WORLDWIDE MONITORING OF BLOOD PRESSURE

GERMAINE CORNELISSEN, FOR BIOCOS

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.

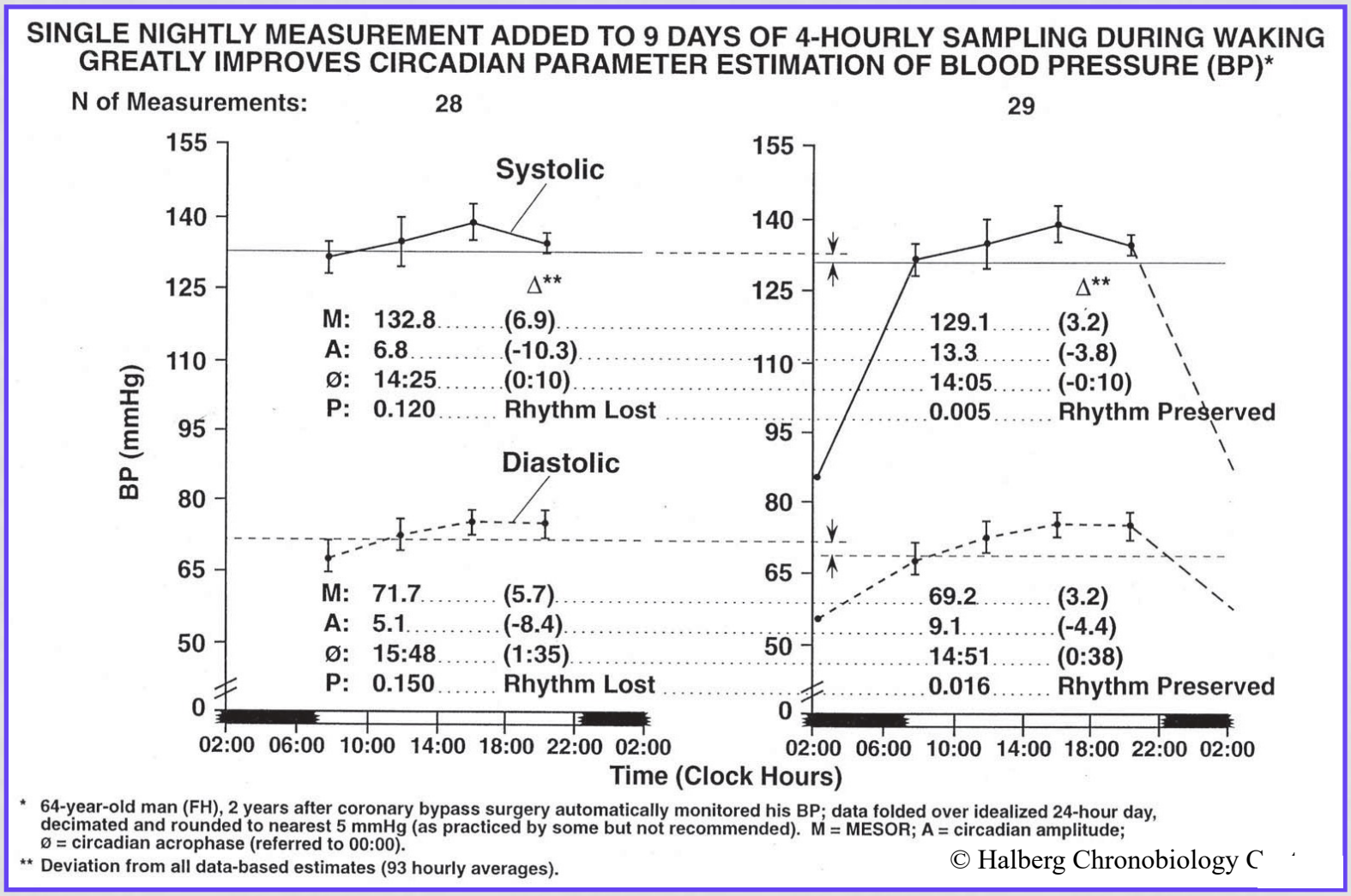
Self-Measurements

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.

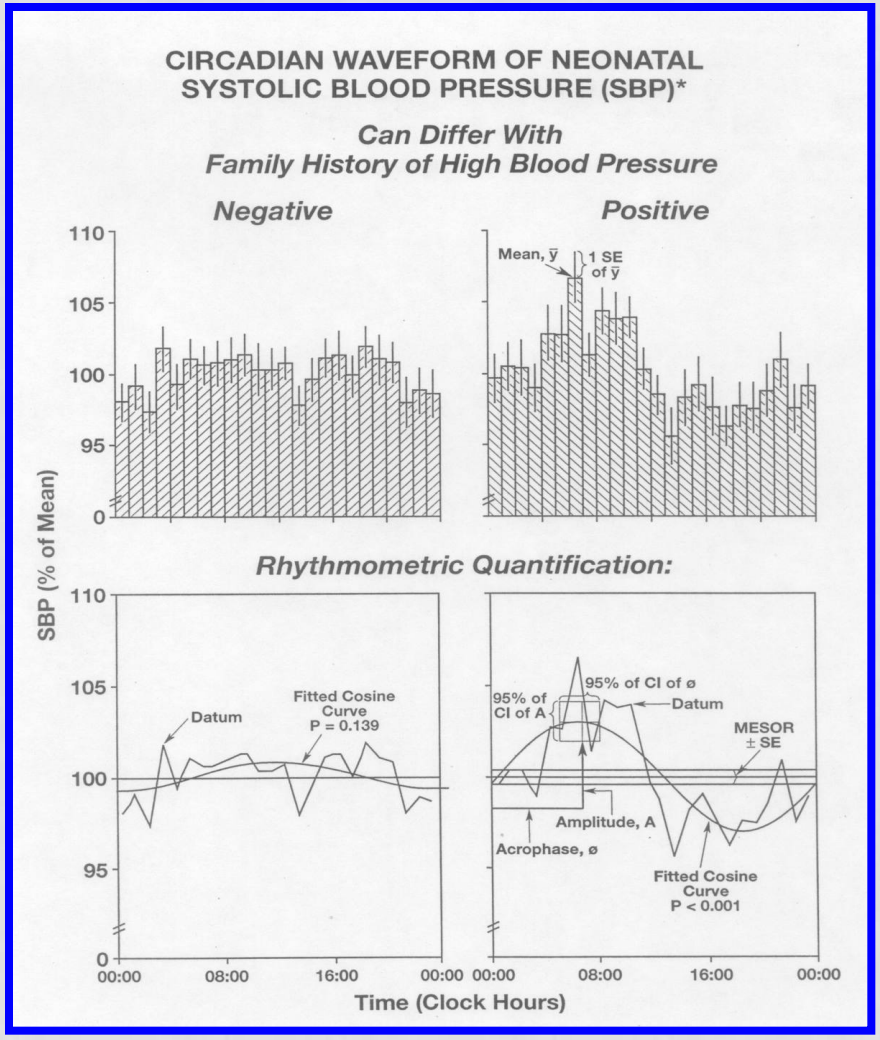
Despite the obvious shortcomings of self-measurements, important findings were made that laid the **foundation for recognizing the importance of BP variability**.

Self-Measurements



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.

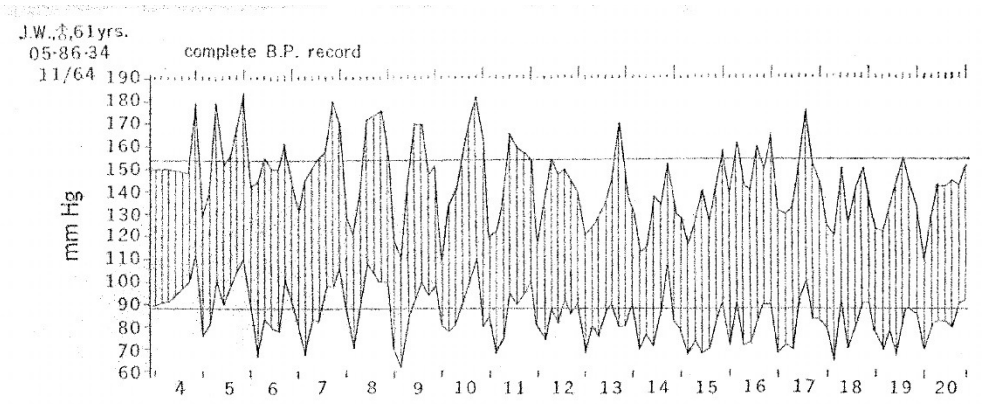


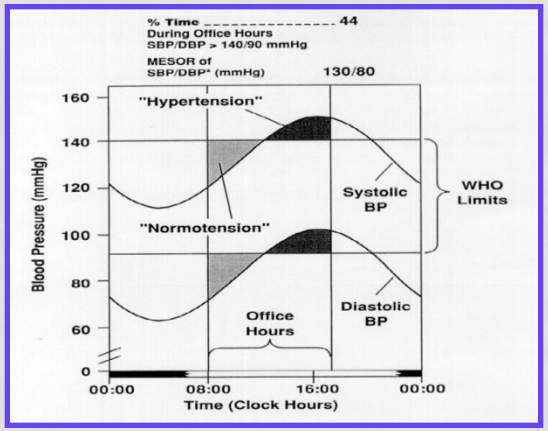
Staff Measurements

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. …"

