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13. ABSTRACT (Maximum 200) <p>Screening of the population in intervention areas continued. By the end of July 1997, 119,976 were interviewed and examined. Three thousand were detected positive for a lump and referred for diagnosis to the tumour clinics corresponding to a positivity rate of 2.8%. Compliance with referral was only 21%. Motives of non-compliance were assessed on a sample of 1,000 positive women who did not turn up at the tumour clinics for further clinical investigation. The survey indicated that costs and cultural barriers are the main reasons of non-compliance with diagnosis and treatment. Non-compliers are now being visited at their place by medical teams equipped to perform needle biopsies, set up for this purpose. However, this action has improved compliance by only 9%.</p> <p>Since all remedies put in place to improve attendance of clinics for final diagnosis and treatment failed to improve clinical attendance, it is now clear that the program as a whole will not be able to reduce mortality from breast cancer in this population.</p> <p>We conclude that the intervention should be discontinued once the first round of screening is completed. Both intervention and control cohorts will be followed up to study the onset of breast cancer and resulting mortality in relation to screening. In addition, the incidence of breast and other cancers will be studied in relation to the data collected at interview during the initial examination.</p> <p>A revision of the Statement of Work is proposed.</p>			
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FOREWORD

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D.M. Paul *28/11/97*
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INTRODUCTION

In 1990 breast cancer accounted for 837,000 new cases per year (WHO World Health Report 1997), and it was the most frequent cancer in women. Incidence rates are still rising in many countries, particularly in the developing world (Coleman and Estève, 1993). It seems that these trends are likely to continue, since the current pattern of later childbearing, decreasing fertility, and 'westernization' of diets will all be associated with increased risk.

At present, our knowledge of environmental risk factors does not permit formulation of any practical primary prevention programs. The introduction of adjuvant therapy with Tamoxifen has improved survival of older cases and a decline of mortality from breast cancer below age 50, observed in some high-risk countries, has also been attributed to adjuvant therapy (Nab *et al.*, 1994, Olivotto *et al.*, 1994). However, further improvements in surgical techniques, or in radiotherapy, are very unlikely to provide more than marginal changes in mortality rates.

A much greater decrease in deaths from breast cancer is achievable through screening programs which lead to detection of cancers which are smaller, at an earlier stage, and less malignant than those which surface clinically. Several randomized trials of screening for breast cancer have been carried out; in the majority the screening modality used was mammography, with or without physical examination of the breasts. There is a clear consensus that such screening programs are capable of decreasing the risk of mortality from breast cancer in women aged 50 or older (Miller *et al.*, 1990; Day, 1991; Moss, 1996). The efficacy of mammography in women below 50 is still a very controversial issue resulting in contradictory recommendations and policies (Moss, 1996; Nelson, 1997). At best, mortality reduction in this age group would be only 15% or one-half that of older women (based on meta-analyses of randomized trials). The reason of lower efficiency of mammography in younger women is not clear; possible causes are cancers growing faster in these ages or sensitivity of mammography in the pre-menopausal breast being relatively low.

Population screening programs which depend upon mammography require extensive provision of expensive technology and highly trained radiologists and radiographers. The cost per life-year saved is therefore relatively high (Barnum and Greenberg, 1991), and clearly an inappropriate use of health care resources for many countries (WHO, 1984).

The alternative screening strategies which have been proposed are physical examination of the breasts (PE), and breast self-examination (BSE). Short-term results of a large scale trial of BSE among 300,000 textile workers in Shanghai, China, conducted by researchers of the University of Washington have been recently published (Thomas *et al.*, 1997). Biases such as low compliance with the intervention, failure of proper randomization or low proficiency in performing BSE could be confidently excluded. No significant reduction of breast cancer mortality in the intervention group has been detected after 5 years of follow-up and the distribution of stage at diagnosis in screen and control groups were very similar. As discussed by the Authors, both results are not definitive; even in trials of mammography a reduction of mortality appeared only after 5 years from entry into the study and stage at diagnosis, which is assessed retrospectively, may well be affected by a rate of misclassification which can obscure existing differences in the intervention and control groups. Nevertheless, the small size of the lesions diagnosed in the control subjects in this trial (47% \leq 2 cm diameter) suggests a high level of health-awareness in the Shanghai population, and may give little scope for improvement in outcome through early detection by BSE.

