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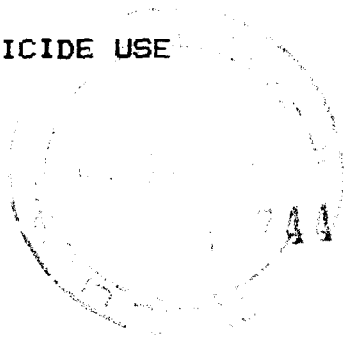
# INCREASED MORTALITY IN RURAL CENTRAL LUZON, PHILIPPINES

# IS CORRELATED WITH INSECTICIDE USE



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RUNNING HEAD: INSECTICIDE USE AND MORTALITY

## ABSTRACT

In a major rice growing area of the Philippines, widespread adoption of insecticides by small farmers was followed by a 27% increase in non-traumatic mortality among economically-active men ($P < .001$). Several factors suggest a causal link: highly toxic chemicals have been used under unsafe conditions; mortality has increased only in the age and sex class occupationally exposed; the death rate has declined among unexposed urban men; specific death rates have increased for those conditions likely to be confounded with insecticide poisoning and have declined for others; and both within and between years the pattern of mortality among men has reflected that of insecticide use. The results suggest strongly that the currently accepted figure of 10,000 deaths annually worldwide due to accidental intoxication is a substantial underestimate.



## KEY WORDS

Pesticides; Insecticides (organochlorine, organophosphate); Asia, southeastern; Philippines; Cerebrovascular disorders

# INTRODUCTION

The spread of modern cereal varieties and farming practices, often referred to as the Green Revolution, has made possible major increases in developing country food production, notably in the rice producing countries of tropical Asia. However, widespread and poorly regulated use of pesticides under unsafe conditions has led to concern about the impact on public health and in particular about the occupational poisoning of farmers and labourers (1,2).

The hazard agricultural workers face may be substantial. Results of a recent study (3) suggest that a person applying "Endrin", an organochlorine insecticide that has been widely used in several countries in Asia, with a backpack sprayer in good repair and under typical conditions would be expected to come into direct contact with 41 mg of active ingredient per hour. At that rate, a worker weighing 55 kg would be exposed to 33% of the mammalian dermal $LD_{50}$ (the lethal dose for 50% of a population) in treating an average holding once*. This estimate excludes

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* Assuming 3 hours to treat a hectare; 2.5 ha/holding; a solution of 0.7 mg active ingredient/ml spray solution; 87% of the spray contacting the operator falling on the parts of the body often left uncovered (4), the hands, lower legs and feet, and a dermal $LD_{50}$ for endrin of 15 mg/kg (5).

exposure during handling of the concentrate and in mixing, which may be significant, though highly variable (3).

Efforts to estimate the actual impact of pesticide exposure on the health of field workers in developing countries encounter important methodological problems. Clinical signs of intoxication, notably acetylcholinesterase depression, provide one objective measure; however the uncertainty of the relationship between cholinesterase levels and morbidity (6) and difficulties in monitoring representative samples of workers over sufficiently long periods limit the conclusions that can be drawn by this method.

Retrospective studies based on reported cases have also been conducted. In Sri Lanka, 13,000 people are admitted to hospital each year for pesticide poisoning, of whom some 1,000 die (7). However, the accuracy of such estimates depends on the proper diagnosis of poisoning and on the completeness of reporting. In developing countries the scarcity of diagnostic tools, high patient-doctor ratios, unfamiliarity of health workers with the signs and symptoms of poisoning and lack of access by the poor to formal health care undermine the reliability of reporting.

A different form of retrospective analysis is employed in the present study. It focuses on an area of the Philippines where

pesticide use has been relatively well studied and where the comparative ease of access to government services makes gross under-reporting of at least adult mortality unlikely. Specific changes are predicted in death rates from what is known of the temporal and spatial patterns of use and the clinical toxicology of the compounds in question. A close fit between observation and expectation then allows one to estimate the excess mortality that has occurred. More specifically, it is hypothesized that: (1) increased mortality due to occupational intoxication will be concentrated among men, who are primarily involved in pesticide application; (2) no such effect will be apparent in unexposed urban groups; (3) the trend of death rate over the years will parallel that of pesticide use; (4) within the year, increased mortality will be concentrated in the months of greatest pesticide use and will closely reflect changes in the cropping pattern; (5) the specific death rates of conditions associated with or likely to be confounded with pesticide poisoning will rise disproportionately and (6) these rates will be significantly correlated with that of diagnosed fatal poisoning.