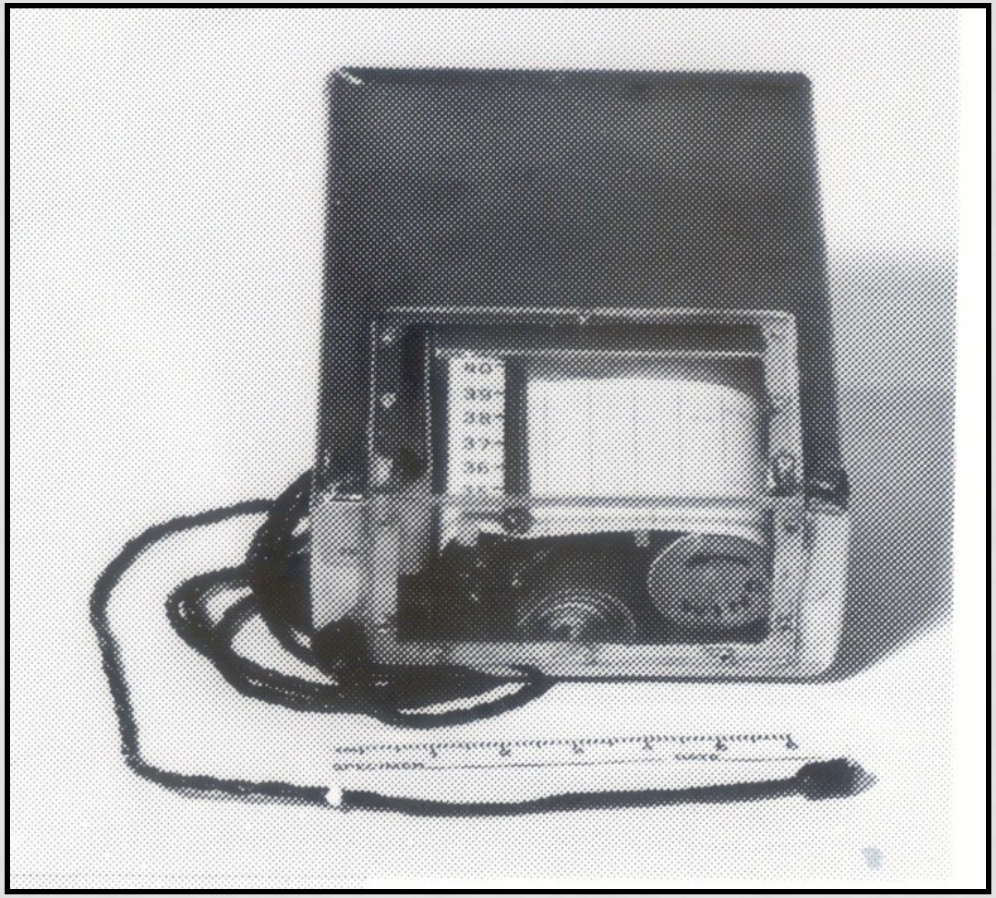
Bartter's patient diagnosed as normotensive in the morning and hypertensive in the evening





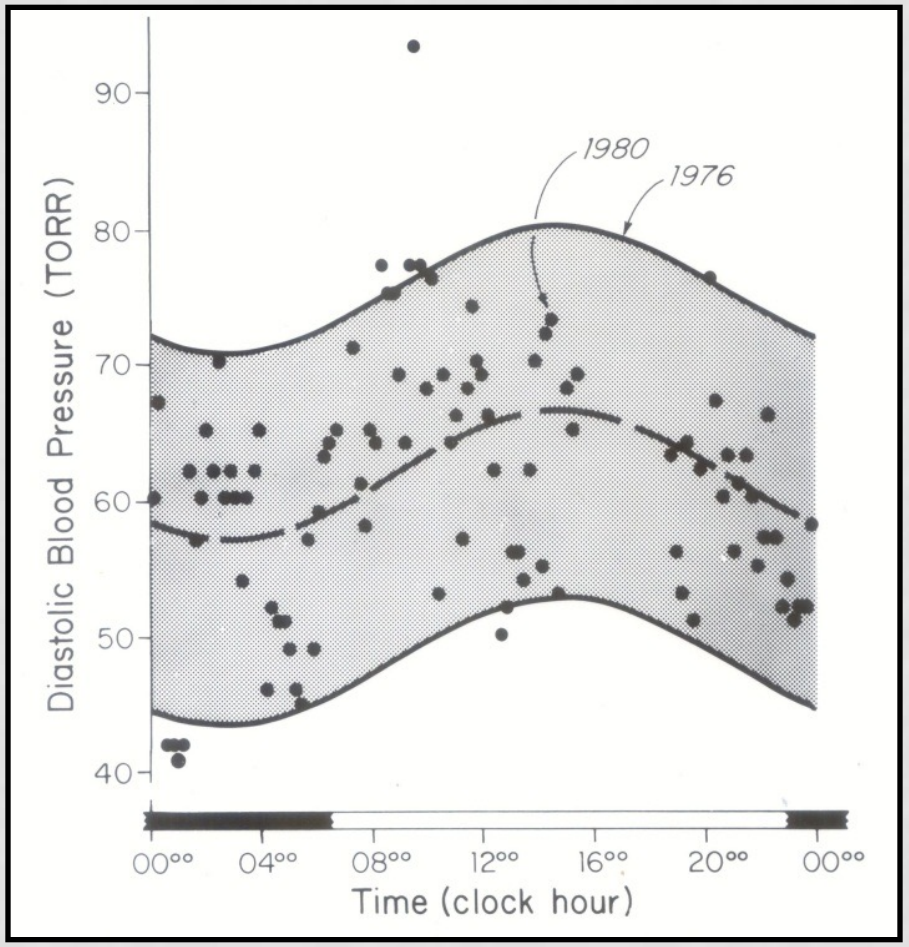
Arteriosonde: an analog BP monitor (1970s)

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**.



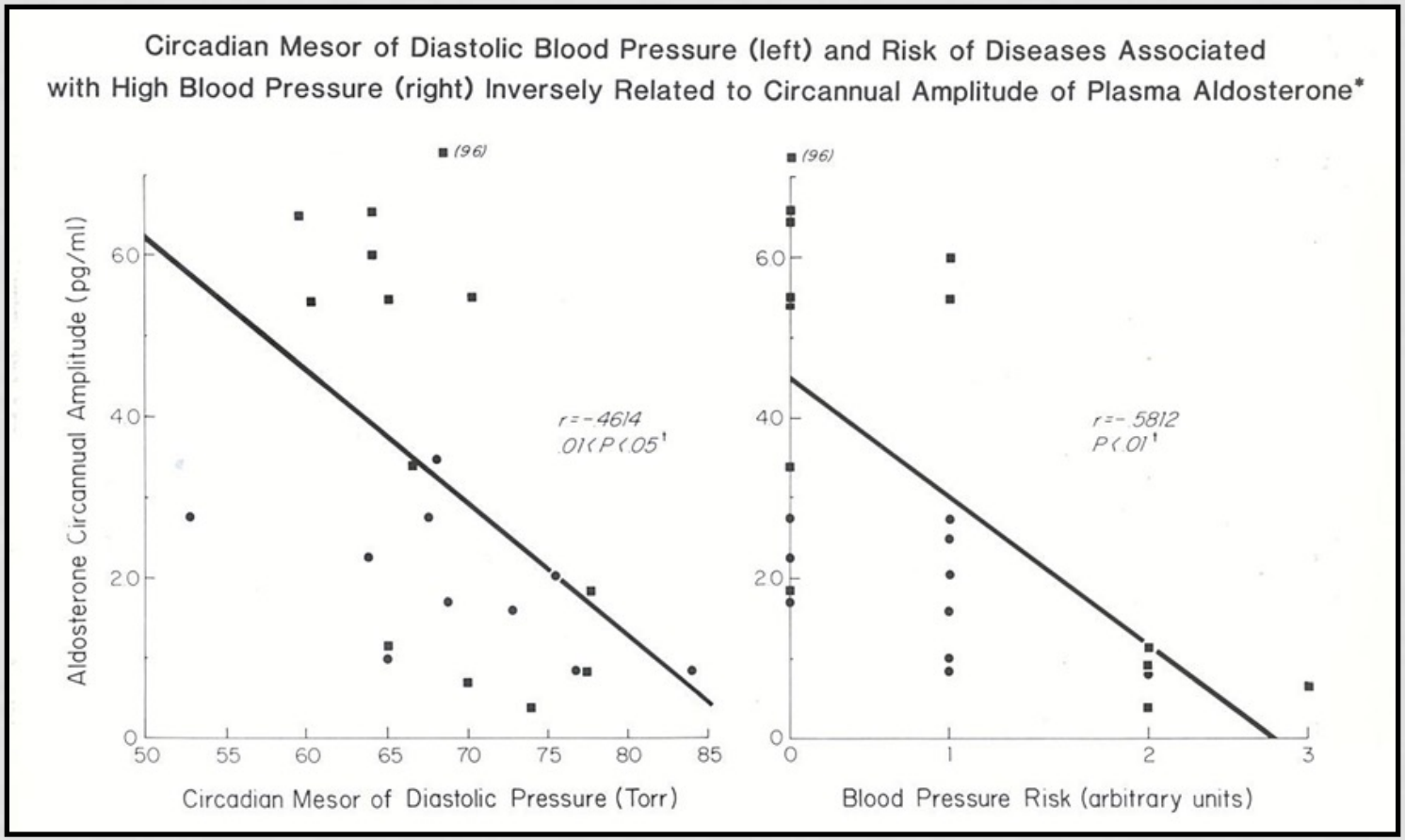
Arteriosonde: an analog BP monitor (1970s)

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.



