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THE AUCKLAND SUBURBS
CORONARY STUDY

Gary E. Fraser

A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Medicine
University of Auckland, 1979
ACKNOWLEDGEMENTS

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ABSTRACT

The Auckland Suburbs Coronary Study is designed to provide information concerning acute coronary events in Auckland. Within New Zealand, information previously depended on either hospital data or death certificate data. The present study is community based and has provided more extensive information than has previously been available.

A random sample of 125 primary care doctors was selected. The patients of these doctors were considered a random sample of the community and formed the study population. The size of this population was estimated using a postal survey, taking names from the electoral roll. A statistical theory is developed to allow a confidence interval to be placed about the maximum likelihood estimate. Hypothesis testing theory is applied to the problem of comparing disease frequencies at different locations or at different times at the same location.

During overlapping one year periods, 293 cases of definite myocardial infarction, 178 cases of sudden cardiac death and 99 cases of possible myocardial infarction were collected. Information concerning demographic variables, past and prodromal medical histories, the acute event, the electrocardiograph, cardiac enzymes, mortality within 28 days and postmortem results, was collected.

As about 80% of sudden deaths are all over before any help is sought and in view of the geographic nature of Auckland city the utility of 'cardiac arrest' ambulances would not seem to be great. For sudden deaths surviving longer than five minutes after onset (about 50% of total) there was a significant tendency
for there to be a lower social class predominance. This may imply inade-
quacies of acute health care--either availability or notification.

Persons dying suddenly differed from persons experiencing definite
myocardial infarction (but not dying suddenly) by experiencing less prodromal
chest pain, taking digoxin and frusemide more frequently, consuming more
alcohol and the acute event occurring in the cooler months proportionately
more often. At postmortem, they had significantly more myocardial scarring
and/or fibrosis.

Persons experiencing definite myocardial infarction differed from persons
experiencing possible myocardial infarction (who did not die suddenly) by
being more likely a male, having less history of past acute coronary
insufficiency, using less of beta-blocking drugs or frusemide/ethacrynic acid
and describing prodromal lethargy less frequently. Clinical shock was more
common in the acute phase and death more common in the succeeding 30 days.

Persons dying suddenly differed from those suffering possible myo-
cardial infarction (but not dying suddenly) by being older, more likely to be male
and less likely to have had chest pain in the prodrome.

The data could be interpreted as suggesting that a separate primary
myocardial process is contributing towards sudden death. Alcohol may be a
risk factor for sudden death. A hypothesis is, that in the presence of acute
infarction, a history of chronic, moderate to high alcohol intake is associated
with an increased likelihood of sudden death.
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CHAPTER I

INTRODUCTION
Section 1.1: HISTORICAL REVIEW

The group of heart diseases that are frequently associated with coronary artery atheroma, represent the major cause of death for middle-aged and elderly men and women in many westernized countries (1).

This fact is a development of the 20th century. Prior to this, infectious diseases, even in well-developed countries were the major killers. With sound public health measures (and antibiotics to a lesser degree) the situation is now reversed. We are in the midst of an epidemic of 'coronary heart disease' which 'almost certainly outstrips the tuberculosis rate at its zenith late in the nineteenth century, when the 'great white plague' was the nation's Number One health problem' (2) (referring to USA).

The apparent increase in disease frequency could well be a distortion due to the use of crude mortality measures. Age specific measures are a much more powerful tool for epidemiological investigations, and enable a consideration of other aetiological factors, apart from that associated with inevitable ageing. When infectious diseases were controlled, the population age-structure changed to include a much higher proportion of older citizens, all at higher risk of 'coronary heart disease'. Thus a more useful question is whether age-specific incidence and prevalence rates for 'coronary heart disease' have been changing with time.

Historically there is considerable evidence, of a necessarily imprecise nature, that coronary disease may well have existed from antiquity. Sandison (3) has documented arteriosclerotic and atherosclerotic diseases of arteries on a number of Egyptian mummies despite having very few
specimens to work on. Long (4) describes a calcified coronary artery with a thickened intima, coexisting, with what appeared to be fine myocardial scars in another Egyptian specimen. It thus seems likely that atherosclerotic arterial disease was not uncommon among higher social class persons at least, in ancient Egypt. Whether or not this caused symptoms is less certain, but the quotation below from the Papyrus Ebers (5), seems very reminiscent of angina pectoris.

'When you examine a man for illness in his cardia, he has pains in his arm, in his breast, on the side of his cardia; it is said thereof: this is the w3d-illness. Then you shall say thereof: it is something which entered his mouth; it is death which approaches him. Then you shall prepare for him stimulating herbal remedies: fruits of pea, bryony (and other vegetable remedies); let them be boiled in fat [Ebers 38: in beer] and be drunk by the man.

Put then your bended hand on him, until the arm gets well and free of pains. Then you shall say: this illness has descended to the rectum, to the anus.

The remedy shall not thence be repeated.'

In 1972, for the first time in China a complete human body from ancient times was unearthed. The woman, approximately 50 years of age, in a remarkable state of preservation apparently lived during the second century B.C. The medical report, among other things showed a severely occluded left coronary artery. Found in the tomb were packets of herbal medicines---cinnamon, magnolia, bark and peppercorns. These are still prescribed today for heart disease by herb doctors in China, and apparently were known also during the period of her life.
It seems likely this 'lady died of a heart attack', quoting Dr. T. O. Cheng, a cardiologist who studied the material. It also seems possible that she had symptomatic pre-existing heart disease requiring medication. Coronary disease may not have been uncommon amongst high ranking persons in ancient China, being found in the first such body examined (6).

Leibowitz (7) in his book The History of Coronary Heart Disease, quotes many suggestive histories from Ancient Greece and Rome, the middle ages, and from the sixteenth century on. While the more recent histories over the last 300 years are in general clearer, it seems possible that this is due to differences in physiological and anatomical knowledge and more familiar language usage. It seems very likely that atheromatous coronary disease has existed in some populations at least over very long periods, and has manifested itself by chest pains and sudden death, very much as today.

Heberden (8) in 1772 described, with clarity, the clinical syndrome of angina pectoris but it was not until 1788 that Parry (9) connected these symptoms, and sudden death to a disorder of the coronary arteries. In 1775 Albrect von Heller (10) introduced the concept of arteriosclerosis and described atheromatous deposits, in detail. Less well described arterial abnormalities which may well have been atheromatous had been noted well before this (11, 12, 13), despite the rarity of postmortem examination. Vogel (1843) (14), and later Aschoff (1907) (15), demonstrated an excess of the doubly refractive material, cholesterol, in these lesions.

Virchow (16) in 1846, described thrombosis in vessels without relating it to coronary pathology. Weigert (17) (1880) gave the first clear pathological
description of myocardial infarction. Leyden (18) (1884) and later more
clearly and definitively, Herrick (19) (1912) finally 'tied together' the clinical
manifestations, atheromatous coronary artery disease, thrombosis and the
pathology of myocardial infarction, to a unified pathophysiological hypothesis.

In 1919 Herrick (20) and Pardee (21) described the electrocardiographic
changes of myocardial infarction. In 1954 enzymes (SGOT) were used by
La Due (22) as an indication of myocardial necrosis. Earlier, features such
as pyrexia (1905) (23, 24), leucocytosis (1916) (23, 24) and elevated ESR (1933)
(25) had been associated with myocardial infarction.

Many years passed between the first clear association of myocardial
infarction with the clinical features, and the acceptance of this relationship
by the medical profession at large. Concepts such as chronic myocarditis
(describing scarring of the myocardium), which is now known often to be a
manifestation of coronary disease, persisted for a long period. One still
hears such diagnoses made by older practitioners in New Zealand.

It is only since the late 1940's that epidemiologists have begun to
investigate this disease from an aetiological point of view. It is true that
there had been isolated previous correlations attempted (e.g., C. D. De Langen
(26) referred to the contrasting diets of the Javanese and Dutch (1941) and
related this to atherosclerosis). The sex differential and age dependence of
coronary disease incidence had been noted previously by clinicians. On
pathophysiological and epidemiological grounds and also based on the results
of animal experiments, several variables (physiological, biochemical,
behavioral and socio-economic) were selected for concentrated longitudinal
population investigations as possible aetiological agents. The Framingham study (27) and somewhat later Ancel Keys' Seven Countries Study (28) were two of the earliest, largest and most successful of these prospective studies.

As a result of their findings, the concept of risk-factors has arisen. Subpopulations have been defined that contribute to the total incidence of coronary disease many more cases than would be expected on a population size basis. These subpopulations are 'at risk' and are said to possess and to be definable by risk factors such as, 1. cholesterol levels above the community average, 2. elevated blood pressure, 3. cigarette smoking.

Other seemingly less significant risk factors have also been progressively defined, e.g., obesity, lack of exercise, family history, water hardness, glucose intolerance, left ventricular hypertrophy on the ECG, stress and psychosocial factors. Some of these are not independent of the three main risk factors mentioned in the previous paragraph and may reflect the same causative variables.

The multifactorial nature of the disease has been made clear and the application of multivariate statistics, including the logistic transformation model has enabled a much more powerful analysis of the data. Nevertheless, the conclusions reached can only be in terms of Factor A being associated with an increased risk of coronary disease, rather than there necessarily being a causal association. The aetiological significance of a correlation, is a matter of judgement rather than statistics, although these contribute to the decision. Certainty that a relationship is aetiological may ultimately be impossible to prove.
From a practical point of view however, the decision of importance is - If Factor A is reduced or eliminated, will the risk of coronary disease to the individual and/or the community be reduced? Whether such a reduction takes place primarily due to the reduction of Factor A or whether it is due primarily to the reduction of Factor B which is closely linked to Factor A, is of secondary importance. This introduces the latest cycle of research endeavour concerning this disease; that of preventive trials. Studies have been designed, usually using large populations, to try to modify behaviour (e.g., diet, smoking) or pathophysiology (e.g., Hypertension). Patients are then followed over several years to try to assess whether these changes are altering the pattern of the disease. Three examples of such studies are a) Multiple Risk Factors Intervention Trial (MRFIT) (29); b) Hypertension Detection and Followup Program (HDFP) (30); c) Lipid Research Clinics (LRC) (31). A major problem with these studies is the difficulty of achieving behavioural modification and maintaining it in large populations. They are also enormously costly, e.g., MRFIT had an initial budget estimate of $50 million (29).

Ongoing with the studies last mentioned, have been coronary disease registers (32, 33, 34, 35, etc) assessing incidence in various places of the earth and trying to relate these to the habits and environments of the populations considered. It seems clear that further aetiological factors must be found, and geographic comparisons represent a powerful tool to point out potential variables for aetiological investigation. (The larger longitudinal studies of course also gave this type of information.)
One of the remarkable features of this disease is the wide geographic variation in the frequency of clinical and pathological manifestations (1). Many countries, particularly economically poor countries with a lower standard of living, and usually a more vegetarian diet have low incidences and prevalences. Countries with a westernized style of life have by far the highest frequencies.

In summary, it seems likely that coronary disease manifestations were not rare from very early times. It is not possible to say more than this and indeed, the evidence relating to incidence and prevalence trends in modern times is still controversial.
Section 1.2: NEW ZEALAND

New Zealand is situated about latitude 40° South and has a temperate climate, varying somewhat from North to South. Extremes in temperature are unusual. Mean Daily Maximum Summer temperatures are generally around 22° C and Mean Daily Minimum Winter temperatures about 5° C. Due to the oceanic position precipitation tends to be high, e.g., Auckland 1243 mm/year.

The original settlers of New Zealand, the Maoris, are a Polynesian race. Although today there are few pure Maoris remaining, about 8% of the population are 50% or more of Maori blood. The remainder of the slightly more than 3 million inhabitants is virtually all European. The population is predominantly urban with only 18.5% living in rural areas, even though the country is economically dependent on farm production. Slightly over 50% of the population lives in the four main centres of Auckland, Wellington, Christchurch and Dunedin.

Despite its South Pacific location, New Zealand having been a British colony, has a westernized life style. Settlers were almost all of British extraction and even today there are still rather restrictive conditions imposed on migration from non-Commonwealth countries. Polynesia is considered as a special region and there are many Samoan and Cook Islanders who immigrate, particularly to Auckland.

The predominant religion is Protestant Christianity--about 16% of the population being Roman Catholics. The standard of living is generally accepted
as being very similar to such countries as Canada, Australia, United Kingdom, using social and economic indicators.

Health expenditure accounts for 4.7% of the gross national product.

Medically, the general practitioner is the primary care doctor and over 94% of New Zealanders are on the records of such a doctor (36). There were on average 844 persons per doctor in 1971, but 2400 persons to each active general practitioner. An emphasis on social security particularly in its application to medical services has been a feature of New Zealand government for about 40 years.

Public hospitals give free treatment for acute care and have also a limited number of geriatric beds. Doctors, both general practitioners and specialists are subsidized by the government on a fee for service basis. However, the patient still pays about 2/3 of the total charge for visits to surgeries (offices) or for domiciliary visits. Prescriptions are made out by the pharmacist free of charge to the patient, the pharmacist being subsidized by the government.

Hospital beds (including maternity) are provided at 7.4/1000 of population, about 25% of these being in privately run institutions. Ischaemic Heart Disease accounts for about 3.6% of all admissions to public hospitals, with a hospital mortality of 18.6%.

Table 1 shows the life expectancy for Maoris and non-Maoris at different ages.

Maoris seem more susceptible to several diseases, e.g., Diabetes, Tuberculosis, Gout, Rheumatic Fever, Cardiac death (females only), Glomerulonephritis and Hypertension (37, 38, 39).
Life Expectancy:

<table>
<thead>
<tr>
<th>Years</th>
<th>Non-Maoris</th>
<th></th>
<th>Maoris</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>a) At birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1896-1900</td>
<td>57.37</td>
<td>59.95</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>1955-1957</td>
<td>68.88</td>
<td>73.88</td>
<td>57.23</td>
<td>56.68</td>
</tr>
<tr>
<td>1965-1967</td>
<td>68.67</td>
<td>74.84</td>
<td>61.44</td>
<td>64.78</td>
</tr>
<tr>
<td>1970-1972</td>
<td>69.09</td>
<td>75.16</td>
<td>60.96</td>
<td>64.96</td>
</tr>
<tr>
<td>b) At age 40 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1896-1900</td>
<td>30.10</td>
<td>31.73</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>1955-1957</td>
<td>32.84</td>
<td>36.65</td>
<td>27.31</td>
<td>26.55</td>
</tr>
<tr>
<td>1965-1967</td>
<td>32.23</td>
<td>37.16</td>
<td>27.49</td>
<td>29.10</td>
</tr>
<tr>
<td>1970-1972</td>
<td>32.40</td>
<td>37.46</td>
<td>26.56</td>
<td>29.22</td>
</tr>
<tr>
<td>c) At age 60 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1896-1900</td>
<td>15.33</td>
<td>16.54</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>1965-1967</td>
<td>15.82</td>
<td>19.68</td>
<td>12.89</td>
<td>15.09</td>
</tr>
<tr>
<td>1970-1972</td>
<td>15.82</td>
<td>19.91</td>
<td>12.96</td>
<td>14.60</td>
</tr>
</tbody>
</table>

Table 1. Life Expectancy for Maoris and Non-Maoris (in Years).

This evidence is largely from death certificate or hospital admission records which probably roughly reflect the true situation. However, it is clear that infectious diseases are still a predominant cause of serious morbidity in Maoris, whereas this is not true amongst European populations. In part this can be explained by the markedly younger population structure of the Maoris.

The New Zealand diet follows the pattern of most other westernized countries. However it is outstanding in terms of calories per person per day and the percentage of these calories that are of animal origin. Presumably this is related to the agricultural economy. According to Table 2 (40) New Zealanders lead the world in both of these measures.
<table>
<thead>
<tr>
<th>Country</th>
<th>Cereals</th>
<th>Potatoes etc</th>
<th>Sugar</th>
<th>Pulses and Nuts</th>
<th>Meat</th>
<th>Milk and Milk Products*</th>
<th>Fats**</th>
<th>Calories</th>
<th>Per person per day</th>
<th>Percentage of animal origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>1964-65</td>
<td>85</td>
<td>43</td>
<td>50</td>
<td>4</td>
<td>106</td>
<td>8</td>
<td>14</td>
<td>3160</td>
<td>43</td>
</tr>
<tr>
<td>Canada</td>
<td>1964-65</td>
<td>67</td>
<td>72</td>
<td>46</td>
<td>6</td>
<td>86</td>
<td>7</td>
<td>19</td>
<td>3090</td>
<td>43</td>
</tr>
<tr>
<td>New Zealand</td>
<td>1967</td>
<td>86</td>
<td>66</td>
<td>50</td>
<td>5</td>
<td>109</td>
<td>10</td>
<td>23</td>
<td>3468</td>
<td>50</td>
</tr>
<tr>
<td>U.K.</td>
<td>1963-64</td>
<td>80</td>
<td>101</td>
<td>46</td>
<td>6</td>
<td>70</td>
<td>8</td>
<td>24</td>
<td>3280</td>
<td>44</td>
</tr>
<tr>
<td>Rep. of Ireland, South Africa</td>
<td>1964</td>
<td>101</td>
<td>136</td>
<td>49</td>
<td>3</td>
<td>69</td>
<td>9</td>
<td>19</td>
<td>3460</td>
<td>40</td>
</tr>
<tr>
<td>U.S.A.</td>
<td>1965</td>
<td>66</td>
<td>45</td>
<td>40</td>
<td>8</td>
<td>100</td>
<td>8</td>
<td>22</td>
<td>3140</td>
<td>38</td>
</tr>
<tr>
<td>Argentina</td>
<td>1963</td>
<td>120</td>
<td>75</td>
<td>33</td>
<td>2</td>
<td>97</td>
<td>4</td>
<td>16</td>
<td>3040</td>
<td>30</td>
</tr>
<tr>
<td>Denmark</td>
<td>1964-65</td>
<td>75</td>
<td>106</td>
<td>48</td>
<td>8</td>
<td>63</td>
<td>9</td>
<td>29</td>
<td>3330</td>
<td>44</td>
</tr>
<tr>
<td>France</td>
<td>1960-62</td>
<td>98</td>
<td>100</td>
<td>30</td>
<td>7</td>
<td>77</td>
<td>6</td>
<td>4</td>
<td>3050</td>
<td>44</td>
</tr>
<tr>
<td>Netherlands</td>
<td>1964-65</td>
<td>73</td>
<td>93</td>
<td>43</td>
<td>5</td>
<td>51</td>
<td>8</td>
<td>22</td>
<td>2890</td>
<td>42</td>
</tr>
<tr>
<td>Sweden</td>
<td>1964-65</td>
<td>69</td>
<td>96</td>
<td>39</td>
<td>3</td>
<td>52</td>
<td>10</td>
<td>22</td>
<td>2950</td>
<td>42</td>
</tr>
<tr>
<td>India</td>
<td>1963-64</td>
<td>142</td>
<td>11</td>
<td>17</td>
<td>22</td>
<td>1</td>
<td>2**</td>
<td>3</td>
<td>1980</td>
<td>6</td>
</tr>
<tr>
<td>Japan</td>
<td>1964</td>
<td>147</td>
<td>67</td>
<td>17</td>
<td>15</td>
<td>10</td>
<td>1</td>
<td>7</td>
<td>2320</td>
<td>11</td>
</tr>
</tbody>
</table>

Table 2. Total Consumption in Calories (per person per day) and some Foodstuffs for Selected Countries from the Food and Agriculture Organization Production Yearbook and the United Nations Statistical Yearbook.

* Excluding butter; ** Including butter; † Tentative data (Source: New Zealand Official Yearbook 1969).
The current theory of aetiology of coronary disease would thus lead one to expect a high incidence of coronary disease in New Zealand. If New Zealand follows the pattern of European countries, Keys work (28) would also predict a high incidence.

A recent dietary survey in Carterton, New Zealand (41) of 16 families included 60 persons. The average caloric intake expressed as adult 'man value' was 3,350 cal; 13% of total calories were from protein, 39% from fat, 47% from carbohydrate and 1% from alcohol. It was estimated that about 90% of the fat came from animal sources, 33% from meat and 57% from dairy products. The average cholesterol intake/day/person was 620 gms. (children and adults included).

In 1943, McLaughlin surveyed 63 urban families among basic wage-earners (42). Average daily caloric consumption per head was 3,107 with 12.2% of these as protein. Compared to US families, the New Zealand families obtained more calories from meat, eggs, butter, and less from fruit and vegetables. Overall, however, differences did not seem large.
Section 1.3: ISCHAEMIC HEART DISEASE IN NEW ZEALAND

(Previous Data)

Most previous New Zealand epidemiological data has been concerned with coronary deaths and has usually been extracted from death certificates.

On this basis (see Table 4), New Zealand is ranked tenth for males and ninth for females (all ages).

However, a fairer comparison is allowed by standardizing all countries to a fixed population age structure. The statistics as quoted for all ages reflect partly differing population age structures, rather than underlying coronary death risk.

On standardizing to Auckland's population age structure Table becomes changed to Table 3.

<table>
<thead>
<tr>
<th>Country</th>
<th>Males Death Rates/100,000 (all ages)</th>
<th>Country</th>
<th>Females Death Rates/100,000 (all ages)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scotland</td>
<td>396.1</td>
<td>Israel</td>
<td>221.3</td>
</tr>
<tr>
<td>USA</td>
<td>396.0</td>
<td>USA</td>
<td>216.3</td>
</tr>
<tr>
<td>Australia</td>
<td>382.3</td>
<td>Australia</td>
<td>192.5</td>
</tr>
<tr>
<td>Finland</td>
<td>362.9</td>
<td>Scotland</td>
<td>190.6</td>
</tr>
<tr>
<td>NZ</td>
<td>348.5</td>
<td>NZ</td>
<td>174.8</td>
</tr>
<tr>
<td>Canada</td>
<td>336.1</td>
<td>Sweden</td>
<td>173.7</td>
</tr>
<tr>
<td>Ireland</td>
<td>315.2</td>
<td>Ireland</td>
<td>171.2</td>
</tr>
<tr>
<td>England, Wales</td>
<td>314.8</td>
<td>Canada</td>
<td>167.6</td>
</tr>
<tr>
<td>Denmark</td>
<td>313.1</td>
<td>Denmark</td>
<td>166.8</td>
</tr>
<tr>
<td>Sweden</td>
<td>311.4</td>
<td>Finland</td>
<td>148.0</td>
</tr>
<tr>
<td>Israel</td>
<td>311.0</td>
<td>England, Wales</td>
<td>143.7</td>
</tr>
<tr>
<td>Norway</td>
<td>265.1</td>
<td>Norway</td>
<td>265.1</td>
</tr>
</tbody>
</table>

Table 3. Standardized Incidence Rates for Ischaemic Heart Disease Death

Thus, in this more valid comparison, New Zealand ranks fifth for males and females.
<table>
<thead>
<tr>
<th>Country</th>
<th>MALES</th>
<th>FEMALES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25-34</td>
<td>35-44</td>
</tr>
<tr>
<td>Scotland</td>
<td>9.2</td>
<td>94.9</td>
</tr>
<tr>
<td>Sweden</td>
<td>2.3</td>
<td>25.3</td>
</tr>
<tr>
<td>U.S.A. (1971)</td>
<td>9.3</td>
<td>85.5</td>
</tr>
<tr>
<td>Denmark</td>
<td>3.5</td>
<td>39.4</td>
</tr>
<tr>
<td>England, Wales</td>
<td>6.3</td>
<td>66.4</td>
</tr>
<tr>
<td>Ireland</td>
<td>7.0</td>
<td>63.2</td>
</tr>
<tr>
<td>Norway</td>
<td>4.2</td>
<td>39.5</td>
</tr>
<tr>
<td>Finland</td>
<td>6.7</td>
<td>113.3</td>
</tr>
<tr>
<td>Australia (1971)</td>
<td>6.3</td>
<td>68.0</td>
</tr>
<tr>
<td>New Zealand</td>
<td>6.6</td>
<td>58.9</td>
</tr>
<tr>
<td>Canada</td>
<td>5.8</td>
<td>59.5</td>
</tr>
<tr>
<td>Israel</td>
<td>6.4</td>
<td>39.1</td>
</tr>
<tr>
<td>Netherlands</td>
<td>5.2</td>
<td>53.5</td>
</tr>
<tr>
<td>Germany (Fed. Republic)</td>
<td>4.7</td>
<td>36.5</td>
</tr>
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<td></td>
<td>2.6</td>
<td>26.2</td>
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</tr>
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<td>3.1</td>
</tr>
<tr>
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<td>2.5</td>
<td>19.4</td>
</tr>
<tr>
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<td>Denmark</td>
<td>1.1</td>
<td>10.0</td>
</tr>
<tr>
<td>England, Wales</td>
<td>1.3</td>
<td>10.1</td>
</tr>
<tr>
<td>Ireland</td>
<td>1.2</td>
<td>12.0</td>
</tr>
<tr>
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<td>18.3</td>
</tr>
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<td>Netherlands</td>
<td>1.1</td>
<td>10.3</td>
</tr>
<tr>
<td>Switzerland</td>
<td>0.2</td>
<td>3.0</td>
</tr>
<tr>
<td>Greece</td>
<td>1.0</td>
<td>2.4</td>
</tr>
<tr>
<td>Japan</td>
<td>1.0</td>
<td>2.8</td>
</tr>
</tbody>
</table>

In common with many other Westernized countries, CHD accounts for a sizeable proportion of all deaths (28% in N. Z.) and represents the greatest single cause of death for men over the age of 45 years (Maori and non-Maori), second only to cancer in women aged 45-64, and again dominant in women over 65 years of age (Maori and non-Maori). (See Figures 1 and 2) (44).

![Major Causes of Death in New Zealand](image)

**Figure 1.** Major Causes of Death in New Zealanders aged 45-65 years in 1973

Trends in coronary mortality are not easy to assess on the basis of death certification but the evidence suggests no dramatic change in Europeans between 1964-73. In Maoris, however, there does seem to be a substantial increase in both sexes and in most age groups (although absolute numbers are small). Such a pronounced difference between the two races is unlikely to be due solely to error or some collection bias and may well reflect the continuing change in life style of the Maori to conformity with European customs. (See Table 5) (45).
Table 5. Coronary Heart Disease: Mortality, 1964-73 (45)

| Year | Non-Maori Males | | | | | Non-Maori Females | | | | |
|------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|      | 35-- 45-- 55-- 65-- 75-- 85+ | | | | | 35-- 45-- 55-- 65-- 75-- 85+ | | | | | |
| 1964 | 65 284 814 1829 3312 5554 | | | | | 10 57 250 823 1986 3798 | | | | | |
| 1965 | 62 278 855 1729 3144 5238 | | | | | 9 41 279 837 1986 3813 | | | | | |
| 1966 | 62 299 849 1937 3373 5496 | | | | | 16 68 283 843 1983 3769 | | | | | |
| 1967 | 68 336 900 1781 3055 5166 | | | | | 20 65 309 784 1906 3849 | | | | | |
| 1968 | 73 309 928 1981 3667 7186 | | | | | 15 82 283 895 2149 4267 | | | | | |
| 1969 | 69 282 852 1865 3646 6200 | | | | | 16 62 268 838 2201 4478 | | | | | |
| 1970 | 73 269 879 1905 3715 5864 | | | | | 14 63 261 862 2103 4409 | | | | | |
| 1971 | 58 308 876 1889 3623 6272 | | | | | 18 69 238 809 2182 4468 | | | | | |
| 1972 | 55 269 833 1810 3707 6397 | | | | | 16 79 264 879 2267 4742 | | | | | |
| 1973 | 58 272 858 1930 3558 6732 | | | | | 17 67 269 777 2059 4489 | | | | | |

Maori Males

| Year | Non-Maori Males | | | | | Non-Maori Females | | | | |
|------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| 1964 | -- 252 687 1544 3333 | | | | | 37 154 586 711 2857 | | | | | |
| 1965 | 47 300 928 1775 4272 | | | | | -- 243 816 1240 3182 | | | | | |
| 1966 | 67 209 960 1722 4954 | | | | | 78 128 746 1868 2115 | | | | | |
| 1967 | 139 292 822 1073 3269 | | | | | 43 159 485 970 1942 | | | | | |
| 1968 | 82 335 842 1377 4600 | | | | | 51 375 526 1333 5200 | | | | | |
| 1969 | 81 332 890 2764 5252 | | | | | 71 269 730 474 3433 | | | | | |
| 1970 | 128 372 1077 2156 3404 | | | | | 39 178 585 1373 2979 | | | | | |
| 1971 | 104 344 1237 2197 4143 | | | | | 9 285 947 1572 3131 | | | | | |
| 1972 | 109 554 1188 2527 2707 | | | | | 27 243 720 1429 3369 | | | | | |
| 1973 | 107 458 1024 2460 4068 | | | | | 71 232 490 1932 2982 | | | | | |
Figure 2. Major Causes of Death in New Zealanders over 65 years in 1973

Foster and Hay (46) recently have published more detailed information concerning acute coronary deaths in New Zealand. They analyzed 4885 deaths from death certificates as the source document. These cases included any certificates stating that a form of acute or subacute ischaemic heart disease caused death, if such condition had been present less than two months. If the condition was more chronic than this, only acute myocardial infarction as the cause of death, was accepted. Thus a proportion of these cases were persons who did not have a Sudden Cardiac Death as usually defined and doubtless died of severe cardiac failure. All ages were considered and the study covered all of New Zealand.

They found that two-thirds of all coronary deaths occurred outside hospital and that one-half occurred within one hour of onset of the final illness. About 33% of European cases died in public hospitals, less than 1% died in the ambulance and about 47% died at their place of residence.
Rather surprisingly, it is also possible to show an excess of late deaths in younger persons occurring in the interval 1-8 weeks after onset of final illness \((p < .005)\). A problem here may be uniformity in criteria for fixing the onset of the final illness, among the hundreds of general practitioners filling in the death certificates. Overall, 29\% of cases had a postmortem performed.

A study of all 757 patients with myocardial infarction admitted to Auckland's three public hospitals was reported by Norris et al. (47) in 1968. Criteria for this diagnosis were that two of the following three be satisfied:

1. characteristic clinical presentation;
2. pathological Q waves, ST elevation, or T-wave inversion with evolutionary changes;
3. rise in serum aspartate aminotransferase to over 40 units/ml.

Of the 757 patients, 195 died during the hospitalization (26\% hospital mortality) and 50\% of these had portmortems. Thirty-four percent of deaths in these hospitalized cases occurred within the first 3 days, most of this due to the excess mortality from cases admitted within six hours of onset of symptoms. They found that admission status was of much greater value in predicting survival than past history.

In 1973 Norris and Caunt reported on delays in admission to the Greenlane Coronary Care Unit (48). In the setting of initial coronary care, the hospital mortality was now 17-20\%. However, there had been a large increase in the number of cases admitted to the hospital since 1967, almost certainly representing a change in distribution of severity of cases admitted. Milder cases, which would previously have been treated at home, were now probably
admitted due to increased public and doctor awareness of the epidemiology and risks of the condition. Fifty-five per cent of cases were admitted within six hours compared with 45% in 1967. This would be expected to increase observed mortality.

Time of onset was recorded as the time of the most severe chest pain preceding admission to hospital. 'The median time for total admission delay was approximately four hours, while the medians for patient, doctor, transport, and hospital delays were approximately 1\(\frac{1}{2}\) hours, 2 hours, 20 minutes and 10 minutes, respectively.' Norris comments that 'doctor-delay' did not occur in those patients who came straight to hospital by ambulance or private transport (1/6 of total).

