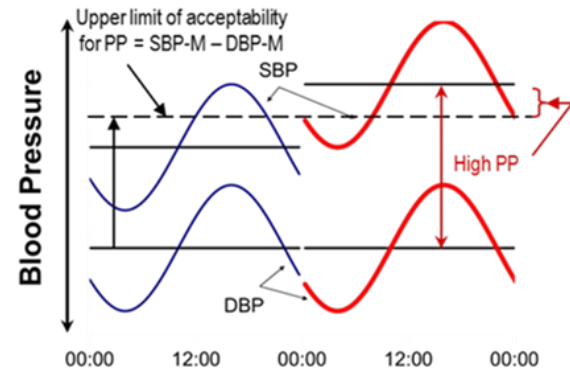
## Incidence of Actual Morbidity



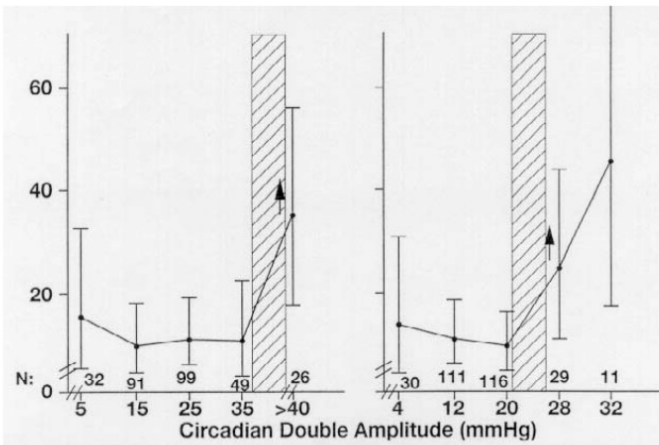
# Ambulatory BP monitoring



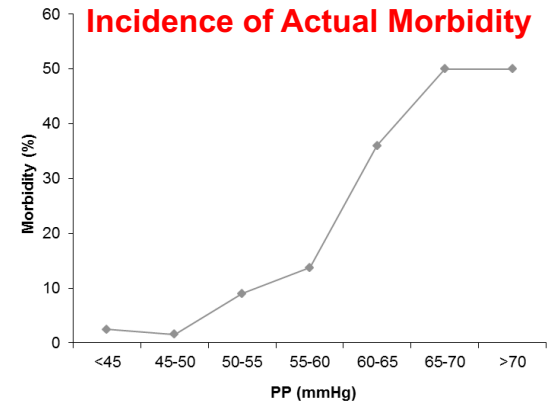
### Excessive Pulse Pressure



### Incidence of Actual Morbidity

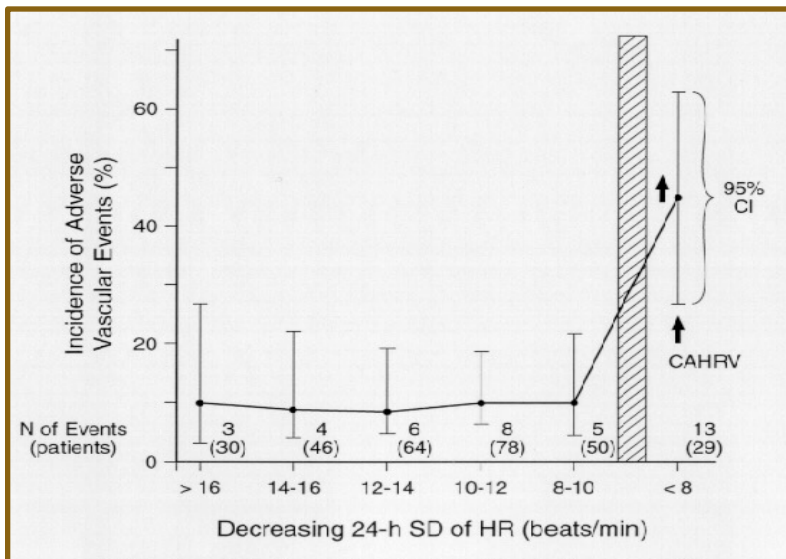