At present PE has never been used as the sole modality of screening, so that its effectiveness is not known. Indirect evidence based on estimates of the accuracy of PE relative to mammography suggests that this type of examination could reduce mortality rates by 2/3 to 3/4 of that achievable by mammography screening in women aged 50 or more. PE alone may be effective in younger women, among whom up to 25% cancers are missed by mammography; in addition, there is evidence that PE improves the performance of mammography. The working group who reviewed in 1979 the results of the Breast Cancer Detection Demonstration Project, the first large non-experimental evaluation of mammography, stated that high priority should be given to the evaluation of PE as a single screening modality. The recommendation was not followed by action until the project

described here, possibly because of the rapid spreading of mammography in most developed countries which vitiated the feasibility of an unscreened control group.

The purpose of the present work was to establish 1) whether a program of mass screening by PE performed by trained paramedical personnel could be set up in a developing country as part of the routine activity of first level health services, and 2) whether and to what extent such a program could reduce mortality from breast cancer. The location is Metro Manila and Rizal Province of the Philippines. This population has a relatively high incidence of breast cancer, considerably above that of other Asian populations, and comparable to that in southern Europe.

BODY

The study is a randomized controlled trial of the effect of annual physical examination (PE) of the breasts performed by trained nurses/midwives, in reducing mortality from breast cancer. The study area comprises the central, more urbanized municipalities of the National Capital Region (Districts I, II, III and IV), which includes 12 municipalities each having municipal health centers in the township area and barangay health stations in more rural areas. In 1990, the estimated size of the female population aged 35-64 was about 340,000. The units of randomization are health centers (HCs) within the selected municipalities of the Manila - Rizal area.

Women aged 35-64 years resident in the intervention HC areas were offered annual breast examinations, carried out by specialized midwives/nurses. At the first visit, these women were also instructed in the technique of breast self-examination (BSE) and provided with a leaflet in the local language explaining the purpose and methodology of BSE.

Women in the control area received no active intervention, but were exposed to the general health education campaigns carried out by municipal authorities and voluntary bodies.

The examiners were trained using a program already developed and tested in the Philippines, making use of breast silicon models. Training was repeated for selected groups of examiners with detection rates markedly above or below the mean. Women eligible for screening were invited to participate through a variety of mechanisms but mainly by home visits.

At the first visit women were interviewed to record demographic variables and risk factors for breast cancer. Instruction in BSE was given and PE performed. Demographic characteristics of women who refused PE were also recorded .

Women with detected abnormalities were referred for final diagnosis to special clinics, made available in 3 major hospitals staffed by project personnel.

Results

During 1995 a coordinating center was set up. Two hundred and two Health Centers were randomized to intervention and control arms. Hospital clinics for referral of positive women and mechanisms for documentation of results were established. Personnel from the intervention HCs were recruited and trained.

A) Results: Intervention

New administrative procedures which defined the responsibilities and duties of the various bodies involved in delivering health care were implemented by the Philippine Government. These allow substantial periodic reshuffling of the field personnel between HCs. Moreover, it soon became evident that the regular personnel of HCs could not reach the scheduled rate of 14,000 woman-examinations per month. Therefore, nurses were recruited to work full-time for the project (FTNs) who became operational in March 1996. Table 1 summarizes the results of accomplishments to 31 July 1997.

Comparison of characteristics of compliers and refusers.

Table 2 compares the prevalence of some characteristics of a sample of women who accepted PE and of those who refused it. The 2 groups do not differ by age, prevalence of smoking or compliance with screening for cervix cancer, the latter being an indication of general attitude towards preventive practices. In contrast with what is observed in western countries, refusers are of higher social class, as indicated by greater average income and significantly lower parity.

B) List of individuals in the target population

Manual lists of the eligible population residing in the intervention and control areas were compiled in 1996 by a door-to-door survey. Electoral rolls could not be released then because of the concomitant national elections. Print-outs of electoral rolls were obtained in 1997; these are called Comelec lists. They have been computerized and are regularly matched with the lists of women examined by automatic record linkage. Nominal lists of the target population are necessary to allow estimation of non-compliance in the intervention arm, and to follow-up the reference control group who were not interviewed.

