

UNIVERSITY OF LAUSANNE

MÉMOIRE DE MAÎTRISE EN MÉDECINE NO 928

Lack of seasonal variation in cardiovascular mortality in a country near the equator

ETUDIANT

ALEKSANDAR DABETIC

TUTEUR

PROF. PASCAL BOVET

INSTITUT UNIVERSITAIRE DE MÉDECINE SOCIALE ET PRÉVENTIVE

CO-TUTEUR

SILVIA STRINGHINI, PHD

INSTITUT UNIVERSITAIRE DE MÉDECINE SOCIALE ET PRÉVENTIVE

EXPERT

PROF. BLAISE GENTON

CENTRE AMBULATOIRE DES MALADIES INFECTIEUSES ET TROPICALES DE LA PMU

LAUSANNE, LE 15 JANVIER 2013

Lack of seasonal variation in cardiovascular mortality in a country near the equator

Aleksandar Dabetic (1), Rosalie Isnard (2), Silvia Stringhini (1), Pascal Bovet (1, 2)

1) Institute of social and preventive medicine, Lausanne University Hospital, Lausanne, Switzerland

2) Statistics Unit, Ministry of Health, Republic of Seychelles

Addresses for correspondence:

Prof. Pascal Bovet

Institut universitaire de médecine sociale et préventive

Biopôle 2

Rue de la Corniche 10

1010 Lausanne, Suisse

Email: pascal.bovet@chuv.ch

Aleksandar Dabetic

Av. de Cour 8

1007 Lausanne, Suisse

Email: aleksandar.dabetic@unil.ch

Part of this work was presented as a poster at the FBM Day congress, Lausanne, Switzerland, 7 June 2012.

A. Dabetic, R. Isnard, S. Stringhini, P. Bovet. Lack of seasonal variation in cardiovascular mortality under the tropics. Poster: MCV-9.

Index

Abstract	4
Introduction	5
Methods and Participants	6
Results	7
Discussion/Conclusion	8
References	11

Table 1: Number of deaths from CVD and other broad causes according to month and difference (in %) from expected numbers assuming no seasonal variation 7

Figure 1: Number deaths according to month and selected broad causes of deaths 7

ABSTRACT

Introduction: Mortality from cardiovascular disease (CVD) varies according to seasons in countries that are located far away from the equator, likely linked to concomitant seasonal variation in underlying CVD risk factors. We assessed temporal variation in CVD mortality in the Seychelles, a small island state situated near the equator and where the climate is virtually constant throughout the year. Seychelles is one of the few countries located near the equator where all deaths are registered.

Methods: We recoded all deaths along broad causes, including CVD (n=5643), stroke (2112) and myocardial infarction (MI, 804). Stroke and MI were considered as the cause of death if the diagnosis appeared in any of the four fields for underlying causes of death in the death certificates. In view of the small size of the population, we pooled all deaths (n=13'163) between 1989 and 2010.

Results: Mortality for all CVD, stroke and MI did not systematically vary according to month or season (chi square >0.05). A lack of variation was also observed within sex and age categories.

Conclusion: The lack of seasonal variation in CVD mortality in a country located near the equator is consistent with the hypothesis that seasonal variation in CVD decreases along decreasing a country's latitude.

Keywords: Cardiovascular disease - Africa - Trends - Mortality - Variation

INTRODUCTION

Mortality from cardiovascular diseases (CVD), particularly stroke and acute myocardial infarction (AMI), varies according to seasons in countries with large seasonal variations in temperature (1;2;3), with highest mortality rates during cold months (4;5). Inversely, less variation in CVD mortality is apparent in regions with minimal seasonal changes such as Taiwan (6). Seasonal variation in CVD mortality may relate to seasonal variations in CVD risk factors, e.g. blood pressure (7), stress levels (8), thrombotic activity (1), fibrinogen blood levels (9), and blood cholesterol levels, which may be associated in turn to seasonal variations in the diet (10;11). However, the exact contributions of these factors have not been assessed precisely. A few studies have also suggested that seasonal variation in CVD mortality is larger in older persons, which may relate to differences in thrombotic activity according to age (12).

