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Long-term health effects after DES exposure in utero

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projected half-life in 1995 be 13.3 years for whites and 7.2 years for blacks but 13.8 years overall?

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The authors reply:

To the Editor: Parikh and Ellison correctly note that from the patient's perspective, improvement in the short-term and long-term survival of renal transplants is additive and directly affects the prognosis.

We found that there has been steady improvement in the survival of renal transplants since the introduction of cyclosporine in the 1980s. Over 90 percent of the 1988 cohort received cyclosporine, and therefore the improved outcomes in later cohorts could be related to changes in doses or timing.¹ However, the improvement is probably not related to cyclosporine alone. The causes of this improvement cannot be pinpointed, but they include a reduction in episodes of acute rejection and improvements in the control of hypertension and in the prevention and management of infections. The decrease in panel-reactive antibodies is probably due to a reduction in the transfusion rate (15 percent with more than 10 prior transfusions in 1988 vs. less than 4 percent after 1992), a decrease that is correlated with the introduction of erythropoietin.

Sam and Leehey raise a question about discrepancies between the text and Table 2 of our article with respect to the improvement in the projected half-life of transplants in blacks, nonblacks, and all recipients. The projected half-life values given in the text (7.2 years for blacks and 13.3 years for nonblacks) were for 1994, not 1995; the value of 11.0 years for all recipients of cadaveric transplants, shown in Table 2, is correct.

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1. Tejani A, Sullivan EK. Higher maintenance cyclosporine dose decreases the risk of graft failure in North American children: a report of the North American Pediatric Renal Transplant Cooperative Study. *J Am Soc Nephrol* 1996;7:550-5.

Prevalence of Gynecologic Cancer in Women Exposed to Diethylstilbestrol in Utero

To the Editor: Exposure to diethylstilbestrol (DES) in utero is related to an increased risk of clear-cell adenocarcinoma of the vagina and cervix at a young age.¹ However, the long-term risk of cancer in the daughters of women given DES during pregnancy (DES daughters) is still unknown. To date, only one study has examined the risk of cancer in adult DES daughters, and no increased risks were found in that study, except for an increased risk of clear-cell adenocarcinoma of the vagina and cervix.²

TABLE 1. PREVALENCE RATIOS FOR TUMORS AMONG 5421 DES DAUGHTERS.

SITE OR TYPE OF TUMOR	TUMORS IN DES DAUGHTERS				PREVALENCE RATIO (95% CI)†	STATISTICAL POWER‡
	SELF-REPORTED	MEDICAL RECORD REVIEWED	OB-SERVED	EXPECTED*		
	no. of tumors					
Vulva	4	2	1	0.11	8.8 (0.2-49.0)	<0.50
Cervix	68	56	12§	2.22	5.4 (2.8-9.5)	0.95
Breast	13	11	9	5.87	1.5 (0.7-2.9)	<0.50
Ovary	11	10¶	4	1.36	2.9 (0.8-7.5)	<0.50
Melanoma	13	9	6	4.37	1.6 (0.6-3.3)	<0.50
Colon	2	1	1			
Total	111	89**	33††			

*The expected number of tumors was calculated on the basis of age- and period-specific prevalence rates according to data from the Eindhoven Cancer Registry.

†CI denotes confidence interval.

‡The values indicate the probability that the null hypothesis is rejected at an alpha level of 0.05 in favor of the alternative hypothesis.

§There were 10 squamous-cell carcinomas and 2 adenocarcinomas.

¶The tumors included two borderline carcinomas.

||A total of 111 tumors were reported by 105 DES daughters.

**The medical records of 85 DES daughters who reported a total of 89 tumors were reviewed.

††A total of 33 tumors reported by 33 DES daughters were confirmed by a review of the medical records.

We analyzed data from a questionnaire mailed to 13,350 DES daughters registered at the Netherlands DES Information Center. Self-reported information on cancer was validated by reviewing information from medical records. Prevalence ratios for cases of cancer were calculated as the ratio of the observed number of cases to the expected number, on the basis of age-specific and calendar-period-specific prevalence rates based on data from the Eindhoven Cancer Registry. The 95 percent confidence intervals and the statistical power (with an alpha level of 0.05) were calculated on the basis of a Poisson distribution.³ To quantify selection bias, we also calculated the prevalence of melanoma and colon cancer, for which no association with DES was assumed, as "marker" tumors. Cases of clear-cell adenocarcinoma of the vagina and cervix were excluded from the analysis.