### Incidence of Actual Morbidity

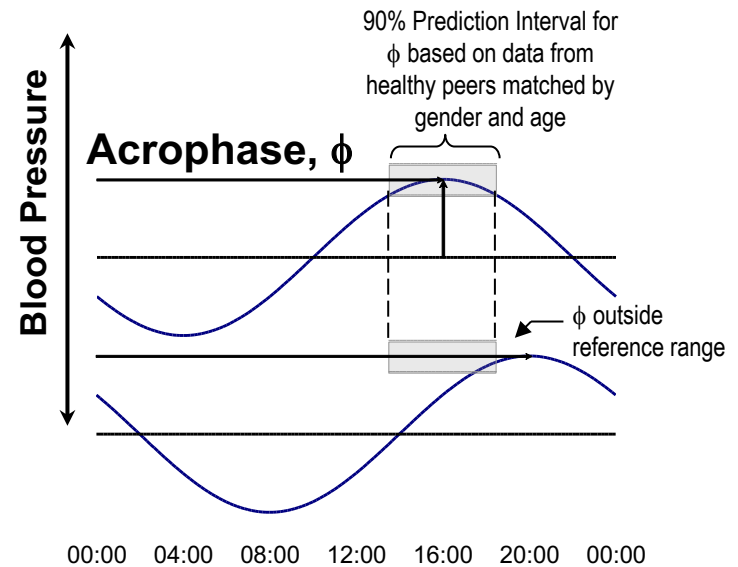


# Ambulatory BP monitoring

## Decreased Heart Rate Variability

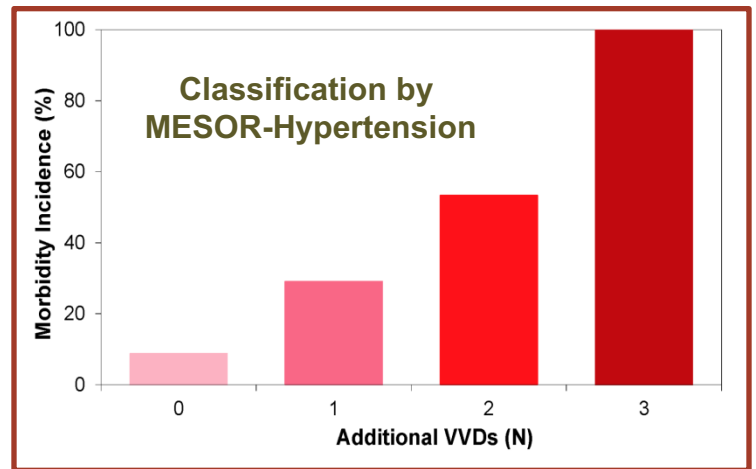
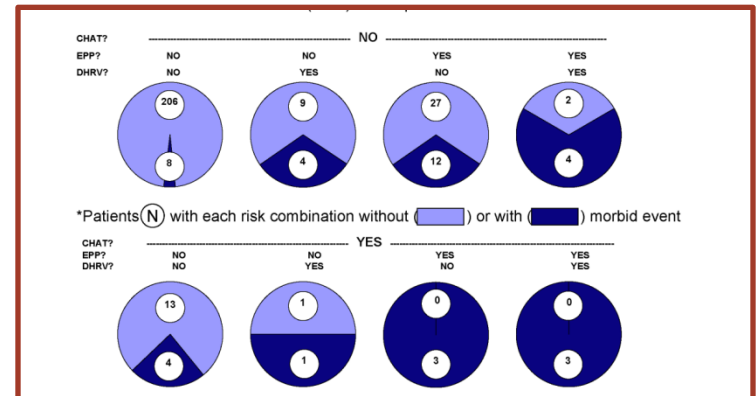
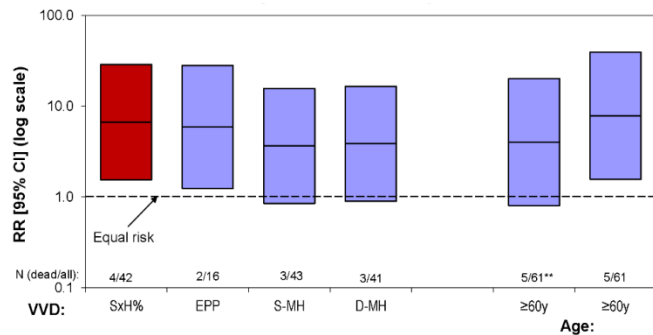
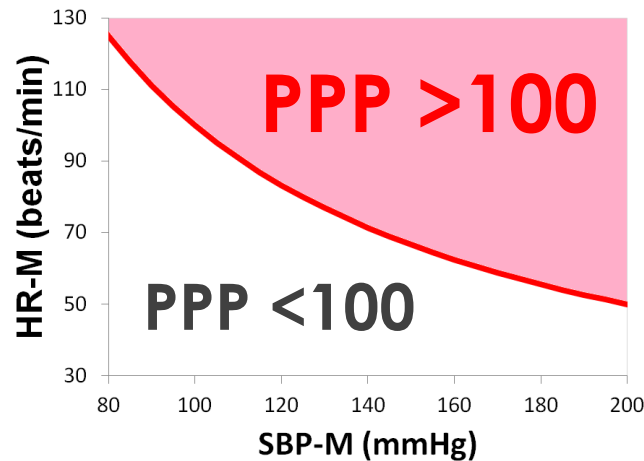