Variation in stroke and AMI (13) mortality has also been observed in relation to the day of the week (13, 14), possibly in relation to work or stress conditions. CVD mortality also varies according to hour of the day (3;15;16), likely related to circadian rhythm in several CVD risk factors, e.g. physical activity, adrenergic hormones and blood pressure (17).

In this study, we assessed seasonal variation in CVD mortality in the Seychelles, an island state near the equator (4° South) where the temperature and several other environment related factors, including the diet is relatively constant throughout the year.

Seychelles is one of the few countries near the equator where all deaths at the entire population level are medically certified through vital statistics. Because information on the exact time of death is not available and some deaths may be recorded in vital statistics on the next days (e.g. for deaths occurring during the week end), we focus on variation of mortality according to month and seasons and not on day-to-day or circadian variations.

Based on vital statistics, total mortality rates standardized for age (per 100,000 population, using the WHO Ahmad population) decreased by approximately 25% between 1990 and 2010 (from 1669 to 1113 in men and from 710 to 535 in women), consistent with downward trends found in many middle income countries (18). Of note, the age-adjusted mortality from CVD decreased by 40-50% in the interval. However, because of the population increased in size (from 68'000 to 87'000 in 2010) and age (e.g. median age increased by approximately 10 years in the interval), the total number of deaths per year increased from 552 to 670 in the interval.

METHODS AND PARTICIPANTS

Original data of the vital statistics were available electronically for the period between 1989 and 2010. Death certificates allow for up to three separate underlying causes of death and associated conditions can be mentioned in another field. We recoded all deaths according to broad cause categories, including cardiovascular disease (CVD, n=5'643), stroke (2'112) and myocardial infarction (804), using the WHO ICD 10 classification of diseases. Stroke and MI were considered as the cause of death if the diagnosis appeared in any of the four fields for the underlying causes of death in the death certificates. We also considered deaths from cancer (n=2'260) and from external causes (n=1064). Because of the small size of the country (87'000 inhabitants in 2010), we pooled all deaths (n=13'163) between 1989 and 2010 when examining seasonal variation of deaths according to month. We used the chi square test to test for differences in mortality between months. Although they can provide useful information, statistical tests are not formally required in this study since data come from the total population (i.e. they are not based on population samples).

RESULTS

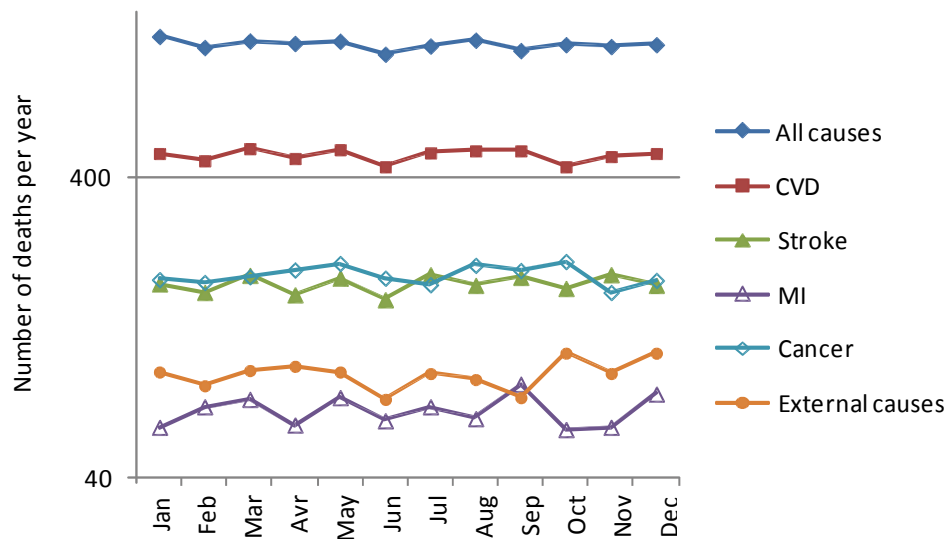
Among a total of 13'163 deaths (57% of men), there were 5643 deaths from CVD (52% of men), 2112 deaths from stroke (51% of men), 804 from MI (63% of men). There were 2260 deaths from cancer (60% of men) and 1064 from external cause (79% of men).