He recommended that 'the treatment of choice for a patient with continuous ischaemic pain of more than 30 minutes' duration is to be transported by the quickest means of transport available to the nearest hospital which has a coronary care unit.'

There have been a few assessments of coronary risk factors in New Zealand populations. In 1961, Hunter and Wong (49) studied 1000 symptom free, actively employed males, coming from two broad occupational groups. Cholesterol was measured and found to rise with age until 47 years, thereafter falling. Representative figures of Mean Cholesterol levels (mg/100 mls) for age ranges 15-19 years, 45-49 years, 60-64 years are 187, 248, 236. Evans and Prior in 1969 (50) published the results of an investigation of residents of the small Wairarapa town of Carterton. Higher cholesterol
values were obtained than the previously quoted study but a different method was used to estimate cholesterol (Abell-Kendall method) (see Fig. 3 and 4).

Results were higher than those for Tecumseh (USA) residents (Abell-Kendall method also used). Conceivably this could relate to New Zealanders' dietary habits (see end Section 1.2).

Blood pressures (51) were also recorded in the Carterton study and the conclusions drawn were as follows, 'The mean blood pressure of adults in Carterton are of the same order of magnitude as those of some other urban populations of European origin and show similar variation with age. Owing to differences in technique and study design it is not appropriate to make more detailed comparisons between these surveys.'
Smoking habits (50) were recorded in Carterton and are shown in Table 6.

<table>
<thead>
<tr>
<th>Smoking Habit</th>
<th>Never Smoked</th>
<th>Given Up</th>
<th>Light (&lt;10/day)</th>
<th>Moderate (10-20/day)</th>
<th>Heavy (&gt;20/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>21%</td>
<td>24%</td>
<td>6%</td>
<td>20%</td>
<td>29%</td>
</tr>
<tr>
<td>Females</td>
<td>55%</td>
<td>10%</td>
<td>8%</td>
<td>17%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Table 6. Smoking Habits in Carterton (Evans et al. (50)).

These figures seem quite comparable with Keys Seven-Country data (28) for males at least.

Thus, on the data available the patterns of disease occurrence, treatment and distribution of risk factors, seem very similar to those of many European countries and the USA.
Data from the 1976 Population Census (52) is shown in Table 7.

<table>
<thead>
<tr>
<th>Category</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never smoked</td>
<td>37.4%</td>
<td>55.2%</td>
</tr>
<tr>
<td>Ex-smokers</td>
<td>21.4%</td>
<td>11.4%</td>
</tr>
<tr>
<td>0-9 per day</td>
<td>6.5%</td>
<td>8.2%</td>
</tr>
<tr>
<td>10-19 per day</td>
<td>12.6%</td>
<td>12.4%</td>
</tr>
<tr>
<td>20-39 per day</td>
<td>16.6%</td>
<td>9.8%</td>
</tr>
<tr>
<td>40+</td>
<td>2.7%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Not specified</td>
<td>3.1%</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

Table 7. Smoking Questionnaire Results From the 1976 Population Census.
Section 1.4: OBJECTIVES OF THIS STUDY

Indirect evidence suggests a modest increase in CHD deaths may have occurred during the last 30 years in many countries (53). However, 'reliable' records in most places have only been available since 1940 or later. Such records are usually death certificates and their validity must often be doubtful, bearing in mind the rather limited knowledge of the disease and crude diagnostic techniques used until recently. Nevertheless, it is clear that mortality remains high. Symptomatically, one British male in five will be afflicted by age 65 years (54), and one U.S. male in five will be afflicted by age 60 years (55).

Added to this is a further major difficulty. Of all CHD deaths, 42-58% occur within 1-2 hours of onset of acute symptoms (56-59, 33, 35). About as many die in the first 24 hours following an acute episode as in the next 5 years (60). Sudden death is the first manifestation of CHD in about 20% of these cases (61, 62).

At present the only reasonable solution seems to be a preventive rather than therapeutic approach, though this does not deny that therapy is important for those cases already suffering the disease. Intervention in a preventive approach needs a good knowledge of aetiological factors (or strongly associated factors). On a nationwide basis about 65% of the incidence variance is explained by dietary saturated fat intake. This was based on the correlation between prediction applying the USA data model to European and USA populations (28). Its significance for individuals within a population is probably considerable but this remains controversial.
It seems possible that the agreement would be improved further if the coefficient of determination was found for any one particular set of population data, using a logistic model which included second order terms.

The most important risk factor known seems to be the level of serum cholesterol and one of the important areas of intervention is assumed to be diet. However, the evidence that dietary differences exist, within populations between the hypercholesterolaemic CHD prone persons and those at lower risk, is controversial (63, 64, 65, 66).

New approaches seem indicated for further progress. The aims of these should be (a) (i) to consolidate present indications as to risk factors using more elegant statistical techniques than have commonly been used; (ii) to refine existing variables which have importance in risk of CHD, by more intensive investigation on previously studied populations. (b) Define further important variables by studying further the data relating to widely differing populations. This would allow correlations between differences in disease incidence and attributes of the populations, to be studied. Thus further intensive and further extensive studies are needed.

This present study contributes to several of these aims. It is in part a feasibility study as such has not previously been attempted in New Zealand for Europeans. The populations response, and the cooperation of the doctors were unknown quantities. The primary aim is to provide age specific incidence rates for acute coronary events in Auckland City. In so doing a random sample of all such events is defined and so data collected on these cases should be representative of all such events.
Statistically, a multivariate approach is clearly essential in relating personal habits, attributes, symptoms to either some facet of coronary disease, or the risk of developing the disease. Most studies previously done, with some outstanding exceptions have used only one, two or three independent variables at a time to investigate differences in the dependent variables between the corresponding subpopulations. These analyses have often been categorical - lumping observations within a particular range together (e.g., high cholesterol, low cholesterol etc.).

A more sophisticated approach uses multivariate regression. The stepwise approach is best, entering successively variables with the highest partial correlation coefficient. Epidemiologically, I believe, this is a sensible approach, as of several correlated independent variables, the one which is entered preferentially, is that which correlates highest with the dependent variable and thus is likely to be closer to this variable in any causal chain or other linkage. One can easily go on to calculate the multiple correlation coefficient and by squaring it obtain an estimate of the proportion of the total variance explained by the regression which has been performed. A Binary outcome (i.e., dependent variable) is harder to handle, but using the logistic transformation and preferably the maximum likelihood technique, it is possible to relate several independent variables to the binary dependent variable and thus obtain the estimated risk of an event (67).

Wherever possible these techniques will be used in this study.
Epidemiological investigations are usually expensive and particularly demanding in terms of time commitment. In view of this, and the nearly worldwide economic problems at the present time, any increase in efficiency should be useful. Sampling techniques are well known to increase efficiency and the design of the present study has utilized this fact.

This study does not contribute substantially to (ii) above, but is concerned particularly with (b), as it studies a population, which has many similarities but also some differences (e.g., diet) from populations previously studied. Any substantial differences in disease incidence between New Zealand and other countries could suggest hypotheses to explain these differences. Such hypotheses could conceivably involve new variables. The incidence of acute coronary events was previously unknown in Auckland and such knowledge is important for public health planning and awareness and hospital planning. Also the establishment of incidence at this point in time will provide a baseline to assess change at some future date.

A knowledge of the proportion of cases treated at home was also lacking and made incidence calculations on hospital data unreliable. An assessment of delays by patient in seeking treatment or delays in ability to obtain treatment would obviously be of considerable interest and would assist health care planners and guide as to the feasibility of coronary care ambulances.

The study is largely descriptive, but there are several hypotheses that it is intended to test whether:

1) Prodromal or longer term symptoms discriminate between the likelihood of development of the various coronary syndromes.
2) Unalterable characteristics of an individual (e.g., age, sex) also discriminate between the likelihood of development of the various coronary syndromes.

3) Habits or life-style characteristics (e.g., smoking, alcohol consumption) discriminate between the likelihood of development of the various coronary syndromes.

There are some limitations associated with the design of the study. The most serious is that of reliance on symptoms for notification and diagnosis (except for sudden death). Totally asymptomatic cases are thus missed. Other overseas investigations have shown that between 11-25% of all acute myocardial infarctions are silent (68, 69, 70). Also missed are cases where the symptoms are relatively mild or unrecognized in a stoical individual. Cases who present to the doctor late (e.g., after seven days) may miss being classified as a definite myocardial infarction due to lack of evidence, but would often have had symptoms sufficient to include them as a possible infarction.

Specifically excluded, are cases whose main symptoms prior to death have been due to severe cardiac failure and in whom death intervened without any episode particularly suggestive of acute myocardial infarction. Thus sudden death cases must not have been bed-ridden in the twenty-four hours prior to the acute deterioration.

Consequently, the study strictly relates only to diagnosed myocardial infarction and this will be assumed from here on.
Section 1.5: AUCKLAND CITY AND SUBURBS

Auckland city is situated in the northern part of New Zealand's North Island on and about a narrow isthmus which represents the narrowest part of the North Island. It is distributed around two large harbours, the Waitemata and Manukau. Temperatures (°C) are Mean Max: - Jan 21.9°, July 14.5°; Mean Min: - Jan 15.6°, July 8.4° and rainfall averages 1243 mm/year. (See Figs. 5 and 6). The region is volcanic with about a dozen extinct volcanic cones within the city area. The city and suburbs cover an area of more than 260 square kilometres (100 square miles).

For the purposes of this study, the author defined Auckland city and suburbs to be the area bounded by Kumeu and Albany in the north; Henderson and Titirangi in the west; Papatoetoe and Whitford in the south; and the coast on the eastern side. (See map, Fig. 7.) This region is mainly urban, but includes some more rural areas (e.g., Kumeu, Albany, Whitford). The total population included within these bounds is 635,985 (71). The age structure for the Central Auckland area is shown in Table 8 (71).

In the defined collection area which is a little smaller than the Central Auckland statistical division referred to in Table 8, the age range 35-69 years is slightly over represented with a total of 220,375 persons. It is this age range that data is collected from.
<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
<th>Percentage</th>
<th>Telephone Extension</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>84</td>
<td>96.64%</td>
<td>RR</td>
</tr>
<tr>
<td>60</td>
<td>58</td>
<td>65.10%</td>
<td></td>
</tr>
<tr>
<td>40 other</td>
<td>26</td>
<td>65.10%</td>
<td></td>
</tr>
<tr>
<td>ARCO5</td>
<td>66</td>
<td>80.7%</td>
<td>RR</td>
</tr>
<tr>
<td>45%</td>
<td>35-64</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>55% rest</td>
<td>30</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td>Age Range</td>
<td>0-4</td>
<td>5-14</td>
<td>15-19</td>
</tr>
<tr>
<td>-----------</td>
<td>-----</td>
<td>------</td>
<td>-------</td>
</tr>
<tr>
<td>%</td>
<td>10.2%</td>
<td>20.2%</td>
<td>8.9%</td>
</tr>
<tr>
<td>45-49</td>
<td>5.7%</td>
<td>5.0%</td>
<td>4.7%</td>
</tr>
<tr>
<td>50-54</td>
<td>3.3%</td>
<td>2.4%</td>
<td>1.6%</td>
</tr>
<tr>
<td>55-59</td>
<td>0.5%</td>
<td>0.2%</td>
<td></td>
</tr>
<tr>
<td>60-64</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70-74</td>
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<td></td>
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<tr>
<td>75-79</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80-84</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>85-89</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Figure 5. Mean Monthly Temperatures in Auckland, April 1974-March 1975
A particular feature of Auckland is the Polynesian population of 50,958 Maoris and 27,589 Pacific Islanders (71) (26.8% Cook Islanders, 13.8% Niuean and Tokelauan, 49.7% Samoan, 9.7% Other Islands). Hence Auckland contains the largest concentrated population of Pacific Islanders in the world - mostly Samoans and Cook Islanders. These people largely live in lower social class areas and are employed usually in unskilled or semi-skilled jobs. However, an increasing proportion of them are now New Zealand born and thus better educated.

In 1974, there were approximately 350 general practitioners and physicians in Auckland claiming the fee for service from the Health Department. Of these, 313 were in the defined area and had claimed more than $1000 in the previous year (72). Unfortunately, doctors in general have only a vague idea of their practice populations' sizes and most tend to serve the area surrounding their practice rooms. By far the majority of acute coronary
Figure 7. Map of Auckland
As Defined in this Study
cases would present either directly to hospital or to their general practitioner. A few specialist physicians have some cases for whom they act as the general practitioner, but generally see patients only on a referral basis.

The area is served by three large public hospitals - a) Auckland Hospital serves the central city area, eastern suburbs and the North Shore; b) Greenlane Hospital serves the western suburbs; c) Middlemore serves the southern suburbs. All three hospitals have modern Coronary Care Units staffed by well trained nurses, cardiologists and resident medical staff. As usual, monitoring and defibrillating equipment is standard. Patients normally spend 1-3 days in the unit depending on severity of infarct, complications and bed pressure.

There must be a death certificate written for any deceased person, usually by the patient's usual doctor. However not infrequently, the usual doctor feels uncertain as to the cause of death, has not seen the patient in the 3 months prior to death, or else is unable to be contacted over the weekend or a holiday period. So the case is referred to the coroner. In this eventuality a post mortem is performed. In general, unless the patient dies in hospital (when permission for post mortem may be sought) this is the only source of postmortem. One such coroner's office exists in Auckland.

Thus Auckland represents an ideal setting for an epidemiological study. The population is well educated and health conscious. Since 1969 a National Heart Foundation has been operative and actively promotes coronary disease prevention and research. The population is easily accessible and
nearly all citizens are able to name a local doctor as their own. A big advantage over, for instance USA, is that nearly all cases hospitalized for nonsurgical complaints would go to one of the three public hospitals. Also the local general practitioner is well acquainted with all facets of the patient's health as the primary care doctor is not a specialist. The population is not nearly as mobile as some overseas populations and this makes for easier followup.
CHAPTER 2

METHODS
Section 2.1: INTRODUCTION

A community-wide study of acute coronary events had never previously been attempted in New Zealand. The initial problem was to find an estimate of the number of cases likely to be encountered, and thus an estimate of the potential work load of the project. Our resources were limited. One professional person, (the author) and a secretary who worked four hours per day were the only personnel.

Norris' figures (47) were used as a guide to myocardial infarction numbers assuming the frequency of hospitalized cases had not altered substantially over the previous seven years. We guessed also the cases treated at home could amount to about 20% of the total.

Thus it was expected that about 500 cases of Definite Myocardial Infarction under 70 years of age would reach coronary care units, and about 100 would be treated at home. Also from death certification records and overseas figures it was expected that about 250 patients would suffer Sudden Cardiac Death - a few of whom would be represented in one of the previously mentioned groups.

Thus about 850 'definite' acute coronary events were predicted for Auckland in one year.

In addition, it was decided to include a further category of patient defined by W.H.O. (73) as Possible Myocardial Infarction. (Definitions considered later—p. 67). Such patients have been particularly noted since the advent of coronary care units where only about 55% of all admissions
constitute definite infarction (47). The majority of the remaining 45% constitute this group of cases. Little is known regarding the natural history or pathophysiology of this acute event. These Possible Infarction cases were also studied for one year which partially overlapped the collection period for the definite acute events. From the initial period of data collection an impression of the likely number of possible infarcts was gained and was thought to total around 320.

It was immediately clear that it would not be possible to cope with all cases. The only alternative seemed to be to take a sample of Auckland's population, and try to relate this to the whole population at risk. After some discussion it was decided that a random sample would be most advantageous and in particular would be superior to selecting a particular area or areas of Auckland to study in isolation. The problem with the latter design was the difficulty in ensuring that the selected population was representative of all of Auckland. It would have been possible to control for many factors of importance but in a disorder where only a modest proportion of the important risk factors or associated factors are known, there was no way of effectively controlling for the unknown factors. A random sample surmounts this problem.

The upper age limit of 69 years was selected for several reasons. It was clearly impossible to cope with infarctions and sudden deaths at all ages, as the incidence rises substantially over 70 years of age, in other similar communities. Secondly, elderly people are often not admitted to hospital for chest pains and sometimes not investigated as fully. Many patients are not able to give an adequate account of themselves in this age range. Also, the local practice was to admit all hospitalized patients up to 70 years of age
to coronary care units thus providing the opportunity for better documentation.

The lower age limit was arbitrary and selected as it was felt that acute coronary
events in persons less than 35 years of age would form a very small percentage
of the total. In fact such events were recorded, but in the 'postal survey',
there was no corresponding category defined except a broad group 'less than
35 years'. 
Section 2.2: REGISTRATION METHOD

Introduction

Conventionally, the estimation of disease incidence has involved the collection of all cases (73, 74) over a specified time period, usually in the form of a disease register. Such an enumeration of cases also allows further characteristics of the cases to be tabulated. Comparisons between defined subpopulations of the group can be made.

The collection of all cases is frequently difficult for several reasons:

1. Problems of manpower and finance in many centers.
2. Enlisting the continuing cooperation of professional people (often busy primary care doctors), for case notification over long periods of time is not easy.
3. Usually several investigators would be required for such a task and the problem of non-uniformity of use of diagnostic criteria arises.

This section describes a technique, whereby disease frequency is estimated with statistical credibility limits, using only a representative sample of the total population. Satisfactory information for most purposes can thus be gained by a single investigator.
Method

A) Sampling Technique

Find a personal characteristic which is assignable to every person in the population and has at least thirty reasonably equally distributed subtypes. A characteristic with fewer subtypes may be satisfactory so long as it is known not to be correlated with risk for the disease under investigation. Perhaps the most suitable characteristic would be the citizen's doctor, which may of course be correlated with disease risk, but as there are likely to be more than thirty doctors in the community this should not be a problem.

The method will be discussed below using disease incidence and the person's doctor as the selected characteristic as was used for this register. Select a suitable proportion of the doctors, so calculated, that their estimated cases of the disease can be coped with by the resources available. The selection should ideally be done using random numbers. Thus the population sample consists of the practice populations of the selected doctors, and the cases collected are the cases of these doctors only. Calculation of incidence requires the knowledge of the number in the sample population.

B) Sample Population Size Estimation

In most circumstances, the age/sex specific practice population of a particular practitioner will not be known with accuracy. Accordingly an independent assessment must be made. This is accomplished by a random selection of N' names off the electoral (or other convenient) community roll. Letters are sent to these N' citizens, simply requesting their age decade and who their local doctor is, or whom they would seek aid from, in the event of becoming ill.
This postal survey presents the usual response problems, but in the author's experience we anticipated and achieved a good response to two letters, where necessary a phone call and/or a visit.

This good response was attributed to:

1) The brevity of the questionnaire.
2) Community interest in medicine.

The number of letters $N'$ should be selected according to statistical criteria, which will be referred to in a later section. The proportion of replies who give one of the randomly selected doctors as their local doctor enables the formation of an estimation of the proportion of the community in our population sample. The expected proportion would be the same as the proportion of the total doctors selected. However the practice populations of the specific doctors randomly selected, may vary from that, hence this subsidiary survey (see Fig. 8).

C) Statistical Model (usually would refer to a single age-sex specific group)

Let:

$I$ = The underlying incidence of the disease for this community eliminating year to year random fluctuations.

$T$ = Total population at risk.

$D$ = Total number of doctors in the community.

$K$ = Total number of doctors randomly selected to participate.

$N$ = The number of letters returned from the $N'$ sent out to citizens in the postal survey.

$\Theta$ = True proportion of the population selected using the $K$ selected doctors (unknown).
\( \lambda \) = Expected number of disease cases from the \( T \) \( \theta \) individuals in the randomly selected population (unknown). \( \lambda = I \theta \ \cdot \ T \).

\( Y \) = Number of letters returned which named one of the \( K \) selected doctors as the citizen's doctor.

\( X \) = Observed number of disease cases from the \( K \) doctors' practices.

(Lower case letters represent realizations of the corresponding random variable in the sections which follow.)

It can readily be seen that \( Y \) is distributed binomially with the unknown parameter \( \theta \), as each letter reply can be represented as a random event with probability \( \theta \). Thus \( Y/N \) is an unbiased estimate of \( \theta \) and \( Y/N \cdot T \) an unbiased estimate of the population sample size.

\( I \cdot \theta \cdot T \) is the expected number of cases. As this is small compared with \( \theta \cdot T \) for most diseases, the binomial distribution of \( X \) observed cases from the randomly selected sample of \( \theta \cdot T \) is closely approximated by a Poisson
distribution with parameter \( I \cdot \theta \cdot T = \lambda \). Thus \( X \) is an unbiased estimate of \( I \cdot \theta \cdot T \).

It can be shown that to a close approximation, when \( N \) is large, that

\[
E \left[ \frac{X}{Y} \cdot \frac{N}{T} \right] = I + I \cdot \frac{(1 - \theta)}{N \cdot \theta}
\]

Thus the relative error involved in this approximation is less than

\[
\frac{1 - \theta}{N \cdot \theta}
\]

It can be seen that for practical purposes \( \frac{X \cdot N}{Y \cdot T} \) is an unbiased estimate of \( I \), providing \( N \) is of sufficient size.

D) Credibility Interval for Sample-Determined Incidence Ratio

In this section, in many cases, the use of the terms \( \text{Pr}(a = b) \) or \( L(a = b | c) \) is not strictly appropriate as we are dealing with continuous variables and should be considering the probability density function value associated with the point \( a = b \). For ease of understanding the discrete nomenclature has been used. \( \text{Pr}(I \mid X = x, Y = y, N, K, T) = \int_0^1 \text{Pr}(\lambda \mid X = x, \theta, T) \cdot \theta \cdot T \cdot \text{Pr}(\theta \mid Y = y, K, N) \cdot d\theta \ldots \ldots \ldots \) (Eqn. 1). To preserve the characteristics of a density function it is necessary to multiply by \( \frac{d\lambda}{dI} \) as in Eqn. 1 above.

By Bayes' theorem (75)

\[
\text{Pr}(\lambda \mid X = x, \theta, T) = \frac{L(X = x \mid \lambda = I \cdot \theta \cdot T, \theta, T) \cdot \text{Pr}(\lambda \mid T, \theta)}{\int_0^T L(X = x \mid \lambda = I \cdot \theta \cdot T, \theta, T) \cdot \text{Pr}(\lambda \mid T, \theta) \cdot d\lambda}
\]
Now the prior probability here $\Pr(\lambda)$, is taken to be constant for all values of $\lambda$ likely to contribute significantly in the calculation of $L(X|\lambda)$, having observed a value of $X$. The bases for this decision are:

I. Usually this kind of investigation is conducted in the specific circumstance of loss of confidence in or lack of previous information.

II. Commonly, previous studies would have used different definitions for diagnosis and may have taken nonrandom populations.

III. The form of the distribution of $\lambda$, the underlying true mean number of cases due to random factors, over time, is usually completely unknown, in part due to the common lack of knowledge of the factors that contribute aetiologically to the disease.

If a prior distribution can be estimated, this could be inserted.

Note that the denominator of the last mathematical expression is

$$\int_{0}^{\theta \cdot T} \frac{e^{-\lambda} \lambda^{x}}{x!} \cdot M, \ d\lambda$$

(where $M$ is the constant prior density assumed for $\lambda$)

$\frac{1}{\hat{M}}$, where $\hat{\theta} \cdot \hat{T}$ is large. Therefore $\Pr(\lambda|X=x, \theta, T.) = \frac{e^{-I \cdot \theta \cdot T}}{x!} (I \theta T)^{x}$

substituting $I \cdot \theta \cdot T.$ for $\lambda$.

Similarly considering the latter portion of Eqn. (1)

$$Pr(\theta|Y=y,K,N) = \frac{L(Y=y|N,\theta)Pr(\theta|\text{letter replies,K})}{\int_{0}^{1} L(Y=y|N,\theta)Pr(\theta|\text{letter replies,K}) \cdot d\theta}$$

(where the letter replies are used to estimate $\sigma^2$ (see Appendix A)).
\[
(N \choose y) \theta^y (1-\theta)^{N-y} \frac{1}{\sqrt{2\pi} \sigma} e^{-0.5(\theta \frac{K}{D})^2 / \sigma^2} \\
= \int_0^1 \int_0^1 \int_0^1 \int_0^1 \frac{e^{-I \cdot \theta \cdot T \cdot x \cdot \theta \cdot T \cdot \theta \cdot (1-\theta)^{N-y} \cdot e^{-0.5(\theta \frac{K}{D})^2 / \sigma^2}}}{e^{-I \cdot \theta \cdot T \cdot x \cdot \theta \cdot T \cdot \theta \cdot (1-\theta)^{N-y} \cdot e^{-0.5(\theta \frac{K}{D})^2 / \sigma^2}}} \, d\theta \, d\theta \, d\theta \, d\theta
\]

where \( \sigma^2 \) is the variance of \( \theta \) when a 100. \( K/D\% \) random sample of the \( D \) doctors is made many times. This will be a function of the variability of individual practice sizes.

\[ E(\theta) = K/D \] and by the central limit theorem, it can be assumed that \( \theta \) is distributed Normal \( (K/D, \sigma^2) \) to a close approximation (see Appendix A for fuller explanation of this).

Thus from Equation (1) \( \Pr(I \mid X = x, Y = y, K, N, T) = \)

\[ \int_0^1 \int_0^1 \int_0^1 \int_0^1 \frac{e^{-I \cdot \theta \cdot T \cdot x \cdot \theta \cdot T \cdot \theta \cdot (1-\theta)^{N-y} \cdot e^{-0.5(\theta \frac{K}{D})^2 / \sigma^2}}}{e^{-I \cdot \theta \cdot T \cdot x \cdot \theta \cdot T \cdot \theta \cdot (1-\theta)^{N-y} \cdot e^{-0.5(\theta \frac{K}{D})^2 / \sigma^2}}} \, d\theta \, d\theta \, d\theta \, d\theta \]

This expression must be integrated with respect to \( I \) over \( 0 \leq I < Z \) where \( 0 \leq Z < 1 \) to give the probability distribution function of \( I \). Notice that the denominator does not contain \( I \) and can be calculated initially and retained as a constant. A Romberg double integration routine has been used by the author, for the distribution function calculation.

E) Prior Distribution of \( \theta \) and Estimation of \( \sigma^2 \) (See Appendix A).
F) Simple Evaluation for the Planning Stage

The number of cases obtained and the number of letters sent to randomly selected citizens will clearly influence the credibility interval surrounding the obtained incidence result.

A preliminary guide as to satisfactory values for these variables, in terms of the width of the credibility interval can be estimated as follows.

A well known formula (77), states:

$$\text{Var} \frac{Z_1}{Z_2} = \frac{\text{Var}(Z_1)}{\{E(Z_2)\}^2} + \frac{\{E(Z_1)\}^2}{\{E(Z_2)\}^2} \cdot \text{Var}(Z_2)$$

where $Z_1$ and $Z_2$ are independent random variables and where $Z_2$ has a small coefficient of variation. Consider $\lambda$ and $\theta$ as the random variables $Z_1$ and $Z_2$ and consider them to have approximately normally distributed probabilities with estimated means $x'$, $K/D$ and estimated $\text{Var}(\lambda) = x'$, where $x'$ is a guessed value of $X$.

Then approximate 95% credibility interval width for $I$ is

$$\hat{C} = \frac{4D}{T,K} \cdot \sqrt{(x' + \frac{x'(D-K)}{N,K})}$$

Table 9 shows a comparison of this estimate ($\hat{C}$) with the true estimate (C). Agreement is reasonably close. However, in the real situation the calculation of C would be made with values of $\frac{Y}{N}$ randomly differing from $K/D$, whereas here $\frac{Y}{N}$ was taken as equal to $K/D$ in calculating $C$. This would alter the credibility interval, to a limited extent as would a higher $\sigma^2$ than the value of 0.0001 assumed. However, the computation was found to be relatively insensitive to the value of $\sigma^2$. With this estimated credibility range and the
estimated value of \( I \) using \( \frac{K}{D} + \frac{Y}{N} \) in the formula \( I \approx \frac{X}{Y} \cdot \frac{N}{T} \), a basis for choice of \( N \) and \( K \) is established.

Another question would be to investigate the results of neglecting the variation of practice sizes, omitting the postal survey and estimating the credibility interval by consideration of the Poisson variable only, as in the total collect situation. The Poisson interval is calculated using the Bayesian approach, assuming constant prior density over the range of interest (See Part C). It was found (See Table 9) that the credibility interval width closely approximated to \( C \) at least under the restrictive conditions described above. However, it can be shown that the mean value will frequently be significantly biased, so that the credibility interval although similar in size will potentially be different in location (See Appendix B).

Although the Poisson method seems, under these circumstances at least, to give a good credibility interval width approximation, it is more difficult to calculate than the variance ratio method. Due to the potential bias mentioned above, the Poisson method alone will generally be unsuitable for the 'exact' description of the distribution of \( I \), hence the previous theory.

G) Discussion

It may be thought a disadvantage that the incidence result obtained is not absolute but comes as an estimate, with a credibility interval. To a limited extent this is true. However, it should be realized that even where a total collect is obtained, over say a one year period, the result is still an estimate in the sense of relating it to the underlying factors at work in the community producing this incidence. Although, it is an exact result for the
year in question, if one postulates in the next year that there has been no significant change in any of the major underlying causal factors, a different observed incidence would be expected due only to random factors. Thus data often reported as exact, is so only in a superficial sense.

In making comparisons at different points in time or between different places this random variation should be acknowledged and makes the seeming loss of accuracy using the sampling technique of lesser significance.

Consider a null hypothesis that the 'super-population' over different times and places is homogeneous and has the one underlying value of I. Then a one year total collect at a particular place during a particular year is statistically similar to a random sample from the 'super-population'. The number of events observed in such a sample should be binomially distributed with parameters T and I. Where I is small and T large this will be well approximated by a Poisson distribution with parameter I.T.

For the within population sampling scheme as described in this paper, the situation would be similar with binomial parameters \( \theta, T \) and I or Poisson parameter I. \( \theta, T \), if \( \theta \) was accurately known. This follows, as a random sample (K of D doctors) of a random sample (specific year and place) is still a random sample. The simple Poisson form, however, is complicated by the need to estimate \( \theta \) in this case.

The efficiency of the sampling scheme in terms of effort reduction, compared with credibility interval width extension, is generally high where the number of cases observed is not too small. Table 10 compares a total collect with various percentage collects in this regard.
<table>
<thead>
<tr>
<th>Alternative Incidence</th>
<th>PROP</th>
<th>X</th>
<th>$\hat{C}$ (Poisson)</th>
<th>(Ratio) $\hat{C}$ (Variance)</th>
<th>$C$ ('Exact')</th>
</tr>
</thead>
<tbody>
<tr>
<td>.0005</td>
<td>10%</td>
<td>1</td>
<td>.00267</td>
<td>.00202</td>
<td>.00270</td>
</tr>
<tr>
<td></td>
<td>20%</td>
<td>2</td>
<td>.00165</td>
<td>.00143</td>
<td>.00165</td>
</tr>
<tr>
<td></td>
<td>50%</td>
<td>5</td>
<td>.00095</td>
<td>.00090</td>
<td>.00095</td>
</tr>
</tbody>
</table>

| .005                  | 10%  | 10 | .0064             | .00687                        | .0067       |
|                       | 20%  | 20 | .0045             | .00482                        | .0046       |
|                       | 50%  | 50 | .0028             | .00296                        | .0028       |

| .05                   | 10%  | 100| .020              | .0334                         | .025        |
|                       | 20%  | 200| .014              | .0228                         | .014        |
|                       | 50%  | 500| .009              | .0125                         | .009        |

**TABLE 9**

Illustrative Comparative 95% Confidence or Credibility Interval Using Approximate and 'Exact' Techniques (N = 500, $T = 20,000$, $S^2 = .0001$)

The effect of sampling on the probability of detecting an incidence change has been investigated and will be presented elsewhere.

