# What Are We BIF-fing About?

## Science Needs Impact Metrics

***To the Editor:***

The recent lively discussion of bibliographic impact factors (BIF) in EPIDEMIOLOGY highlights the importance given to publications when assessing the impact of scientists' work.[1–5] Subsequent correspondence[6–10] has focused largely on the limitations of the Impact Factor algorithm and has not addressed broader approaches already in use. We argue that the scientific community should wholeheartedly support the ongoing development and validation of metrics for describing the quality and impact of science. The Hirsch index and the journal strike rate index are examples of second generation metrics derived from citation data, the first providing good power to predict future performance of scientists and the second permitting comparisons of journals across disciplines.

Data on citations have been collected in Science Citation Index since 1961. The initial objective of comparing authors was subsequently broadened to include quantifying the impact of journals.[11] Journal impact factors and author citation statistics have attracted for a number of years the slavish attention of many (if not most) participants in the scientific community. Resources are limited at every level of the science enterprise, and science administrators, grant reviewers, librarians, academic publishing houses, and scientists all need to assess the greatest likely return on the investment of their dollars and time. As these personal and commercial decisions can affect the careers and livelihoods of individuals and institutions, there is a strong need for objective means to assess past performance and predict future performance of individuals, groups of scientists, and the media they publish in.

The limitations of citation metrics have been widely discussed. Citation counts form the basis for most metrics, but rewarding scientists for the impact factor of journals they publish in merely rewards them for the company they keep, rather than the contribution of their own work. Recognition of these limitations has spurred interest in metrics with less bias and better comparability across disciplines. Examples include the Hirsch (h) index[12] and the journal strike rate index.[13] In a recent empirical study, Hirsch[14] found that the h-index (the number [N] of papers with $\geq$N citations) was a better predictor of future performance of scientists than total paper count, total citation count, or citations per paper. Hirsch indexes are now computed in the ISI Web of Science and Scopus, and can readily be estimated from Google Scholar; however, a recent study found discrepancies among h-indexes calculated from the ISI, Scopus, and Google Scholar databases.[15] Importantly, the hit counts and citation counts for Google Scholar are untraceable and may be inflated. Barendse's strike rate index (10 log h/log N), where h is the Hirsch index for a journal and N the total number of citable items in the journal during the interval under examination, has a similar distribution across disciplines; thus, it seems to have greater utility in comparing the quality of journals across disciplines than does BIF. Other metrics are under development.[11]

The need for quantitative measures of science performance and journal quality may differ among sectors of the science enterprise. To aid the development of informative metrics we need clearer articulation of the particular needs of administrators, government, investors, publishers, collection curators, and scientists when they assess performance and quality. Some criteria such as power to predict future performance and ability to compare performance across disciplines may be of interest to all sectors. Broader knowledge of the strengths and weaknesses of each metric is needed to increase the awareness of other participants' gamesmanship. Support from journals such as EPIDEMIOLOGY for the development of robust metrics should be a high priority.

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# Physical Fitness During Adolescence and Adult Mortality

***To the Editor:***

Numerous studies have demonstrated a strong inverse relationship between physical fitness during middle and older ages and subsequent mortality.[1–5] Likewise, a lack of physical fitness during adolescence is associated with the subsequent development of cardiovascular risk factors such as obesity.[6] However, it has not been reported whether physical fitness during adolescence could be a predictor of long-term mortality. We investigated this in a historical cohort of Japanese women.

All 510 female students (mean age = 16.8 [SD, 2.0] years) from Ochanomizu University Senior High School underwent a physical fitness examination in December 1943. The observational period ended in April 2007. The subjects' vital status was determined through records of the alumni association, and the follow-up rate was 98%. Subjects who died before the age of 20 years were excluded.

The physical fitness of each subject was determined by the sum of scores for 4 fitness performance tests (a 1000-m run, rope skipping [time until failure to skip;frequency of rope turn, 100–120/min], throwing a 300-g wooden club [distance], and running while carrying a heavy weight [total time to run 100 m with a 16-kg weight]). Each of these 4 tests was assigned a score of 1–10 based on a decile, with 1 representing the lowest level of performance. Thus, the physical fitness score could range from 4 to 40. All analyses were performed using SPSS 15.0 for Windows (Chicago, IL).

