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MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL

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TO William H. Foege, M.D.
Director, Center for Disease Control (CDC)

DATE: November 9, 1979

Thru: Philip S. Brachman, M.D.
Director, Bureau of Epidemiology (B.E.)

FROM Michael J. Rosenberg, M.D., M.P.H.
Family Planning Evaluation Division, BE

SUBJECT: Foreign Trip Report (AID/RSSA): Rio de Janeiro, Brazil, September 28-30, 1979; Campinas, Brazil, October 1-12, 1979

SUMMARY

	Page
I. PLACES, DATES AND PURPOSE OF TRAVEL	2
II. PRINCIPAL CONTACTS	2
III. ACCOMPLISHMENTS	3
A. Background on breast tumor study and purpose of visit	3
1. Sample size considerations	3
2. Editing and coding	5
3. Preparation of data tape	6
4. Analysis	7
5. Project timeline	7
B. Seminar on epidemiologic methods presented at Department of Statistics and Applied Mathematics, State University of Campinas	7
C. Training of project personnel	8
D. Meetings with BEMFAM and CDC	8

SUMMARY

Between September 28 and October 12, I visited Brazil to assist with a case-control study to evaluate the number of ovulatory menstrual cycles during a woman's reproductive lifetime as a risk factor for malignant and benign breast disease. As of September 28, 587 interviews have been completed, of which 304 (52%) are control subjects, 167 (28%) have breast malignancies, and 116 (20%) have benign breast lesions. I determined that this number of cases and controls is sufficient to address the question of risk due to number of ovulatory cycles and use of anovulatory agents as well as other major risk factors for breast disease. Since sufficient

funds exist to continue interviewing, however, we decided to extend the data collection through the coding phase in order to permit greater flexibility in analysis. Medical editing was completed for all questionnaires, and a coding manual was written and edited. Coders were trained, and coding was started. Computer editing programs were written and partially debugged. Priorities for the project were established along with a detailed timetable which calls for completion of the analysis by May 1980.

While in Brazil, I also held discussions with BEMFAM, Brazil's family planning agency, regarding CDC participation in contraceptive prevalence surveys and presented a seminar on epidemiologic design and analysis of the University of Campinas, where the Breast Cancer Project is being done, to the Department of Statistics and Applied Mathematics.

I. PLACES, DATES AND PURPOSE OF TRAVEL

Rio de Janeiro, Brazil, September 28-30, 1979, and Campinas, Brazil, October 1-12, 1979, at the request of AID/POP/DS/FPSD and AID/POP/DS/LA to confer with officials of BEMFAM and the CDC in Rio regarding CDC assistance to present and future population studies and to provide background for the breast disease project in Campinas; in Campinas to assist with the study to evaluate the effect of number of ovulatory menstrual cycles as a risk factor for breast disease which is underway at the Faculty of Medicine, State University of Campinas.

II. PRINCIPAL CONTACTS

A. State University of Campinas, Faculty of Medicine

1. Ellen Hardy - Principal Investigator, Breast Cancer Project
2. Ana Vichi - Associate Investigator, Breast Cancer Project
3. Ronaldo Araki - Computer Specialist, Breast Cancer Project
4. Anibal Faundes, Population Council Representative to Brazil and Director of Maternity, Department of Obstetrics and Gynecology, Faculty of Medicine
5. José Pinotti - Dean, Faculty of Medicine, Chairman, Department of Obstetrics and Gynecology
6. Henrique Brenelli - Professor, Department of Obstetrics and Gynecology
7. Emilio Marussi - Professor, Department of Obstetrics and Gynecology

B. State University of Campinas, Department of Statistics and Applied Mathematics

1. Hermanna Rohrer - Professor and Chairman

C. Sociedade Bem-Estar do Familiar no Brasil--BEMFAM (IPPF Affiliate)

1. José Maria Arruda - Director
2. Eliane Reis - Evaluation Section

III. ACCOMPLISHMENTS

A. Background on breast tumor study and purpose of visit

This project considers the number of ovulatory cycles during a woman's reproductive lifetime as an indicator of hormonal influences which may affect development of either a benign or a malignant breast lesion. The study takes into consideration the effect of oral and other contraceptive agents as well as additional factors which affect ovulation such as pregnancy, lactation, and menstrual disorders. This follows previous studies which indicate that oral contraceptive use decreases the incidence of benign breast lesions but has no effect on the incidence of malignancies.[1] The acceptability of anovulatory agents as a means of contraception will be based on the safety which studies such as this are able to demonstrate. My trip was to review progress to date and to help decide when to terminate the data collection phase as well as to formulate a plan for analysis of the data.

The project is being conducted by Ellen Hardy, a sociologist working at the Faculty of Medicine of the State University of Campinas, Brazil. Funding comes from the Population Council and the Rockefeller Foundation with assistance provided for this visit through the Agency for International Development and the Center for Disease Control.

1. Sample Size Considerations

As of October 1, 1979, 587 interviews have been completed (Table 1), of which 52% are control subjects, 28% are subjects with breast malignancies, and 20% are subjects with benign breast lesions. Since sufficient funding remains to continue interviews, the questions of how many additional subjects, if any, should be collected to assure adequate statistical power and how additional data collection should be allocated between cases and controls need to be addressed.

Since the single most important objective of this study is the establishment of dose-response relationships between

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[1] Ory HW: Oral Contraceptive Use and Breast Diseases in Garattini S and Berendes HW (eds): Pharmacology of Steroid Contraceptive Drugs. New York, Raven Press, 1977, pp 179-183

number of ovulatory cycles and incidence of benign and malignant breast lesions, considerations of numbers required for statistical significance is not a simple issue. It is possible, for example, that 2 adjacent strata of number of cycles can fail to differ significantly yet can contribute to a significant trend, or that 2 significantly differing strata can be part of a non-significant trend. The issue is best considered as a series of dichotomous exposure variables such as proportion with greater than a certain number of cycles, or proportion with positive family history of breast disease, or proportion of ever-users of anovulatory agents. The question of required numbers at this time and as the study progresses can be considered from 3 perspectives: (1) should one seek cases, controls, or both in equal proportion; (2) how many cases and controls are required to provide statistical validity for consideration of a specific exposure factor; and (3) with given number of cases and controls in which allocation ratios (proportion of cases to controls) remain roughly the same as those at present, which exposure factors can be adequately evaluated?

