



Malattia Diverticolare del Colon

Sabato 12 maggio 2012

Aspetti cronobiologici

Roberto Manfredini

Clinica Medica
Azienda Ospedaliera-Universitaria di Ferrara

Cronobiologo: l'esperto del *tempo*



Cronobiologo: l'esperto del *tempo*





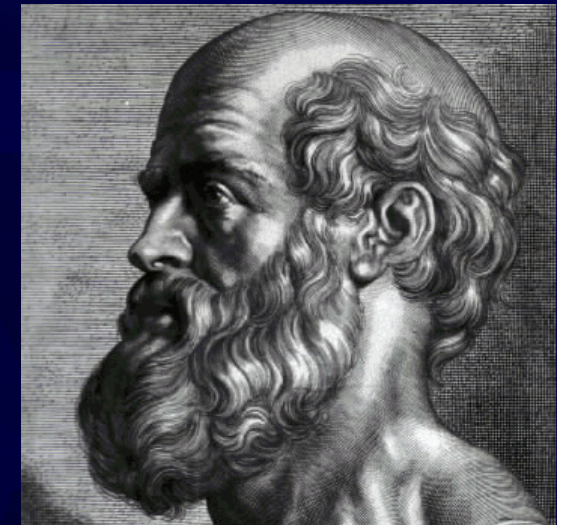
A service of the National Library of Medicine
and the National Institutes of Health

Seasons

Divisions of the year according to some regularly recurrent phenomena usually astronomic or climatic.

67587

Una stagione per le malattie?



Arie, Acque e Luoghi

Ippocrate

400 A.C.



PART 1

Whoever wishes to investigate medicine properly, should proceed thus:

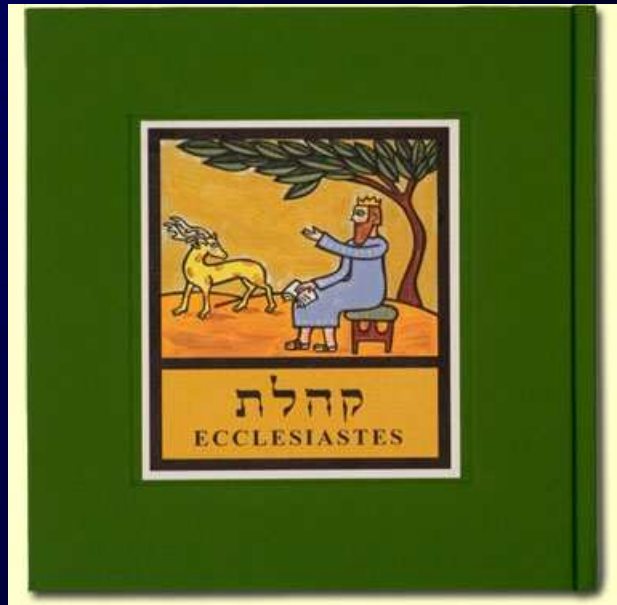
in the first place to consider the seasons of the year, and what effects each of them produces for they are not at all alike, but differ much from themselves in regard to their changes.

Then the winds, the hot and the cold, especially such as are common to all countries, and then such as are peculiar to each locality.

We must also consider the qualities of the waters, for as they differ from one another in taste and weight, so also do they differ much in their qualities.

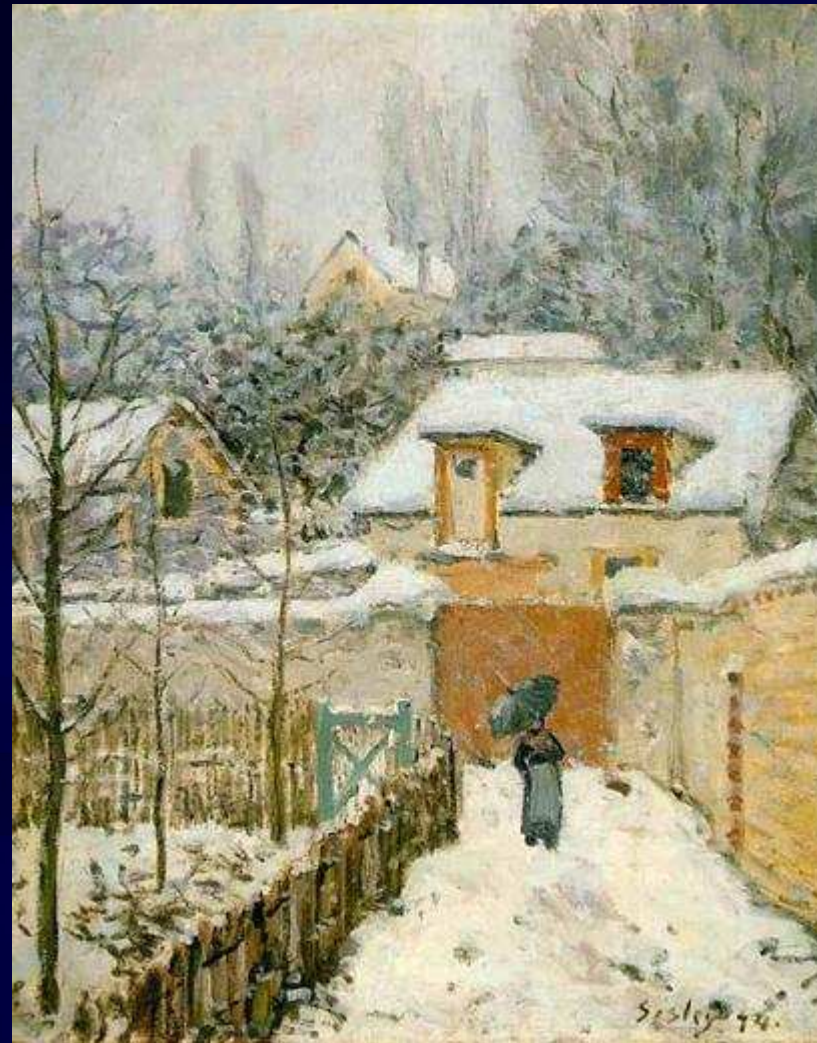
In the same manner, when one comes into a city to which he is a stranger, he ought to consider its situation, how it lies as to the winds and the rising of the sun; for its influence is not the same whether it lies to the north or the south, to the rising or to the setting sun.

**..per ogni cosa c'è la sua stagione,
c'è un tempo per ogni situazione sotto il cielo..**



To Everything
there is a Season,
and a time
to every Purpose
under Heaven.
Ecclesiastes 3:1

Inverno



Alfred Sisley, 1878
Neve a Louveciennes

Infarto miocardico acuto

2° Registro Nazionale USA, 1994-1996 (n = 259.891)

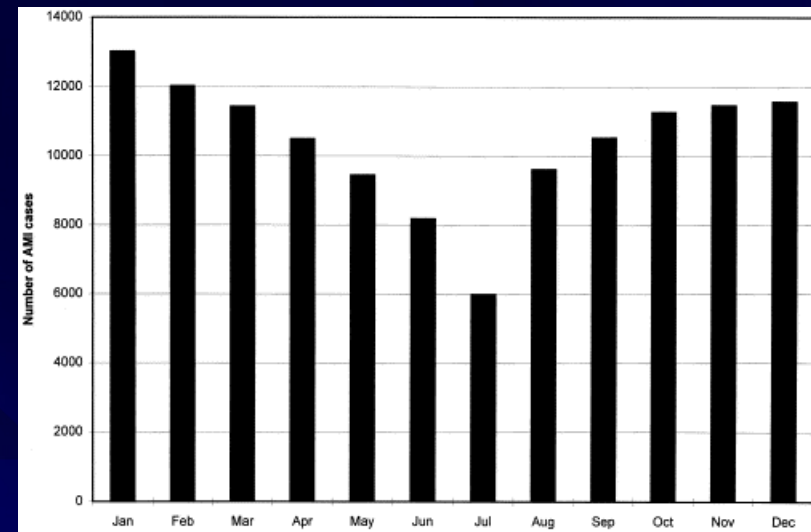
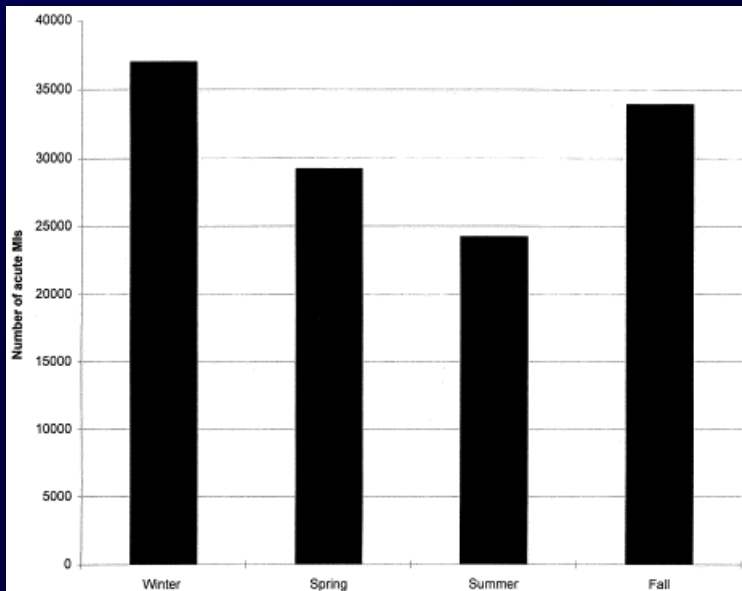


CLINICAL STUDIES

MYOCARDIAL INFARCTION

Seasonal Distribution of Acute Myocardial Infarction in the Second National Registry of Myocardial Infarction

FREDERICK A. SPENCER, MD, ROBERT J. GOLDBERG, PhD, RICHARD C. BECKER, MD,
JOEL M. GORE, MD, FACC, FOR THE PARTICIPANTS IN THE NATIONAL REGISTRY OF
MYOCARDIAL INFARCTION*
Worcester, Massachusetts



Infarto miocardico acuto

Ferrara, 1998-2004 (n = 4.014)



SEASONAL VARIATION IN ONSET OF MYOCARDIAL INFARCTION—A 7-YEAR SINGLE-CENTER STUDY IN ITALY

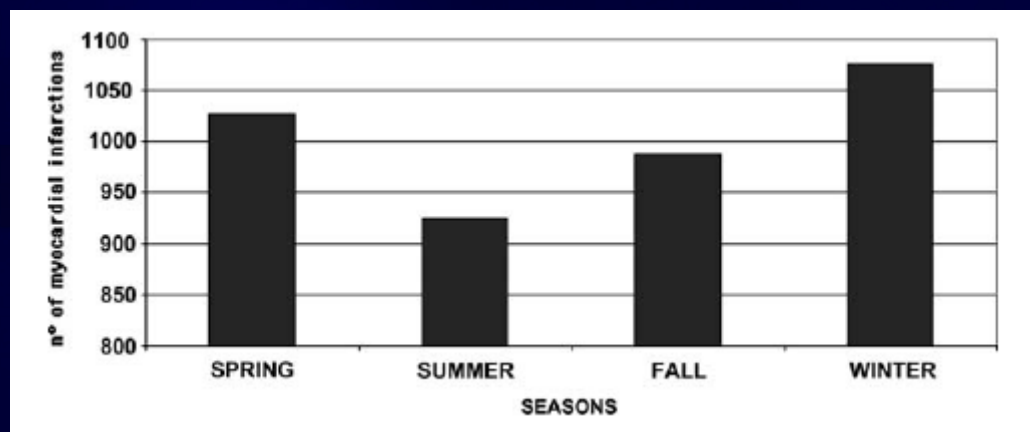
Roberto Manfredini,¹ Benedetta Boari,¹ Michael H. Smolensky,²
Raffaella Salmi,³ Massimo Gallerani,³ Franco Guerzoni,⁴ Valentina Guerra,⁴
Anna Maria Malagoni,¹ and Fabio Manfredini¹

¹*Vascular Diseases Center, University of Ferrara, Ferrara, Italy*

²*School of Public Health, University of Texas-Houston Health Sciences Center, Houston, Texas, USA*