The number of deaths according to month of the year is tabulated in **Table 1** and graphed in **Figure 1**. There was not systematic difference in the numbers of CVD, stroke and MI deaths according to month or seasons. Despite the fact that we pooled all deaths occurring between 1989 and 2010, the number of deaths was fairly small and fluctuations occur in the month-to-month numbers of CVD deaths: however there was no pattern for systematic differences according to month or season. Age-stratified analysis (results not shown) also showed that there was no consistent seasonal pattern among young, middle aged or older person and in men or women considered separately. Analysis also suggests the absence of seasonal variation for mortality due to cancer and external causes.

Table 1. Number of deaths from CVD and other broad causes according to month and difference (in %) from expected numbers assuming no seasonal change time

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
All causes	1167	1073	1128	1107	1125	1020	1085	1135	1048	1097	1081	1097	13163
% Δ	4.6	6.5	1.3	2.2	0.1	-6.7	-3.5	1.3	-2.7	-2.3	-0.2	-2.3	
CVD	478	452	496	460	492	432	480	488	488	432	467	478	5643
% Δ	0.1	4.2	3.6	-0.2	2.4	-6.7	0.1	1.3	4.5	-10.2	1	0.1	
Stroke	176	165	188	162	184	156	189	174	185	170	189	174	2112
% Δ	-2.3	1.7	4.6	-6.7	2.4	-11	4.6	-3.5	6.7	-6.1	7.7	-3.5	
MI	59	69	73	60	74	62	69	63	82	58	59	76	804
% Δ	-16.3	10.9	6.7	-9.5	7.7	-6.7	1.3	-8.8	19.5	-17.9	-12.5	10.7	
Cancer	182	178	186	196	206	184	175	203	195	209	165	181	2260
% Δ	-4.8	3	-3.5	5.6	6.7	-1.4	-10.2	5.7	4.5	7.7	-12.5	-6.1	
External causes	90	81	91	94	90	73	89	85	74	104	89	104	1064
% Δ	0.1	-0.9	1.3	6.7	0.1	-19	-1	-6.1	-17.3	13.4	2.2	13.4	

Figure 1. Number of deaths from CVD and other broad causes according to months (logarithmic scale of the Y axis)



DISCUSSION

This first study to examine seasonal variation in CVD mortality in the African region suggests that cardiovascular mortality did not vary according to the month or season in the Seychelles. This finding is consistent with the view that seasonal variation in CVD mortality decreases along decreasing country latitude and, possibly, concomitant smaller variation in several CVD risk factors in tropical countries than in countries with marked seasons.

Seasonal variation of CVD mortality has been observed in countries that are remote from the equator, e.g. in Italy (4), Greece (5), New Zealand (2;12) and California (19). CVD mortality is highest during the coldest months in all these countries. Seasonal variation in CVD mortality has been related to concomitant seasonal variation in factors such as temperature (1;2;3;12); light and/or related vitamin D (16); or nutrition, e.g. a diet possibly more atherogenic in winter (fats, meat, alcohol, etc) than in summer (salads, fruits) (10;11). Fibrinogen levels were also found to increase by up to 23% in winter in England (9). Seasonal variation in physical activity, tobacco habits and other potential triggers of CVD can also play a role (20). Seasonal variation in CVD mortality can also be associated with social events, e.g.

end of the year festive times with caloric excess or more atherogenic/prothrombotic diet on these occasions, or stress related to these events (9;21).