The work of Rosenberg[1] dictates that in the present study, statistical power can most efficiently be increased by preferential addition of controls, since the scarcity of cases makes their ascertainment cost appreciably greater than that of controls. A small number of incident cases can be expected to show up locally over the next few months, however, and if these cases are able to be interviewed without the necessity of laborious location and travel, these will also be added.

When considering numbers of cases and controls necessary to evaluate the influence of a specific exposure factor, the proportion of exposed controls must be known along with the minimum acceptable statistical power, (defined as $1-\beta$, where the β represents the β or Type II error and is the probability of mistakenly concluding there is no difference between the two groups being compared when there actually is a difference), the maximum acceptable probability of an α or Type I error (the chance of concluding there is a difference when none actually exists), and desired level of risk detection as compared to the control group (relative risk). Table 2 presents several exposure factors present in a sample of 50 (16%) of control subjects, and this project's protocol specifies a

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[1]Rosenberg MJ: How many cases, how many controls? Presented at Epidemic Intelligence Service Conference, Atlanta, Georgia, April 1979

power of at least 0.8 (corresponding to a maximum acceptable beta error of 0.2) to detect a relative risk of 2.0. Figure 1 demonstrates the effect of study size on power for a series of different exposure factors. This graph assumes an allocation ratio (controls/cases) of 2 (actual present allocation ratios for malignant and benign disease are 1.8 and 2.6, respectively), and so provides an estimate of the required numbers. Exact numbers can be calculated by the method of Miettinen[1] with programs for hand calculators[2] For example, Table 2 shows that use of anovulatory agents for more than 12 months is present in 20% of controls. The curve corresponding to 20% exposure intersects a power of 0.8 where the total sample size requirement is read as just under 300 subjects, or about 100 cases and 200 controls.

A similar but more precise answer to which exposure factors can be evaluated with a given number of subjects is presented in Figure 2. This has 2 lines, representing current allocation ratios for the malignant and benign groups. Assuming these ratios do not change greatly and previously specified relative risk and power parameters, the graph demonstrates that adequate numbers of subjects presently exist for evaluation of an exposure factor with prevalence of greater than 0.14 in the benign group (304 controls + 116 cases = 420 subjects) and greater than 0.10 in the malignant group (304 controls + 167 cases = 471 subjects).

Although adequate numbers presently exist to evaluate major risk factors, greater numbers will allow increased flexibility in analysis, and ability to control for confounding a more precise estimate, and will permit addressing a number of less common factors. Figure 1 indicates that with slightly over 400 cases and controls in each group, we are at a point on the power curves where there is still an appreciable marginal increase in power for each case or control added. The decision was thus made to continue collection of controls as they become available. However, a small number of incident cases can be expected over the next few weeks, and resources will be shifted to include these since their cost will approximate that of controls. Interviewing is expected to continue until approximately 1 week before coding of present questionnaires are completed so that the recently completed questionnaires can be edited and coded without delaying data editing and analysis.

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[1]Miettinen OS: Individual matching with multiple controls in the case of all or none responses. Biometrics 1969; 25:339-354

[2]Rothman KJ, Boice JD: Epidemiologic analysis with a programmable calculator. U.S. Department of HHealth, Education, and Welfare, NIH Publication No. 76-1649, 1979

2. Editing and Coding

All completed questionnaires have been edited for consistency and to eliminate ambiguous responses. I reviewed the narratives provided for each woman who identified a relative as having had a breast lesion. Of approximately 70 such subjects, medical review resulted in the changing of 2 responses: one woman answered that she did not know whether the relative's lesion was malignant or benign and gave a history clearly consistent with a benign lesion, and another thought that a family member had a malignant lesion but gave a history which indicated a benign lesion.

Review of the questionnaire during preparation of a coding manual made it clear that more than straightforward transcription of responses would be required. Because the questionnaire was formated to facilitate interviewing, there is redundancy in certain portions, some questions used to help guide the interview are not used in analysis, it was possible to condense a group of questions to a single coding option in several cases, and it was necessary to rearrange the logical flow in other cases. For example, question 3.1 (Appendix A) asks whether a woman is pregnant, but that information is also available elsewhere in the questionnaire, and question 3.3 helps guide the interviewer to a complete pregnancy history and does not of itself provide useful information. The history of pregnancies was recorded during the interview by first listing the dates of each pregnancy, then selecting one detail (such as outcome, duration, and whether the child was breastfed) and chronologically reviewing each pregnancy as regards that detail before selecting the next detail and again reviewing each pregnancy. The great variability in complexity of pregnancy histories (1 woman had 18 pregnancies) necessitated coding by considering all the details of each pregnancy before recording the responses for the next pregnancy. These complexities mandate a clearly written and unambiguous coding manual, meticulous training and supervision of coders, and frequent quality control checks.

The coding manual with an English translation is on file in the Epidemiologic Studies Branch of the Family Planning Evaluation Division, Center for Disease Control, Atlanta, Georgia, for examination. Eleven coders were selected by recommendation or past experience with the team conducting this study and underwent 3 days of training, culminating in the practice coding of several questionnaires, each of

which was individually checked by a supervisor. During the coding, a minimum of 15% of the questionnaires will be independently checked in their entirety in addition to frequent supervisory spot checks and computer editing. It is anticipated that coding and checking will be completed by mid-December 1979.

3. Preparation of Data Tape

Keypunching and verification will be performed at the computer facility of the State University of Campinas under the direction of the principal investigator and Ronaldo Araki, a computer specialist working on the project. He and I wrote computer edit programs for internal consistency and illegal characters which have been partially debugged. Ronaldo will be visiting the United States during October and November 1979 and will bring a set of approximately 20 punched and verified questionnaires. With these and additional dummy data cards, debugging will be completed and a set of analysis tables generated as a guide for preliminary analysis of the completed data set which will occur in Brazil. A clean data tape is expected by March 1979.

