

# Statistics in the News

Nancy Reid

January 6, 2005

**GLOBEANDMAIL.COM** News

Investing

Technology

Home | Business | National | International | Sports | Travel | Entertainment



Search Site [More Search Options/Archives](#)

Search Tips

go

[Privacy Policy](#)  
[Subscribe to Globe](#)  
[Publisher's Note](#)

Breaking News

Home Page  
 Business  
 Personal Finance  
 National  
 International  
 From the Field  
 Sports  
 Entertainment

TODAY'S PAPER

## HEALTH

### Eating smart is good for your brain

Research is piling up that getting certain nutrients can help you concentrate and learn today, and ward off brain aging in the long run

By LESLIE BECK

Wednesday, September 8, 2004 - Page A17

## TOXICOLOGY

## Salmon Survey Stokes Debate About Farmed Fish

Salmon's popularity has boomed in the past 2 decades as aquaculture has made salmon available year-round at low cost. The fish is a good source of protein, vitamin D, and heart-friendly fats. But fish farms have boosted less welcome ingredients: The largest survey yet of pollutants in salmon, reported on page 226, has found that farmed fish have higher levels of polychlorinated biphenyls (PCBs) and other organochlorine compounds than do wild-caught salmon. The source, as many researchers suspected, is the feed.

"This is a definitive study," says nutritionist and toxicologist Miriam Jacobs of the University of Surrey, U.K., and Royal Veterinary College, London. "Further action has to be taken to reduce the contaminant levels in feed." The authors argue that consuming more than one meal of farmed salmon per month may hike the risk of cancer. "The punch line is that eating the wrong kind of fish has real dangers," says team member David Carpenter of the State University of New York, Albany, in Rensselaer.

Other experts say the risk is outweighed by the benefits of eating farmed salmon. Avoiding the fish would mean giving up its nutritional benefits, including protection against heart attacks. What's more, they say,

the contaminant levels aren't high enough to pose real dangers. "In my view, the study says we should be eating more farmed salmon," says toxicologist Charles Santerre of Purdue University in West Lafayette, Indiana.

While nutritionists debate the study's implications, consumers can use its data to try to select the cleanest fish possible. "I think we can begin to make informed choices about what kind of fish to eat," says toxicologist Linda Birnbaum of the U.S. Environmental Protection Agency (EPA).

The massive study, funded by the Pew Charitable Trusts' Environment program and conducted by six scientists, sampled about 700 salmon from around the world and ana-



**Seeing red.** Farmed salmon has more PCBs than wild salmon, but scientists don't agree on how much one should eat.

lyzed them for more than 50 contaminants. The greatest differences were between farmed and wild salmon. Farmed salmon was in only 14 of these chemicals, whereas wild salmon was in 14 of these chemicals. Farmed salmon had more contaminants than wild ones. Farmed salmon in Europe had the highest levels, followed by farmed salmon from North America, whereas Chilean farmed salmon were the cleanest. Researchers also tested for oil and meal feed in the fish and found a similar pattern. Feeding salmon fish meal boosted their growth and nutrition, but it also concentrated contaminants.

The team took a closer look at PCBs

and other persistent pesticides called dioxins and toxaphene, all of which have been related with risk of liver and other diseases. The researchers used EPA guidelines to calculate the maximum amount of fish that can be eaten before boosting

## Did FDR Have Guillain-Barré?

A new analysis of Franklin Delano Roosevelt's symptoms suggests he might not have been stricken by polio but by Guillain-Barré syndrome.

In 1921, at the beginning of his political career, Roosevelt became feverish and developed paralysis, which started in his legs and moved up to his neck. Although he recovered partially, he remained permanently wheelchair-bound.

Immunological pediatrician Armond Goldman of the University of Texas Medical Branch in Galveston now says FDR's symptoms are more concordant with Guillain-Barré syndrome, a bacterially induced autoimmune disease. For example,

emerged as the more likely cause of his paralysis, they report in the 1 November *Journal of Medical Biography*.

"The result is interesting both historically and neurologically," says neurologist Deborah Green of the University of Hawaii School of

Medicine at Manoa. FDR's misdiagnosis—if such it was—may have changed the course of history, because his affliction gave great momentum to efforts to develop a polio vaccine. But Green notes that "there's no way to prove [a misdiagnosis] without testing the spinal cord fluid." Neurologist H. Royden Jones of Harvard Medical School in Boston adds that the researchers could be wrong in assuming that "Guillain-Barré is the same now as it was back then."

### Getting Into a

# Statistical error leaves pollution data up in the air

Jonathan Knight, San Francisco

An off-the-shelf statistics package has tripped up pollution researchers in North America and Europe who are studying the effects of airborne soot on human health.

