TIME PATTERNS IN STROKE INCIDENCE

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Disclosures

- I have no financial relationships or other conflict of interests to disclose, and I will not discuss off label use and/or investigational use in my presentation

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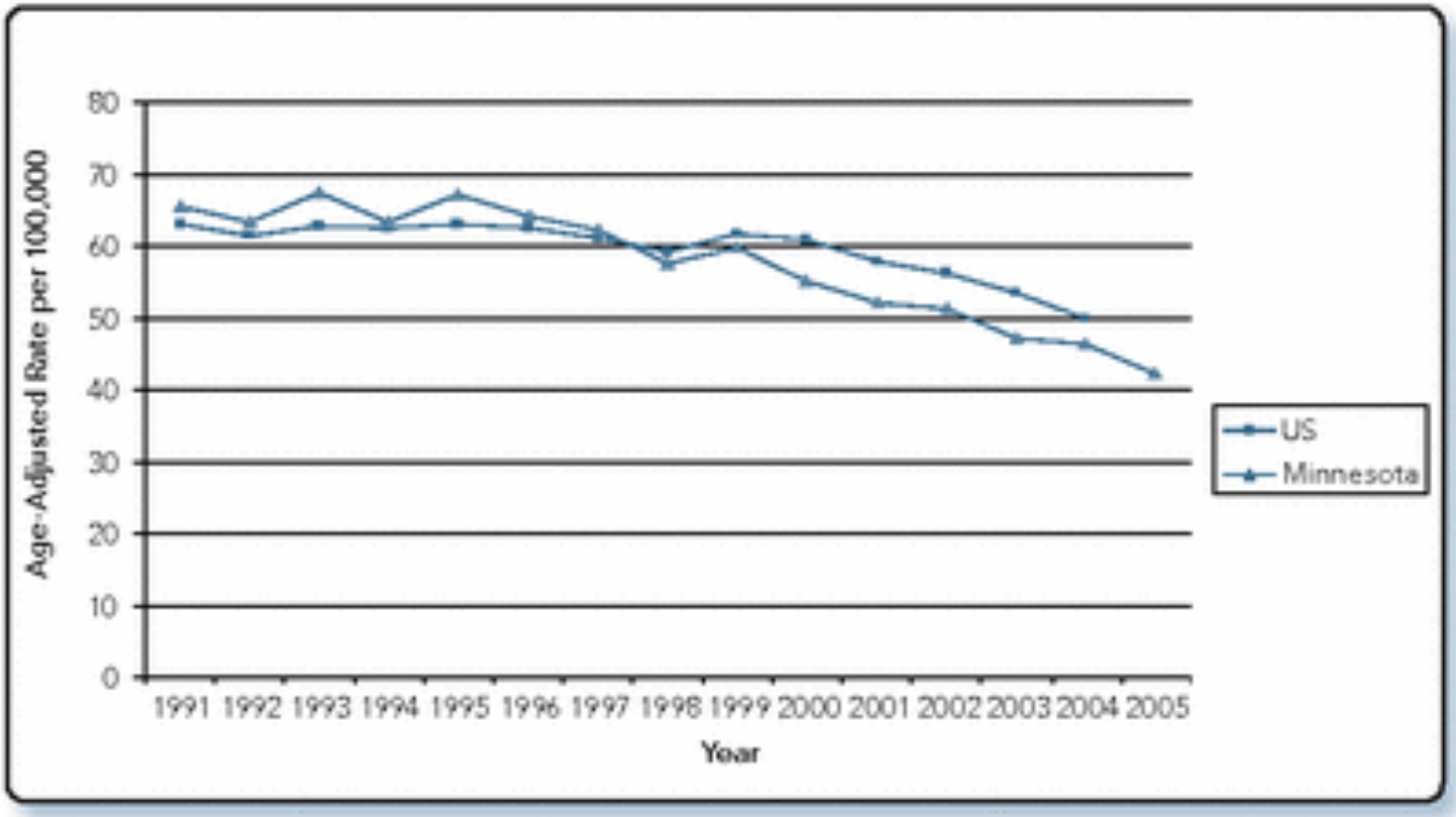
- Ownership interest in ---
- Consultant for ---

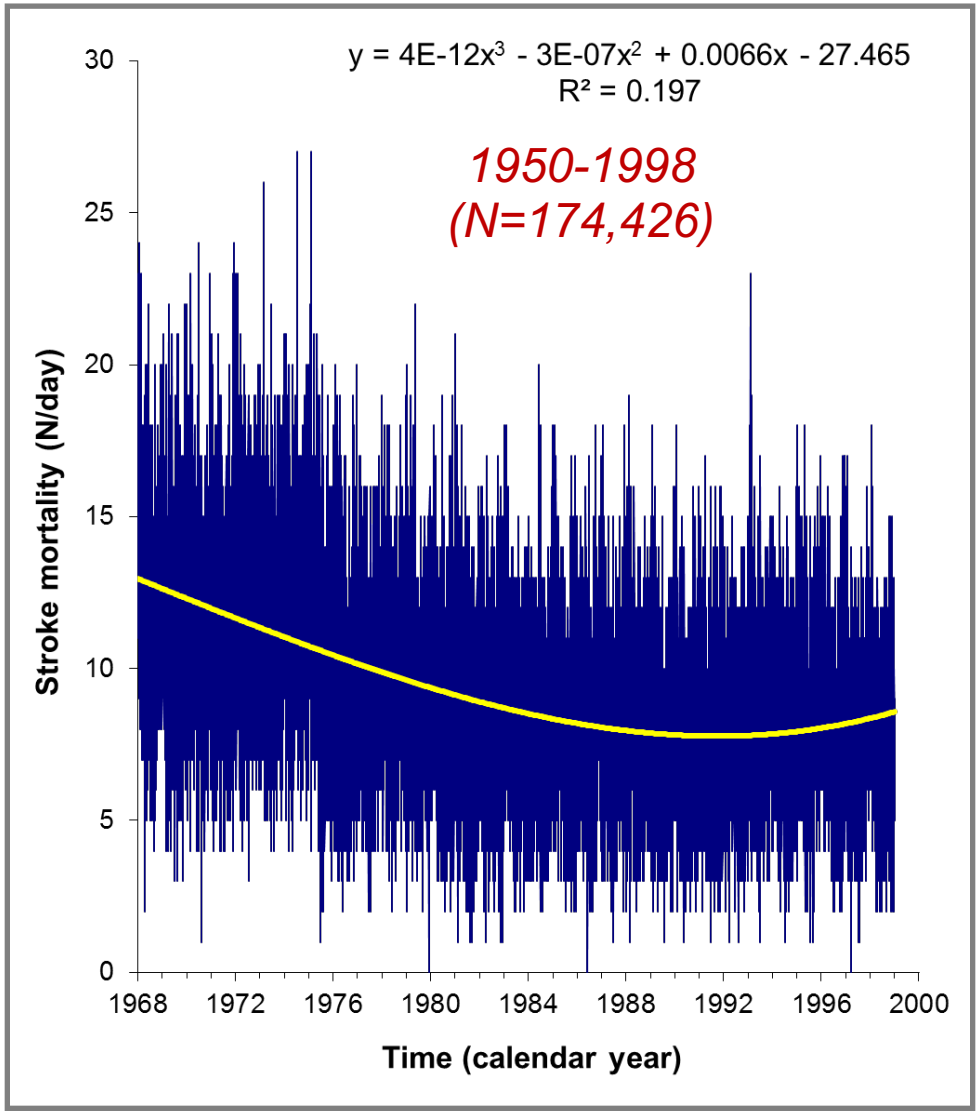
Stroke in Minnesota: 2014

- About 2.2% adults reported ever having had a stroke in their lifetime (>90,000 people)
- >5% (2,172) of all deaths are due to stroke
- >12,000 hospitalizations for acute stroke events at a cost of $418 million
- Compared to Caucasians, African-Americans have a 25%, and Asians have a 30% higher stroke death rate

From the MN Department of Health, Stroke Mortality is Declining in MN and Nationwide



This Decline is Part of a Longer-Term Trend

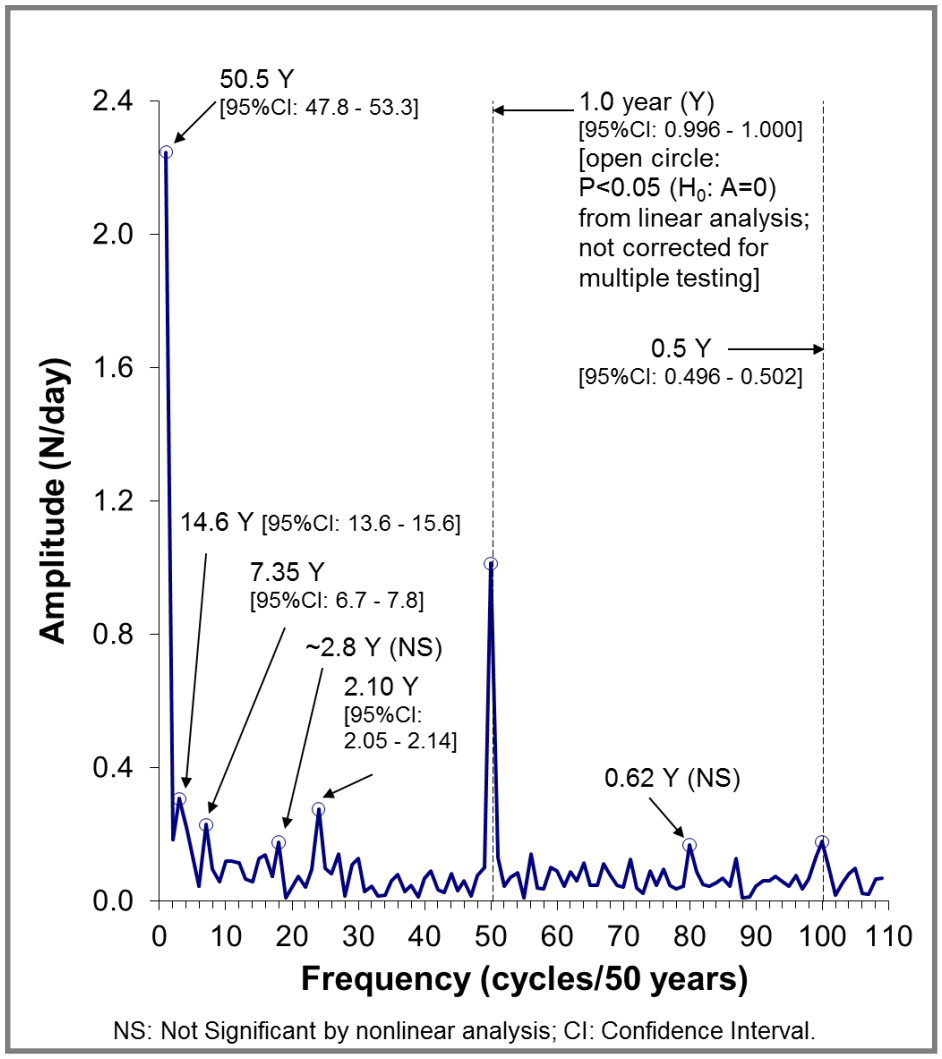


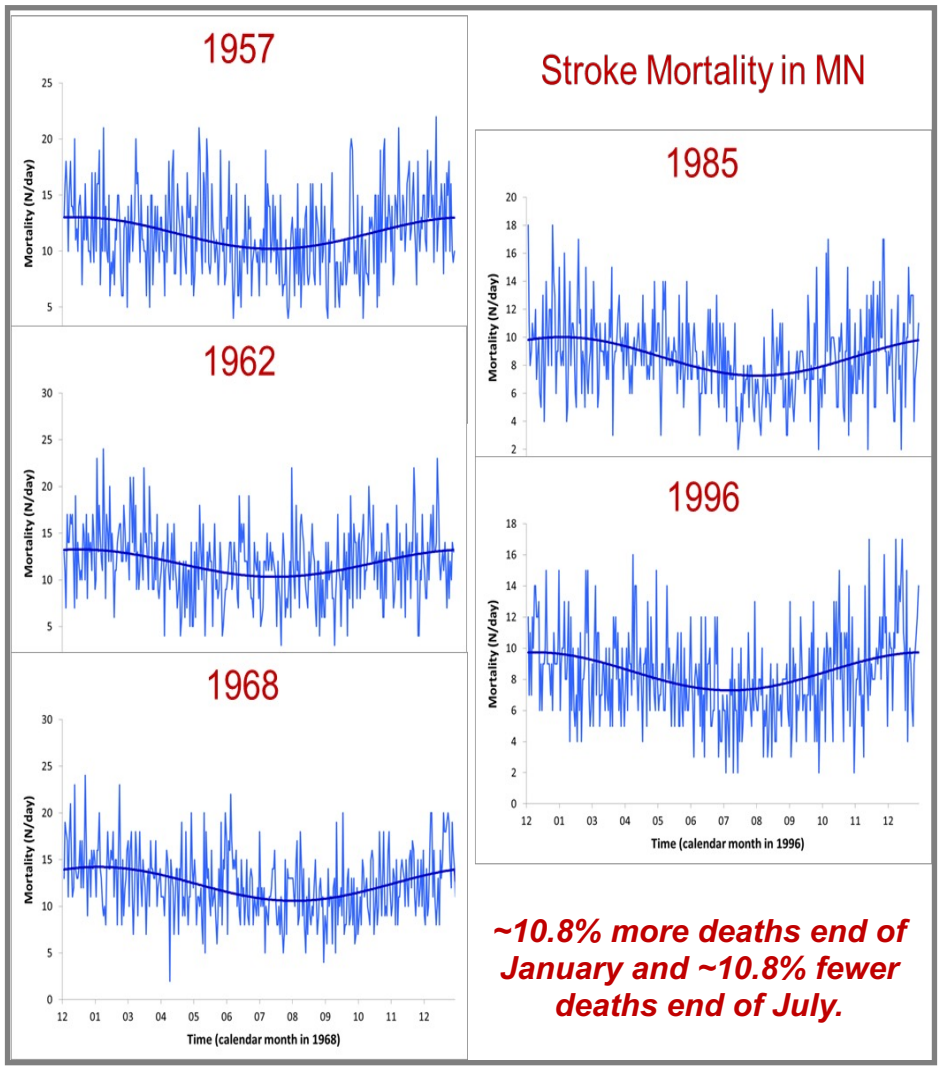
Stroke in Minnesota: 1950 -1998

Careful spectral analysis of these data – the daily incidence of stroke deaths in MN during half a century – reveals predictable patterns:

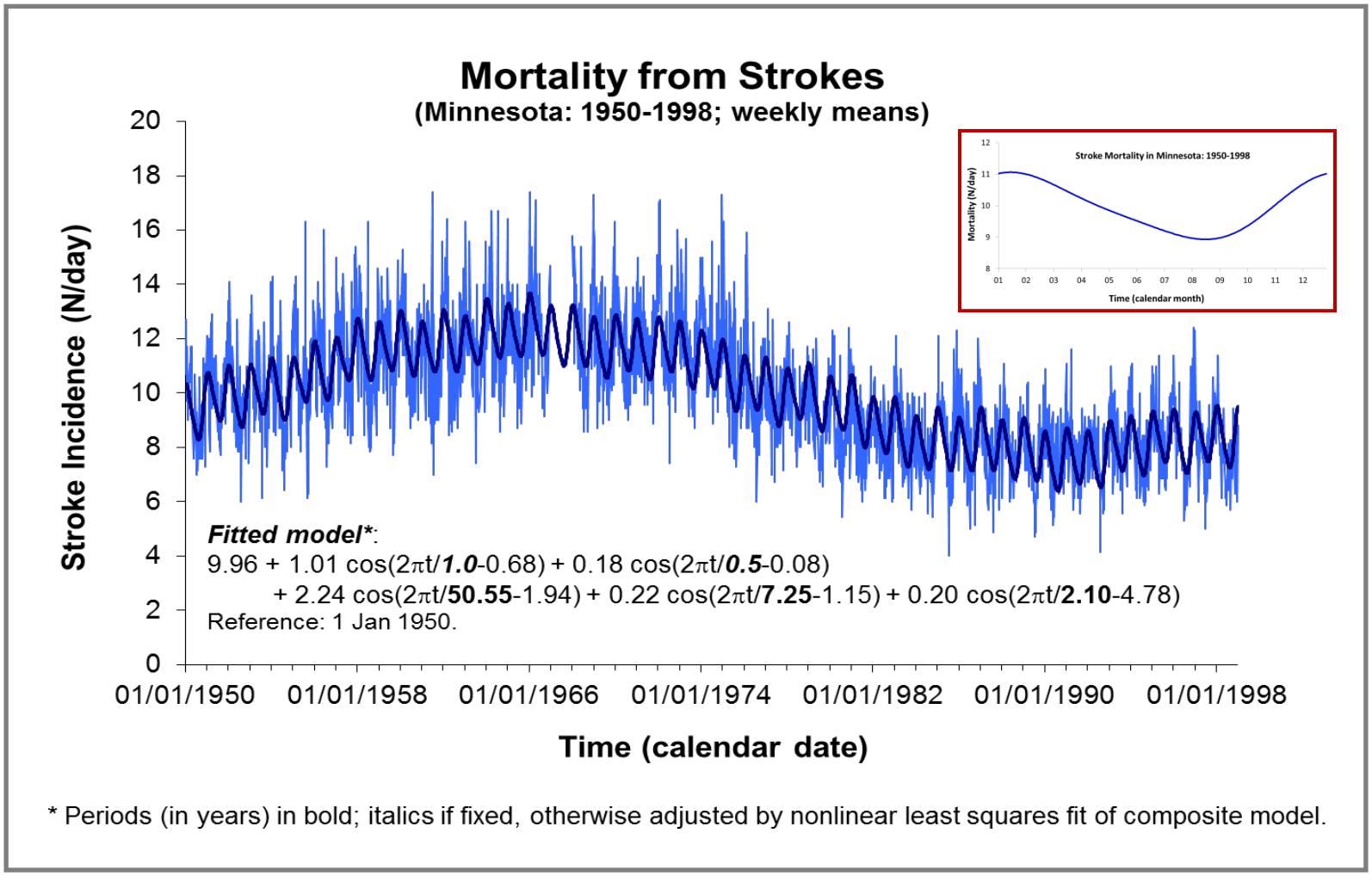
- About yearly cycles peaking in winter;
- About weekly cycles;
- Other components such as the half-year accounting for the waveform of the yearly variation;
- Other periodicities that have counterparts in our broader environment.

Stroke Mortality in MN Varies with the Seasons



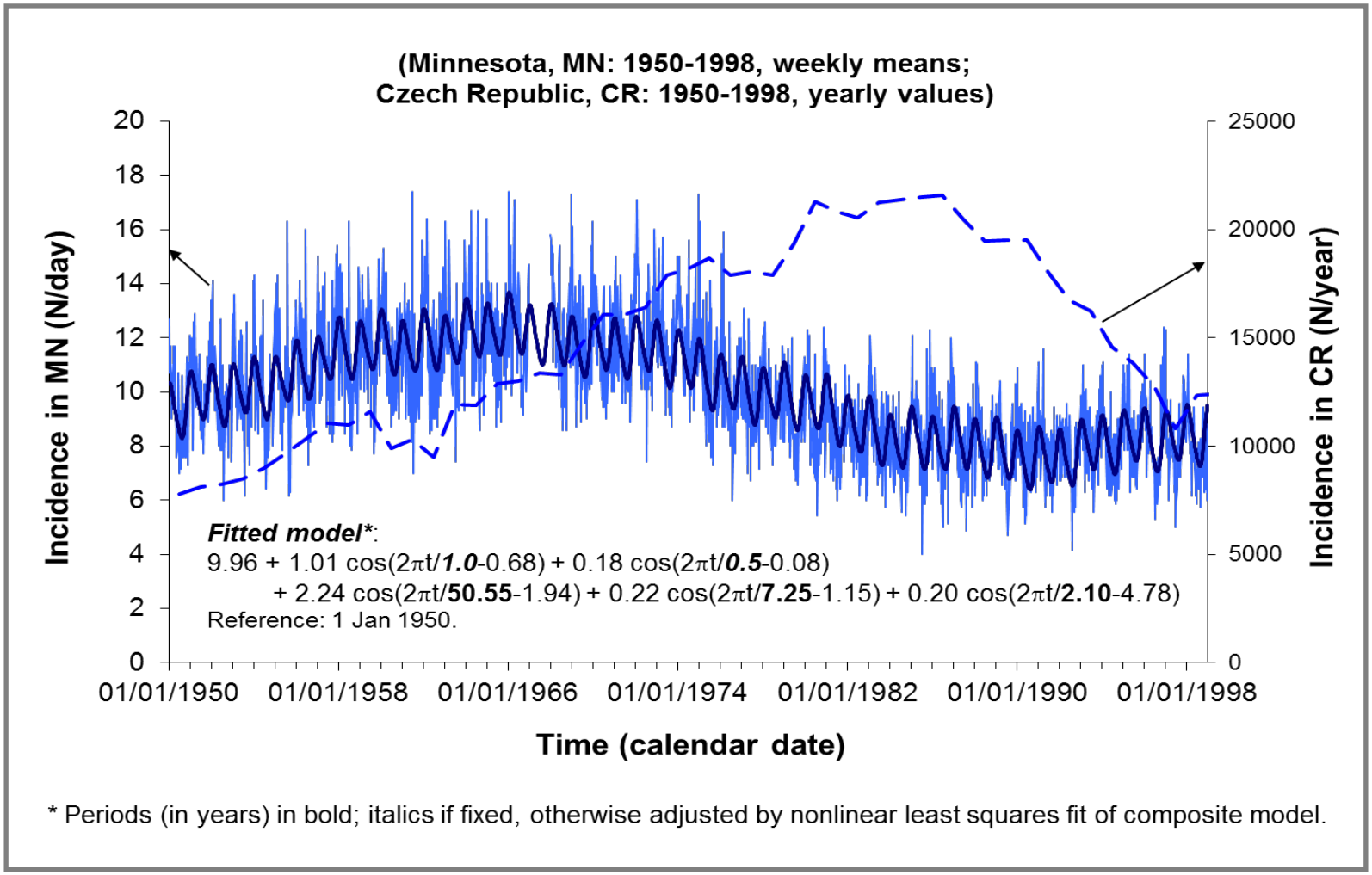


Modeling and Prediction of Stroke Mortality Based on Components Identified in Spectral Analysis



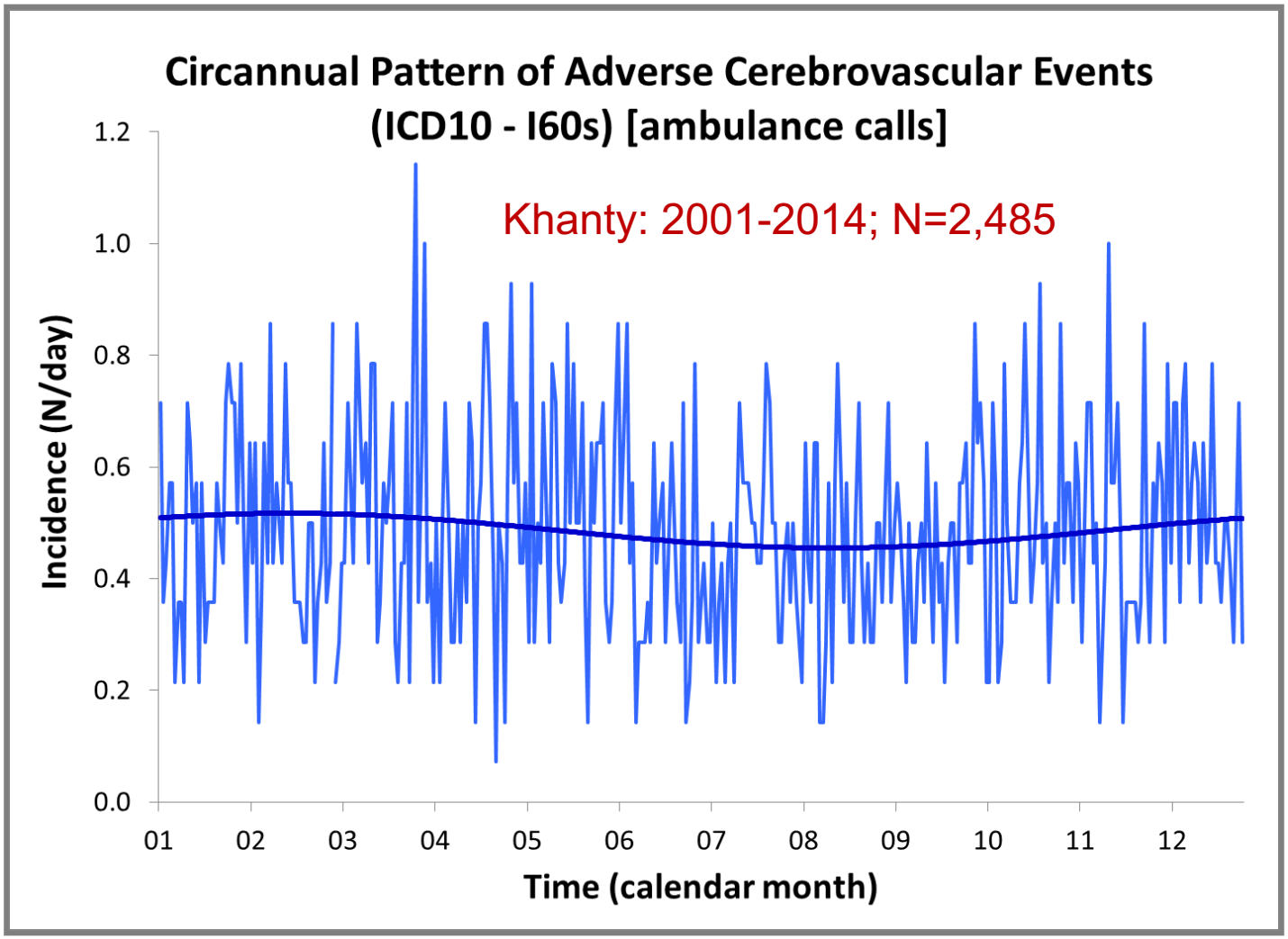
* Periods (in years) in bold; italics if fixed, otherwise adjusted by nonlinear least squares fit of composite model.