4. Analysis

Preliminary cross-tabulations will be run in Brazil and will be analyzed by Ellen Hardy. A duplicate set will be sent to me at the CDC. Ellen will complete the analysis under my supervision. This could take place either at the CDC or in Brazil, but the possible need for interaction with various members of the study team and access to original records dictate that the work could most easily be done in Brazil. This plan also has the advantage of permitting others on the project and at the Faculty of Medicine of the University of Campinas to gain familiarity with analysis.

Results will be presented as relative risks estimated by the methods of Gart[1] with test-based confidence intervals calculated according to Miettinen.[2] Confounding will be controlled by the method of Mantel and Haenszel.[3] Trend testing will be done with the Mantel extention test.[4]

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[1]Gart SS: Point and interval estimation of the common odds ratio in the combination of 2x2 tables with fixed margins. Biometrics 57:471-475, 1970

[2]Miettinen OS: Simple interval estimation or risk ratio. Am J Epidemiol 103:226-235, 1976

[3]Mantel N, Haenszel W: Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst 22:719-748, 1959

[4]Mantel N: Chi-square tests with one degree of freedom: Extention of the Mantel-Haenszel procedure. J Amer Stat Assoc 59:690-700, 1963

5. Project Timeline

Appendix B presents a detailed schedule for completing of the project. We anticipate finishing the analysis by May 1980.

B. Seminar on epidemiologic methods presented at the Department of Statistics and Applied Mathematics, State University of Campinas

An important objective of this trip is the encouragement of local epidemiological expertise. When problems arose with study design before my visit, they were referred to the Department of Statistics and Applied Mathematics at the State University of Campinas and resulted in faculty interest in learning more about epidemiology, particularly about methods of sample size selection and analysis. I presented a seminar entitled, "Epidemiologic Design and Analysis: An Overview," to members of the Statistics Faculty which generated a good deal of interest. An outline of the material covered is presented on the following pages. I expect this interest to be of appreciable potential benefit to the scientific community in Campinas and have made tentative plans to discuss more specific components of epidemiology, particularly sample size selection, on my return visit.

Epidemiologic Design and Analysis: An Overview

STUDY TYPES

COHORT

	Exposed	Non-Exposed	
Cases	a	b	M_1
Person-years	N_1	N_0	T

$$RR = \frac{\frac{a}{N}}{\frac{b}{N_0}}$$

CASE CONTROL -

	Case	Control	
Exposed	a	b	a+b
Non-exposed	c	d	c+d
	a+c	b+d	a+b+c+d

$$RR = \frac{ad}{bc}$$

PRINCIPLES OF STUDY DESIGN

Precision - (Random error)

beyond control but can and should be measured. Precision is a function of:

1. Size - increased study size generally means greater precision, but it does not guarantee it because random error is not simply a reflection of size.

2. Efficiency in using data available for each subject - for example:

Cases	Controls		Cases	Controls	
50	50	better than	90	10	better than

Cases	Controls
0	100

Validity - (systematic error or bias)

- Two types:

  1. Internal - pre-requisite for external validity
  2. External - ability to generalize to larger groups

  Bias:

  1. Selection - is one group more likely to be included?
  2. Information - is information gathered differently?
  3. Confounding - have other effects which may lead to outcome been taken into account?

Confounding -

1. Tested for by stratification in analysis, not by statistical tests. Statistical tests measure chance as a contributor to bias.

2. Degree of confounding depends on:
   (a) degree of risk indicator
   (b) degree to which it is present

3. Statistical tests cannot be used because they:
   (a) don't measure integrated effects of 2a & 2b
   (b) are basically inferential tests and do not measure internal validity
   (c) are tes's which are a function of size (i.e., large studies lead to small p-values and small studies lead to large p-values)

4. Can be controlled by:
   (a) Restriction - deciding who gets into the study. If a factor does not vary, it cannot confound.
   (b) Matching - in analysis, comparing a series of smaller groups in which the factor does not vary (either always present at the same level or always absent)
   (c) multivariate analysis - complex analysis not generally understood and leads to loss of feel for data.

HYPOTHESIS TESTING

1. Keep in mind that nothing can be proved

2. If a study establishes that a cause leads to an effect, it does not prove the hypothesis, but if the study does not establish a cause leading to an effect, it disproves the hypothesis.

3. Most studies reported as significant or not by p-values (0.05). This is not good because:

   (a) Value of 0.05 is arbitrary

   (b) p-values do not reflect strength of association, which is the most important result of a study

4. Instead, estimates of relative risk should be used with confidence intervals.

EVALUATION OF AN EPIDEMIOLOGIC STUDY

Three explanations for why an association is observed:

1. Bias - selection, information, confounding

2. Chance

3. Causality - look for

   (a) Strength of association - size of relative risk

   (b) Consistency - has it been repeated?

   (c) Specificity - i.e. only vinyl chloride workers get angiosarcomas (a specific workers getting a rare and specific tumor)

   (d) Timing - does the exposure come before the disease?

   (e) Dose response - is the greater risk with more exposure?

   (f) Plausibility - does the association make sense in light of what we know?

   (g) Coherence - the association should not seriously conflict with known facts

   (h) Natural experiment - when corrective action is taken, does the disease disappear?

C. Training of Project Personnel

This project provides partial fulfillment of Ellen Hardy's requirements for a master's degree in epidemiology through Goddard College in Vermont. During my visit, we used various portions of the project as a basis for more academic discussions, particularly aspects of informational and selection bias and their effects on outcome. I also reviewed her plan for her degree work and made several suggestions which were discussed with Howard Ory, M.D. of the CDC, the supervisor for her degree work.

Ronaldo Araki has an undergraduate degree in computer sciences and is handling the computational aspects of the project. He will be in the United States during October and November 1979 visiting the International Fertility Research Program in Research Triangle Park, North Carolina, to gain additional training in the use of computer statistical packages. I will use the opportunity to work with him in completing the work previously outlined in this report, and his presence also provides the opportunity for him to gain experience with epidemiologic analysis. I will meet with him at IFRP to try to arrange for additional work, preferably at the CDC, as his schedule permits.