³*Department of Internal Medicine, St. Anna General Hospital, Ferrara, Italy*

⁴*Department of Medical Statistics, St. Anna General Hospital, Ferrara, Italy*



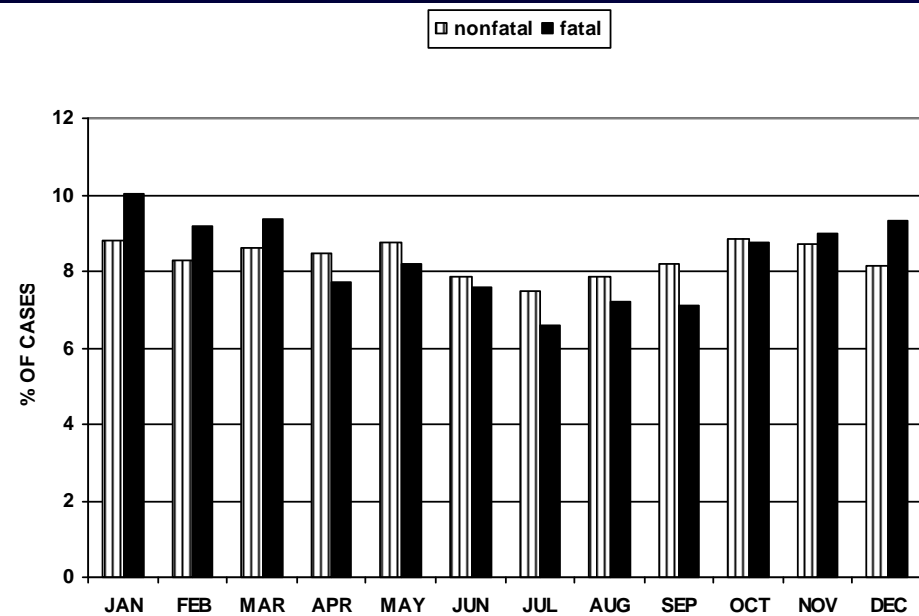
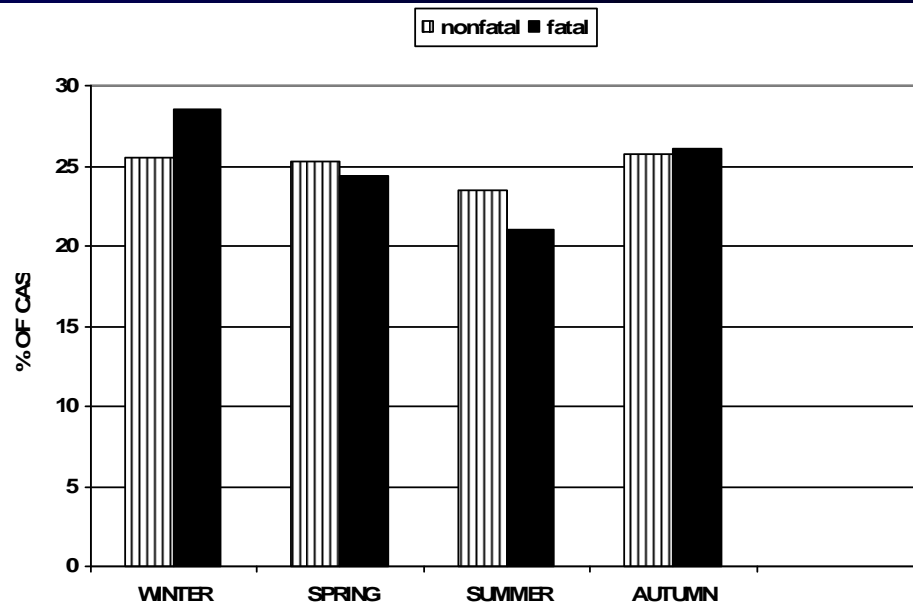
Infarto miocardico acuto

Regione Emilia Romagna, 1998-2006 (n = 40.386)



Seasonal and weekly patterns of hospital admissions for nonfatal and fatal myocardial infarction ☆

Roberto Manfredini MD^{a,b,*}, Fabio Manfredini MD^c, Benedetta Boari MD^d,
Elisabetta Bergami MD^d, Elisa Mari MD^d, Susanna Gamberini MD^b,
Raffaella Salmi MD^d, Massimo Gallerani MD^d



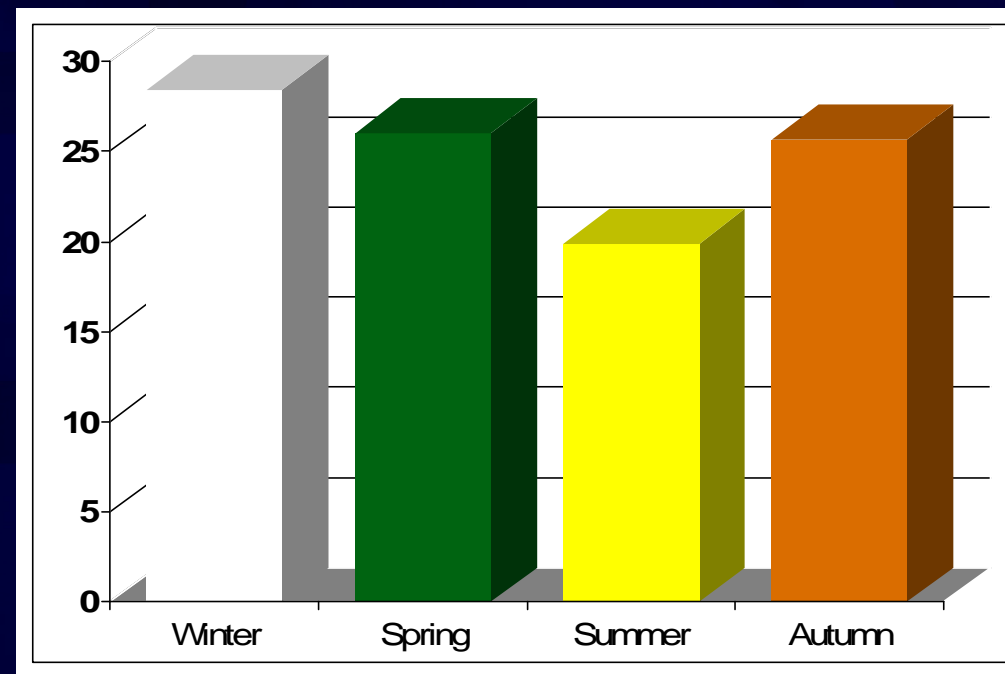
Patologie aortiche acute

Registro Internazionale IRAD, 1996-2000 (n = 957)



Chronobiological Patterns of Acute Aortic Dissection

Rajendra H. Mehta, MD; Roberto Manfredini, MD; Fauziya Hassan, MD; Udo Sechtem, MD;
Eduardo Bossone, MD; Jae K. Oh, MD; Jeanna V. Cooper, MS; Dean E. Smith, PhD;
Francesco Portaluppi, MD; Marc Penn, MD; Stuart Hutchison, MD; Christoph A. Nienaber, MD;
Eric M. Isselbacher, MD; Kim A. Eagle, MD;
on Behalf of the International Registry of Acute Aortic Dissection (IRAD) Investigators



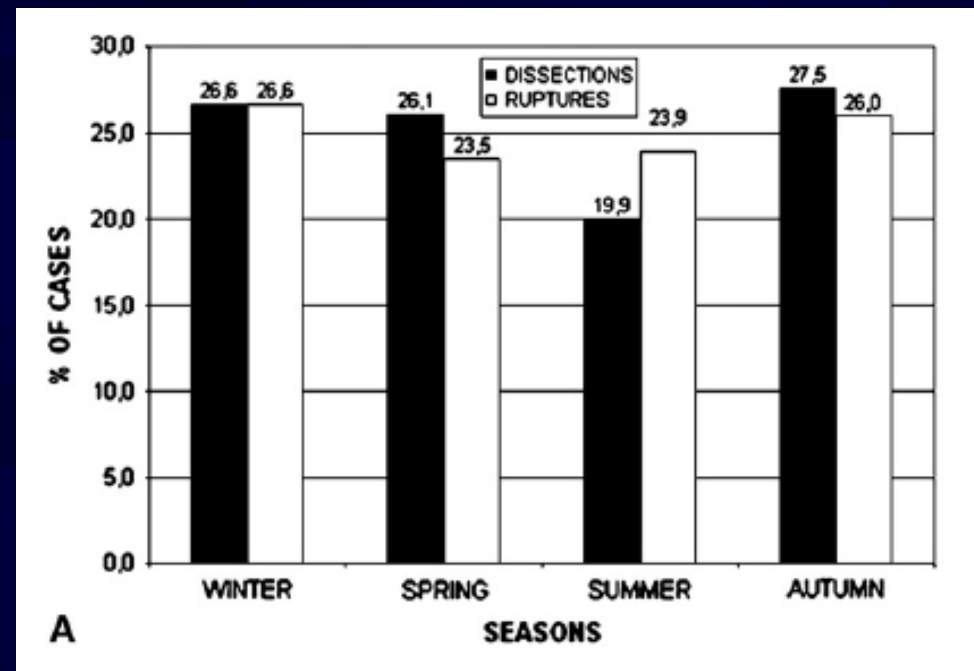
Patologie aortiche acute

Regione Emilia-Romagna, 2000-2006 (n = 4.615)



Seasonal variation in occurrence of aortic diseases: The database of hospital discharge data of the Emilia-Romagna region, Italy

Roberto Manfredini, MD,^a Benedetta Boari, MD,^b Fabio Manfredini, MD,^c Raffaella Salmi, MD,^b Eduardo Bossone, MD,^d Davide Fabbri, MD,^e Edgardo Contato, MD,^f Francesco Mascoli, MD,^g and Massimo Gallerani, MD,^b Ferrara and Milan, Italy



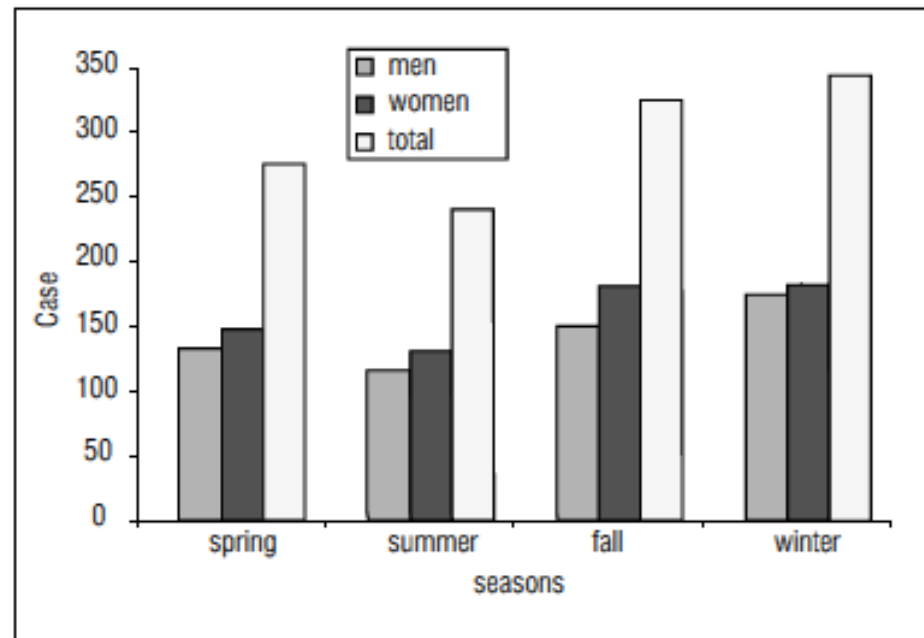
Trombosi venosa profonda

Ferrara, 1998-2002 (n = 1.166)



Seasonal variation in the occurrence of deep vein thrombosis

Massimo Gallerani¹, Benedetta Boari², Damiana de Toma¹,
Raffaella Salmi², Roberto Manfredini¹