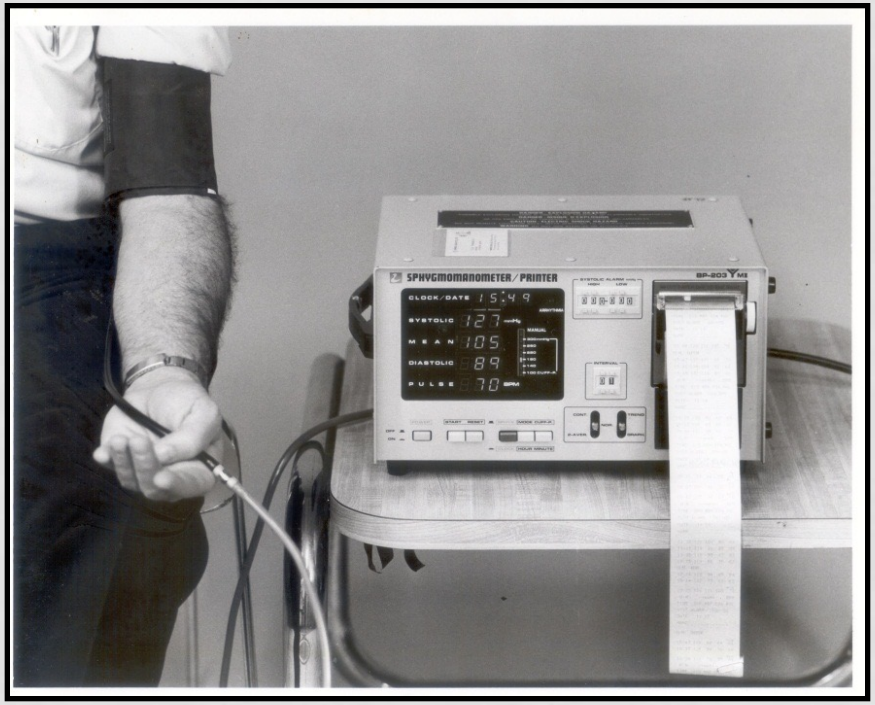
Arteriosonde: an analog BP monitor (1970s)

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



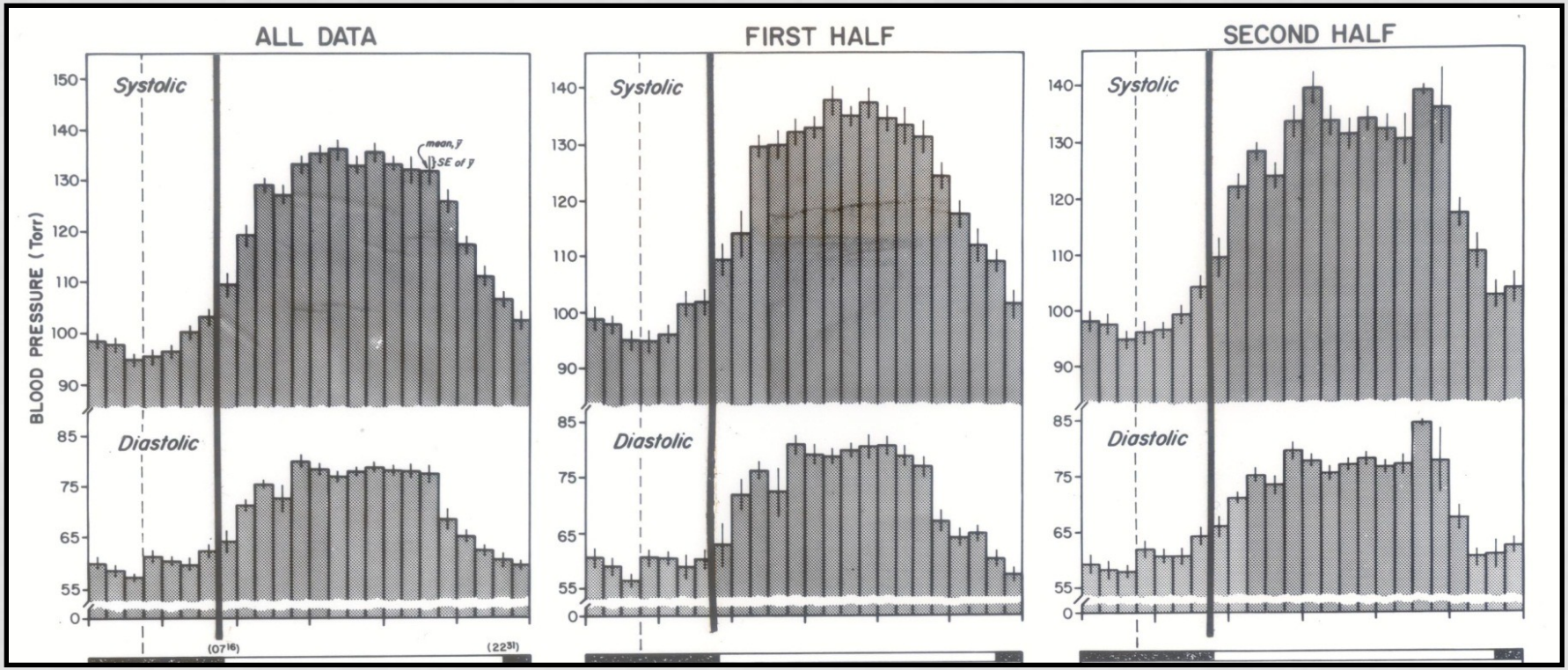
Portable Nippon-Colin BP monitor (1980s)

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



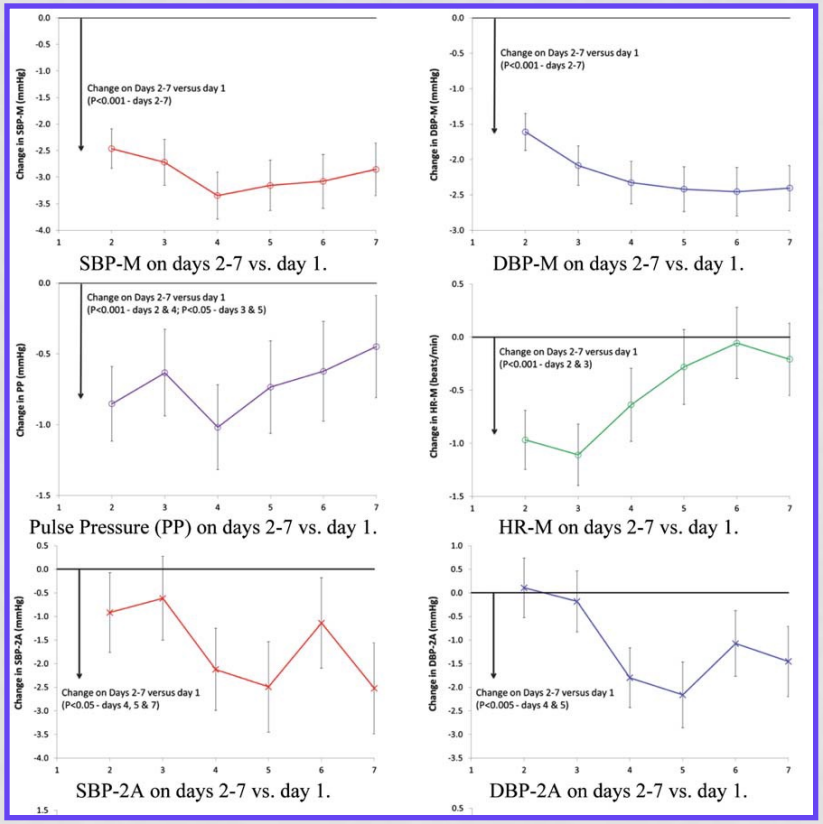
Portable Nippon-Colin BP monitor (1980s)

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**.

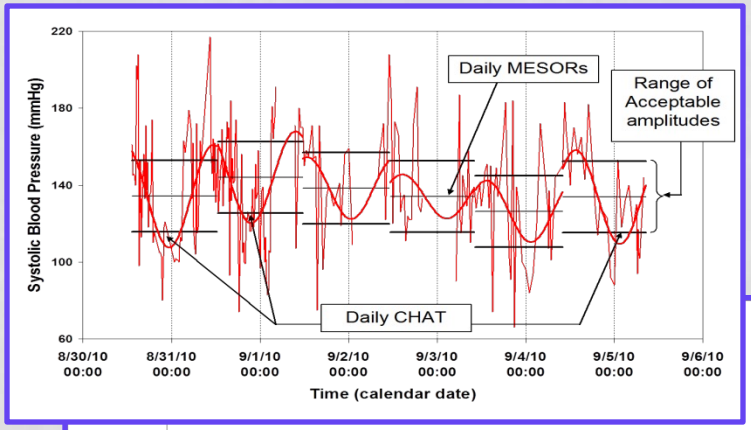


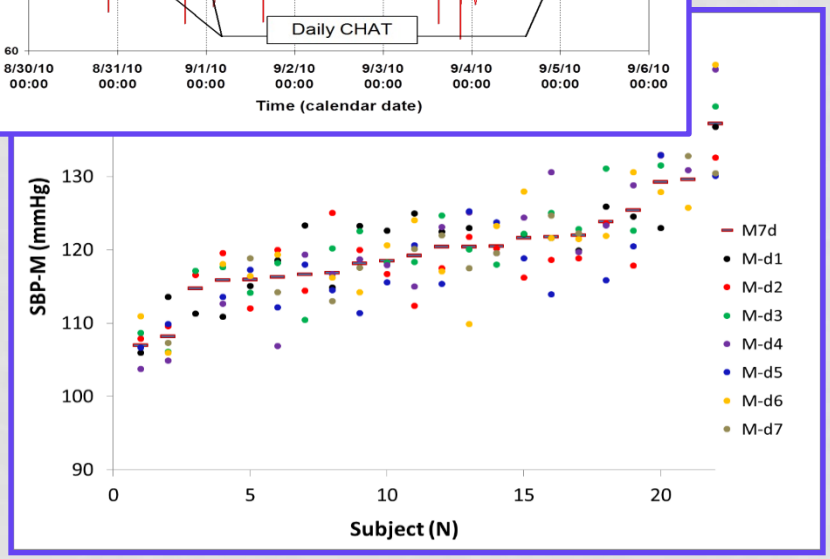
Portable Nippon-Colin BP monitor (1980s)

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



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





Portable Nippon-Colin BP monitor (1980s)

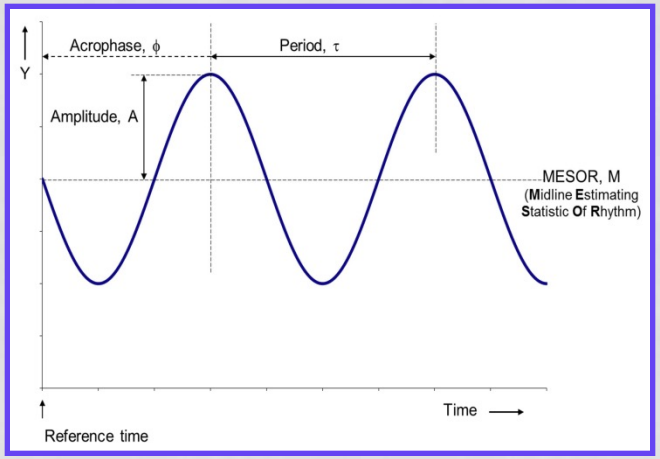
We showed that by extending the monitoring span from 24 to 48 hours, the uncertainty on the estimation of circadian parameters was reduced by 30%, with another 10% gain by prolonging the record to 7 days.