Similar but Delayed Long-Term Trend in Stroke Mortality in the Czech Republic vs MN

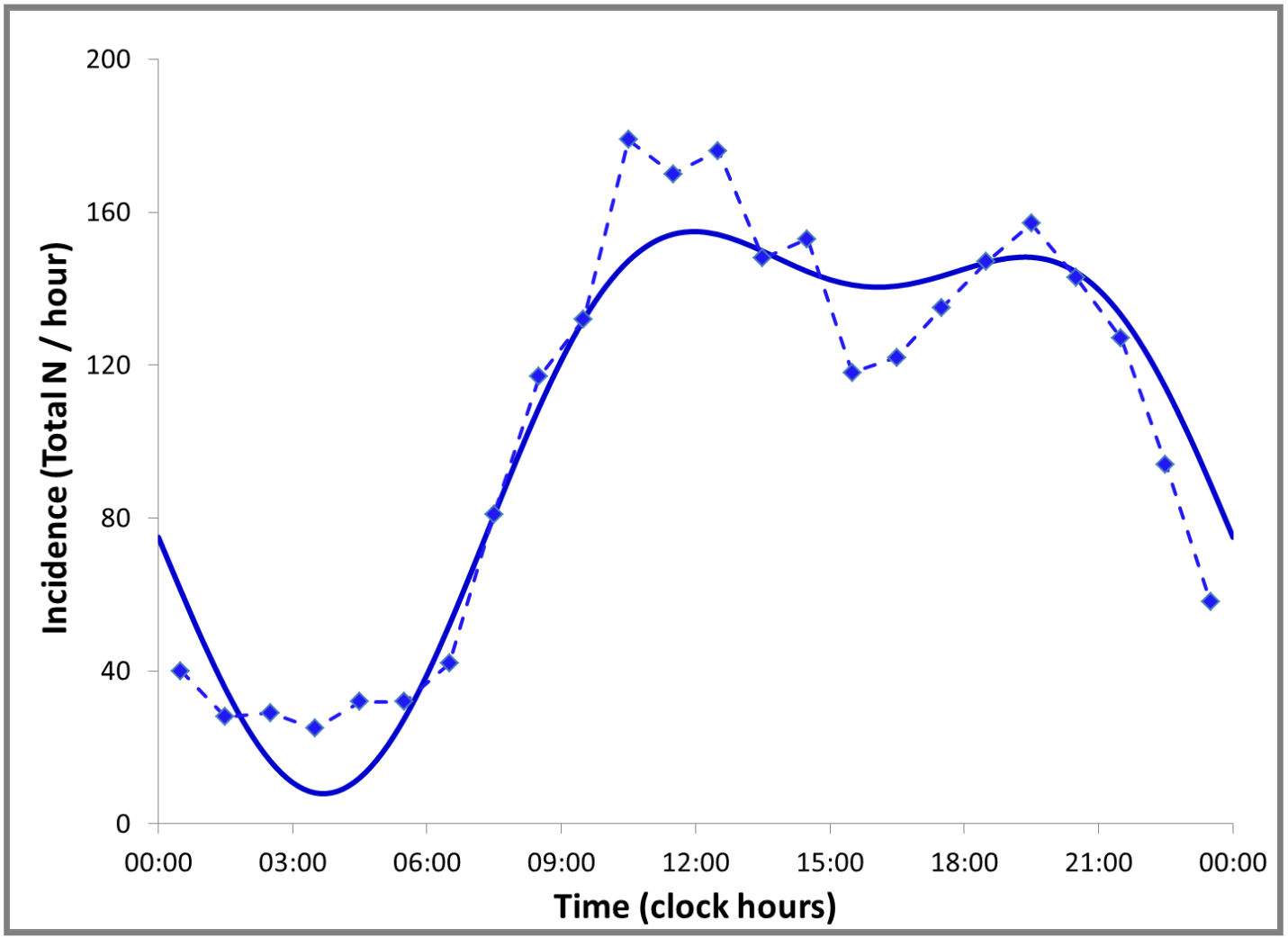


* Periods (in years) in bold; italics if fixed, otherwise adjusted by nonlinear least squares fit of composite model.

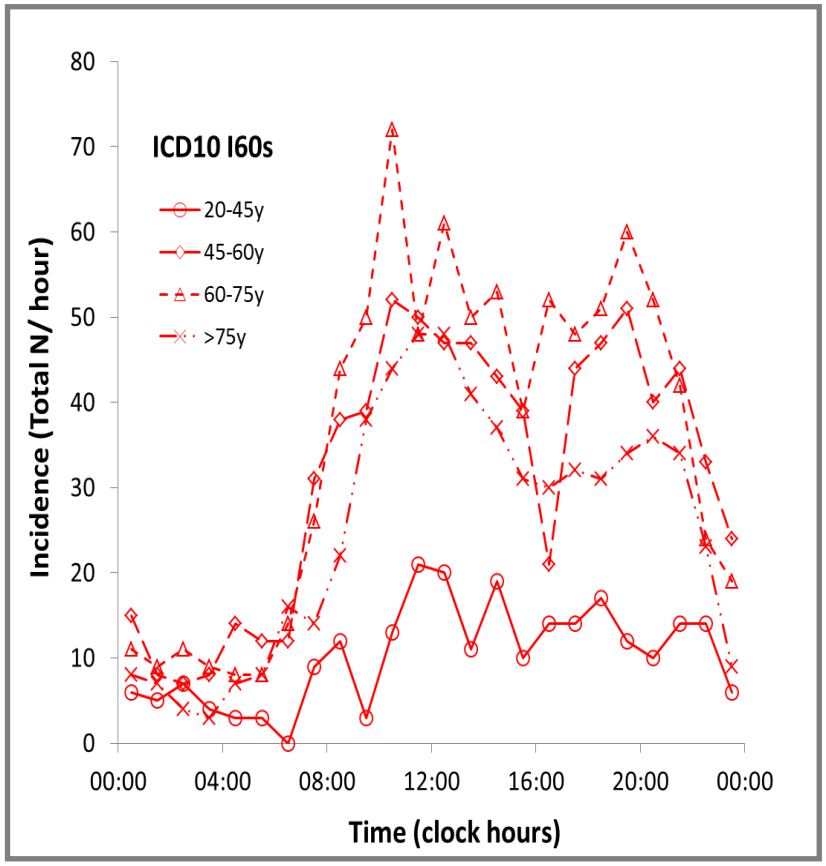
Similar Yearly Pattern Characterizes Incidence of All Adverse Cerebrovascular Events in Siberia

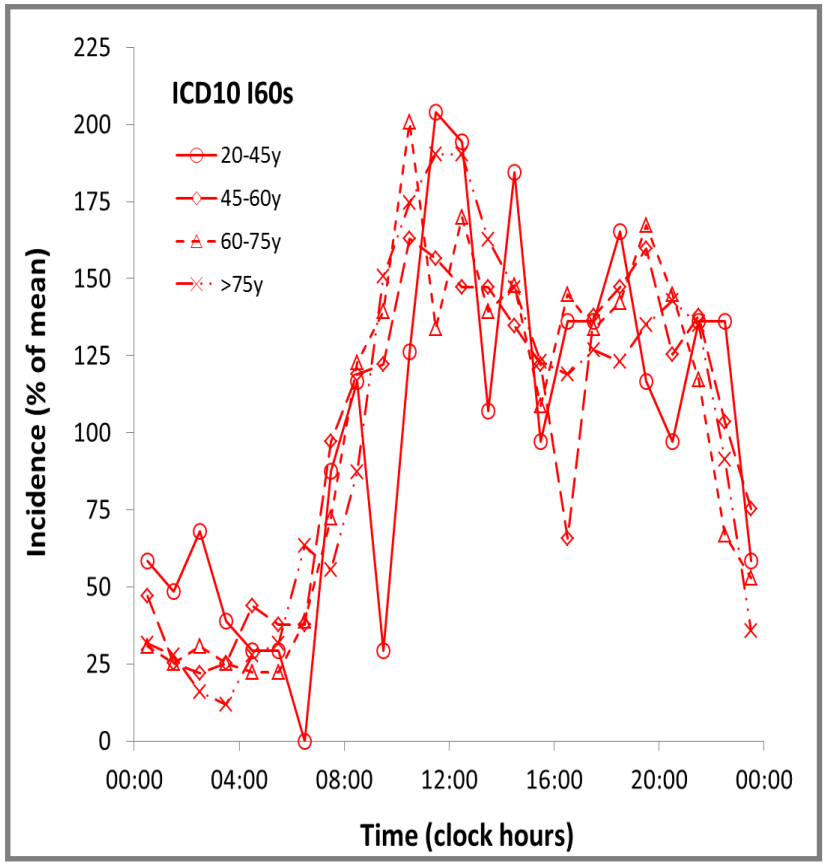


Circadian Pattern of Adverse Cerebrovascular Events in Khanty, Siberia (2001-2014; N=2,485)