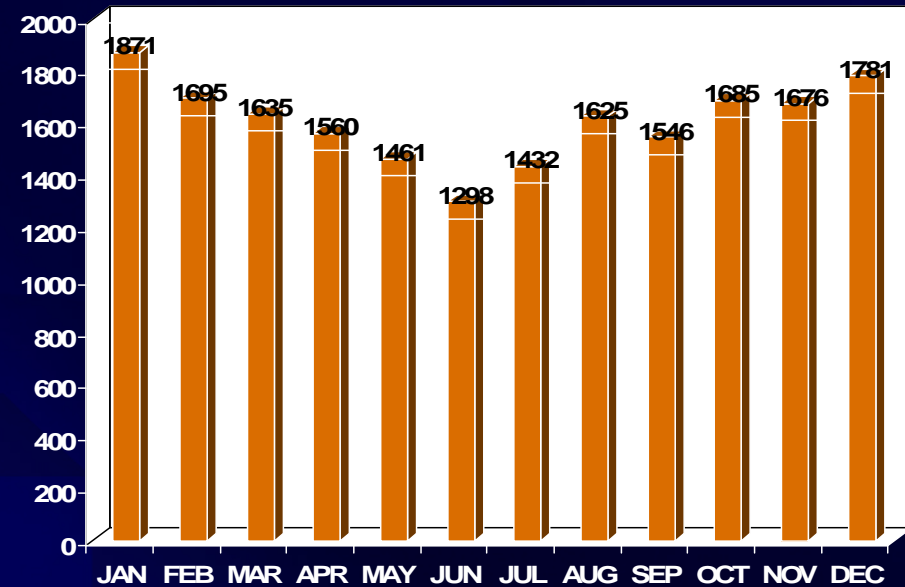
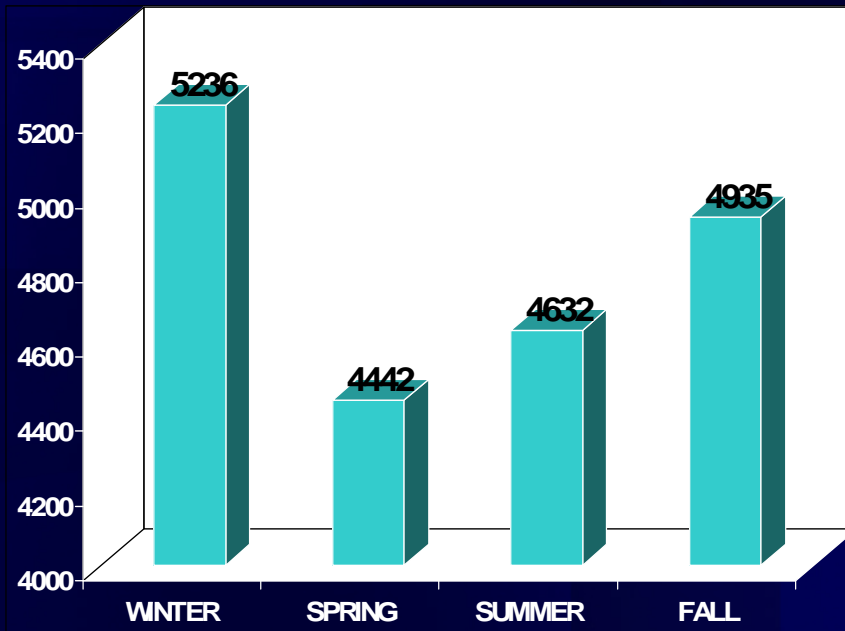
Tromboembolia polmonare

Regione Emilia-Romagna, 1998-2005 (n = 19.245)



SEASONAL VARIATION IN OCCURRENCE OF PULMONARY EMBOLISM: ANALYSIS OF THE DATABASE OF THE EMILIA-ROMAGNA REGION, ITALY

Massimo Gallerani,¹ Benedetta Boari,¹ Michael H. Smolensky,² Raffaella Salmi,¹ Davide Fabbri,³ Edgardo Contato,⁴ and Roberto Manfredini⁵



Tromboembolismo venoso

Metanalisi studi letteratura (17 studi, n = 23.469)



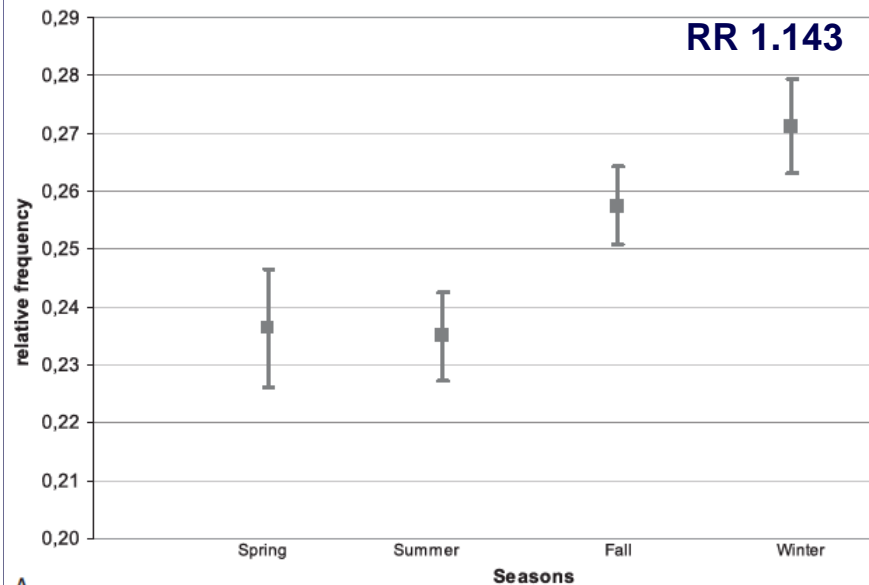
Seasonal and monthly variability in the incidence of venous thromboembolism

A systematic review and a meta-analysis of the literature

Francesco Dentali¹; Walter Ageno¹; Elena Rancan¹; Alberto V. Donati¹; Luca Galli¹; Alessandro Squizzato¹; Achille Venco¹; Pier Mannuccio Mannucci²; Roberto Manfredini³

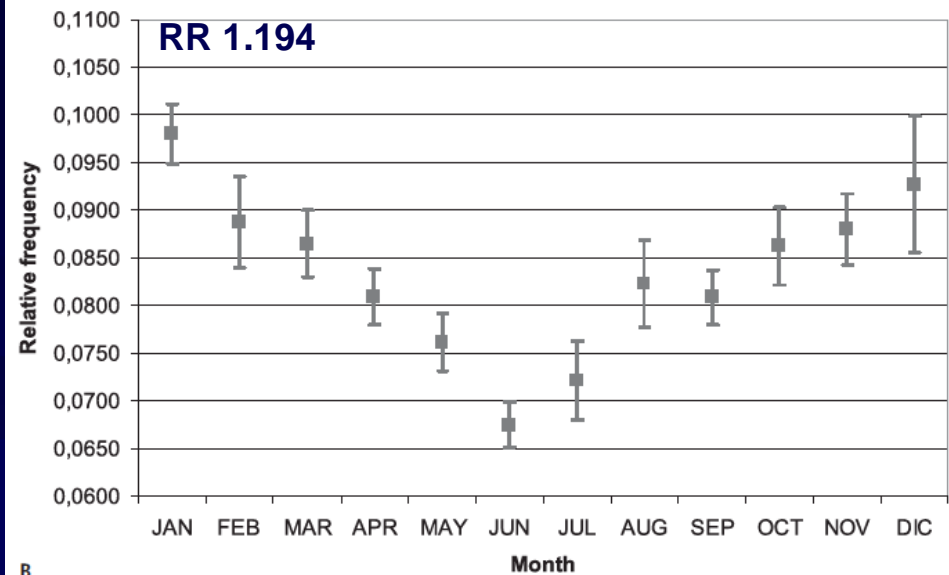
¹Department of Clinical Medicine, University of Insubria, Varese, Italy; ²Department of Medicine and Medical Specialties, IRCCS Cà Granda Foundation Maggiore Policlinico Hospital, Milan Italy; ³Department of Clinical and Experimental Medicine, Clinica Medica and Vascular Diseases Center, University of Ferrara, Italy

Relative frequency of average seasonal variation with 95% CI bars



A

Relative frequency of average monthly variation with 95% CI bars



B

Autunno



Alfred Sisley, 1873
Autunno: la Senna presso Bougival

Malattia tromboembolica venosa

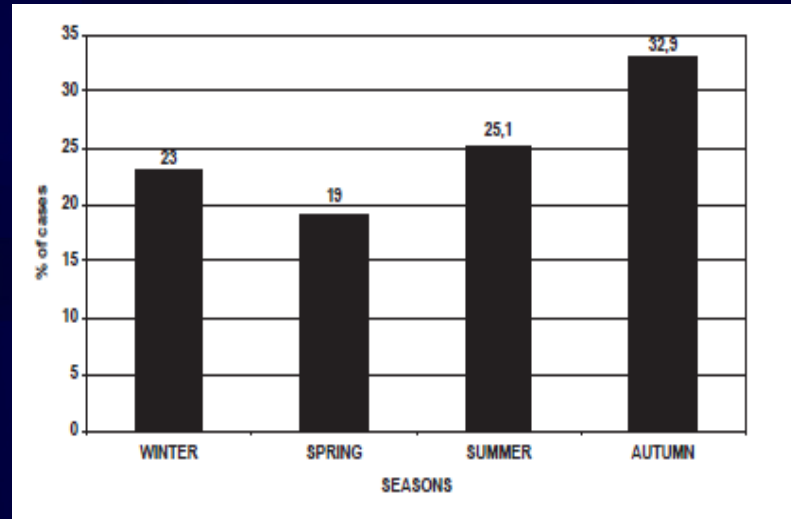
Registro multicentrico prospettico italiano, 2002-2004 (n = 2.119)



Seasonal Variation in the Occurrence of Venous Thromboembolism: Data From the MASTER Registry

Clinical and Applied
Thrombosis/Hemostasis
Volume 15 Number 3
June 2009 309-315
© 2009 The Author(s)
10.1177/1076029608319947
<http://cah.sagepub.com>

Roberto Manfredini, MD, Davide Imberti, MD, Massimo Gallerani, MD, Melina Verso, MD, Riccardo Pistelli, MD, Walter Ageno, MD, and Giancarlo Agnelli, MD



Attacco ischemico transitorio

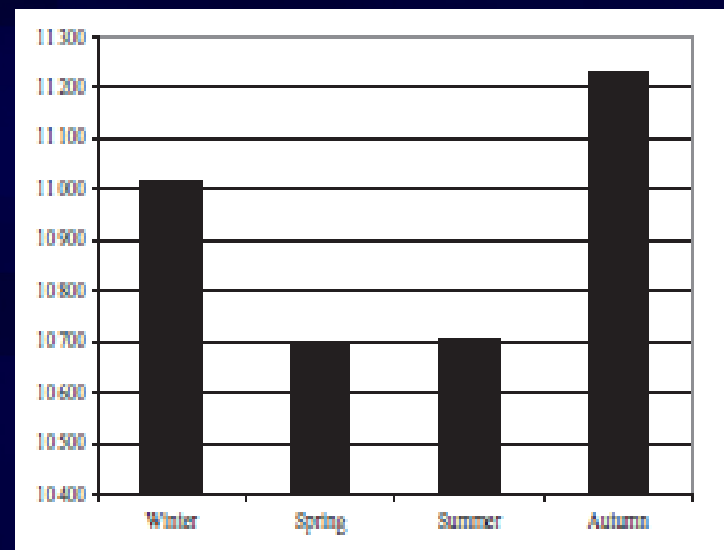
Regione Emilia-Romagna, 1998-2006 (n = 43.642)



Clinical and Applied
Thrombosis/Hemostasis
Volume 16(2) Number 2
March/April 2010 153-160
© 2010 The Author(s)
10.1177/1076029609342111
<http://cah.sagepub.com>

Temporal Patterns of Hospital Admissions for Transient Ischemic Attack: A Retrospective Population-based Study in the Emilia-Romagna Region of Italy

Roberto Manfredini, MD, Fabio Manfredini, Benedetta Boari, MD, Anna Maria Malagoni, MD, Susanna Gamberini, MD, Raffaella Salmi, MD, and Massimo Gallerani, MD



Chirurgia carotidea

Ferrara, 1996-2008 (n = 159)