D. Meetings with BEMFAM and CDC

My work in Campinas was preceded by 3 days of discussions in Rio de Janeiro with Leo Morris, Ph.D., Chief, Program Evaluation Branch, Family Planning Evaluation Division, CDC, and with José Maria Arruda and Eliane Reis of Sociedade Bem Estar da Familiar do Brasil (BEMFAM). We discussed general background information on gathering information in Brazil and its reliability, in addition to contraceptive surveys in which CDC participates.

Michael J. Rosenberg, M.D., M.P.H.

TABLE 1

Number of Interviews Completed as of October 1, 1979
Study of Ovulatory Cycles as a Risk Factor
University of Campinas

	Group				
Age	Malignant	Benign	Control	Total	%
≤ 29	5	5	12	22	3.7
30-34	11	10	23	44	7.5
35-39	14	13	28	55	9.4
40-44	25	23	44	92	15.7
45-49	35	29	59	123	21.0
50-54	16	12	32	60	10.2
55-59	15	13	34	62	10.6
60	46	11	72	129	22.0
TOTAL	167	116	304	587	
%	28.4	19.8	51.8		100.0

TABLE 2

Proportion of controls with exposure factors present (n=504)
Study of Ovulatory Cycles as a Risk Factor
University of Campinas

Use of anovulatory agents:	
- Never	.66
- 1 - 12 months	.14
- >12 months	.20
Family history of malignant breast disease:	
- Present	.16
- Absent	.84
Mother's age at first birth:	
- < 30 years old	.89
- ≥ 30 years old	.11
Number of children breast fed:	
- None	.12
- 1 - 2	.30
- 3 - 4	.30
- 5 +	.28
Number of nine-month pregnancies:	
- None	.10
- 1 - 2	.28
- 3 - 4	.24
- 5 +	.38

n=45

FIGURE 1

Effect of Study Size on Power for
Differing Exposure Proportions
Campinas, 1979

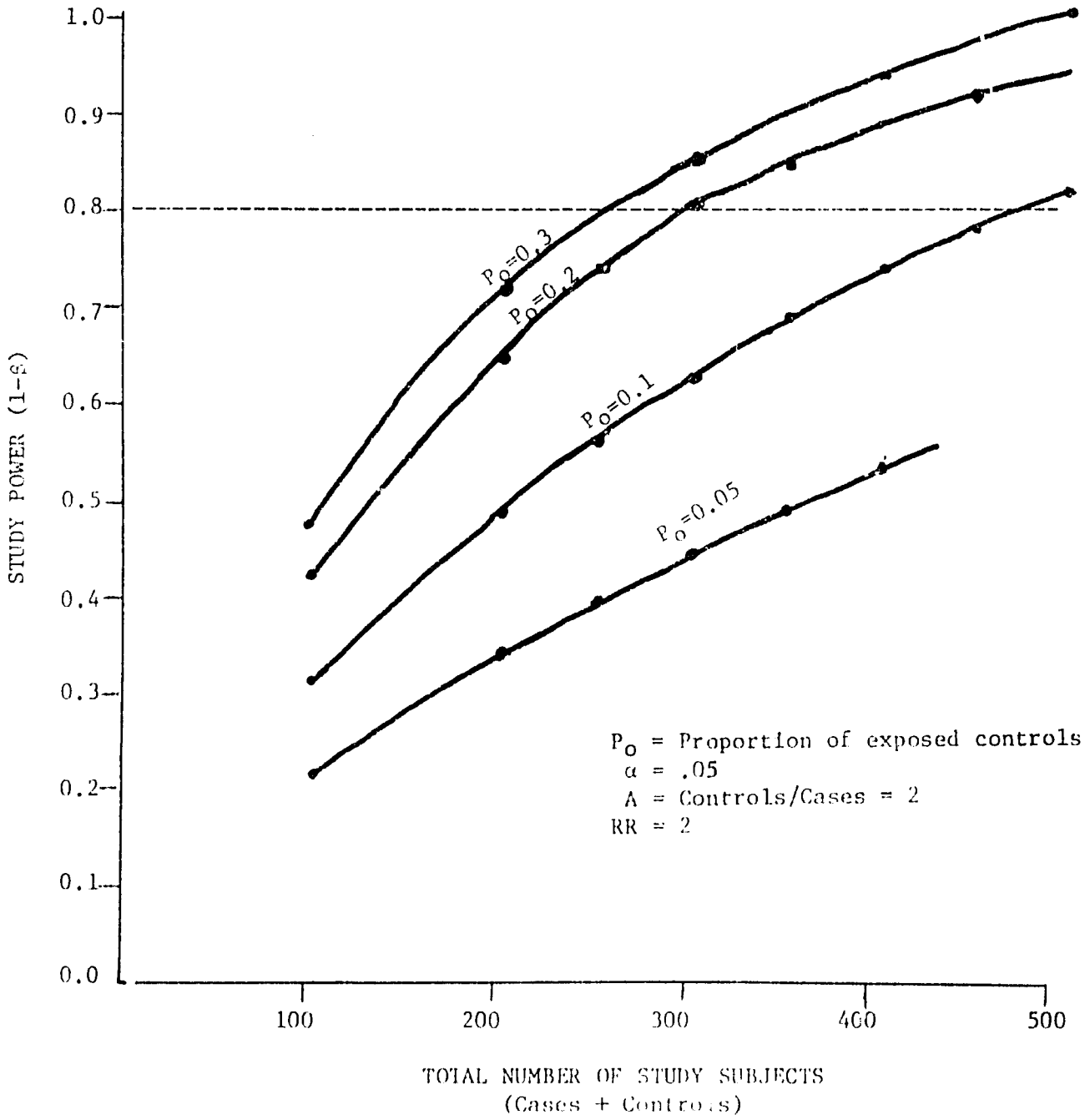
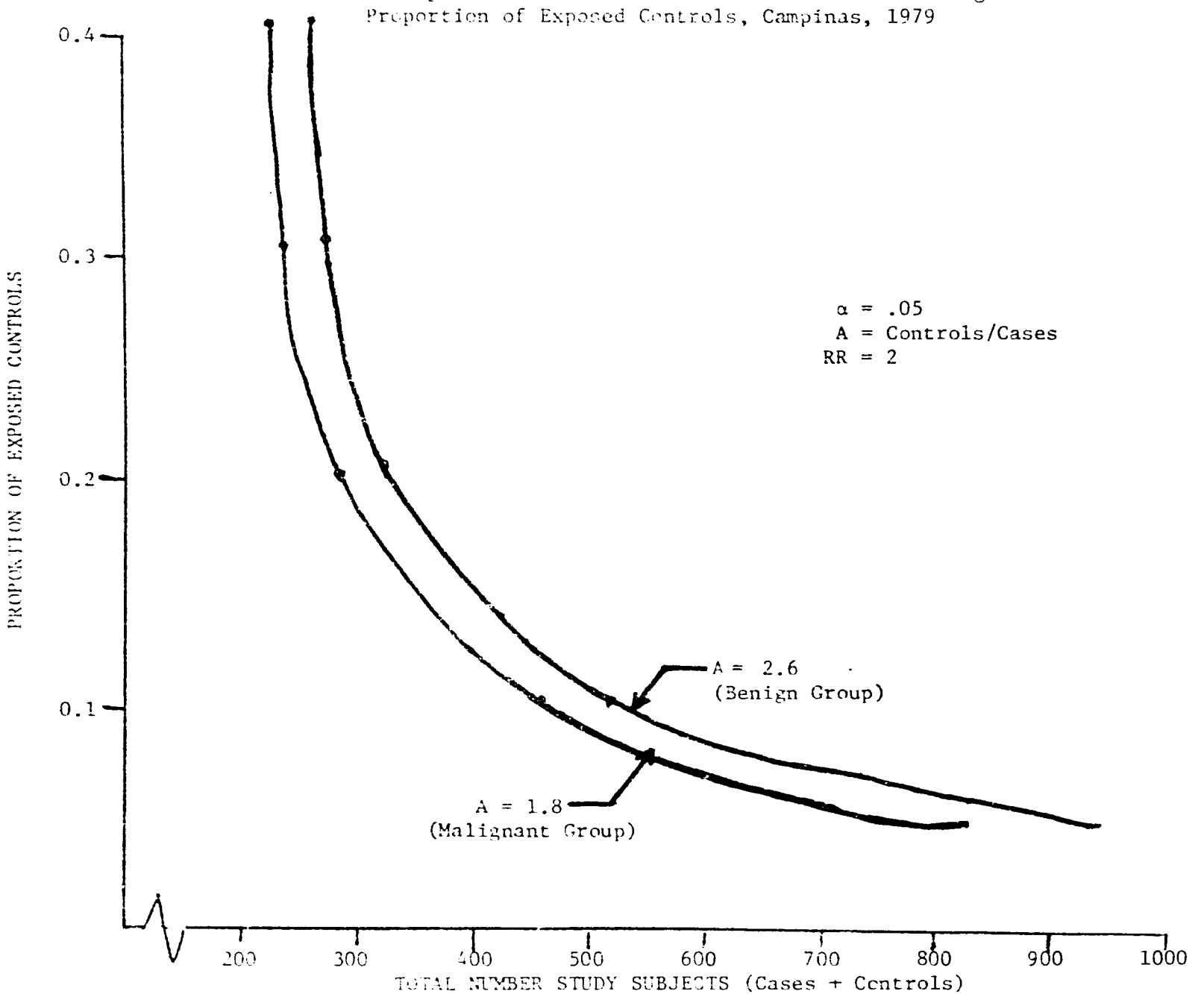