The role of infections (influenza, etc) related to cold weather has also been suggested to act as a trigger of CVD. However, flu-like syndromes tend to occur with less seasonal variation in Seychelles than in countries with cold seasons and the epidemics are often limited in magnitude (e.g. less than 500 cases of influenza-like syndrome are generally notified in a year) (22). Little systematic seasonal variation is also observed in Seychelles for other frequent infectious agents on most years, e.g. viral fever (3000-6000 cases notified every year on average), gastroenteritis (3000-6000 cases notified every year on average) and other occasional viruses (e.g. 4650 chikungunya cases notified in 2 months in 2006). Because we merged mortality data from several years and epidemics of infectious diseases do not consistently occur on the same months over years in Seychelles, we cannot assess whether CVD mortality is related to these epidemics.

Inversely, the absence of seasonal variation in CVD mortality in Seychelles is indirectly consistent with the lack of variation in temperature, day light length, and diet throughout the year. A lack of seasonal variation in CVD mortality has also be observed in Taiwan, a country close to the equator (6) and characterized by a fairly constant climate and, likely, diet throughout the year.

As stated in the introduction, CVD mortality also varies also according to day of the week and hour of the day. However, we could not examine these weekly or daily variations in CVD mortality because the exact time of death was not available and some deaths could be reported on a next day.

Our study has some limitations. Because of the small number of deaths occurring in the small population of the Seychelles, we had to merge data from different years: this

precluded us to analyze seasonal trends separately in different years. This should not obscure variation by month or season if a systematic seasonal trend was indeed present. As already mentioned, our data lack information on the exact time of death, which precluded analysis of circadian or day-to-day variations in CVD mortality. Finally, although we merged mortality data from several years, the number of deaths in this study is still not very large and our study lacks power to identify small seasonal variation. A strength of this study was the availability, in a country in the African region, of information on all deaths occurring in the entire population with reasonable accuracy of the causes of death.

In conclusion, our finding of a lack of systematic seasonal variation of CVD mortality in the Seychelles is consistent with the view that CVD mortality is attenuated or abolished in countries located near the equator. Our findings also indirectly support a role of the cardiovascular risk factors which vary in intensity according to seasons. Few data on CVD variation are available in countries located near the equator and further studies in other equatorial countries are needed to confirm our findings.

REFERENCES

- (1) Myint PK, Vowler SL, Woodhouse PR, Redmayne O, Fulcher RA. Winter excess in hospital admissions, in-patient mortality and length of acute hospital stay in stroke: a hospital database study over six seasonal years in Norfolk, UK. *Neuroepidemiology* 2007;28(2):79-85.
- (2) Douglas AS, Russell D, Allan TM. Seasonal, regional and secular variations of cardiovascular and cerebrovascular mortality in New Zealand. *Aust N Z J Med* 1990;20(5):669-76.
- (3) Ricci S, Celani MG, Vitali R, La Rosa F, Righetti E, Duca E. Diurnal and seasonal variations in the occurrence of stroke: a community-based study. *Neuroepidemiology* 1992;11(2):59-64.
- (4) Manfredini R, Boari B, Smolensky MH, Salmi R, Gallerani M, Guerzoni F, et al. Seasonal variation in onset of myocardial infarction--a 7-year single-center study in Italy. *Chronobiol Int* 2005;22(6):1121-35.
- (5) Spengos K, Vemmos KN, Tsvigoulis G, Synetos A, Zakopoulos N, Zis VP, et al. Seasonal variation of hospital admissions caused by acute stroke in Athens, Greece. *J Stroke Cerebrovasc Dis* 2003;12(2):93-6.
- (6) Lee HC, Hu CJ, Chen CS, Lin HC. Seasonal variation in ischemic stroke incidence and association with climate: a six-year population-based study. *Chronobiol Int* 2008;25(6):938-49.
- (7) Green MS, Harari G, Kristal-Bonneh E. Excess winter mortality from ischaemic heart disease and stroke during colder and warmer years in Israel. *Eur J Public Health* 1994;4:3-11.