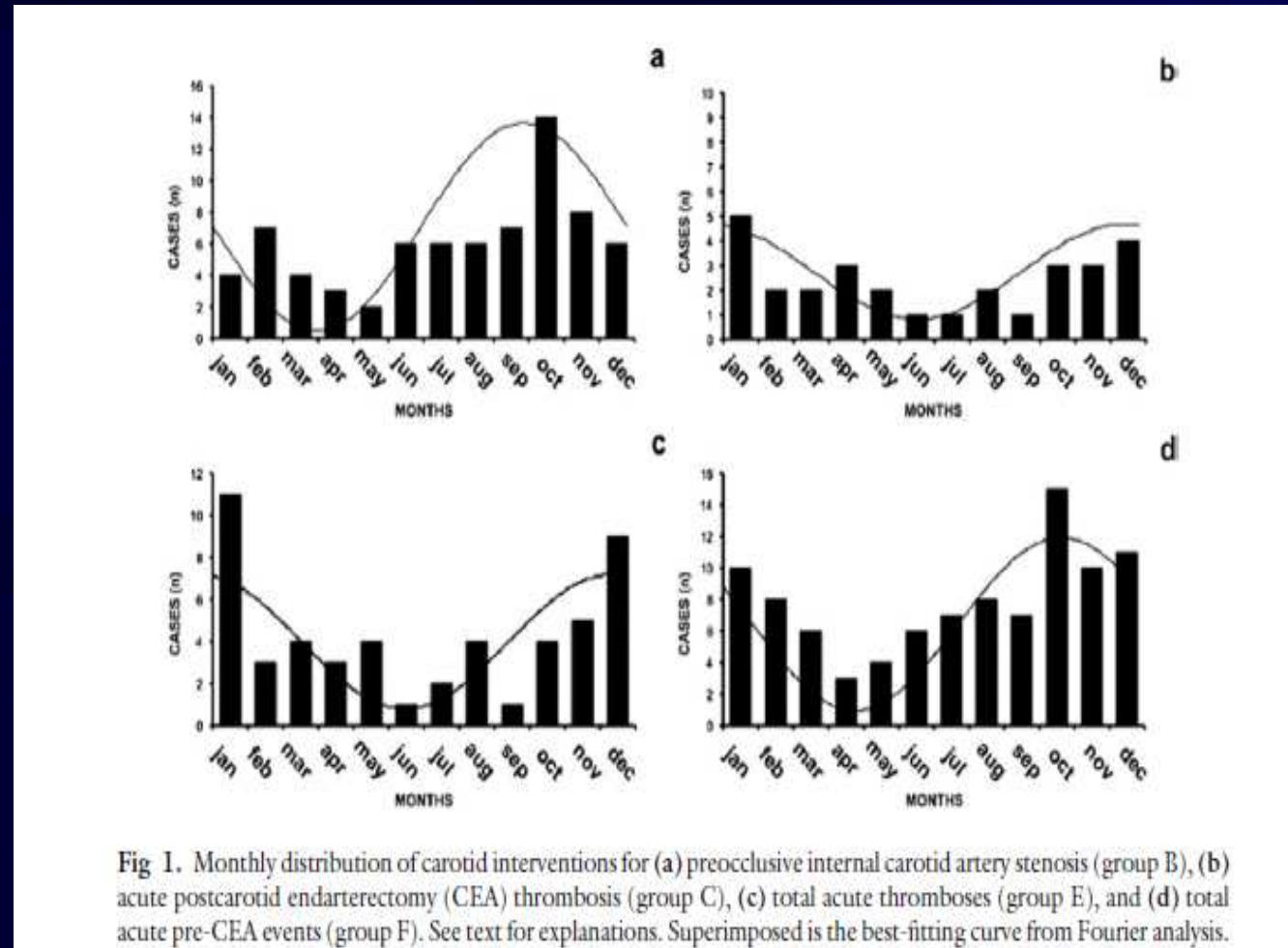


Fig 1. Monthly distribution of carotid interventions for (a) preocclusive internal carotid artery stenosis (group B), (b) acute postcarotid endarterectomy (CEA) thrombosis (group C), (c) total acute thromboses (group E), and (d) total acute pre-CEA events (group F). See text for explanations. Superimposed is the best-fitting curve from Fourier analysis.

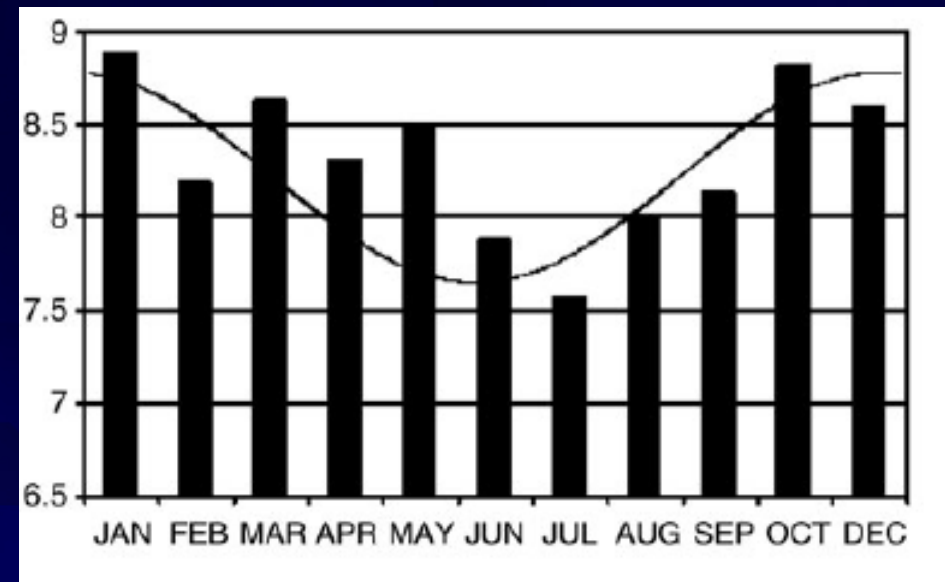
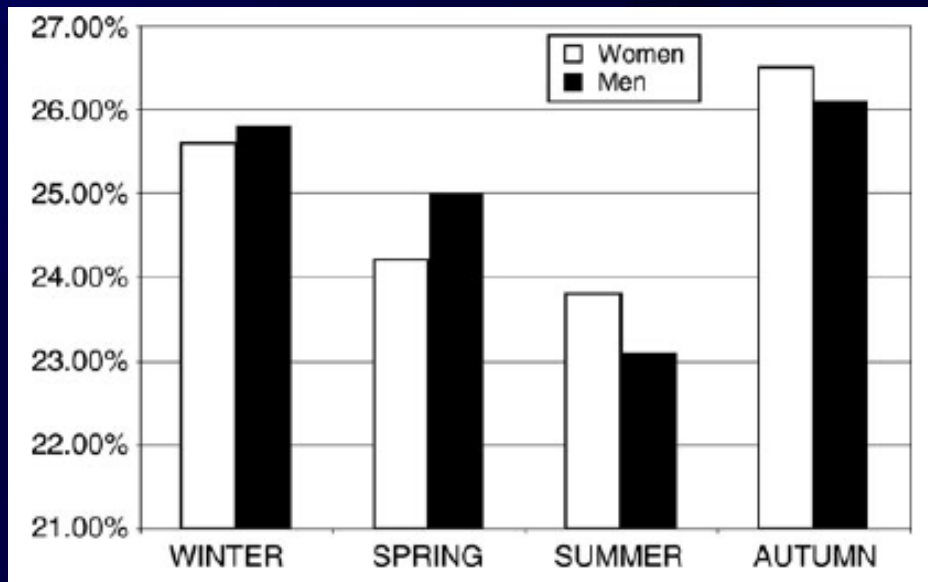
Eventi acuti cardiovascolari globali

Ferrara, 1998-2006 (n = 130.693)



Seasonal and Weekly Patterns of Occurrence of Acute Cardiovascular Diseases: Does a Gender Difference Exist?

Roberto Manfredini, M.D.,¹ Fabio Fabbian, M.D.,¹ Marco Pala, M.D.,¹ Ruana Tiseo, M.D.,¹ Alfredo De Giorgi, M.D.,¹
Fabio Manfredini, M.D.,² Anna Maria Malagoni, M.D.,² Fulvia Signani, PsyD,³ Candida Andreati, M.D.,³
Benedetta Boari, M.D.,⁴ Raffaella Salmi, M.D.,⁴ Davide Imberti, M.D.,⁴ and Massimo Gallerani, M.D.⁴



Ulcera peptica

Regione Emilia-Romagna 1998-2005 (n = 26.848)

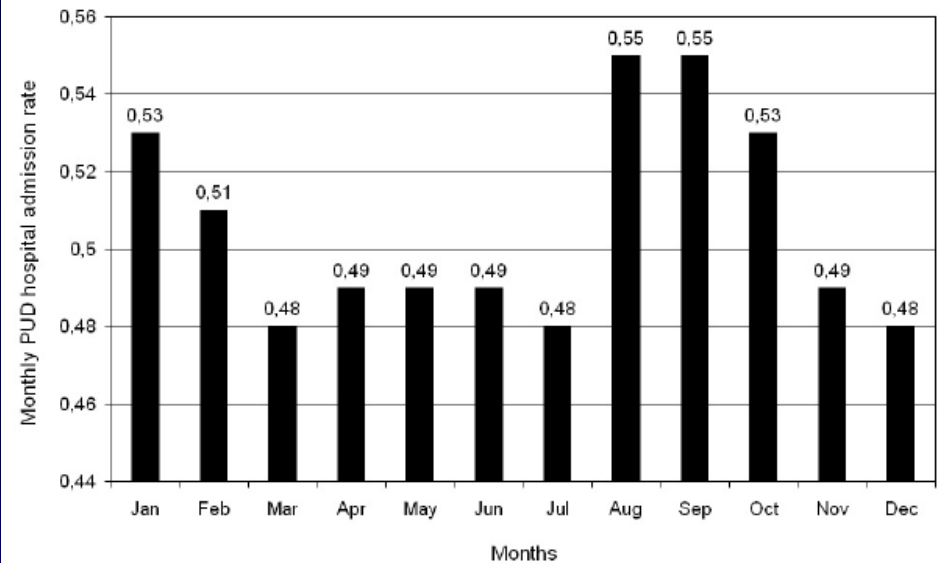
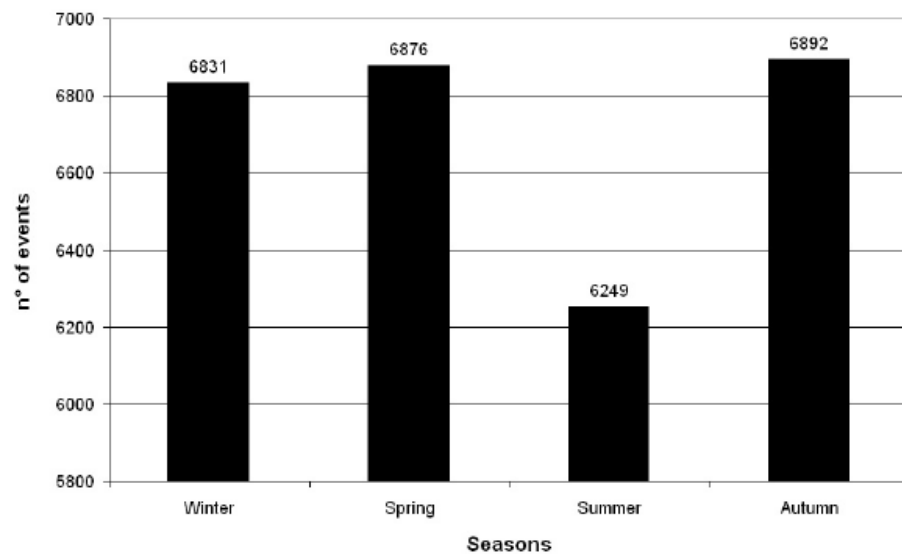


RESEARCH ARTICLE

Open Access

Seasonal pattern of peptic ulcer hospitalizations: analysis of the hospital discharge data of the Emilia-Romagna region of Italy

Roberto Manfredini*^{1,2}, Roberto De Giorgio³, Michael H Smolensky⁴, Benedetta Boari⁵, Raffaella Salmi⁵, Davide Fabbri⁶, Edgardo Contato⁷, Mauro Serra³, Giovanni Barbara³, Vincenzo Stanghellini³, Roberto Corinaldesi³ and Massimo Gallerani⁵



Estate



Alfred Sisley, 1888
Il ponte di Moret d'Estate

Cardiomiopatia Tako-Tsubo

Tako-Tsubo Italian Network 2002-2007 (n = 88)