During 64 years of observation (30,823 person-years), 72 women died. Using Kaplan-Meier analysis with log-rank tests, cumulative all-cause mortality in subjects with a total score above 22 (the median) was lower than in those with a score below the median ($P = 0.027$; Figure).

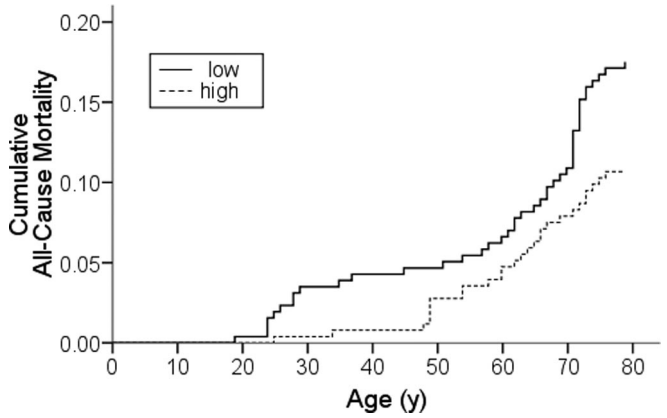


**FIGURE.** Kaplan-Meier cumulative mortality curve for all-cause mortality during follow-up, according to the physical fitness level in 510 women.

Our results demonstrated that a high degree of physical fitness early in life was associated with lower mortality.[1–5] The difference between curves of those with low and high physical fitness was remarkable before 50 years of age and after 70 years of age. The difference in premature death could have been partially modified by malnutrition or infection such as tuberculosis, which was a leading cause of death during the postwar period. The reasons for the difference in later deaths are yet to be determined. However, cardiovascular disease, which accounts for one-third of mortality in the general population of Japanese women, may be a candidate, based on findings of a recent review,[6] suggesting that both cardiorespiratory and muscular fitness are associated with cardiovascular disease risk factors.

This study has several limitations. First, these data are only on Japanese women. Second, causes of death are unknown. Third, information on lifestyle factors at baseline and during the observational period is not available, and so we cannot adjust the results by these parameters. Despite these limitations, our results suggest that a low level of physical fitness even during adolescence could be a risk factor for mature and premature death in Japanese women.

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## ACKNOWLEDGMENTS

*The authors thank Emiko Suzuki at the Ochanomizu University, Kazuko Sakurai, Toshiko Kobayashi, Yoko Nakatani, Syoko Oshita, staff and member (all from the alumni association of Ochanomizu University Senior High School), Kazuhiko Murooka, Hajime Nagano, Tomoko Ishii, and Kayano Masuda (all from Ochanomizu University Senior High School) for providing assistance in the acquisition of the data.*

*Supported in part by the Japanese Ministry of Health, Labor and Welfare, as well as the Japan Society for the Promotion of Science.*

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# Thinness in Japanese Young Women

***To the Editor:***

The desire to be thin is widespread among young women. In some European countries, fashion models are required to have a body mass index (BMI; weight [kg]/height$^2$ [m$^2$]) of 18 kg/m$^2$ or greater to discourage severe emaciation.[1] Unhealthy dietary regimens for weight loss during youth can lead to unfavorable outcomes, including eating disorders[2] or low bone mineral content,[3] in adulthood. Asian young women, especially Japanese women, have been reported to strongly desire to be thin, even though they have a lower BMI than other ethnic groups.[4] In Japan, more than 20% of women in their 20s are underweight (BMI $<$18.5 kg/m$^2$),[5] a percentage much higher than in most developed countries. In the United States, the prevalence of obesity continues to rise among children, adolescents and adult men, but not women.[6] The BMI physiologically increases throughout life after approximately 6 years of age.[7] We compared BMI curves by age among young people from Japan, Korea, and the United States. We also examined the period during which unhealthy emaciation began in Japanese women.

We performed an ecologic study, using national health statistics from the United States (NHANES 2003–2004 and 2005–2006), Korea (KNHANES 2005), and Japan (NNS-J 1957–2006). We calculated BMI, using information on height and weight from these databases and compared the BMI curves from age 10 to 29 years among men and women in the 3 countries. We also chronologically rearranged cross-sectional data on Japanese women according to birth year.