A default setting that produced erroneous results went unchecked for years, despite significant statistical expertise in all of the groups. "It was already such standard software when we started using it, I didn't

even question it," says Francesca Dominici, a public-health researcher at Johns Hopkins University in Baltimore, Maryland.

On 4 June, Dominici posted revised figures on her website after discovering that the error had doubled her group's estimate of the risk to health posed by particulates in the air. Two other groups that used the same tool, one in Canada and one in Greece, are now redoing their calculations.

The groups were looking for correlations between death rates and particulates in the air, which come mainly from diesel engines and power plants. Their data on air quality, hospitalizations and deaths from dozens of cities cover a seven-year period up to 1994.


Death rates vary throughout the year because of such factors as changes in temperature and disease outbreaks. To tease out the effects of particulates, the groups used a statistics program known as S-Plus.

S-Plus searches for correlations using an iterative process in which confounding effects are gradually peeled away. The default parameter in question determined how many times the procedure would iterate before stopping to produce a final result.

"For most applications the value is perfectly fine," says David Smith, product manager of Seattle-based Insightful, which sells S-Plus. Smith says that the Hopkins case was exceptional, but that users should always check whether changing the parameter affects the outcome, and adjust it if necessary. Smith says that Insightful will tighten the default value of the parameter — slowing the programme slightly — on future releases of S-Plus.

Richard Burnett, a statistician with Health Canada in Ottawa, which is conducting a similar study, says that his group will probably revise its estimates of the impact of airborne soot on mortality downwards by 20–50%. The findings of a study run by a group at the University of Athens may also have to be adjusted, he says.

The health risk posed by particulates is a source of fierce environmental controversy in the United States, and the Bush administration is considering rules to restrict emissions. Opponents of tighter rules are likely to seize on the revisions as evidence that the research linking soot in the air to harmful effects on health is not to be trusted. ■



Clouding the issue: particulates are seen as a health risk, but how reliable are the data?

# Data Revised on Soot in Air and Deaths

## Scientists Lower Their Estimate of Risk From Bad-Air Days

By ANDREW C. REVKIN

Revisiting their own data with new methods, scientists who conducted influential studies that linked sooty air pollution with higher death rates have lowered their estimate of the risk posed by bad-air days.

The findings do not challenge what is now a well-established link between air pollution and premature death. But the new analysis is highly likely to delay the final review of new regulations on small-particle pollution, officials of the Environmental Protection Agency said yesterday.

The review was projected to end, and the new rules to take effect, by the end of next year.

"This may clearly push it beyond that," a spokesman for the E.P.A., Joe Martyak, said last night.

The fine particles in question come mainly from power plants and diesel engines, and the proposed rules have been at the center of a long legal, political and public-relations battle between private environmental groups and power plant owner and vehicle manufacturers.

The researchers, at the Johns Hopkins University, have been distributing their new analysis to scientists and government officials by fax and e-mail. Yesterday, they set up a Web site, [biostat.jhsph.edu/~fdominic/biosun01.biostat.jhsph.edu](http://biostat.jhsph.edu/~fdominic/biosun01.biostat.jhsph.edu), that details their new findings.

"This is a very important finding that needs to be probed," said Daniel S. Greenbaum, president of the Health Effects Institute, the organi-

zation that can be deeply inhaled into the lungs and stay there. In the original analysis, the rise was 0.4 percent above the typical mortality rate for each jump of 10 micrograms of soot per cubic meter of air. In the new analysis, the increase is half that.

The researchers said the change was small but significant. The average level in the average city is now about 24 micrograms a cubic meter.

The work has been published for several years in a variety of leading journals like *The New England Journal of Medicine* and *The American Journal of Epidemiology*. The project, the National Morbidity, Mortality and Air Pollution Study, was given extra weight by policy makers because of the reputation of the Health Effects Institute and the Johns Hopkins group, led by Dr. Jon-

*New research may delay a review due next year on small-particle pollution.*

athan M. Samet, chairman of epidemiology at the public health school there.

As part of a continuing effort to check for flaws, those scientists in recent weeks used a new method to

re-analyze the data. Dr. Scott L. Zeger, said other researchers who used the software, S-Plus, should check for similar problems. It is widely used for research in fields like pharmacology, genetics, molecular biology and stock-market forecasting, as well as serving as a mainstay of other environmental studies.

Dr. Zeger and Mr. Greenbaum stressed that the new findings did not overturn the basic link between soot and illness. They also pointed to the recent publication of other studies on the long-term effects of soot that do not use the same analytical tools.

Still, industry officials said the new findings called into question the validity of some research underlying the new federal standards.

"This study is really one of the ones creating the path for the future on air-quality regulation," said Allen Schaeffer, executive director of the Diesel Technology Forum.

The new results, Mr. Schaeffer said, show that "particle science is still evolving, and so are the analytical tools to look at it."