The method with some minor adjustments can also be used to measure disease prevalence.

**H) Conclusions**

A sampling technique may allow case collection over an entire age range, or an entire geographical area, where before only part could have been investigated. In many parts of the world, resources may be such that a total collect is not feasible. Thus, this method could potentially allow accumulation of data from many more centers with greater efficiency. As it is by the comparison of disease frequencies, relating to differing environments and groups of people, that aetiological clues are gained, such data would be valuable.
<table>
<thead>
<tr>
<th>Rs/Ri</th>
<th>95% Credibility Range</th>
<th>Expected number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.95</td>
<td>2.26</td>
</tr>
<tr>
<td></td>
<td>0.0645</td>
<td>0.0571</td>
</tr>
<tr>
<td></td>
<td>0.0396</td>
<td>0.0428</td>
</tr>
<tr>
<td></td>
<td>0.0227</td>
<td>0.032</td>
</tr>
<tr>
<td></td>
<td>0.0049</td>
<td>0.0078</td>
</tr>
<tr>
<td></td>
<td>0.0004</td>
<td>0.0017</td>
</tr>
<tr>
<td></td>
<td>0.0004</td>
<td>0.0017</td>
</tr>
<tr>
<td></td>
<td>0.0004</td>
<td>0.0017</td>
</tr>
<tr>
<td></td>
<td>0.0004</td>
<td>0.0017</td>
</tr>
</tbody>
</table>

**TABLE 10**

Ri = Credibility interval using a total cohort.
Re = Credibility interval using a sample.
Section 2.3: COMPARISON OF DISEASE FREQUENCIES
ESTIMATED BY THE USE OF EITHER
TOTAL OR SAMPLE POPULATIONS

Comparisons of disease frequencies between populations at the same
location at different times or between populations at different locations is a
fundamental tool of epidemiology. It is by such comparisons that clues can be
gained as to aetiology. A significant change in disease frequency implies a
cause, which can be searched for.

As discussed previously (Section 2.2), even where the whole population
has been used to estimate the disease frequency, this result is still an
estimate in terms of relating it to possible causal factors, although the result
is exact for the period of collection. Such an estimate should be associated
with a credibility interval.

This implies that an apparent difference in disease frequency, even
where two complete populations have been used for the estimate may be due
to chance factors only and could be substantially different if repeated. The
question now is when does a difference become large enough to be meaningful
and suggest a true difference between the populations. The magnitude of the
apparent difference and the number of persons involved in each estimate are
clearly the important parameters in making this decision.

The methodology for making the comparison is straight-forward if the
whole population has been used for both estimates, thus collecting all cases
of the disease for the relevant time period. If however a random sample of
the population has been used to estimate disease frequency as in the present
study the comparison is not so easy.
The purpose of this section is to consider means of making pairwise comparisons where a sample population has either i) not been used for either frequency estimate, ii) been used for one of the frequency estimates, iii) been used for both frequency estimates. Initially, consideration is given to simultaneous comparisons of disease frequency from more than two populations. Illustrative examples will be given using results from the WHO myocardial infarction community registers for total population estimates (32), and results from the present study as a sample population estimate. The decreased power associated with the sample population estimates will be balanced against the decreased effort and resources required in data collection.

Definitions

Let:

i) \( X_1, X_2 \) be the number of cases observed during the two respective periods of collection. This is regardless of whether a sample or a total population was used.

ii) \( T_1, T_2 \) be the total populations at risk in the communities under investigation (not sample population numbers).

iii) \( \lambda_1, \lambda_2 \) be the true disease frequencies for each population (unknown).

iv) \( \hat{I}_1, \hat{I}_2 \) be the estimated disease frequencies for each population.

v) \( \lambda \) be the hypothesized underlying disease frequency for both populations under the null hypothesis that \( \lambda_1 = \lambda_2 \).

vi) \( \lambda_1, \lambda_2 \) be the expected number of disease cases detected from either total or sample populations, as appropriate, if random variations could be eliminated (unknown).
The following variables are relevant only to sample population estimates.

vii) $N_1, N_2$ be the number of letters returned from randomly selected citizens inquiring as to their doctor.

viii) $Y_1, Y_2$ be the number of letters returned naming one of the selected doctors as that citizen's doctor.

As previously discussed (Section 2.2), it is assumed that the $X_i$ are distributed according to binomial distributions closely approximated by Poisson distributions varying about the respective $\lambda_i$. The $Y_i$ are distributed according to binomial distributions with parameters $N_i, \theta_i$ ($i = 1, 2$).

ix) $\theta_1, \theta_2$ be the actual proportion of the populations served by the selected doctors (unknown). Then $N_1, \theta_1$ and $N_2, \theta_2$, respectively, are the expected numbers of letters returned from citizens naming a selected doctor.

The following portion of this section derives two tests, for the situation of information being available for $n$ populations where a total population was used and $m$ populations where a sample population was used. In this situation where a multiple comparison is made a simultaneous test is appropriate. As special cases of this theory, tests for pairwise comparisons are readily derived. This is so whether one or both populations are sample populations.

Let $L$ be the likelihood of the observations $X_1, X_2, \ldots, X_{n+m}$ $Y_{n+1}, \ldots, Y_{n+m}$.
Consider the null hypotheses \( H_0: \lambda_1 = \lambda_2 = \ldots = \lambda_n = \ldots = \lambda_{n+m} = \lambda \)

Set \( \hat{\lambda}_i = \hat{\lambda}_i T_i, \quad i = 1, 2, \ldots, n, \quad \hat{\lambda}_j = \hat{\lambda}_j T_j, \quad j = n+1, \ldots, n+m \)

Take the logarithm of the likelihood and differentiate with respect to \( \lambda \).

Then solving for \( \hat{\lambda} \)

\[
\hat{\lambda} = \frac{x_1 + x_2 + \ldots + x_n + x_{n+1} + \ldots + x_{n+m}}{T_1 + T_2 + \ldots + T_n + T_{n+1} + \ldots + T_{n+m}}
\]

Equation (1)

Next differentiate the log likelihood function with respect to \( \hat{\theta}_j \) and find that

\[
\hat{\theta}_j = \frac{\hat{\lambda} T_j + \hat{\lambda} N_j - \sqrt{(\hat{\lambda} T_j + \hat{\lambda} N_j)^2 - 4\hat{\lambda} T_j (\hat{\lambda} N_j + \hat{\lambda} y_j)}}{2\hat{\lambda} T_j}
\]

Equation (2)

by solving the quadratic equation in \( \hat{\theta}_j \). That the negative root is appropriate is shown. Suppose the positive square root is in fact correct. Then in this situation notice that if the quantity under the square root sign (say \( A \)) is greater than \( (\hat{\lambda} T_j - N_j - X_j)^2 \) (=B, say), then \( \hat{\theta}_j > 1 \) which is impossible.

By expanding \( A \) and \( B \) it is easy to show that \( A = B + \hat{\lambda} T_j (N_j - Y_j) \). As \( N_j - Y_j \) is always \( > 0 \), then \( A > B \). Consequently the postulated positive
square root sign is incorrect.

Now substituting for \( \hat{\theta}_j \) in equation (1) rearranging it slightly

\[
\sum_{i=1}^{n} (x_i) + \sum_{j=n+1}^{n+m} (x_j) = \hat{\theta}(2, \sum_{i=1}^{n} (T_i) + \sum_{j=n+1}^{n+m} (T_j)) + \sum_{j=n+1}^{n+m} (N_j - \sqrt{(T_j + x_j + N_j)^2 - 4(x_j + y_j)^2 T_j})
\]

\[
\text{Equation (3)}
\]

This can be solved numerically for \( \hat{\theta}_j \). Once \( \hat{\theta}_j \) is found, the \( \hat{\theta}_j \) can be found by substituting in the \( m \) equations of the same form as equation (2).

Then using the defined relationships, the \( \hat{\lambda}_k \), \( k = 1, 2, \ldots, n+m \) can be found.

Having then found the maximum likelihood parameters, the test to be used must be decided. The author has investigated the characteristics of two types of test: i) the minimum chi-squared 'goodness of fit' test, ii) the likelihood ratio test.

i) Minimum Chi-squared Test

This test can be constructed by noting that there are \( n+2m \) deviations from maximum likelihood estimates of parameters, viz. \( (X_i - \hat{\lambda}_i) \), \( i = 1, \ldots, n \); \( (Y_j - N_j \cdot \hat{\lambda}_j) \), \( j = n+1, \ldots, n+m \). The test could then be considered a goodness-of-fit test, performed by the use of the well known \( \chi^2 \) technique. Such a test, using maximum likelihood values for the expected values gives, to a close approximation, a minimum chi-squared statistic (79). There are \( m+1 \) constraining equations corresponding to equation (3) and the \( m \) equations of the form of equation (2).
Thus \[ \chi^2_{n+m-1} = \sum_{i=1}^{n} \left( \frac{x_i - \hat{\lambda}_i}{\hat{\lambda}_i} \right)^2 + \sum_{j=n+1}^{n+m} \left( \frac{y_j - \hat{\theta}_j}{\hat{\theta}_j} \right)^2 + \sum_{j=n+1}^{n+m} \left( \frac{y_j - N_j \hat{\theta}_j}{N_j \hat{\theta}_j} \right)^2 \]

is the simultaneous test as required.

ii) **Likelihood Ratio Test**

Under the hypothesis \( H_0 \) \( \lambda_1 = \lambda_2 = \cdots = \lambda_{n+m} = \hat{\lambda} \)

Thus \[ R = \frac{L_{H0}(\hat{\lambda}, \hat{\theta}_{n+1}, \cdots, \hat{\theta}_{n+m}; x_1, \cdots, x_{n+m}, y_{n+1}, \cdots, y_{n+m})}{L(\hat{\lambda}, \hat{\theta}_{n+1}, \cdots, \hat{\theta}_{n+m}; x_1, \cdots, x_{n+m}, y_{n+1}, \cdots, y_{n+m})} \]

Then \(-2 \ln R \sim \chi^2_{n+m-1}\) for large numbered observations of the constituent distributions (80).

On substituting for the numerator and denominator in \( R \), the test becomes

\[ -2 \ln R = -2 \left\{ \frac{\sum_{i=1}^{n} \{ (x_i - \hat{\lambda}_i)^2 \} + x_i \ln \left( x_i / \hat{\lambda}_i \right) }{\sum_{i=1}^{n+m} \{ (x_i - \hat{\lambda}_i)^2 \} + \sum_{j=n+1}^{n+m} \{ (y_j - \hat{\theta}_j)^2 \} / \hat{\theta}_j \} \right\} \]

The situations of \( n=2, m=0; m=2, n=0; n=1, m=1 \), correspond to the various types of pairwise tests using combinations of either total or sample populations. Most comparisons would likely be pairwise and of course involve a \( \chi^2_1 \) test.

Which of these two tests should be used? The maximum likelihood technique is more commonly used in statistical testing and theoretically involves somewhat closer approximations. Mr. Peter Hannan and the author performed a simulation study (to be published) for the circumstances
of either \( m=2, n=0; m=1, n=1 \). For many differing values of the \( \lambda_k \)'s and \( N_j \theta_j \)'s (where appropriate) random variables were generated 1000 times and the two tests performed on each occasion. It was found that when the smallest \( \lambda_k \) is \( \geq 10 \), the power of the two tests was essentially identical. Where one or both of the \( \lambda_k \)'s was very small (say < 10), the minimum chi-squared test seemed the test of choice. It gave results very close to the prescribed level even for \( \lambda_k \)'s = 1. Sometimes the observed \( \alpha \) was a little higher, sometimes a little lower than the \( \alpha \) expected if the approximations had been satisfied. In contrast, the likelihood ratio test became consistently nonconservative where small numbers were involved.

This result seems in good agreement with that of Larntz who investigated these two tests in the closely related problem of a 2x2 contingency table (81). Therefore, as the minimum chi-squared test is also computationally easier, there seems little point in using the likelihood ratio test for either small or large numbers.

Where \( n=2, m=0 \), i.e., a pairwise comparison where both centers used total populations, the usual test for comparison of Poisson variables can be used. This is essentially a 2x2 contingency table \( \chi^2_1 \) test where the second line of the table is neglected as the \( T_i \) so greatly exceed the \( X_i \). The minimum chi-squared test, as derived, corresponds exactly to this usual test, without continuity correction. The author has not used continuity corrections even for small numbers as according to the work of Larntz (81) errors are quite small with the minimum chi-squared technique, and fluctuate about the correct value. The use of the continuity correction results
in quite over conservative results and Larntz does not recommend its use (personal communication).

When incidence estimates become available either at different centres, or else at the same place at different points in time, a logical further investigation is to investigate the habits and environments of two populations experiencing differing attack rates of ischaemic heart disease. It would clearly be important to establish that the apparent differences given by estimates of disease frequency, were likely to be real. If the differences were not statistically significant, it is quite possible that the apparent differences in disease frequency would have disappeared, or even reversed if the registers had been repeated one year later.

Where comparisons are to be made, it is important that definitions of disease and methods of case collection be comparable. The application of these tests to situations where this is not so would likely give misleading results due to comparisons of slightly different disease entities.
A) Data Collection

It was clear that a major portion of the effort would have to be spent on making the diagnosis according to defined criteria.

Cases could be collected from several possible sources.

i. Hospitals were an obvious source as some patients present directly to the Accident and Emergency Departments, and most cases are admitted here.

ii. The general practitioner would also need to be involved to find cases treated at home. He would provide a back up source of notification for the hospital cases which he admitted. These should be ascertained both from the hospital and the general practitioner. He would be an important source of Sudden Death cases not surviving to be admitted to hospital and for various reasons not being referred to the coroner.

iii. The remaining Sudden Deaths must be referred to the coroner by the police. Thus a liaison with the coroner was also necessary.

Collection from hospitals was quite feasible as there were only 3 public hospitals admitting medical patients. None of the few private hospitals have coronary care units and it was thought that no acute coronary patients below 70 years of age would be admitted to such hospitals. An exception was the
Mater Misericordae Hospital which is the largest private hospital. A few patients may be admitted here, and for this reason, a liaison was established with the Medical Superintendent of this hospital.

It was decided to visit the three public hospitals twice weekly. The admitting list for the previous week was readily available and could rapidly be reviewed. Any cases with diagnoses similar to the following would be followed up:

a) Myocardial infarction  
b) Heart attack  
c) Chest pain  
d) Ischaemic Heart Disease  
e) Left Ventricular Failure  
f) Breathlessness  
g) Atrial Fibrillation  
h) Arrhythmia  
i) Collapse

These diagnoses are usually provided by the admitting doctor.

While it is recognized that this list does not cover all possible presentations of acute myocardial infarction, there were two possible ways of minimizing error.

a) Before reaching the ward most patients were seen by a hospital medical officer, who would admit to the coronary care unit if he was at all worried by the possibility of acute myocardial infarction. Thus the diagnosis was, in effect, checked. Consequently, any case with an admitting diagnosis
not included above, but who was admitted to a coronary unit, was also followed.

b) Hopefully, the general practitioner could let us know of any missed cases; this would occur after patient discharge, when he would be advised of the diagnosis by the hospital.

The general practitioners were a key collection source and it was thought necessary to personally visit each selected doctor before the study commenced, to ensure his understanding and cooperation. Thereafter, it was proposed that the general practitioner should telephone into the author's office with the name of any definite or suspect case of myocardial infarction, or any case of Sudden Death—presumed cardiac. A phone which would be rapidly answered during business hours was a requisite and, as the author's secretary was part-time, it was necessary to install an extension to a more central office where instruction was given the secretarial staff. In addition, each month, the author's secretary would routinely contact any doctor who had not already advised a case during that month. She would simply ask if he had had any cases of suspected heart attacks or sudden deaths.

The coroner's office would be visited twice weekly by the author's secretary, who would be instructed in the relevant diagnoses, pathological terms and clinical presentations. She would select cases for further investigation and only patients of the selected doctors would be included in the study. Having made the diagnosis, further data concerning the patient was collected either from the patient or from close friends or relatives, should he be deceased. The doctor was contacted in all cases by the author and any
difficult areas of history were discussed. Also antecedent blood pressures and serum lipid results were requested. Most contact was by telephone but a few doctors requested that we use the mail. (See Appendix C and D for the two forms used.) As the study design ensured a random sample of Auckland's acute coronary events, there was clearly an opportunity to assemble some unbiased descriptive data concerning these disorders. Using this data, certain hypotheses could be tested.

Some personal data such as age, residence, height, weight, cigarette and alcohol consumption, and country of birth were collected. The acute medical history (often supported by a more long-term history) was usually necessary to make the diagnosis. Both acute and longer term cardiac histories were documented, with special attention being paid to the prodromal period, defined as the previous 28 days. Times of: onset of symptoms, call for medical aid, arrival of aid, arrival in hospital and arrival in coronary care unit were documented where relevant. The initial examining doctor's findings were recorded briefly, with emphasis on the cardiac findings (these were most commonly the findings of an examining practitioner outside hospital). Certain ECG characteristics had to be recorded to make the diagnosis, and a few further ECG characteristics were also documented. The Minnesota code was not used due to time limitations. Such a sophisticated record did not seem essential due to the fact that there was only one investigator using well defined criteria in a standard fashion. The outcome of the acute event in terms of life or death within 28 days was recorded. For fatal cases, relevant postmortem findings were recorded either from the hospital pathologist or the coroner.
The author endeavored to ask questions in a standardized way, particularly those relating to cigarette and alcohol consumption, where it is well known that interviewer bias can be important (82). The form of these questions was as follows:

a) 'Do you smoke cigarettes?'
   i) Response: 'Yes'
      'How many a day would you smoke on average?'
   
   or
   
   ii) Response: 'No'
      'Have you smoked within ten years?'

b) 'Do you drink any alcohol?'
   Response: 'Yes'
   'Thinking over the last one year, how much would you average each week?'
   Response: Usually rather lengthy and imprecise but gave a general overview of the consumption.

Then for each of Beer, Spirits, Wine and Sherry
   'How many (glasses, bottles, cans, flagons, nips - as appropriate) of (specific alcohol source) would you drink each week, then?'
   'Does this also include the weekend?'

In many cases it was necessary to consider weekdays and weekends separately and, occasionally, on a day-by-day basis.

A copy of the questionnaire can be found in Appendix E.
Several potential problem areas of data collection were immediately apparent and some thought was given to these. General practitioners are often overworked and every effort was made to minimize their time commitment in order to achieve maximum cooperation. The information required from them was scrutinized and any non-vital questions were omitted. It was realized that not all practitioners would order serum enzyme tests on suspected cases treated at home, or else they would commonly do so only for the first day. Thus it was arranged with a private laboratory to collect blood from such cases under the author's direction, if the practitioner's permission had been obtained. A copy of results would automatically be sent to the patient's doctor.

It was decided that an ECG machine would be essential to further investigate suspected cases who were treated at home. In many such cases ECGs may not be routinely ordered by the practitioner caring for the case and this would hinder our diagnosis. It was decided, in consultation with other cardiologists, that the results of such ECGs would normally be unavailable to the general practitioner. Only in circumstances where they revealed the patient to be in unrecognized danger would this not be adhered to. We proposed to take the ECG within 24 hours of notification of the case.

Another problem would be that of general practice locum tenens. When the usual doctor was to go on holiday, it would be stressed that he should tell his locum briefly of the objectives and organization of this study, so case notification could continue. The secretary's regular monthly phone call could also help here if she found a locum caring for the surgery. Weekend and night cover would sometimes be done by a locum service who would not
be aware of the study. This problem was not major as the locum service, not knowing the patients, would tend more readily to hospitalize suspect coronary cases. In addition, it is their policy to let the practitioner know within two to three days of any of his cases they had treated. Notification could then proceed normally.

Group practices are common in Auckland and emergency cover is often shared between the group members. In this case, the doctor(s) selected from the group to be in this study simply had to inform other group doctors of the project. In any event it would be normal practice for the emergency cover doctor to inform the patient's usual doctor the next day and referral would then be routine.

These last difficulties are important only for cases treated at home as any hospitalized would be ascertained from the hospital.

A more serious problem would be the occasional group practice which shared patients in such a way that as patients arrived for consultation they consulted with whoever of the partners was free at that time. Thus patients are group patients rather than patients of a specific doctor. Knowing that such situations would be uncommon, it was decided that if some partners of such a practice were selected then all partners would be involved, but only a proportion of their referred cases would be randomly accepted—corresponding to the proportion of all partners initially selected for participation in the study.

By comparison with census data, it was found that the electoral roll contained only about 88% of the population in this age range. This limitation
was accepted for the postal survey, as we had no alternative. However, it seems unlikely that those citizens not on the roll would have a significantly different proportion served by the selected doctors, as these doctors were randomly selected.
Section 2.5: DEFINITIONS

Definitions for the first two types of acute coronary events were those defined by W. H. O. (1969), (73), as follows:

i) Definite Acute Myocardial Infarction
   1. ECG shows unequivocal serial changes, or
   2. history typical or atypical, together with ECG equivocal and elevated enzymes, or
   3. typical history and elevated enzymes with ECG negative or not available, or
   4. fatal cases, whether sudden or not, with naked-eye appearances of fresh myocardial infarction and/or recent coronary occlusion found at necropsy (antemortem thrombus, haemorrhage into an atheromatous plaque or embolism)

ii) Possible Acute Myocardial Infarction
   1. Living patients, with typical pain, whose ECG and enzyme results do not place them in the definite acute myocardial infarction group. There must be no good evidence for any other diagnosis for the attack, or
   2. fatal cases whether sudden or not (where there is no good evidence for another cause of death, clinically or at autopsy, and not in the definite acute myocardial infarction category)
a) with a history of pain, typical or atypical, or
b) without a history of pain, but with evidence of chronic coronary occlusion, or stenosis, or old myocardial scarring at necropsy, or
c) with clinical evidence of chronic ischaemic heart disease.

iii) Sudden 'Coronary' Death

Death within 24 hours of some distinct change in the patient's state of health, provided:

a) the new symptoms were consistent with a primary cardiac cause for the change in health status,
b) the patient had not been bedridden during the 24 hours before the symptomatic change,
c) the new symptoms may constitute the fatal event,
d) any postmortem conducted did not reveal pathological change which would suggest that ischaemic heart disease was not the primary cause of death,
e) there was no history or antemortem physical findings of severe valvular dysfunction or other nonischaemic cardiac disease that may have caused the death.

iv) Electrocardiographic Changes Supporting Acute Infarction

The ECG classification was based on consideration of all ECG records following the attack and, if available, records taken immediately beforehand.
Unequivocal ECG Changes of Acute Infarction (Type A in Questionnaire)

1. Development of a pathological Q wave, and/or
2. the evolution of an injury current which lasts for more than one day (where an S-T elevation above the baseline of at least 2mm was necessary for consideration as an injury current).

The interpretation of at least two ECG records is therefore necessary for the establishment of this category.

Equivocal ECG Changes of Acute Infarction (Type B in Questionnaire)

1. Evolution of an injury current that disappears within 24 hours or where an injury current is present when only one record is available, or
2. a stationary injury current, or
3. symmetrical inversion of the T wave, or
4. bundle branch block with additional Q wave, or
5. pathological Q wave where only a single record is available.

Other ECG abnormalities (Type C in Questionnaire)

1. Where morphological abnormalities exist that do not conform to the pattern as described under unequivocal or equivocal changes above, e.g., (Heart block, bundle branch block, old Q waves where multiple records available).

v) Other Specified ECG Abnormalities

a) Left Ventricular Hypertrophy

This was defined as any two of the following:
1. Left axis deviation beyond 0°;
2. Either of, $S_2 + R_5 > 35\text{ mms.}$, or $R > 20\text{ mm in AVL}$;
3. ST-T segment depression of a 'left ventricular strain type' (i.e., $J$ point less depressed than the rest of the segment, the S-T segment has a straight line slope downwards from the $J$ point and terminates in a $T$ wave which is in an opposite direction from the major direction of the QRS complex).

b) **First-Degree Heart Block**

The P-R interval is fixed and consistently greater than 0.21 sec.

c) **Second-Degree Heart Block**

A variable P-R interval but some ventricular response to a supraventricular pacemaker still exists.

d) **Third-Degree Heart Block**

Total incoordination between the supraventricular pacemaker and ventricular response in the presence of a bradycardia.

e) **Left Anterior Hemiblock**

Left axis deviation to at least -30°, where the initial ventricular vector is superiorly directed and the final vector inferiorly directed, in the frontal plane.

vi) **Serum Enzyme Level Criteria**

Most enzyme results came from the laboratories of the three main hospitals which worked largely independently, employing slightly different ranges of tests and using their own 'normal' limits. However,
in each case, these were clearly specified. A more difficult problem related to elevations due to non-cardiac causes, this particularly relating to SGOT and CPK. In view of this it was deemed necessary to use rather conservative criteria for abnormality, and in each case to have an equivocal and unequivocal range of elevation as follows:

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Normal Range (units)</th>
<th>Equivocal Range (units)</th>
<th>Unequivocal Range (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum glutamic-oxaloacetic transaminase (Aspartate amino-transferase) (83, 84)</td>
<td>0 - 40</td>
<td>41 - 99</td>
<td>100</td>
</tr>
<tr>
<td>Creatine phosphokinase (Auckland Hospital) (85)</td>
<td>0 - 4</td>
<td>5 - 14</td>
<td>15</td>
</tr>
<tr>
<td>Creatine phosphokinase (Greenlane Hospital) (86)</td>
<td>0 - 60</td>
<td>61 - 99</td>
<td>100</td>
</tr>
<tr>
<td>Hydroxybutyrate dehydrogenase (Greenlane Hospital) (87)</td>
<td>100 - 200</td>
<td>-</td>
<td>200</td>
</tr>
</tbody>
</table>

An **Enzyme Elevation** was defined as elevation of any one enzyme into the unequivocal range, or elevation of more than one enzyme into the equivocal range, where there was no other diagnosis which could have accounted for the elevations (e.g., hepatic disease).

vii) **Acute Symptoms**

The criteria for the symptoms of acute myocardial infarction are those defined by W.H.O. (73), as follows:
A Typical History is characterized by retrosternal pain with the following characteristics:

a) diffusion through the chest, anteriorly or generally, which may remain localized in the chest or radiate to the shoulders, arms, jaws or abdomen on one or both sides;

b) resistance to nitroglycerine if taken during the attack;

c) duration of more than 20 minutes;

d) usually severe and at times of agonizing intensity.

An Atypical History is characterized by symptoms such as dyspnoea, a sense of suffocation, 'indigestion', syncope, general malaise, sweating or acute cardiac failure.

viii) Geographical Area

Each patient's place of residence was placed in the relevant population census subdivision. This was coded and recorded. (See Fig. 9). The total area considered as 'Auckland' for the purposes of this study is defined in Section 1.5.

ix) Social Class

This was determined solely on the basis of area of residence. Bowman and Hosking (88) performed a factorial analysis of the socioeconomic and ethnic structure of the Auckland community as related to urban area. They used 53 variables from the 1966 Population Census to perform this analysis. One of the two main
factors derived (factor II) clearly related to social class. They were able to divide the 64 census subdivisions of the Auckland suburbs to Low, Medium and High social class categories (see Fig. 9), and we have followed this classification.

x) Race

The difficulties of precisely defining a person's race were deemed too complex to deal with in this study. Consequently, the race as stated by the person was simply accepted. This problem relates particularly to Maoris where mixed descent is now the rule.
xi) **Place of Treatment**

A person was considered to have been treated in hospital only, if he reached hospital within 24 hours of the onset of the acute event. If hospital was reached between 24-72 hours after the onset, he was considered to have been treated at hospital and at home. If hospital was reached more than 72 hours after onset, or not at all, he was considered to have been treated at home.

xii) **Angina** was considered to be a nonlocalized retrosternal pain, (with or without radiation to throat, shoulder or arm), brought on usually by exertion or emotional influences, responding to rest or nitroglycerine (if used) within 20 minutes.

xiii) **Acute Coronary Insufficiency** was considered to be a nonlocalized retrosternal pain (with or without radiation to throat, shoulder or arm), often occurring without obvious cause, and not responding to rest or nitroglycerine within 20 minutes.

xiv) **Previous Myocardial Infarctions** were accepted as such, only when documentation was seen by the author to warrant classification as a definite myocardial infarction according to the criteria used in this study.

xv) **Breathlessness** was accepted as such only when it was present to such a degree as to interfere with the person's daily activities. Specific situations were mentioned as follows: a) climbing a flight
of stairs, b) fast walking on the flat, c) walking at a normal pace on the flat, d) at rest. Particular notice was taken of a definite change in a person's breathing capacity as judged by symptoms. Positive answers to b), c), d) were considered abnormal and any breathlessness necessitating a pause or slowing of activity after one flight of stairs was also considered abnormal.

xvi) **Peripheral Vascular Disease** was judged on historical grounds. An affirmative reply to the following question was accepted. 'Do you suffer pains in the calf muscles on walking up a rise, at the time of the walk, and relieved by rest within two to three minutes?'

xvii) **Diabetes** was accepted only on the evidence of a positive glucose tolerance test.

xviii) **Hypertension** was defined as any previously recorded blood pressure deemed high enough to warrant treatment, by the examining doctor.

xix) The **Prodrome** was defined as the 28 day period prior to the acute event. Increased or more severe angina, acute coronary insufficiency or breathlessness was accepted as any deterioration of these symptoms during the prodromal period, even if this just represented the latter part of a more prolonged deterioration.

xx) **Time of Onset of Acute Symptoms**

a) **Myocardial Infarction.** This is a difficult area, most particularly in deciding whether a severe but undocumented antecedent symptom
was part of the prodrome or whether it, rather than a later severe symptom prompting admission, represented the acute event. It was decided that the onset of the acute event would be defined as the most severe pain, if severe pain had been felt (or if severe pain had never been a symptom, the most severe 'cardiac-type' symptom) in the preceding 28 days. In addition consideration would have to be taken of still changing ST segment elevation or Q wave depth, or deepening T waves, on the ECG, or still elevated enzyme levels. If any of these were present it would suggest onset of the acute event within the last three to four days. It is realized that this neglects the possibility that the event which resulted in medical attention was an extension of an original infarction. In practice it was clear that this was an uncommon problem and that the above criterion represented a reasonable compromise.

b) **Sudden Death.** Onset is defined as the time when symptoms required a major change in the individual's activities (remembering that the person must have been mobile during the 24 hours prior to onset).

xxd) **Clinical Shock** was defined as unusual pallor or sweating noted by the examining doctor. This is intended to act as a crude measure of increased sympatho/adrenal activity.
xxdii) Cardiac Arrest

Although this was initially conceived to refer to all cases of cardiac arrest, it was utilized in practice, to refer to Ventricular Fibrillation as far as it was possible to identify this condition. (Thus any cases dying of documented asystole were not recorded as a 'cardiac arrest' in box 15, page 7 of the questionnaire (Appendix E). If, as usual, the asystole was fatal, the death was recorded in box 16 and a note made of the nature of the final arrhythmia.)