C) Data management

Procedures to computerize the data collected have been established and regular data entry ensures the maintenance of data bases of women examined, women detected positive and final diagnoses. Data entered are subject to systematic checks for errors of coding and typing and for inconsistencies in the information recorded. As mentioned above, the population lists are also computerized; these are regularly matched with the file of the women recruited by means of a software program developed in Lyon for this purpose. The program makes use of the usual basic demographic items - names and surname, date of birth, age and detailed address - and allows for differences in spelling or variations in the reported date of birth. Each variable contributing to the matching process is assigned a weight which summarizes its discriminating power and the likelihood that it is reported incorrectly. The resulting matching score allows linkage of records from different files pertaining to the same woman.

D) Follow-up

Procedures in the 2 cancer registries serving the study populations (Manila-PCS and Rizal-DOH) have been improved, so that general case finding is taking place in a more timely manner than previously. Additional staff have been recruited and trained to trace cases and report data by means of new abstract forms which include extensive information on extent of disease (tumor size, spread and nodal involvement). Table 3 summarizes the clinical characteristics of the incident cases recorded up to July 1997.

E) Action taken to improve compliance with clinical investigation among women detected positive.

One thousand women who were positive for a lump at the initial visit but who had not subsequently turned up at a referral clinic were visited a second time to assess the motives for non-compliance. The survey indicates that the main reasons for non-compliance are inconvenience and costs (Table 4). In order to induce greater motivation to seek medical attention, medical teams formed by a doctor and a nurse and equipped to perform needle biopsies, were sent to visit non-compliers at home in order to obtain a final diagnosis. This activity commenced in March 1997 (recruitment and training of doctors) and is currently ongoing. Table 5 compares the outcome of diagnoses of 472 women who complied with referral and of 388 who had a biopsy at home. Of the 860 lumps referred by PE, 40% were not detected by the referral oncologist. The remaining 514 underwent biopsies which resulted in 27 malignant cancers and 349 benign lumps. Of all the fine-needle biopsies carried out, 138 were inadequate and need to be repeated; the majority of these (80%) were performed at home.

CONCLUSION

The experience of the first 2 years of field activity indicates that a screening program by PE can attain high coverage in this urban population. The positivity rate (2.8%) is sufficiently low to make this type of intervention cost-effective provided that the positive predictive value and sensitivity of the test prove to be high.

However, at present, the positive predictive value of the screening test appears rather low (27 cancers out of 663 referrals for whom a final diagnosis is available, i.e. around 4%). Sensitivity will be estimated eventually by comparing the incidence of interval cancers (not detected by screening) in the intervention group, with the incidence in the control group. These data will be provided by the cancer registries.

The potential of the intervention is seriously compromised by the very low rate of compliance with referral of women detected positive at PE. This is far too low to have any impact on the risk of dying from breast cancer in the intervention group. The low compliance rate was the main problem shown by the pilot study conducted in 1990-1991; the reason for this was identified in the cost of transport and diagnostic examinations which most women could not afford. Therefore, provision to reimburse diagnostic expenses was made in the project protocol. It appears that this mechanism is not sufficient to compensate for loss of working-days. The project is now bringing the diagnostic facilities to positive women; it was hoped that the relatively few who result positive for malignant cancer would have a strong motivation to seek medical care. Unfortunately this remedy improved compliance with clinical investigation only by a depressing 9%, with the cost of treatment and cultural barriers remaining the main obstacles to further clinical investigation.

As described in the previous sections it is now clear that the program as a whole will not be able to reduce mortality from breast cancer in this population. The reason for this is the low compliance with clinical investigation and treatment of women found positive at PE. Moreover, all remedies put in place to overcome, at least, logistical problems linked to referral failed to improve the compliance. A better understanding of the cultural determinants of the attitude of this population towards health practices would help the Department of Health in developing future strategies.

It was concluded that the intervention should be discontinued once the first round of screening is completed. The control cohort is being established with data entry completed by the end of November 1997. Follow up of the 2 groups will be performed. This will provide information on the effectiveness of the prevalent screen (incidence and mortality rates in the 2 groups), as well as identifying the risk factors for breast and other female cancers in this population.

The cohorts will be followed up for 5-10 years to study the onset of breast cancer and resulting mortality in relation to screening. In addition the incidence of breast and other cancers will be studied in relation to the data collected at interview during the initial examination. The association between reproductive factors and cancer of the breast has never been studied in a prospective study of this size in a population with fertility rates characteristic of developing countries but showing patterns of cancer risk quite high for Asian standards. Other cancer sites which will be related to reproductive factors, tobacco smoking, alcohol consumption and family history of cancer are cervix, ovary, corpus uteri, colon, lung, kidney and gallbladder. Table 6 shows the number of cases expected in the next 5 to 20 years in the cohort interviewed, by cancer site. Cancers of the kidney and gallbladder have been associated with parity in women however, being rather rare cancers the association has been investigated only in small studies.