FIGURE 2

Number of Subjects Needed to Attain Power of 0.8 According to Proportion of Exposed Controls, Campinas, 1979



APPENDIX A

Nº [ ][ ][ ][ ]
1 4

NAME: _____

STREET: _____ Nº _____ APT Nº _____

SUBURB: _____ CITY _____ FONE: _____

INTERVIEWER'S NAME: _____

Nº ANNEXES: 1 _____ P.H. _____

VISIT	DATE	RESULT	RETURN
1			
2			
3			

COMMENTS:

_____

_____

_____

COMMENTS ON THE INTERVIEW:

DONE AT: ☐ HOSPITAL ☐ CLINIC ☐ HOME ☐ OTHER

_____

_____

_____

_____

_____

Nº [ ][ ][ ][ ]
1 4

SECTION 1. INTERVIEWEE'S CHARACTERISTICS

RESIDENCE: Campinas [1] Other City [2] Rural [3]

DONE AT: Hospital [1] Clinic [2] Home [3] Other [4]

1.1 What is your date of birth? (USE DOCUMENT)

_____ DAY _____ MONTH _____ YEAR D.K. [ ]

1.2 How old were you on your last birthday? _____ YEARS

I.1 - INTERVIEWER: CORRECT IN CASE OF INCONSISTENCY

1.3 Did you go to school?

NO [0] YES [1]

GO TO 1.5

1.4 What was the last grade you completed? _____ GRADE

1.5 Are you currently: single, married, in a common law union, separated or a widow?

[1] SINGLE → GO TO 1.6

[2] MARRIED
[3] COMMON LAW
[4] SEPARATED
[5] WIDOW
} GO TO 1.7

1.6 Have you ever been married or had a common law union?

NO [0] MARRIED [1] COMMON LAW [2]

GO TO 1.9

1.7 What was the last grade your husband completed in school?

_____ GRADE

1.8 What work does (did) your husband do? TEXT: _____

_____

I.2 - INTERVIEWER: IF HUSBAND IS A STUDENT, SPECIFY THIS FACT AND RECORD NAME OF COURSE

1.9 Do you have any health insurance such as: INPS, IAMSPE, UNIMED, FUNRURAL or any other?

I.3 - INTERVIEWER: MARK AS MANY CODES AS NECESSARY

[0] NONE [3] UNIMED

[1] INPS [4] FUNRURAL

[2] IAMSPE [5] OTHER: SPECIFY _____

1.10 Have you ever worked?

NO [0] YES [1]

GO TO 1.13

1.11 Are you currently working?

NO [0] YES [1]

1.12 What work do (did) you do?

TEXT: _____

1.13 Has anybody in your family had breast cancer?

NO [0] YES [1] D.K. [9]

GO TO 1.16 GO TO 1.16

1.14 How many persons have had breast cancer? _____ Number

1.15 Whom in your family had breast cancer?

TEXT: _____

F.I - INTERVIEWER: ONLY BLOOD RELATIONS ARE OF INTEREST, PROBE AND CHECK ALL APPROPRIATE BOXES

[1] MOTHER ___ [4] AUNT

___ [2] SISTER ___ [5] COUSIN

___ [3] DAUGHTER ___ [6] GRANDMOTHER

OTHER [8] IF SHE DID NOT ALSO MENTION ANY CODE FROM 1 to 6 GO TO 2.1

I.4 - INTERVIEWER: FOR EACH RELATIVE FROM CODE 1 THROUGH 6 APPLY QUESTIONS IN ANNEX 1.