## Ecphasia (and Ecfrequency)

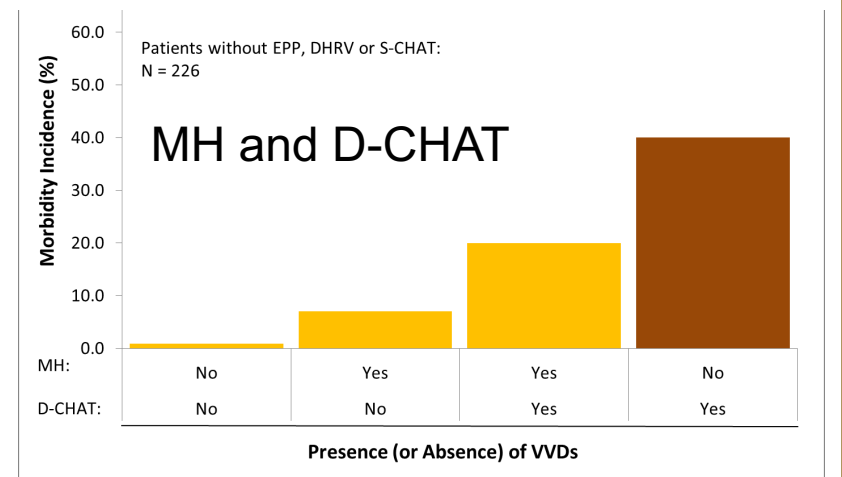
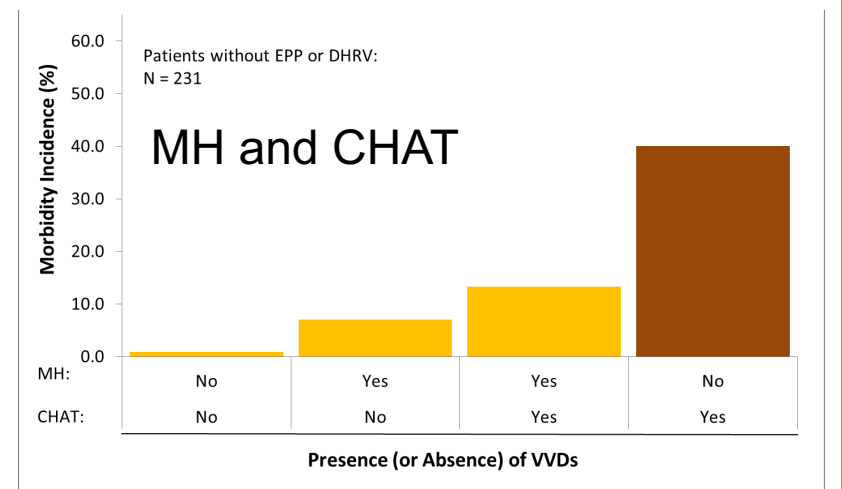
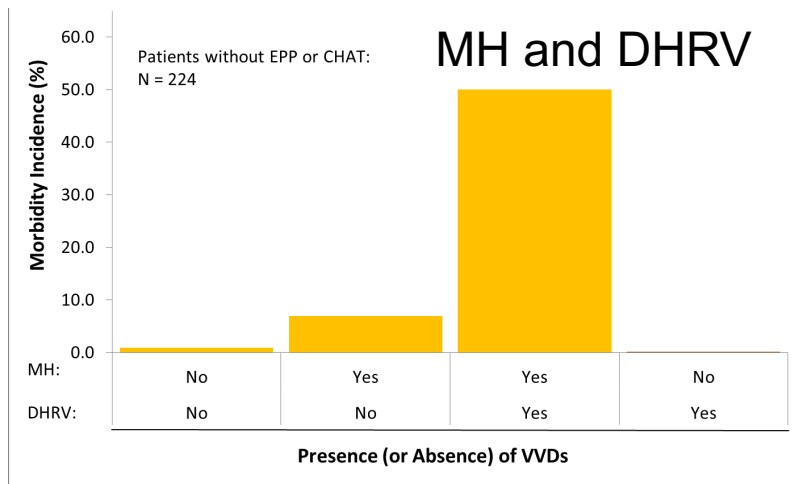
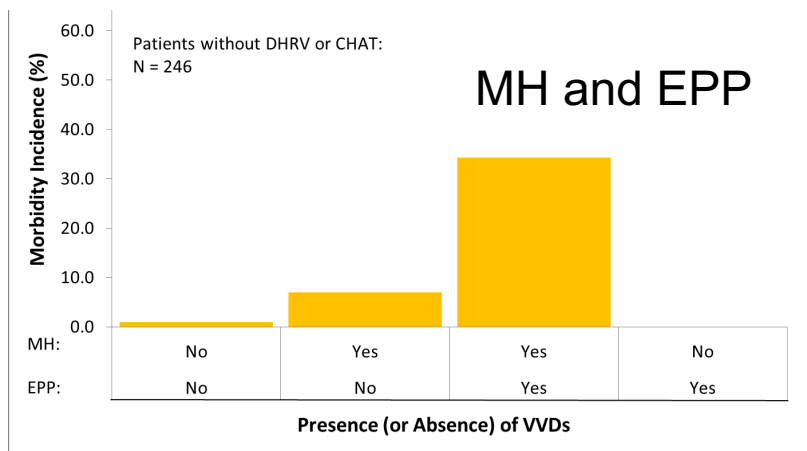