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Table 1.
Accomplishments at 31 July 1997.

<i>Intervention</i>		
No. offered the intervention	119,976	
No. interviewed and examined	108,102	89.7%
No. refused PE	12,404	10.3%
Average monthly recruitment rate since FTN operative	7,499	
<i>Women detected positive</i>		
Number of women detected positive and referred to tumor clinics	3,004	
	positivity rate:	2.8%
No. referred who attended clinic:	629	
	percent compliance with referral:	20.9%
	No. with final diagnosis:	393 13.1%
No. referred who did not attend clinic and were visited at home (see text and table 5)	620	
	No. with final diagnosis	270 9.0%
Outcome of diagnoses (3,004 women):		
	no mass	346 11.5%
	malignant breast cancer:	27 0.9%
	benign breast disease:	349 11.6%
	actively refused further investigation (at clinics or home visits):	242 8.1%
	attended other clinic:	73 2.4%
	pending diagnoses:	1,967 65.5%

Table 2.
Comparison of characteristics of women who refused examination
and of those who accepted.

	compliers N=92091	refusers N=12404
age in years (mean±SD)	44.9±8.3	44.9±8.6
attended college/university (%)	12.8%	18.5%
monthly income (pesos)		
mean±SD	4,960± 4,496	10,276±12,898
median	4000	5000
mean age at menarche	13.7±1.7	13.6±1.6
mean age at first fullterm pregnancy	23.2±4.6	23.9±4.9
mean age at first pregnancy if <20 years	17.9±1.2	17.9±1.2
ever used contraception (%)	33.0%	26.9%
nulliparous (%)	9.7%	15.7%
more than 5 fullterm pregnancies (%)	34.0%	23.9%
never had a PAP smear (%)	70.6%	71.0%
reporting family history (%)	1.8%	1.8%
smokers (%)	8.2%	7.5%
drinkers (%)	7.7%	12.5%

Table 3
Clinical Characteristics of Breast Cancer Cases diagnosed in Metro Manila
(study area - intervention and control) in 1995-1997 (provisional)

	number	%
Number of cases	769	
mean age in years	50.54	
Tumour size		
<1 cm	4	0.8
1 - 2.9	78	16.2
3 - 3.9	78	16.2
4+	320	66.5
TNM Stage		
0	7	0.9
I	32	4.2
II	386	50.2
III	177	23.0
IV	64	8.3
unstaged	103	13.4

Table 4
Reasons given for non-compliance with referral - results from 1020 woman

Reason Given	number	%
went to special clinic in the interim period	96	9.4
do not have time/do not want to miss work	412	40.4
no money to pay for treatment	59	5.8
prefer to see a faith healer	6	0.6
afraid of what the diagnosis may be - cancer	68	6.7
hospital too far from home	20	2.0
afraid of hospitals/doctors	12	1.2
prefer to leave it up the Lord	27	2.7
do not feel ill	59	5.8
other reasons	259	25.4
Total	1020	

Table 5.
Pathology outcome of screen-detected lumps in referral clinics and after home fine needle biopsy (FNB).

	referral clinics	%	home visits & FNB	%	Total	%
total evaluated:	472		388		860	
no mass	233	49.4	113	29.1	346	40.2
unsatisfactory biopsy	27	5.7	111	28.6	138	16.1
benign disease	194	41.1	155	40.0	349	40.6
malignant	18	3.8	9	2.3	27	3.1

Table 6
 Expected number of cases in the intervention cohort, by follow-up and cancer site.

	follow-up	
	5 years	10 years
Colon	77	187
Rectum	56	130
Gallbladder	16	38
Lung	154	387
Breast	676	1,484
Cervix uteri	321	700
Corpus uteri	85	195
Ovary etc.	133	297
Kidney	26	60
Thyroid	109	232

Appendix

Details of future plans and Revised Statement of Work

Future plans

The intervention will be discontinued once the first round of screening is completed. The control cohort is being established with data entry completed by the end of November 1997. Follow up of the 2 groups will be performed. This will provide information on the effectiveness of the prevalent screen (incidence and mortality rates in the 2 groups), as well as identifying the risk factors for breast and other female cancers in this population.