How is pesticide poisoning likely to be misdiagnosed? In Central Luzon, two types of pesticide of marked acute toxicity have been widely used by small farmers: organophosphate (OP) and cyclodiene and hexachlorocyclohexane (CYC-HCH) organochlorine insecticides. Intoxication by each type can occur by the dermal, respiratory

and oral routes. Symptoms of severe OP poisoning include generalised convulsions, psychic disturbances, intense cyanosis, bradycardia, pulmonary oedema and coma (8). Pneumonia, asthma and bronchospasm are frequently encountered sequelae (9-11). Unpublished observations by Dr. Nelia Maramba and her colleagues at the Philippines General Hospital indicate that when rural doctors were presented with the signs and symptoms of acute OP intoxication in mock examinations, they most frequently diagnosed a variety of cardio-vascular and respiratory conditions. I predict therefore that, as the use of OP insecticides rises, misdiagnosis of poisoning will inflate the combined death rates of cardio-vascular and respiratory diseases.

The clinical picture of acute CYC-HCH intoxication is very different. The primary locus of action of these compounds is the CNS and severe poisoning is marked by tonic and clonic convulsions, generally epileptiform in nature (12-13). Kubrich and Urban (14) describe a case of apparent dermal intoxication by endrin that under other circumstances would have been diagnosed as stroke. Increasing use of and intoxication by CYC-HCH insecticides will, I predict, be followed by rising death rates attributed to epilepsy, brain tumor, stroke and related conditions (cerebral hemorrhage, embolism, aneurysm etc.) as a result of misdiagnosis.

## METHODS

In Nueva Ecija, the major rice-producing province in Central Luzon (Fig. 1), four jurisdictions were selected where pesticide use and cropping patterns had been closely studied (15,16). Aliaga, Jaen and Zaragoza are entirely rural municipalities (combined 1980 population 96,000). Cabanatuan (population 138,000) is a nearby centre encompassing both urban neighbourhoods, in which the occupational exposure to insecticides is likely to be low, and rural villages. More than 80% of the heads of household in typical villages find their primary employment in rice farming and together the four jurisdictions account for 16% of the provincial production.

fig 1 here

Pesticide use in Central Luzon rose markedly following the adoption of modern varieties in the late 1960's, the introduction of a government-sponsored credit scheme in 1972 and a series of pest and disease outbreaks beginning in 1971. Between 1970 and 1974, the value of insecticides applied to rice rose more than 250%. Among the compounds in widespread use during the 1970's were carbofuran (oral $LD_{50}$ 8 mg/kg), endrin (8 mg/kg), methyl parathion (14 mg/kg) and monocrotophos (14mg/kg) (17,5). The liquid formulations sold in Central Luzon are classified as "extremely" or "highly hazardous" by the World Health Organization (18).

In the study area in 1978, farmers applied insecticide 4-5 times per crop, with a mean dosage of 0.3 kg of active ingredient per hectare. Treatments were concentrated in the vegetative stage of the crop, particularly during the month subsequent to transplanting (15). Insecticides were applied by backpack sprayer, generally by men, either farmers themselves, family members or hired labourers. Protective clothing was not worn and none was available locally. Since the late 1970's the use of insecticides has remained constant or declined slightly in the face of rising prices and scarcity of credit. In what follows, I examine mortality in relation to two periods, one of low use of insecticides (1961-71) and one of high (1972-84).

Population estimates were obtained from four national censuses (19) and by interpolation in intervening years. Mortality statistics were obtained from civil registries derived from death certificates. The cause or causes ascribed were noted and the entries assigned to one of 4 age classes: children 1-5 years and 6-14 years and men and women 15-54 years. Deaths due to traumatic causes were excluded, save non-suicidal poisonings involving pesticides or unspecified substances.