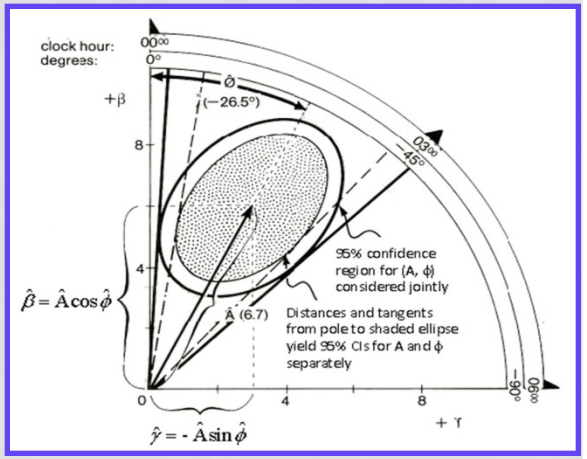
Monitoring for 7 days at the outset has been recommended in several consensus meetings

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

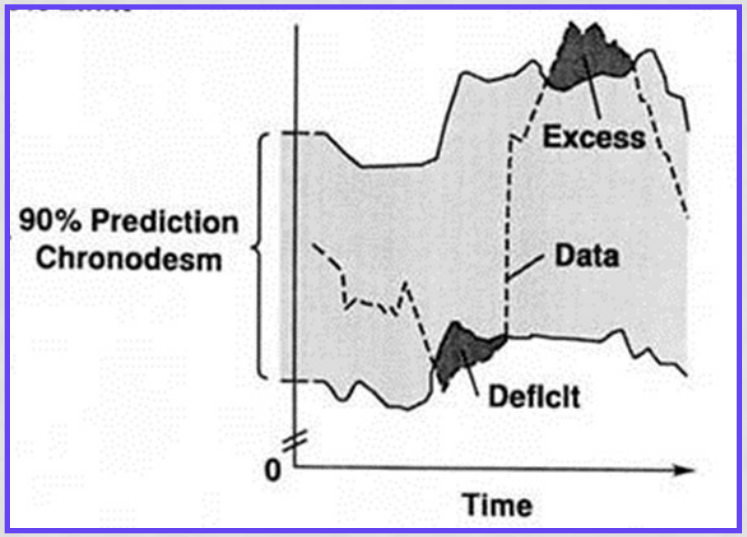
Ambulatory BP monitoring: ABPM-630

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.





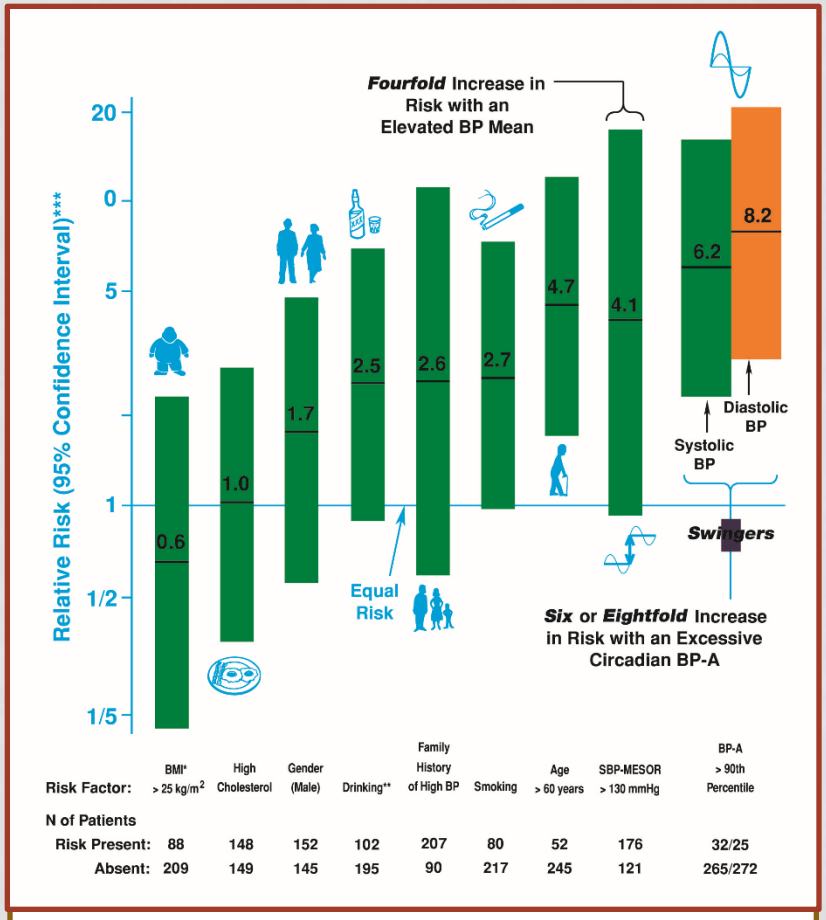
These data were essential to derive **time-specified reference values qualified by gender and age**, on which our **sphygmochron** analysis is based.



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**.

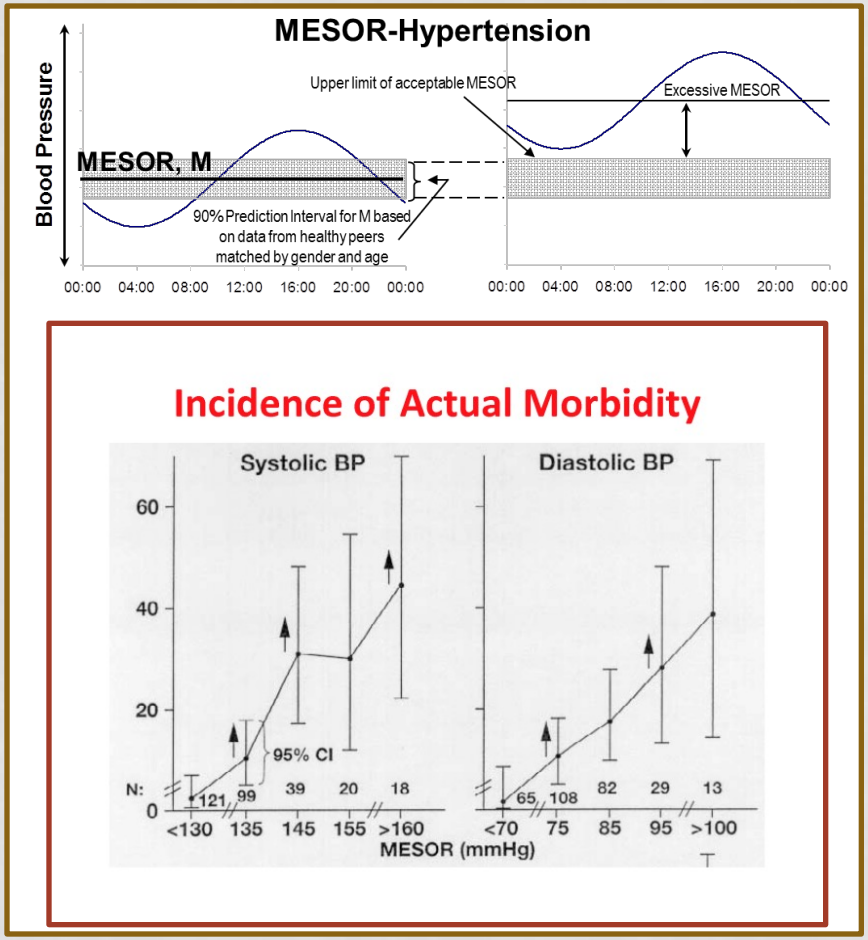
Outcome studies corroborated the **risk associated with an excessive circadian amplitude of BP (CHAT**, brief for Circadian Hyper-Amplitude-Tension).