Scientists involved with the soot standard said that there was much other evidence that pointed to the dangers of soot but that the errors in the Johns Hopkins work were still significant.

"It certainly brings into question the precision of the data," said Dr. Jane Q. Koenig, a professor of environmental health at the University of Washington and a consultant involved with the soot review. "That's very unfortunate, because this re-

Nov. 5, 2004. 06:29 AM

## Health officials examine Celebrex safety

TANYA TALAGA  
HEALTH POLICY REPORTER

Federal health officials and the maker of Celebrex were scrambling yesterday to alleviate fears over the safety of the popular drug used to treat arthritis.

A published report suggested Celebrex, a product of Pfizer Canada Inc., is suspected of contributing to just over a dozen deaths and numerous heart and brain-related complications in Canada. The report is based on numbers obtained from an adverse drug reaction database, a surveillance tool Health Canada uses to monitor drugs in the marketplace. Dr. Maria Valois, Health Canada's director of marketed pharmaceuticals, told a group of journalists from across North America yesterday she was awaiting more information from Pfizer on the drug's safety in clinical trials and results from other countries.

She set a Nov. 18 deadline for the reports. Further action would depend on the material submitted, she said. "It's still premature to conclude what intervention is required in this case," Valois said.

She said information pulled from the database shows Celebrex may "possibly" be connected to six deaths in Canada. There is no proof the drug caused deaths. "Any health product has some benefit and some risk," Valois said. Drug-maker Pfizer issued a statement from its New York headquarters saying the safety profile for Celebrex was supported by worldwide clinical trials. Millions have taken Celebrex since it was approved in 1998.

"The news report, based on voluntary spontaneous event reporting to Canadian health authorities, is misleading," Pfizer said in a statement. "The story is not supported by any clinical or epidemiological studies and has the potential to cause undue confusion among patients and physicians."

The database the numbers came from uses information collected through voluntary reporting by doctors, pharmacists, health professionals and others.

Cox-2 inhibitors like Celebrex and Vioxx — drugs that block an enzyme in the body that contributes to inflammation and pain — have recently come under scrutiny. The arthritis drug Vioxx was pulled off the market worldwide

### GTA COLUMNISTS

- > [Jim Coyle](#)
- > [Rosie Dimand](#)
- > [Joe Fiorito](#)
- > [Christopher F](#)
- > [Royson James](#)



## Press Release

[Prescribing Information](#)

[Patient Product Information](#)

[Refund Information for Patients](#)

[Information for Patients](#)

[Information for Healthcare Professionals](#)

[Information for Direct and Indirect  
Pharmacy Wholesaler and Retailer  
Customers](#)

[Information for Canadian Residents](#)

## Merck Announces Voluntary Worldwide Withdrawal of VIOXX<sup>®</sup>

WHITEHOUSE STATION, N.J., Sept. 30, 2004—Merck & Co., Inc. today announced a voluntary worldwide withdrawal of VIOXX<sup>®</sup> (rofecoxib), its arthritis and acute pain medication. The company's decision, which is effective immediately, is based on three-year data from a prospective, randomized, placebo-controlled clinical trial, APPROVe (Adenomatous Polyp Prevention on VIOXX) trial.

The trial, which is being stopped, was designed to evaluate the efficacy of VIOXX in preventing recurrence of colorectal polyps in patients with a history of colorectal adenomas. In this study, there was an increased relative risk for confirmed cardiovascular events, such as heart attack and stroke, beginning after 18 months of treatment in the patients taking VIOXX compared to those taking placebo. The results of the first 18 months of the APPROVe study did not show any increased risk of cardiovascular events on VIOXX, and in this respect, are similar to the results of placebo-controlled studies described in the current U.S. labeling for VIOXX.



# Data Revised on Soot in Air and Deaths

## Scientists Lower Their Estimate of Risk From Bad-Air Days

By ANDREW C. REVKIN

Revisiting their own data with new methods, scientists who conducted influential studies that linked sooty air pollution with higher death rates have lowered their estimate of the risk posed by bad-air days.

The findings do not challenge what is now a well-established link between air pollution and premature death. But the new analysis is highly likely to delay the final review of new regulations on small-particle pollution, officials of the Environmental Protection Agency said yesterday.

The review was projected to end, and the new rules to take effect, by the end of next year.

"This may clearly push it beyond that," a spokesman for the E.P.A., Joe Martyak, said last night.

The fine particles in question come mainly from power plants and diesel engines, and the proposed rules have been at the center of a long legal, political and public-relations battle between private environmental groups and power plant owner and vehicle manufacturers.

The researchers, at the Johns Hopkins University, have been distributing their new analysis to scientists and government officials by fax and e-mail. Yesterday, they set up a Web site, [biostat.jhsph.edu/~dominic/research.html](http://biostat.jhsph.edu/~dominic/research.html), that details their new findings.