As the breakdown of Cabanatuan's urban and rural populations was not consistent between censuses, indices of mortality by age class were calculated as the number of deaths in the urban or

rural areas divided by the city's population in that year. These indices will be proportional to the death rate if the urban/rural mix remains constant. Cabanatuan has grown rapidly in recent years as a result of immigration; if, as appears likely, most immigrants settled in the urban neighbourhoods, the index would underestimate both true decreases in death rate in the urban neighbourhoods and increases in the rural villages.

For both men and women 15-54 years, death rates in the rural municipalities and indices of mortality in Cabanatuan were adjusted to the city's age distribution in 1960 by the direct method.

Overall trends in mortality in the 1-5 and 6-14 years age classes were analysed by means of Armitage's test (20), and by least squares regression of arc sine-transformed rates for men and women (as these had been age-adjusted). The t-test was used to compare mortality in the periods of low and high use of insecticides, again using arc sine-transformed rates. However, in the case of diagnosed poisoning a more conservative non-parametric method, the Mann-Whitney U-test, was employed due to the large number of years in the low-use period in which no fatalities were recorded. Changes in the distribution of deaths by cause and month were analyzed by means of the appropriate Chi-square test.

## RESULTS

### Mortality by Age and Sex

While the non-traumatic death rate in the three entirely rural municipalities has declined significantly since 1961 among children 1-5 years ($\chi^2 = 58.5$, $P < .001$), those 6-14 years ($\chi^2 = 7.20$, $P < .01$) and women 15-54 years ($r = -.58$, $P < .01$), it has increased markedly for men ($r = .61$, $P < .01$). Note that for the latter there is no evidence of trend prior to 1972, when low cost credit became widely available to farmers, nor in the years 1976-84, a period of rough constancy in insecticide use (fig. 2). Comparing the periods 1961-71 and 1972-84, the mean non-traumatic death rate increased 27.4%, from 2.15 to 2.74 per 1000 ($t = 4.09$, $P < .001$).

fig 2 here

### Urban/Rural Comparisons

Significant and opposite changes in adult male mortality have occurred in the two sections of Cabanatuan (table 1): the index increased 29.3% in the villages ($t = 2.28$, $P < .05$) while declining 37.2% in the urban neighbourhoods ($t = -3.14$, $P < .05$). If, as suggested earlier, the city became more urban over the period, both trends would be accentuated. Among women in rural Cabanatuan, the index of mortality did not increase significantly ($t = 1.12$, ns), while as for men there was a marked decline in the urban areas of 52% ($t = -5.45$, $P < .001$).

table 1 here

Causes of Death

In the 3 rural municipalities, mortality due to diagnosed poisoning increased 247% ($U = 29$, $P < .01$) and that from associated or potentially confounded conditions 41% ($t = 4.53$, $P < .001$) between the periods of low and high use of insecticide (table 2). As predicted, there is a significant correlation between the two series ($r = .47$, $.01 < P < .02$). The trend in both cases has been similar to that of overall male mortality (Fig. 2): death rates were low prior to 1972 (fatal diagnosed poisonings were recorded in only three of 11 years between 1961 and 1971), rising rapidly thereafter and remaining roughly constant after the late 1970's. In contrast, the death rate from all other causes, save cancer, declined 33.7% ($t = -2.78$, $P < .02$) over the period. Similar changes in the causes of death occurred in the rural areas of Cabanatuan, but not the urban.

table 2 here

Though this paper focuses on the impact of acute intoxication, chronic effects are also to be expected. Several of the insecticides in widespread use in Central Luzon are known or suspected carcinogens, including DDT and endrin (21,22). While overall cancer rates (excluding brain tumor) have not increased significantly (table 2), marked changes have occurred in the death rates for specific cancers, notably leukemia. Growing evidence suggests a link between exposure to insecticides, both organochlorine and organophosphate, and subsequent development of

this disease (23-25). In the three rural municipalities, mortality among men attributed to leukemia increased 580%, from 0.6 to 3.6 x $10^{-5}$, between the 1961-71 and 1972-84 periods ($\chi^2$ = 4.5, P < .05). The rise has been most marked in recent years: 7 of the 11 cases recorded since 1961 occurred in the 6 years 1979-84. In contrast, among women the death rate has remained virtually unchanged: 0.6 x $10^{-5}$ (1961-71) and 0.7 x $10^{-5}$ (1972-84), representing 1 and 2 cases respectively.

