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Dear Jim:

I have read the paper Ovarian Cancer and Talc: A Case-Control Study by Cramer, DW, Welch, WR, Scully RE, and Wojciechowski CA, which you sent me. I have also read, or re-read, some of the relevant papers referred to in that paper. The paper describes the findings in 215 white females with epithelial ovarian cancer and 215 controls from the general population matched for age, race and residence. 92 (42.8%) of the cancer cases are reported to have regularly used talc either as a dusting powder on the perineum or on sanitary napkins compared with 61 (28.4%) of the controls. This gives a crude relative risk of 1.89. When adjusted for differences in parity and menopausal status between cases and controls, this relative risk became 1.92. The comparable adjusted relative risk for women who had regularly engaged in both practices was 3.28 compared with women with neither exposure. These differences were statistically significant ($p < .003$ and $< .001$ respectively.) The possibility that talc from condoms or diaphragms or from pelvic surgery could contribute to the risk was explored; but no significant differences were observed between cases and controls. Expected large differences were, however, found with parity and marital status.

Selection of cases. The 215 cases were obtained from 297 English-speaking residents of Massachusetts diagnosed November, 1978 to September, 1981 at 12 participating hospitals in the Greater Boston Area. Identification was through pathology logs or tumor boards. 256 cases were interviewed. Physicians refused permission to contact patients in 13 instances; 14 patients refused and 14 had died or moved. On the basis of histology, the 256 cases were reduced to 215 epithelial cancers, which included 39 with tumors of borderline malignancy.

Selection of controls. Controls were drawn at random from Massachusetts Town Books matched by precinct of residence, race and age + 2 years. 475 potential controls were identified. 56 (12%) of them could not be reached because they had moved, died or had disconnected or unlisted phones. 29 (6%) of the total were ineligible because of bilateral salpingo-oophorectomy, 29 (4%) were wrong age or race or did not speak English. 155 (33%) refused to participate.

Table 1
Comparison of Cases and Controls

	Cases	Controls
Total	297	475
Dead, etc.	14 (4.7)	56 (11.8)
Refused incl. physician	27 (9.1)	155 (32.6)

Table 1 shows there were large differences between cases and controls in the proportions who died or moved and refused. The reference to "dis-connected or unlisted phones" is interesting. It suggests the controls may have been interviewed by phone while the cases were interviewed in a clinic.

Conduct of interviews. It is not clear how the interviews were conducted. The only description tells us they were conducted personally; but what this means is not explained. i.e. Did the same interviewers interview both cases and controls? How many interviewers were there? Were observer differences considered either in the design or analysis? Were the interviews at home, in a clinic, telephone or in person?

Information was collected on menstrual and reproductive history, medical and family history, and on environmental exposures. This paper, however, deals only with exposure, potential or definite, to talc from contraceptive practices, operations, or perineal hygiene. It would have been interesting to have some statement on such ovarian cancer risk factors as previous history of mumps and possible environmental or occupational exposures, particularly to asbestos.

Results and analysis. The analysis ignores matching. It is confirmed to comparison of the frequency of factors in all cases and controls. The usual effect of this is to make the findings less sensitive than they otherwise might be, however, and it is unlikely to have produced spuriously significant differences.

While no striking differences were noted in most of the potential confounding factors, large differences were noted between cases and controls between never married and nulliparous. The cases were roughly twice as likely to be never married or nulliparous (57.7% compared with 29.3%). Although these differences are said to be allowed for in the results, I think it would be interesting to see the findings for the stratified groups.

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No results are presented on the degree of exposure. There is thus no evidence on dose/response. Nor is it made clear how long talc had been regularly used. For example, it might be relevant to know whether exposure occurred before asbestos contamination was removed from cosmetic talc.

Regular use of talc is not defined in the paper. The reader is not told the minimum duration and frequency needed for inclusion in the category.

In general, this paper provides some evidence for an association between talc use and ovarian cancer. The likelihood that this was due to bias introduced by refusal rates, the way the data were collected, or because cases and controls differed in other respects than talc usage of the kind described here, seems to me to be high. There is also the possibility that reporting bias whereby the cases who will naturally be concerned to identify any potential cause of their disease might be more prone than the controls to report the use of talc.

I should perhaps add that I have some difficulty in accepting the likelihood of the hypothesis. The evidence that cosmetic talc is carcinogenic is lacking. And although it seems clear that particles placed in the vagina can reach the abdominal cavity via the fallopian tubes, it is difficult to envisage this happening much from perineal application. If the hypothesis is correct and this paper is demonstrating cause and effect, one is forced to conclude that talc is a potent ovarian carcinogen. I do not think this is so.

I have tried to reach Dr. Cramer in Boston, but so far without success. I will, however, continue to try and will let you know any additional facts I may glean from him.

Yours sincerely,



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