'Cardiac arrest' was considered to have occurred if the patient was rendered unconscious by the arrhythmia (e.g., a few cases of fast, ineffective ventricular tachycardia were included, on the basis that outside hospital these would almost certainly have led to fatal ventricular fibrillation).

xxdiii) Alcohol Consumption

A large brewery was contacted regarding the alcohol content of common alcoholic beverages. The grams of alcohol were calculated on the following basis:

- i) Beer 3 Gms Alcohol / 100 mls
- ii) Wine 12 Gms Alcohol / 100 mls
- iii) Sherry 22 Gms Alcohol / 100 mls
- iv) Spirits 42 Gms Alcohol / 100 mls
<table>
<thead>
<tr>
<th>Containers</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>i) Quart bottle</td>
<td>750 mls</td>
</tr>
<tr>
<td>ii) Can of beer</td>
<td>340 mls</td>
</tr>
<tr>
<td>iii) Beer glass</td>
<td>300 mls</td>
</tr>
<tr>
<td>iv) Wine glass</td>
<td>100 mls</td>
</tr>
<tr>
<td>v) Sherry glass</td>
<td>50 mls</td>
</tr>
<tr>
<td>vi) Nip spirits</td>
<td>20 mls</td>
</tr>
<tr>
<td>vii) Jug</td>
<td>1100 mls</td>
</tr>
</tbody>
</table>
Section 2.6: VALIDATION OF COLLECTION TECHNIQUES

As in any data collection scheme, it was felt wise to try to establish the effectiveness of the collection technique. There were several possibilities which could cause the omission of some cases. The most important of these was in the notification of nonhospitalized cases and cases not referred to the coroner, by general practitioners. General practitioners have on average only two to three definite infarction cases and one to two sudden deaths, in this age range, each year. Despite our regular phone calls it was possible that some cases may not have been notified.

In the case of Sudden Deaths, validation was relatively easy and required that every death certificate written in Auckland over the one year period be perused. This was done, and it was found that about 15% of these cases had not been notified. This was due to several circumstances. Usually the death had occurred when the doctor was off duty and a partner had told the usual doctor of the death, but due to lack of active involvement the doctor seemed to have forgotten of the case before our next phone call. Occasionally a doctor had been misinformed, or not checked a patient's age and so considered him too old for inclusion. All Sudden Death cases not previously included, but found by the validation, were followed up and relatives and/or friends interviewed in the normal way. Thus, the author believes a total collect for Sudden Deaths was achieved.

The situation with non-hospitalized myocardial infarction (Definite and Possible) is much more difficult. The only possible way to validate the
collection technique seemed to be to go through a proportion of several doctors' records, hunting for unreported cases occurring during the correct period and in the correct age range. As the incidence of these disorders treated at home is of the order of 0.1-0.5/1000 and missed cases were hopefully of the order of 5%, this would have necessitated on average the search of about 100,000 records in the correct age range (about 1/3 of total population), i.e., probably about 300,000 records to find just one missed case. Practically speaking, with the resources available, even going through 5,000 records in the correct age range which would have to have been spread through a representative group of general practitioners, would have been a major task. Getting the practitioners' permission could have been difficult and reading their writing often impossible!

Assume that it had been organized to peruse 5,000 records and that we found no missed cases. Assuming a Poisson distribution of missed cases, we could be about 95% sure that the true value was not more than three missed cases/5000 average relevant records, i.e., a total of 18 missed cases/80,000 people (which was roughly the population size collected from). As the total number of cases treated only at home was only about 25 this would imply an upper bound for the collection error of 18 missed cases out of a total of 43, i.e., 41.9% error. As it was most likely that no cases would be found in such a limited search, it was felt that such a high upper bound for missed cases was unrealistic, and, in fact due to small numbers widening the confidence interval. Thus this validation was not proceeded with.
As the proportion of 'missed' Sudden Deaths was about 15%, it seems clear that the proportion of missed home treated myocardial infarctions should be substantially lower, e.g., 5-8% or less. This is due to the fact that in such cases, the time commitment by the practitioner is usually substantial involving several visits, electrocardiographs and serum enzyme tests. He would seem unlikely to forget such a sequence of events within one month. Nevertheless, the author recognizes that a small proportion of diagnosed cases may have been missed.

As previously mentioned, it is recognized that there is a significant proportion of myocardial infarctions undiagnosed and no attempt was able to be made to establish an incidence for this group in Auckland.
Section 2.7: USE OF RESOURCES IN PRACTICE

It soon became obvious that an important area contributing to the success of a study such as this was 'public relations,' with general practitioners, hospital staff, the public, and officials at the coroner's office. It was not thought necessary to undertake any publicity through recognized news media and as far as the public were involved in the postal survey, we relied on their general interest in health and awareness of coronary disease. Thought was also given to the selection of my secretary, who would do most communicating with the public and general practitioners, and she should be pleasant in appearance and manner. This substantially contributed to the success of this study, which relied heavily on cooperation from lay people and professional groups alike.

We endeavoured to keep the participating doctors informed as to the progress of the study in our routine telephone conversations and also by letter (see Appendix F). A list of all general practitioners in the Auckland area was supplied by the Health Department. This was searched and any doctors located outside our defined area of Auckland were deleted. The remainder were given a number 1 - 313.

Consideration of available resources suggested it would be possible to cope with the patients of approximately 120 - 130 doctors. Statistical considerations also suggested this was a reasonable number. This then represented about 40% of all doctors in the defined area. Using random numbers the first 127 numbers between 1 and 313 were selected and matched to the corresponding doctor. On assessing the chosen group, it was felt that this
seemed a representative group in terms of doctor age, location of practice, and proportion of group practices.

Having decided to visit the selected doctors, it was now apparent that this would occupy about four or five weeks, after making appointments. Of the 127 doctors, only one refused an appointment with the author, on the grounds that he objected to surveys. He was thus excluded. About 1100 miles were travelled and it proved an interesting experience, observing a wide range of practices, surgeries and gaining the impressions of general practitioners regarding epidemiological research and such matters as home treatment of coronary patients.

The cooperation of these doctors was excellent. Some were obviously very enthusiastic and others less so, but 126 agreed to cooperate. About three months into the study, a further doctor withdrew on the grounds of lack of time. The remaining 125 doctors, as far as we could judge, did their best to inform us of all cases and made time for phone conversations in a manner exceeding our expectations. Thus we ended up with 125/313 as a proportion of Auckland's doctors, i.e., 39.9%.

During the 20 month total period of collection, two of the elderly doctors died and three gave up practice. In three of these changes, the practice was directly taken over by another doctor, whom we then incorporated into the study. The other two changes affected very small practices and occurred towards the end of the study, so it was felt reasonable to neglect these.

For the postal survey, it was necessary to select a random sample of about 5100 names from the electoral roll. This was done by computer using
a random number generator. On statistical grounds, it was decided that about 1500 letters for the first collection year and about the same for the second overlapping collection year would be adequate. From census data it was estimated that only about 60% of persons on the electoral roll would fall within our defined age range of 35-69 years (inclusive). This explains the need for the 5100 letters.

Unfortunately, the electoral roll was about three years old at the time it was used and a proportion of people had moved house. Initially about 10% of letters were returned 'wrong address'. This was partially overcome by stamping on the envelope after the person's name 'present house occupant'. A pilot study of 50 letters was sent to see whether the method was likely to give results sufficient to warrant its use. Despite some dire predictions, the public cooperation was excellent. The letter used to explain the purpose of the study was included with a reply-paid self addressed envelope. A copy of this letter, and the second letter sent if there was no response to the first after 10-14 days, is included in Appendix G.

The breakdown of response pattern for the complete postal survey is as follows:

<table>
<thead>
<tr>
<th>Response to two letters</th>
<th>69%</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Phone call</td>
<td>6%</td>
</tr>
<tr>
<td>(Visit</td>
<td>9%</td>
</tr>
<tr>
<td>(Refused when contacted</td>
<td>3%</td>
</tr>
<tr>
<td>or had no doctor</td>
<td></td>
</tr>
<tr>
<td>(Not contacted</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>100%</td>
</tr>
</tbody>
</table>

Thus overall response rate was 84%. This was a little lower than had been predicted and could have been increased by trying to contact some of the 13% above. It was decided that it was not worth pursuing this too far as
it seemed intrinsically unlikely that the randomly selected 125 doctors should divide the non-respondents in any very different way to the respondents. Clearly, the 13% must include a higher proportion of persons who had no doctor if the figure given by Dixon for Auckland (36) is accepted.

Sixty-nine per cent of the total replies were in the age range 35-69 years. Of the total number of 3034 replies in this group, 42.2% gave one of the selected 125 doctors as their doctor (compared to the 39.9% expected). Altogether about 487 visits and 296 contacts by phone were made (all ages), by the author's secretary.

The replies to letters were used to estimate the $\sigma^2$ values for the 3 age ranges: 35-49 years, 50-59 years, 60-69 years. This was done using the 32 replies from the first year of the study. The 313 doctors were randomly split into ten equal groups for the calculation.

The calculations used the equation developed for $S^2$ in Appendix A relating to Section 2 of this chapter. Results are given in Table 11.

<table>
<thead>
<tr>
<th>Age</th>
<th>Var $Y_k$</th>
<th>S</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>35 - 49</td>
<td>254.9</td>
<td>0.027</td>
<td>856 letters</td>
</tr>
<tr>
<td>50 - 59</td>
<td>45.15</td>
<td>~0</td>
<td>538 letters</td>
</tr>
<tr>
<td>60 - 69</td>
<td>81.38</td>
<td>0.023</td>
<td>446 letters</td>
</tr>
</tbody>
</table>

Table 11. Estimated Values of $\sigma$. 

85
As expected, as much time was taken diagnosing cases, as interviewing. Finding patients in hospitals, perusing their notes and returning for further enzyme/ECG results occupied a substantial proportion of the author's time. A liaison was established with the admitting offices of each of the hospitals and the admission lists were readily made available, with admission diagnoses and the ward to which the patient was admitted.

Patients treated at home, necessitated home interviews. However, these were relatively few and presented no problem. A particular point was made of stressing to practitioners our interest in home treated cases, both at the initial interview and subsequently where convenient, as we realized this was the weakest link in notification. Notification of these cases was totally dependent on the general practitioner and we had no practicable means of validation.

Contacting the relatives of deceased patients presented at times considerable difficulty. A liaison was established with the coroner's office without difficulty. However, the records were not always easy to find depending on whether there had been an inquest, when the records may be sent elsewhere for up to two months. However, by frequent checking and record searching this problem was overcome. The author's secretary soon became proficient in recognizing the relevant kinds of history and postmortem result (usually no acute pathological cause found). A problem was that in about 20% of the records, the police had not filled in the deceased's usual doctor, which of course was vital for this particular study. This situation improved after we explained the difficulty, but still occurred occasionally. In such circumstances we contacted the next of kin by phone or telegram and obtained the information.
The next of kin were interviewed in every case included in the study, occasionally necessitating a long-distance telephone call, but usually by personal visit. Information was clearly of variable reliability and the author had to make a decision on the reliability of the witness. If the spouse was being interviewed there was usually little difficulty, although it was clear that some men confided little in their wives. It was felt that there should be a relatively low threshold for rejecting information as unreliable and counting it as missing information, rather than including much information of doubtful value which could mask the reliable data which had already been gathered.

The regular telephone calls to the general practitioners were time consuming. Afternoons off, answer-phones, the wrong surgery for that day, persistently engaged phones, doctors consulting and unable to speak, all made these calls at times very frustrating. About 2,500 phone calls were conducted over the period of collection. Once contacted the doctors were without exception always pleasant and cooperative.
CHAPTER 3

RESULTS -

INTRODUCTION AND INTERNATIONAL COMPARISONS

OF CORONARY DISEASE FREQUENCY
SECTION 3.1: INTRODUCTION TO PRESENTATION OF RESULTS

The presentation of results such as these raises several problems, a major one of which has to do with classification. Groups of cases can be separated on a univariate or multivariate basis and according to pathological or clinical criteria. The epidemiological aim is directed towards the identification of causal factors. With this in mind, it would seem best to classify where possible on a multivariate basis as different patterns of aetiological influences will probably be related to different coronary syndromes. A pathological basis should also be preferred, if feasible, as this is likely to be more objective.

The nosology of ischaemic heart disease at present is largely on a univariate basis (e.g., sudden death or not sudden death; angina or not angina) rather than using a constellation of symptoms or examination data which may allow cases to be grouped together as an aetiological unit, even if what we now see as the major manifestation is absent in some cases. Similarly, cases manifesting multiple univariate syndromes (e.g., definite myocardial infarction coexisting with sudden death) may be classifiable as a single grouping not totally dependent on either one of these manifestations.

The methods of the present study hopefully may give some ideas as to other variables separating the major groupings (described in Chapters 4, 5, and 6) apart from the major manifestation. In so doing, it is likely that the major manifestations will become subdivided to some extent and perhaps amalgamated to some extent.
Many studies have presented results relating to 'all coronary disease', 'all acute events of coronary disease', or have separated as discrete entities 'sudden death' (with several possible definitions), 'all fatal coronary events' or 'medically unattended deaths', etc. The present study has used sudden death, definite and possible myocardial infarction as basic divisions, but recorded sufficient data to subdivide further as required.

The major objective of the present study was to provide incidence and other basic data on cases suffering an acute coronary event. For this reason, data is not available for normal persons. This limits the type of aetiological investigations that can be performed as it is impossible to compare the characteristics of persons with the disease and those without. However, potential for aetiological investigation still remains, due to the ability to compare between the three syndromes investigated. Differences found may have aetiological significance either in a disease provoking or in a protective sense.

A further problem already alluded to in Chapter 2 is that a proportion of historical sudden deaths, not having a postmortem, may not be cardiac sudden deaths fulfilling the pathological criteria had postmortems been performed, i.e., conditions such as pulmonary embolus, aortic rupture, severe valvular heart disease previously undiagnosed, may masquerade as coronary disease. Spain (89) and Wickland (90) have investigated this problem and found that the diagnosis is likely to be correct in at least 90% of such cases.
In the present series, 98 sudden deaths (55%) did have a postmortem. Of these, 5 which had been accepted on historical grounds as sudden cardiac deaths were later excluded due to the postmortem findings. The pathological findings were

a) 2 cases with severe aortic stenosis
b) one case with mitral incompetence and stenosis
c) one case of myocarditis? viral
d) one case with severe bronchopneumonia.

The valvular lesions were undiagnosed during life. However, there were also two cases which could be excluded on careful historical documentation as most probably due to cerebrovascular accidents. This decision was made after the cases had been referred by the local doctor. Thus it seems quite likely that of the 80 cases which did not have a postmortem, there will be a few who were incorrectly diagnosed. However, it is unlikely to be a problem of much significance, particularly as a careful clinical history was always taken.

Although the succeeding chapters are concerned basically with the presentation of results, some comments have been added, in appropriate places drawing attention to areas where comparisons can be made with published studies. These comments have been inserted at these points in order to simplify the Discussion section of this thesis.
Section 3.2: COMPARISONS BETWEEN THE AUCKLAND INCIDENCES AND THOSE OF THE WHO EUROPEAN AND AUSTRALIAN REGISTERS

The results of a series of myocardial infarction registers directed by WHO have recently been published (32). These involved the use of whole populations to estimate disease frequency in nineteen different locations. Definitions of disease were standardized for all centres.

The Auckland myocardial infarction register was conducted about the same time as the WHO registers and used the same definitions of disease. The Auckland register however used a 40% random sample of the population of Auckland as described in Chapter Two.

Thus these results allow the opportunity to illustrate the methods of Section 2.3. For comparability the Auckland categories 'possible myocardial infarction', 'definite myocardial infarction' not associated with sudden death, plus all 'sudden deaths' are combined to give an attack rate for all acute ischaemic heart disease events. This is compared to the results in Table 17 of WHO Ischaemic Heart Disease Registers (32). Population figures are given in Table 8 of the same publication.

The following centres were chosen from the WHO registers: Gothenburg, Berlin, Boden, Innsbruck, Sofia, Tel Aviv, Perth (Australia), Helsinki, Dublin, London. For Dublin and London, collection periods were greater than one year. To allow for this the populations at risk were multiplied by the number of years of observation. This allows the advantage of the greater number of cases collected over the extended period to be retained.
That this is an appropriate way to handle this situation can be shown by consideration of the likelihood function of \( X_1 \) for say Centre 1 where a two year collection was performed. It is assumed that the population was stable over this period.

\[
L = \frac{e^{-(2T_1)}}{x_1!} \left( \frac{(2T_1)^{x_1}}{x_1!} \right)
\]

Clearly exactly the same function is found by considering the incidence acting on twice the population i.e., \((2T_1) = I(2T_1)\).

The results of the pairwise comparisons (including Auckland) are given in Figures 10, 11, 12. In addition, for each age-sex grouping a \( X^2_{10} \) statistic with the corresponding P value is given for the simultaneous test (S.T.). As an illustration of the pairwise comparison of disease frequencies where both estimates used samples of the population several comparisons were made within the Auckland data as follows:

a) Males - Less than 40 years compared with 50-54 years

\[
X^2_1 = 240.4. \quad P < 0.001
\]

b) Females - Less than 40 years compared with 50-54 years

\[
X^2_1 = 51.3. \quad P < 0.001
\]

c) Males - 50-54 years compared with 60-64 years

\[
X^2_1 = 3.52. \quad P < 0.10
\]

d) Females - 50-54 years compared with 60-64 years

\[
X^2_1 = 10.60. \quad P < 0.005.
\]
Figures 10, 11, 12. Comparisons of Acute Coronary Disease Frequency between WHO Centres and Auckland for Three Selected Age Groups. (Results for Females above the Diagonal and for Males below the Diagonal.)
It can be seen that for pairwise comparisons, for instance, some superficially unpredictable results have occurred. For instance for males less than 40 years old, the London attack rate is not significantly higher than that of Boden, but does differ significantly from that of Sofia. This is despite the fact that the estimated Sofia attack rate is the closer to the estimated London attack rate. The explanation is the larger number of cases gathered from the larger Sofia population (15 cases from 72,670 persons at risk) compared to Boden (1 case from 5,220 persons at risk).

It can be seen that Auckland usually falls in the upper three or four centres in estimated disease frequency. Auckland has usually significantly higher frequencies than Scandinavian centres, Sofia and Berlin. It is sometimes significantly lower in frequency than Helsinki. Centres with results consistently similar to those of Auckland (for men particularly) are London, Dublin and Perth.
CHAPTER 4

RESULTS--

DEFINITE MYOCARDIAL INFARCTION
Section 4.1: DEFINITE MYOCARDIAL INFARCTION IN AUCKLAND

This chapter summarizes the data gathered on 293 patients suffering a definite myocardial infarction, who should be a 40% representation sample of all such patients in Auckland, between April 1974 - March 1975. Forty-one of these cases were associated with sudden cardiac death and thus will also be included in Chapter 5.

(M.I. = Myocardial Infarction)

Demographic Data

a) Sex

225 males (76.8%)

68 females (23.2%)

Of the cases who were also sudden deaths, 20% were females.

These figures are similar to many overseas studies e.g., Tower Hamlets (London) (91) 19% female; Nashville, Tennessee Whites (33) 24% females; Goteborg, Sweden (92) 18% female.

In London and Goteborg the age range was only up to 64 years, whereas in Nashville it was up to 75 years. This may account for the variations seen with the females having an even lower proportionate incidence in the younger populations.

b) Age Specific Incidence

This is depicted in Table 12 and Figure 13.
Table 12. Age-Sex Specific Incidence Estimates for Definite Myocardial Infarction.

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Cases (% in brackets)</th>
<th>Total Census Population</th>
<th>Letters Returned naming one of the selected doctors</th>
<th>Max. Likelihood Estimate of Incidence &amp; 95% Credibility Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-29</td>
<td>M</td>
<td>1(0.4)</td>
<td>21758</td>
<td>Not recorded¹</td>
<td>0.00012 (0.00002–0.00065)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>0(0)</td>
<td>23138</td>
<td>&quot;</td>
<td>0.00040 (0.0–0.00041)</td>
</tr>
<tr>
<td>30-34</td>
<td>M</td>
<td>3(1.3)</td>
<td>19327</td>
<td>&quot;</td>
<td>0.00013 (0.00003–0.00072)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>1(1.4)</td>
<td>19652</td>
<td>&quot;</td>
<td>0.00090 (0.00042–0.00195)</td>
</tr>
<tr>
<td>35-39</td>
<td>M</td>
<td>6(2.7)</td>
<td>17054</td>
<td></td>
<td>0.00015 (0.00004–0.00085)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>1(1.4)</td>
<td>16749</td>
<td></td>
<td>0.00137 (0.00072–0.00295)</td>
</tr>
<tr>
<td>40-44</td>
<td>M</td>
<td>10(4.4)</td>
<td>18575</td>
<td></td>
<td>0.00289 (0.00009–0.00102)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>2(2.9)</td>
<td>18069</td>
<td></td>
<td>0.0014 (0.00058–0.00225)</td>
</tr>
<tr>
<td>45-49</td>
<td>M</td>
<td>21(9.3)</td>
<td>18111</td>
<td></td>
<td>0.0059 (0.00058–0.00225)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>8(11.8)</td>
<td>17906</td>
<td></td>
<td>0.0089 (0.00052–0.00956)</td>
</tr>
<tr>
<td>50-54</td>
<td>M</td>
<td>44(19.6)</td>
<td>15335</td>
<td></td>
<td>0.00118 (0.00063–0.00239)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>8(11.8)</td>
<td>16264</td>
<td></td>
<td>0.00762 (0.00585–0.01053)</td>
</tr>
<tr>
<td>55-59</td>
<td>M</td>
<td>45(20)</td>
<td>14184</td>
<td></td>
<td>0.00254 (0.00162–0.00426)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>16(24)</td>
<td>15108</td>
<td></td>
<td>0.0101 (0.00784–0.01384)</td>
</tr>
<tr>
<td>60-64</td>
<td>M</td>
<td>52(23)</td>
<td>11832</td>
<td></td>
<td>0.00231 (0.00139–0.00409)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>13(19)</td>
<td>12965</td>
<td></td>
<td>0.01089 (0.00824–0.01530)</td>
</tr>
<tr>
<td>65-69</td>
<td>M</td>
<td>43(19)</td>
<td>9075</td>
<td></td>
<td>0.00395 (0.00259–0.00640)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>19(28)</td>
<td>11068</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total 35-69 yrs = 212,388. Male Mean Age = 56.5 years
Female Mean Age = 56.9 years
Overall Mean Age = 56.6 years

¹ The 35-49 year proportion is assumed for the purposes of incidence estimation.
Comparisons with results from other places are difficult to make precisely due to differences in definitions and differences in age ranges considered. The Auckland data has however been adapted to calculate figures for the same age ranges used in the study with which it is being compared. Auckland figures are given in brackets in Table 13.
<table>
<thead>
<tr>
<th>Age Group</th>
<th>Goteborg (92)</th>
<th>Nashville USA (33)</th>
<th>Tower Hamlets London (91)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td>Males</td>
</tr>
<tr>
<td>25-29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-39</td>
<td>0.46</td>
<td>0.08</td>
<td>1.84</td>
</tr>
<tr>
<td></td>
<td>(1.37)</td>
<td>(0.28)</td>
<td>(1.13)</td>
</tr>
<tr>
<td>40-44</td>
<td>1.94</td>
<td>0.32</td>
<td>5.50</td>
</tr>
<tr>
<td></td>
<td>(2.95)</td>
<td>(1.14)</td>
<td>(4.86)</td>
</tr>
<tr>
<td>50-54</td>
<td>3.99</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(6.89)</td>
<td>(1.18)</td>
<td></td>
</tr>
<tr>
<td>55-59</td>
<td>7.85</td>
<td>1.96</td>
<td>9.82</td>
</tr>
<tr>
<td></td>
<td>(7.62)</td>
<td>(2.54)</td>
<td>(9.32)</td>
</tr>
<tr>
<td>60-64</td>
<td>11.35</td>
<td>2.10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(10.10)</td>
<td>(2.31)</td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Seattle USA (93)</th>
<th>Helsinki (94)</th>
<th>Honolulu Japanese (95)</th>
<th>Perth (96)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>25-29</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-34</td>
<td>0.44</td>
<td>0.06</td>
<td>0.84</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td>(0.62)</td>
<td>(0.14)</td>
<td>(0.90)</td>
<td>(0.15)</td>
</tr>
<tr>
<td>35-39</td>
<td>2.16</td>
<td>0.32</td>
<td>2.61</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>(2.11)</td>
<td>(0.69)</td>
<td>(1.37)</td>
<td>(0.28)</td>
</tr>
<tr>
<td>40-44</td>
<td>3.17</td>
<td>0.06</td>
<td>4.80</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>(1.37)</td>
<td>(0.28)</td>
<td>(2.95)</td>
<td>(1.14)</td>
</tr>
<tr>
<td>45-49</td>
<td>6.36</td>
<td>1.02</td>
<td>9.57</td>
<td>3.73</td>
</tr>
<tr>
<td></td>
<td>(2.95)</td>
<td>(1.14)</td>
<td>(7.62)</td>
<td>(2.54)</td>
</tr>
<tr>
<td>50-54</td>
<td>9.06</td>
<td>0.97</td>
<td>14.62</td>
<td>4.98</td>
</tr>
<tr>
<td></td>
<td>(6.89)</td>
<td>(1.18)</td>
<td>(7.62)</td>
<td>(2.54)</td>
</tr>
<tr>
<td>55-59</td>
<td>12.59</td>
<td>2.50</td>
<td>19.18</td>
<td>5.32</td>
</tr>
<tr>
<td></td>
<td>(7.62)</td>
<td>(2.54)</td>
<td>(10.10)</td>
<td>(2.31)</td>
</tr>
<tr>
<td>60-64</td>
<td>15.49</td>
<td>5.33</td>
<td>2.87</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(10.10)</td>
<td>(2.31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>7.93</td>
<td>3.24</td>
<td>19.18</td>
<td>5.32</td>
</tr>
<tr>
<td></td>
<td>(11.35)</td>
<td>(3.33)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 13. Comparisons of the Incidence of Definite Myocardial Infarction in Different Places.
c) **Social Class**

Social classes I, II and III were defined purely on an area of residence basis (see 'Definitions', Section 2.4).

### Social Class

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-49</td>
<td>14(14.1)</td>
<td>31(27.5)</td>
<td>9(12.4)</td>
</tr>
<tr>
<td>Age</td>
<td>50-59</td>
<td>52(47.6)</td>
<td>33(32.1)</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>57(52.2)</td>
<td>37(36.0)</td>
</tr>
</tbody>
</table>

Table 14. Social Class and Definite Myocardial Infarction.

No significant differences from expectation were demonstrated (see Table 14) and the social class analysis thus gave a predictable result. The method of ascertainment of social class may seem crude, but has been used previously (97). This 'ecological' approach may well measure something different than other social class measures, e.g., occupation, education. Previous studies relating myocardial infarction to social class (98, 99, 100) are not common (usually a global 'coronary disease' or 'coronary deaths' is used as the dependent variable). Most of the studies considering just myocardial infarction showed results similar to those presented here, although Brown (100) showed a higher frequency in Class I persons. Results for coronary disease considered as a whole are conflicting (97, 101).
d) **Race**

Of all myocardial infarction cases, the division was as follows:

- 95.9% were European (281 cases)
- 2.7% were Maori (6 male, 2 female)
- 1.0% were Other Polynesians (3 cases)
- 0.3% were Indian (1 case)

In view of the previously reported high coronary death rates of Maoris (102) and the possibly high angina rates particularly for Maori women (103), using the Rose questionnaire (104), it is perhaps a little surprising to find only 8 Maori cases when the expected number on an age-specific population basis would be about eleven cases. However numbers are clearly small. The possibility of underdiagnosis must be mentioned, as Maoris could be less likely to present for medical care. However there must be some doubt about the validity of using the Rose questionnaire for angina in a Maori population, until it has been formally validated in this racial group.

**Personal Characteristics and Habits**

a) **Height and Weight**

Table 15 shows means and standard deviations for these variables.
<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Height (cms)</td>
<td>173.29</td>
<td>159.4</td>
</tr>
<tr>
<td>(No. of cases)</td>
<td>(224)</td>
<td>(67)</td>
</tr>
<tr>
<td>Weight (kgs)</td>
<td>75.75</td>
<td>64.02</td>
</tr>
<tr>
<td>(No. of cases)</td>
<td>(223)</td>
<td>(66)</td>
</tr>
</tbody>
</table>

Table 15. Height and Weight in Definite Myocardial Infarction Patients.

Table 16 presents age-sex specific Quetelet's index\(^2\) in the myocardial infarction patients as compared with the figures obtained for the Carterton population (105).

<table>
<thead>
<tr>
<th>Males</th>
<th>Auckland M.I. Patients</th>
<th>Carterton Citizen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Q. Index</td>
</tr>
<tr>
<td>30-39yrs</td>
<td>9</td>
<td>0.272</td>
</tr>
<tr>
<td>40-49yrs</td>
<td>31</td>
<td>0.265</td>
</tr>
<tr>
<td>50-59yrs</td>
<td>88</td>
<td>0.252</td>
</tr>
<tr>
<td>60-69yrs</td>
<td>93</td>
<td>0.247</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-39yrs</td>
<td>2</td>
<td>0.282</td>
</tr>
<tr>
<td>40-49yrs</td>
<td>10</td>
<td>0.228</td>
</tr>
<tr>
<td>50-59yrs</td>
<td>24</td>
<td>0.271</td>
</tr>
<tr>
<td>60-69yrs</td>
<td>32</td>
<td>0.240</td>
</tr>
</tbody>
</table>

Table 16. Quetelet's Index for Auckland MI Patients and Carterton Citizens.

\(^2\) Quetelet's Index = 100 \times \frac{\text{Weight (kg)}}{\text{Height (cms)}}^2.
There is no significant difference for any age-sex group from the normal population body build. It is noted that there seems to be a consistent trend amongst the male myocardial infarct cases of a decreasing index with age but all male results combined are not significantly higher than male Carterton results combined, taking into account differences in age structure of the populations.

The Busselton Community study when compared with a Sydney coronary study showed a highly significant difference in Quetelet's Index with the coronary patients having higher indices (106). This could be due to other differences between the populations. The present study does not show this finding clearly, perhaps due to small numbers, although the trend is in this direction. For young men the differences were at a level of $0.10 > p > 0.05$.

The Framingham study (107) showed no significant differences in obesity, from normal, for myocardial infarction cases (as distinct from angina). However, in that study Quetelet's Index was not used, a 'relative weight' measure being employed. Keys et al. (108) found results similar to those presented here if only the 'hard criteria' of sudden death or myocardial infarction were used.

The heights and weights of the 41 cases associated with sudden death were not significantly different from the whole group.
b) Cigarette Smoking

Table 17 shows the results for cigarette smoking in this definite myocardial infarction population.

<table>
<thead>
<tr>
<th>Category</th>
<th>% in each category</th>
<th>Mean No. per day</th>
<th>Mean for smokers only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>28.6</td>
<td>14.2</td>
<td>23.4</td>
</tr>
<tr>
<td>(290)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>25.6</td>
<td>15.2</td>
<td>24.6</td>
</tr>
<tr>
<td>(223)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>37.2</td>
<td>10.9</td>
<td>19.16</td>
</tr>
<tr>
<td>(67)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases who also died</td>
<td>17.1</td>
<td>15.2</td>
<td>21.5</td>
</tr>
<tr>
<td>suddenly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(41)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 17. Cigarette Smoking in Definite MI Patients.