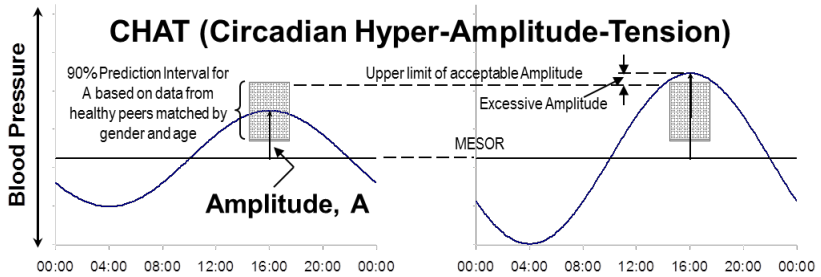
CHAT carries a higher risk of morbidity than high BP

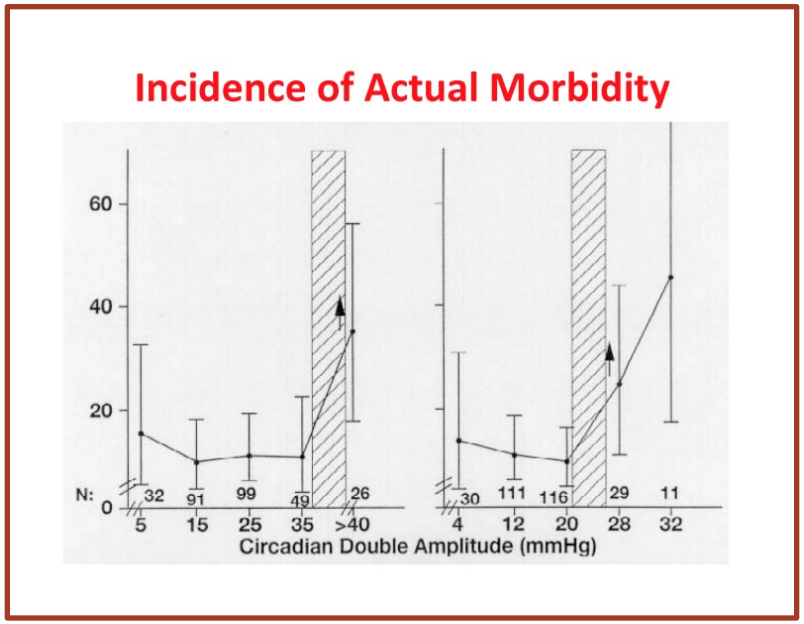
Ambulatory BP monitoring

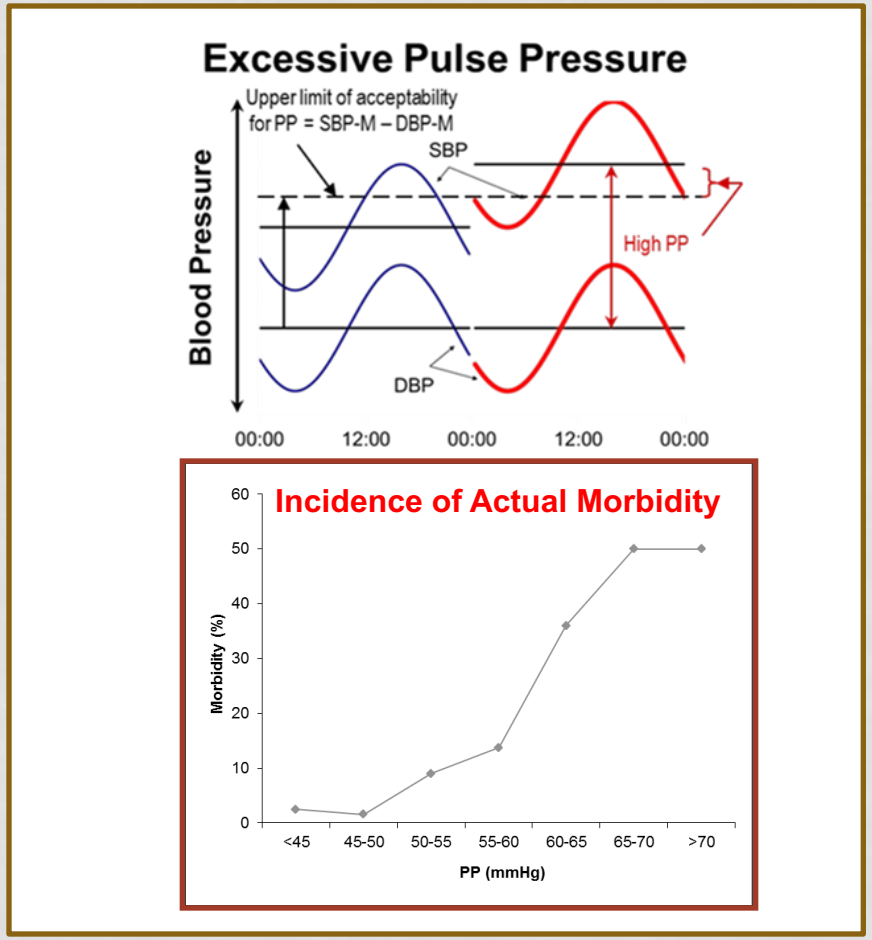
Outcome studies in Japan, Taiwan, Minnesota, the Czech Republic, and Germany further identified other abnormalities in the variability of BP and heart rate, which we named **Vascular Variability Disorders** (**VVDs**).



