Journal of the American College of Cardiology
© 2011 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 57, No. 7, 2011
ISSN 0735-1097/$36.00

CORRESPONDENCE

Research Correspondence

Is Cardiovascular Mortality Related to the Season of Birth?

Evidence From More Than 6 Million Cardiovascular Deaths Between 1992 and 2007

To the Editor: There is increasing evidence that environmental factors in early pre- and post-natal life have significant impact on the development of various diseases later in adulthood. The "fetal origins hypothesis" proposes that risk of cardiovascular disorders originates in the exposure to certain factors during a critical period of development, with lasting effect on the disease process (1).

Season of birth presents a well-defined variable associated with various environmental factors in early life, which are most likely not directly related to the genetic background. Not only meteorological factors, daily sunlight exposure, and alterations in air pollution and food supply, but also many behavioral changes, including dietary habits and physical activity levels throughout the year, are to be discussed as potential influences associated with the season of birth.

In the present study, we analyze the association between the month of birth and age at death in subjects dying from cardiovascular cause in Germany between 1992 and 2007 to test the hypothesis that environmental factors during early pre- or post-natal life may determine cardiovascular mortality later in adulthood.

Data from all subjects dying in Germany between 1992 and 2007 were obtained from German research data centers (Forschungsdatenzentrum der Statistischen Landesämter [Düsseldorf], Statistisches Landesamt des Freistaates Sachsen, [Kamenz]), including age at death, date of birth, date of death, sex, cause of death (International Classification of Diseases [ICD]-9/10), and location where the subject was living (classified according to the NUTS [Nomenclature des Unités Territoriales Statistiques] system, a classification of states, governmental regions, and districts in the European Union).

Age at death (mean ± SD) was calculated separately in 12 groups categorized by the month of birth (exclusion of subjects dying at the age of <18 years), compared by analysis of variance and analyzed for a seasonal effect (2) (SPSS 17-syntax [SPSS Inc., Chicago, Illinois]) ($p < 0.05$: statistically significant). The following subgroups were analyzed: women and men dying of cardiovascular cause (ICD-9 [1992 to 1997]: 401 to 448, ICD-10 [1998 to 2007]: I10 to I79, from official death certificates) and all-cause deaths; subgroups categorized according to the month of death, to the year of death, and in each of the 16 federal states; and in four groups categorized according to the settlement structure (urban region/core cities, urban environment, rural environment, rural districts) (adopted from Bundesinstitut für Bau-, Stadt-, und Raumforschung).

In both sex subgroups, age at death was lowest in subjects born in May and highest in subjects born in November (Figs. 1A to 1B). On average, the difference between age at death in subjects dying from cardiovascular cause born in May and those born in November was 7.3 months for women (83.67 ± 9.47 years for those born in November and 83.07 ± 9.72 years for those born in May) and 11.7 months for men (75.88 ± 12.17 years for those born in November and 74.90 ± 12.21 years for those born in May). For all-cause deaths (as well as noncardiovascular causes), age at death followed a similar pattern (Figs. 1C to 1D), with a mean difference between subjects born in May and those born in November of 9.4 months for men (71.75 ± 14.49 years for those born in November and 70.97 ± 14.46 years for those born in May) and 9.6 months for women (80.13 ± 12.50 years for those born in November and 79.33 ± 12.75 years for those born in May). These relationships were similar in women and men categorized according to the year of death between 1992 and 2007, without a significant trend over time. They were also similar in subgroups categorized according to the month of death (irrespective of the year of death), in each of the 16 federal states, in rural districts, rural environments, urban environments, and core cities.

In all of these subgroups a highly significant seasonal effect was demonstrated for both cardiovascular deaths and all-cause deaths ($p < 0.001$).

It is well established that prevalence and incidence of many diseases, including cardiovascular disorders, are subject to seasonal variation (1,3). Environmental factors associated with the season of the year may also have significant impact in early pre- and post-natal life. For example, arterial blood pressure in adulthood and other cardiovascular alterations were shown to be significantly related to the month of birth in some smaller studies (4). Whether these associations result in differences in cardiovascular mortality was subject of the present investigation.

Age at death was significantly different in subjects categorized according to the month of birth. The effect of environmental factors associated with the season of birth on age at death appeared to be independently superimposed on a variety of other factors with obviously substantial influence on life expectancy, as this relationship could be demonstrated in various subgroups: women and men, in each of the 16 federal states, in rural and urban regions, and also in subgroups categorized according to the month of death with a similar seasonal distribution. Of note, the latter finding excludes that differing death rates throughout the months of the year are the basis for the observed relationship solely due to arithmetical reasons. The observations parallel other investigations demonstrating a statistically significant relationship between season of birth and survival from all causes, even if the seasonal distribution is not consistent in all of these studies (5,6).