Among the conditions associated with or likely to be confounded with acute CYC-HCH intoxication, by far the most frequently recorded in the study area is stroke. While the specific death rate for all men in Cabanatuan and the 3 rural municipalities rose significantly between the 1961-71 and 1972-82 periods ($\chi^2$ = 49, P < .005), the increase was greater among younger men, generally at low risk of stroke ($\chi^2$ = 5.4, P < .02; table 3A). Among those 15-24 years, no deaths attributed to stroke had been recorded before 1972, whereas 20 were noted from 1972 to 1982.

table 3 here

During the 1982 wet season, the Philippines Fertilizer and Pesticide Authority banned the use of endrin, the most widely used and toxic CYC-HCH insecticide available to rice farmers. In the two years subsequent to the ban mortality attributed to stroke declined for all men relative to the level immediately prior ($\chi^2$ = 4.8, P < .05; table 4B), but again to a

significantly greater extent in the younger age class ($\chi^2$ =3.8, P < .05). Similar trends are seen in the 3 rural municipalities considered alone.

## The Monthly Distribution of Mortality

In the vicinity of Cabanatuan, the wet season crop is generally transplanted in late July and August and, since the completion of a large irrigation scheme in 1976, a dry season crop is now planted as well in late January and February. Insecticide use, as noted earlier, is greatest in the period after transplanting, and one would therefore expect the increase in acute occupational poisoning to be concentrated in these months.

Figure 3 illustrates the monthly ratio of observed-to-expected mortality during two periods, where the expectation is taken from the monthly distribution of deaths from 1961 to 1971, when insecticide use was low. Before the arrival of irrigation (Fig. 3A), the ratio was greatest, 50% above expectation, in August, the month of maximum insecticide use in the wet season. After double cropping became widespread. two peaks occurred (fig 3B): in February, when insecticides are most intensively used during the dry season crop, and again in August. (1983 and 1984 are excluded from consideration as low water levels in the reservoir disrupted the usual irrigation schedule.) A straighforward test of the significance of this pattern can be calculated from the

fig 3 here

prior probability of the two highest peaks coinciding with the months of greatest insecticide use in the wet and dry seasons: $P = 1/12 \times 1/11 = .008$.

Although dry season cropping schedules and peaks in observed/expected mortality are not as well defined in the 3 rural municipalities that lie downstream of Cabanatuan, August remains a major period of transplanting and insecticide application during the wet season. The crude death rate during the month rose 66% between 1961-71 and 1972-82, while the increase was only 15% over the rest of the year. Taking all rural areas together, the proportion of deaths among men occurring during August rose from 7.3% in 1961-71 to 10.1% in 1972-82 ($\chi^2 = 4.7$, $P < .05$).

## DISCUSSION

The data presented provide strong evidence linking a marked increase in mortality in Central Luzon and occupational exposure to insecticides: only men in rural areas have been affected, both within and between years, male death rates have reflected the pattern of insecticide use, and increased mortality has been concentrated in those conditions associated or likely to be confounded with pesticide poisoning, most strikingly seen in the relationship between endrin use and deaths attributed to stroke. Although the

evidence is retrospective in nature, the close fit between observation and expectation lends credence to the postulated causal relation.

Other factors may however have contributed to the observed changes in mortality:

1) Impoverishment due to falling rural incomes in the region (17) might in part account for the changing monthly distribution of mortality, if its impact is greatest during periods of notable stress. For men, one such time may be early in the crop season, during land preparation. However, widespread reduction in the food supply of near-subsistence communities is generally thought to affect young children in greatest measure (26), whereas in the study area only death rates among men were found to have risen.