# Ambulatory BP monitoring

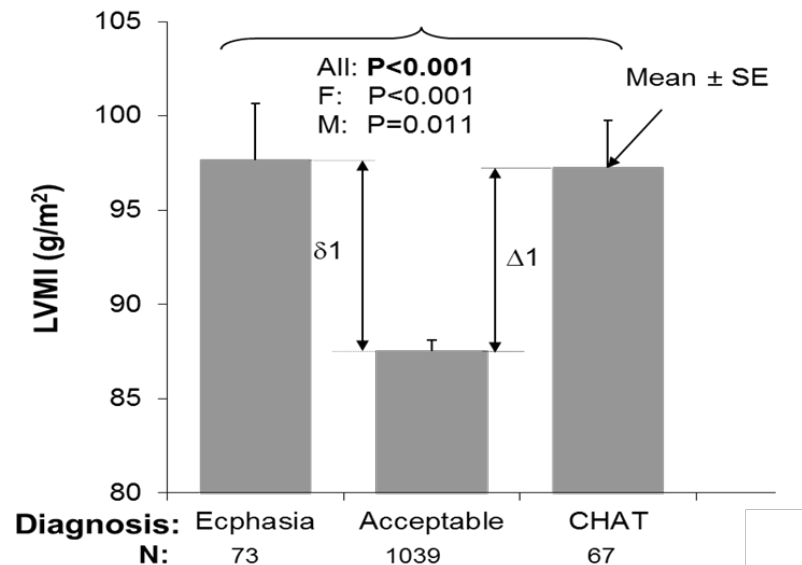
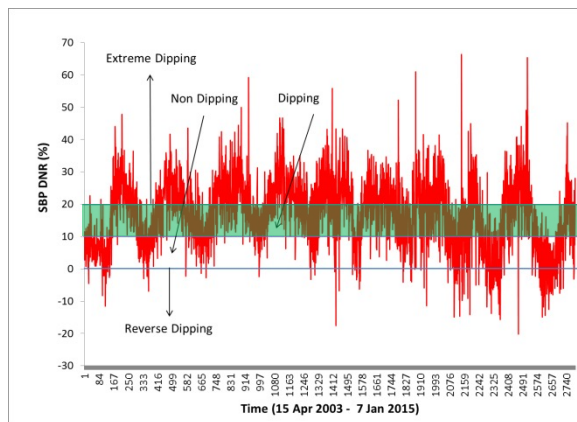
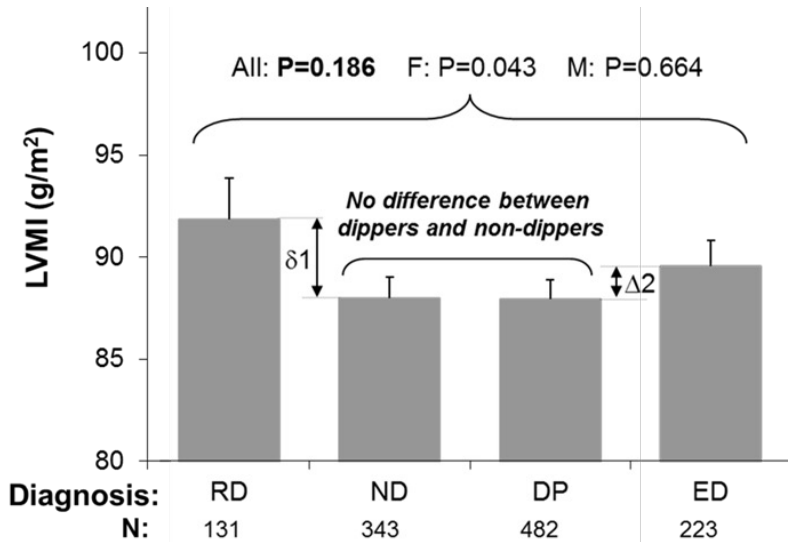
## Excessive Pulse Pressure Product