Enrollment

Enrollment into the screened cohort will continue until the end of 1997, aiming to get as close to the target of 170,000 screened women as possible. The existing population lists should be sufficient for this without the need for updated Comelec lists. The FTNs can choose the most effective method possible to maximize the recruitment rate. It was agreed that they may enroll any women in the target age range who are resident in the intervention areas, even though they do not appear on the population lists.

A second round of screening will be completed on 5000 women. This has already begun in Pateros. This sample of second screens will provide indirect information on the performance of PE; in fact, if first examinations detected the majority of prevalent lumps the prevalence of positive women should decrease at subsequent examinations.

Control cohort

The control cohort will be established by combining the population lists compiled manually in 1996 and the Comelec lists for the control areas; only women present on both files will be included. A random sample of 1000 women will be drawn from the resulting list to be traced and interviewed by the same questionnaire adopted for the intervention. This will take place in January - February 1998. The purpose of this sample survey is to estimate the actual proportion of the control cohort that is present in early 1998, and to compare the characteristics of this cohort with those of the intervention group as a check on the randomization procedure. If randomization was successful women in the control cohort will show the same pattern of risk factors.

Follow-up of screened positive women

The current procedures to trace and examine as many as possible of the women found positive in the screening examination will be continued, including the special clinics, financial incentives, and mobile teams. As the screening will continue until the end of December, the clinical follow-up will continue until the end of March 1998.

Database

The screening databases (first round screen and second screen) should be completed soon after the end of enrollment into these 2 cohorts (end of February 1998). The data on clinical follow-up will be added by the end of April 1998. Data entry of the control cohort lists will be completed by November 1997 to draw the 1000 sample. The questionnaires of the sample interview will be computerized in February-March 1998.

After 2 years, a sample of the intervention cohort will be drawn, and an attempt will be made to trace the subjects, noting those who have moved (and to where), and those who have died.

Long Term Follow-up: The Cancer Registry

Two cancer registries cover together the whole area of Metro Manila. The Rizal Cancer Registry covers the 12 municipalities involved in the trial and 14 neighboring municipalities, The Manila-Philippine Cancer Society Registry (PCS- MCR) covers 4 additional urban areas of Manila not included in the trial. The Rizal registry will be responsible for long term follow-up. This will comprise:

- (1) Recording stage of disease (tumor size, lymphatic spread and metastases) using the SEER extent of disease (10 digit) coding scheme, and TNM stage for all breast cancer cases occurring in residents of the study municipalities.
- (2) Matching all registered cancer cases occurring in the 2 registry areas with the study database for a period of 5 (minimum) - 10 years.

All registered cancer cases occurring in women in the age groups who were recruited into the study will be matched with the study database. Linkage will be aided by the recording of the address in full on the cancer registration forms (although only municipality of residence is coded and entered into the registry regular database). Recording the address in full will require some extra work by the registry clerks only for those cases where it is currently missing.

Although the study cohort was recruited in just 12 municipalities, linkage with registration of women resident in the whole of Manila/Rizal will be performed, in order to identify women moving within the urban area.

As noted above, a special nominal file of study subjects has been created for record linkage purposes, comprising study number, and demographic data (name, date of birth, address), but without the interview results. This will be retained in the Rizal Cancer Registry. Any cancer cases identified will be 'flagged' in this nominal file as already identified.

Breast cancer cases

Linked breast cancer cases (registrations which have been identified as belonging to the study cohort) will be entered into a separate breast cancer file. The details of stage, already recorded for residents of the 12 study municipalities, will be added to the records in this file. Matched registrations of women no longer resident in the 12 municipalities will not have stage available on the registration form. The hospital records of these women must be actively traced by registry staff, details of stage and treatment abstracted, and added to these records. Records on the breast cancer file will contain the hospital record number, and subjects contact details (address/ telephone/next of kin) to facilitate follow-up. Breast cancer cases will be carefully followed up at annual intervals updating status (alive/dead/not traced) and contact details. The flow-chart in figures 1 and 2 describes the whole procedure.