2) Increased tobacco consumption among men might contribute to some of the observed trends, notably an increase in respiratory and cardiovascular diseases. Conflicting results emerge from studies concerning the link between smoking and stroke (27,28), however none report a disproportionately increased risk for those under 35, or even 25 years, as found here. Moreover, though smoking appears to be at least as prevalent among urban as rural men, mortality has fallen markedly in the urban neighbourhoods.

3) Greater efficiency in the reporting of vital events would result in an apparent but spurious rise in death rates. However, specific biases in reporting are required to account for the selectiveness of the increases by age, sex, cause, month and place of residence.

The overall increase in non-traumatic mortality among rural men between the periods of low and high use of insecticides was estimated at 27%. The actual occurence of fatal poisoning may well be greater than this figure suggests if one assumes that in the absence of exposure mortality would have declined, as it did among women and children in the rural areas and among men in urban Cabanatuan. Extrapolating, even on the basis of the 27% value, to other rice growing areas in the Philippines and elsewhere in Asia where pesticides have been widely adopted suggests an annual excess mortality of several tens of thousands. The figure of 10,000 deaths worldwide from accidental and occupational poisoning that is often cited (29,30) must on this evidence be considered a serious underestimate. That it is economically-active men, often the heads of households, who are most at risk of intoxication implies that the overall social impact is greater than such numbers alone indicate.

Further epidemiological research is required to confirm these results and to catalyse efforts to confront the poisoning issue

in smallhold agriculture. Techniques similar to those used here might be employed in areas where mortality and pesticide use have been adequately monitored; participatory research designs might be considered where monitoring is less reliable and as a means of making the issue visible among those at risk. In some instances it may be possible to employ rigorous case-control methods.

Exposure to pesticides can be significantly reduced by increased reliance on alternative methods of pest control. In crops such as rice and cotton, "economic thresholds" for insecticide application, resistant plant varieties, and biological and cultural controls permit reduced pesticide use without sacrificing output or farmers' incomes (31-33). These practices require vigorous adaptive research and extension to make them accessible to the majority of farmers and must be supported by effective pesticide regulation.

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## Table 1

Trends in indices of mortality among men 15 - 54 years in rural and urban areas of Cabanatuan, Philippines.

| | 1961-71 | 1972-84 |
|---|---|---|
| Rural | 1.84 ± .180 * | 2.38 ± .138 |
| Urban | 1.64 ± .210 | 1.03 ± .058 |

* Mean index per thousand ± standard error.

Table 2

Trends in specific death rates among men 15-54 years in 3 rural municipalities in Nueva Ecija, Philippines.

| | 1961-71 | 1972-84 |
|---|---|---|
| diagnosed pesticide poisoning | 2.39 ± 1.34 * | 8.29 ± 2.30 |
| all potentially confounded conditions | 130 ± 9.20 | 183 ± 7.10 |
| cancer (all sites except brain) | 21.1 ± 3.49 | 25.9 ± 4.02 |
| all other causes | 62.0 ± 6.04 | 41.1 ± 4.62 |

* Mean rate per 100,000 ± standard error.

Table 3

Mortality attributed to stroke among men 15 - 54 years in Cabanatuan and three rural Philippine municipalities combined in: (A) periods of low and high endrin use; (B) the two years immediately prior and subsequent to the ban on endrin's use.

| | A. | | | B. | | |
|---|---|---|---|---|---|---|
| Age class (years) | Death rate ‡ | | Percent change | Death rate | | Percent change |
| | 1961-71 | 1972-82 | | 1981-82 | 1983-84 | |
| 15 - 34 | 4.59 (12) ‡‡ | 18.0 (70) | +291% | 26.0 (27) | 9.91 (11) | -62% |
| 35 - 54 | 33.2 (41) | 80.9 (135) | +144% | 91.2 (38) | 79.1 (34) | -13% |

‡ Per 100,000. ‡‡ Values in parentheses are numbers of deaths.

## FIGURE LEGENDS

### Figure 1

The study area in Central Luzon, Philippines.