Ambulatory BP monitoring

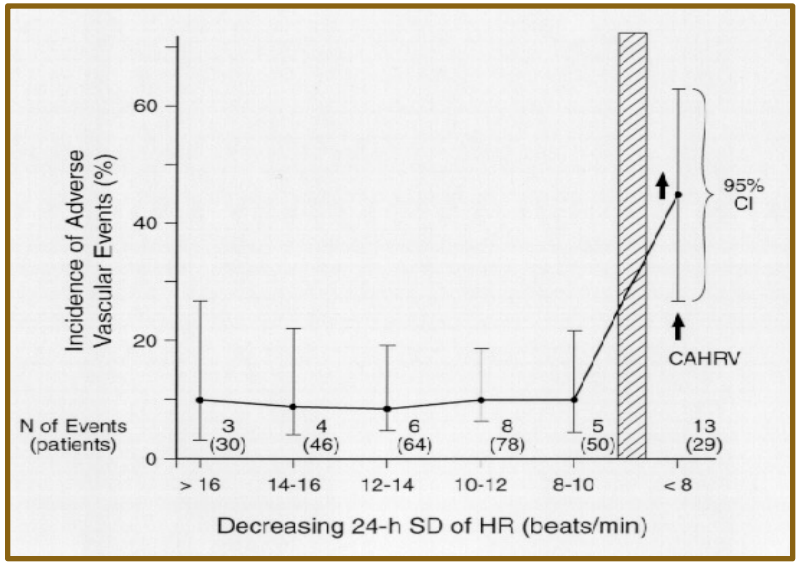




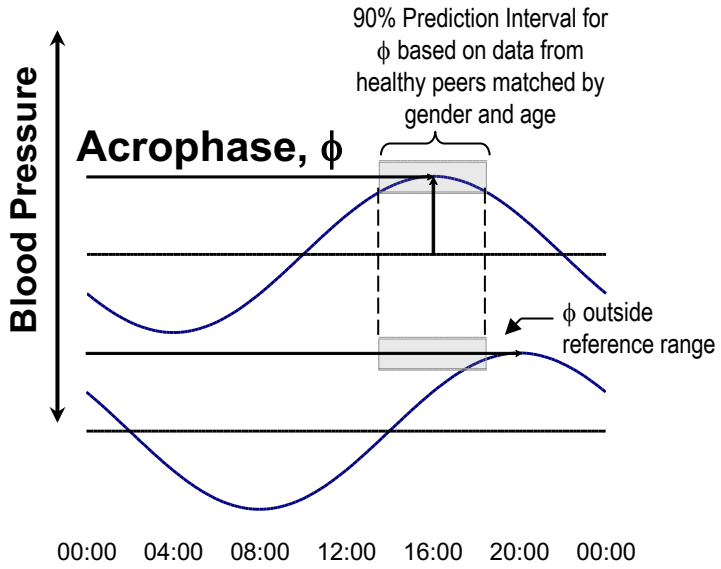


Ambulatory BP monitoring

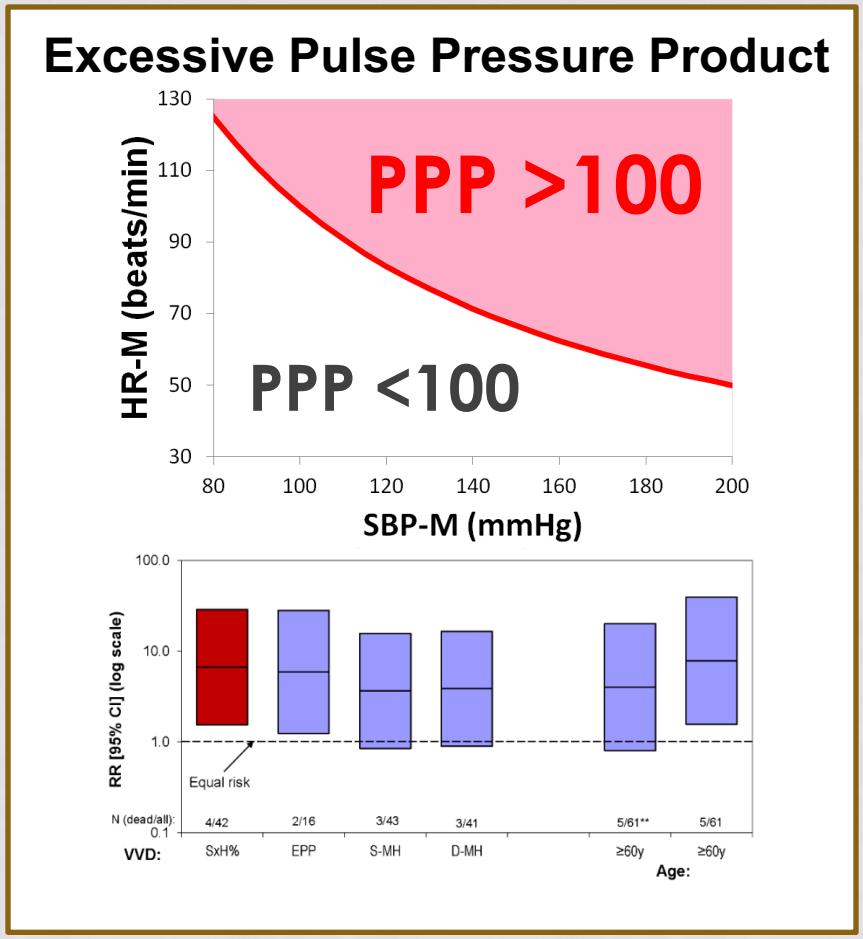
Decreased Heart Rate Variability

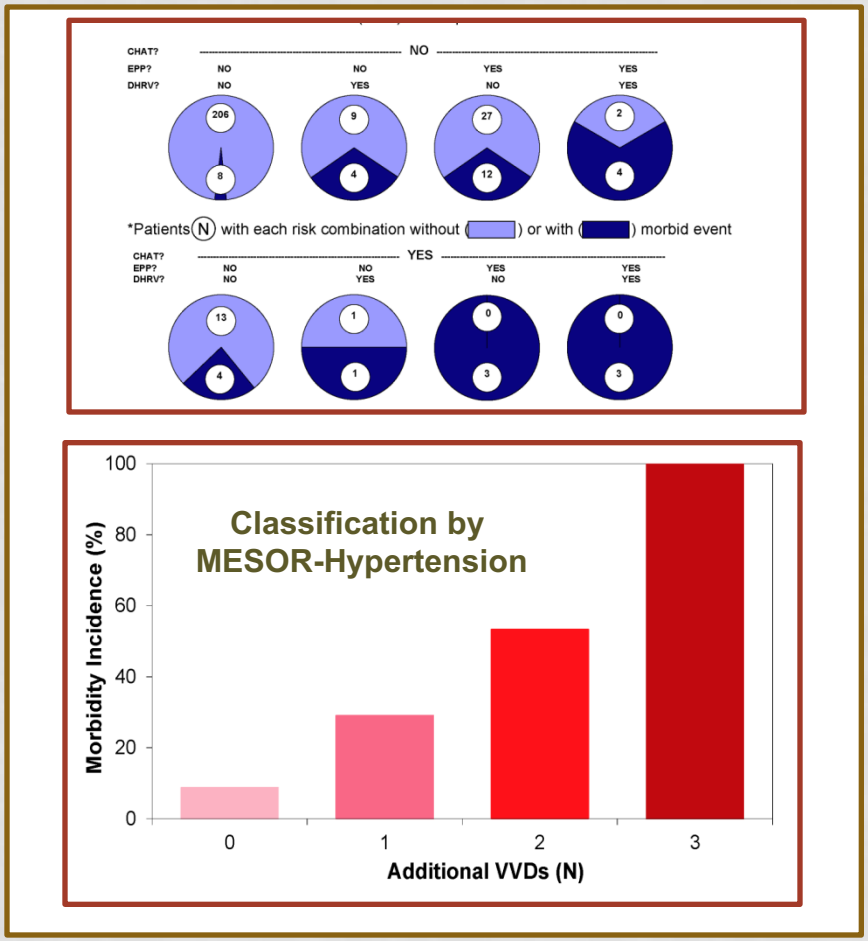


Ecphasia (and Ecfrequency)



Ambulatory BP monitoring





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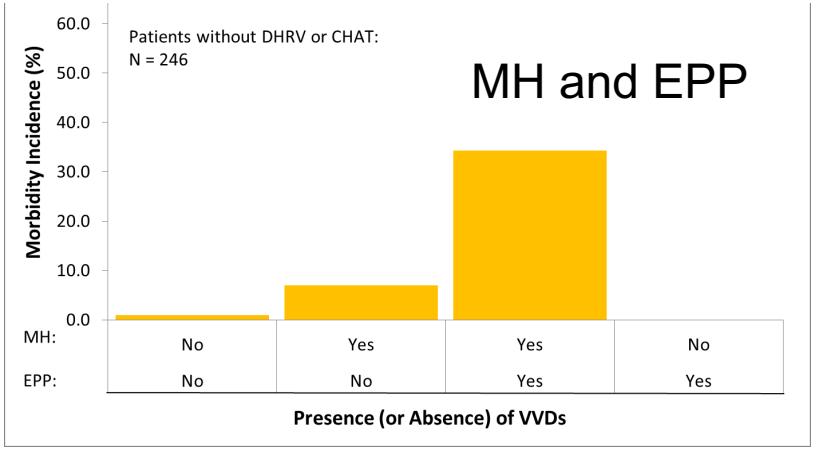

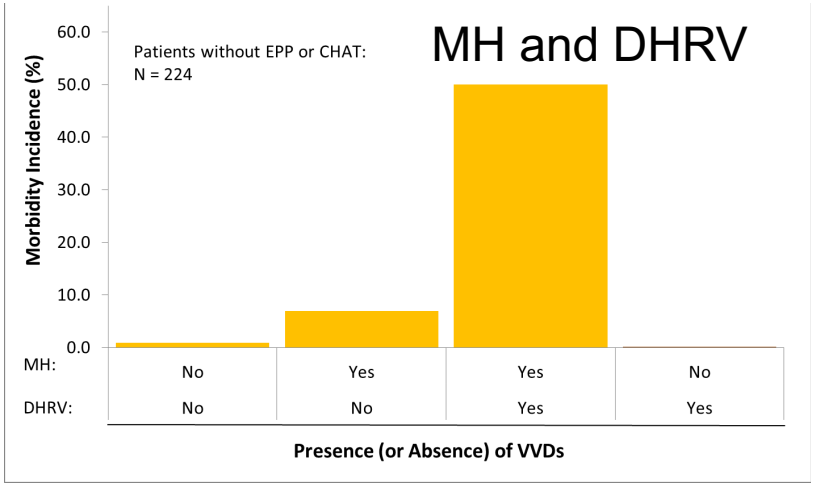

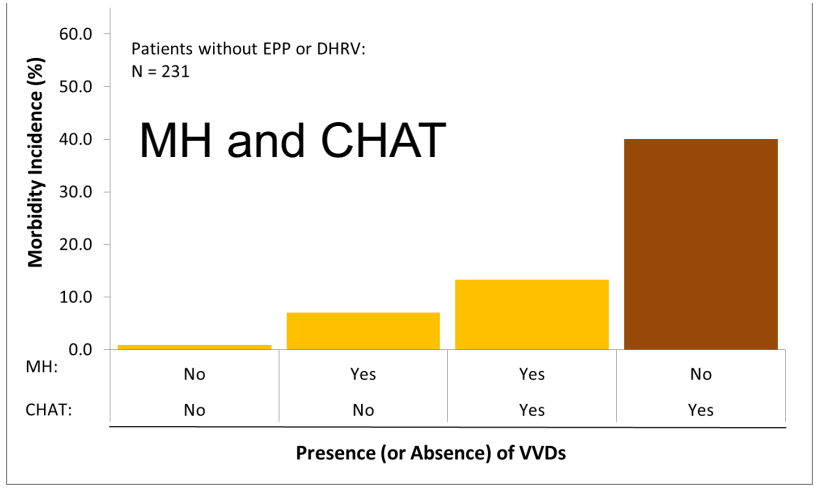

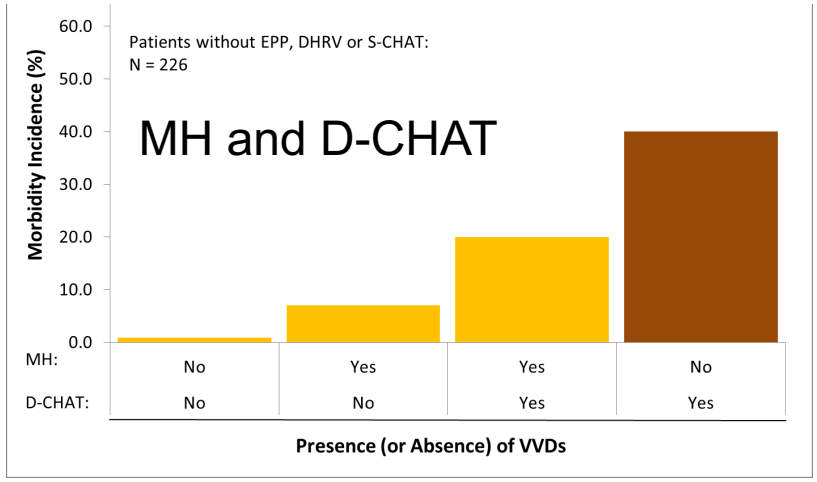

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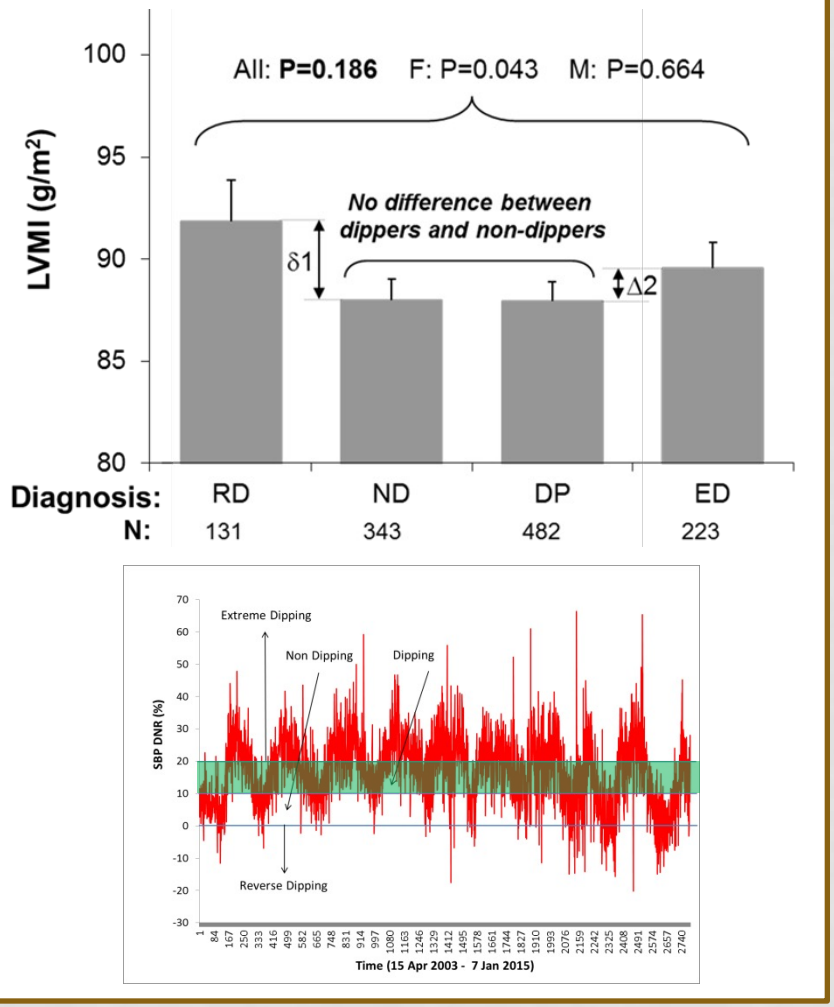