Forty-one percent of the women (5421) responded to the mailing. The median age of the respondents was 30 years (range, 19 to 45). A total of 111 cancers were reported by 105 women, and the medical records of 85 of these women were reviewed to confirm the reported tumors (Table 1). The agreement between the information reported by the respondents and the information from the medical records was poor for cervical cancer (21 percent), since many women reported a carcinoma in situ as an invasive cancer. The prevalence ratio for confirmed cervical cancer was significantly elevated (5.4; 95 percent confidence interval, 2.8 to 9.5); the prevalence ratios for the other tumors were not significantly elevated.

DES daughters with health problems might have been more likely to respond to our questionnaire than DES daughters without health problems. However, adjustment for the elevated prevalence ratio for the combined marker tumors (1.6; 95 percent confidence interval, 0.6 to 3.3) still resulted in a tripled risk of cervical cancer. DES daughters might actually be expected to have a lower prevalence of invasive cervical cancer than women in the general population, since DES daughters are screened more intensively for cervical cancer and since precursor lesions detected on screening are usually treated aggressively. Our finding is therefore particularly striking.

Robboy and colleagues reported that the risk of squamous-cell dysplasia and carcinoma in situ was doubled in DES daughters.⁴ They hypothesized that DES daughters might have an elevated risk of cervical cancer because of the presence of a wider transformation zone of metaplastic squamous epithelium, which might make them more susceptible to external carcinogenic factors. Larger studies, preferably with incidence data, are needed to confirm our observations.

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1. Waggoner SE, Mittendorf R, Biney N, Anderson D, Herbst AL. Influence of in utero diethylstilbestrol exposure on the prognosis and biologic behavior of vaginal clear-cell adenocarcinoma. *Gynecol Oncol* 1994;55: 238-44.
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3. Breslow NE, Day NE. Statistical methods in cancer research. Vol. 2. The design and analysis of cohort studies. Lyon, France: International Agency for Research on Cancer, 1987. (IARC scientific publications no. 82.)
4. Robboy SJ, Noller KL, O'Brien P, et al. Increased evidence of cervical and vaginal dysplasia in 3,980 diethylstilbestrol-exposed young women: experience of the National Collaborative Diethylstilbestrol Adenosis Project. *JAMA* 1984;252:2979-83.

Women Physicians in Academic Medicine

To the Editor: Nonnemaker (Feb. 10 issue)¹ presents her results without much editorializing about the woes of women in medicine. Articles on this topic always worry me, since the victim mentality is so prevalent in our society.

When I was in high school, I worked for a woman physician by watching her children. She told me some of the things she had to endure while in medical school in the 1960s. Some of the treatment she received was appalling. However, I believe that the climate in medicine has changed substantially since that time. I graduated from medical school in 1989. I have experienced very little prejudice on the basis of my being a woman. I cannot say that my experience holds true for all women in medicine, particularly women who are members of minority groups, but my own experience has been good overall, with only a few minor problems.

I was in academic medicine until the summer of 1999. I observed no inequalities with respect to the promotion of women as compared with men. I also saw that fewer

women chose to put in the hours required to progress rapidly to full professorship. Most of these women cited the value they placed on family life as the reason for not putting in the required extra hours. I fall into that category. I recently left full-time medicine in order to care for my children myself. I still work part-time, but such a career choice, as compared with those of many men in academic medicine, could be one of the reasons for the skewed statistics on the promotion of women relative to men in academic medicine. I suggest that lifestyle choices are a possible cause of the lower numbers of women in the higher ranks of academic medicine.

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1. Nonnemaker L. Women physicians in academic medicine: new insights from cohort studies. *N Engl J Med* 2000;342:399-405.

To the Editor: If the goal referred to by Nonnemaker is to provide equal opportunity to women to advance academically, I suggest that her study has not proved that women do not have equal opportunity. To prove this, one would have to know the proportion of junior faculty members of both sexes who have met the criteria for advancement to senior rank and have not yet been promoted. At that point, one could determine whether equal opportunity did or did not exist. Likewise, it would be interesting to know the relative qualifications of recently promoted male and female faculty members at each academic level to ascertain whether efforts at affirmative action within faculty organizations have been successful. It is easy to imply sex bias through the use of statistics that show an imbalance, when in fact the imbalance may be due to factors not studied, such as time (and effort) spent away from academia, which would contribute to a lower level of academic achievement as compared with that of colleagues.

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To the Editor: Is it the goal of academicians to promote women, as opposed to promoting the best and most qualified candidates? It seems to me that medicine — at least as much as, if not more than, any other profession — should be blind to sex and color.

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To the Editor: Nonnemaker and De Angelis, in her accompanying editorial,¹ highlight the continuing problems that confront women physicians in their pursuit of academic promotion. The problem of whether women physicians receive recognition equivalent to that of men is also highlighted on the page following the editorial in the same issue of the *Journal*.