Proposed revision of Statement of Work

The budget remaining can cover remaining field activities (first 6 months of 1998) and the follow-up of the cohort for 6 years from 1998 to 2003. The main costs are due to search of information (hospitals, death certificates and direct contacts) and abstraction and reporting in a timely manner; maintenance of the data bases including automatic record linkage and manual handling of uncertain matches, coordination and periodic analyses. A detailed cost estimate is given in attached and reflects the following Statement of Work.

Year 1 – 1998

Complete data entry of forms relative to women examined during the first round of screening completed by December 1997.

Complete home visits (home biopsies) of women detected positive who do not attend referral clinics for final diagnosis.

Re-examine a random sample of 5,000 women screen-negative at first examination.

Interview a random sample of 1,000 women drawn from the population lists of the control areas.

Recruit and train cancer registry personnel to trace and abstract clinical information and vital status of breast cancer cases.

Set up procedures to update the file of breast cancer cases (enter new cases, record changes of address, record changes of vital status and related information), and match files of cases with those of the intervention and control cohorts and of death certificates.

Undertake routine activity of follow-up.

Perform periodical analyses of the data collected and report on current status.

Years 2 to 5 – 1999 to 2002

Continue follow-up activities, analysis and reporting. Undertake special procedures to trace cases lost to follow-up, by direct contact of next of kin or home visits.

Year 6 – 2003

Perform formal evaluation of the outcome of the intervention by comparing incidence and mortality from breast cancer in the screened and control cohorts.

Perform analysis of the risk of cancer at various sites in relation to reproductive history, tobacco and alcohol consumption and family history of breast cancer.

Budget revision for Annual report 24 Nov. 1997

Detailed cost estimate (US\$)

Appendix - table 1

		exchange rate=					US\$1= P30	
		year					Total	
		1998	1999	2000	2001	2002	2003	Total
A.	<i>IARC, Lyon coordination</i>							
A.1	<u>Direct labour cost</u>							
	Computing technician for periodical analyses, selection of matched controls 6 month/yr	20,262	20,870	21,496	22,141	22,805	23,189	130,763
	Data entry and file maintenance in Manila	15,000	12,000	12,000	12,000	12,000	12,000	75,000
	A.1 Total	35,262	32,870	33,496	34,141	34,805	35,189	205,763
A.2	<u>Equipment</u>							
	Hardware and software	5,000			3,000			8,000
	A.2 Total	5,000	0	0	3,000	0	0	8,000
A.3	<u>Travel costs</u>							
	i) by IARC staff							
	2 trips Lyon-Manila, per diem 7 days each	10,862	10,862	10,862	10,862	10,862	10,862	65,172
	1 trip Manila-Lyon , per diem 21 days	6,957	6,957	6,957	6,957	6,957	6,957	41,742
	ii)Co-investigator in Manila							
	1 trip Manila-Lyon, per diem 7 days	5179	5179	5179	5179	5179	5179	31,074
	A.3 Total	22,998	22,998	22,998	22,998	22,998	22,998	137,988
A.4	<u>Material supplies and consumable</u>							
	Total supplies	5,000	5,000	5,000	5,000	5,000	5,000	30,000
	A. total	68,260	60,868	61,494	65,139	62,803	63,187	381,751

Appendix tale 1 - continued

	year					Total
	1998	1999	2000	2001	2002	2003
B.3 Travel cost						
B.3.1 DOH (3 month clinical follow up of referred women)						
Transportation for health workers on referrals, P25*600 referrals	500					500
Transportation for patients on referral, P25*600 referrals	500					500
B.3.2 Rizal Cancer Registry						
Transportation allowance registry clerks, P1,300/month/clerk x12 months x 5 clerks	2,600	2,600	2,600	2,600	2,800	16,000
B.3.3 Training registry clerks Manila/Lyons + subsistence	5,000	5,000	5,000			15,000
B.3 Total	8,600	7,600	7,600	2,600	2,800	2,800
B.4.1 Material, supplies and consumable DOH (3 month clinical follow up of referred women)						
Biopsy material	600					600
Office consumable	300					300
B.4.2 Rizal Cancer Registry						
Supplies and consumable	6,000	6,000	6,500	7,000	7,000	39,500
Maintenance of equipment (car & computers)	4,000	4,000	4,500	4,500	4,500	26,000
B.4 Total	10,900	10,000	11,000	11,500	11,500	66,400
B total direct costs	45,800	33,790	35,600	31,830	33,080	213,180
Indirect costs 13%	14,828	12,306	12,622	12,606	12,465	77,341
Grand total	128,888	106,964	109,716	109,575	108,348	672,272

N.B. 'Supplies and consumables' under B.4.2 include, office supplies and consumable, petrol, communication (fax, telephone and e-mail) and miscellaneous costs such as hospital reimbursement for extra work due to retrieval of documents.