Mean BMI for men and women in the United States increased with age, as it did for men in Korea and Japan; however, the increase was not as steep for Asian men as for US men and women (Fig. 1). The increase in Korean women stopped at around 18 years of age and remained constant thereafter, whereas in Japanese women, the BMI started to decrease at approximately age 18 years.

Data according to period of birth (Fig. 2) showed no tendency toward leanness among Japanese women born between 1945 and 1949 (age 59–63 in 2008); the curve was similar to that of Korean women born during this time.

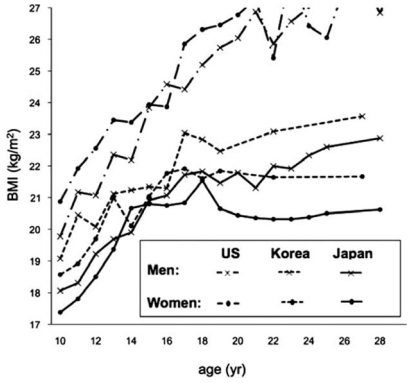


**FIGURE 1.** Cross-sectional relationship between age and BMI in young men and women in the United States (2003–2006), Korea (2005), and Japan (2003–2005).

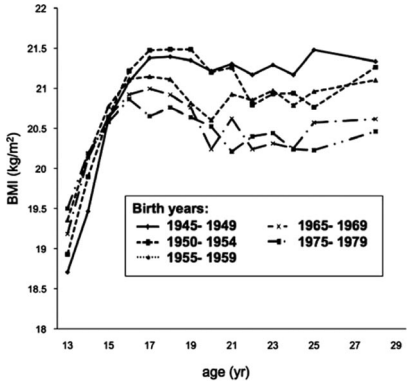


**FIGURE 2.** Longitudinal changes in BMI in young Japanese women between the age of 10 and 29 years, depending on birth year.

However, the BMI of those born between 1950 and 1954 (age 54–59 in 2008) sharply dropped after the age of about 20 years. Then, in those born between 1955 and 1959 (age 49–53 in 2008), the drop in BMI began at age around 15 years and, in subsequent 5-year period, the magnitude of decline intensified. Thus, leanness among Japanese young women (late teens–early 20s) became apparent in the 1970s. The curves for BMI before the age of 15 years were similar regardless of the period of birth.

In the 1970s, during the period when decreases in BMI became evident, Japan experienced an economic growth spurt similar to that currently being experienced in other Asian countries. Lifestyle and cultural changes, including vast exposure to media, might have fostered the desire of women to be thin.

At present, a reduction in mean BMI among young women has not been reported in other countries, despite the widespread desire to be thin.[4] Most concerns today are with increasing BMI. This should not overshadow concerns about possible declines in BMI among young women. The social background or rationale for this apparently nonphysiologic drop in BMI among Japanese women may be useful in addressing this issue in other developed countries.

## ACKNOWLEDGMENTS

*The authors thank Young Seol Kim and Sang Youl Rhee from the Kyung Hee University for providing assistance in the acquisition of the Korean data.*

*Supported in part by the Japanese Ministry of Health, Labor and Welfare, as well as the Japan Society for the Promotion of Science.*

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# Risk Factors for Retinal Detachment

***To the Editor:***

We recently reported a case-control study[1] testing the hypothesis that heavy occupational lifting or manual handling (requiring the Valsalva maneuver) may be a risk factor for retinal detachment among people who are myopic (near-sighted). This study also suggested a possible role for obesity. To evaluate the study hypothesis, we had restricted our analysis to myopic subjects, adjusting for degree of myopia. Other etiologic studies of retinal detachment,[2,3] although not restricted to myopic subjects, have provided little information on risk factors among nonmyopic people. We therefore did a supplementary analysis of our data to explore how risk factors for retinal detachment vary in nonmyopic subjects compared with near-sighted people.

In the absence of data for suitable nonmyopic control subjects, we conducted a case-case analysis of all the myopic cases of retinal detachment included in the parent study[1] (26 women, 35 men), alongside the previously excluded nonmyopic cases (29 women, 30 men). We analyzed risk factors such as heavy lifting/manual handling, body mass index (BMI), and alcohol consumption, along with age, head/eye trauma, and eye surgery. Occupational lifting of at least 10 kg (commonly requiring the Valsalva maneuver) was again evaluated by a cumulative lifting index, calculated as the product of load (kg), frequency (number of lifting maneuvers/wk), and number of years of lifting (using the same cut-offs: heavy lifting, >8000 kg × frequency × year; reference category, no lifting).[1] For multivariate analysis, we used ordered logistic regression analysis to take into account severity of myopia (mild/moderate/severe), additionally adjusting for sex.