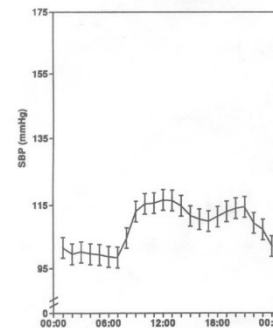
# Ambulatory BP monitoring



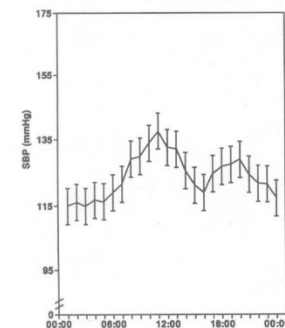
# Ambulatory BP monitoring



20 - 40 Year Olds  
(n = 51)



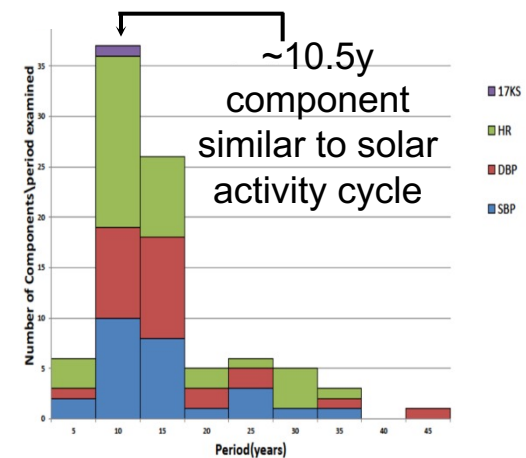
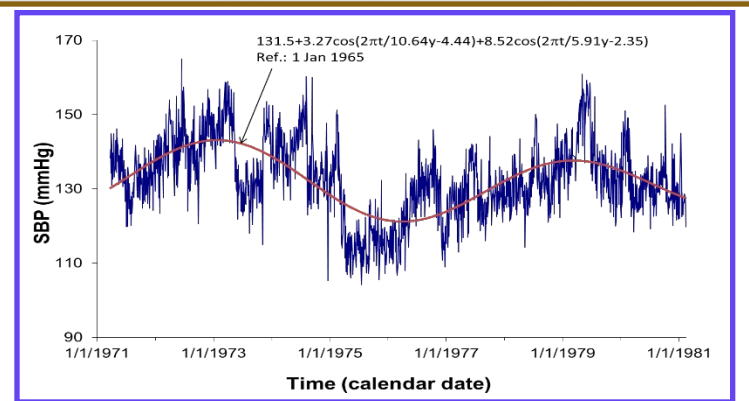
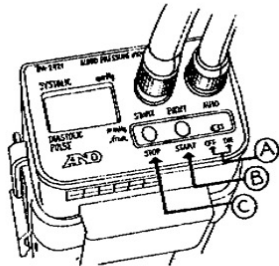
60 - 80 Year Olds  
(n = 31)



# Ambulatory BP monitoring



With smaller and lighter devices, **continued surveillance** became more readily feasible. Uncovered **long-period cycles** suggested **cosmic influence**.