Category
1 = Not smoked within 10 years
2 = Stopped smoking between 6 months and 10 years ago
3 = Smoked 1-9/day regularly within 6 months
4 = Smoked 10-19/day regularly within 6 months
5 = Smoked 20-39/day regularly within 6 months
6 = Smoked ≥ 40/day regularly within 6 months

A comparison between the definite myocardial infarction cases and the general population was made possible by the 1976 population census (52). Here the results of the census have been adjusted to the age-structure of the definite MI population to allow a fair comparison (see Table 18).
<table>
<thead>
<tr>
<th>Smoking Category</th>
<th>Male Census</th>
<th>Female Census</th>
<th>MI who Died Suddenly</th>
</tr>
</thead>
<tbody>
<tr>
<td>None or Given up</td>
<td>62.1% 38.2%</td>
<td>73.5% 41.6%</td>
<td>29.3%</td>
</tr>
<tr>
<td>0-9/day</td>
<td>5.7% 9.4%</td>
<td>7.6% 10.5%</td>
<td>12.2%</td>
</tr>
<tr>
<td>10-19/day</td>
<td>12.3% 16.1%</td>
<td>10.8% 24.0%</td>
<td>24.4%</td>
</tr>
<tr>
<td>20-39/day</td>
<td>16.7% 26.9%</td>
<td>7.5% 20.8%</td>
<td>29.3%</td>
</tr>
<tr>
<td>&gt;40/day</td>
<td>3.1% 9.4%</td>
<td>0.7% 2.9%</td>
<td>4.9%</td>
</tr>
</tbody>
</table>

\[ X^2_4 = 67.8 \quad X^2_3 = 40.7 \]

Table 18. Cigarette Smoking in Definite MI Cases and the Age-Adjusted Census Population.

Although the cases of MI who died suddenly had a higher percentage of present smokers than non-sudden death MI's, this was not statistically significant.

c) Alcohol Consumption

Intake was recorded in Grams Alcohol/week and is presented in Table 19. Figures in brackets refer to the number of cases on whom information was available. Alcohol data was only recorded on the latter 214 cases.

\[ \text{Number of cases}. \]

\[ \text{Two classes were amalgamated due to low numbers. In both cases the major portion of these high } X^2 \text{ statistics came from an excess of MI cases who were heavy smokers}. \]
<table>
<thead>
<tr>
<th></th>
<th>Beer</th>
<th></th>
<th>Wine &amp; Sherry</th>
<th></th>
<th>Spirits</th>
<th></th>
<th>Total Alcohol</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>Drinkers</td>
<td>All</td>
<td>Drinkers</td>
<td>All</td>
<td>Drinkers</td>
<td>All</td>
<td>Drinkers</td>
</tr>
<tr>
<td>All Cases (4)5</td>
<td>60.3</td>
<td>(210)</td>
<td>151.5</td>
<td>(84)</td>
<td>22.4</td>
<td>(210)</td>
<td>77.1</td>
<td>(62)</td>
</tr>
<tr>
<td>No. of Cases</td>
<td>(210)</td>
<td>(84)</td>
<td>(210)</td>
<td>(62)</td>
<td>(210)</td>
<td>(69)</td>
<td>(210)</td>
<td>(136)</td>
</tr>
<tr>
<td>Males (3)5</td>
<td>75.6</td>
<td>(165)</td>
<td>152.0</td>
<td>(82)</td>
<td>25.8</td>
<td>(165)</td>
<td>81.9</td>
<td>(52)</td>
</tr>
<tr>
<td>No. of Cases</td>
<td>(165)</td>
<td>(82)</td>
<td>(165)</td>
<td>(52)</td>
<td>(165)</td>
<td>(59)</td>
<td>(165)</td>
<td>(118)</td>
</tr>
<tr>
<td>Females (1)5</td>
<td>4.0</td>
<td>(45)</td>
<td>90.0</td>
<td>(2)</td>
<td>9.9</td>
<td>(45)</td>
<td>49.5</td>
<td>(10)</td>
</tr>
<tr>
<td>No. of Cases</td>
<td>(45)</td>
<td>(2)</td>
<td>(45)</td>
<td>(10)</td>
<td>(45)</td>
<td>(10)</td>
<td>(45)</td>
<td>(18)</td>
</tr>
<tr>
<td>M. I.'s who died</td>
<td>76.3</td>
<td>(30)</td>
<td>134.6</td>
<td>(17)</td>
<td>53.8</td>
<td>(30)</td>
<td>120.0</td>
<td>(14)</td>
</tr>
<tr>
<td>suddenly (1)5</td>
<td></td>
<td>(30)</td>
<td>(17)</td>
<td></td>
<td>(30)</td>
<td>(14)</td>
<td></td>
<td>(10)</td>
</tr>
<tr>
<td>Non Sudden Death</td>
<td>58.0</td>
<td>(180)</td>
<td>155.8</td>
<td>(67)</td>
<td>17.5</td>
<td>(180)</td>
<td>65.6</td>
<td>(48)</td>
</tr>
<tr>
<td>M. I.'s (3)5</td>
<td></td>
<td>(180)</td>
<td>(67)</td>
<td></td>
<td>(180)</td>
<td>(48)</td>
<td></td>
<td>(59)</td>
</tr>
<tr>
<td>No. of Cases</td>
<td>(180)</td>
<td>(67)</td>
<td>(180)</td>
<td>(48)</td>
<td>(180)</td>
<td>(59)</td>
<td>(180)</td>
<td>(115)</td>
</tr>
</tbody>
</table>

Table 19. Alcohol Consumption (Grams per week) over the Previous One Year.

5 Number of cases for whom information was not available. These cases were not included in the 'No. of Cases' values.
Amongst M.I.'s who died suddenly 47% were wine and sherry drinkers, 33% were spirit drinkers and 70% drank alcohol in some form, whereas amongst non-sudden death cases, 27% drank wine or sherry, 33% drank spirits and 64% drank alcohol in some form.

Figures for the New Zealand population aged 20 years and over in 1971 were:

Beer consumption - 118.5 gms alcohol/week, wine consumption - 26.2 gms alcohol/week, spirits consumption - 29.4 gms alcohol/week (113).

Thus amongst the M.I. cases alcohol intake is representative of the New Zealand population except for beer. The author suspects this latter difference is due to the different age structure of the M.I. cases, including a much higher proportion of older persons.

The role of alcohol in coronary disease has been controversial for many years. Initially, it was thought possibly to be protective when it was found that cirrhotics tended to have less atherosclerosis (114,115). However Hirst et al. (116) observed that while this may be true of cirrhotics it does not seem to be true of non-cirrhotic alcoholics. Palmer (106) observed that in cases of established coronary disease in Sydney (86% survived infarcts), heavy drinking was more common than Busselton controls, at all ages. The role of alcohol will be further discussed in Chapters 5 and 7.

Animal work has also suggested alcohol may affect both lipid levels and atherosclerosis (117).
CARDIOVASCULAR HISTORY

This section refers to symptoms prior to the prodromal period.

a) Number of Previous Symptoms (see Fig. 14)

Figure 14. Number of Previous Symptoms (Definite Myocardial Infarctions)

The symptoms included are

a) Angina   b) Acute coronary insufficiency

c) Breathlessness   d) Documented definite myocardial infarction

b) Individual Symptoms

Recorded in Table 20 is the percentage of patients admitting to this symptom.
### Table 20. Individual Previous Symptoms in Definite MI Patients.

This pattern was essentially unchanged for cases who died suddenly with their M.I.

c) Duration of Symptoms

Mean durations are recorded in Table 21 with the number of cases evaluated given in brackets.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Males(^6)</th>
<th>Females(^6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>48.2%(^7)</td>
<td>53.5%</td>
</tr>
<tr>
<td>Acute Coronary Insuff.</td>
<td>12.6%</td>
<td>16.3%</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>36.7%(^7)</td>
<td>52.7%</td>
</tr>
<tr>
<td>1 Previous Infarct</td>
<td>24.6%(^6)</td>
<td>13.6%</td>
</tr>
<tr>
<td>2 Previous Infarcts</td>
<td>4.9%(^6)</td>
<td>7.3%</td>
</tr>
<tr>
<td>3 Previous Infarcts</td>
<td>0.4%(^6)</td>
<td>0%</td>
</tr>
<tr>
<td>No Previous Infarcts</td>
<td>70.1%(^6)</td>
<td>79.1%</td>
</tr>
</tbody>
</table>

Table 21. Mean Duration of Previous Symptoms in Definite MI Patients.

\(^6\) Number of cases evaluated in brackets.

\(^7\) Significant difference between males and females \(p < 0.025\).
Figure 15. Probability of Onset of Previous Symptoms (Definite Myocardial Infarctions)
The histograms of Figure 15 were essentially similar for both sexes and whether or not the M.I. was associated with sudden death. They show the probability of onset of the named symptoms during the period before the prodromal phase.

Pedoe records in London (91) that 63% of men and 79% of women had had previous cardiovascular symptoms. Also 50% had suffered angina and 21% previous proven myocardial infarction. However Pedoe's study included also sudden death and possible myocardial infarction cases.

Solomon recorded that 41% of his cases had experienced previous angina (118).

Kinlen recorded a 43.8% past history of angina and a 19.1% incidence of previous infarction, for both sexes combined (74), in Oxford, U.K.

d) Drugs

Table 22 refers to a selection of the more common medications taken within three weeks of the infarction with the number of cases evaluated given in brackets.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Digoxin 8</th>
<th>Blocker</th>
<th>T. N. T.</th>
<th>Thiazide or Lasix 9</th>
<th>Other Antihypertensive</th>
<th>Tricyclics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>7.1% (225)</td>
<td>12.9% (225)</td>
<td>21.3% (225)</td>
<td>17.3% (225)</td>
<td>10.2% (225)</td>
<td>2.2% (225)</td>
</tr>
<tr>
<td>Female</td>
<td>17.4% (68)</td>
<td>14.5% (68)</td>
<td>27.9% (68)</td>
<td>30.1% (68)</td>
<td>10.0% (68)</td>
<td>7.1% (68)</td>
</tr>
</tbody>
</table>

Table 22. Drug Therapy Within Three Weeks of the Infarction.

8 Difference between males and females significant p < 0.02.
9 Difference between males and females significant p < 0.05.
e) **Serum Lipids**

Unfortunately only 24% of cases had had a serum cholesterol estimation in the one year prior to the acute event, and only 8% of cases had had a fasting serum triglyceride estimation in the same period. As results may well not be representative of the group as a whole they will not be considered.

f) **Other Vascular Disease**

Six percent of cases gave a history of stroke and 14% a history of intermittent claudication. This compares with Pedoe's London figures (91) of 7% and 12% respectively.

g) **Antecedent Blood Pressure**

Sixty-eight percent of these patients had had their blood pressures checked in the one year prior to the infarction (64% of males and 79% of females). Forty percent (36% of men and 52% of women) of the 224 persons for whom information was available were either hypertensive during that year, or had at some time in the past been treated for hypertension. Thus a few cases who had no recording or a normal recording within one year, but who gave a definite history of hypertension are included. A negative answer was recorded only if there was no history of treatment and a normal pressure had been recorded during the one year period. All other cases were considered as 'missing data.'

Of the 68% who had had recordings taken Table 23 shows the mean results with the number of cases given in brackets.
Table 23. Mean Antecedent Blood Pressure Readings for MI Patients.

There was no significant difference between cases who were or were not associated with sudden death.

Pedoe recorded frequencies of past hypertension substantially lower than those above - 30% for women and 15% for men but his cases are not limited to definite myocardial infarction alone.

Kinlen (74) recorded in Oxford, U.K., a past history of hypertension in 30.4%, for both sexes combined.

The Carterton community results (51), when adjusted for age structure, are for males 149.0/91.4 and for females 149.3/91.6, taking mean results. Surprisingly our figures are lower, but comparisons are difficult due to possible different social and other circumstances associated with location of the populations. Also the Carterton blood pressures were done as part of a research project, whereas the Auckland blood pressures were done as routine checks by the patients' usual doctors. Most known hypertensives were on treatment, as they had often presented for attention with ischaemic heart disease symptoms.

h) Antecedent Electrocardiographic Features

For many cases, ECG's before the acute event were not available. If this was the case the ECG feature was scored as 'possibly present before the
acute event if it was present after the event. The lower bounds given below refer to the frequency of the feature when it was definitely known to precede the acute event. The upper bound represents the addition of the cases in whom the feature was possibly present before the acute event. (See Table 24.)

<table>
<thead>
<tr>
<th>Left Bundle Branch Block</th>
<th>Right Bundle Branch Block</th>
<th>Left Anterior Hemiblock</th>
<th>$1^\circ$ Heart Block</th>
<th>$2^\circ$ Heart Block</th>
<th>$3^\circ$ Heart Block</th>
<th>AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.7-2.2%</td>
<td>0.7-2.6%</td>
<td>3.8-18.8%</td>
<td>0.7-2.2%</td>
<td>0-0.7%</td>
<td>0-0.7%</td>
<td>2.3-</td>
</tr>
</tbody>
</table>

Table 24. Antecedent ECG Findings

**PRODROMAL SYMPTOMS**

![Bar chart](image)

Figure 16. Number of Prodromal Symptoms
(Definite Myocardial Infarctions)
a) **Number of prodromal symptoms**

The prodromal symptoms enumerated in Figure 16 are those listed in Table 25.

b) **Specific prodromal symptoms**

Table 25 shows specific prodromal symptoms with the numbers of cases given in brackets.

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>Sudden Death &amp; MI cases</th>
<th>MI &amp; no Sudden Death cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Angina</td>
<td>16.6%</td>
<td>13.4%</td>
<td>5%*</td>
<td>17.6%*</td>
</tr>
<tr>
<td></td>
<td>(223)</td>
<td>(67)</td>
<td>(40)</td>
<td>(250)</td>
</tr>
<tr>
<td>Increased Angina</td>
<td>22.7%</td>
<td>34.8%</td>
<td>21.1%</td>
<td>26.2%</td>
</tr>
<tr>
<td></td>
<td>(220)</td>
<td>(66)</td>
<td>(38)</td>
<td>(248)</td>
</tr>
<tr>
<td>New Coronary Insufficiency</td>
<td>24.4%</td>
<td>19.1%</td>
<td>17.9%</td>
<td>24.1%</td>
</tr>
<tr>
<td></td>
<td>(222)</td>
<td>(67)</td>
<td>(39)</td>
<td>(250)</td>
</tr>
<tr>
<td>Increased Coronary Insufficiency</td>
<td>4.6%</td>
<td>4.0%</td>
<td>2.6%</td>
<td>4.8%</td>
</tr>
<tr>
<td></td>
<td>(222)</td>
<td>(66)</td>
<td>(39)</td>
<td>(249)</td>
</tr>
<tr>
<td>New or Increased Breathlessness</td>
<td>18.6%</td>
<td>23.5%</td>
<td>18.4%</td>
<td>20.1%</td>
</tr>
<tr>
<td></td>
<td>(221)</td>
<td>(67)</td>
<td>(38)</td>
<td>(250)</td>
</tr>
<tr>
<td>Lack of energy</td>
<td>36.7%</td>
<td>41.8%</td>
<td>39.5%</td>
<td>37.8%</td>
</tr>
<tr>
<td></td>
<td>(218)</td>
<td>(67)</td>
<td>(38)</td>
<td>(247)</td>
</tr>
<tr>
<td>All chest pains</td>
<td></td>
<td></td>
<td>37%*</td>
<td>56%*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(38)</td>
<td>(247)</td>
</tr>
</tbody>
</table>

Table 25. Specific Prodromal Symptoms in Definite MI Patients.

*Significant difference p < 0.05.
c) **Duration of Specific Prodromal Symptoms**

The histograms of Figure 17 depict the pattern of onset of the symptoms in the 28 days before the acute event.

![Graphs showing probability of onset of prodromal symptoms](image)

**Figure 17.** Probability of Onset of Prodromal Symptoms (Definite Myocardial Infarctions)
Overseas data corresponds well with the Auckland figures.

Alonzo (119) reported 67% of MI cases experienced new or increased angina in the prodromal period (probably including also what is referred to in this study as acute coronary insufficiency), 38% experienced excessive fatigue and 36% dyspnoea.

Solomon (118) recorded a 65% incidence of prodromata, with 59% of cases having some kind of pain in this period.

*Most of these cases represent a continuing decline in a longer term health deterioration.*
Kileen (74) recorded prodromal symptoms in Oxford, U.K., as
a) New pain 23.7%, b) Changed pain 25.3%, c) Dyspnoea 19.1%, d) Tiredness 19.6%, for both sexes combined.

**Acute Phase**

a) **Description of symptoms**

The following describes the acute phase symptoms:

- 86% had classical Type I pain,
- 8.7% had atypical symptoms,
- 5.2% had no pain (2/3 of these were sudden deaths),
- 52.7% had some degree of abnormal breathlessness, and
- 72% experienced abnormal sweating.

There were no significant differences between males and females.

Of those cases associated with sudden death about 25% had no known pain.

These cases died within a few seconds of apparently normal health and included cases with developed myocardial infarction that had not been symptomatic. (See comment under 'Postmortem Findings,' this chapter.)

Kileen reported from Oxford (74) that chest or epigastric pain was the presenting symptom in 82% of cases, but this includes also all sudden deaths. He noted also that 63% reported abnormal sweating.

Pedoe (91) found that 77% of surviving MI patients had experienced chest pain in the acute phase.

Hagstrom (33) in Nashville, U.S.A., found that 74% of the MI cases met the typical symptom pattern criteria.
Bean (120) has summarized the various clinical masquerades of myocardial infarction. However, it seems that the atypical presentations (e.g., dyspnoea alone, angina, arhythmia, neurological symptoms, apprehension, weakness) were either uncommon alone, or else such cases were seldom diagnosed, in Auckland.

b) **Time of onset of acute event**

(i) **Month.** Table 26 shows the number of cases each month.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25</td>
<td>24</td>
<td>21</td>
<td>18</td>
<td>19</td>
<td>24</td>
<td>21</td>
<td>32</td>
<td>21</td>
<td>28</td>
<td>32</td>
<td>28</td>
</tr>
</tbody>
</table>

Table 26. Distribution of Definite MI Cases Over One Year.

In Auckland, the coolest six months are April - September. (See Chapter 1, Figure 5 for temperatures April 1974 - March 1975.)

Thus there were 135 cases in the cooler months and 158 in the warmer months. This difference is not statistically significant.

(ii) **Time of day.** Table 27 shows the distribution of definite MI cases throughout the day.

<table>
<thead>
<tr>
<th>Time Period</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>12mn - 6am*</td>
<td>59</td>
</tr>
<tr>
<td>6am - 12md*</td>
<td>89</td>
</tr>
<tr>
<td>12md - 6pm</td>
<td>70</td>
</tr>
<tr>
<td>6pm - 12mn</td>
<td>72</td>
</tr>
</tbody>
</table>

Table 27. Distribution of Definite MI Cases Throughout the Day.

*This represents a significant difference (p < 0.05) between the number of cases whose symptoms start between 12mn - 6am as compared to 6am - 12md.
Pedoe (91) confirms the time relationships found here, with no significant three monthly variation, but with a deficit of cases during the early hours of the morning and an excess at the time of rising and going to work.

Pell and D'Alonzo (121) found the same pattern in the employees of Du Pont & Co. in the U.S.A.

Most, in Seattle, reported (34) that the most frequent hospitalization period for MI's was the winter, but does not state if the difference was significant statistically.

Treatment

a) Place

Of the 293 cases i) Twenty-five were treated only at home for at least the first three days, ii) Twenty-one were finally treated in hospital but took between 24-72 hours after onset of symptoms to be admitted, iii) Two hundred and eleven were admitted to hospital less than 24 hours after onset of symptoms, iv) Thirty-two died within 24 hours of onset of symptoms, before receiving treatment, and v) Four received no treatment within 3 days. See Figure 18.

b) Reasons for treatment at home or delay beyond 24 hours in hospitalization

i) Cases taking more than 24 hours to reach hospital

48% due to initial uncertainty of diagnosis by doctor
48% due to no initial medical care
5% due to patient request
5% due to other reasons.

ii) Cases treated only at home

70% due to initial uncertainty of diagnosis by doctor
30% due to patient request
17% due to no initial medical care
9% due to other reasons.

The most frequent incorrect initial diagnosis was that of hiatus hernia (usually despite the absence of demonstrated reflux).

Figure 18. Place of Treatment (Definite Myocardial Infarctions)

11 Note percentages add to more than 100 as there were frequently multiple reasons.
The category represented by the first bar in Figure 18 is almost certainly markedly under-represented as only 55% of the sudden death cases had postmortems. Those that never were usually forced into the possible myocardial infarction category. It also seems likely that a proportion of cases that had no macroscopic infarct or coronary artery thrombosis would have developed such pathological evidence if their survival had been longer.

Of the MI cases who died suddenly nine or 22% were treated in hospital. The proportion of non-hospitalized cases was rather lower than expected, but still higher than many overseas reports which seem to be usually 0-5% compared with 8% in Auckland (91, 92, 33, 122). However, in Oxford (74) and Edinburgh (56), home treatment accounted for 15-25% of cases. These higher figures relate to the period before the full acceptance of coronary care units.

c) Treatment delays are expressed as a flow diagram in Figure 19.

Cumulative probabilities for delays are shown in Table 28.

<table>
<thead>
<tr>
<th>a) Onset of Symptom to Call for Doctor</th>
<th>b) Call for Doctor to Arrival of Doctor</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 mins 35.3%</td>
<td>30 mins 55.9%</td>
</tr>
<tr>
<td>1 hour 49.3%</td>
<td>1 hour 73.7%</td>
</tr>
<tr>
<td>2 hours 69.7%</td>
<td>2 hours 83.8%</td>
</tr>
<tr>
<td>6 hours 79.5%</td>
<td>4 hours 92.3%</td>
</tr>
<tr>
<td>12 hours 93.0%</td>
<td>6 hours 95.0%</td>
</tr>
<tr>
<td></td>
<td>12 hours 96.6%</td>
</tr>
</tbody>
</table>
c) Arrival of Doctor to Arrival at Hospital

<table>
<thead>
<tr>
<th>Time</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 hour</td>
<td>30.2%</td>
</tr>
<tr>
<td>2 hours</td>
<td>61.7%</td>
</tr>
<tr>
<td>4 hours</td>
<td>84.5%</td>
</tr>
<tr>
<td>6 hours</td>
<td>88.9%</td>
</tr>
<tr>
<td>12 hours</td>
<td>95.3%</td>
</tr>
</tbody>
</table>

d) Onset of Symptoms to Arrival in C. C. U.

<table>
<thead>
<tr>
<th>Time</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 hour</td>
<td>4.4%</td>
</tr>
<tr>
<td>2 hours</td>
<td>23.7%</td>
</tr>
<tr>
<td>4 hours</td>
<td>58.9%</td>
</tr>
<tr>
<td>6 hours</td>
<td>74.2%</td>
</tr>
<tr>
<td>12 hours</td>
<td>88.5%</td>
</tr>
</tbody>
</table>

e) Arrival at Accident and Emergency Department to Arrival at C. C. U.

<table>
<thead>
<tr>
<th>Time</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 mins</td>
<td>19.7%</td>
</tr>
<tr>
<td>1 hour</td>
<td>52.7%</td>
</tr>
<tr>
<td>4 hours</td>
<td>92.3%</td>
</tr>
</tbody>
</table>

Table 28. Cumulative Probabilities for Several Delay Intervals.

Figure 19. Treatment Delays for Various Admissions Routes (Definite Myocardial Infarctions)
No significant differences were observed between males and females. In particular, this was true for the delay in seeking medical aid.

Norris (47) in 1973 reported from Auckland delays for the 1972 year to one hospital, expressed as median time for total admission of approximately four hours. Median times for patient, doctor, transport and hospital delays to coronary unit were one and one half hours, two hours, twenty minutes and ten minutes respectively. Norris' figures for doctor delay are not strictly comparable with the doctor delay of the present study which includes only time from call for medical aid until the doctor's arrival. Norris' doctor delay included also the period until the doctor made a decision to call for transport to hospital. Nevertheless there seems to have been some improvement in patient delay particularly, since Norris' Auckland study.

Pedoe (91) recorded that in London 46% of persons suffering acute MI had called for medical aid within two hours, 60% within four hours, and 72% by eight hours. At four hours, 45% had reached hospital and 31%, the ward.

Armstrong in Edinburgh (56) found
i) Median delay to call for G.P. - 1 hour 30 mins
ii) Median delay in G.P.'s arrival a further 44 mins
iii) Median delay between onset of symptoms and hospitalization of 3 hours 35 mins
iv) Median delay in reaching ward after hospital arrival - 29 mins

Pole (124) recorded that in Perth the median delay for the patient to call for medical aid and total admission delay were two and a half hours and five and a quarter hours respectively.
Thus Aucklanders seem quicker than most to seek aid, but hospital delay in reaching the coronary unit could be improved.

First Assessment Post Infarction

This record was usually made by the general practitioner but if not recorded, the house surgeon's observations on arrival at hospital were used. The median time of these observations after the onset of the acute event was two hours and thirty minutes and 75% were within seven hours and forty minutes.

Average Systolic B. P. - 135.3 mm Hg
Average Diastolic B. P. - 87.9 mm Hg

For the 57% who had had a previous blood pressure recording within one year and also survived to have a recorded post-infarct pressure, the pattern of differences (Old B. P. - Recent B. P.) were as in Table 29.

<table>
<thead>
<tr>
<th>Pressure Difference (mm Hg)</th>
<th>-80</th>
<th>-60</th>
<th>-40</th>
<th>-20</th>
<th>0</th>
<th>+20</th>
<th>+40</th>
<th>+60</th>
<th>+80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systole (No. of cases)</td>
<td>1</td>
<td>4</td>
<td>19</td>
<td>32</td>
<td>56</td>
<td>32</td>
<td>18</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Diastole (No. of cases)</td>
<td>0</td>
<td>2</td>
<td>14</td>
<td>52</td>
<td>71</td>
<td>24</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 29. Blood Pressure Differences 'Previous B. P. - First Assessment B. P.' for Definite MI Cases.

Thus, for this group of 167 cases (which is biased against sudden death and towards having had a previous B. P. recording), both systolic and diastolic pressures post-infarct are a little lower than previously reported, on the average.
The proportion of cases with a positive difference is significantly higher than the proportion with a negative difference (p < 0.005 for systolic and p < 0.05 for diastolic).

Fourteen per cent of cases had post-infarct systolic pressures in excess of 20 mm Hg higher than the previous casual recordings. Fox et al. (125) has found a similar group to have increased mortality and SGOT levels. The present study did not confirm the excess mortality. The risk of death or cardiac arrest seemed highest in those with systolic post infarct pressures more than 20 mm Hg lower than previous recordings, and lowest in those with systolic post infarct pressures \( \geq 20 \text{ mm Hg} \) higher than previously (p = 0.07). Similarly for diastolic pressures differing more than 10 mm Hg than the previous recording. This is in keeping with the previous Auckland findings of Norris et al. (126).

In 40% of the 227 patients in whom sufficient record was made, clinical manifestations of shock, such as pallor and/or sweating were noted. In 28% of the 226 patients in whom sufficient record was made, bilateral basal crepitations were heard.

In 7.4%, the first pulse rate recorded post-infarct was less than 60/minute. In 24% it was greater than 100/minute. The average pulse rate was 84.5.

Norris (127) recorded a 21% proportion of cases with bradycardia less than 60/min and a 36% proportion of cases with tachycardia greater than 100/min. These higher figures are probably due to the fact that they were based on several hourly recordings whereas the present study figures were based only on the first post-infarct recordings.
Acute E.C.G. (for the 259 cases in which an acute E.C.G. was available)

a) **Type of Infarct**

The following are the findings:

i) Full thickness (Persistent S.T. elevation and/or new Q waves) - 58.3%.

ii) Partial thickness (New persistent T wave inversion) - 28.6%.

iii) Other abnormality only (e.g., LBBB, old Q waves or transient ST-T change) - 11.2%.

iv) Normal E.C.G. - 1.9%.

Nine per cent of cases of full thickness infarction also had other abnormalities (e.g.; RBBB, heart block), whereas 24% of cases of partial thickness infarction has such other abnormalities coexisting. (Significant difference \( p < 0.01 \).)

Norris (47) found 64.5% transmural infarction in hospitalized cases.

b) **Site of infarction by E.C.G. criteria**

The sites were as follows:

- 52.6% of infarctions were Anterior
- 37.8% of the infarctions were inferior or infero-lateral
- In 9.6% the site was not determined by E.C.G.

**Cardiac Arrest**

Sixty-six (22.7%) cases (16% of females and 24% of males) developed apparently primary cardiac arrest, within twenty-eight days. Of these, twelve (22%) survived for 28 days or more after onset of the attack.
The place of arrest was as follows:

53% occurred before any decision on treatment was made (and 17% of the successful resuscitations occurred here).

0% occurred after a decision to treat at home

3% occurred in the ambulance

18% occurred in the coronary care unit (but 66% of the successful resuscitations occurred here)

20% occurred in the hospital ward usually after discharge from the coronary unit (and 17% of the successful resuscitations occurred here).

6% occurred elsewhere.

Two arrests in proved infarcts occurred during the period of delay between reaching hospital or reaching the coronary unit. One died.

Probably the category 'before decision on treatment' is under-represented because as previously mentioned it is likely that some of the early deaths were MI's but evidence was not obtainable, and so they will be included in the chapter on sudden death.

Libethson (128) recorded that of 426 prehospital sudden cardiac deaths only 72% were due to ventricular fibrillation. This figure was for all sudden cardiac deaths, not only proven myocardial infarction. In Auckland there was evidence that at least 21% of the fatal MI's were not due to primary ventricular fibrillation, but these were all deaths within 28 days, not sudden deaths.

Pedoe (91) recorded in London that 23% of Definite MI cases died outside hospital (it is not clear whether some of these were being treated at home).
However, depending on the postmortem rate, the number of early deaths included as definite MI cases will vary substantially, as the diagnosis of definite MI depends on the postmortem in a proportion of the cases.

Chapter 7 contains a discussion of characteristics of persons suffering documented ventricular fibrillation compared to those not doing so.

Death

Overall the death rate was 24.7% within 28 days. (Males 24.1%, Females 26.5%). Of the 232 cases who reached hospital alive, mortality was 15.2%. The overall death rate is probably artificially low due to lack of evidence to correctly classify some sudden death cases as definite MI. The death rate in cases previously having suffered myocardial infarction was 28.4%. This nonsignificant short-term mortality increase with previous infarction is similar to the previous Auckland findings of Norris et al. (126).

