tion for further study of the problem of thrombo-embolic phenomena, I find vastly more cause for concern than is represented by the use of this method in arriving at the present position. I emphasize that the method does not approach the reliability of a well conducted prospective study and is not a suitable basis on which to draw firm conclusions in a case such as the present one.

p. 49—The choice of two controls for each case is described here—the purpose being to have a second chance if the first control were unavailable for interview. It is a truism in sample survey practice that such substitution can often lead to highly disturbing selection biases. The rate of unavailability was non-negligible (it appears to be in the neighborhood of 20 per cent), but this potential contribution to bias is not discussed in the report.

p. 53—A dozen lines are devoted to the affirmation of a difference in risk between sequentials and combinations. Prof. John Fertig has calculated an over-all chi-square for the 12 different products and gets a chi-square of about 15 (11 d.f.) which does not approach significance. The decision to group the sequentials together (15:0) but to leave Enovid E (14:1) with the other group requires explanation, and none is given. Without additional input to justify it, there is no evident ground from the data itself to justify this separation into the two groups presented. A description of the results, based on the data, would certainly take note of the situation of Enovid E. (Significance levels, based on selected comparisons do not have the unequivocal interpretation of those related to a single predetermined question.)

p. 60—It is suggested that the possible bias due to oral contraceptive users being more likely to be hospitalized for equally severe thrombo-embolic phenomena than non oral contraceptive users is satisfactorily tested for by comparing the situation for severe and mild cases. This is certainly one comparison worth making, but it is by no means justifies a firm judgment on this point.

p. 61—The issue of religion is dealt with in a short paragraph which I believe misses the major point. The point discussed is the possible effect of the correlation between pairs in religious background. No special point need be made about religion in this regard. If the matching is at all effective, many variables which were not ascertained will be similarly associated. The important point—for which this one might be mistaken—is that discrepancy in religion between cases and controls—for which there is some evidence—could introduce an apparent risk where there might be none. This very serious problem is not discussed.

p. 62—It is claimed here that "most of the women in the population who use oral contraceptives have none of the predisposing conditions." Evidence on this point could have been obtained by additional interviews, but no evidence is given. Rather mild predisposing factors led to exclusion, and the point is an important one.

p. 72—The data in table 7 are used to justify the conclusion that discontinuance of oral contraceptives leads to prompt elimination of risk (p 51). I have no judgment of the relative likelihood of alternatives, but it should be pointed out that table 7 is equally open to the interpretation that the physicians predisposition to hospitalize is higher for current oral contraceptive users than for others, but that this predisposition does not exist for those no longer using oral contraceptives.

Appendix 2B

The conclusion stated is that the vital statistics "are consistent" with an increase in thrombo-embolic phenomena among women due to use of oral contraceptives. They are at least equally consistent with the opposite.

Summary

In sum, I feel most strongly that the problem of risks associated with use of oral contraceptives are too important to be assessed solely by means of retrospective studies. As I suggested in the meeting on November 6 with Dr. Ley, I believe that prospective studies are feasible and should be initiated without delay. I should welcome the opportunity to contribute to the planning of such studies.

Sincerely yours,

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Professor of Statistics.