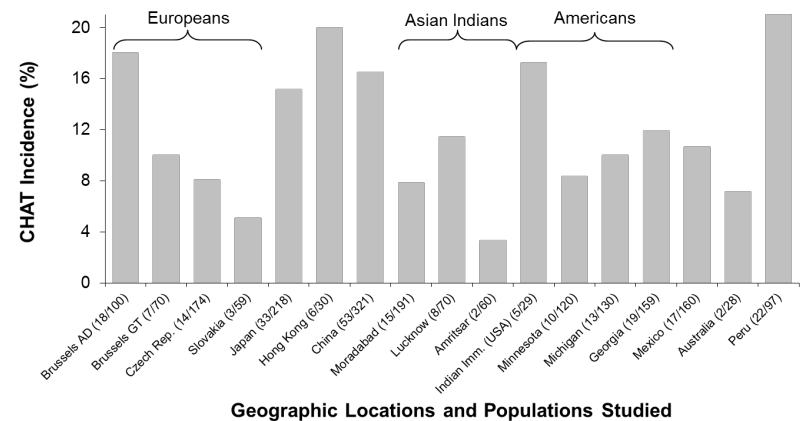


# ABPM: Refined Diagnosis

Ongoing monitoring around the world continues to accumulate evidence for the need to

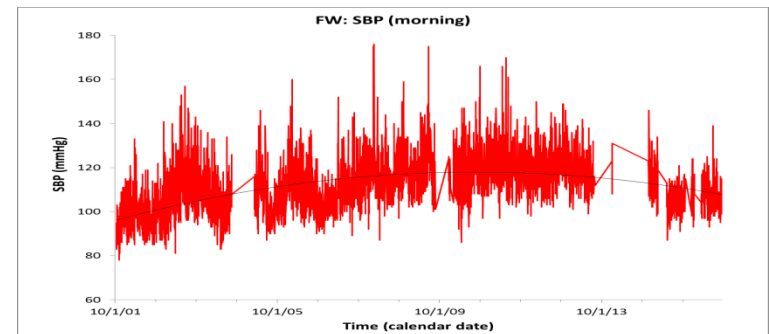
- **routinely screen for VVDs** (VVDs like CHAT are diagnosed in all geographic locations examined thus far)
- **perform continued monitoring** when needed (e.g., patients on anti-hypertensive treatment).

**Worldwide Blood Pressure Overswinging (CHAT\*), A Silent Risk (Greater than that of Hypertension) of Stroke and Other Morbid Events**



**Geographic Locations and Populations Studied**

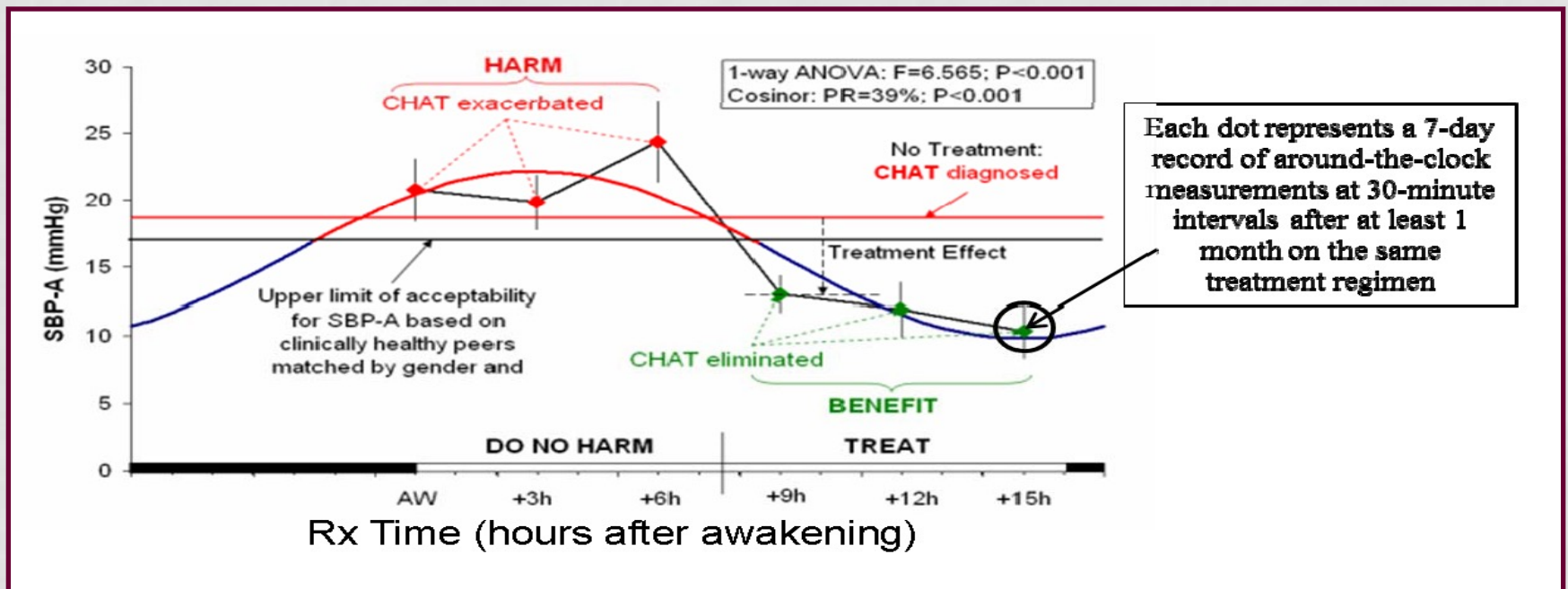
\* CHAT (Circadian Hyper-Amplitude-Tension) incidence in several geographic locations.