Figure 1

BREAST CANCER REGISTRATIONS

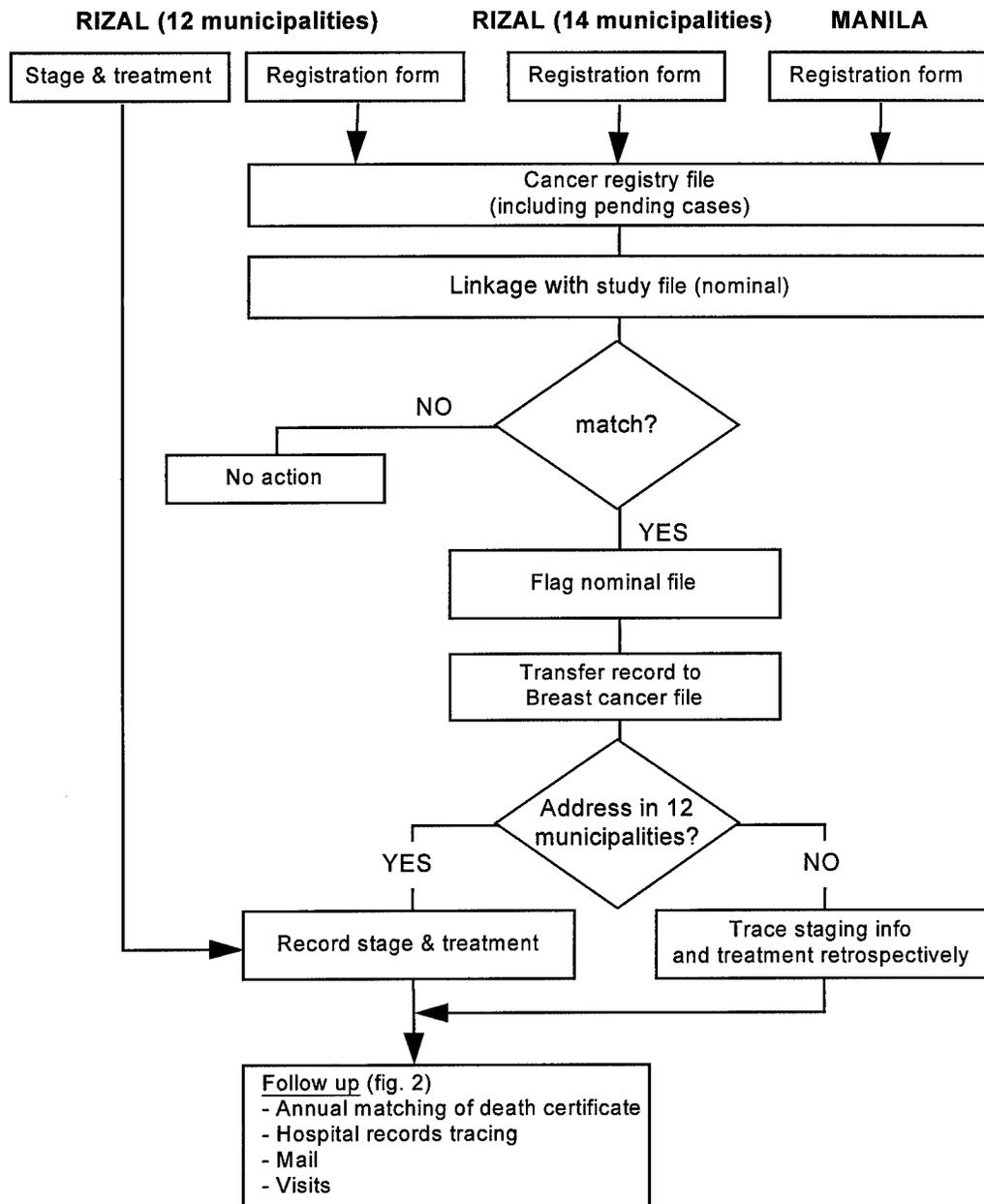


Figure 2

MORTALITY FOLLOW-UP