GO TO I.10 IN ANNEX 1

1.16 Did anyone in your family have a breast or a breast cyst removed?

NO [0] YES [1] D.K. [9]

GO TO 2.1 GO TO 2.1

1.17 How many people had a breast or breast cyst removed?

_____ NUMBER

1.18 Whom in your family had a breast or breast cyst removed?

TEXT: _____

F.2 - INTERVIEWER: ONLY BLOOD RELATIONS ARE OF INTEREST. PROBE AND CHECK ALL APPROPRIATE BOXES.

[1] MOTHER ___ [4] AUNT OTHER [8]

___ [2] SISTER ___ [5] COUSIN

___ [3] DAUGHTER ___ [6] GRANDMOTHER

IF SHE DID NOT ALSO MENTION ANY CODE FROM 1 TO 6 GO TO 2.1

I.5 - INTERVIEWER: FOR EACH RELATIVE FROM CODE 1 THROUGH 6 APPLY QUESTIONS IN ANNEX 1

GO TO I.12 IN ANNEX 1

SECTION 2. MENSTRUAL HISTORY

2.1 How old were you when you first menstruated?

_____ AGE D.K. [ ] → GO TO 2.4

2.2 Had you already completed _____ years of age when you first menstruated?

NO [0] YES [1] D.K. [9]

2.3 Do you remember in what month you menstruated for the first time?

_____ MONTHS D.K. [ ]

2.4 How old were you when you first had sexual relations?

_____ AGE NEVER HAD S.R. [ ]

2.5 Do you menstruate?

NO [0] YES [1]

2.6 Why don't you menstruate?

TEXT: _____

_____

_____

[ ] PREGNANT/BREAST FEEDING
GO TO 2.18

[ ] OTHER REASON
GO TO 2.12

2.7 Are your periods the same as they have always been?

NO [0] YES [1]

GO TO 2.10

2.8 How often do you menstruate?

TEXT: _____

F.3 - INTERVIEWER: CHECK APPROPRIATE BOX

EVERY 20 DAYS OR LESS [0]

EVERY 40 DAYS OR MORE

EVERY 21 TO 39 DAYS [1]

GO TO 2.10

2.9 Since what month and year (since when) do you menstruate every _____ days?

TEXT: _____

2.10 How many days does your period last?

TEXT: _____

F.4 - INTERVIEWER: CHECK APPROPRIATE BOX

LESS THAN 1 DAY
7 OR MORE DAYS [0]

1 TO 6 DAYS [1]

GO TO F.5

2.11 Since what month and year (since when) do your periods last _____ days?

TEXT: _____

GO TO F.5

2.12 In what month and year did you menstuate the last time?

_____ MONTH _____ YEAR D.K. [ ]

2.13 How old where you when you menstruated the last time?

_____ AGE D.K. [ ]

GO TO I.6

2.14 Had you already completed _____ years of age when you menstruated the last time?

NO [0] YES [1] D.K. [ ]

I.6 - INTERVIEWER: IF SHE ANSWERED 'D.K.' TO 2.12, 2.13 OR 2.14, ASK 2.15. IF NOT, GO TO 2.16

2.15 How long ago, more or less, did you menstruate the last time?

TEXT: _____

2.16 Before this last menstruation, were you menstruating every month?

NO [0] YES [1]

GO TO F.5

2.17 Since what month and year (since when) did you stop menstruating every month?

TEXT: _____

2.18 Every how often do you menstruate?

TEXT: _____

2.19 How many days do your menstruations last?

TEXT: _____

SECTION 3. PREGNANCY HISTORY

F.5 - INTERVIEWER: CHECK APPROPRIATE BOX

NO S.R. [0]	STILL MENSTRUATES [1]	NO LONGER MENSTRUATES [2]	PREGNANT [3]
GO TO 5.1		GO TO 3.2	GO TO 3.4

3.1 Are you pregnant now?

D.K. NO [0] YES [1]

GO TO 3.4

3.2 Were you ever pregnant? (Have you every been pregnant?)

NO [0] YES [1]

GO TO 3.6

3.3 Did you ever have a pregnancy that lasted only a few weeks or months?

NO [0] YES [1]

GO TO 5.2 GO TO 3.7

3.4 How many months are you pregnant? _____ MONTHS

3.5 Is this your first pregnancy?

NO [0] YES [1]

GO TO 5.1

3.6 Did you every give birth to a live born child?

NO [0] YES [1]

GO TO 3.9

3.7 Did you ever have a stillborn child?

NO [0] YES [1]

GO TO 3.17

3.8 Did you every have an abortion?

NO [0] YES [1]

CORRECT ERROR GO TO 3.19

HISTÓRIAS DE GRAVIDEZ

Nº ☐☐☐☐

I ORDER	A LIVE CHILDREN			B CHILDREN WHO DIED		C STILL BORN	D ABORTIONS	E DATES		F INTERVALS	G	H
I-J Number the events according to date of occurrence	3.10 Which are the names of your live children. Start by the oldest	3.11 How many months pregnant were you when (name) was born?	3.12 How old is (name)? In completed years	3.13 Did you have any children who were born alive and died? Yes ☐ No ☐ Go to 3.16 3.14 Which are the names of your children born alive who died? Start by the oldest	3.15 How many months pregnant were you when (name) was born?	3.16 Did you ever have a still born? Yes ☐ No ☐ 3.17 How many months pregnant were you?	3.18 Did you ever have an abortion? Yes ☐ No ☐ 3.19 How many months pregnant were you?	For each pregnancy ask: 3.20 What date did you have (name, c.b. abortion)		For each interval including before 1st pregnancy and after last, ask: 3.21 Why didn't you become pregnant between ____ and ____?	For each time she declares use of pills and/or injections ask 3.22 What date (month) did you start using ____?	For each time she declares use of pills and/or injections ask: 3.23 What date (month) did you stop using ____?
								Month	Year		Started	Finished