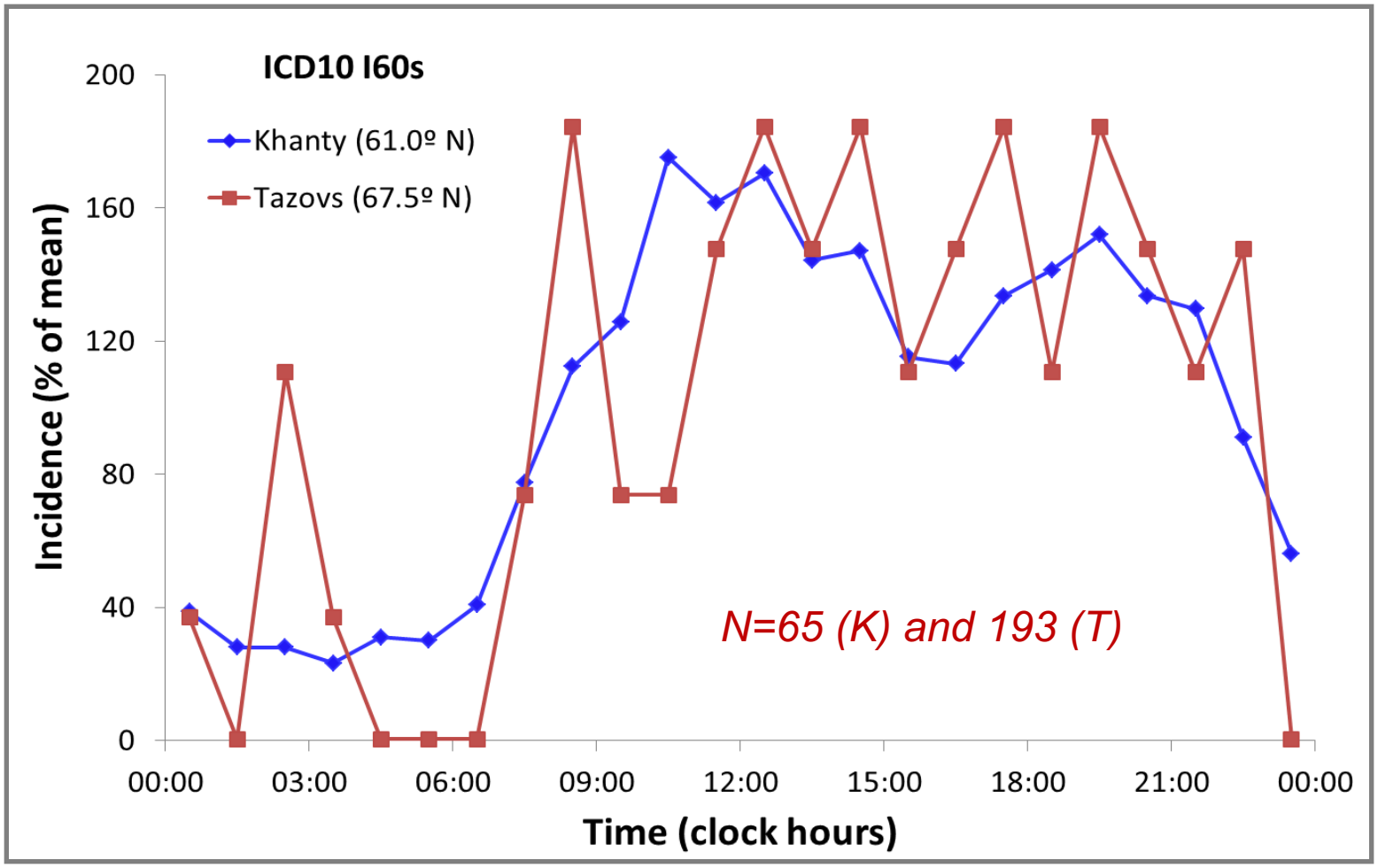


Similar Circadian Pattern at All Ages

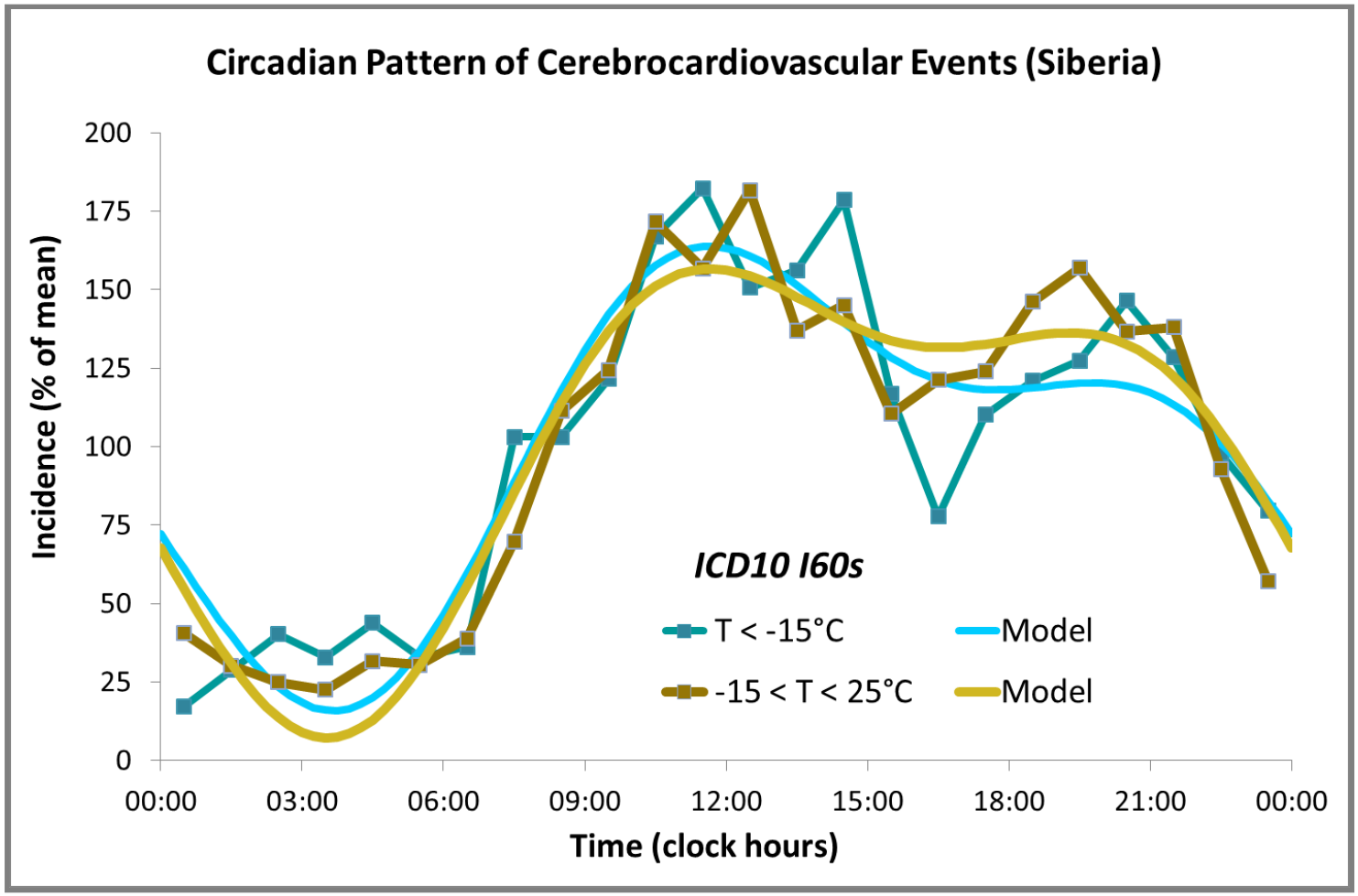




Similar Circadian Pattern in Different Geographic Locations



Similar Circadian Pattern at Different Environmental Temperatures



Influence of Weather on Stroke Incidence

(K Ohshige et al. Int J Biometeorol 2006; 50: 305-311)

- Computerized records of ambulance transport
- Jan 1992 – Dec 2003 (N=53,585)
- Yokohama, Japan
- Age, gender, residential area, date/time of emergency call, reason for transport, illness category
- First diagnosis (emergency department)
- Patients 50 years and older
- Stroke: ICD-9 430-438 (<2001); ICD-10 I60-I67 (>2001)

Influence of Weather on Stroke Incidence

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Poisson regression analysis:

$$\ln N_{ik} = \ln P_k + \alpha + \beta_1 TEMP_{ik} + \beta_2 HUMD_{ik} + \beta_3 PRES_{ik} + \beta_4 HOLIDAY_{ik}$$

Meteorological conditions divided into 96 weather pattern categories (6q5°C; 4q20%h; 4hPa)
Ordinary least squares regression analysis: daily incidence/100,000 vs. daily ranges of temperature, relative humidity, barometric pressure, holiday
96 weather patterns classified into 5 weather-risk categories (LS regression estimates ≥1.3, 1.2 - <1.3, 1.1 - <1.2, 1.0 - <1.1, and <1.0)

Stroke Incidence Higher at Lower Temperature and Relative Humidity

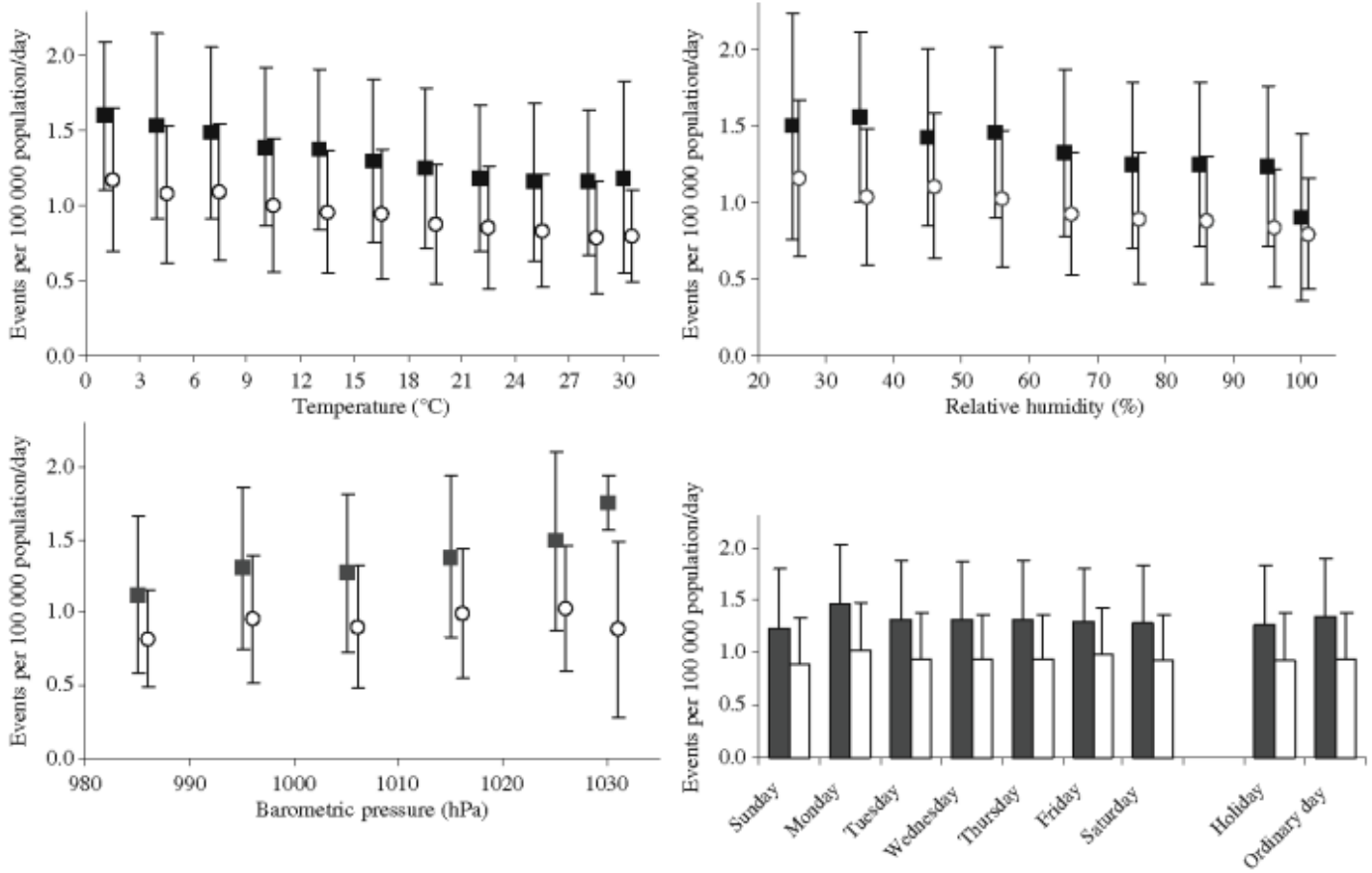
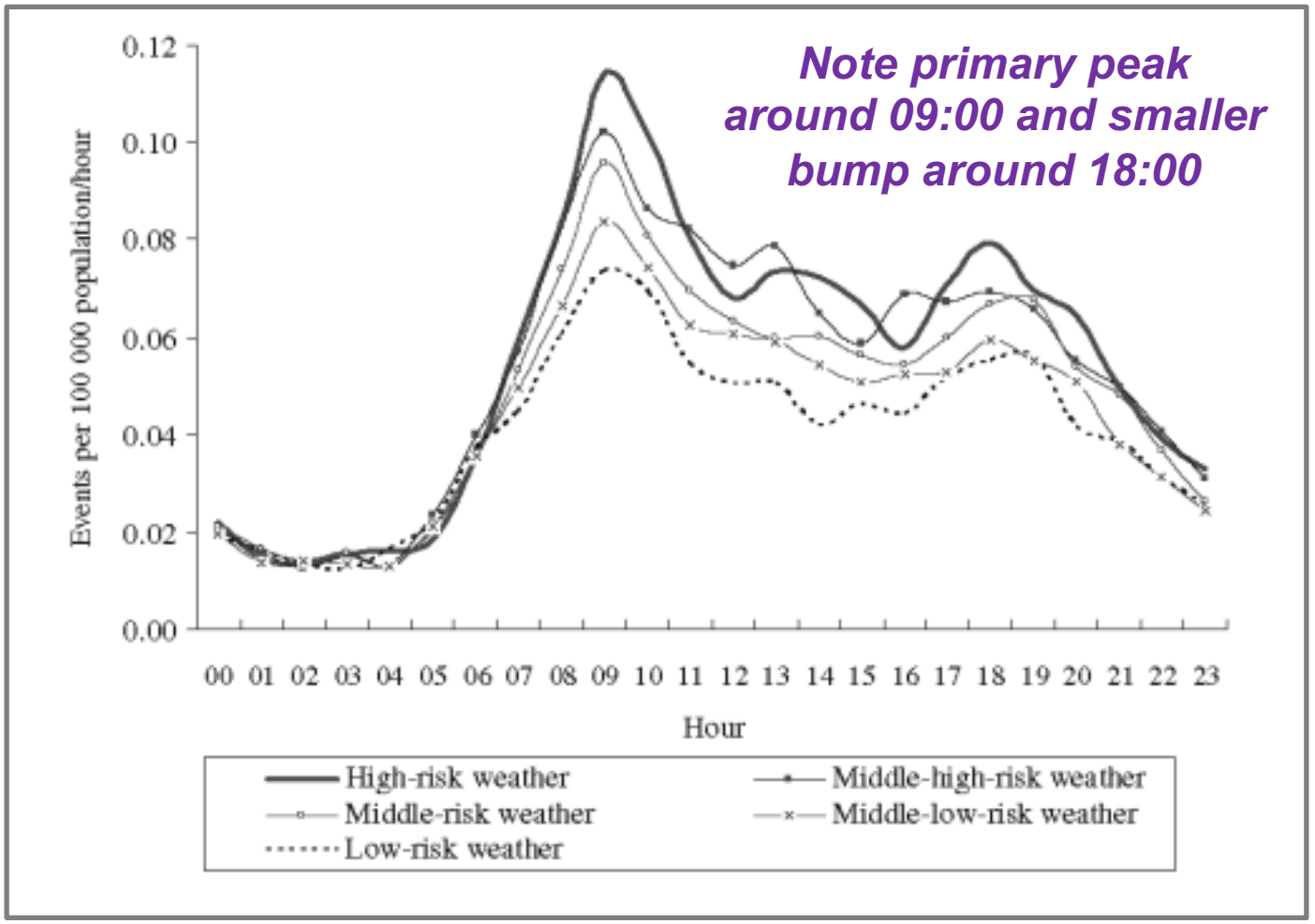


Fig. 1 Mean number of daily emergency transport events coded as stroke per 100,000 population according to daily mean ambient temperature in intervals of 3°C, daily mean relative humidity in intervals of 10%, daily mean barometric pressure in intervals of 10 hPa and each of the days of the week. ■: Men, □: Women, Bar: standard deviation