<table>
<thead>
<tr>
<th>Time of Death after Onset of Symptoms</th>
<th>Number</th>
<th>Cumulative %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5 mins</td>
<td>15</td>
<td>21.75%</td>
</tr>
<tr>
<td>5-15 mins</td>
<td>3</td>
<td>26.10%</td>
</tr>
<tr>
<td>15-30 mins</td>
<td>2</td>
<td>29.00%</td>
</tr>
<tr>
<td>30-60 mins</td>
<td>2</td>
<td>31.90%</td>
</tr>
<tr>
<td>1-3 hours</td>
<td>3</td>
<td>36.25%</td>
</tr>
<tr>
<td>3-6 hours</td>
<td>2</td>
<td>39.15%</td>
</tr>
<tr>
<td>6-24 hours</td>
<td>9</td>
<td>52.20%</td>
</tr>
<tr>
<td>1-7 days</td>
<td>12</td>
<td>69.60%</td>
</tr>
<tr>
<td>1-2 weeks</td>
<td>8</td>
<td>81.20%</td>
</tr>
<tr>
<td>2-3 weeks</td>
<td>5</td>
<td>88.40%</td>
</tr>
<tr>
<td>3-4 weeks</td>
<td>8</td>
<td>100%</td>
</tr>
</tbody>
</table>

TOTAL 69*

Table 30. Time of Death after Onset of Symptoms

*In three cases the circumstances of death could not be determined or even the time of death within 24 hours. These cases are omitted from the above table, although they clearly fall into one of the categories before or including '1-7 days'.
These results are shown as estimated probability density histograms in Figures 20 and 21. Table 30 shows the cumulative probability of death.

The hospital mortality of 15% in Auckland is virtually identical to that recorded from Edinburgh (56).

Pedoe (91) recorded a 28 day case fatality among males (females similar) of 35%, but only 17% among those cases who reached hospital alive and only 13% among those treated in coronary care units. The differences in these figures may largely reflect the reducing risk of cardiac arrest as time progresses.

Norris (47) recorded a hospital mortality of 26% and quotes several other studies showing figures varying between 15-40%.
Figure 21. Probability of Death in First 28 Days (Definite Myocardial Infarctions)

Thus the figures of the present study seem lower than most, despite the postmortem rate being higher than many studies, allowing the classification of more sudden deaths as also definite MI's. (The mortality for all definite acute coronary events, i.e., sudden death plus definite MI was 48.7%.)

Postmortems

Of those fatal cases diagnosed as definite myocardial infarction, 76.4% had a postmortem (55 cases). In fact, that diagnosis depended on the postmortem in 52% of all fatal definite MI's (i.e., 12.6% of total definite MI cases). The results are shown in Table 31.
<table>
<thead>
<tr>
<th>Macroscopic coronary infarction &amp; no coronary artery lesion</th>
<th>Acute coronary infarction</th>
<th>Both infarction and coronary lesion</th>
<th>Left ventricle hypertrophy</th>
<th>Fine myocardial fibrosis</th>
<th>Cardiac rupture</th>
<th>Mural thrombosis</th>
<th>Old myocardial infarction</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>17</td>
<td>22</td>
<td>14</td>
<td>12</td>
<td>1</td>
<td>8</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

29% 31% 40% 25% 22% 1.8% 14.5% 24% %

Table 31. Selected Post Mortem Results for Definite MI Cases.
Of eighteen cases with clinical evidence of definite acute infarction before death and who had a postmortem, only one did not also have macroscopic evidence of infarction at postmortem (but did have an acute thrombosis).

Postmortems on 98 of 178 sudden deaths revealed the only evidence of definite MI in 37 cases. It seems likely, though unable to be confirmed, that those sudden death cases who had a postmortem were not biased in any important way. The circumstances resulting in a coroner's referral were largely time related (see Chapter 1, p. 33). Such biases as did exist would be towards cases who did not have previously recognized coronary disease and towards cases who had not recently visited their doctor. How these factors might influence the proportion of observable definite infarction in these sudden deaths cases is speculative. If one accepts that the proportion of definite MI's could be the same in those who did not have postmortems, as those who did, it seems that a further approximately thirty definite MI cases may have been found if a 100% postmortem rate had been possible, for the sudden deaths. Thus the 'true' incidence of definite MI could be about 10% higher than stated. Also the proportion of fatal cases dying in the first 24 hours could be substantially higher than the stated 52% (about 65%). The mortality rate would rise to about 34%.

The frequency of acute arterial lesions has been the subject of much study in recent years (129, 130). The Aucklands results are compatible with overseas findings.
Miller (131) found that of cases with pathological infarction 66% had also an acute coronary occlusion. The Auckland figure is 58%. Defining left ventricular hypertrophy as '50% heavier than normal', Miller found left ventricular hypertrophy in 74% of 49 cases without an acute coronary artery lesion and 42% of 94 cases with an acute coronary artery lesion, i.e., overall 53%. However there was no upper age restriction on this series.

Mitchell et al. (132) found in a group of patients again with pathological MI (69% of the Auckland MI fatalities), that more than 50% of male patients had fine fibrotic lesions (apparently not associated with acute or chronic coronary lesions), which was no different to the 'normal' male population. This was a microscopic study and this fact probably accounts for the excess over the Auckland results.

For women, Mitchell found about 30% of an unselected female population had fine lesions but over 80% of females with an old or new MI. This may well be consistent with the findings of the present study that women having suffered an acute MI were more likely to have had a history of breathlessness or have been taking digoxin and/or a diuretic prior to the acute event.
CHAPTER 5

RESULTS-
SUDDEN DEATH IN AUCKLAND
This chapter summarizes the data gathered on 178 cases of sudden cardiac death, who should be a 40% representative sample of all such cases occurring in Auckland April 1974 - March 1975. As previously mentioned, 41 (23%) of these cases were also proven definite myocardial infarctions, and are thus included in Chapter Three.

Baum (133) in an investigation of 146 resuscitated survivors of ventricular fibrillation found that only 10% of the patients collapsed at the time the ambulance arrived went on to show evolution of typical acute transmural infarction compared with 50% of those cases who developed ventricular fibrillation after the arrival of the ambulance. Forty-two per cent of the first group and 79% of the second group showed enzyme evidence of myocardial necrosis, which may have been induced by the arrest or the cause of the arrest.

The Auckland figures are of course based on pathological evidence if available and/or clinical evidence if available. Included are both the 'instantaneous' and later deaths in the first 24 hours. The frequency of acute myocardial infarction undoubtedly would have been higher had the postmortem rate been higher.

**Demographic Data**

a) **Sex**

136 males (76.4%)

42 females (23.6%)

Kuller in Baltimore found that 23.0% of sudden deaths aged 25-64 years were female (35).
Hagstrom in Nashville, U.S.A., reported 26.0% of deaths in whites were female, but 36.9% of sudden deaths in blacks were female. The age range was up to 75 years (33).

McNeilly and Pemberton (134) in Belfast Ireland found 23.9% of coronary deaths (not only sudden deaths) less than 70 years, were female.

Romo in Helsinki (94) reported 19.9% of sudden deaths, under 65 years to be female.

Thus agreement is good in various places and very similar to myocardial infarction figures.

b) Age Specific Incidence

This is depicted in Table 32 and Figure 22.

![Figure 22. Age and Sex Specific Incidence Rates for Sudden Death (With 95% Credibility Intervals)](image-url)
<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Cases (% in brackets)</th>
<th>Total Census Popn.</th>
<th>Proportion of letters naming a selected GP</th>
<th>Max. likelihood est. of incidence &amp; 95% credibility range</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-29</td>
<td>M</td>
<td>1(0.7)</td>
<td>21758</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>0(0.0)</td>
<td>23138</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>1(0.7)</td>
<td>19327</td>
<td>Not recorded¹</td>
<td></td>
</tr>
<tr>
<td>30-34</td>
<td>F</td>
<td>0(0.0)</td>
<td>19652</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>3(2.2)</td>
<td>17054</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-39</td>
<td>F</td>
<td>0(0.0)</td>
<td>16749</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>5(3.7)</td>
<td>18575</td>
<td>336/856</td>
<td></td>
</tr>
<tr>
<td>40-44</td>
<td>F</td>
<td>3(7.1)</td>
<td>18069</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>11(8.1)</td>
<td>18111</td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-49</td>
<td>F</td>
<td>3(7.1)</td>
<td>17906</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>23(16.8)</td>
<td>15335</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-54</td>
<td>F</td>
<td>3(7.1)</td>
<td>16264</td>
<td>224/538</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>22(16.0)</td>
<td>14184</td>
<td></td>
<td></td>
</tr>
<tr>
<td>55-59</td>
<td>F</td>
<td>7(16.7)</td>
<td>15108</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>33(24.2)</td>
<td>11832</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-64</td>
<td>F</td>
<td>12(28.6)</td>
<td>12965</td>
<td>194/446</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>38(27.8)</td>
<td>9075</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>F</td>
<td>14(33.3)</td>
<td>11068</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 32. Age-Sex Specific Incidence Estimates for Sudden Death.

Average Age Males = 58.3 yrs; Average Age Females = 59.8 yrs; Overall Average Age = 58.6 yrs.

¹For the calculation of credibility ranges in ages 25-34 years, the proportion of letters for the ages 35-49 years was used.
### Table 33: Comparisons of the Incidence of Sudden Death in Different Places

<table>
<thead>
<tr>
<th>2°0 (2°48)</th>
<th>5°0 (9°09)</th>
<th>5°8 (4°39)</th>
<th>5°7 (6°74)</th>
<th>5°6 (6°49)</th>
<th>5°5 (6°24)</th>
<th>5°4 (6°00)</th>
<th>5°3 (5°75)</th>
<th>5°2 (5°51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0°7 (1°43)</td>
<td>0°4 (0°72)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
</tr>
<tr>
<td>0°6 (2°12)</td>
<td>0°4 (0°44)</td>
<td>0°0 (0°72)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
</tr>
<tr>
<td>0°2 (2°8)</td>
<td>0°0 (0°48)</td>
<td>0°0 (0°13)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
</tr>
<tr>
<td>0°0 (2°2)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
</tr>
<tr>
<td>0°0 (1°3)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
<td>0°0 (0°00)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
<th>Male</th>
<th>Female</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>36-69</td>
<td>60-64</td>
<td>55-59</td>
<td>50-54</td>
<td>45-49</td>
<td>40-44</td>
</tr>
<tr>
<td>35-39</td>
<td>30-34</td>
<td>36-69</td>
<td>60-64</td>
<td>55-59</td>
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<td>36-69</td>
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<td>50-54</td>
</tr>
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<td>30-34</td>
<td>36-69</td>
<td>60-64</td>
<td>55-59</td>
<td>50-54</td>
</tr>
</tbody>
</table>

**Note:**
- 24-hour period
- 3-hour period
- 1-hour definition
- Various medical and non-medical definitions
Comparisons with other places are made difficult by differing definitions, particularly the time period from onset of symptoms to death. Here, for a fair comparison the Auckland data is adjusted to whichever definition has been used in the other study.

Table 33 shows the figures for four other places.

c) Sudden Deaths and Social Class

Social class is defined as before and the results are as presented in Table 34

<table>
<thead>
<tr>
<th>Young (35-49 years)</th>
<th></th>
<th></th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Class</td>
<td>I</td>
<td>II</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>---------------------</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>-------</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>12</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>(6.5)</td>
<td>(12.7)</td>
<td>(5.8)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Middle Aged (50-59 years)</th>
<th></th>
<th></th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Class</td>
<td>I</td>
<td>II</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>----------------------------</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>-------</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>22</td>
<td>23</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>(15.9)</td>
<td>(23.4)</td>
<td>(15.7)</td>
<td></td>
</tr>
<tr>
<td>$X^2 = 5.67$</td>
<td></td>
<td></td>
<td></td>
<td>$P &lt; 0.06$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Old (60-69 years)</th>
<th></th>
<th></th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Class</td>
<td>I</td>
<td>II</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>-------</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>30</td>
<td>36</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>(29.3)</td>
<td>(39.4)</td>
<td>(27.2)</td>
<td></td>
</tr>
<tr>
<td>$X^2 = 5.10$</td>
<td></td>
<td></td>
<td></td>
<td>$P &lt; 0.07$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>All Ages (35-69)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Class</td>
<td>I</td>
<td>II</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>-------</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>64</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(51.7)</td>
<td>(75.6)</td>
<td>(48.7)</td>
<td></td>
</tr>
<tr>
<td>$X^2 = 6.85$</td>
<td></td>
<td></td>
<td></td>
<td>$P &lt; 0.05$</td>
</tr>
</tbody>
</table>

Table 34. Sudden Death and Social Class in Different Age Groups. (Expected values in parentheses)
A problem here is the differing age structure of the social classes with slightly more elderly persons in classes I & III. The above expected values take this into account. Thus we find a significant excess of sudden deaths occurring in the lowest social class. This is supported by several overseas studies when coronary deaths (as opposed to all coronary disease cases) are considered (94, 135, 136, 137, 138).

Race

Of all sudden deaths:

- 90.4% were European (161 cases)
- 5.1% were Maori (nine cases)
- 3.4% were Other Pacific Islander (six cases)
- 1.1% were Other races (two cases)

The Maori figure is above expectation once adjustment for the differing age structures is made (expected number is 5.7). However, with such small numbers, such differences could be due to random fluctuations. Death certificate data certainly suggest a higher Maori rate, but this is for all coronary deaths, not just sudden death.

Personal Characteristics & Habits

a) Height and Weight

Table 35 shows means and standard deviations for these variables.
Mean
Male Female

Standard
development
Male Female

| Height (cms)  | 173.2  | 161.0 | 10.39 | 5.96 |
| No. of cases  | (133)  | (42)  |       |      |
| Weight (kgs) | 74.0   | 63.6  | 15.04 | 12.86 |
| No. of cases  | (124)  | (41)  |       |      |

Table 35. Height and Weight in Sudden Death Cases.

Table 36 presents age-sex specific Quetelet's index for the sudden death patients.

<table>
<thead>
<tr>
<th>Age</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>S.D.</td>
</tr>
<tr>
<td>30 - 39</td>
<td>.330</td>
<td>.100</td>
</tr>
<tr>
<td>No. of cases</td>
<td>(3)</td>
<td></td>
</tr>
<tr>
<td>40 - 49</td>
<td>.261</td>
<td>.034</td>
</tr>
<tr>
<td>No. of cases</td>
<td>(14)</td>
<td>(6)</td>
</tr>
<tr>
<td>50 - 59</td>
<td>.246</td>
<td>.040</td>
</tr>
<tr>
<td>No. of cases</td>
<td>(39)</td>
<td>(10)</td>
</tr>
<tr>
<td>60 - 69</td>
<td>.244</td>
<td>.041</td>
</tr>
<tr>
<td>No. of cases</td>
<td>(65)</td>
<td>(23)</td>
</tr>
</tbody>
</table>

Table 36. Age Specific Quetelet's Index (for cases 30-69 years).

Comparing these figures with the Carterton data (105), there are no significant differences.

This finding is in keeping with more recent reports of some of the larger overseas studies. Results had been conflicting, but when multivariate techniques were used, it became clear that even Framingham data (139) gave little support for obesity being important in sudden death, as opposed to angina.
b) **Cigarette Smoking**

Table 37 shows the results for cigarette smoking in this sudden death population.

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Mean no.</th>
<th>Mean for smokers per/day only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>28.6%</td>
<td>14.9%</td>
<td>8.0%</td>
<td>14.3%</td>
<td>27.4%</td>
<td>6.9%</td>
<td>13.5</td>
<td>23.9</td>
</tr>
<tr>
<td>Males</td>
<td>24.1%</td>
<td>18.8%</td>
<td>9.0%</td>
<td>13.5%</td>
<td>27.8%</td>
<td>6.8%</td>
<td>13.5</td>
<td>31.5</td>
</tr>
<tr>
<td>Females</td>
<td>42.9%</td>
<td>2.4%</td>
<td>4.8%</td>
<td>16.7%</td>
<td>26.2%</td>
<td>7.1%</td>
<td>13.4</td>
<td>29.7</td>
</tr>
</tbody>
</table>

1 = Not smoked within ten years  
2 = Gave up < ten years but > six months ago  
3 = 1 - 9 cigarettes/day  
4 = 10 - 19 cigarettes/day  
5 = 20 - 39 cigarettes/day  
6 = ≥ 40/day

Table 37. Cigarette Smoking in Sudden Death Patients.

These results are very similar to those of definite myocardial infarction with the same significant differences holding when comparing 1976 census data with the sudden death case data, and age adjusting (see Table 38).

Libethson reported (128) 62.5% of cases smoked ten or more cigarettes per day.

These results are also very similar to those reported by Romo (94) where 49% of women were current smokers, 12% were ex-smokers, and 39% non-smokers. For men he found 62% to be current smokers, 22% ex-smokers, and 16% non-smokers.
### Table 38. Cigarette Smoking in Sudden Death Cases and the General Population.

<table>
<thead>
<tr>
<th>Category</th>
<th>Males Census</th>
<th>Sudden Death(133)</th>
<th>Females Census</th>
<th>Sudden Death (42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None or given up</td>
<td>63.2%</td>
<td>42%</td>
<td>74.7%</td>
<td>45%</td>
</tr>
<tr>
<td>0 - 9/day</td>
<td>5.9%</td>
<td>9%</td>
<td>7.4%</td>
<td>5%</td>
</tr>
<tr>
<td>10 - 19/day</td>
<td>12.6%</td>
<td>14%</td>
<td>10.5%</td>
<td>17%</td>
</tr>
<tr>
<td>20 - 39/day</td>
<td>15.5%</td>
<td>28%</td>
<td>6.9%</td>
<td>26%</td>
</tr>
<tr>
<td>≥ 40/day</td>
<td>2.9%</td>
<td>7%</td>
<td>0.6%</td>
<td>7%</td>
</tr>
</tbody>
</table>

\[ \chi^2_4 = 53.6 \ (p < 0.001) \quad \chi^2_3 = 68.4 \ (p < 0.001) \]

Chiang (57) in Tecumseh however, found no significant difference between sudden death cases' smoking habits and a similar aged Tecumseh population. Hickey (140) reported from Dublin that sudden deaths were equally distributed between smokers and non-smokers.

The combined Framingham-Albany data (109) suggests smoking the most potent of the several tested risk factors in predicting sudden death for the age group 45-64 years.

---

5 Numbers of cases for which information was available is given in brackets.

6 Two classes were amalgamated due to small numbers.
c) Alcohol Consumption

Note that alcohol data recording was only attempted for the latter 143 cases. Table 39 records mean intakes.

Thus 45% of all cases were beer drinkers, 28% were wine and sherry drinkers, 28% were spirit drinkers and 63% drank alcohol in some form.

Figures for the New Zealand population (113) aged 20 years and over in 1971 were:

- Beer consumption: 118.5 gms alcohol per week
- Wine consumption: 26.2 gms alcohol per week
- Spirits consumption: 29.4 gms alcohol per week.

The sudden death cases' alcohol intakes were substantially above average (except for beer), despite the much older age of this population when compared with the general New Zealand population.

Several studies (141, 142) have suggested that alcohol consumption could be a risk factor for cardiac death. This will be discussed further in Chapter 7.

Cardiovascular History

This section refers to symptoms prior to the prodromal period.

The symptoms included are:

i) Angina
ii) Breathlessness
iii) Acute coronary insufficiency
iv) Documented definite myocardial infarction.

The number of previous symptoms are depicted in the histogram of Figure 23.
<table>
<thead>
<tr>
<th>Category</th>
<th>Beer</th>
<th></th>
<th>Wine &amp; Sherry</th>
<th></th>
<th>Spirits</th>
<th></th>
<th>Total Alcohol</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All cases</td>
<td>Drinkers</td>
<td>All cases</td>
<td>Drinkers</td>
<td>All cases</td>
<td>Drinkers</td>
<td>All cases</td>
<td>Drinkers</td>
</tr>
<tr>
<td>All cases (6*)</td>
<td>75.3</td>
<td>(143)</td>
<td>165.7</td>
<td>(65)</td>
<td>55.0</td>
<td>(142)</td>
<td>195.3</td>
<td>(40)</td>
</tr>
<tr>
<td>No. of cases</td>
<td>(32)</td>
<td>(6)</td>
<td>35.8</td>
<td>(32)</td>
<td>12.2</td>
<td>(32)</td>
<td>65.0</td>
<td>(6)</td>
</tr>
<tr>
<td>Males (5*)</td>
<td>86.7</td>
<td>(111)</td>
<td>163.1</td>
<td>(59)</td>
<td>67.3</td>
<td>(110)</td>
<td>217.7</td>
<td>(34)</td>
</tr>
<tr>
<td>No. of cases</td>
<td>(30)</td>
<td>(17)</td>
<td>76.3</td>
<td>(29)</td>
<td>134.6</td>
<td>(13)</td>
<td>120.0</td>
<td>(10)</td>
</tr>
<tr>
<td>Females (1*)</td>
<td>35.8</td>
<td>(32)</td>
<td>190.9</td>
<td>(6)</td>
<td>12.2</td>
<td>(32)</td>
<td>65.0</td>
<td>(6)</td>
</tr>
<tr>
<td>Sudden death with proven MI (1*)</td>
<td>75.1</td>
<td>(113)</td>
<td>176.8</td>
<td>(48)</td>
<td>55.3</td>
<td>(113)</td>
<td>231.4</td>
<td>(27)</td>
</tr>
<tr>
<td>No. of cases</td>
<td>(30)</td>
<td>(17)</td>
<td>76.3</td>
<td>(29)</td>
<td>134.6</td>
<td>(13)</td>
<td>120.0</td>
<td>(10)</td>
</tr>
</tbody>
</table>

Table 39. Alcohol Consumption During the Past One Year (Grams per week)

* These are not included in the 'No. of cases' totals.

7 Bracketed numbers in this column represent the number of cases for which information was not available.
b) **Individual Symptoms**

Table 40 shows the percentage of cases suffering the given previous symptoms.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>52.6 (133)</td>
<td>43.6 (39)</td>
</tr>
<tr>
<td>Acute Coronary Insufficiency</td>
<td>19.2 (130)</td>
<td>19.5 (41)</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>53.7 (134)</td>
<td>51.2 (41)</td>
</tr>
<tr>
<td>1 Previous Infarct&lt;sup&gt;8&lt;/sup&gt;</td>
<td>30.8 (133)</td>
<td>11.9 (42)</td>
</tr>
<tr>
<td>2 Previous Infarcts</td>
<td>3.0 (133)</td>
<td>4.8 (42)</td>
</tr>
<tr>
<td>3 Previous Infarcts</td>
<td>3.0 (133)</td>
<td>0 (42)</td>
</tr>
<tr>
<td>No Previous Infarcts&lt;sup&gt;9&lt;/sup&gt;</td>
<td>63.2 (133)</td>
<td>83.3 (42)</td>
</tr>
</tbody>
</table>

Table 40. Percentage of Case Suffering Individual Previous Symptoms.

<sup>8</sup>Significant difference between male and female p < 0.02

<sup>9</sup>Significant difference between male and female p < 0.05
Duration of Symptoms

Mean durations are recorded for various symptoms in Table 41.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Angina</th>
<th>Acute Coron. Insufficiency</th>
<th>Breathlessness</th>
<th>Time since first M.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>177 weeks</td>
<td>99 weeks</td>
<td>190 weeks</td>
<td>76 months</td>
</tr>
<tr>
<td></td>
<td>(86)</td>
<td>(34)</td>
<td>(92)</td>
<td>(48)</td>
</tr>
</tbody>
</table>

Table 41. Mean Durations for Given Previous Symptoms in Sudden Death Cases.

Both sexes were similar except that for females acute coronary insufficiency had mean duration of 144 weeks (nine cases) compared with males' duration of 84 weeks (25 cases).

The histograms of Figure 24 show the pattern of onset of symptoms.

Chiang et al. (57) reported that 40% of 45 Tecumseh sudden deaths had had previous coronary disease.

Myeburg and Davis (143) found that 59.2% of sudden death cases had definite or suggestive symptoms of coronary disease before death.

Kuller also recorded (35) that over half of his cases in Baltimore had a prior history of heart disease.

Libethson (128) found 32.5% gave a history of previous M.I. and 48.5% a history of angina pectoris. Hagstrom (33) found that 37.2% of white males and 29.8% of white females had suffered a previous M.I. (from a 93% non-random sample of the total cases), whereas 20% of black males and 0% of black females had suffered a previous M.I.
Figure 24. Probability of Onset of Previous Symptoms (Sudden Deaths)
Kannel et al. (144) found that 41% of sudden deaths had previous evidence of coronary disease.

Variation therefore is quite wide, but could be due to definitions differing rather than the disease process.

d) Drugs

Table 42 refers to a selection of the more common medications taken within three weeks of the acute event.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Digoxin</th>
<th>blocker</th>
<th>TNT</th>
<th>Thiazide or Lasix</th>
<th>Other antihypertensive</th>
<th>Tricyclics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>20.6%</td>
<td>15.4%</td>
<td>28.7%</td>
<td>24.3%</td>
<td>12.5%</td>
<td>3.7%</td>
</tr>
<tr>
<td></td>
<td>(136)</td>
<td>(136)</td>
<td>(136)</td>
<td>(136)</td>
<td>(136)</td>
<td>(136)</td>
</tr>
<tr>
<td>Female</td>
<td>11.9%</td>
<td>14.3%</td>
<td>19.0%</td>
<td>31.0%</td>
<td>26.2%</td>
<td>4.8%</td>
</tr>
<tr>
<td></td>
<td>(42)</td>
<td>(42)</td>
<td>(42)</td>
<td>(42)</td>
<td>(42)</td>
<td>(42)</td>
</tr>
</tbody>
</table>

Table 42. Drug Therapy Within Three Weeks of Sudden Death.

e) Serum Lipids

Only 21% of these persons had had a serum cholesterol and 11% a serum triglyceride measured in the previous one year. Due to possible bias in the selected samples these results will not be reported.

f) Other Vascular Diseases

Of all cases, 13.8% gave a history of intermittent claudication, 9.6% gave a history of a previous stroke; and 8.4% had diabetes mellitus proven by glucose tolerance tests.

10 Significant difference between males and females p < 0.05.
Chiang (57) in Tecumseh found 18% of sudden death cases diabetic.
Libethson (128) found about 10.5% of cases to have a history of diabetes.
Hagstrom (33) found among whites in Nashville that 14.7% of men and 23.4% of women gave a history of diabetes (information from an 88% non-random sample of the total).

g) **Antecedant Blood Pressure**

Seventy-two per cent of these cases had had a blood pressure measured in the preceding one year (74% of females and 72% of males). Assessing hypertension in the same way as for definite myocardial infarction, of the 136 for whom useful information was available, 38.2% either had a history of antihypertensive therapy or had had documented treated hypertension in the past one year (45.5% for females and 35.9% for males).

Of the 72% who had had a recording taken in the previous one year mean results are given in Table 43.

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>147.4</td>
<td>151.4</td>
</tr>
<tr>
<td></td>
<td>(98)</td>
<td>(31)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>87.9</td>
<td>92.1</td>
</tr>
<tr>
<td></td>
<td>(98)</td>
<td>(31)</td>
</tr>
</tbody>
</table>

Table 43. Mean Results for Blood Pressure
Before the Acute Phase.

Libethson (128) found a history of hypertension in 34% of cases,
Hagstrom (33) recorded a history of hypertension in 40.95% of white males
and 51.21% of white females and in 29.62% of black males and 66.66% of black females. Kuller (35) found that 42% of sudden deaths had previously diagnosed hypertension.

Auckland figures seem comparable with the findings in other European populations.

h) Antecedent Electrocardiographic Characteristics

For a few cases, an electrocardiograph was available after the onset of the acute event. If a particular characteristic was then absent, it was considered to have been absent prior to the onset of the event. The only exception relates to left ventricular hypertrophy which could not be assessed in this fashion in the presence of an acute anterior infarction which could likely account for reduced voltages and so negative findings.

Either antecedent electrocardiographs or electrocardiographs as described above were available in only 62 of the 178 cases. The results are shown in Table 44.

<table>
<thead>
<tr>
<th>LVH (ECG criteria)</th>
<th>LBBB</th>
<th>RBBB</th>
<th>Left Anterior Hemiblock</th>
<th>1st, 2nd or 3rd degree Heart Block</th>
<th>Atrial Fibrillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>23.7%</td>
<td>8.4%</td>
<td>1.8%</td>
<td>20.9%</td>
<td>4.8%</td>
<td>12.2%</td>
</tr>
</tbody>
</table>

Table 44. Antecedent Electrocardiographic Criteria.

Chiang et al. (57) found left axis deviation in 17.8%, 1st degree A.V. block in 6.6%, complete LBBB in 11%, complete RBBB in 6.6% and atrial fibrillation in 2.2%. It could well be that the Auckland sample is biased towards inclusion
of atrial fibrillation cases who would have been more likely to have had a previous electrocardiograph due to symptoms. This effect could be true of the other characteristics also, to a lesser extent, although they seem fairly comparable with the Tecumseh findings which themselves are based only on 45 cases.

**Prodromal Symptoms**

a) **Number of Prodromal Symptoms**

The number of prodromal symptoms are shown in Figure 25. The prodromal symptoms considered are those listed below under specific symptoms (except for the last).

![Figure 25. Number of Prodromal Symptoms (Sudden Deaths)]
b) Specific Prodromal Symptoms

The proportion of cases suffering specific prodromal symptoms are listed in Table 45.

**Prodromal Symptoms in S.D. Cases**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Angina</td>
<td>7.6% (129)</td>
<td>7.3% (41)</td>
</tr>
<tr>
<td>Increased Angina</td>
<td>19.1% (131)</td>
<td>17.9% (39)</td>
</tr>
<tr>
<td>New AcI</td>
<td>8.5% (130)</td>
<td>20% (40)</td>
</tr>
<tr>
<td>Increased AcI</td>
<td>5.4% (132)</td>
<td>10% (40)</td>
</tr>
<tr>
<td>New or Increased Breathlessness</td>
<td>20.1% (130)</td>
<td>31.7% (41)</td>
</tr>
<tr>
<td>Lack of Energy</td>
<td>46.4% (129)</td>
<td>39% (41)</td>
</tr>
</tbody>
</table>

---

**All Chest Pain**

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30.5% (128)</td>
<td>41.0% (41)</td>
</tr>
</tbody>
</table>

(33.1% of both sexes)

Table 45. Specific Prodromal Symptoms in Cases Dying Suddenly.

Alonzo et al. (119) found a 39% frequency of prodromal dyspnoea, a 42% frequency of fatigue/weakness and a 35% frequency of prodromal new or accelerated chest pain. Sixty-four per cent of the cases had experienced some prodromal symptoms.

Kuller recorded (35) that over the two weeks prior to death, increasing angina occurred in 13% of cases, worsened dyspnoea occurred in 18% of cases (although 42% were breathless to some extent), and 38% noted increasing fatigue.
Figure 26. Probability of Onset of Prodromal Symptoms (Sudden Deaths)
Figure 26. Probability of Onset of Prodromal Symptoms (Sudden Deaths)

Thus these figures are very comparable to those found in Auckland. The fact that Kuller's figures are a little lower could well be due to the shorter prodromal period. The patterns of onset of prodromal symptoms are shown in Figure 26.

Acute Phase (for information regarding definition of time of onset see Chapter Two, page 76).

The circumstances at the time of collapse were witnessed within five minutes (i.e., a time when resuscitation could still be successful) in only 61.8%. This compares with 64% of deaths witnessed in Simon's study (145). *Most of these cases represent a continuing decline in a longer term health deterioration.
a) **Description of Symptoms**

For 76.1% of cases, information was available concerning the acute pain.  
29.9% had classical Type 1 pain  
34.0% had atypical pain (frequently severe, but death supervening before 20 mins).  
36.1% had no pain (frequently dying in sleep).