Perhaps unsurprisingly, there was no sign of any association for either eye surgery or head trauma retinal detachment (Table). The point estimates close to unity suggest that the effects of these 2 major predisposing factors on retinal detachment[4] are similar in nonmyopic and myopic people. The more pronounced age-related risk in nonmyopic cases (4-fold after 65 years) can be attributed to the impact of near-sightedness as a predisposing factor for retinal detachment across the age spectrum.

Regarding heavy lifting/manual handling, the absence of any clear association (between nonmyopic and myopic cases) with retinal detachment leads us to hypothesize that this factor may increase the risk of retinal detachment regardless of myopia. As for BMI, there were signs of a possible dose-response relation, suggest-

**TABLE.** Case-Case Analysis of Risk Factors for Nonmyopic Cases Compared With Myopic Cases of Retinal Detachment

| Variables | Myopia[a] (No.) None | Low | Medium | High | Univariate[b] Analysis OR (95%CI) | Multivariate[b,c] Analysis OR (95%CI) |
|---|---|---|---|---|---|---|
| Age (y) | | | | | | |
| <65[d] | 21 | 18 | 12 | 10 | 1.0 | 1.0 |
| ≥65 | 38 | 17 | 2 | 2 | 4.1 (2.0–8.5) | 4.8 (2.1–11) |
| BMI (kg/m$^2$) | | | | | | |
| <25.0[d] | 22 | 13 | 6 | 7 | 1.0 | 1.0 |
| 25.0–29.9 | 27 | 18 | 7 | 4 | 1.3 (0.6–2.6) | 1.2 (0.5–2.5) |
| ≥30.0 | 10 | 4 | 1 | 1 | 2.2 (0.7–6.6) | 3.5 (0.9–13) |
| Cumulative lifting (kg × freq × y) | | | | | | |
| No manual lifting[d] | 22 | 14 | 6 | 5 | 1.0 | 1.0 |
| ≤8000 | 14 | 6 | 4 | 3 | 1.1 (0.4–2.7) | 0.8 (0.3–2.2) |
| >8000 | 23 | 15 | 4 | 4 | 1.2 (0.6–2.6) | 0.8 (0.3–1.9) |
| Alcohol consumption (g/d) | | | | | | |
| Little/none (<1)[d] | 17 | 11 | 4 | 6 | 1.0 | 1.0 |
| Light (1–19) | 6 | 7 | 6 | 3 | 0.5 (0.2–1.4) | 0.7 (0.2–1.9) |
| Moderate (20–59) | 20 | 8 | 3 | 3 | 1.8 (0.7–4.5) | 1.9 (0.7–5.1) |
| Heavy (≥60) | 16 | 9 | 1 | 0 | 2.5 (1.0–6.6) | 4.1 (1.3–13) |
| Eye surgery (including cataracts) | | | | | | |
| No[d] | 35 | 21 | 9 | 9 | 1.0 | 1.0 |
| Yes | 24 | 14 | 5 | 3 | 1.3 (0.7–2.6) | 1.1 (0.5–2.4) |
| Eye or head trauma | | | | | | |
| No[d] | 40 | 21 | 9 | 8 | 1.0 | 1.0 |
| Yes | 19 | 14 | 5 | 4 | 0.9 (0.4–1.7) | 0.8 (0.4–1.8) |

[a]None indicates up to −0.5 diopters; low, −0.5 to −4.75; medium, −5 to −9.75; and high, at least −10.
[b]Ordered logistic regression model. (Ordered according to severity of myopia.)
[c]Additionally adjusted for sex.
[d]Reference category.
OR indicates odds ratio; CI, confidence interval.

ing that obesity might conceivably be an even more prominent risk factor for retinal detachment among nonmyopic people.