K Ohshige et al. Int J Biometeorol 2006; 50: 305-311

Circadian Amplitude Gradually Increases with Increasing Weather Risk



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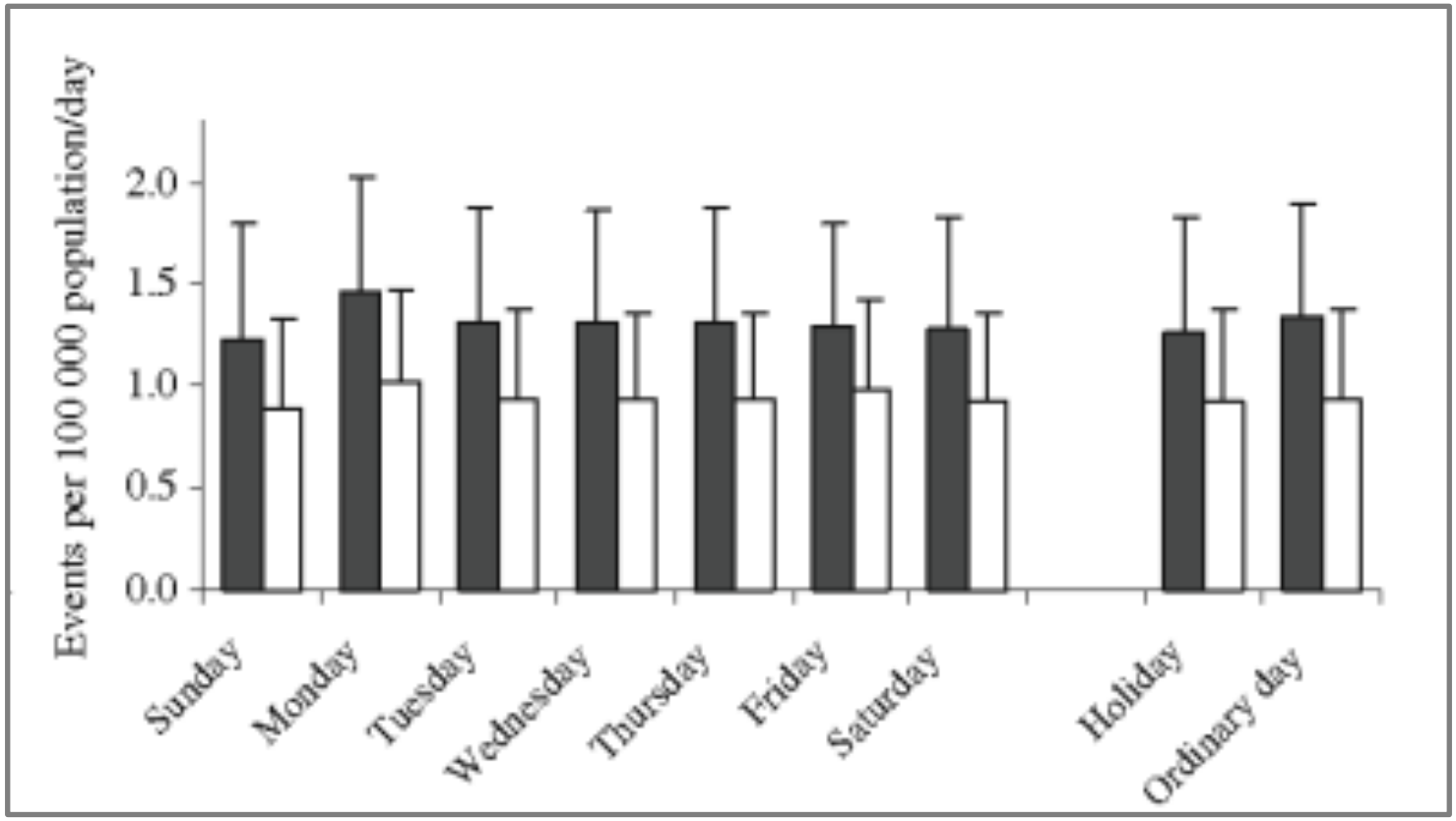
Weekly Pattern with Minimum on Sunday and Maximum on Monday



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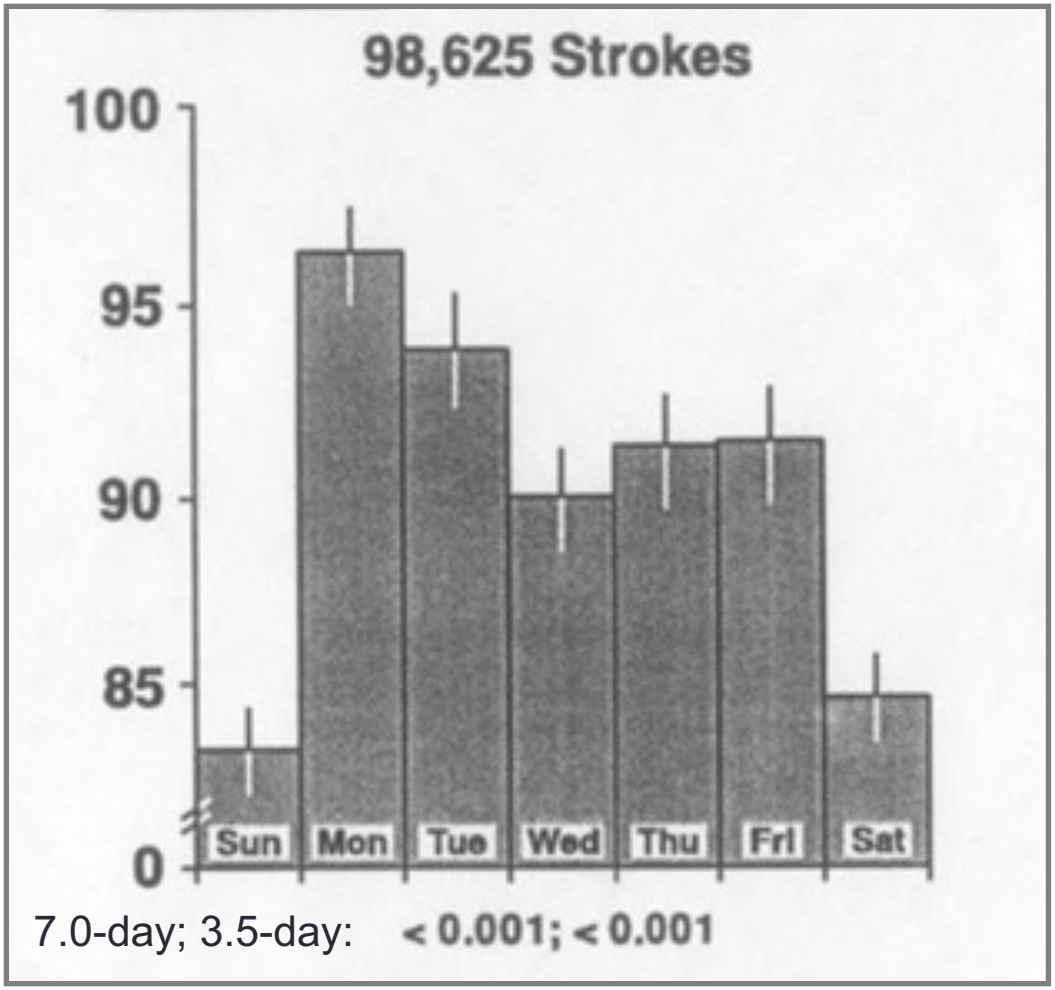
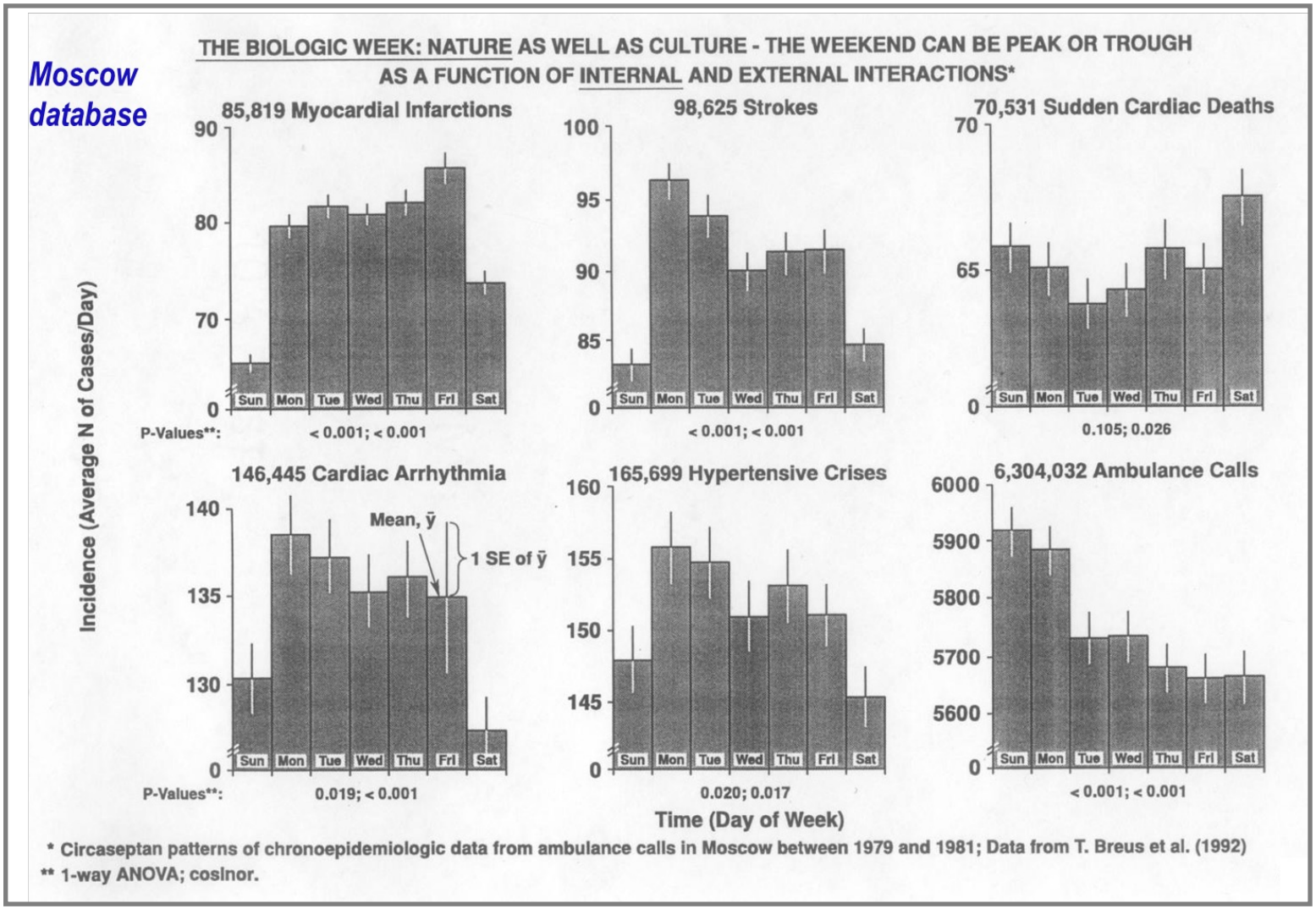
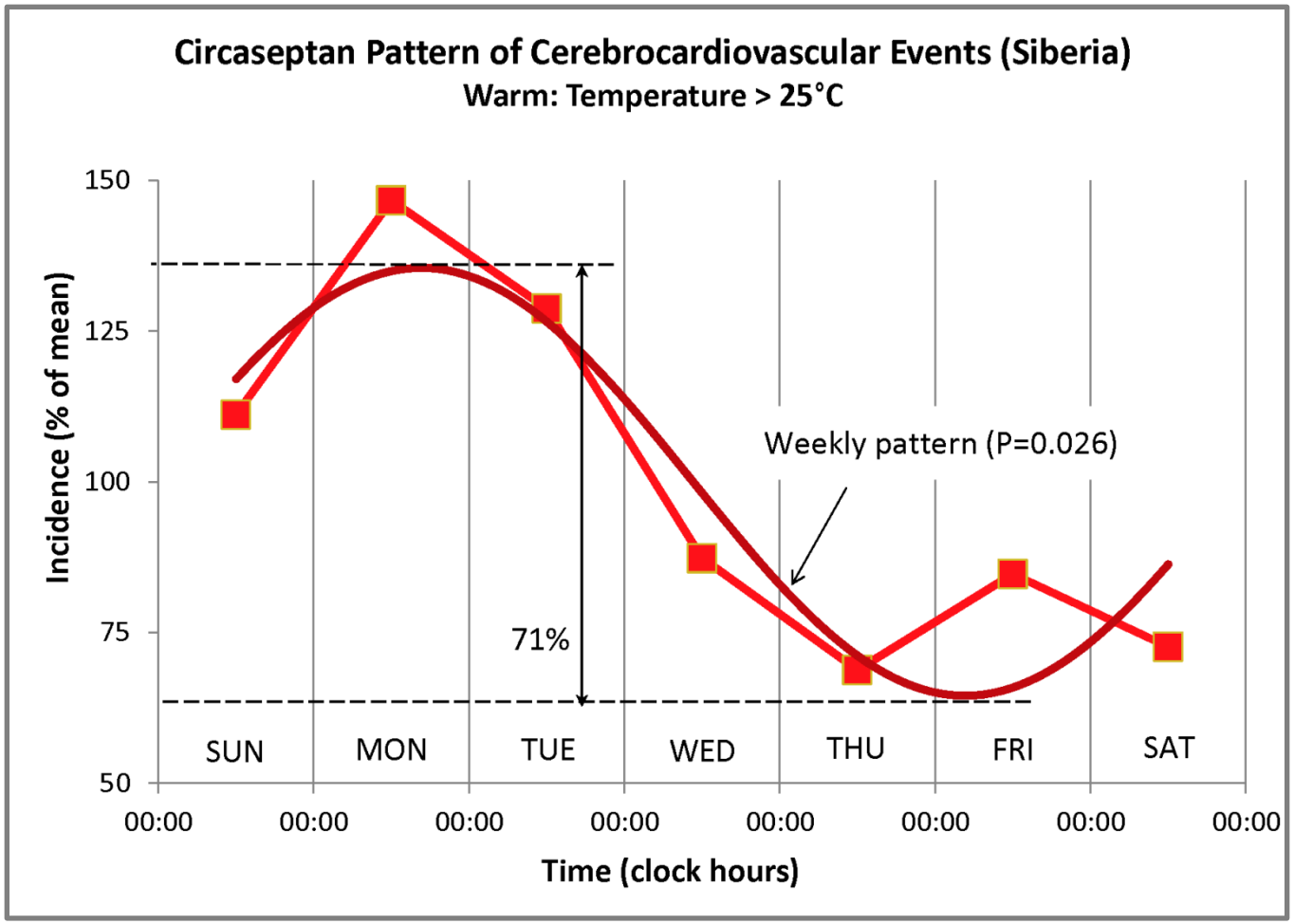
Similar Results Observed in Moscow, Russia (1979-1981)



Weekly Patterns also Characterize Incidence of Other Cardiovascular Events



In Siberia, Weekly Incidence Pattern of Cerebro-cardiovascular Events Depends on Air Temperature