- (8) Manfredini R, Manfredini F, Boari B, Bergami E, Mari E, Gamberini S, et al. Seasonal and weekly patterns of hospital admissions for nonfatal and fatal myocardial infarction. *Am J Emerg Med* 2009;27(9):1097-103.
- (9) Stout RW, Crawford V. Seasonal variations in fibrinogen concentrations among elderly people. *Lancet* 1991;338(8758):9-13.
- (10) Culic V. Seasonal distribution of acute myocardial infarction: a need for a broader perspective. *Int J Cardiol* 2006;109(2):265-6.
- (11) Robinson D, Bevan EA, Hinohara S, Takahashi T. Seasonal variation in serum cholesterol levels--evidence from the UK and Japan. *Atherosclerosis* 1992;95(1):15-24.
- (12) Marshall RJ, Scragg R, Bourke P. An analysis of the seasonal variation of coronary heart disease and respiratory disease mortality in New Zealand. *Int J Epidemiol* 1988;17(2):325-31.
- (13) Allegra JR, Cochrane DG, Allegra EM, Cable G. Calendar patterns in the occurrence of cardiac arrest. *Am J Emerg Med* 2002;20(6):513-7.
- (14) Wang H, Sekine M, Chen X, Kagamimori S. A study of weekly and seasonal variation of stroke onset. *Int J Biometeorol* 2002;47(1):13-20.
- (15) Arntz HR, Willich SN, Schreiber C, Bruggemann T, Stern R, Schultheiss HP. Diurnal, weekly and seasonal variation of sudden death. Population-based analysis of 24,061 consecutive cases. *Eur Heart J* 2000;21(4):315-20.
- (16) Kriszbacher I, Bodis J, Boncz I, Koppan A, Koppan M. The time of sunrise and the number of hours with daylight may influence the diurnal rhythm of acute heart attack mortality. *Int J Cardiol* 2010;140(1):118-20.
- (17) Millar-Craig MW, Bishop CN, Raftery EB. Circadian variation of blood-pressure. *Lancet* 1978;1(8068):795-7.

- (18) Stringhini S, Simon F, Didon J, Gedeon J, Paccaud F, Bovet P. Declining stroke and myocardial infarction mortality between 1989 and 2010 in a country of the African region. *Stroke* 2012;43:2283-88.
- (19) Ebi KL, Exuzides KA, Lau E, Kelsh M, Barnston A. Weather changes associated with hospitalizations for cardiovascular diseases and stroke in California, 1983-1998. *Int J Biometeorol* 2004;49(1):48-58.
- (20) Izzo JL, Jr., Larrabee PS, Sander E, Lillis LM. Hemodynamics of seasonal adaptation. *Am J Hypertens* 1990;3(5 Pt 1):405-7.
- (21) Kloner RA. Natural and unnatural triggers of myocardial infarction. *Prog Cardiovasc Dis* 2006;48(4):285-300.
- (22) Health Statistics 2010. Statistics Unit, Ministry of Health, Victoria, Seychelles, 2011
- (23) Lin HC, Lin SY, Lee HC, Hu CJ, Choy CS. Weekly pattern of stroke onset in an Asian country: a nationwide population-based study. *Chronobiol Int* 2008;25(5):788-99.
- (24) Wolf K, Schneider A, Breitner S, von Klot S, Meisinger C, Cyrys J, et al. Air temperature and the occurrence of myocardial infarction in Augsburg, Germany. *Circulation* 2009;120(9):735-42.
- (25) Gerber Y, Jacobsen SJ, Killian JM, Weston SA, Roger VL. Seasonality and daily weather conditions in relation to myocardial infarction and sudden cardiac death in Olmsted County, Minnesota, 1979 to 2002. *J Am Coll Cardiol* 2006 Jul 18;48(2):287-92.
- (26) Faeh D, Gutzwiller F, Bopp M. Lower mortality from coronary heart disease and stroke at higher altitudes in Switzerland. *Circulation* 2009;120(6):495-501.
- (27) Marques-Vidal P, Arveiler D, Amouyel P, Ducimetiere P, Ferrieres J. Myocardial infarction rates are higher on weekends than on weekdays in middle aged French men. *Heart* 2001;86(3):341-2.

(28) Muller JE, Ludmer PL, Willich SN, Tofler GH, Aylmer G, Klangos I, et al. Circadian variation in the frequency of sudden cardiac death. *Circulation* 1987;75(1):131-8.