Perhaps the most intriguing finding relates to alcohol consumption: heavy drinking appeared to be associated with a roughly 4-fold higher risk of retinal detachment in nonmyopic cases compared with myopic cases. Notably, there were signs of a dose-response relation through light to moderate to heavy drinking (and, considering the nondrinkers, perhaps also of the J-shaped curve often observed in etiologic studies of cardiovascular diseases[5]). Available data regarding the possible role of heavy drinking as a risk factor for eye diseases are contradictory.[6] Our observations suggest that the plausible etiologic role of heavy drinking in retinal detachment might be more relevant (or more evident) in nonmyopic people, and underline the need[6] for clarification of the effect of heavy drinking on this and other eye conditions.

These results may provide useful hints for future hypothesis-driven research into plausible risk factors for retinal detachment, including high alcohol intake, heavy lifting, and obesity. They also highlight the need for analytic studies to evaluate risk factors separately for nonmyopic people—especially because retinal detachment often occurs in the absence of myopia.

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# Birth Prevalence of Congenital Heart Disease

***To the Editor:***

Congenital heart defects occur in 1 of every 100–150 newborns.[1] Periconceptional use of folic acid may reduce the incidence of some of these defects, including conotruncal heart defects.[2,3] In November 1998, the Canadian government instituted mandatory fortification of flour and enriched pasta with folic acid.[4] This is estimated to increase the daily intake of folic acid among women 18–34 years of age by approximately 50%.[5] We assessed whether the birth prevalence of conotruncal heart defects subsequently decreased in the Canadian province of Quebec.

Using echocardiography databases and medical records of Quebec's 4 pediatric cardiology referral centers, we identified all children born alive from 1 January 1993 to 31 December 1996 and from 1 January 1999 to 31 December 2002 with one of the following diagnoses: tetralogy of Fallot, pulmonary atresia and ventricular septal defect, double-outlet right ventricle, truncus arteriosus, interrupted aortic arch, pulmonary atresia and intact ventricular septum, transposition of the great arteries, and hypoplastic left heart syndrome. The first 5 are conotruncal defects. Since fortification was optional between December 1996 and November 1998, this period was not included.

We used segmented Poisson regression to investigate changes in birth prevalence. We considered 2 groups: conotruncal defects and other congenital heart defects. Year was included as a linear factor. We used a segmented model allowing for 2 regression slopes, one before and one after 1998, described as follows:

$$\begin{aligned}\ln(\mu_{ij}) = {} & \ln(\text{number of births}_i) + \beta_0 \\ & + \beta_1 \text{type}_j + \beta_2 \text{year}_i + \beta_3 \text{type}_j \\ & \times \text{year}_i + \beta_4 (\text{year}_i - 1998) \\ & \times I(\text{year}_i > 1998) + \beta_5 \text{type}_j \\ & \times (\text{year}_i - 1998) \times I(\text{year}_i > 1998),\end{aligned}$$

where $\mu_{ij}$ is the mean number of congenital heart defects of type $j$ during year $i$. The variable type $j$ takes the value 0 for conotruncal defects and 1 for other congenital heart defects. The years considered are 1993–1996, and 1999–2002. The indicator I (year >1998) is a function that takes the value 1 if year >1998, and 0 if year <1998.

The model for conotruncal defects before 1998 is:

$$\begin{aligned}\ln(\mu_{ij}) = {} & \ln(\text{number of births}_i) + \beta_0 \\ & + \beta_2 \text{year}_I\end{aligned}$$

and after 1998 is:

$$\begin{aligned}\ln(\mu_{ij}) = {} & \ln(\text{number of births}_i) + \beta_0 \\ & - 1998\beta_4 + (\beta_2 + \beta_4)\text{year}_i.\end{aligned}$$

Similarly, the model for other congenital heart defects before 1998 is:

$$\begin{aligned}\ln(\mu_{ij}) = {} & \ln(\text{number of births}_i) + \beta_0 \\ & + \beta_1 + (\beta_2 + \beta_3)\text{year}_I\end{aligned}$$

and after 1998 is:

$$\begin{aligned}\ln(\mu_{ij}) = {} & \ln(\text{number of births}_i) + \beta_0 \\ & + \beta_1 - 1998(\beta_4 + \beta_5) + (\beta_2 + \beta_3 \\ & + \beta_4 + \beta_5)\text{year}_i.\end{aligned}$$

From these equations, the change in the slope between the 2 periods for the birth prevalence of conotruncal defects is $\beta_4$ and