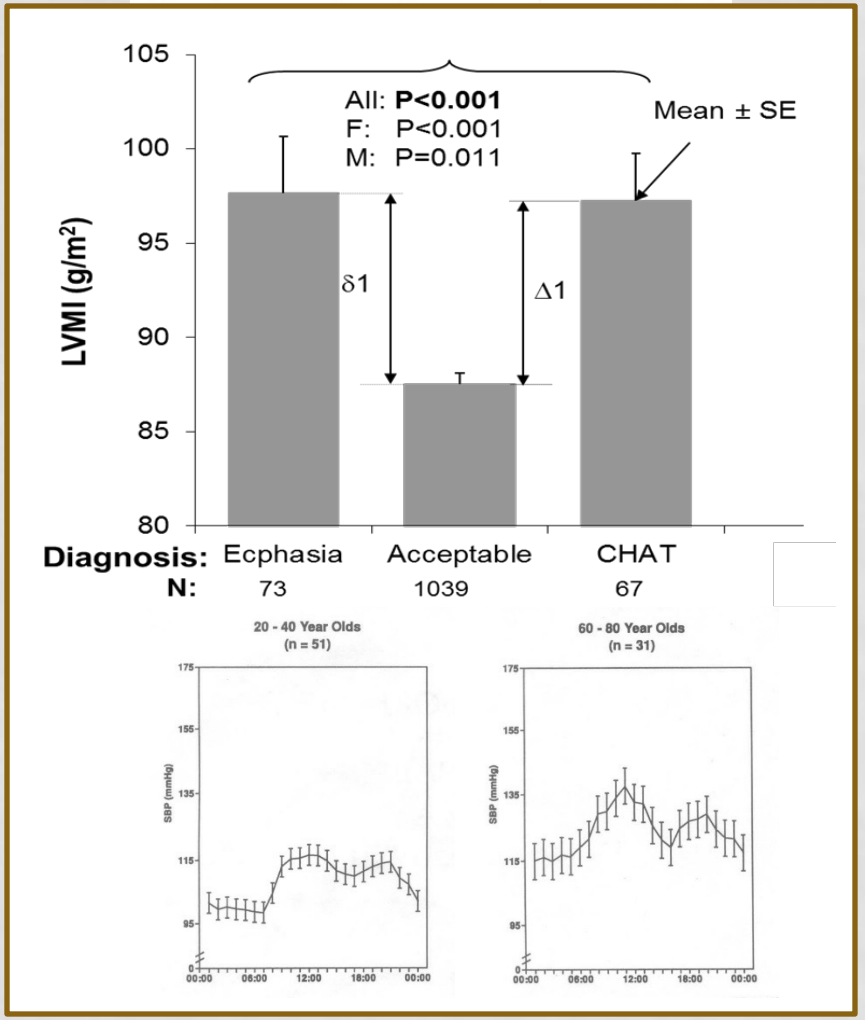

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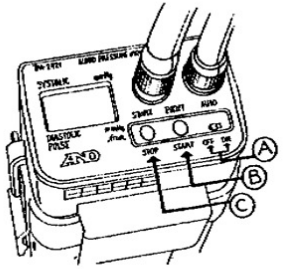
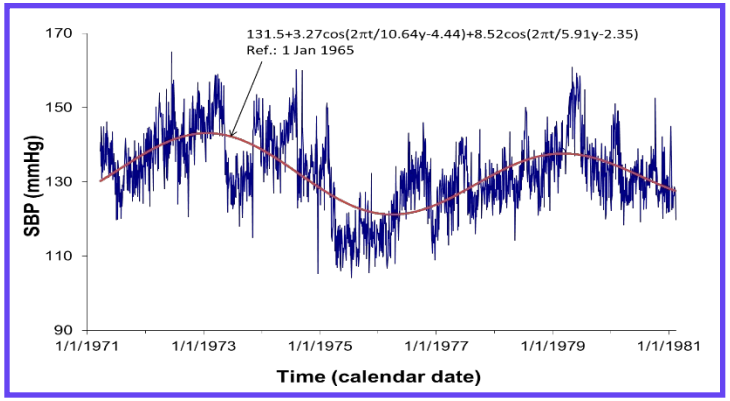
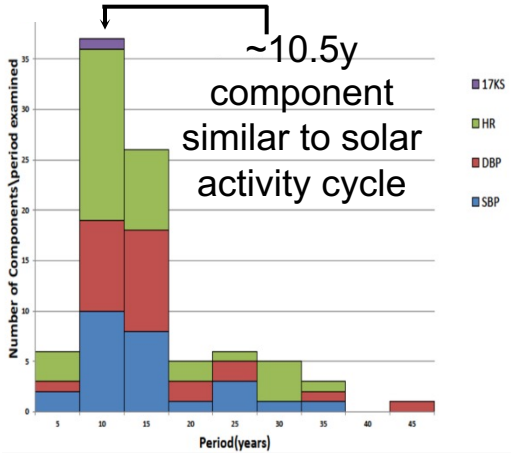


With smaller and lighter devices, continued surveillance became more readily feasible.

Uncovered long-period cycles suggested cosmic influence.