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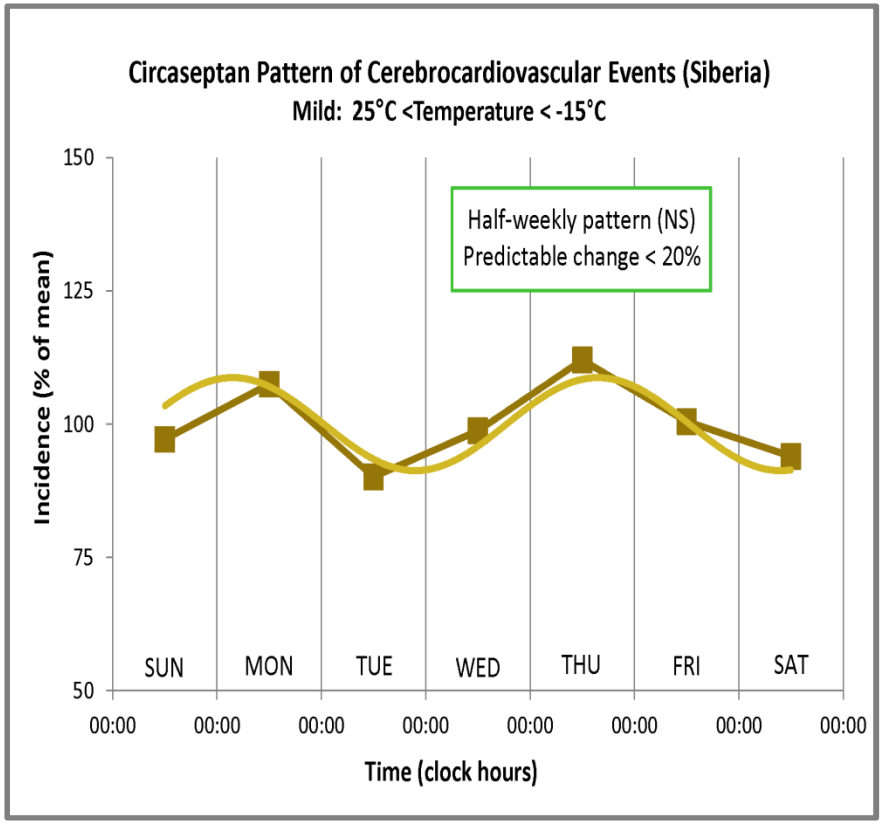
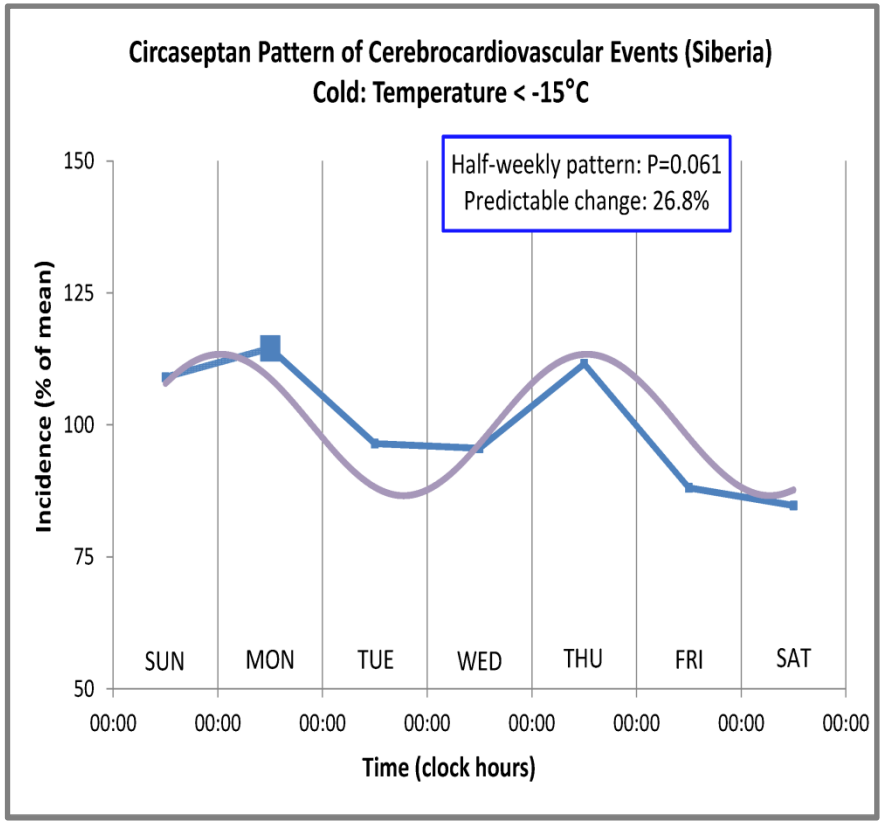




Similar About-Daily, -Weekly, and -Yearly Patterns are Reported by Others

- Spengos K et al. Neuroepidemiology 2003; 22: 204-210.
- Jimenez-Conde J, Roquer J. Medicina Clinica 2009; 132: 671-676.
- Turin TC et al. Neuroepidemiology 2010; 34: 25-33.
- Turin TC et al. Acta Neurologica Scandinavica 2012; 125: 206-212.
- Terayama Y. Japanese Journal of Clinical Medicine 2013; 71: 2130-2134.
- Lorenzano S et al. Stroke 2014; 45: 176-184.
- Mao Y et al. Chronobiology International 2015; 32: 881-888.

Similar About-Daily, -Weekly, and –Yearly Patterns are Reported by Others

- *Johansson BB et al. Progress in Clinical & Biological Research 1990; 341A:427-436.*

- University hospital Lund/Orup, Sweden
- Sep 1987-Aug 1988; N=497 (278M & 219F)
- Classified into different etiologies:
- Subarachnoid hemorrhage (SH, N=15)
- Intracerebral hemorrhage (IH, N=48)
- Large vessel disease infarction (LVH, N=233)
- Lacunar infarction (LA, N=57)
- Infarct due to cardiac embolism (CE, N=144)

Circadian, Circaseptan, and Circannual Incidence Patterns in Lund, Sweden

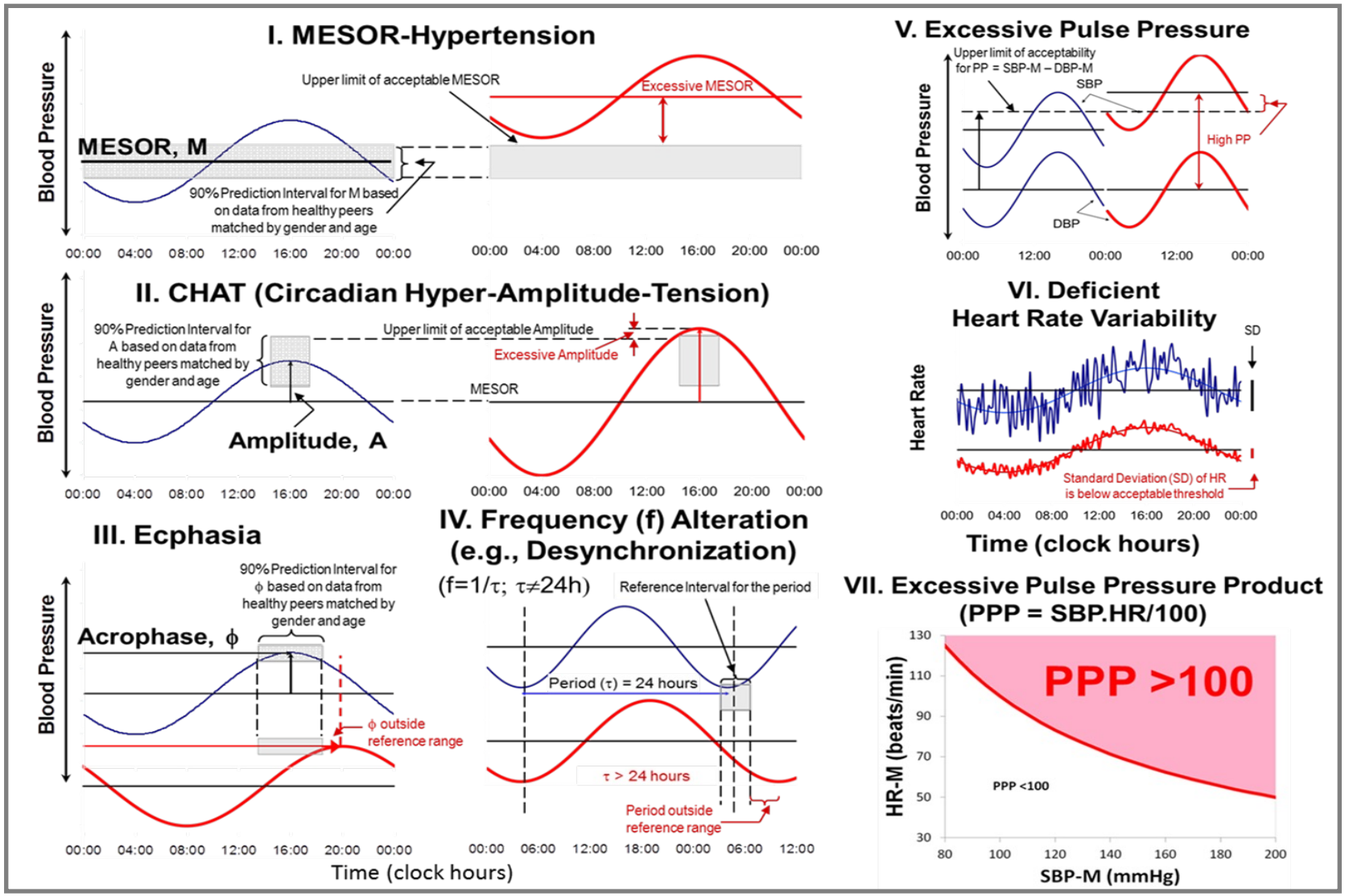
	N	P	MESOR	Amplitude	Acrophase	(95% CI)
				Circadian		
All	497	<0.001	16.6	10.4	10:56	09:08 , 12:48
SH	15	0.012	0.6	0.5	17:16	14:40 , 19:52
IH	48	0.241	1.6	0.9	10:08	,
LVD	233	<0.001	7.7	5.0	11:48	10:20 , 13:16
LA	57	0.087	2.2	1.2	09:20	,
CE	144	0.007	4.5	3.6	10:12	07:48 , 12:32
				Circaseptan/Circasemiseptan		
LVD	7.0d	0.050	33.29	7.47	-113	early TUE
SH	3.5d	0.016	2.14	1.49	-83	late SUN, early THU
LA	3.5d	0.059	5.71	2.25	-240	early TUE, late FRI
				Circannual		
LVD						peak in MAR
CE						peaks in DEC & JUL

Risk factors for Stroke

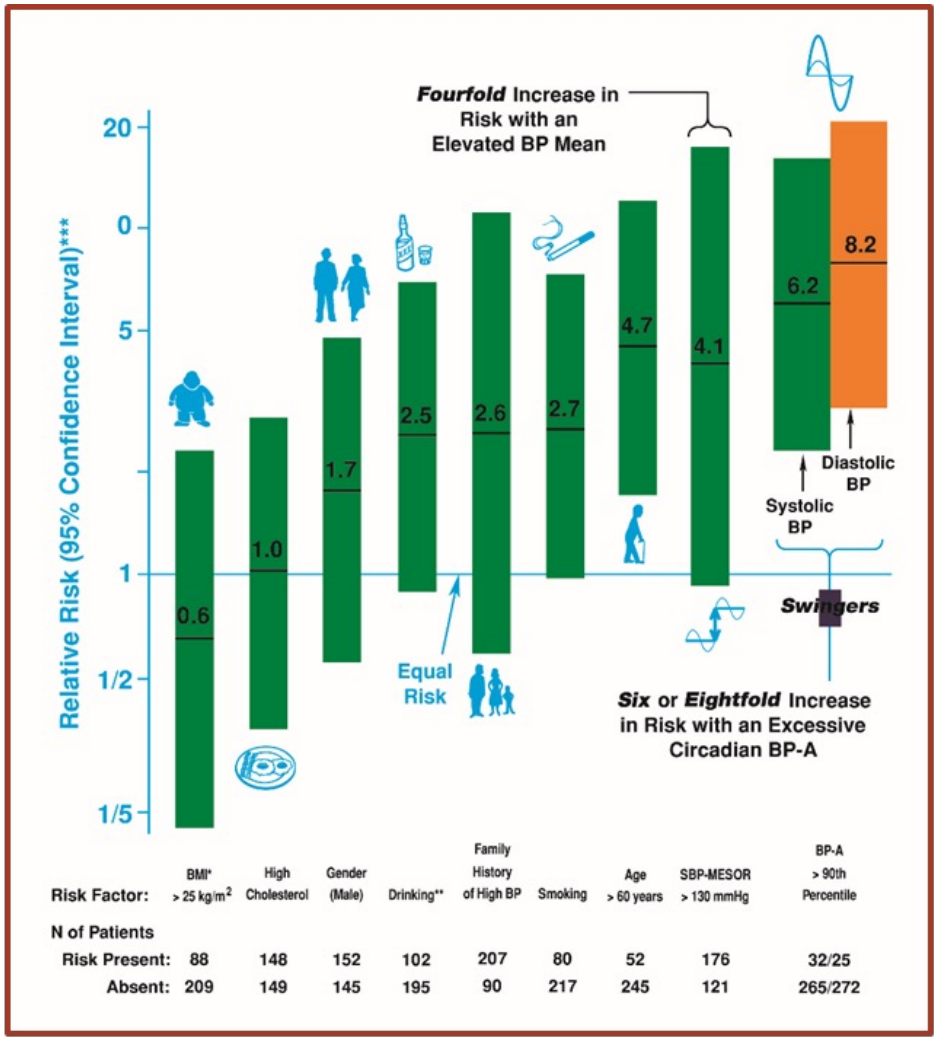
- Prior Stroke or Transient Ischemic Attack
- ***Hypertension***
- Myocardial Infarction
- Diabetes
- Atrial Fibrillation
- Hyperlipidemia
- Carotid Artery Disease
- Cigarette Smoking
- ***Excessive Alcohol***
- Heredity