**TABLE.** Prevalence (per 10,000 live births) of 8 Major Congenital Heart Defects in the Province of Quebec Before and After Mandatory Fortification of Flour and Enriched Pasta With Folic Acid

| Diagnosis | 1993–1996 Prevalence (no.) | 1999–2002 Prevalence (no.) |
|---|---|---|
| Tetralogy of Fallot | 3.7 (130) | 3.1 (91) |
| Double-outlet right ventricle | 1.6 (56) | 1.2 (34) |
| Pulmonary atresia with a ventricular septal defect | 0.9 (32) | 0.7 (21) |
| Truncus arteriosus | 0.4 (15) | 0.3 (10) |
| Interrupted aortic arch | 0.3 (9) | 0.2 (6) |
| Transposition of the great arteries | 2.8 (101) | 2.7 (80) |
| Hypoplastic left heart syndrome | 1.4 (49) | 1.4 (42) |
| Pulmonary atresia with an intact ventricular septum | 0.7 (24) | 0.9 (25) |
| Conotruncal defects | 6.8 (242) | 5.6 (161) |
| Other defects | 4.9 (174) | 5.0 (147) |
| Total | 11.7 (416) | 10.6 (309) |

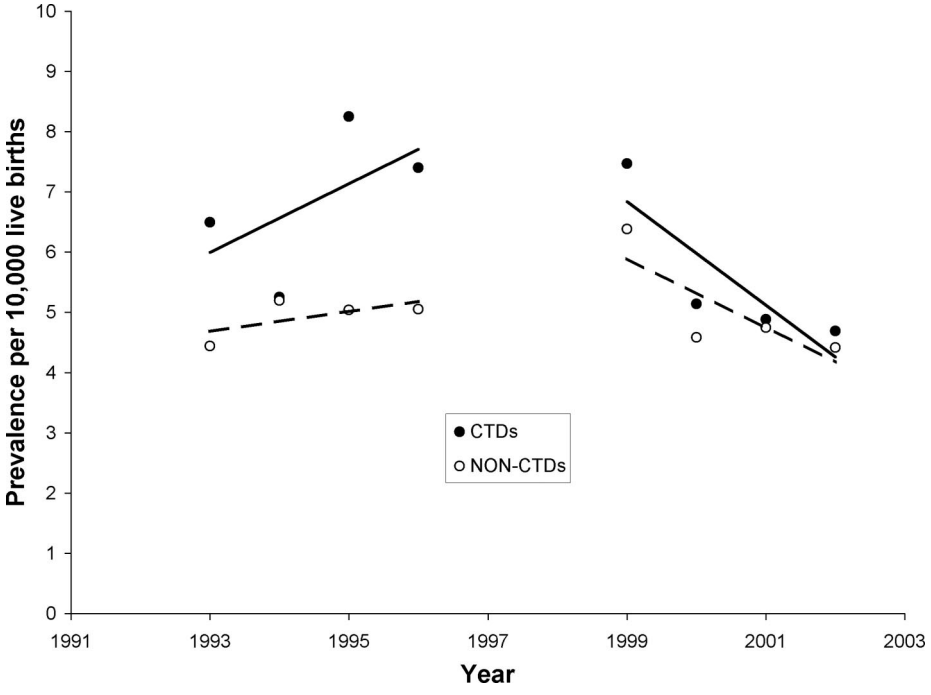


**FIGURE.** Birth prevalence of conotruncal defects (CTDs) and other congenital heart defects (NON-CTDs) in the province of Quebec during the 2 studied time periods, with their corresponding slopes.

the change in the slope for the prevalence of other congenital heart defects is $\beta_4 + \beta_5$.

Data were analyzed using SAS software, version 9.1 (SAS Institute, Inc., Cary, NC).

The Table shows the birth prevalence of congenital heart defects during the 2 time periods. There was a marked decline in the slope of prevalence of conotruncal defects between the 2 periods (−0.24; 95% confidence interval = −0.42 to −0.06) with less evidence for a decrease in the slope for other congenital heart defects (−0.15; −0.35 to 0.04) (Figure).

The evidence for periconceptional use of folic acid in primary prevention of congenital heart defects is inconsistent.[6] This ecologic study of selected congenital heart defects in Quebec following food fortification with folic acid, suggests that the birth prevalence of conotruncal defects has decreased, and perhaps of other congenital heart defects as well. Potential ascertainment bias was minimized by having the same investigator collecting the data in all 4 centers.