# ABPM: Treatment Optimization by Timing

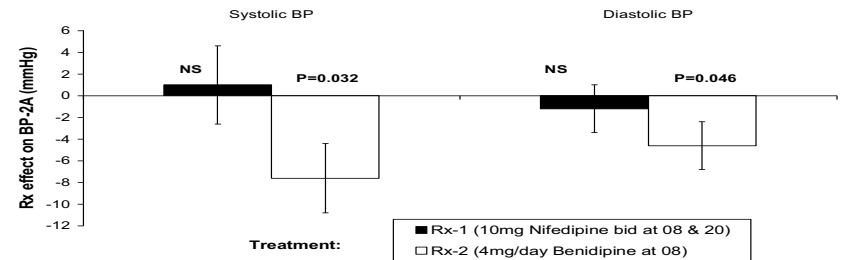
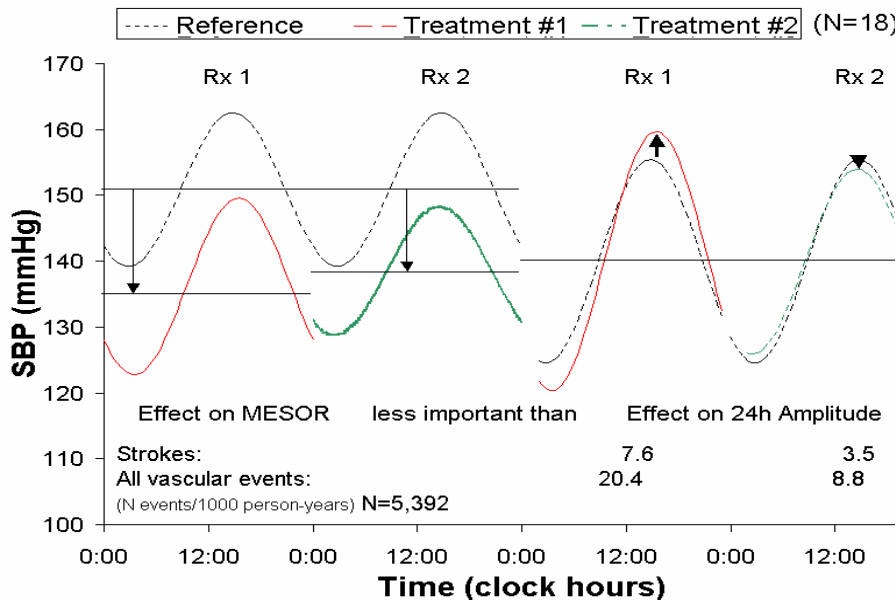
Treatment is best optimized by timing (**chronotherapy**) on an individualized basis. The **same dose** of the **same anti-hypertensive medication** given to the **same patient** has **different effects** on BP and BP variability depending on **when** it is taken daily. The optimal treatment time **differs among patients**, in part because of **differing VVDs**. About 2/3 of patients are expected to benefit.



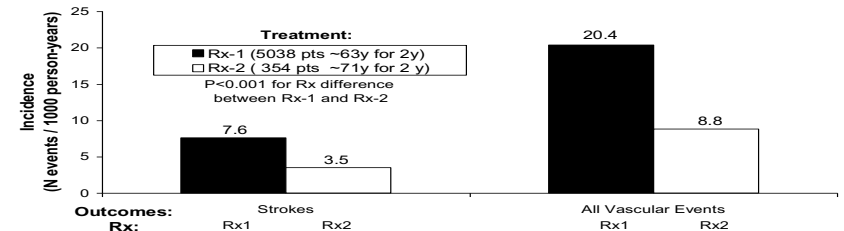
# ABPM: Treatment Optimization by Timing

Some VVDs can be treated.

Reducing an excessive BP amplitude (alleviating CHAT) reduces adverse cardiovascular events by more than a factor 2.