"This is a very important findi-

ng that can be deeply inhaled into the lungs and stay there. In the original analysis, the rise was 0.4 percent above the typical mortality rate for each jump of 10 micrograms of soot per cubic meter of air. In the new analysis, the increase is half that.

The researchers said the change was small but significant. The average level in the average city is now about 24 micrograms a cubic meter.

The work has been published for several years in a variety of leading journals like *The New England Journal of Medicine* and *The American Journal of Epidemiology*. The project, the National Morbidity, Mortality and Air Pollution Study, was given extra weight by policy makers because of the reputation of the Health Effects Institute and the Johns Hopkins group, led by Dr. Jon-

*New research may delay a review due next year on small-particle pollution.*

athan M. Samet, chairman of epidemiology at the public health school there.

kins biostatistics department, Dr. Scott L. Zeger, said other researchers who used the software, S-Plus, should check for similar problems. It is widely used for research in fields like pharmacology, genetics, molecular biology and stock-market forecasting, as well as serving as a mainstay of other environmental studies.

Dr. Zeger and Mr. Greenbaum stressed that the new findings did not overturn the basic link between soot and illness. They also pointed to the recent publication of other studies on the long-term effects of soot that do not use the same analytical tools.

Still, industry officials said the new findings called into question the validity of some research underlying the new federal standards.

"This study is really one of the ones creating the path for the future on air-quality regulation," said Allen Schaeffer, executive director of the Diesel Technology Forum.

The new results, Mr. Schaeffer said, show that "particle science is still evolving, and so are the analytical tools to look at it."

Scientists involved with the soot standard said that there was much other evidence that pointed to the dangers of soot but that the errors in the Johns Hopkins work were still significant.

"It certainly brings into question the precision of the data," said Dr. Jane Q. Koenig, a professor of environmental health at the University of Washington and a consultant in-

- ▶ “the new analysis is highly likely to delay the final review of new regulations on small-particle pollution”
- ▶ “industry officials said the new findings called into question the validity of some research underlying the new federal standards”
- ▶ “ ‘It certainly brings into question the precision of the data’, said Dr. Jane Q. Koenig”
- ▶ “The health risk posed by particulates is a source of fierce environmental controversy in the United States”
- ▶ “Opponents of tighter rules are likely to seize on the revisions as evidence that the research linking soot in the air to harmful effects on health is not to be trusted”
- ▶ “A default setting that produced erroneous results went unchecked for years, despite significant statistical expertise in all the groups”

- ▶ “The findings do not challenge what is now a well established link between air pollution and premature death”
- ▶ “The work has been published for several years in a variety of the leading journals like the New England Journal of Medicine and the American Journal of Epidemiology”
- ▶ “The project, the National Morbidity, Mortality and Air Pollution Study, was given extra weight by policy makers because of the reputation of the Health Effects Institute and the Johns Hopkins group”
- ▶ **Not as well known that the effect was first discovered at Health Canada, by Tim Ramsay and Rick Burnett**
- ▶ their work also drew attention to the incorrect calculation of standard errors in the `gam` software
- ▶ Original estimate 0.41% increase in mortality rate associated with increase of  $10\mu\text{g}/\text{m}^3$  increase in  $PM_{10}$ .
- ▶ Revised estimate 0.22%.
- ▶ these are small effects; approximately 12 additional deaths per year in Montreal, perhaps 15 in Toronto

## The data

- ▶ daily mortality counts from NCHS (National Center for Health Statistics) 1987-1994
- ▶ hourly temperature and dewpoint data from National Climatic data Center
- ▶ data on pollutants  $PM_{10}$ ,  $O_3$ ,  $CO$ ,  $SO_2$ ,  $NO_2$  from EPA

## The model

- ▶  $Y_t$  mortality rate on day  $t$  follows a Poisson distribution with mean  $\mu_t$
- ▶  $\log \mu_t$  depends on a number of inputs: pollution on day  $t - 1$ , age and size of population, weather, day of the week, time
- ▶ effect of pollution is linear, effect of **confounders** is 'smooth'
- ▶ fit the same model for each city, pool effect estimates

## ... the model

- ▶  $\log \mu_{at} = \beta X_{t-1} + \gamma DOW + S_1(t, 7) + S_2(temp_0, 6) + S_3(temp_{1-3}, 6) + S_4(dew_0, 3) + S_5(dew_{1-3}, 3) + \alpha_a + S_{6a}(t, 8)$
- ▶  $a$  indexes age groups,  $t$  time (days)
- ▶  $S(z, 8)$  is a non-specified, but smooth, function of  $z$  with 8 'degrees of freedom', can think of it as a spline with a pre-specified number of knots. Large df means wiggly function, 1 df is linear
- ▶ mortality rates change with season, weather, changes in health status, ...
- ▶ Is there anything left for pollution?