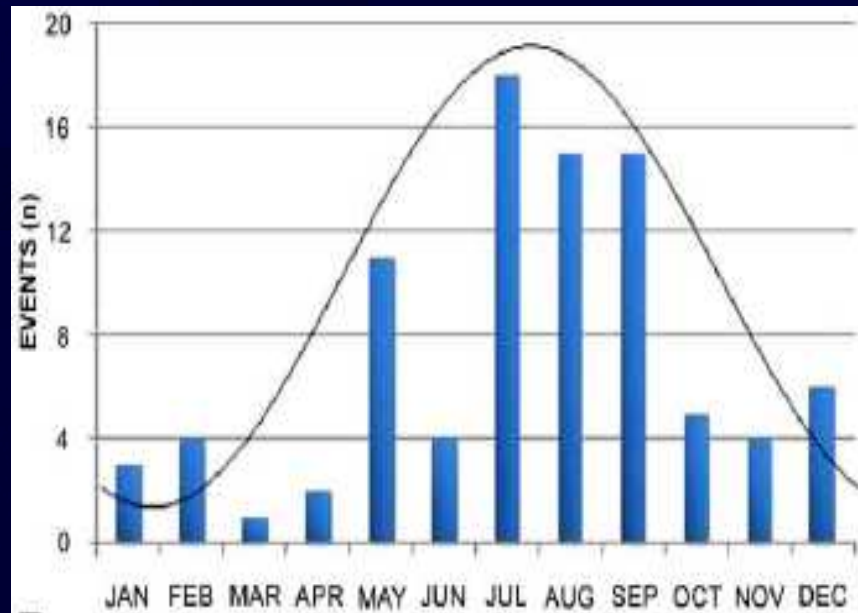


CORRESPONDENCE

Research
Correspondence

Chronobiological Patterns of
Onset of Tako-Tsubo Cardiomyopathy

A Multicenter Italian Study



*Rodolfo Citro, MD

Mario Previtali, MD

Daniella Bovelli, MD

Olga Vriza, MD

Costantino Astarita, MD

Marco Mariano Patella, MD

Gennaro Provenza, MD

Corinna Armentano, MD

Quirino Ciampi, MD

Giovanni Gregorio, MD

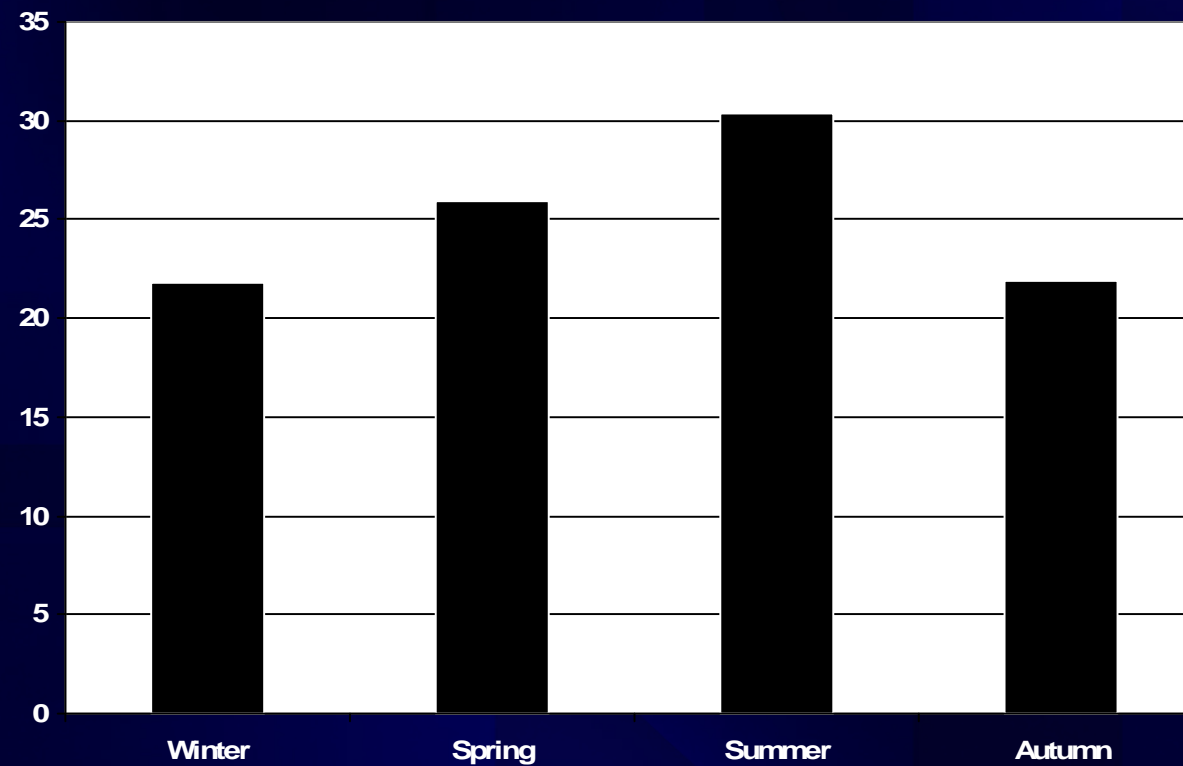
Massimo Piepoli, MD

Eduardo Bossone, MD, PhD

Roberto Manfredini, MD

Infezioni da Herpes Zoster

Ferrara 1992-1998 (n = 845)



Appendicite acuta

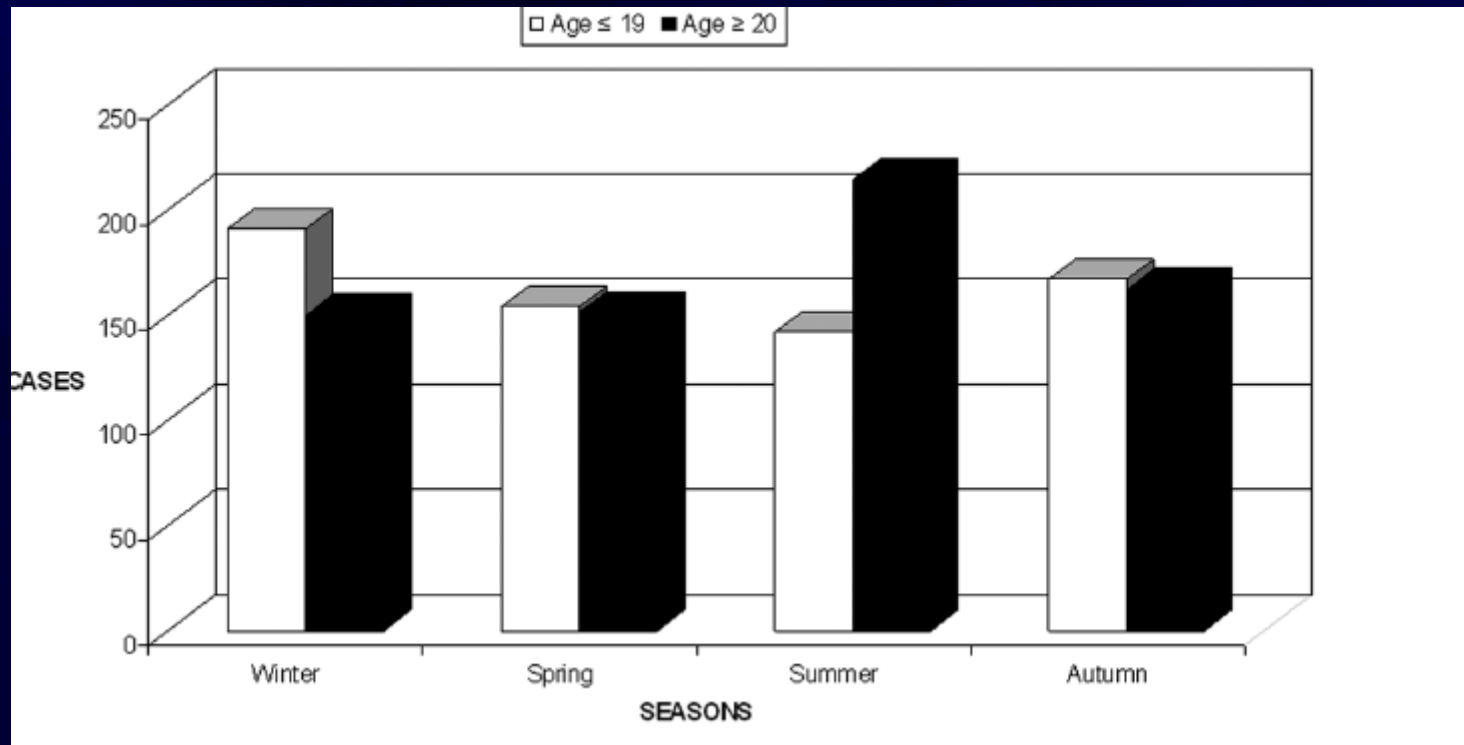
Ferrara 1998-2004 (n = 1.331)



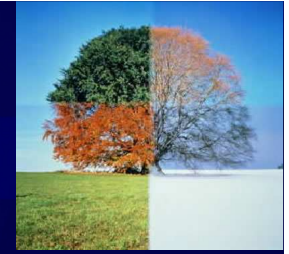
Seasonal variation in onset of acute appendicitis

¹M. Gallerani, ²B. Boari, ³G. Anania, ³G. Cavallesco, ²R. Manfredini

¹Department of Internal Medicine, St Anna Hospital Ferrara; ²Department of Clinical and Experimental Medicine; ³Department of Surgical, Anaesthesiologic and Radiological Sciences, University of Ferrara, Italy



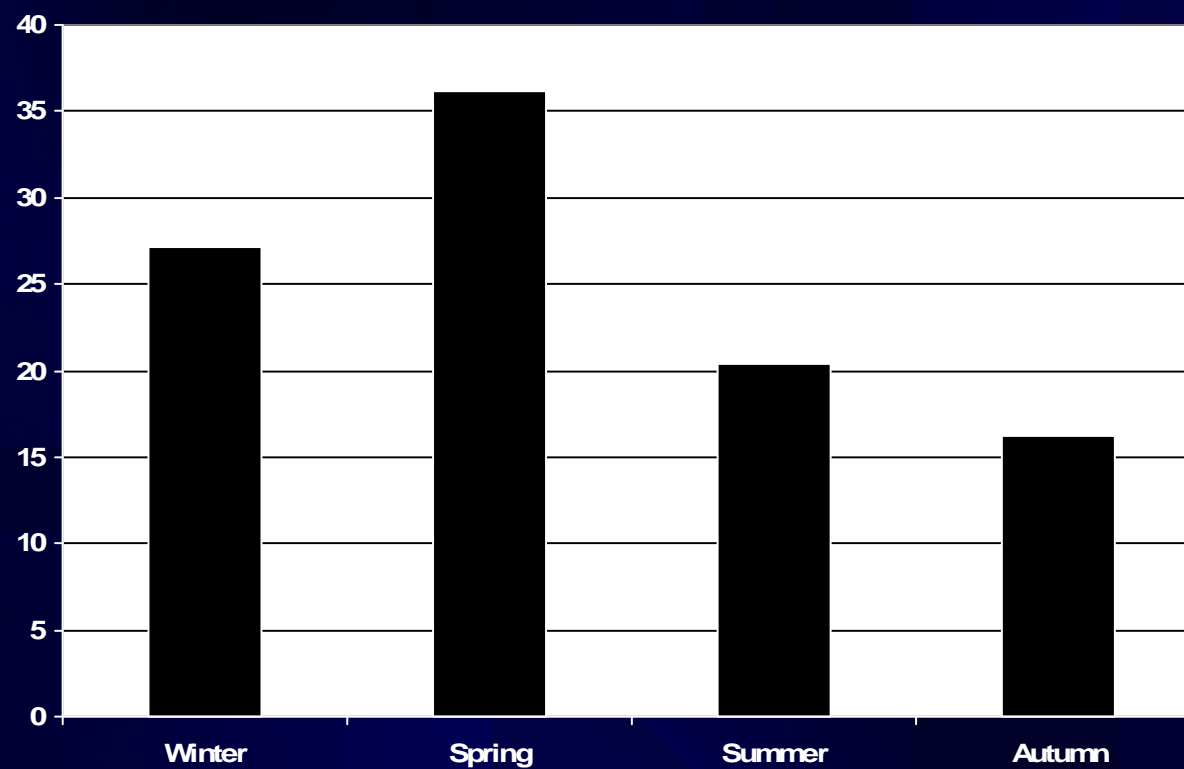
Primavera



Alfred Sisley, 1881
Frutteto in Primavera

Gotta acuta

Ferrara, 1990-1997 (n = 210)



Sclerosi multipla (recidiva)

Bologna, 2007-2008 (n = 164)



Salvi et al. *BMC Neurology* 2010, **10**:105
<http://www.biomedcentral.com/1471-2377/10/105>



RESEARCH ARTICLE

Open Access

A seasonal periodicity in relapses of multiple sclerosis? A single-center, population-based, preliminary study conducted in Bologna, Italy

Fabrizio Salvi¹, Ilaria Bartolomei¹, Michael H Smolensky², Angelo Lorusso¹, Elena Barbarossa¹, Anna Maria Malagoni³, Paolo Zamboni³, Roberto Manfredini^{3,4,5*}