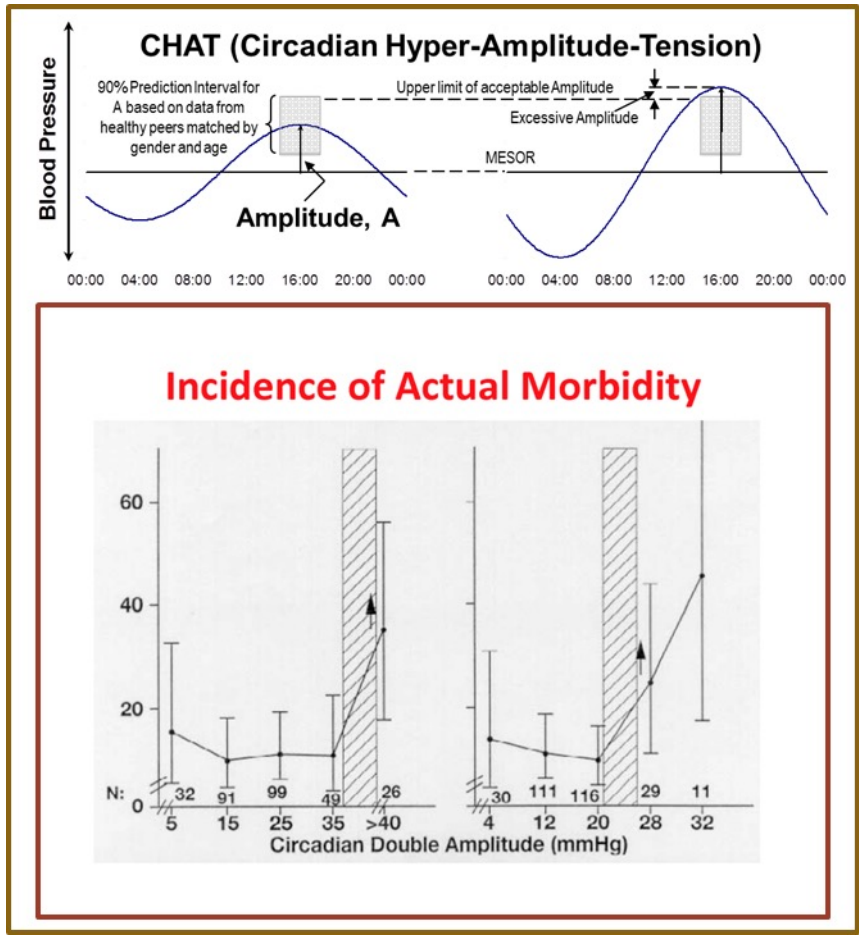
http://www.activebeat.co/your-health/women/10-risk-factors-for-stroke/2/

High BP is only One of Several Vascular Variability Disorders (VVDs) – ***Alterations*** of ***Variability*** in ***BP*** and/or ***HR***

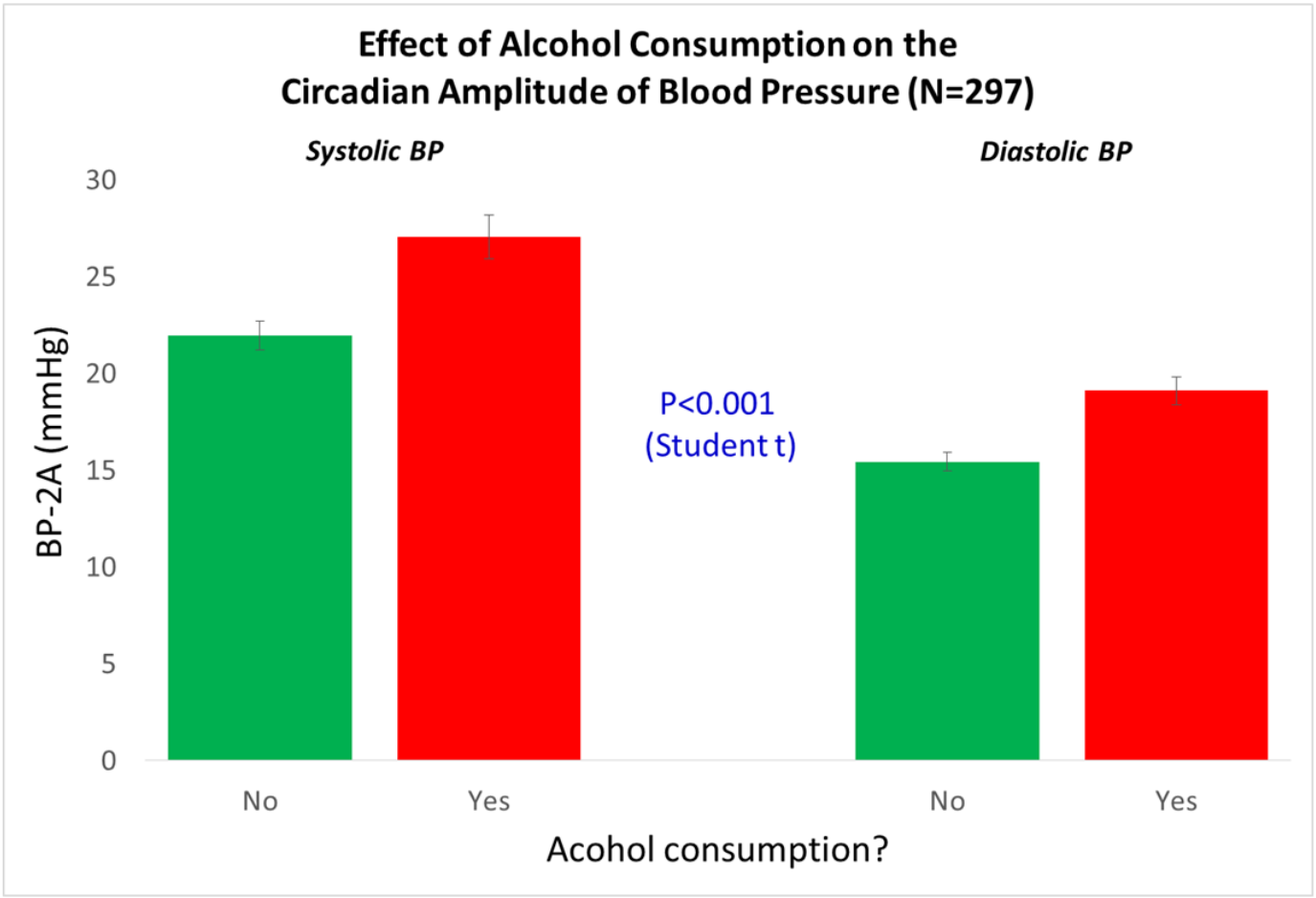


Circadian Hyper-Amplitude-Tension (CHAT) Raises Risk of Ischemic Cerebral Event Most

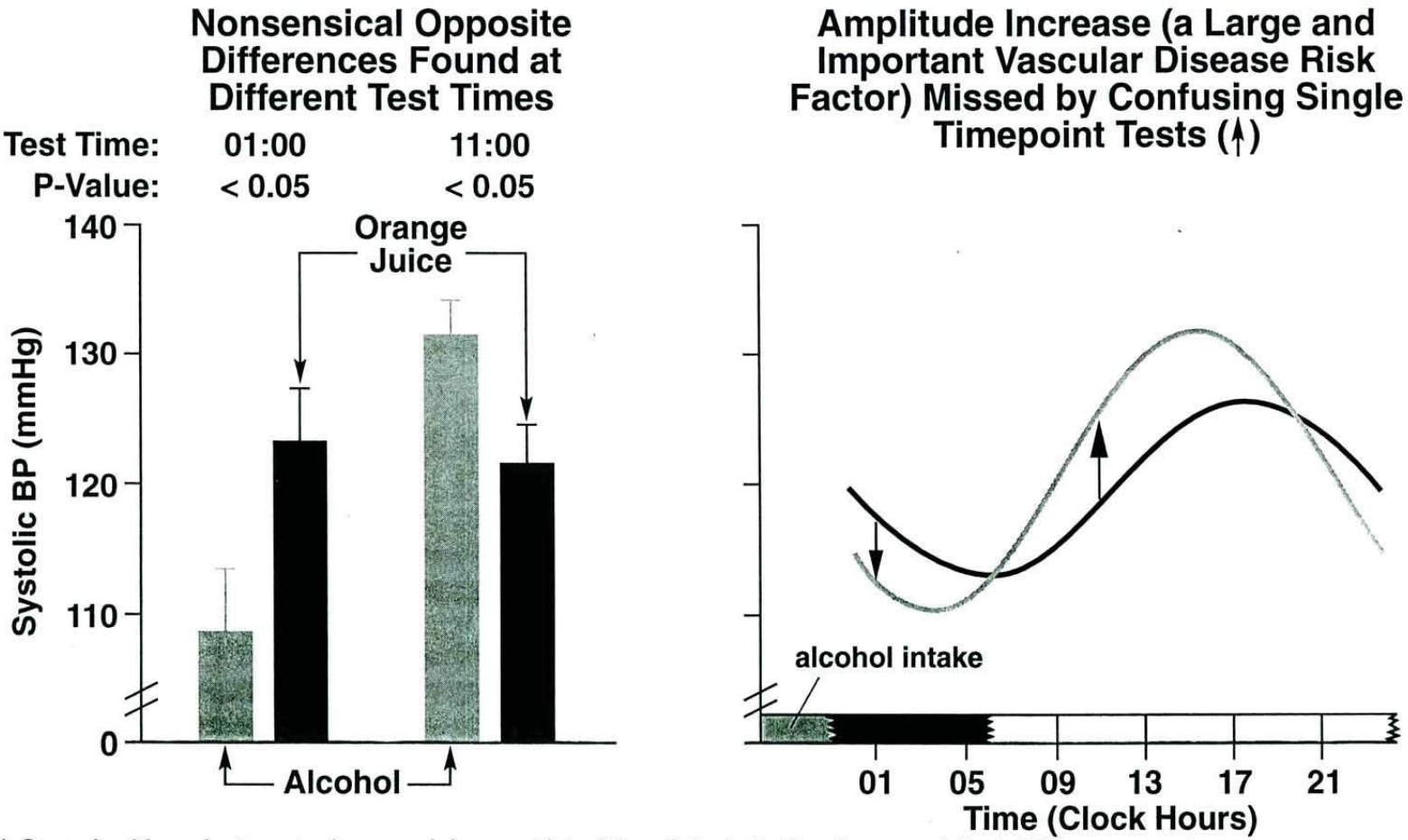




Alcohol Consumption is the Only Risk Factor Found to Correlate with the Circadian BP Amplitude (BP-A)