One might speculate that meteorological parameters, the duration of sunlight exposure, differing incidence of infectious diseases, amount of air pollution, many habits including dietary habits and

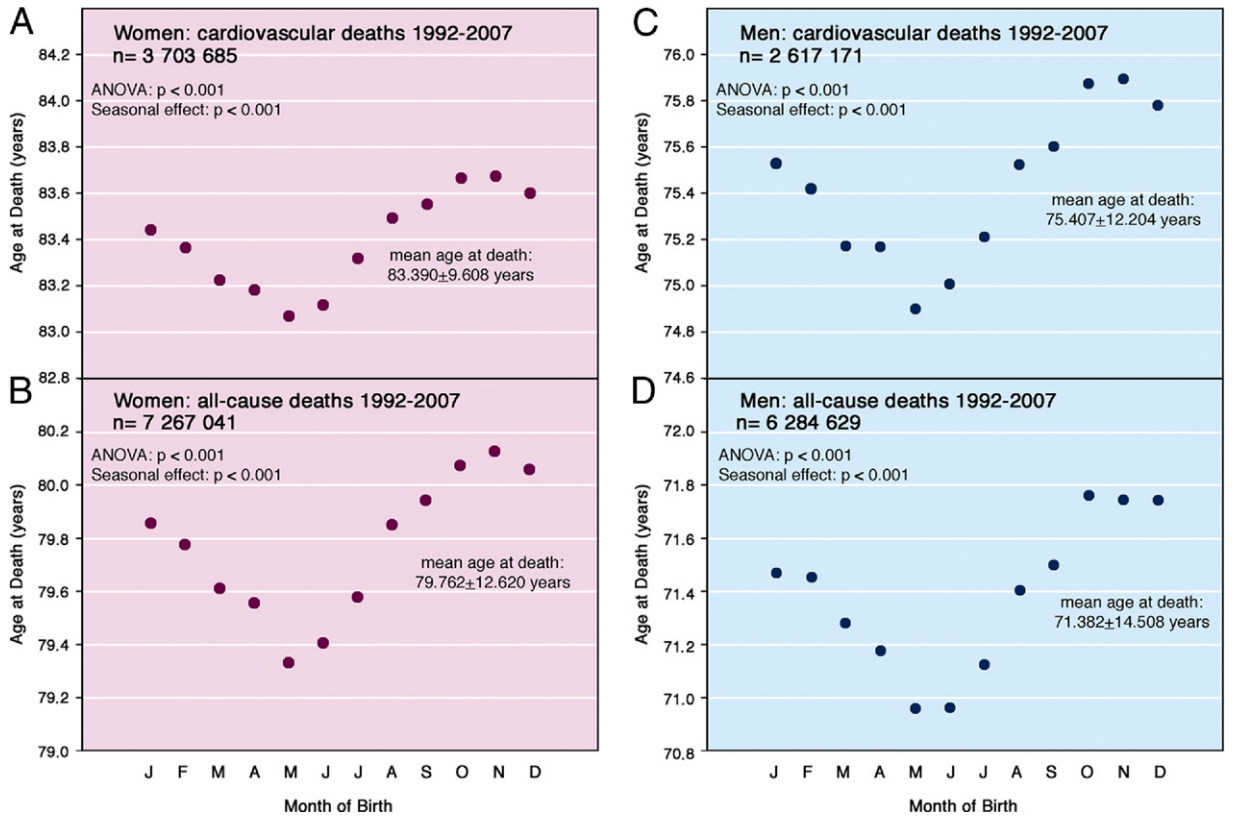

Figure 1 **Age at Death in Relationship to Month of Birth in Women and Men Dying of Cardiovascular Cause and All-Cause Death Between 1992 and 2007**

(A) Age at death was lowest in subjects dying from cardiovascular cause born around May and highest in subjects born around November. On average, the difference between age at death in subjects born in May and those born in November was 11.7 months for men and 7.3 months for women for cardiovascular deaths. **(B)** Similar patterns were observed for all-cause death. Standard deviation was 9.47 to 9.76 years for **A** (women), 12.13 to 12.25 years for **B** (men), 12.48 to 12.76 years for **C** (women), and 14.42 to 14.59 years for **D** (men). Figure illustration by Craig Skaggs. ANOVA = analysis of variance.

the level of physical activity, or the specific food supply could contribute to the effects. Prospective studies should be initiated, with detailed documentation of factors that are potentially the underlying cause of the observed relationship.

***Thorsten Reffelmann, MD**

*Klinik und Poliklinik für Innere Medizin B
Universitätsklinikum der
Ernst-Moritz-Arndt-Universität Greifswald
Friedrich-Löffler Str. 23 a
17487 Greifswald
Germany
E-mail: ThorstenReffelmann@web.de

Till Ittermann
Klaus Empen, MD
Marcus Dörr, MD
Stephan B. Felix, MD

doi:10.1016/j.jacc.2010.10.021

Please note: The cooperation and contributions of Dr. U. Janisch and Dr. O. Schoffer, Forschungsdatenzentrum Standort Kamenz im Statistischen Landesamt des Freistaates Sachsen, Kamenz, Germany, are highly appreciated.

REFERENCES

1. Barker DJP. The developmental origins of adult disease. J Am Coll Nutr 2004;23:588S–95S.
2. Le CT, Liu P, Lindgren BR, Daly KA, Scott Giebink G. Some statistical methods for investigating the date of birth as a disease indicator. Stat Med 2003;22:2127–35.
3. Kloner RA, Poole WK, Perrit LR. When throughout the year is coronary death most likely to occur? A 12-year population-based analysis of more than 220 000 cases. Circulation 1999;100:1630–4.
4. Banegas JR, Rodríguez-Artalejo F, de la Cruz JJ, Graciani A, Villar F, del Rey-Calero J. Adult men born in spring have lower blood pressure. J Hypertens 2000;18:1763–6.
5. Doblhammer G, Vaupel JW. Lifespan depends on month of birth. Proc Natl Acad Sci U S A 2001;98:2934–9.
6. Muñoz-Tudurí M, García-Moro C. Season of birth affects short- and long-term survival. Am J Phys Anthropol 2008;135:462–8.