Increased use of folic acid supplements by pregnant women between the 2 periods could have contributed to this decline, and thus overestimate the effect of fortification. However, surveys of Quebec women have shown no substantial change in the intake of folate-containing multivitamin supplements before conception between the 2 periods.[7,8] Selective pregnancy termination may have had an impact on the results, although the prevalence of hypoplastic left heart syndrome (frequently associated with termination of pregnancy) did not decrease between the 2 time periods, suggesting that prenatal diagnosis did not

have a substantial impact on the results. Our findings add further support to the body of literature implicating folic acid deficiency in the pathogenesis of congenital heart defects.

## ACKNOWLEDGMENT

*We thank Jean-Luc Bigras, Christine Houde, Marc Bellavance, and Gregor Andelfinger for their contributions to this study.*

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# Fractal Epidemiology

***To the Editor:***

In the book *Fundamental Aspects of Fractal Epidemiology*,[1] we present a simple theory of complexity and the fundamental aspects of fractal epidemiology, based on conventional epidemiology and this complexity theory. "We see complex phenomena around us so often," says Per Bak in his book *How Nature Works*,[2] "that we take them for granted without looking for further explanation." We present ideas for study designs, procedures and methods by which one can identify fractals and causative complexities that occur studying epidemiologic data.[1] We have modified conventional concepts of exposure, response, and study setting, and made them more fit for the dynamics of prospective studies, so that researchers might more easily discover fractals in their studies and examine the correlation between complexity-exposure and complexity-response. By means of these tools, epidemiologists may discover many fractals and find complexities hidden in their studies.[3,4] We demonstrate how these methods can be applied to hypotheses such as the climatologic hypothesis that there is a deterministic relationship between global air carbon dioxide and global air temperature.

We firmly believe that the time has come for antireductionist study planning, investigation and understanding of outcomes. In the hope that the book might create some interest in complexity theory and fractal epidemiology, a free copy will be sent—as far as the impression goes—to everyone who e-mails Eystein Skjerve at eystein.skjerve@veths.no giving his/her name and postal address.

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# Snuff Use and Stroke

***To the Editor:***

Hergens et al recently concluded that "[s]nuff use may elevate the risk of fatal stroke, and particularly of fatal ischemic stroke."[1] We note apparent errors in Table 3, in which the relative risks and confidence intervals for "fatal" ischemic stroke are identical to those for "all" ischemic stroke, for all 4 snuff doses listed. The errors are obvious because the confidence intervals cannot be the same for the disparate numbers of cases in these 2 categories. Because this table relates to the authors' main points, a correction is in order. (***Editors' note***: *See erratum in this issue*.)

Furthermore, the manuscript clearly illustrates important aspects of the Karolinska group's research studies relating to snuff use among Swedish construction workers. The cohort on which this research is based consists of 2 distinct groups: construction workers enrolled during the period 1978–1992, and those enrolled earlier. Hergens et al[1] wrote that a previous Karolinska Institute study by Bolinder et al[2] provided evidence of increased stroke deaths among snuff users. That study was based on construction workers enrolled only between 1971 and 1974, who Hergens et al excluded from their analysis "because data on tobacco use were incomplete before 1978." In short, Hergens et al accepted the Bolinder findings but rejected the Bolinder cohort.

In a series of studies, the Bolinder cohort has been subjected repeatedly to

a revolving door of inclusion and exclusion by Karolinska investigators,[3] which is unacceptable from a scientific perspective. The subgroup in question consists of 135,000 workers contributing millions of person-years of follow-up, so its inclusion/exclusion may have had a profound effect on the risk estimates reported in the Karolinska studies.

Karolinska publications have also contained conflicting descriptions of snuff use among the Bolinder cohort. A recent Karolinska report,[4] coauthored by Hergens and Bolinder, stated that information on exposure to snuff for the Bolinder cohort ". . . was limited to ever or never use." In contrast, the Bolinder study[2] stated that the study population consisted of "present" (ie, current) snuff users. One of these descriptions of snuff exposure is incorrect.