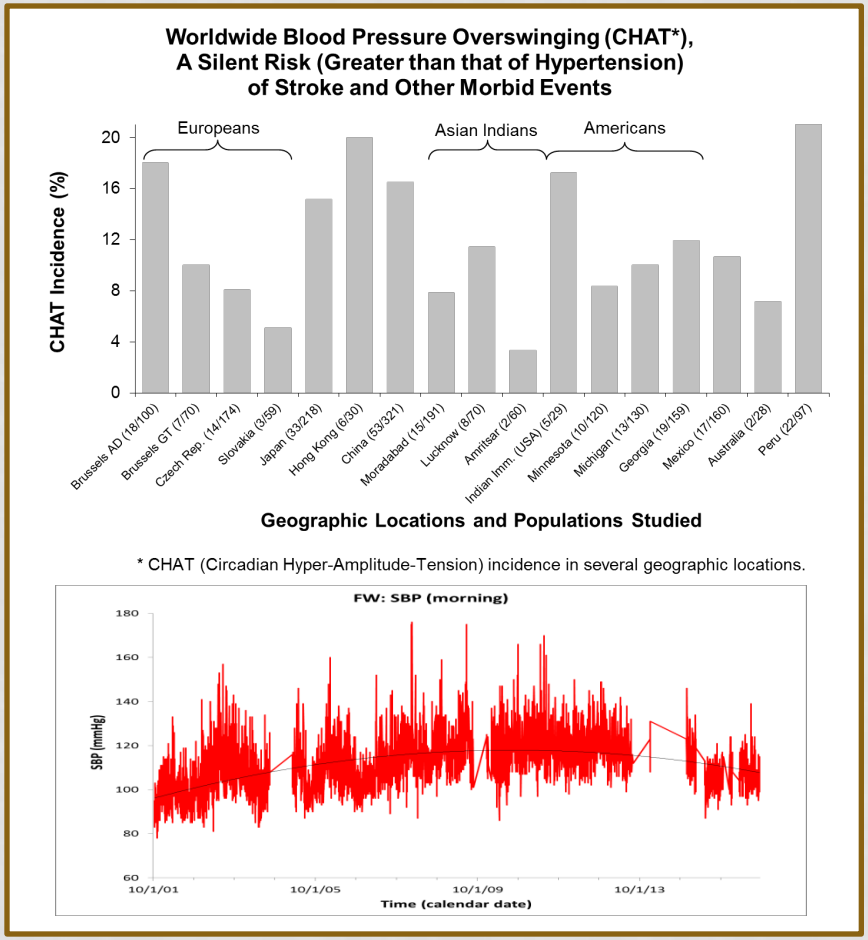




ABPM: Refined Diagnosis

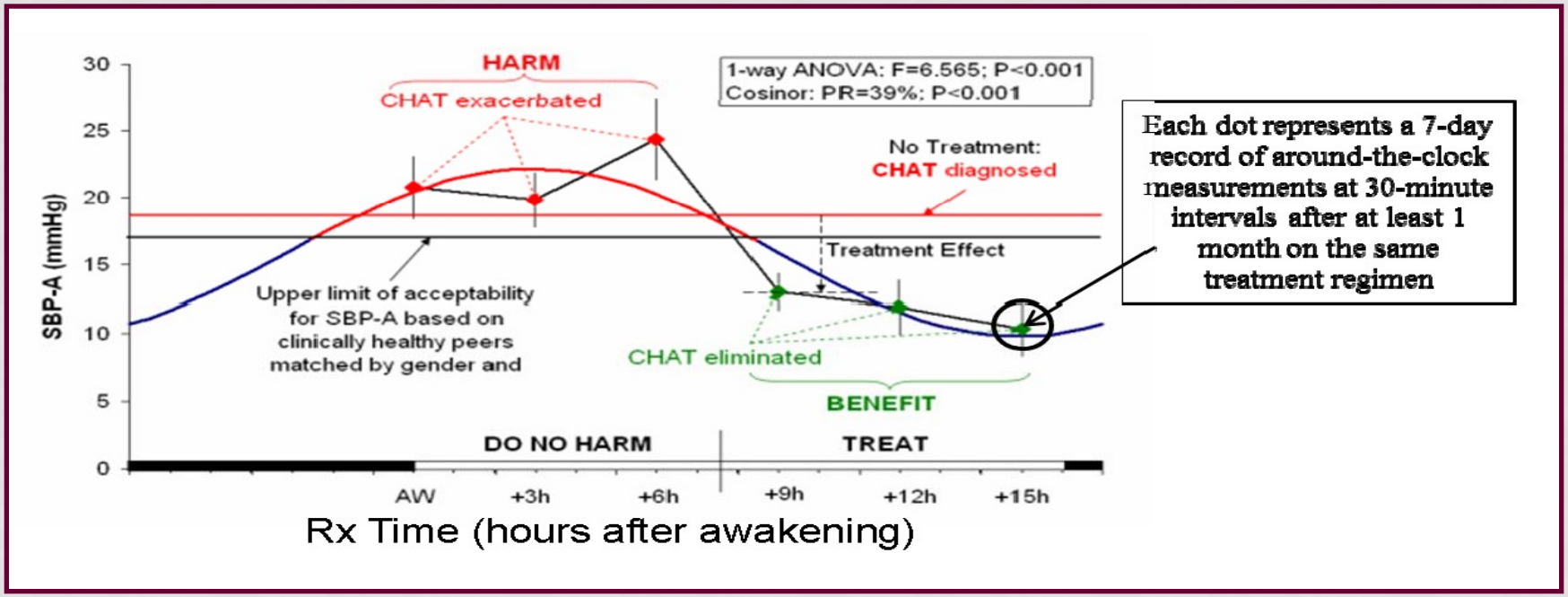
Ongoing monitoring around the world continues to accumulate evidence for the need to

- **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**).



ABPM: Treatment Optimization by Timing

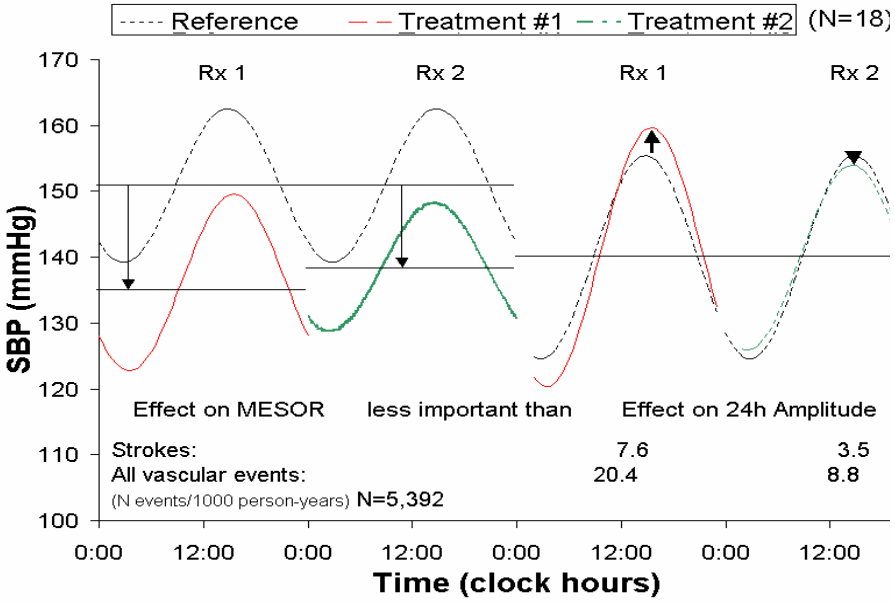
Treatment is best optimized by timing (**chronotherapy**) on an individualized basis. The **same dose** of the **same anti-hypertensive medication** given to the **same patient** has **different effects** on BP and BP variability depending on **when** it is taken daily. The optimal treatment time **differs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

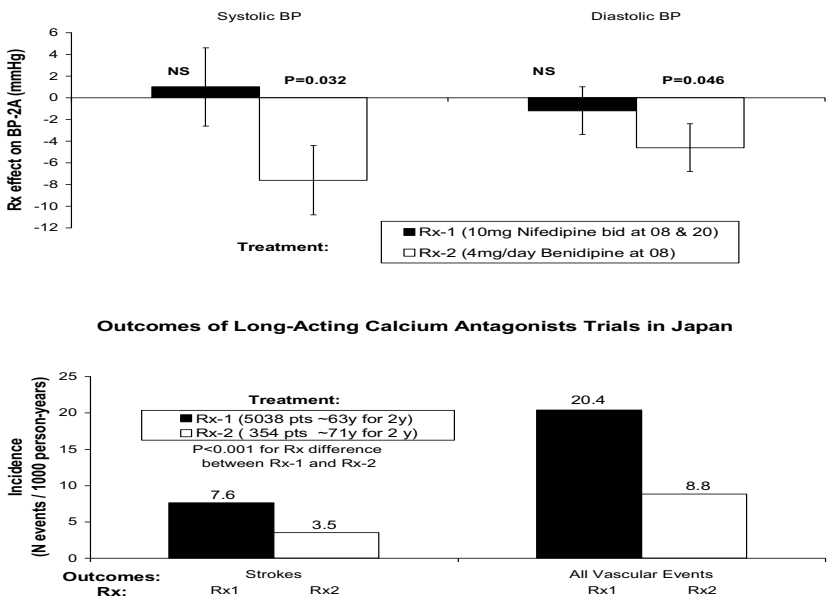


ABPM: Treatment Optimization by Timing

Some **VVDs can be treated**.

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



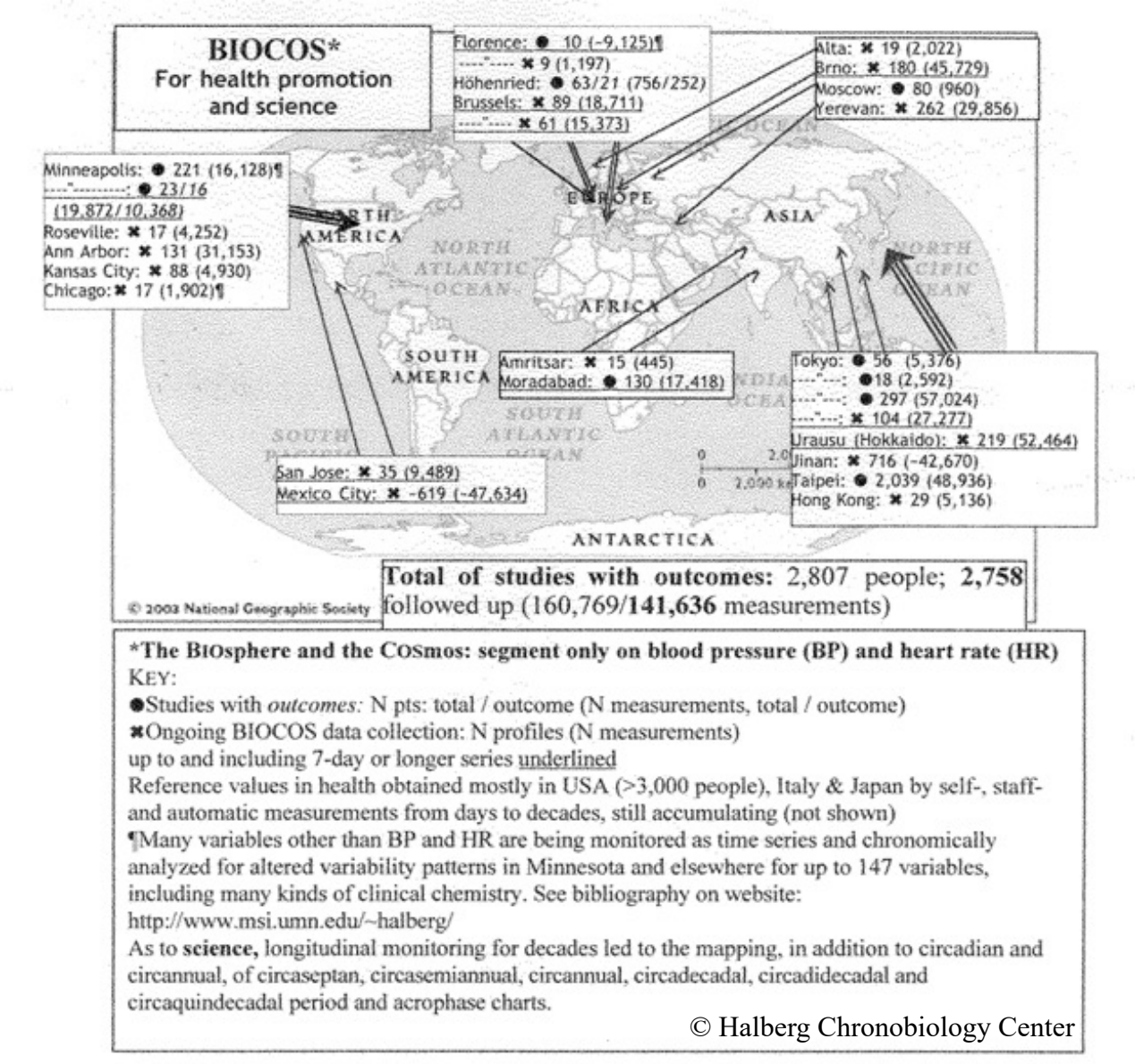


Discussion

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



THANK YOU

Acknowledgements:
BIOCOS Members Worldwide

In fond memory of
Franz Halberg