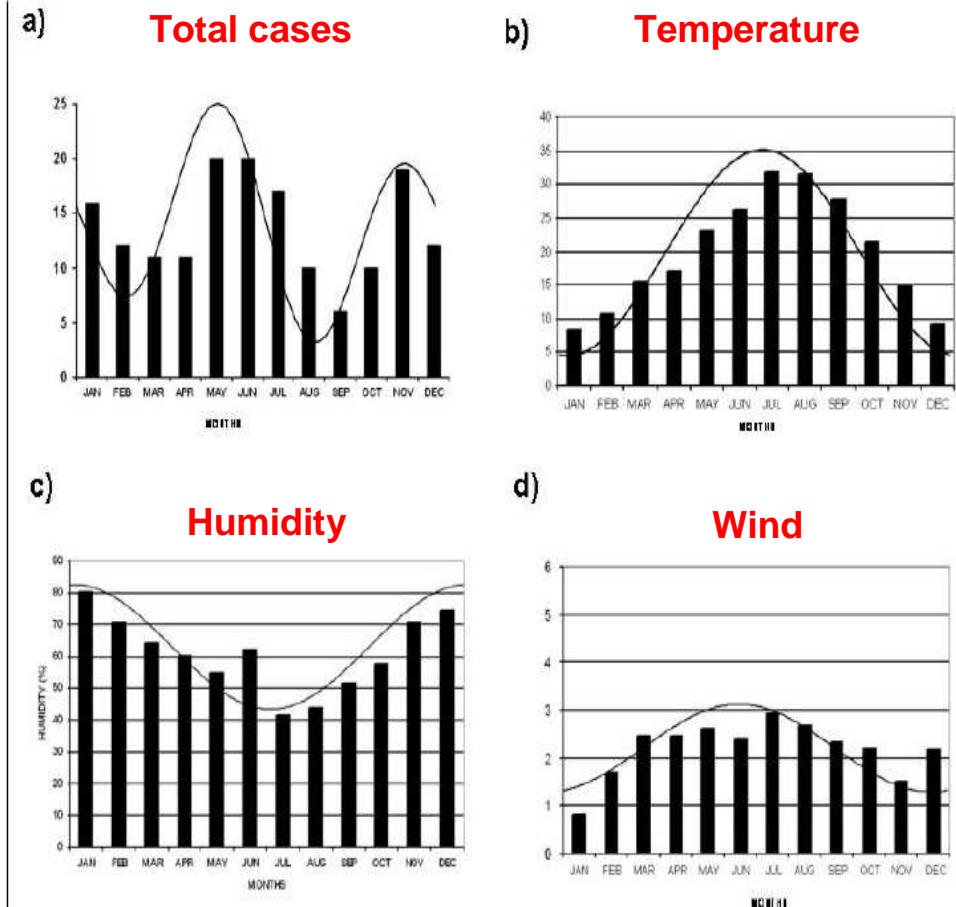
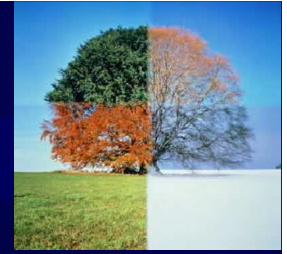


Figure 1 Frequency of relapses of multiple sclerosis by month of the year (a) and average monthly data of ambient temperature in °C (b), relative humidity as % (c), and wind speed as m/sec (d).

***..per ogni cosa c'è la sua stagione,
c'è un tempo per ogni situazione sotto il cielo..***



...e per i diverticoli?



Pillole di epidemiologia



- **Dati USA**

- **Patologia diverticolare**

- 5% della popolazione di età 40
 - 33-50% della popolazione >50
 - 80% della popolazione >80

- **Diverticolite**

- 10-20% dei pazienti con patologia diverticolare
 - È una delle 5 patologie gastroenterologiche più costose, con costi diretti ed indiretti stimati di \$2,5 mld/anno

- **Dati internazionali**

- **Diverticolosi: 0.2% della popolazione**

Pillole di epidemiologia



- **Dati USA**

- **Patologia diverticolare**

- 5% della popolazione di età 40
- **33-50% della popolazione >50**
- 80% della popolazione >80

- **Diverticolite**

- 10-20% dei pazienti con patologia diverticolare
- È una delle 5 patologie gastroenterologiche più costose, con costi diretti ed indiretti stimati di \$2,5 mld/anno

- **Dati internazionali**

- **Diverticolosi: 0.2% della popolazione**



Pillole di epidemiologia



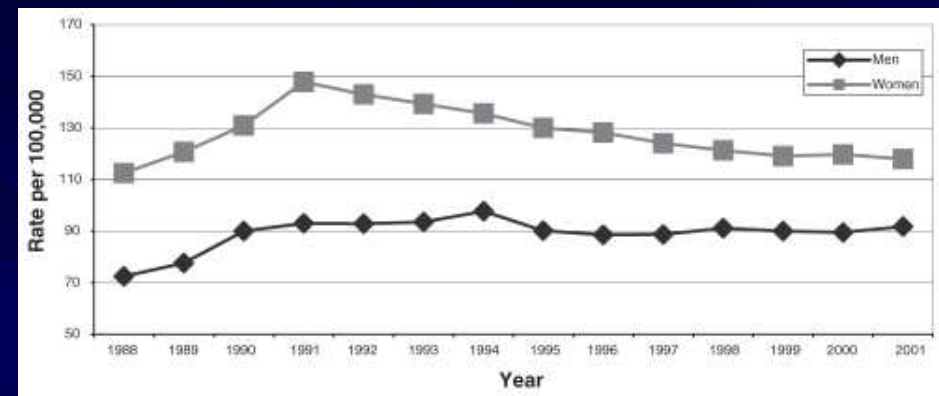
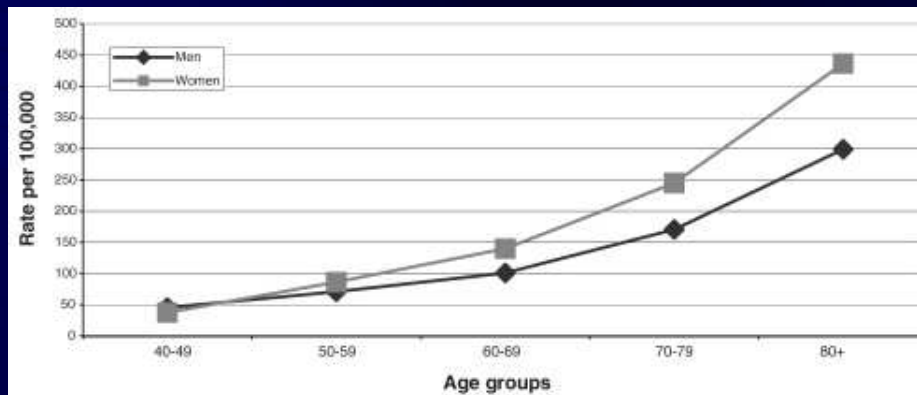
- **Età**
 - La patologia incrementa con l'età
- **Sesso**
 - Nessuna relazione
- **Razza**
 - Popolazione Asiatica predisposta alla diverticolite colon destro
- **Mortalità e Morbilità**
 - 20% richiede terapia chirurgica
 - Tasso di mortalità: 7.7% (se concomita peritonite)



ORIGINAL ARTICLE

Fourteen-year study of hospital admissions for diverticular disease in Ontario

Eiran Warner BSc¹, Eric J Crighton PhD¹, Rahim Moineddin PhD²,
Muhammad Mamdani PharmD MPH^{3,4}, Ross Upshur MA MD MSc CCFP FRCPC^{1,2,3}



Diverticolite acuta

Nationwide Inpatient Sample USA 1997-2005 (n = 374,123)



ORIGINAL ARTICLE

Cyclical Increase in Diverticulitis During the Summer Months

Rocco Ricciardi, MD, MPH; Patricia L. Roberts, MD; Thomas E. Read, MD; Peter W. Marcello, MD; Jason F. Hall, MD; David J. Schoetz, MD; Eugene F. Foley, MD

Diverticulite acuta

Nationwide Inpatient Sample USA 1997-2005 (n = 374.123)

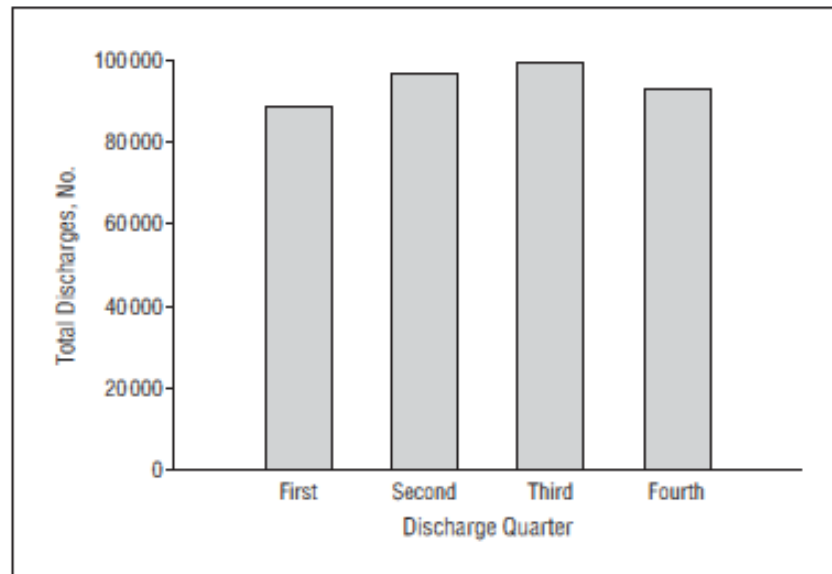


Figure 1. Total number of nonelective diverticulitis discharges in Nationwide Inpatient Sample hospitals by quarter. First indicates January, February, and March; second, April, May, and June; third, July, August, and September; and fourth, October, November, and December.

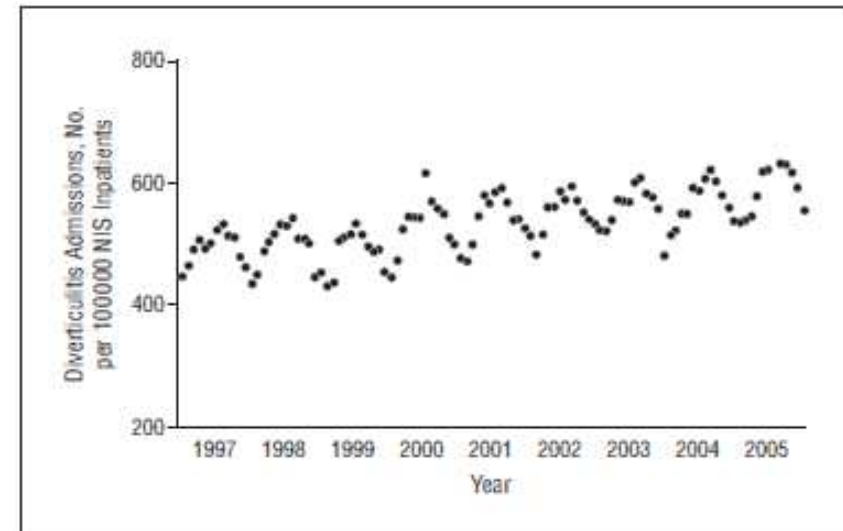


Figure 2. Nonelective diverticulitis admissions in Nationwide Inpatient Sample (NIS) hospitals as a proportion of all inpatients. The ratio of monthly nonelective diverticulitis admissions are plotted as a function of time.