3.9 How many of your children are alive today? _____ No

F.6 - INTERVIEWER: CHECK APPROPRIATE BOX

NONE [0] — GO TO 3.14

1 OR MORE [1] — GO TO 3.10

SECTION 4. BREASTFEEDING AND MENSTRUATION

F.7 - INTERVIEWER: CHECK APPROPRIATE BOX ACCORDING TO PREGNANCY HISTORY

NO LIVE BIRTH [0] HAD LIVE BIRTH [1]

GO TO F.10

4.1 Did you breast feed all or only some of your children?

NONE [0] SOME [1] ALL [2]

GO TO F.8 GO TO I.7

4.2 What are the names of the children you breast fed?

TEXT: _____

I.7 - INTERVIEWER: ASK QUESTIONS 4.3 TO 4.9 THAT APPLY, FOR EACH BREAST FED CHILD?

4.3 How old was _____ (NAME) when you stopped breast feeding him/her?

_____ YEAR(S) _____ MONTH(S) _____ DAY(S)

STILL BREAST FED [ ]

GO TO 4.6

4.4 How old was he/she when you started bottle feeding? (ANY KIND OF MILK)

_____ YEAR(S) _____ MONTH(S) _____ DAY(S)

NEVER BOTTLE FED [ ]

GO TO 4.6

4.5 How long before weaning did you start giving him/her milk in a bottle?

TEXT: _____

4.6 Did (have) you menstruate(d) while breast feeding?
_____ (NAME)

NO [0] YES [1] D.K. [9]

GO TO 4.9

4.7 Did you menstruate after _____ (NAME) was born?

NO [0] YES [1]

GO TO 4.9

4.8 Why didn't you menstruate? TEXT: _____

_____

_____ GO TO NEXT CHILD

4.9 How old was _____ (NAME OF CHILD) when you menstruated again?

_____ YEAR(S) _____ MONTH(S) D.K. [9]

4.3 How old was _____ (NAME) when you stopped breast feeding him/her?

_____ YEAR(S) _____ MONTH(S) _____ DAY(S)

STILL BREAST FED [ ]

GO TO 4.6

4.4 How old was he/she when you started bottle feeding? (ANY KIND OF MILK)

_____ YEAR(S) _____ MONTH(S) _____ DAY(S)

NEVER BOTTLE FED [ ]

GO TO 4.6

4.5 How long before weaning did you start giving him/her milk in a bottle?

TEXT: _____

4.6 Did (Have) you menstruate(d) while breast feeding _____ (NAME)

NO [0] YES [1] D.K. [9]

GO TO 4.9

4.7 Did you menstruate after _____ (NAME) was born?

NO [0] YES [1]

GO TO 4.9

4.8 Why didn't you menstruate? TEXT: _____

_____

_____ GO TO NEXT CHILD

4.9 How old was _____ (NAME OF CHILD) when you menstruated again?

_____ YEAR(S) _____ MONTH(S) D.K. [9]

F.8 - INTERVIEWER: CHECK APPROPRIATE BOX ACCORDING TO 4.1

NONE [0] SOME [1] ALL [2]

GO TO F.10

I.7 - INTERVIEWER: REGISTER THE NAMES OF ALL CHILDREN NOT BREAST FED AND ASK HOW MANY MONTHS (COMPLETED MONTHS) OLD EACH ONE WAS WHEN MOTHER MENSTRUATED AFTER THAT BIRTH:

NAME	COMPLETED MONTHS	NAME	COMPLETED MONTHS
1.		6.	
2.		7.	
3.		8.	
4.		9.	
5.		10.	

I.8 - INTERVIEWER: AFTER OBTAINING THE INFORMATION GO TO F.10

SECTION 5. USE OF ANOVULATORIES

5.1 Did you ever use pills or injections (not to become pregnant) (to regulate your menstruation)?

NO [0] YES [1]

END INTERVIEW GO TO 5.3

5.2 Why didn't you ever become pregnant?

TEXT: _____

F.9 - INTERVIEWER: CHECK APPROPRIATE BOX

USED ANOVULATORIES [1] OTHER ANSWER [0]

END INTERVIEW

5.3 What date (when) did you start using _____

TEXT: _____

5.4 What date (when) did you stop using _____

TEXT: _____

END INTERVIEW

SECTION 6. POST ABORTION OR STILLBORN MENSTRUATION

F.10 - INTERVIEWER: CHECK APPROPRIATE BOX ACCORDING TO PREGNANCY HISTORY

NO ABORTIONS NOR STILLBORNS [0] — END INTERVIEW

HAD ABORTION AND/OR STILLBORN [1]

I.9 - INTERVIEWER: FOR EACH ABORTION AND STILLBORN ASK QUESTIONS 6.1 TO 6.3 THAT APPLY. USE ONE BOX FOR EACH ABORTION OR STILLBORN

6.1 After the stillborn (abortion) you had in _____ (DATE) did you menstruate? (BEFORE BECOMING PREGNANT AGAIN)

NO [0] — YES [1] GO TO 6.3

6.2 Why didn't you menstruate again? TEXT: _____

GO TO NEXT STILLBORN OR ABORTION

6.3 How long after you had the stillborn (abortion) did you menstruate again? TEXT: _____

GO TO NEXT STILLBORN OR ABORTION

6.1 After the stillborn(abortion) you had in _____ (DATE) did you menstruate? (BEFORE BECOMING PREGNANT AGAIN)

NO [0] — YES [1] GO TO 6.3

6.2 Why didn't you menstruate again? TEXT: _____

GO TO NEXT STILLBORN OR ABORTION

6.3 How long after you had the stillborn (abortion) did you menstruate again? TEXT: _____

GO TO NEXT STILLBORN OR ABORTION

6.1 After the stillborn (abortion) you had in _____ (DATE) did you menstruate? (BEFORE BECOMING PREGNANT AGAIN)

NO [0] — YES [1] GO TO 6.3

6.2	Why didn't you menstruate again? TEXT: _____
	GO TO NEXT STILLBORN OR ABORTION
6.3	How long after you had the stillborn (abortion) did you menstruate again? TEXT: _____
	GO TO NEXT STILLBORN OR ABORTION