If these discrepancies cannot be resolved by Karolinska epidemiologists, they must release the data for analysis by independent investigators. In the interim, the results should be considered as potentially unreliable, and unworthy of the certainty that they have been afforded by some European officials.[5]

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## DISCLOSURES

*This work was supported by unrestricted grants from smokeless tobacco manufacturers to the University of Louisville (US Smokeless Tobacco Company [USSTC] and Swedish Match AB) and to the University of Alberta (USSTC). The terms of the grants assure that the grantors are unaware of this work, and thus had no scientific input or other influence with respect to its design, analysis, interpretation or preparation.*

*Dr. Rodu and Dr. Heavner have no financial or other personal relationship with regard to the grantors. Dr. Phillips has provided consulting services to USSTC in the context of product liability litigation and is a member of a British American Tobacco External Science Panel that deals with developing reduced-harm products.*

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***The authors respond:***

Rodu et al[1] have pointed out a typographical error in Table 3 that escaped our attention when reading the proofs of our article titled "Smokeless tobacco and the risk of stroke."[2] Here, we provide the correct estimates for all ischemic stroke among current users by amount used (Table). This error does not affect our conclusion that (1) there was no clear dose-response relationship among current users, and (2) snuff use might be associated with an increased risk of fatal ischemic stroke, especially among current users.

Rodu et al also claim that studies about snuff use and various health outcomes based on data from the Construction Workers Cohort conducted at Karolinska Institutet have been inconsistent regarding inclusion and exclusion criteria. We have previously responded to this critique[3] but repeat the description of our study population and our reasons for exclusions. Between 1969 and 1993, all employees in the Swedish building industry were offered free outpatient medical services during which many other lifestyle factors, including tobacco use, were recorded. The total number of registered visits is over 1,150,000 among 386,000 individuals. More than 200,000 men had more than one health visit. Different questionnaires were used during different time periods. With regard to snuff use, the questions between 1971 and 1974 were: "Do you use snuff or chewing tobacco?" and "Since how many years?" Between 1975 and 1977, no questions on tobacco use were asked. Starting in 1978, the questionnaires included the following inquiries: "Daily consumption of snuff or chewing tobacco, in years," "Time since quitting the use of snuff or chewing tobacco, in years," and "Consumption lately, in grams per week."

Rodu et al criticize us for accepting results by Bolinder et al[4] regarding snuff use and cardiovascular outcome in the Construction Workers Cohort between 1971 through 1974, but excluding from our studies[2,5] the subjects included

**TABLE.** Relative Risk of Ischemic Stroke for Current Snuff Users by Amount Used Compared With Nonusers of Tobacco

| | RR (95% CI) <12.5 g/d | RR (95% CI) 12.5–29.9 g/d | RR (95% CI) 25–49.9 g/d | RR (95% CI) ≥50 g/d |
|---|---|---|---|---|
| All ischemic strokes | *1.10 (0.90–1.34)* | *1.10 (0.91–1.33)* | *1.13 (0.82–1.55)* | *1.27 (0.82–1.96)* |
| Nonfatal | 1.05 (0.85–1.28) | 1.08 (0.89–1.31) | 1.15 (0.83–1.58) | 1.19 (0.76–1.88) |
| Fatal | 2.11 (1.10–4.07) | 1.99 (0.80–3.44) | 0.66 (0.09–4.76) | 3.28 (0.79–13.6) |

Corrected results for all ischemic strokes in Table 3 of the article by Hergens et al.[2]
RR indicates relative risk derived from Cox proportional hazard regression model, adjusted for age (age at follow-up was used as time scale), body mass index, and region of residence; CI, confidence interval.

in the Bolinder study. They seem to believe that the Bolinder study and ours are based on 2 distinct groups, which is not the case. Because of the differences in the questionnaires during different time periods, we chose to use the information on tobacco use collected after 1977. This means that subjects with exposure information from this year are included. In all, 300,637 individuals had tobacco information from health check-ups after 1 January 1978, of which 77,844 (25%) also had exposure information before 1978. These subjects somewhat overlapped with those in the study by Bolinder et al, which is also described in a thesis published at Karolinska Institutet.[6]

Another critique expressed by Rodu et al[1] is the confusing referral to snuff use in the study by Bolinder et al[4] and provided in subsequent studies based on data from the Construction Workers Cohort.[5,7,8] Bolinder et al presented results for current snuff users, but in subsequent studies this is described as ever-use of snuff. However, we do not think that this in any way invalidates our results. The results by Bolinder et al on current snuff use are in line with our more recent findings on current snuff use, as well as for ever-use.[6]

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