### Figure 2

Three-year moving averages of age-adjusted non-traumatic mortality among men and women 15-54 years in three rural municipalities in Nueva Ecija, Philippines.

### Figure 3

Ratio of the observed to the expected number of deaths among men 15-54 years in the rural areas of Cabanatuan, Philippines. A: a period of intensive insecticide use and predominantly single cropping. B: a period of intensive insecticide use and predominantly double cropping.

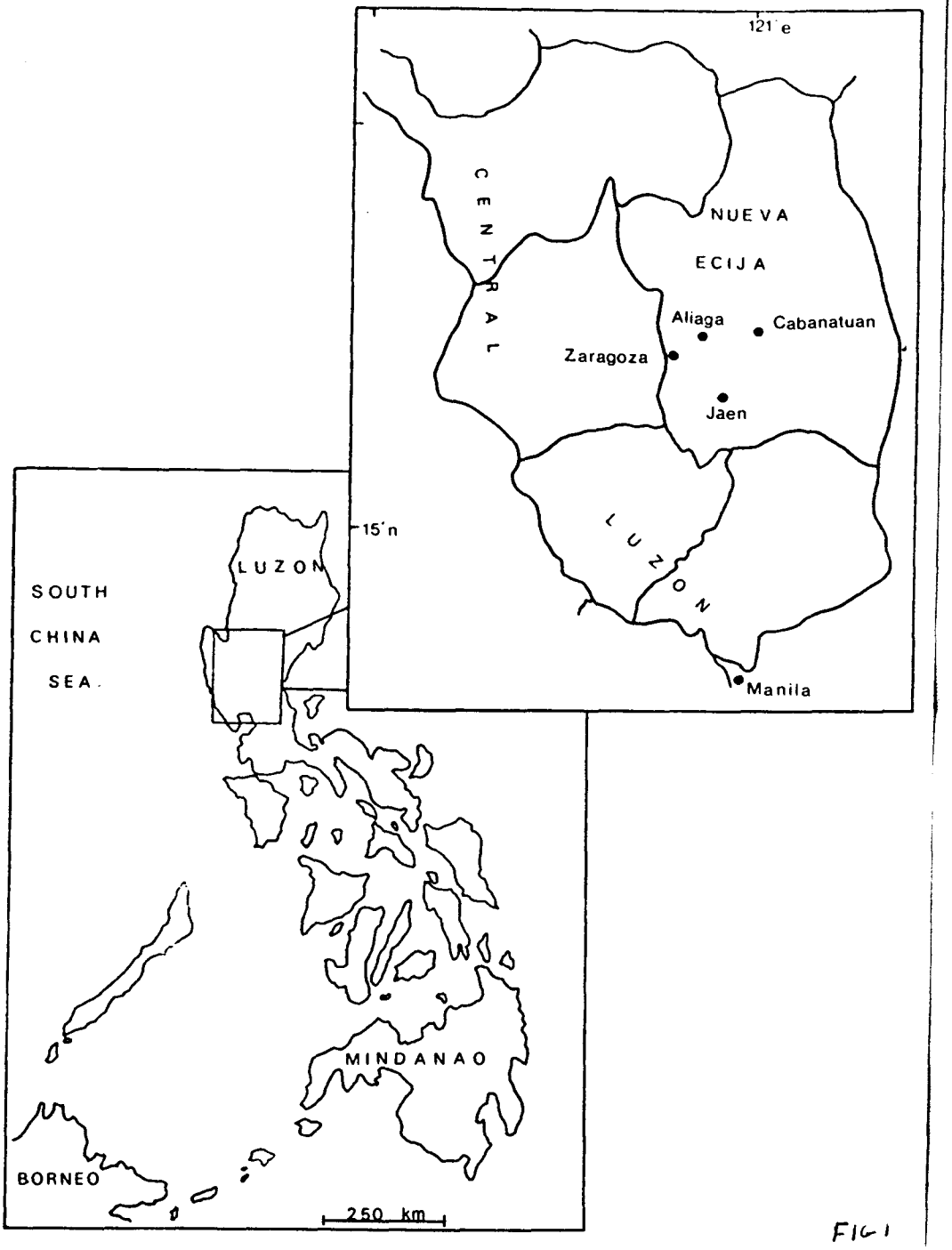