AFTER USING ONE BOX FOR EACH STILLBORN OR ABORTION END INTERVIEW

7. ANNEX 1

I.10 - INTERVIEWER: REGISTER 7.1 THROUGH I.11 FOR EACH RELATIVE CHECKED IN F.1

7.1 What date was your _____ 's cancer diagnosed?

_____ DATE D.K. [ ]

7.2 Did your _____ have a breast operation?

NO [0] YES [1] D.K. [9]

GO TO 7.8 GO TO 7.8

7.3 Was one or both breasts operated on?

ONE [0] BOTH [1] D.K. [9]

GO TO 7.5 GO TO 7.5

7.4 Was the whole breast removed or only a nodule?

[1] ONLY A NODULE

[2] WHOLE BREAST

[3] OTHER OPERATION Which? _____

[4] D.K.

GO TO 7.6

7.5 Were both breasts removed or only a nodule (one breast removed and a nodule from the other?)

[1] BOTH BREASTS

[2] NODULE FROM EACH BREAST

[3] ONE BREAST AND NODULE FROM OTHER

[4] OTHER OPERATION Which? _____

[9] D.K.

7.6 What happened to your _____ after the operation?

DIED [1] IMPROVED [2] CURED [3]

GO TO I.11 GO TO I.11

7.7 What did your _____ die of?

TEXT: _____

GO TO I.11

7.8 What happened to your _____ regarding her illness?

DIED [1] IMPROVED [2] CURED [3]

GO TO I.11 GO TO I.11

7.9 What did your _____ die of?

TEXT: _____

I.11 - INTERVIEWER: DESCRIBE THE EVOLUTION OF THE ILLNESS (BONES BROKE, METASTASIS, BACK PAIN, LACK OF AIR, SORES)

_____

_____

_____

GO TO 2.1

I.12 - INTERVIEWER: REGISTER 7.10 THROUGH I.13 FOR EACH RELATIVE CHECKED IN F.2

7.10 Was your _____ operated on one or both breasts?

ONE [1] BOTH [2] D.K. [9]

GO TO 7.12 GO TO 7.13

7.11 Was the whole breast removed or only a nodule?

[1] ONLY A NODULE

[2] WHOLE BREAST

[3] OTHER OPERATION Which? _____

[9] D.K.

GO TO 7.13

7.12 Were both breasts removed or only a nodule (one breast removed and a nodule from the other)?

[1] BOTH BREASTS

[2] NODULE FROM EACH BREAST

[1] ONE BREAST AND NODULE FROM OTHER

[2] OTHER OPERATION Which? _____

[9] D.K.

7.13 What date was your _____ operated on?

_____ DATE

7.14 What happened to your _____ after the operation?

DIED [1] IMPROVED [2] CURED [3]

GO TO I.13 GO TO I.13

7.15 What did your _____ die of?

TEXT: _____

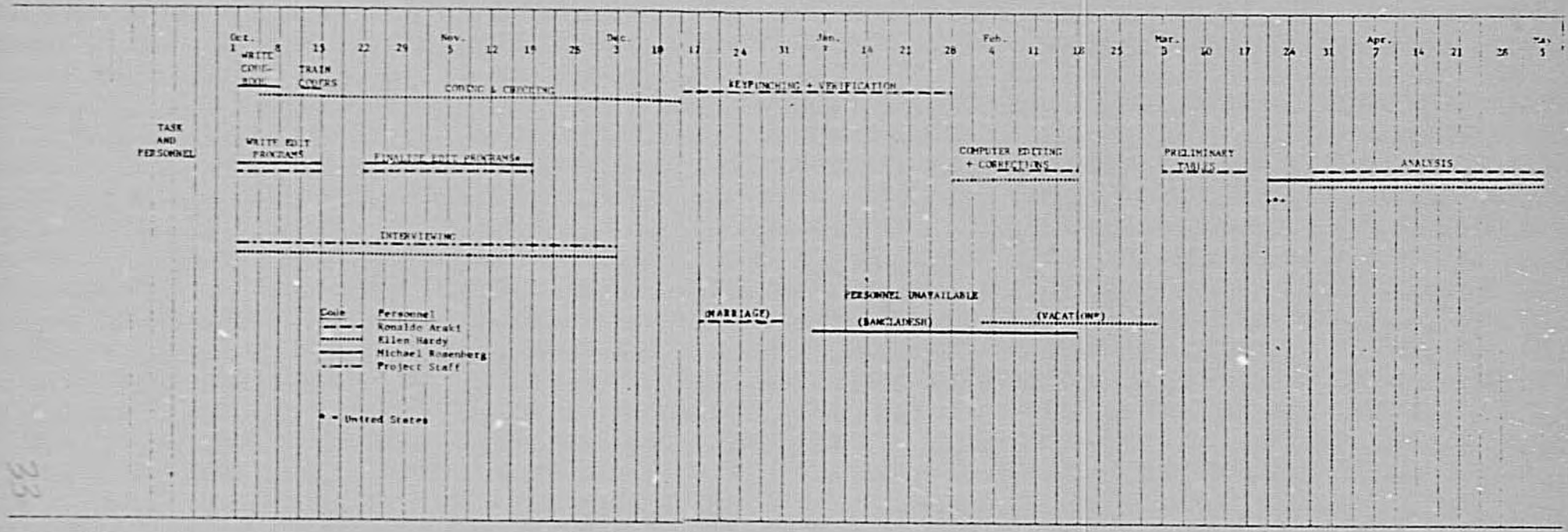
I.13 - INTERVIEWER: DESCRIBE THE EVOLUTION OF THE ILLNESS (BONES BROKE, METASTASIS, BACK PAIN, LACK OF AIR, SORES)

_____

_____

_____

GO TO 2.1

APPENDIX B

BREAST LESION PROJECT TIMETABLE, CAMPINAS, 1979