Information concerning acute dyspnoea was available in 75.6% and of these, 26.7% had acute dyspnoea.  
For 63.7% of cases, information was available concerning acute sweating, and of these 20.3% of cases had abnormal acute sweating. There were no significant differences between males and females.

The very short course of the acute symptoms in a substantial proportion make symptoms such as dyspnoea and sweating less likely to be observed than in acute infarction. Liberthson (128) found that in 23% acute symptoms of chest pain or dyspnoea were present and that 53% suffered instantaneous collapse or death within one minute of acute symptoms.

b) **Time of Onset of Acute Event**

i) **Month**

The distribution of cases throughout the year is shown in Table 46.
Table 46. Distribution of Sudden Death Cases Throughout the Year.

Thus sudden death seems significantly more common in the cooler six-month period.

ii) Time of Day

The distribution of cases throughout the day is shown in Table 47.

\[
\begin{array}{cccccc}
12\text{mn} - 6\text{am} & 6\text{am} - 12\text{md} & 12\text{md} - 6\text{pm} & 6\text{pm} - 12\text{mn} \\
26 & 52 & 52 & 33 \\
\end{array}
\]

\[
\chi^2 = 13.02 \quad p < 0.005.
\]

Table 47. Distribution of Sudden Deaths Throughout the Day.

Note that for 15 cases, accurate information as to time of death was not available. It is true that deaths occurring at nighttime are less likely to have accurately recorded times of death and so be more likely to exclusion as unknown data. Thus these findings should be treated with some caution (as distinct from the definite M.I. findings).

It has previously been shown several times that mortality from ischaemic heart disease tends to be higher in the cooler months (146,147,148). Thus the Auckland findings are certainly in keeping with overseas figures. Pell and D'Alonzo (121) noted a decreased frequency of death due to ischaemic heart
disease between 12mn - 6am compared with 6am - 12md and commented that 'the risk of death varies according to the time of the attack.' Again, this agrees well with the Auckland findings.

**Treatment**

a) **Place of Treatment and Relationship to Cardiac Arrest**

The place and type of treatment was distributed as follows:

i) 85.4% of cases received no treatment (i.e., were medically unattended).

ii) 9.0% of cases were treated in hospital (some after initial resuscitation from arrest outside hospital).

iii) 5.6% of cases were attended by only a doctor or ambulance prior to death.

Nineteen percent of cases called either the doctor or ambulance prior to death, but such aid arrived before death in only 13.4% of cases and only 7.9% of cases reached hospital prior to arrest (this includes two cases who reached hospital successfully using their own transport). See Figure 27.

---

**Figure 27. Treatment Stage in Relation to Cardiac Arrest (Sudden Deaths)**
First Assessment after Onset of Symptoms

Only 23 cases survived for a doctor to make some assessment after onset of symptoms. The average time of this assessment was 1 hour 47 mins after onset of symptoms, with 56.5% being within one hour. Undoubtedly this early assessment was at least partially due to the fact that only those cases seen quickly were seen at all before death.

Although this group is selected, obviously being biased toward a subgroup of sudden deaths who survived longer than most, the results of the assessment are of some interest.

Table 48 records the results for several clinical observations with the number of observations in parentheses.

<table>
<thead>
<tr>
<th>Mean Pulse Rate (per min)</th>
<th>Mean Systolic B.P. (mm Hg)</th>
<th>Mean Diastolic B.P. (mm Hg)</th>
<th>Crepitations at bases of Clinical Shock</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>100.5</td>
<td>122.0</td>
<td>84.2</td>
<td>63.1%</td>
<td>68.9%</td>
</tr>
<tr>
<td>(19)</td>
<td>(20)</td>
<td>(17)</td>
<td>(19)</td>
<td>(16)</td>
</tr>
</tbody>
</table>

Table 48. Some Clinical Variables at First Assessment.

Of the persons who had a 'first assessment' blood pressure measured, seventeen of those who had a systolic pressure recorded, and eighteen of those who had a diastolic pressure recordable, also had had previous blood pressures recorded in the one year prior. The differences (Previous blood pressure) - (Pressure after onset of symptoms), are presented in Table 49 and a summary of directional of blood pressure change is shown in Table 50.
Table 49. Differences (Antecedent-Post-Onset) in Blood Pressures.

<table>
<thead>
<tr>
<th>Systolic Differences</th>
<th>-100</th>
<th>-80</th>
<th>-60</th>
<th>-40</th>
<th>-20</th>
<th>0</th>
<th>+20</th>
<th>+40</th>
<th>+60</th>
<th>+80</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic Differences</td>
<td>1</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 50. Direction of Blood Pressure Change.

There is a significant difference between the directional trend of systolic and diastolic pressure differences. The diastolic pressures tended to rise and the systolic to fall.

Acute Electrocardiograms

Only 22 cases survived to have an electrocardiogram performed after the onset of symptoms.

The results are shown in Table 51.

<table>
<thead>
<tr>
<th>Normal</th>
<th>Full Thickness MI</th>
<th>Partial Thickness MI</th>
<th>Other Abnormality Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>0% (0)</td>
<td>27.3% (6)</td>
<td>13.6% (3)</td>
<td>59.1% (13)</td>
</tr>
</tbody>
</table>

Table 51. Electrocardiographs of those Sudden Death Cases Surviving to Electrocardiography.
The excess of the 'other abnormality only' category is likely due to the short periods of time available before death for more typical changes to evolve. Most of the abnormalities noted here were T wave inversion which could have been old or new.

Death

a) Place of Death

The places of death were distributed as follows:

i) Home 73.0% (130 cases)

ii) Hospital 9.0% (sixteen cases, four of whom arrested prior to admission but were temporarily resuscitated, and three of whom arrested between hospitalization and reaching coronary care).

iii) Work 6.2% (eleven cases)

iv) Elsewhere (mostly public places) 11.8% (21 cases)

Simon et al. (145) found in a Maryland study 76% of deaths occurred in private living quarters, about 14% in ambulances or hospital emergency rooms, 4% at work and 10% in public places. Armstrong et al. (56) found in an Edinburgh study of medically unattended deaths that 74% occurred at home or at hotel or friends' houses etc., 7.9% occurred at work, 15.3% occurred in the street and 2.6% in the hospital. The correspondence between these results is striking.

Of all deaths from acute definite ischaemic heart disease (definite myocardial infarction and sudden death) 79.1% occur before hospitalization is achieved and the mortality in this combined group is 48.7%. The
Albany-Framingham data showed that 60% of all coronary deaths occurred outside hospital (149), but included in this group are also the deaths of persons chronically debilitated and bedridden by the disease, prior to death.

b) **Type of Cardiac Arrest**

Twenty cases were monitored sufficiently to observe the type of arrest. Eight cases (40%) were either ventricular fibrillation or other terminal rhythm, secondary to pump failure or shock. Twelve (60%) were primary ventricular fibrillation (four in the ambulance). Again this is likely to be a selected group of cases.

Liberthson (128) in a report of prehospital arrest observed by fire rescue squads states, that the initial rhythm recorded after collapse, was ventricular fibrillation in 72%, and other terminal rhythms in 28%. (Asystole, idioventricular rhythm, heart block, sinus bradycardia, ventricular tachycardia, junctional rhythm).

c) **Time of Death after Onset of Symptoms**

There were twelve cases where the time of death could not be accurately estimated and they are not included here. Several other cases were not witnessed. For these persons, if no reasonable clue could be gained, the time of death recorded was midway between the time the person was last seen alive and the time he was found dead. If such a case was found beyond twenty-four hours after onset of symptoms or last being observed as apparently well, it was accepted as a sudden death only if there was pathological evidence that death had occurred within the twenty-four hours.
These results shown in Figure 28 are typical of the majority of a large number of previously reported studies (134, 56, 35, 145).

Simon has reported that cases with no previous documented coronary disease tended to die quicker after onset (145). Using the Auckland data, the time of death was compared with the number of previous cardiac type symptoms and no significant differences were found. The figures are shown in Table 52.

<table>
<thead>
<tr>
<th>Time of Death after Onset</th>
<th>0 - 5 min</th>
<th>5 - 60 min</th>
<th>&gt; 60 mins</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of previous symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>18</td>
<td>14</td>
<td>5</td>
<td>37</td>
</tr>
<tr>
<td>1</td>
<td>20</td>
<td>12</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
<td>14</td>
<td>13</td>
<td>52</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>9</td>
<td>7</td>
<td>37</td>
</tr>
</tbody>
</table>

Table 52. Time of Death after Onset Relative to the Number of Previous Symptoms.

However, if the number of prodromal symptoms were considered, there was a significant difference $p < 0.025$ with those with no prodromal symptoms tending to die quicker after onset. This is shown in Table 53.

<table>
<thead>
<tr>
<th>Time of Death after Onset</th>
<th>0 - 60 mins</th>
<th>&gt; 60 mins</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of prodromal symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>52</td>
<td>6</td>
</tr>
<tr>
<td>&gt; 0</td>
<td>81</td>
<td>27</td>
</tr>
</tbody>
</table>

Table 53. Time of Death after Onset Relative to the Number of Prodromal Symptoms.
Some studies have suggested that younger persons tend to die quicker (134, 62). However, the Framingham data did not clearly support this conclusion (149). The Auckland data did not show this trend, as shown in Table 54.

<table>
<thead>
<tr>
<th>Time of Death after Onset</th>
<th>0 - 5 mins</th>
<th>6 - 60 mins</th>
<th>60 mins</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 35-39 yrs</td>
<td>11</td>
<td>8</td>
<td>6</td>
<td>25</td>
</tr>
<tr>
<td>50-59 yrs</td>
<td>24</td>
<td>9</td>
<td>14</td>
<td>47</td>
</tr>
<tr>
<td>60-69 yrs</td>
<td>48</td>
<td>31</td>
<td>12</td>
<td>91</td>
</tr>
</tbody>
</table>

Table 54. Time of Death after Onset Relative to Age.

If McNeilly and Pemberton's data (134) is reanalyzed omitting the over 70 years group (to correspond with the present study), the significant trend also disappears.

Postmortem Findings

Of the 178 cases, 98 (55%) had postmortem examinations, mostly through the coroner's office. The cases that had postmortems either

i) died in hospital

ii) were referred to the coroner because the usual doctor was on holiday or could not be contacted.

iii) were referred to the coroner because the usual doctor had not seen the patient within three months, or the death was unexpected.
Figure 28. Probability of Death during First 24 Hours
(Sudden Deaths)

The cases in category (i) would be biased towards the longest survivors.

The cases in category (ii) would be unbiased as this reason is a function of the doctor rather than the patient.

The cases in category (iii) would be biased towards patients who were well before a rapid collapse.

However, the author believes that these biases would not be too marked and that the results are of some interest. Recorded in Table 55 are the percentages of all sudden death postmortems with the named lesions.
Macroscopic
Recent Infarct.
with no Fresh
Coronary Artery
Lesion

12.5%

Fresh Coronary
Artery Lesion

16%

Macroscopic
Recent Infarct
and Fresh
Coronary
Artery Lesion

12.5%

Fine
Myocardial
Fibrosis

45%

Old
Infarct

33%

Left Ventricular
Hypertrophy

41%

(Moderate to severe coronary atheroma was almost invariable.)

Table 55. Postmortem Results for Cases Dying Suddenly.

Kuller (35) recorded a 12.5% incidence of acute infarction, 18.7% frequency of fresh thrombosis and 58% of hearts weighing more than 450 grams.

Libechson (128) found acute infarction in 29% of cases (mostly more than one day old), acute coronary lesions in 58%. In 37% (Auckland figure 59%) there was no acute coronary or myocardial lesion. An old myocardial infarction was present in 44%. Schwartz and Walsh (150) reviewed the literature on the pathology of sudden death and found the frequency of thrombotic occlusion to vary between 19 - 54.6%.

Variation in these postmortem findings seems high, but could well reflect differences in postmortem technique, definitions, and methods of data collection.
CHAPTER 6

RESULTS -

POSSIBLE MYOCARDIAL INFARCTION
(Excluding Sudden Deaths)
Although the WHO possible myocardial infarction category (73) does include all sudden deaths with no fresh thrombosis or macroscopic infarction at post mortem (and no other cause of death demonstrated), these cases have previously been included in this thesis as sudden deaths in Chapter 5. These sudden death cases almost certainly represent at least two aetiological subgroups, one of which may not be related to acute ischaemia or infarction (133).

For these reasons, it was decided to consider in this chapter only those possible infarctions who did not die within 24 hours, but who experienced severe cardiac pain with nondiagnostic ECG and enzyme tests. Deaths within 24 hours could not be definitely categorized into this 'symptoms only' group of cases as there possibly had not been time enough for positive ECG and enzyme tests to be manifested before death. Also, as judged by a very low post-24 hour mortality, it seems unlikely that many of the 'symptoms only' cases would have suffered sudden death. Similar cases in previous reports from other centres have been labelled acute coronary insufficiency (includes also symptomatically milder cases), or preinfarction angina.

However, it is realized that a proportion of this type of case could conceivably be represented as sudden deaths if it is believed that sudden deaths may occur during an episode of acute ischaemia rather than infarction. Late deaths would be unexpected as there is hypothetically no dead muscle to cause continuing electrical instability.
The WHO and other definitions of possible MI are beset by the difficulty of subjectivity. A decision must be made on the severity of the pain, almost always retrospectively. Using the WHO definition, it was noted that the pain must usually be severe, and at times agonizing. This was interpreted so as to include 1) Patients who had continuous pain they called moderately rather than very severe, but in whom there was objective electrocardiographic evidence compatible with previous coronary disease. 2) All other cases must admit to very severe pain and have nondiagnostic tests, for inclusion. This was an attempt to minimize the inclusion of noncardiac pain, which may have been called moderately severe but probably would have had no electrocardiographic support for ischaemic heart disease.

This chapter summarizes the data on 99 possible infarctions who did not die suddenly and should be a 40% representative sample of all such cases occurring in Auckland, December 1974 through November 1975. Cases progressing to definite myocardial infarction within one month were excluded, and the present acute symptoms considered as prodromal for the definite infarction.

**Demographic Data**

a) **Sex**

63 Males (63.6%)
36 Females (36.4%)

Krauss found almost the identical ratio in Boston (151) being somewhat different to both previously considered categories of ischaemic heart disease in chapters four and five. However Abbott et al. (152) found a
ratio close to that for definite myocardial infarction, whereas an older paper (153) found a much higher male to female ratio.

b) **Age Specific Incidence**

This is given in Table 56 and Figure 29.

![Graph](image)

**Figure 29.** Age and Sex Specific Incidence Rates for Possible Myocardial Infarction (With 95% Credibility Intervals).

The mean age is very similar to that found by Beamish et al. (155), Wood (154) and Vakil (153) but less than the figure of 62 years found by Krauss (151).
<table>
<thead>
<tr>
<th>AGE</th>
<th>SEX</th>
<th>CASES</th>
<th>TOTAL CENSUS POP.</th>
<th>PROPORTION OF LETTERS NAMING A SELECTED G.P.</th>
<th>MAX. LIKELIHOOD ESTIMATE OF INCIDENCE &amp; 95% CREDIBILITY INTERVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-29</td>
<td>M</td>
<td>0</td>
<td>21758</td>
<td></td>
<td>0.00000-0.00044</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>0</td>
<td>23138</td>
<td></td>
<td>0.00000-0.00042</td>
</tr>
<tr>
<td>30-34</td>
<td>M</td>
<td>1(1.6%)</td>
<td>19327</td>
<td>NOT RECORDED1</td>
<td>0.00003-0.00073</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>0(0.0%)</td>
<td>19652</td>
<td></td>
<td>0.00000-0.00050</td>
</tr>
<tr>
<td>35-39</td>
<td>M</td>
<td>2(3.2%)</td>
<td>17054</td>
<td></td>
<td>0.00009-0.00085</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>1(2.8%)</td>
<td>16749</td>
<td></td>
<td>0.00004-0.00085</td>
</tr>
<tr>
<td>40-44</td>
<td>M</td>
<td>6(9.5%)</td>
<td>18575</td>
<td>336/856</td>
<td>0.00038-0.00180</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>2(5.6%)</td>
<td>18069</td>
<td></td>
<td>0.00028</td>
</tr>
<tr>
<td>45-49</td>
<td>M</td>
<td>8(12.7%)</td>
<td>18111</td>
<td></td>
<td>0.00057-0.00222</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>4(11.1%)</td>
<td>17906</td>
<td></td>
<td>0.00057</td>
</tr>
<tr>
<td>50-54</td>
<td>M</td>
<td>17(27.7%)</td>
<td>15335</td>
<td></td>
<td>0.00172-0.00439</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>4(11.1%)</td>
<td>16264</td>
<td>224/538</td>
<td>0.00059</td>
</tr>
<tr>
<td>55-59</td>
<td>M</td>
<td>10(15.9%)</td>
<td>14184</td>
<td></td>
<td>0.00025-0.00155</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>8(22.2%)</td>
<td>15108</td>
<td></td>
<td>0.00096-0.00320</td>
</tr>
<tr>
<td>60-64</td>
<td>M</td>
<td>10(15.9%)</td>
<td>11832</td>
<td></td>
<td>0.00067-0.00258</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>10(27.8%)</td>
<td>12965</td>
<td>194/446</td>
<td>0.00194</td>
</tr>
<tr>
<td>65-69</td>
<td>M</td>
<td>9(14.3%)</td>
<td>9075</td>
<td></td>
<td>0.00109-0.00370</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>7(19.4%)</td>
<td>11068</td>
<td></td>
<td>0.00100-0.00338</td>
</tr>
</tbody>
</table>

Average Age 55.40 years (Males 54.20 years, Females 57.50 years)

Table 56. Age Specific Incidences for Possible Myocardial Infarction Cases.

1 The proportion found for the 35-49 year range was used in the incidence calculation.
c) Possible Infarction and Social Class

These results are shown in Table 57 for the 98 cases between

35-69 years.

35-49 years

<table>
<thead>
<tr>
<th>Social Class</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>(5.95)</td>
<td>(11.75)</td>
<td>(5.3)</td>
</tr>
</tbody>
</table>

\[
X^2 \text{ test NS}
\]

50-59 years

<table>
<thead>
<tr>
<th>Social Class</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>(11.16)</td>
<td>(16.58)</td>
<td>(11.26)</td>
</tr>
</tbody>
</table>

\[
X^2 \text{ test NS}
\]

60-69 years

<table>
<thead>
<tr>
<th>Social Class</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>(10.99)</td>
<td>(14.80)</td>
<td>(10.21)</td>
</tr>
</tbody>
</table>

\[
X^2 \text{ test NS}
\]

All Ages

<table>
<thead>
<tr>
<th>Social Class</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>28</td>
<td>45</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>(27.25)</td>
<td>(45.51)</td>
<td>(25.24)</td>
</tr>
</tbody>
</table>

\[
X^2 \text{ test NS}
\]

Table 57. Possible Myocardial Infarction and Social Class. ²

²Expected numbers given in parentheses.

As can be seen, there was no difference from random expectation.

In this respect, these cases segregated similarly to the myocardial infarction cases.
d) Race

The following distribution was found.

- 93.9% European (93 cases)
- 4% Maori (4 cases, 3 females)
- 2% Other Polynesian (2 cases, both female)

Combining the Polynesian results a contingency table as shown in Table 58 is constructed:

<table>
<thead>
<tr>
<th></th>
<th>Polynesian</th>
<th>European</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>5</td>
<td>31</td>
<td>36</td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
<td>62</td>
<td>63</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>6</strong></td>
<td><strong>93</strong></td>
<td><strong>99</strong></td>
</tr>
</tbody>
</table>

Table 58. Sex Distribution among Polynesian Cases.

Using Fisher's exact test, this result is significant at the 2.5% level, suggesting a difference of the sex ratio between the two racial groups. Beaglehole et al. (103) also, using a questionnaire technique and with some electrocardiographic support has found chest pain to be more common amongst Maori women than Maori men. A similar pattern was not found for definite MI or sudden death.
Personal Characteristics and Habits

a) Height and Weight

Observed height, weight and Quetelet's indices are shown in Tables 59 and 60.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Height (cms)</td>
<td>175.1</td>
<td>161.3</td>
</tr>
<tr>
<td></td>
<td>(62)</td>
<td>(36)</td>
</tr>
<tr>
<td>Weight (kgs)</td>
<td>77.2</td>
<td>68.0</td>
</tr>
<tr>
<td></td>
<td>(62)</td>
<td>(36)</td>
</tr>
</tbody>
</table>

Table 59. Height and Weight for Possible MI Cases. 3

<table>
<thead>
<tr>
<th>AGE</th>
<th>Males</th>
<th></th>
<th>Females</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>S.D.</td>
<td>Mean</td>
<td>S.D.</td>
</tr>
<tr>
<td></td>
<td>(3)</td>
<td>(1)</td>
<td>(14)</td>
<td>(6)</td>
</tr>
<tr>
<td>30-39</td>
<td>0.273</td>
<td>0.084</td>
<td>0.301</td>
<td>--</td>
</tr>
<tr>
<td>40-49</td>
<td>0.260</td>
<td>0.029</td>
<td>0.281</td>
<td>0.095</td>
</tr>
<tr>
<td>50-59</td>
<td>0.245</td>
<td>0.032</td>
<td>0.269</td>
<td>0.067</td>
</tr>
<tr>
<td>60-69</td>
<td>0.250</td>
<td>0.044</td>
<td>0.248</td>
<td>0.042</td>
</tr>
</tbody>
</table>

Table 60. Quetelet's Index for Possible MI Cases. 3

3 Number of cases for whom information is available is given in brackets.

Comparing these figures with the Carterton figures of Prior's study (105) no significant differences are found.
b) Cigarette Smoking

Table 61 compares the smoking habits of possible MI cases with the age adjusted census population (52).

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Possible MI (63)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Census</td>
<td>61.09%</td>
<td>5.28%</td>
<td>12.2%</td>
<td>17.84%</td>
<td>3.51%</td>
<td></td>
</tr>
<tr>
<td>Possible MI (36)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Census</td>
<td>73.33%</td>
<td>7.25%</td>
<td>11.00%</td>
<td>7.72%</td>
<td>0.70%</td>
<td></td>
</tr>
</tbody>
</table>

KEY: 1. Not smoked within 10 years  4. 10-19 Cigarettes/day
2. Gave up < 10 yrs but > 6 months ago  5. 20-39 Cigarettes/day
3. 1-9 Cigarettes/day  6. ≥ 40/day

Using $X^2$ tests, differences between possible MI cases and the census population were highly significant for both males ($p < 0.0005$) and females ($p < 0.005$). Zeiner-Henriksen (156) found in Norway that 60.8% of male possible infarcts were current cigarette smokers, 23% were ex-cigarette smokers. The remainder had either never smoked cigarettes, or currently smoked a pipe or cigars. However this was a prevalence study and thus would be a somewhat different group of cases, including persons who may have had no pain for more than one year.

$^4$The number of cases for whom information is available is given in brackets.
c) Alcohol Consumption

This data is shown in Table 62.

<table>
<thead>
<tr>
<th></th>
<th>BEER</th>
<th>WINE</th>
<th>SPIRITS</th>
<th>TOTAL ALCOHOL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drinkers</td>
<td>Drinkers</td>
<td>Drinkers</td>
<td>Drinkers</td>
</tr>
<tr>
<td>All cases</td>
<td>All</td>
<td>All</td>
<td>All</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td>69.03</td>
<td>157.32</td>
<td>28.60</td>
<td>90.41</td>
</tr>
<tr>
<td></td>
<td>(98)</td>
<td>(43)</td>
<td>(98)</td>
<td>(31)</td>
</tr>
<tr>
<td>Males</td>
<td>103.63</td>
<td>178.68</td>
<td>25.87</td>
<td>72.91</td>
</tr>
<tr>
<td></td>
<td>(62)</td>
<td>(37)</td>
<td>(62)</td>
<td>(22)</td>
</tr>
<tr>
<td>Females</td>
<td>4.27</td>
<td>25.62</td>
<td>33.30</td>
<td>133.30</td>
</tr>
<tr>
<td></td>
<td>(36)</td>
<td>(6)</td>
<td>(36)</td>
<td>(9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 62. Alcohol Consumption in Patients Suffering Possible MI.\(^5\)

These figures show some similarities to the sudden death data. They can be compared with those for the New Zealand Population over 20 years of age (see Chapter 4).

Forty-four per cent of these patients drank beer, 31.6% drank wine and/or sherry, 36.7% drank spirits and 71.4% drank alcohol in some form.

\(^5\) The number of cases for whom information is available is given in brackets.
Previous Cardiovascular History

a) Number of Previous Symptoms

The histogram of Figure 30 shows the number of previous symptoms admitted to by these persons.

![Percentage of Cases vs Number of Previous Symptoms](image)

**Figure 30. Number of Previous Symptoms (Possible Myocardial Infarctions)**

The previous symptoms included are those shown below.

b) Specific Symptoms

The proportion of cases experiencing the named symptoms are shown in Table 63.
Krauss (151) records that 60% of the acute coronary insufficiency patients had previously had chronic angina, 53% had suffered a previous myocardial infarction, 31% had had previous acute coronary insufficiency. Abbott et al. records data for probable infarction cases which is similar (152).

c) Duration of Symptoms

The mean duration of the named symptoms before the acute event is shown in Table 64.

Krauss (151) found that for cases who had had a previous MI, the average duration of ischaemic symptoms had been six years and for those cases who had not previously had an MI, the duration of symptoms was

6 Comparing males with females $\chi^2 = 9.5$, (p < 0.005)

7 No missing data.
Table 64. Mean Durations of Symptoms Before the Possible MI.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Mean Durations</th>
<th>Time From First Def. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>159 weeks</td>
<td>18 weeks</td>
</tr>
<tr>
<td>ACI</td>
<td>112 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>151 weeks</td>
<td>15 weeks</td>
</tr>
<tr>
<td></td>
<td>210 weeks</td>
<td></td>
</tr>
</tbody>
</table>

1.7 years on the average. Corresponding Auckland figures are 3.2 and 1.5 years respectively. The probability of onset of the various symptoms before the acute event is shown in Figure 31.

d) Other Disorders of Cardiovascular Significance

i) 7% of cases had had a stroke
    11% of cases gave a history of intermittent claudication
    11% were diabetic.

ii) Hypertension: 79 (80%) cases had had a blood pressure recorded in the previous one year. In addition, one case gave a history of past treated hypertension, but no recent recorded blood pressure. Of those for whom an opinion was possible 52.2% either were or had previously been hypertensive. Abbott's figure (152) is 30%.

For the 79 recorded pressures, the average blood pressure was 148.7/90.0.

e) Medication

Table 65 shows a selection of the more commonly prescribed drugs, that had been taken at least within the month prior to onset of symptoms.

---

8 Only cases having symptoms are included.
Figure 31. Probability of Onset of Previous Symptoms (Possible Myocardial Infarctions)
<table>
<thead>
<tr>
<th></th>
<th>Male (63)</th>
<th>Female (36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digoxin</td>
<td>14.3%</td>
<td>13.8%</td>
</tr>
<tr>
<td>Blockers</td>
<td>22.2%</td>
<td>27.7%</td>
</tr>
<tr>
<td>Nitroglycerine</td>
<td>23.86%</td>
<td>27.9%</td>
</tr>
<tr>
<td>Thiazides/Furosemide</td>
<td>20.0%</td>
<td>36.0%</td>
</tr>
<tr>
<td>Other Antihypertensives</td>
<td>14.3%</td>
<td>28.2%</td>
</tr>
<tr>
<td>Tricyclics</td>
<td>3.2%</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

Table 65. Selected Drug Consumption in Possible MI Cases (no missing data).

f) Previous Electrocardiographic Characteristics

As previously, this was interpreted to include a finding as a negative antecedent characteristic if the variable was negative at the time of the acute electrocardiogram (except for left ventricular hypertrophy). The findings are shown in Table 66.

<table>
<thead>
<tr>
<th>Left Ventricular Hypertrophy</th>
<th>LBBB</th>
<th>RBBB</th>
<th>Anterior Hemiblock</th>
<th>Atrial Fibrillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of Cases</td>
<td>10.2</td>
<td>1.1-5.1</td>
<td>2.1-5.1</td>
<td>4.1-10.2</td>
</tr>
<tr>
<td>(94)</td>
<td>(95)</td>
<td>(96)</td>
<td>(93)</td>
<td>(95)</td>
</tr>
</tbody>
</table>

Table 66. Some Electrocardiographic Variables in Possible MI Cases.

The lower bound here is given by the number of cases known with certainty, and the upper bound includes in addition these cases who had positive acute electrocardiographs and no previous electrocardiograph. These cases could have also been positive prior to the acute event. (The exception is left ventricular hypertrophy. As the acute event should not have produced this any positive ECG was accepted.) Abbott's cases (152) had a greater frequency

---

9 The number of cases for whom information was available is given in brackets.
of ventricular hypertrophy (39%) and of anterior hemiblock (27%).

**Prodromal Symptoms**

a) **Number of Prodromal Symptoms**

The number of prodromal symptoms are shown in Figure 32, where the symptoms included are those shown in Table 67 (except the last).

![Figure 32. Number of Prodromal Symptoms (Possible Myocardial Infarctions)](image-url)
b) **Specific Symptoms**

The frequency of specific prodromal symptoms is shown in Table 67.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Angina(^{10})</td>
<td>20.6%</td>
<td>5.7%</td>
</tr>
<tr>
<td></td>
<td>(63)</td>
<td>(36)</td>
</tr>
<tr>
<td>Increased Angina</td>
<td>24.2%</td>
<td>28.6%</td>
</tr>
<tr>
<td></td>
<td>(62)</td>
<td>(35)</td>
</tr>
<tr>
<td>New ACI</td>
<td>19.3%</td>
<td>13.8%</td>
</tr>
<tr>
<td></td>
<td>(62)</td>
<td>(36)</td>
</tr>
<tr>
<td>Increased ACI</td>
<td>4.8%</td>
<td>8.7%</td>
</tr>
<tr>
<td></td>
<td>(62)</td>
<td>(35)</td>
</tr>
<tr>
<td>New or Increased</td>
<td>24.6%</td>
<td>27.9%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>(61)</td>
<td>(36)</td>
</tr>
<tr>
<td>Lethargy</td>
<td>46.8%</td>
<td>58.4%</td>
</tr>
<tr>
<td></td>
<td>(52)</td>
<td>(36)</td>
</tr>
<tr>
<td>All Chest Pains</td>
<td>48.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(99)</td>
<td></td>
</tr>
</tbody>
</table>

Table 67. Frequency of Specific Prodromal Symptoms.\(^{11}\)

**c) Duration of Prodromal Symptoms**

The probability of onset of the specified symptoms during the prodrome is shown on the histograms of Figure 33.

Krauss et al. (151) observed that 41% of his cases had had a painful prodrome for less than 24 hours before the acute event. (This apparently also included cases with no true prodrome, only the acute event.) Twenty-nine percent had painful symptoms for one to six days and the remaining twenty-nine percent for one to four weeks.

\(^{10}\)\(^{p}<0.05\)

\(^{11}\) Number of cases for whom information was available is given in brackets.
Figure 33. Probability of Onset of Prodromal Symptoms (Possible Myocardial Infarctions)
The Acute Event

a) Acute Symptoms

By definition, all cases suffered severe ischaemic-type pain, 61.8% were also breathless with the pain, 57.9% noted abnormal sweating.

b) Time of Onset

The time of onset during the year is shown in Table 68.