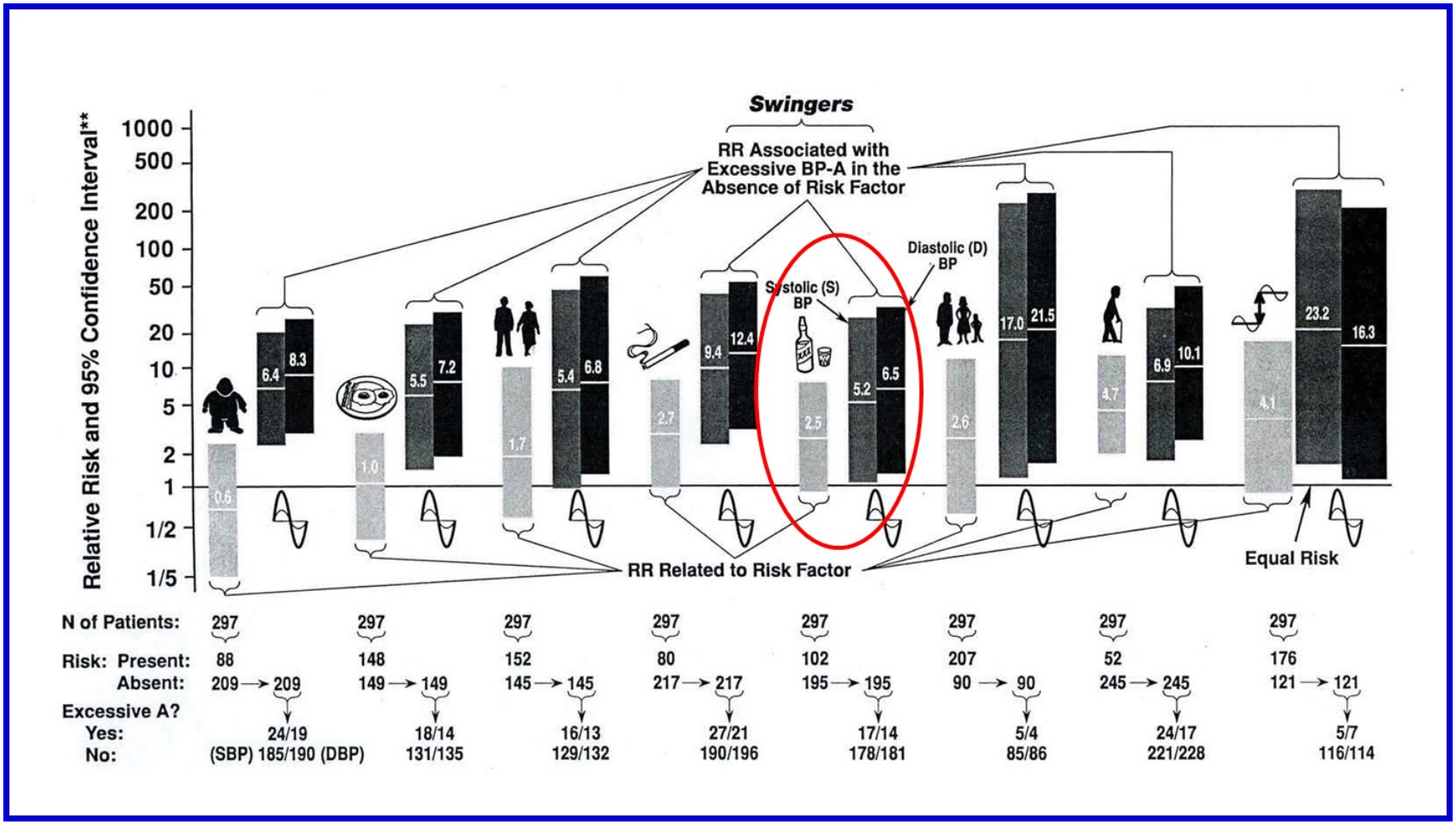


Alcohol in the Evening Amplifies the Circadian Rhythm in BP

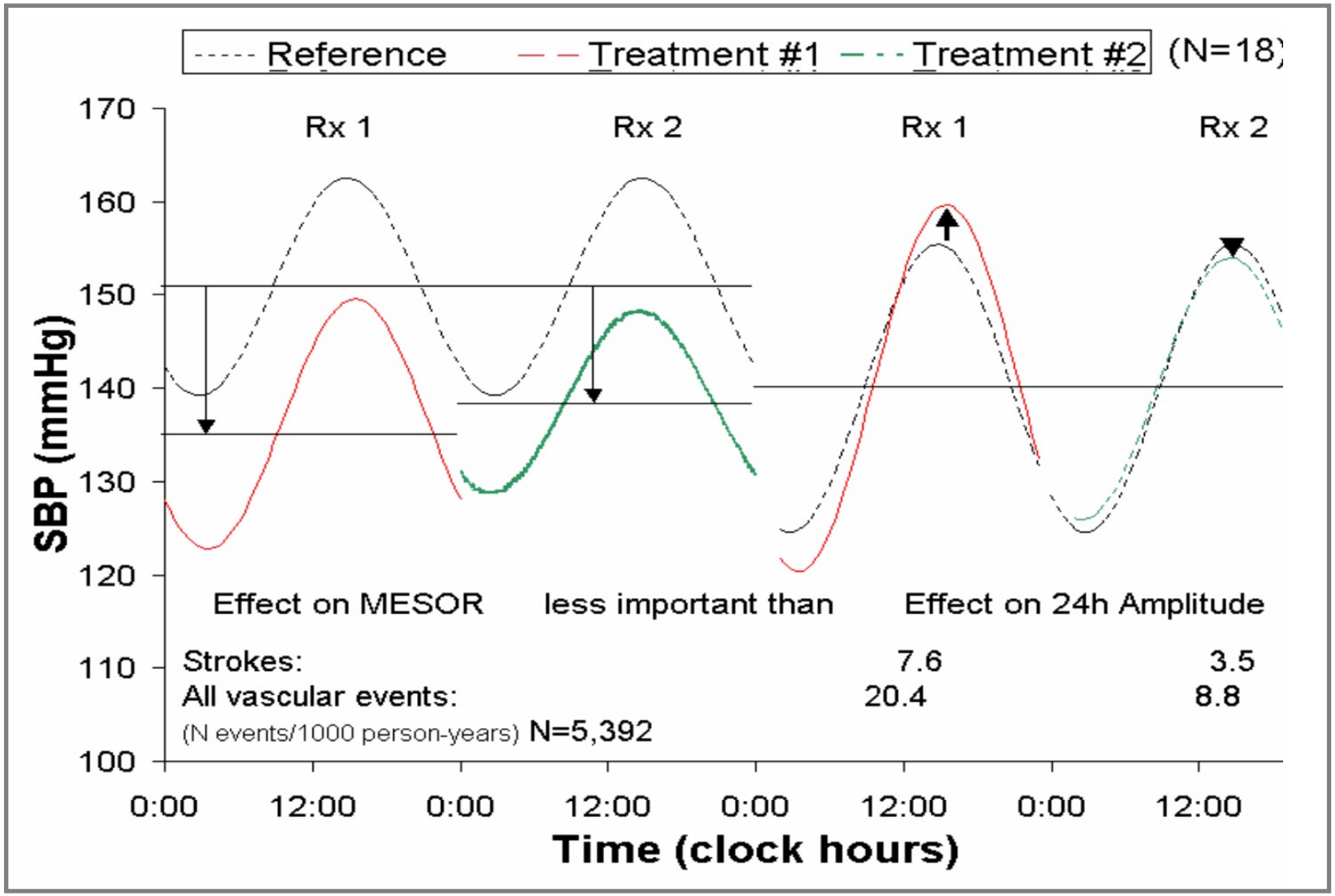


* Seven healthy volunteers took orange juice or whisky (40 g of alcohol) after dinner; amlpitude (A) increase and acrophase (ø) advance revealed by (A, ø) test ($P < 0.05$) in the absence of change in MESOR (M, rhythm-adjusted mean).

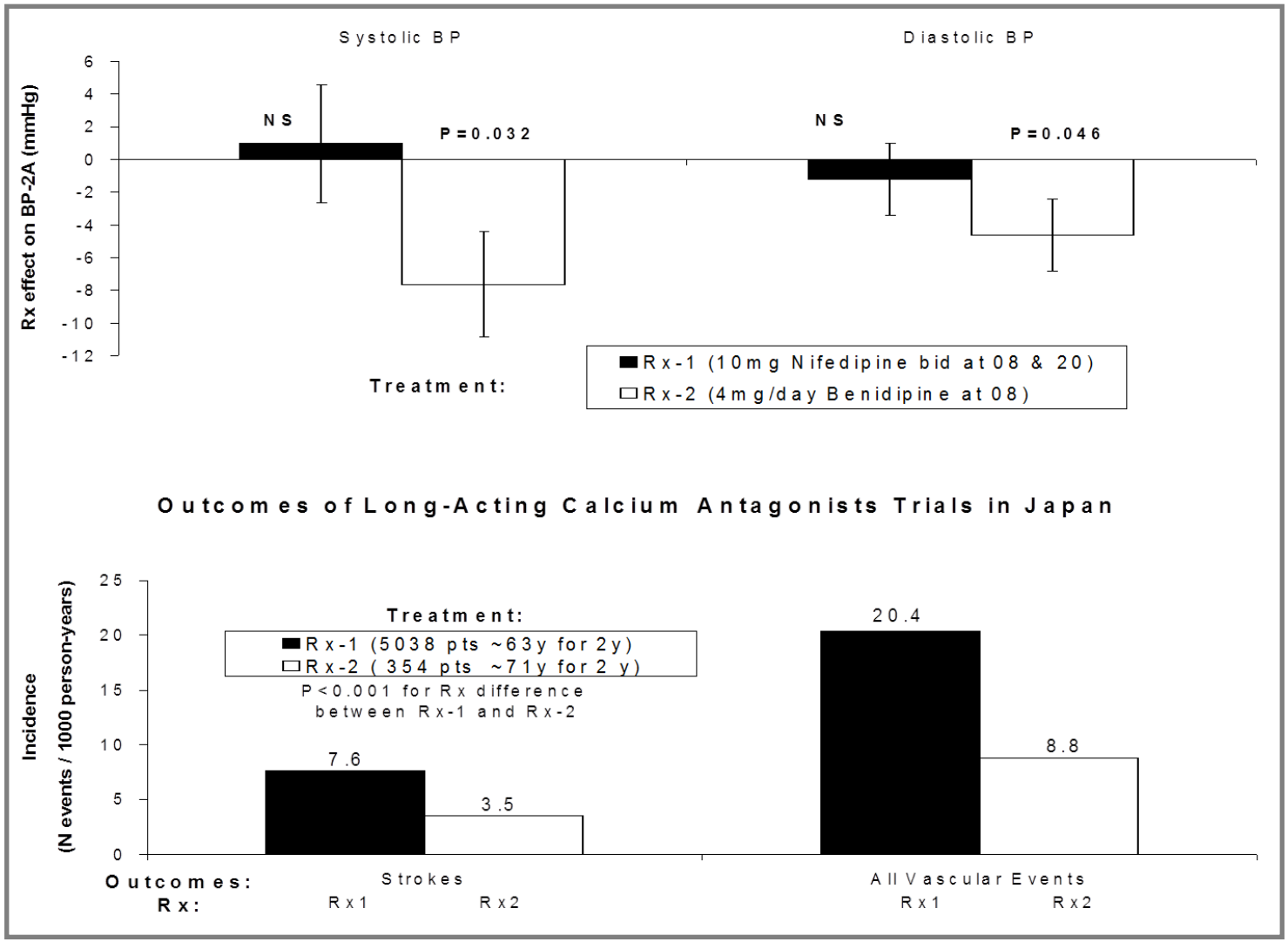
CHAT Remains an Important Risk Factor for Stroke Among Non-Drinkers (and in the absence of other risk factors)



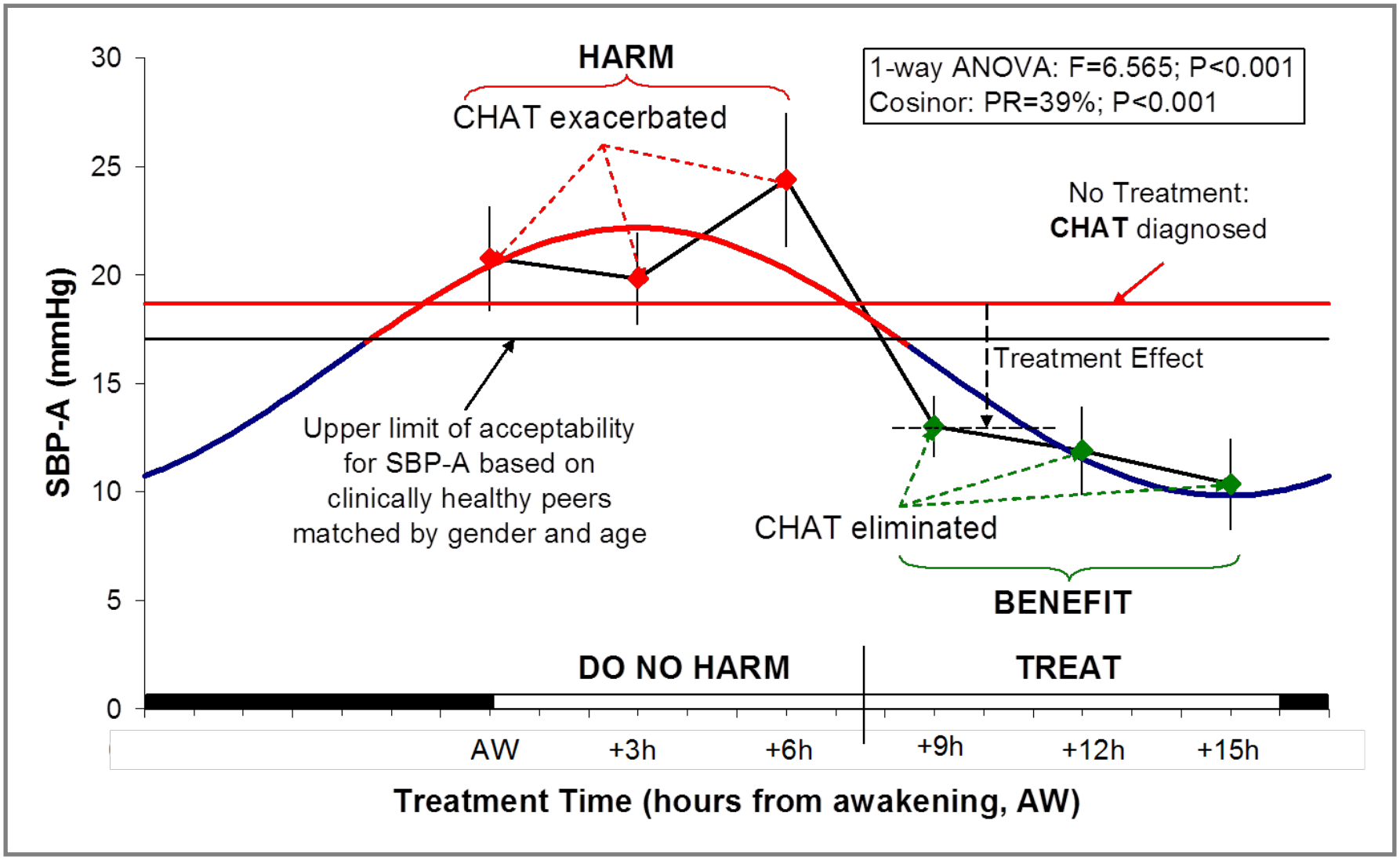
Not All Anti-Hypertensive Drugs Act on BP-A



Decreasing an Excessive BP-A May Be More Important than Decreasing the BP-M



Individualized Timed Rx (Chronotherapy) Helps 2/3 Patients by Reducing VVDs



THANK YOU

Collaborators

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