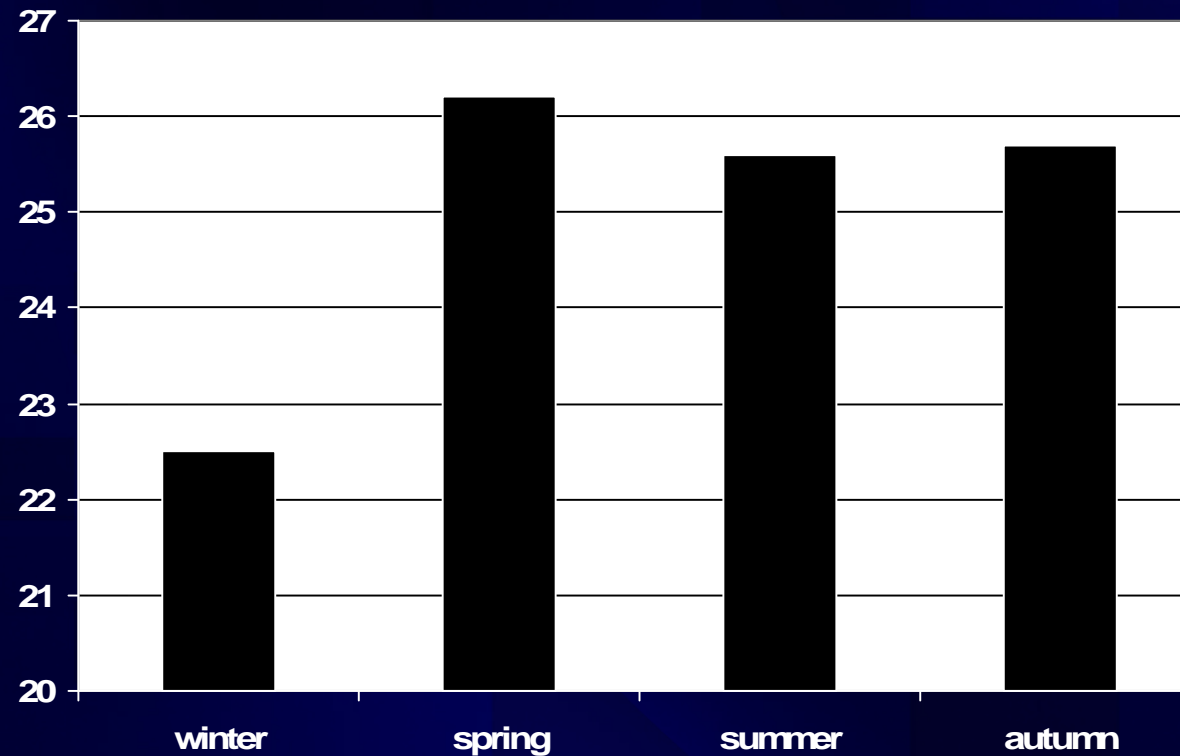
Estate vs Inverno= +12.4%

$P < 0.001$



Diverticoliti acute

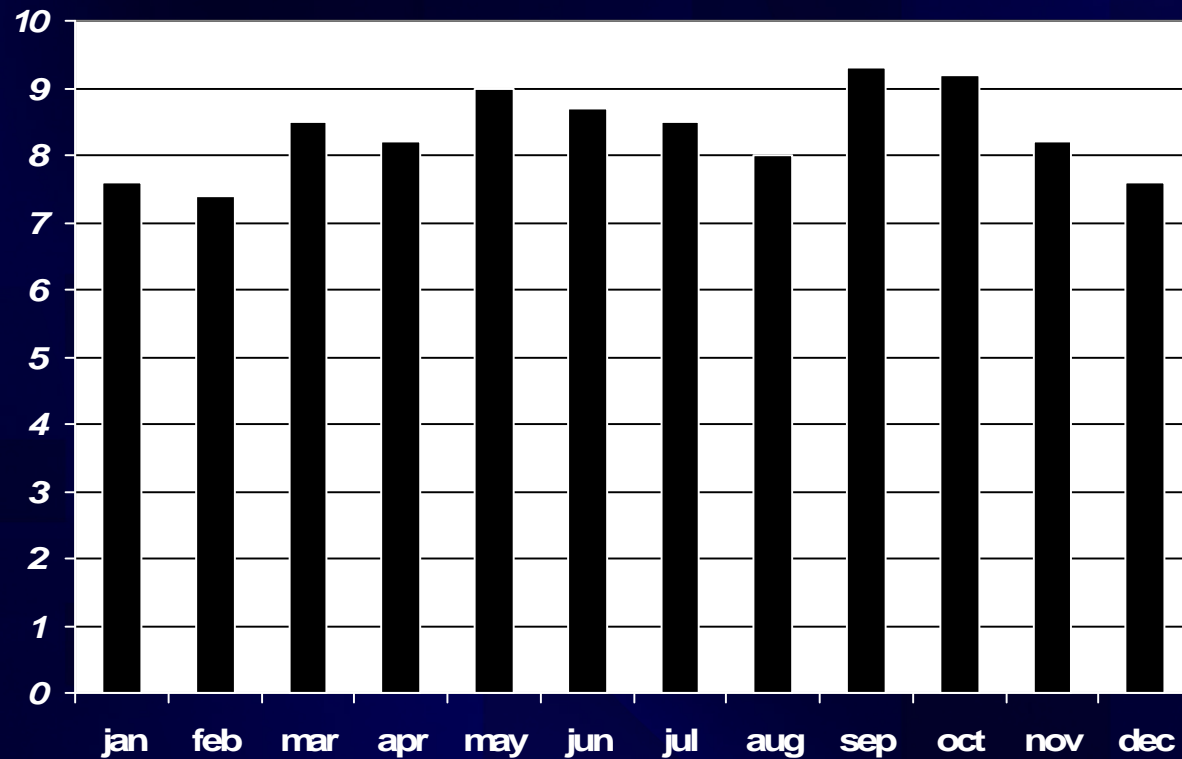
Ferrara 1992-1998 (n = 30.671)



$P=0.020$

Diverticoliti acute

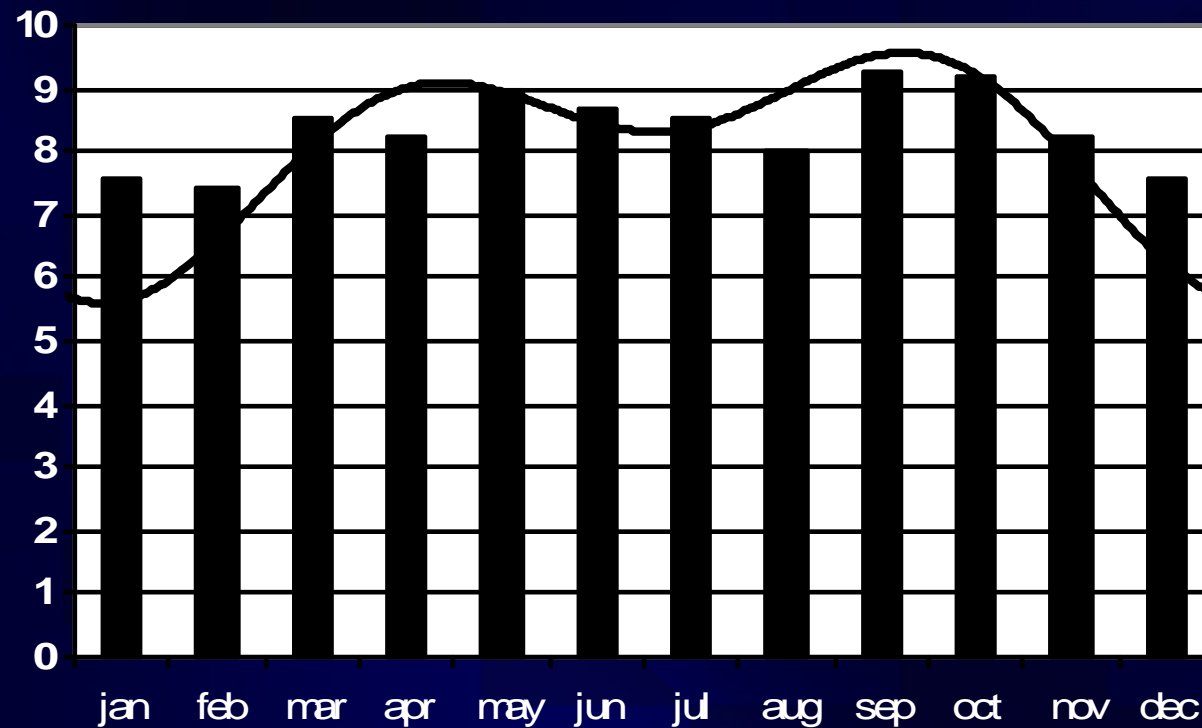
Ferrara 1992-1998 (n = 30.671)



$P=0.071$

Diverticoliti acute

Ferrara 1992-1998 (n = 30.671)



$P=0.0015$

Ipotesi patogenetiche?



- ruolo delle patologie virali (influenza?)
- dieta e triggers alimentari: frutta e verdura; noccioline e popcorn; intake di fibre
- modificazioni climatiche, periodi feriali, fattori di lifestyle
- farmaci (FANS)

Diverticulitis: Something New Under the Sun?



The observation is an intriguing one.

Seasonal variation has been described in acute appendicitis, with the peak incidence occurring during the summer months.

One could hypothesize a variety of factors that might be responsible for the summer seasonality of diverticulitis including dietary change, dehydration, or a hitherto unrecognized pathogen.

But it does provide the reader with food for thought at a time when almost all of our previous notions about diverticular disease have been called into question.

The Cardiomyocyte Circadian Clock

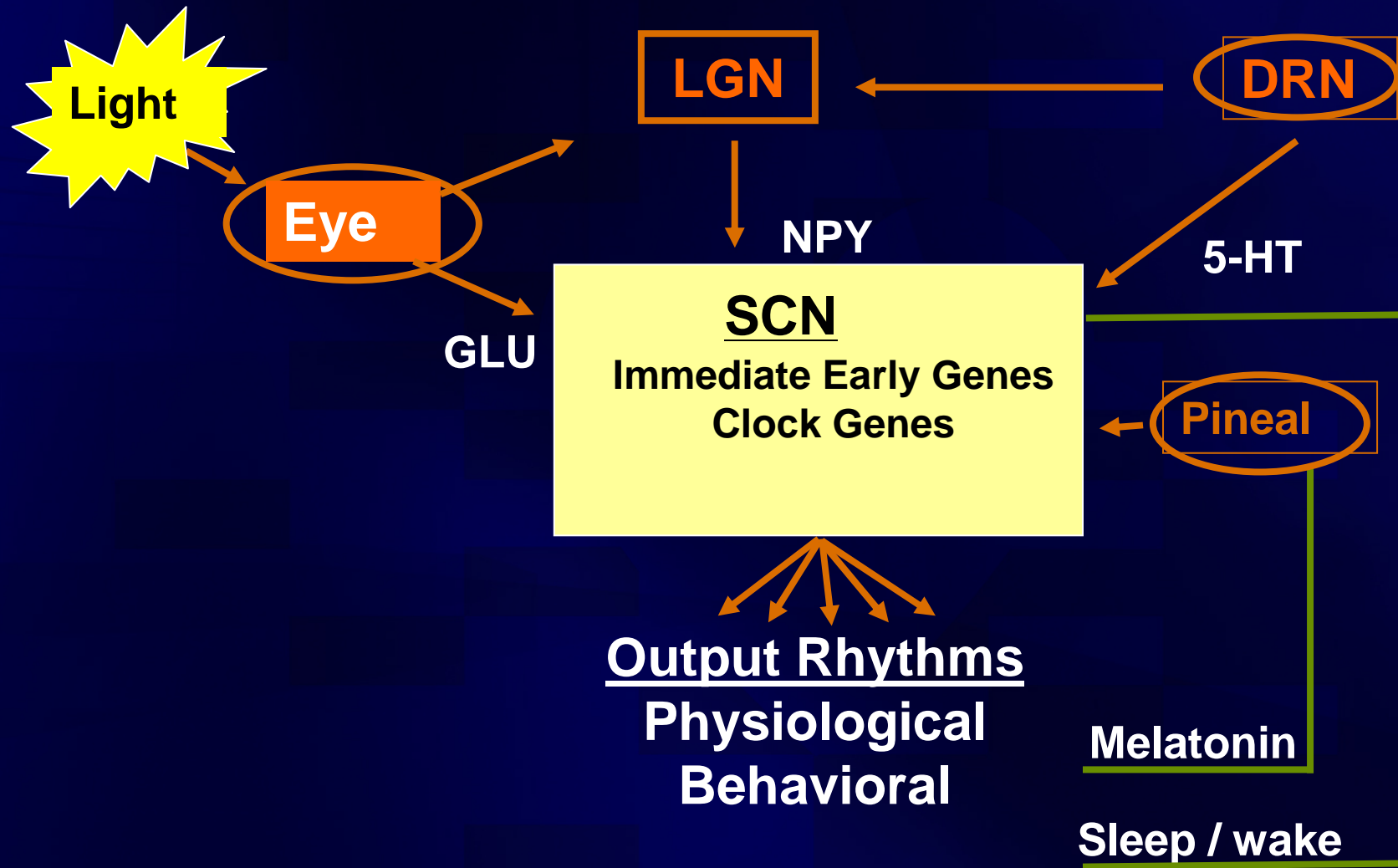
Emerging Roles in Health and Disease

David J. Durgan, Martin E. Young

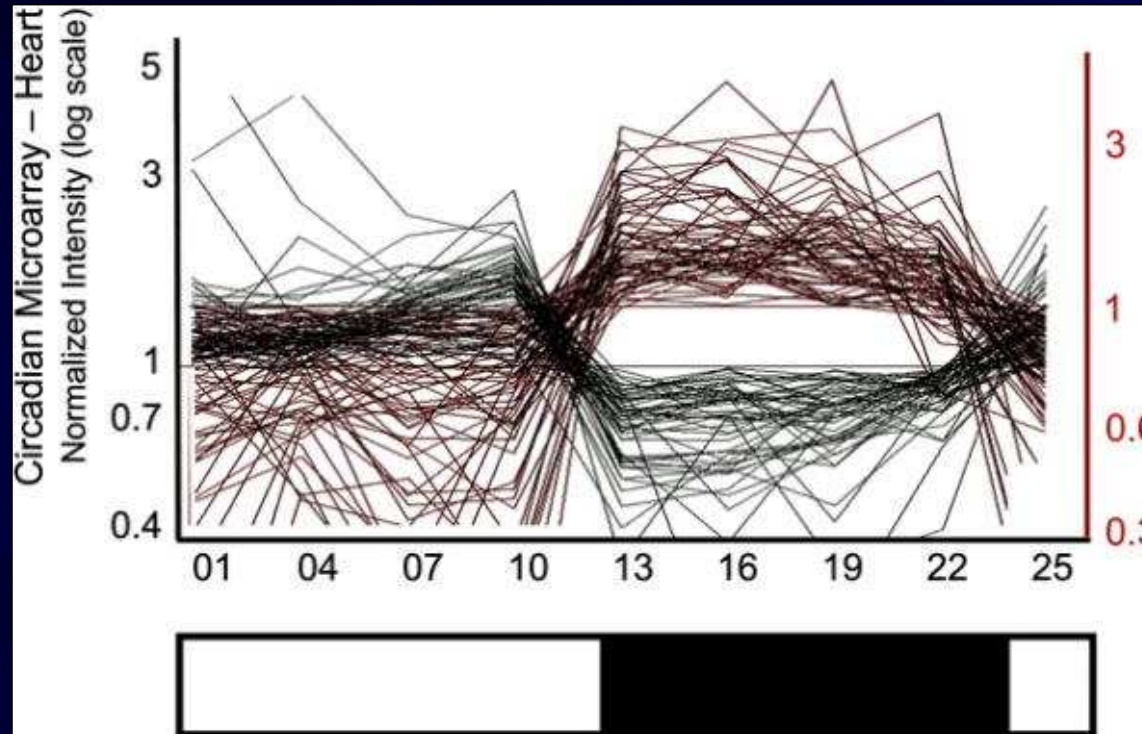


- The onset of CV events, such as MI, stroke, aortic aneurism rupture, and SCD have all been shown to be time-of-day-dependent in humans.
- Many of these diseases have been shown to exhibit both weekly and seasonal variations as well (*Manfredini 2004, 2001*).
- Classically, these rhythms have been ascribed to fluctuations in extracardiac factors, such as sympathetic activity, sheer stress and prothrombotic factors. The possibility that a molecular mechanism intrinsic to the cardiomyocyte, such as the circadian clock, may contribute to cardiovascular diseases, is the subject of contemporary investigation.