Outcomes of Long-Acting Calcium Antagonists Trials in Japan



# Discussion

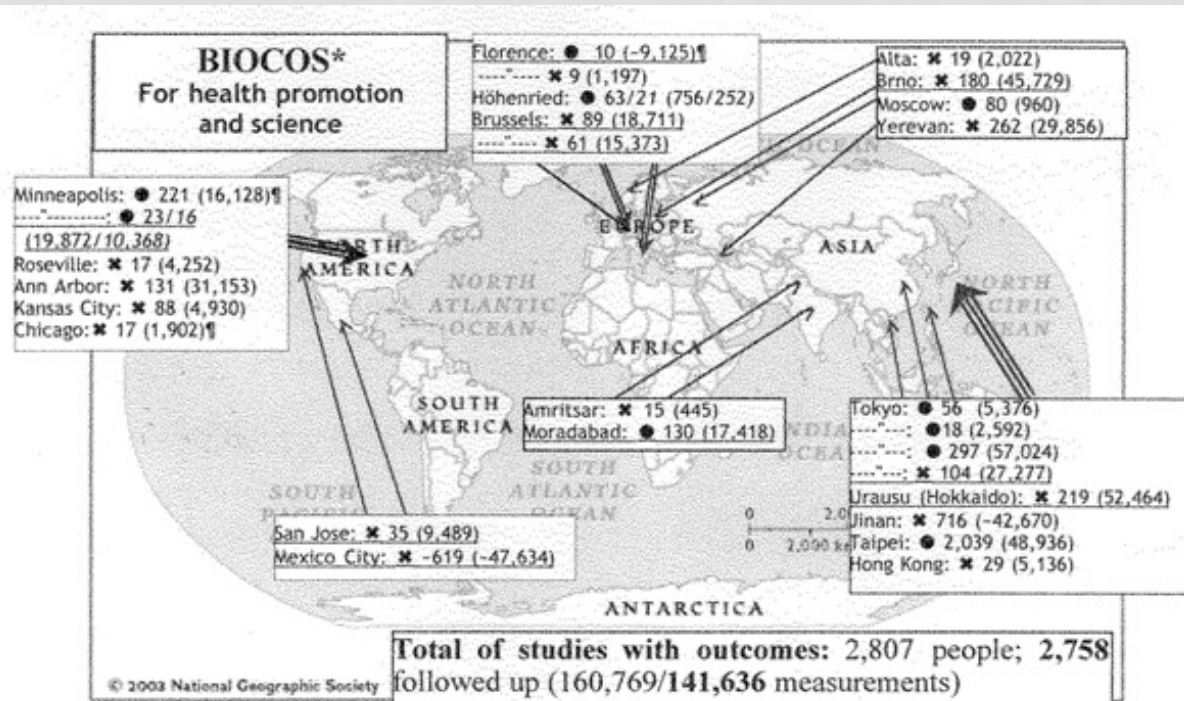
Important lessons were learned from BP monitoring, which now await **introduction into routine clinical care** with focus on both **primary and secondary prevention**.

Many more applications can benefit from a chronobiologic approach to BP monitoring, such as the **determination of healthy lifestyle choices** (e.g., tobacco use, alcohol and salt intake, and prayer), as already done in India.

**Longitudinal monitoring** of BP also contributes invaluable information regarding **environmental and cosmic influences on physio-pathology**.

# BIOCOS: Project on the BIOSphere and the COSmos

## Worldwide monitoring of blood pressure and heart rate



\*The BIOSphere and the COSmos: segment only on blood pressure (BP) and heart rate (HR)

KEY:

- Studies with *outcomes*: N pts: total / outcome (N measurements, total / outcome)
- ✱ Ongoing BIOCOS data collection: N profiles (N measurements) up to and including 7-day or longer series underlined

Reference values in health obtained mostly in USA (>3,000 people), Italy & Japan by self-, staff- and automatic measurements from days to decades, still accumulating (not shown)

¶ Many variables other than BP and HR are being monitored as time series and chronometrically analyzed for altered variability patterns in Minnesota and elsewhere for up to 147 variables, including many kinds of clinical chemistry. See bibliography on website:  
<http://www.msi.umn.edu/~halberg/>

As to **science**, longitudinal monitoring for decades led to the mapping, in addition to circadian and circannual, of circaseptan, circasemiannual, circannual, circadecadal, circadidecadal and circaquindecadal period and acrophase charts.

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# THANK YOU

Acknowledgements:  
BIOCOS Members Worldwide

In fond memory of  
***Franz Halberg***