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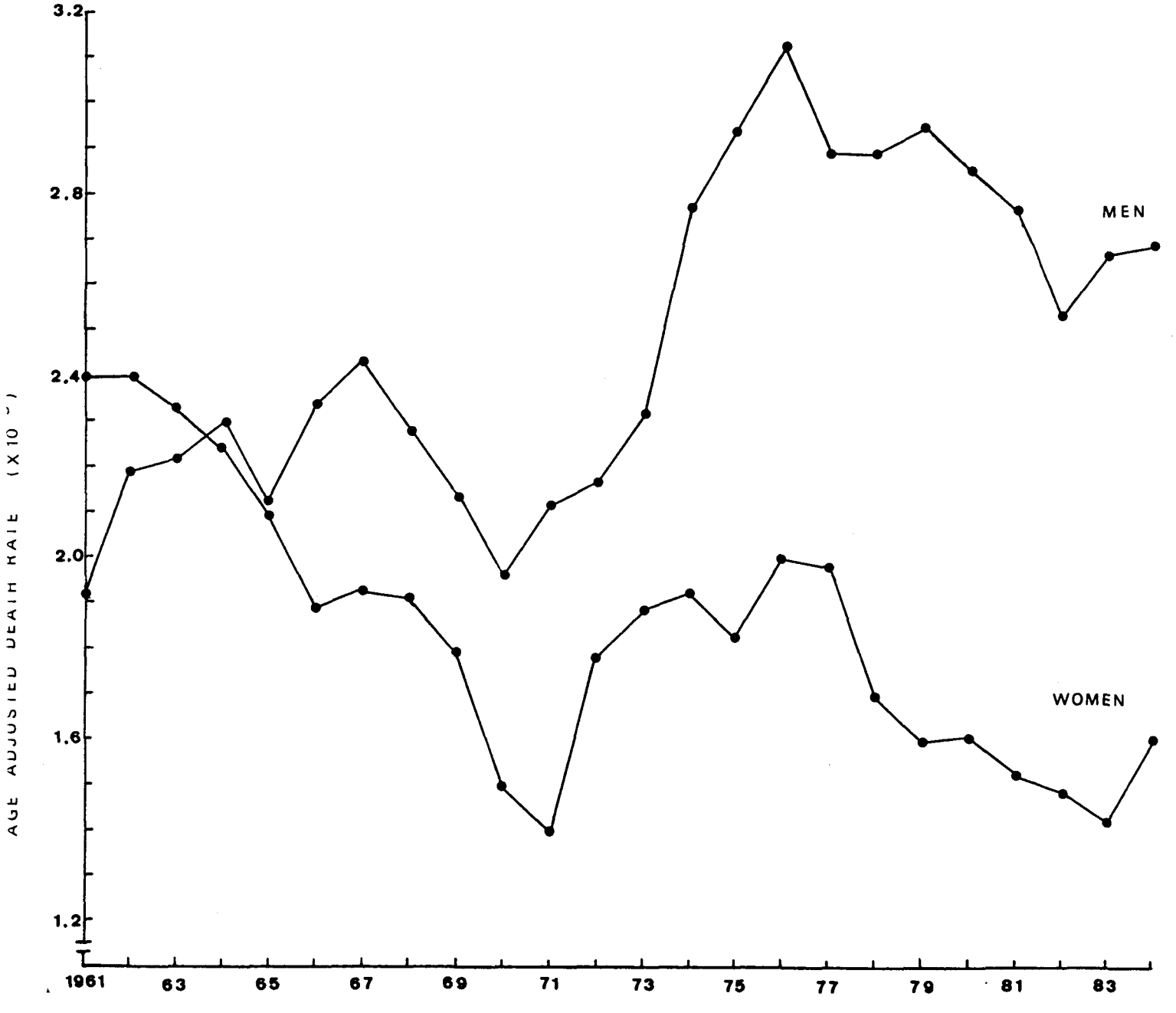
FIG 1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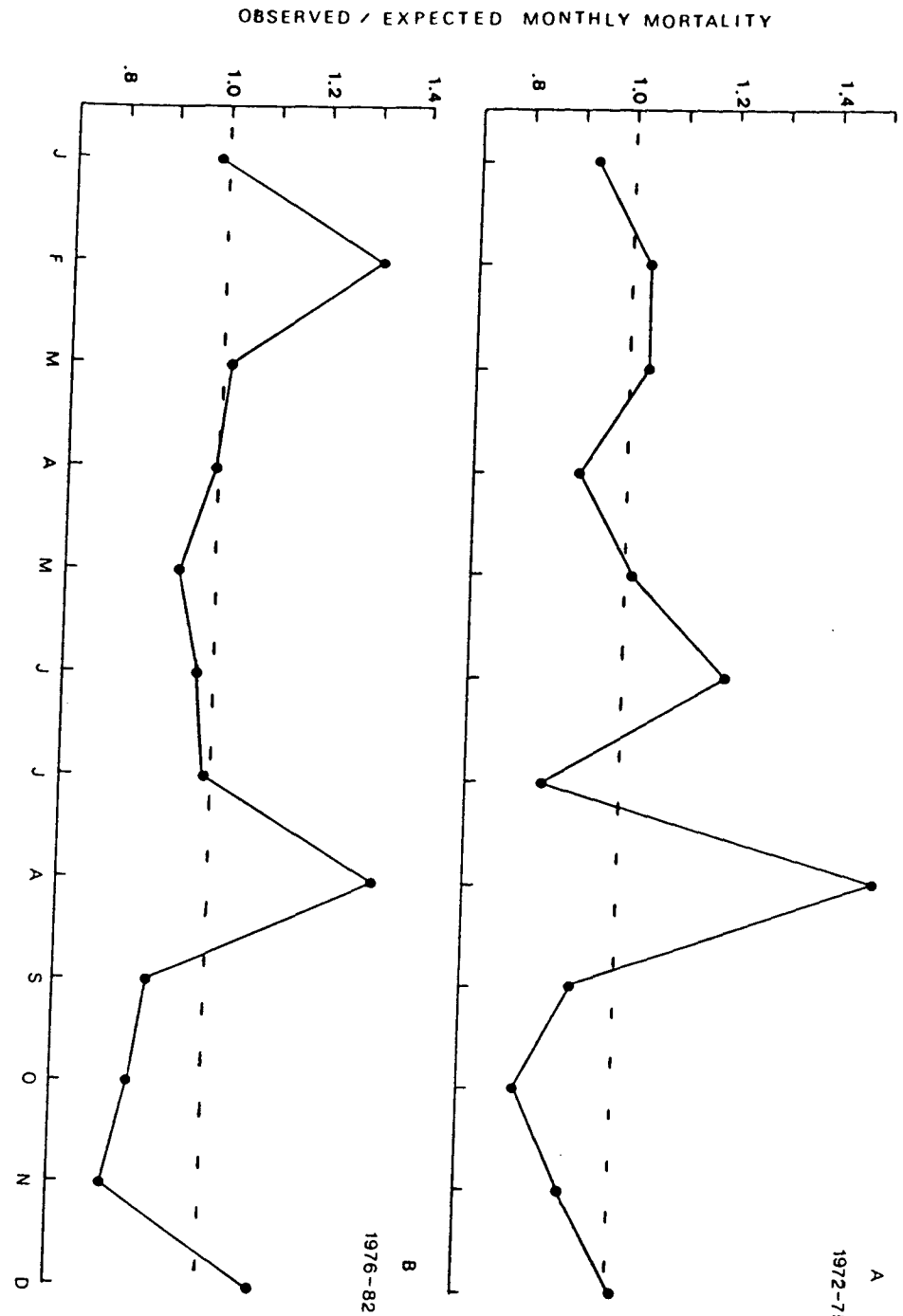
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FIG 3