Organizzazione dei ritmi circadiani

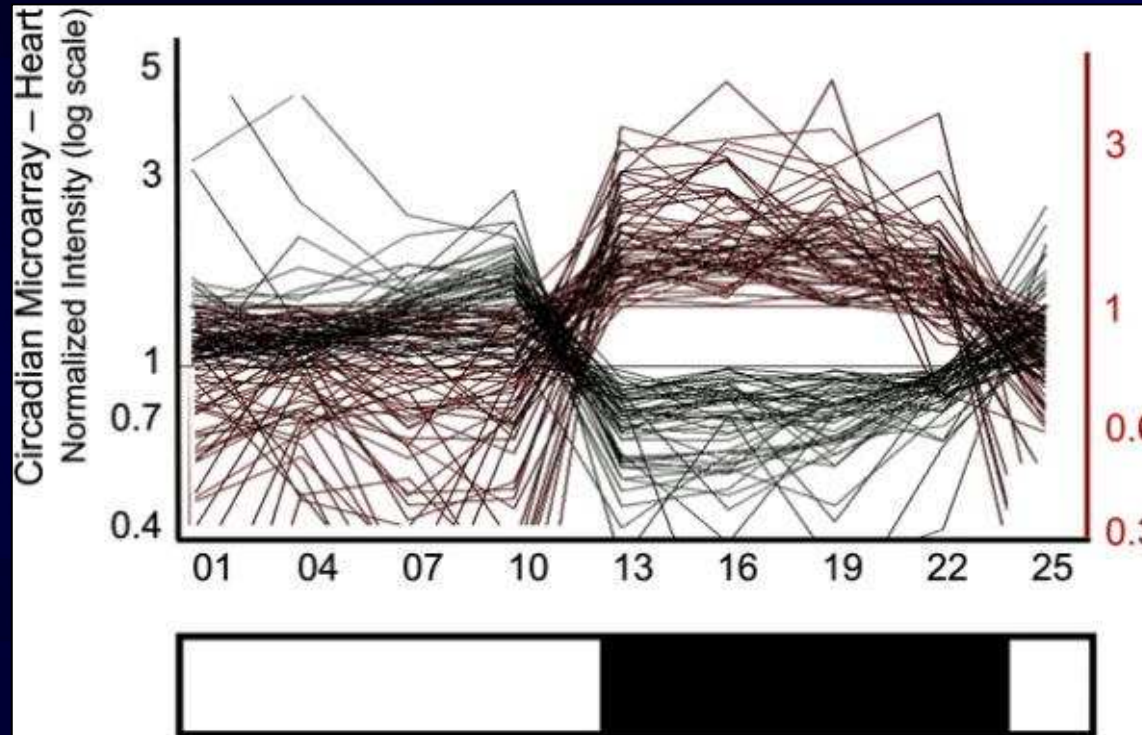


Geni e ritmi circadiani



Transizione luce/buio e modificazione di attività ed espressione dei geni cardiaci
light-activated (or dark-repressed) & dark-activated (or light-repressed)

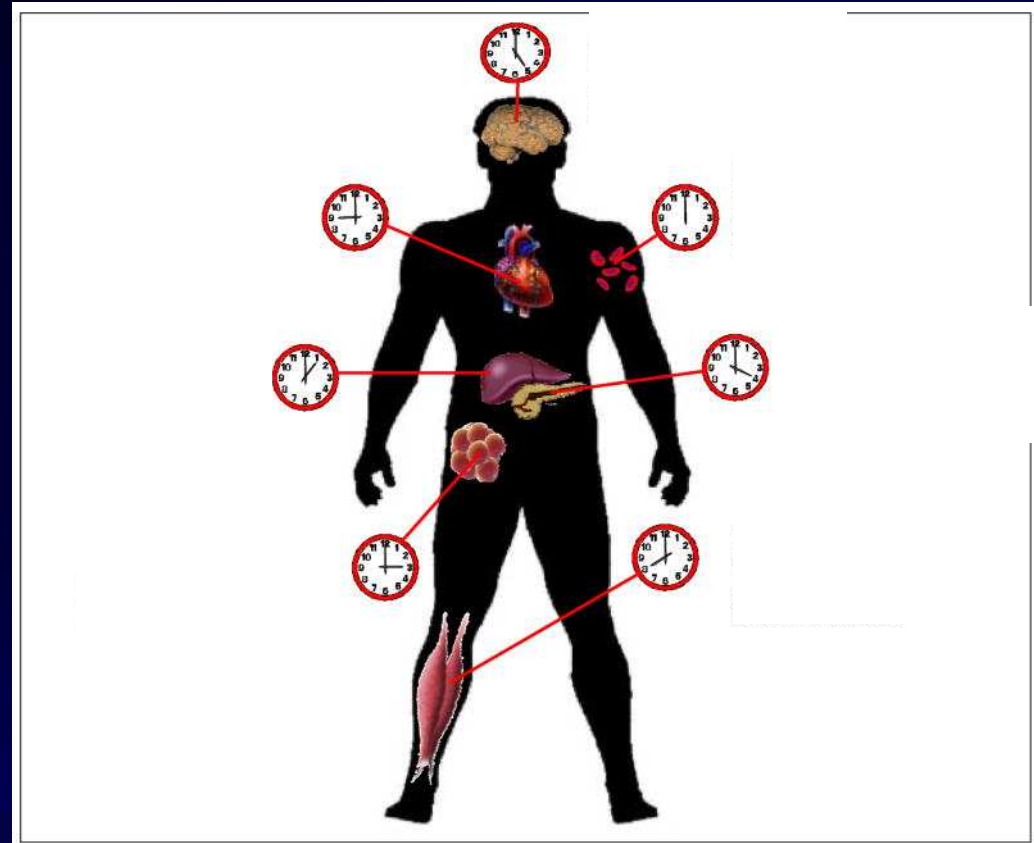
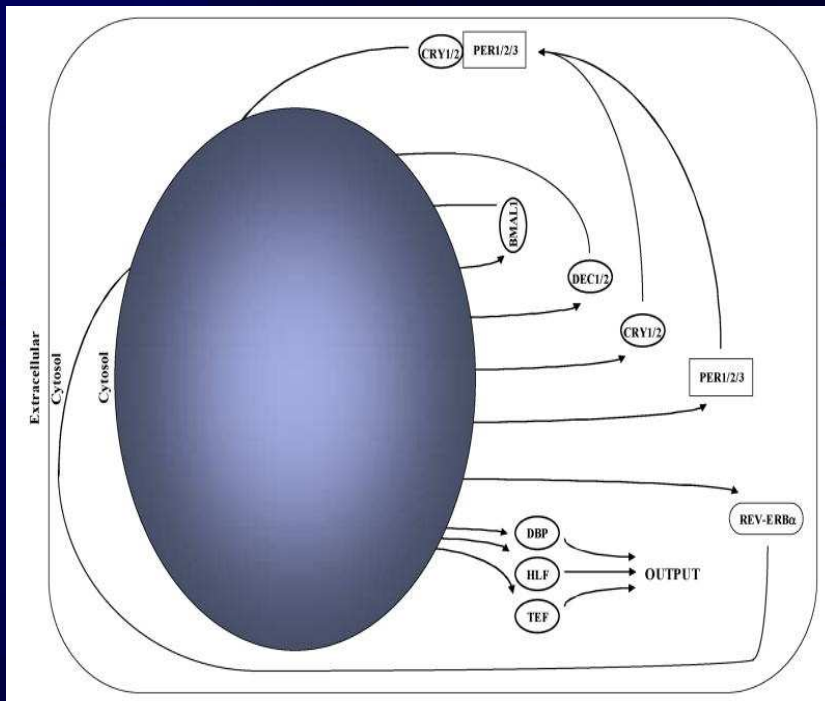
Geni e ritmi circadiani



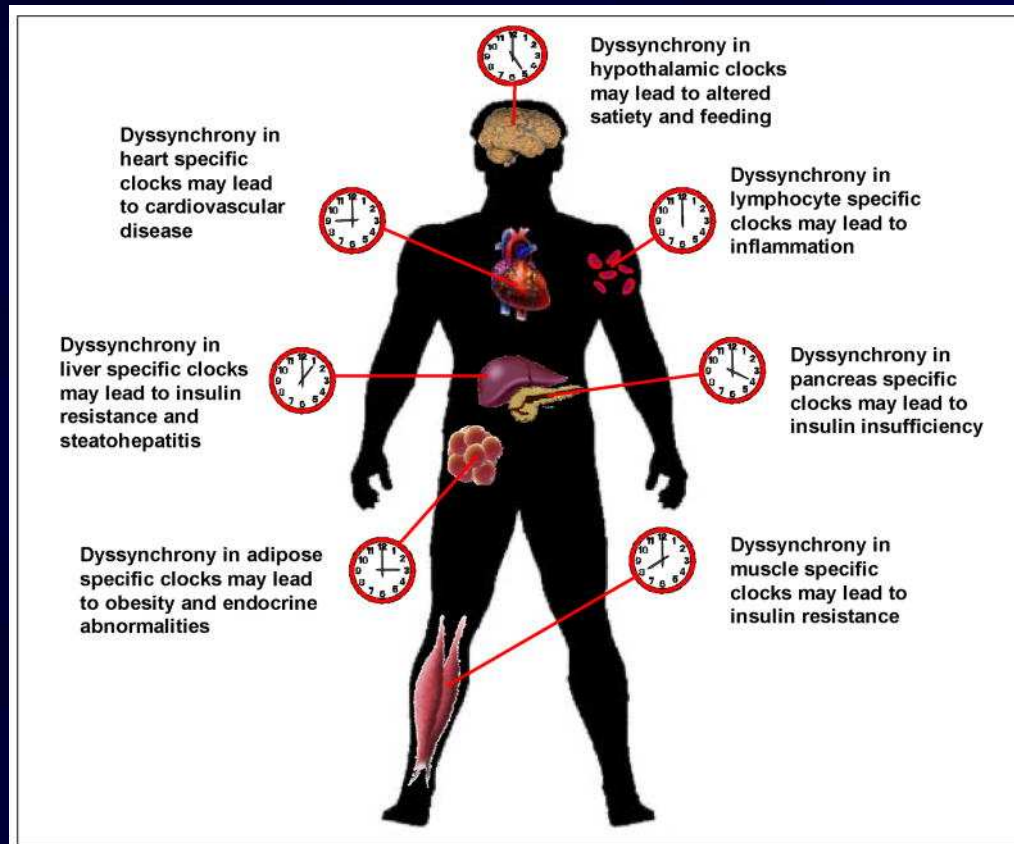
Circa il 35% del patrimonio genico umano è circadiano dipendente



Orologio biologico o orologi biologici?



Orologi biologici: out-of-synch e patologie



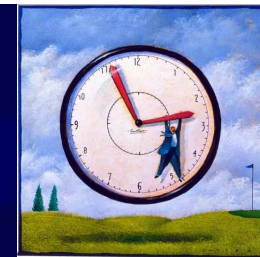


**Così ho
battuto la
diverticolite**



Cronobiologo: l'esperto del *tempo*

GRAZIE!!



Chi dorme non piglia tempo,
chi ha tempo non aspetti pesci.