*Most of these cases represent a continuing decline in a longer term health deterioration.
i) Month

<table>
<thead>
<tr>
<th>Month</th>
<th>JAN</th>
<th>FEB</th>
<th>MAR</th>
<th>APR</th>
<th>MAY</th>
<th>JUNE</th>
<th>JULY</th>
<th>AUG</th>
<th>SEPT</th>
<th>OCT</th>
<th>NOV</th>
<th>DEC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12</td>
<td>4</td>
<td>8</td>
<td>6</td>
<td>5</td>
<td>7</td>
<td>8</td>
<td>13</td>
<td>16</td>
<td>8</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 68. Month During Which the Acute Event Occurred.

This pattern seems to bear no relationship to the average monthly temperatures for December 1974 through November 1975 (see Chapter 1, figure 6), and there is no clear seasonal trend or differences.

ii) Time of Day

The distribution of acute events during the day is shown in Table 69.

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>12 MN-6 AM</th>
<th>6 AM-12 MD</th>
<th>12 MD-6 PM</th>
<th>6 PM-12 MN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>22</td>
<td>27</td>
<td>20</td>
<td>29</td>
</tr>
</tbody>
</table>

Table 69. Onset of Acute Event During the Day.

No significant differences can be shown.
Treatment

a) Place of Treatment

The proportion of events treated at different places is shown in Figure 34.

b) Reasons for Treatment at Home of 12 Cases (12% of total sample)

Ten of the 12 cases remaining at home did so as there was no initial medical case (67%), five cases (33%) were treated at home due to initial uncertainty in diagnosis.
c) Treatment Delays

Cumulative probabilities for delays are shown in Table 70.

<table>
<thead>
<tr>
<th>a) Onset of Symptoms to Call for Doctor (70 cases)</th>
<th>b) Onset of Symptoms to Call for Ambulance (for those cases who did not call a doctor) (23 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 mins</td>
<td>30 mins</td>
</tr>
<tr>
<td>1 hour</td>
<td>1 hour</td>
</tr>
<tr>
<td>2 hours</td>
<td>2 hours</td>
</tr>
<tr>
<td>6 hours</td>
<td>6 hours</td>
</tr>
<tr>
<td>12 hours</td>
<td>12 hours</td>
</tr>
<tr>
<td>0.34</td>
<td>0.43</td>
</tr>
<tr>
<td>0.46</td>
<td>0.57</td>
</tr>
<tr>
<td>0.57</td>
<td>0.83</td>
</tr>
<tr>
<td>0.83</td>
<td>0.96</td>
</tr>
<tr>
<td>0.96</td>
<td>1.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>c) Call for Doctor to Arrival of Doctor (52 cases)</th>
<th>d) Arrival of Doctor to Arrival at Hospital (45 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 mins</td>
<td>30 mins</td>
</tr>
<tr>
<td>1 hour</td>
<td>1 hour</td>
</tr>
<tr>
<td>2 hours</td>
<td>2 hours</td>
</tr>
<tr>
<td>6 hours</td>
<td>6 hours</td>
</tr>
<tr>
<td>12 hours</td>
<td>12 hours</td>
</tr>
<tr>
<td>0.44</td>
<td>0.11</td>
</tr>
<tr>
<td>0.67</td>
<td>0.29</td>
</tr>
<tr>
<td>0.83</td>
<td>0.67</td>
</tr>
<tr>
<td>0.96</td>
<td>0.96</td>
</tr>
<tr>
<td>1.00</td>
<td>0.96</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>e) Onset of Symptoms to Arrival in CCU (81 cases)</th>
<th>f) Arrival at Accident and Emergency Department to CCU (42 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 mins</td>
<td>30 mins</td>
</tr>
<tr>
<td>1 hour</td>
<td>1 hour</td>
</tr>
<tr>
<td>2 hours</td>
<td>2 hours</td>
</tr>
<tr>
<td>4 hours</td>
<td>4 hours</td>
</tr>
<tr>
<td>6 hours</td>
<td>6 hours</td>
</tr>
<tr>
<td>12 hours</td>
<td>12 hours</td>
</tr>
<tr>
<td>0.00</td>
<td>0.05</td>
</tr>
<tr>
<td>0.02</td>
<td>0.33</td>
</tr>
<tr>
<td>0.19</td>
<td>0.76</td>
</tr>
<tr>
<td>0.56</td>
<td>0.93</td>
</tr>
<tr>
<td>0.72</td>
<td>0.93</td>
</tr>
<tr>
<td>0.90</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Table 70. Cumulative Treatment Delays.

12 Includes only cases who passed through the relevant treatment steps.
First Assessment Post-'Infarct' (91 cases)

The median time of first assessment after onset of symptoms was three hours and fifteen minutes and 75% within seven hours and forty minutes. The average pulse rate was 81.1 per minute. The average systolic blood pressure was 139.32 mm/Hg and average diastolic 86.58 mm/Hg. 22.5% of cases were noted to have bilateral crepitations and 19.5% to be abnormally pale and/or sweaty. Seventy-six cases had both previous and post-'infarct' blood pressures recorded and the difference (old BP-new BP) is recorded in Table 71 with the lower contingency table comparing systolic and diastolic directional trends.

<table>
<thead>
<tr>
<th>Systolic</th>
<th>-80</th>
<th>-60</th>
<th>-40</th>
<th>-20</th>
<th>0</th>
<th>+20</th>
<th>+40</th>
<th>+60</th>
<th>+80</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic</td>
<td>5</td>
<td>20</td>
<td>37</td>
<td>13</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BP Difference</th>
<th>Syst.</th>
<th>Diast.</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>49</td>
<td>14</td>
<td>63</td>
</tr>
<tr>
<td>-</td>
<td>27</td>
<td>62</td>
<td>89</td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>76</td>
<td>152</td>
</tr>
</tbody>
</table>

\[ x^2 = 33.20 \]

\[ p < 0.0001 \]

Table 71. First Assessment Changes in Blood Pressure.

Thus recorded systolic pressure post-infarct tended to fall, while a higher proportion of diastolic pressures rose despite both systolic and diastolic mean pressures falling. This implies that the fewer diastolic pressure drops were greater in magnitude than the larger number of rises.

Acute Electrocardiograph (94 cases)

Fifty-two percent has a type B ECG (new ST-T wave change) only. 23.5% had a type C ECG (old changes or changes unable to be proven as new) only.
23.5% had a normal ECG. One percent had both type B and C ECG changes.

Of those cases with a type B ECG, 48% of the changes were inferior and/or posterior in location and 52% anterior.

Cardiac Arrest and Death

Three cardiac arrests were recorded in the 28 days following the possible infarction. One occurred one hour and thirty minutes after onset of symptoms and resuscitation was successful. The other two were fatal and occurred 16 and 21 days after onset of possible MI symptoms. They could well have been considered sudden deaths with a prodrome of severe acute coronary insufficiency. Postmortems were not conducted.
CHAPTER 7

DISCUSSION OF RESULTS
Section 7.1: INTRODUCTION

Discussion of Results

In this chapter selected aspects of each syndrome in isolation will be discussed. In addition univariate and multivariate comparisons will be made between sudden death, definite myocardial infarction and possible myocardial infarction. The final section deals with aetiological aspects of these syndromes. As mentioned previously in Chapter One, it is not possible in this study to define directly possible risk factors, as there is no information available on normal persons. However, differences between the coronary syndromes can be investigated and possibly some clues as to risk factors obtained.

One problem arises immediately. If Syndrome A has factor X significantly greater than Syndrome B it is not possible to say if this is because Syndrome A has an excess of factor X or if Syndrome B has a deficit of factor X with respect to the general population. This problem can be overcome to some extent by utilizing the group of cases who have both Syndrome A and B coexisting (say Syndrome AB) if such cases exist. The comparison of factor X between Syndrome AB and Syndrome A, isolates Syndrome B as the only difference and conversely for the comparison Syndrome AB and Syndrome B. This assumes no interaction effects between the variables.
Section 7.2: DEFINITE MYOCARDIAL INFARCTION

Incidence

The estimated age-sex specific incidences for definite myocardial infarction were high and consistent with the westernized lifestyle of New Zealanders. However, the incidences were perhaps not as high as might have been predicted on a dietary basis alone. The effect of dietary fats however, may be compensated for by other variables not measured (e.g. psychosocial) or not known.

Comparisons with other places are difficult to make precisely due to differences in definitions and the age ranges considered. The Auckland data has, however, been adapted to calculate figures for the same age-ranges and definitions used in other studies with which it is to be compared. Observed incidence estimates from several other studies are given in Table 13 of Chapter 4 with estimated Auckland figures given in brackets.

It is noted that for the age-range 60-69 years, the incidence of definite infarction is significantly higher in Perth than Auckland. However, when the possible infarcts (see Chapter 6) are added for both centres, the difference is effectively obliterated. In several age ranges, Auckland figures are then a little higher. This proportionate difference between 'possible' and 'definite' infarct numbers in Perth and Auckland may be a true finding. Alternatively it may indicate differences in application of the diagnostic criteria for definite infarction, with Auckland relegating a higher proportion of cases to the possible infarction group.

Cigarette Smoking and Possible Consequences

There is a substantial difference in the distribution of smoking habits between definite MI cases and the age-adjusted census population. Thirty-eight
percent of the male census population and 62% of definite MI males smoked. Twenty-six and one-half percent of the female census population and 60.5% of the female MI cases smoked. Thus overall roughly twice as many MI patients smoked as would a comparable census population. Applying a $X^2$ test to these two distributions, for males $X^2_4 = 67.8$ ($p<0.001$) and for females $X^2_3 = 40.7$ ($p<0.001$, two classes amalgamated due to small numbers). In both cases the major portion of these $X^2$ statistics came from the excess of MI cases who were heavy smokers.

The proportions of smokers given above imply a relative risk estimate for male smokers of 2.7 and for female smokers of 4.2. This of course does not prove that smoking is a causal factor, but suggests that either smoking or some other factor statistically correlated with it is one cause of definite myocardial infarction. This result is in agreement with several other studies (157). There was no significant difference between the smoking habits of those MI cases who also died suddenly and those who did not.

Alcohol Consumption and Its Implications

Several differences were however noted between the definite MI cases who died suddenly and those who did not. One of these relates to alcohol consumption. Using a Mann-Whitney-U test, it is found that those cases associated with sudden death had a significantly higher consumption of wine and/or sherry ($p<0.05$) and total alcohol ($p<0.10$) than those cases who did not die suddenly. This test is a univariate test, and it is conceivable that other differences between the two groups of cases may have caused the difference in alcohol intakes. In particular, however, a difference in sex ratio cannot be implicated in this alcohol difference, as the sex ratio difference between the two groups is slight and not
significant \( (p < 0.5) \).

**Significance of Prodromal Chest Pain**

Another similar comparison relates to the occurrence of chest pains in the prodromal period. There was a significant deficit of such painful symptoms in those definite myocardial infarction cases associated with sudden death. Alonzo has also recorded a similar finding (119). In the present study, during the acute phase 18.9% of cases associated with sudden death had no ascertainable pain or other symptoms whereas only 2.4% of cases not associated with sudden death were "silent". The most likely explanation for these differences would be that the roughly 15% of silent infarcts (68, 69, 70) are omitted from the group of cases not associated with sudden death. This was because notification depended upon symptoms. However such cases were able to be ascertained and included in the group associated with sudden death due to the fact that all deaths were checked, regardless of symptoms.

It is to be noted that even in those cases associated with sudden death who were found to have a macroscopic infarction at postmortem, 16% did not apparently experience symptoms in the acute phase. This was despite the fact that in these cases infarction must have occurred several hours prior to death. These findings would seem to indicate that for MI cases associated with sudden death also, the proportion of silent infarctions is in the range of 15-20%. A similar difference in the prodromal phase symptoms indicates that persons who experience a silent infarction also often have a silent prodromal.

**Influence of Sex of Subjects on the Syndrome of Definite M.I.**

As expected there were some differences between male and female cases. The incidence in females was roughly 1/3 of the male incidence, with this altering
surprisingly little even into the older age groups. However in the youngest age groups where numbers are small the ratio was about $1/5$. These results are similar to others as can be seen in Table 13 of Chapter 4. As documented above, the effect of smoking seems to be more important for females even than males.

Significantly more females had a previous history of breathlessness and/or had been prescribed digoxin and/or frusemide or thiazides up to within three weeks of the infarction. This may imply that females tend to have a greater tendency to cardiac decompensation before to the development of frank ischaemia leading to infarction. Perhaps some other process had been responsible for the antecedent cardiac dysfunction, or it could be a manifestation of ischaemic cardiomyopathy where the muscle loss had been of a diffuse microscopic nature and thus not producing usual infarction symptoms. The females were on average slightly older, but to an insignificant extent (0.4 years).

Subdivisions of Definite M.I. Cases

The definite MI cases can be split to many different subgroups for comparisons. For this discussion two further comparisons of interest have been selected: i) those 28 MI cases suffering proven 'primary' ventricular fibrillation (pre-arrest blood pressure $\geq 100$ mm. Hg) are compared with those MI cases known not to have had such an arrhythmia (and also having acute systolic blood pressure $\geq 100$ mm. Hg) (236 cases); ii) those 78 cases suffering subendocardial infarction (new symmetrical T wave inversion without new Q waves, no ST elevation lasting more than 24 hours) compared with those 158 cases suffering transmural infarction according to electrocardiographic criteria.
i) Those persons suffering documented 'primary' ventricular fibrillation as a complication of definite myocardial infarction differed from persons who did not in the following respects. The frequency of pallor and sweating at first clinical documentation was significantly higher 22/26 cf. 78/202 (p<.0005), a higher portion had transmural infarction by electrocardiograph 20/27 cf. 133/235 (p<0.08), a higher proportion of breathlessness was reported with the acute event 16/28 cf. 86/236 (p<0.05), a significantly higher pulse rate 99 cf. 83/min. was recorded at the first clinical assessment after the acute event (p<0.005). Variables such as sex ratio, Quetelet's index, past symptoms or myocardial infarction, site of infarction, total alcohol consumption in the previous one year, smoking habits, were not significantly different between these two groups. A multivariate analysis gave an equation with only pulse rate included as significant, the other univariately significant variables being correlated with this.

These findings suggest that the haemodynamic effect of the infarction still represents an important differentiating factor even when those cases of apparent secondary arrests are extracted. Thus even the seemingly primary arrests are significantly more likely to be associated with more severe haemodynamic decompensation. The pallor and sweating could be interpreted as suggesting higher catecholamine levels. The relative risk of 'primary' ventricular fibrillation in cases showing pallor and sweating is 8.7. Twenty-two percent of cases having this sign (but only 3% without this sign) suffered 'primary' ventricular fibrillation. In cases with first pulse rate $\geq$ 100 the relative risk is 4.0, with 55% of 'primary' fibrillations having this sign but only 6% of cases not suffering 'primary' ventricular fibrillation. About 23% of cases with pulse $\geq$ 100 and systolic blood pressure $\geq$ 100 (but only 6% without this sign) developed 'primary'
ventricular fibrillation. As no significant differences in alcohol consumption were found, this may imply that any postulated effect of alcohol promoting sudden death would not be in lowering the fibrillation threshold in the presence of a definite myocardial infarction.

ii) Persons suffering transmural definite myocardial infarction differed from those suffering subendocardial infarction in the following ways.

They were significantly heavier (on average about 4.3 kg) \((p < 0.02)\) but nearly significantly taller \((p < 0.10)\) so that body mass index was not significantly different, had experienced a lesser frequency of acute coronary insufficiency in the past \((17/157 \text{ cf. } 16/78, p < 0.05)\), a quite significant \((p < 0.005)\) deficit of acute coronary insufficiency in the prodromal period \((28/187 \text{ cf. } 28/78)\), were less likely to have suffered a previous infarction \((30/158 \text{ cf. } 28/78, p < 0.005)\) and were more likely to show pallor and sweating at the first clinical assessment \((65/133 \text{ cf. } 23/73, p < 0.02)\). In addition they were more likely to have an episode of documented ventricular fibrillation \((20/154 \text{ cf. } 4/78, p < 0.06)\) and more likely to die within 30 days \((24/158 \text{ cf. } 5/78, p < 0.06)\), but these differences did not quite reach statistical significance. At post mortem 22\% showed old MI or fibrosis compared to 80\% of subendocardial infarction \((p < 0.02)\) hearts.

Some of these differences seem to probably relate to the greater muscle loss with most transmural infarcts and the consequent haemodynamic and electrical results e.g. pallor and sweating, ventricular fibrillation and death. However the increased frequency of acute coronary insufficiency and old myocardial infarction in the subendocardial group may imply that a different process is accounting for this expression of coronary disease. Such cases may be more closely allied to the possible myocardial infarction group, who also have a
high frequency of previous acute coronary insufficiency and often showed symmetric T wave inversion perhaps implying subendocardial infarction, but without sufficient enzyme evidence.

**Symptoms - Onset of Treatment Delay**

Since it has been realized that serious complications usually occur early, there has been interest in the components of delay from onset of symptoms to the achievement of definitive treatment. The most serious delays of more than 24 hours or perhaps the inadvertent treatment (or lack of treatment) out of hospital entirely, were commonly due to misdiagnosis by the doctor. More than half of such delays had this reason as at least part of the cause. However, this represented only 10% of the total infarcts. The most common incorrect initial diagnoses were hiatus hernia (often without a clinical history of reflux) and angina. Although patient delay in calling for aid is a major problem, a substantially longer period of time is represented by the wait for the doctor's arrival, his assessment, the wait for the ambulance and the time required to travel to the hospital. Travelling time in Auckland to reach the nearest hospital would be a maximum of 30 minutes for most patients. An ambulance should reach most parts of the suburbs within 15 minutes after it is called. Clearly, delays due to other less clearly defined and perhaps unnecessary reasons are common. Although the majority of doctors responded rapidly to the patient's call, 26% took longer than one hour to arrive. It is interesting to again note as did Norris (48), the delay advantage of calling the ambulance directly (Fig. 19). A comparison of delays with the time of death shows that by the time the median patient or "bystander" has called the doctor, 32% of deaths have occurred
and by the time the median patient reaches the hospital only an additional 4% of deaths have occurred. Clearly, then the patient delay is the serious problem in general. However, in individual cases, the doctor-ambulance period may also be that period of extreme vulnerability. This will be particularly true when the doctor has responded with appropriate urgency to the request of a well educated patient.
It is very likely that sudden deaths as defined in this report represent a heterogeneous group of disorders, with some common underlying features. As commented in Chapter 5, one such common feature is the presence of significant coronary atheroma (158). However, it seems likely that perhaps about half of sudden death cases have not suffered an acute myocardial infarction and represent a primary arrhythmia (which tends to be recurrent even after successful resuscitation (159)). These are the findings of Cobb et al in Seattle.

The acute phases can somewhat arbitrarily be divided to three groups:

i) Death occurring within five minutes of the person apparently being in his normal state of health. This includes a group of cases who died during sleep,

ii) Death occurring within twenty minutes of onset of the acute phase, but surviving longer than five minutes after onset.

iii) Cases who experience typical or atypical myocardial infarction symptoms and who survive twenty minutes but not through the first twenty-four hours.

Death may be due to arrhythmia, heart block, heart failure or rarely, cardiac rupture. The proportion of cases in each group is i) 39%, ii) 22%, iii) 39% (77% of these had classical prolonged cardiac pain). These three divisions of acute phases could conceivably encompass the following pathophysiological situations. Group (i) - cases experiencing a primary arrhythmic death or arrhythmia secondary to a previous silent infarction. Group ii) - cases dying of arrhythmia during an ischaemic episode, cases of ventricular tachycardia or severe bradycardia not related to acute ischaemia, cases dying during the early stages of a massive infarction. Group (iii) - cases dying of a later arrhythmia following infarction or of later pump failure from a more extensive infarction.
The significant excess of cases from the lowest social class has been observed by several others, particularly if coronary deaths, as opposed to all coronary disease incidents are considered in isolation (94, 135, 136, 137). The excess in the lowest social class is largely balanced by a deficit of cases from the middle class population with cases from the upper class population being "close to expectation".

Reasons for these differences can only be conjectural. Perhaps medical care inadequacies due to financial problems or less adequate knowledge of disease and its management amongst the lowest social class patients, their relatives and workmates, may allow coronary disease to be expressed as sudden death more frequently. Alternatively perhaps the lower and upper social classes consume more alcohol and this may also predispose to sudden death (see below). Psychosocial stresses may be more important in the lowest (and possibly the upper) social class than the middle class population, but the present study design does not provide information on this point.

Death certificate data had suggested the possibility of a high risk of sudden death in Maoris as total coronary deaths are high (45). Unfortunately the numbers of Maori deaths observed in this population during one year were inadequate to test this hypothesis. On adjusting for the differing age structure of the Maori population, it was found that the expected number of cases was 5.7, whereas nine cases were observed.

Alcohol Consumption and Cigarette Smoking

Bain et al (160) have documented the relationship between cigarette smoking and sudden death. The results presented in this thesis are very similar. As previously discussed (Chapter 4), alcohol differences were significant between
those cases of myocardial infarction not associated with sudden death and those associated with sudden death. The difference between these latter two groups of cases is the presence or absence of sudden death. Consequently this result could be interpreted as suggesting that alcohol consumption is related to the risk of sudden death. Sex ratio differences between these groups do not appear to account for the alcohol consumption results. Some previous studies have also suggested a similar association between alcohol and coronary death (rather than all coronary events) (141, 142). Another recent study finds the opposite trend for low alcohol intakes (161).

**Prodromata**

The most prominent prodromal symptom was lethargy. This has also been found by others (162). This observation must be treated with caution, however. As a symptom it is difficult to define, and is very subjective. An observer, such as the spouse, may have difficulty reporting accurately. Gillum, et al. (163) has found this symptom to be reported by relatives 32% more frequently than if the patient (myocardial infarction patient) is asked.

The author was aware of these difficulties and probed beyond a 'yes/no' answer in evaluating this symptom. If the above finding is accepted at face-value, it could imply a reduction in cardiac output prior to the fatal event, or the concurrence of some systemic (e.g. viral) illness or perhaps side effects from medications (e.g. diuretic induced hypokolemia).

**Differences Between the Sexes**

Few differences were found between male and female cases dying suddenly (apart from expected differences in alcohol and tobacco consumption). It is observed that about 17% of females and 37% of males suffering sudden death
had a documented previous infarction. The difference is statistically significant. It can be shown that this implies that if a patient has had a previous infarction, a female still has only about 42% of the male's risk of dying suddenly subsequently (30 days or more after the previous infarct) before the age of 70 years (see Section 7.7).

Women who died suddenly had a significantly higher frequency of taking "other antihypertensive drugs" (usually methldopa and/or adrenergic neurone blockers) than males who died suddenly. Although there was no clear difference in previous blood pressure levels between the sexes, it may be that the female cases had required more powerful drugs for control. Previous blood pressures had of course been measured by the many different doctors caring for these patients. This may decrease the sensitivity of comparisons but should not completely invalidate them (164).

Comparison of Very Sudden Deaths and Later Sudden Deaths

It seemed possible that the very sudden collapses may represent a different group aetiologically, from the later sudden deaths. Therefore, comparisons between the 48% of cases who died within 5 minutes of onset of symptoms and the rest of the cases, were made. No significant differences were found with respect to sex ratio, previous symptoms, prodromal symptoms, cigarette and alcohol consumption, recorded previous blood pressure levels, time of year of death or postmortem findings. There were nearly significant (p<0.10) findings in two areas, 1) the very rapid sudden deaths had the expected social class distribution with the later deaths being markedly biased towards the lower socio-economic group perhaps implicating the inadequate medical care hypothesis. 2) the very rapid sudden deaths more frequently were taking digoxin.
If this is a true difference, it could represent a toxic effect of digitalis or alternatively suggests that patients with heart failure (e.g., from fibrotic muscle replacement - see below) requiring digoxin frequently die very rapidly. This needs further confirmation, however.

**Influence of Time to Treatment or Lack Thereof On Outcome**

The present data dramatically underlines the difficult logistic problem associated with treatment of this syndrome after onset. Thirty-nine percent of sudden deaths were not witnessed within the time before severe brain damage would have occurred. It is hard to see how this problem could be overcome unless persons at high risk can be identified and monitored continuously. By the time the call for medical aid is made, let alone arrives, 80% of the fatal collapses have occurred. The general practitioner and more so the hospital are dealing with a small remnant of the total cases. Coronary care ambulances have been used in several overseas cities with some success (159, 128). However, only witnessed cases can be treated by such ambulances, thus immediately reducing the potential to 61% of the total. The success of coronary ambulances must be partially dependent on the density of population. The more spread out the population is, the less the chance of an ambulance being able to reach any point within five minutes. Auckland and suburbs covers 100 square miles along a narrow isthmus and around adjoining harbours and inlets of the ocean. Clearly a large fleet of specialized ambulances would be required to be scattered throughout the residential area to be effective. Similar ambulances in other places have been to resuscitate and enable survival to hospitalization in 30-40% of cases in ventricular fibrillation on ambulance arrival. Of such cases, about 40% survived to be discharged, 60% of these free from neurological
deficit (128, 159). Mortality in the one year following discharge was 30% (159). Thus overall about 10% of these patients survive one year or more. Hill et al (165) give a similarly pessimistic view regarding acute out of hospital resuscitation.

Postmortem Results

The postmortem results agree with other reports in the large proportion of cases having had old infarction (166, 167), or showing fine fibrosis (possibly from acute selective myocardial necrosis (168, 169)). Also the frequency of acute macroscopic myocardial infarction is fairly typical of other studies (166, 170), some of which (159, 171) comment on the occurrence of this finding with no history to support an acute infarction. Sixteen percent of cases with macroscopic myocardial infarction in the present study were silent as far as could be ascertained.

Areas of complete or partial fibrosis or areas of selective cellular damage may be due to many different causes (172), e.g., ischaemia, rheumatic heart disease, high alcohol consumption, viral myocarditis, left ventricular hypertrophy and hypertension, sarcoidosis, idiopathic, etc. These abnormal areas may predispose to electrical instability (such as the reentry phenomenon) and ventricular fibrillation. Acute lesions involving the major branches of the conducting system do not seem very common in these cases (173).

Persons dying suddenly may thus be largely those dying in association with an acute infarction (arrhythmia and/or pump failure), and those with chronic electrical instability resulting from damage or scarring of diverse aetiology.
Section 7.4: POSSIBLE MYOCARDIAL INFARCTION (EXCLUDING SUDDEN DEATHS)

The definition of this syndrome is essentially symptomatic. There must be real doubt as to whether it exists as a separate entity pathologically and/or aetiologically. It is quite possible that these cases represent an early phase of either the myocardial infarction or sudden death syndromes or both. Again it is quite likely that on a pathological or aetiological classification basis, more than one subgroup is contained in the possible MI grouping. The subjectivity of the diagnostic criteria make it likely that some cases of chronic 'stable' angina experiencing a severe attack are included. This may well explain the increased proportion of women in this group of cases, as chronic angina is equally common in women and men (59). It is also interesting to notice the high percentage of previous angina in female possible myocardial infarction cases as compared to men. This may imply that while the females often are cases of chronic angina, this is less likely to be so for the male, who may progress more rapidly to definitive syndromes such as definite myocardial infarction.

Incidence and Demographic Factors

The flattening out of the incidence curve for males over the age of 50 years may also imply that males, who of course experience an increase in coronary disease manifestations with age, are tending to 'bypass' this syndrome relatively, in older age groups. However, the evidence for the curves being different in shape between the two sexes is not good, looking at the scatter of points.

The difference in sex ratio between Maoris and Europeans is noteworthy. Although Maori numbers are very small, as the selection is random and the Fisher's test involves no approximation, the conclusion of significant difference
should be valid. It is interesting to note the finding of Beaglehole (103) who found an apparent excess of Maori women giving positive answers to the Rose questionnaire for myocardial infarction (174) and showing electrocardiographic abnormalities. In view of the present findings, it seems quite likely Beaglehole was measuring an excess of possible myocardial infarction cases in Maori women. It is not clear what this means pathophysiologically.

**Cigarettes and Alcohol**

The high proportion of cases who are smokers and have or have had hypertension seems characteristic of all coronary syndromes and suggests that possible myocardial infarction is also related to these coronary atherosclerotic disorders. The roughly 25% frequency of previous documented myocardial infarction also supports this. The high proportion of cases who have had some previous ischaemic-type symptoms is largely expressing the high previous pain rates in females.

Compared to the general population (as far as can be judged (113) ) possible myocardial infarction cases seem to have a fairly high intake of alcohol. This may be significant in view of the fact that alcohol ingestion is known to decrease cardiac performance acutely (175) and in particular lower the threshold for angina as precipitated by physical activity (176). However, it was not possible to demonstrate an unusual acute pattern of alcohol intake before the attack. This was assessed simply and rather crudely by asking whether more or less alcohol than usual had been consumed in the 24 hours before the acute attack. It may be that a high alcohol intake sensitizes the patient to other factors producing acute ischaemia.

The blood pressure changes before and after the acute event are difficult to interpret. On average systolic pressures dropped 7.7 mm. Hg and diastolic
pressures dropped 2.5 mm. Hg. In fact more persons experience rises in diastolic blood pressure, thus the average magnitude of drops must have been greater than the average magnitude of rises. The effect of glycercyl trinitrate, possible morphine injections and the stress of admission to the coronary unit probably prevents any clear physiological interpretation of these results.

It is clear that in some senses this group of cases represents a distinct group from definite myocardial infarction and this will be discussed further in the section dealing with intersyndromal comparisons that follows.
Section 7.5: UNIVARIATE INTERSYNDROMAL COMPARISONS

a) Univariate Comparisons Between Persons Dying Suddenly and Those Suffering Definite Myocardial Infarction (But Not Sudden Death)

On consideration of this section the question immediately arose as to which category the 41 cases suffering both definite myocardial infarction and sudden death should be assigned. The decision indicated by the heading above was prompted by the interest in factors possibly contributing to sudden death. This division of cases separates all persons dying suddenly. The other possibility of placing persons both dying suddenly and suffering definite myocardial infarction with the definite myocardial infarction category will at times be of interest as an attempt to isolate definite myocardial infarction. This is less satisfactory as there are certainly many cases of undiagnosed myocardial infarction in the sudden death group, that then are inappropriately categorized.

Below is summarized several comparisons which gave results either statistically significant or approaching this. These included all comparisons in which the odds ratio looked substantially different from unity. Comparisons were originally considered with respect to the following variables: age, sex, height, weight, Quetelet's index, previous angina, previous acute coronary insufficiency, previous breathlessness, previous definite myocardial infarction, last recorded blood pressures, frequency of taking the various medications documented, smoking history, prodromal angina, prodromal acute coronary insufficiency, prodromal breathlessness, prodromal lethargy, month of onset, time of day of onset, postmortem findings, alcohol consumption.

For each variable, x, there is presented the ratio of the relative risk of sudden death to the relative risk of definite myocardial infarction with respect
to change in variable $x$. (= odds ratio, $\Omega$), the $X^2_1$ statistic (with continuity correction) showing the statistical significance of this observation (177). Missing data can be calculated by recalling that there are 178 sudden death cases and 252 definite MI's (who did not die suddenly).

a) Previous Acute Coronary Insufficiency ($x$)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
<th>$\Omega$</th>
<th>$X^2_1$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$x$</td>
<td>33</td>
<td>33</td>
<td>1.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\bar{x}$</td>
<td>138</td>
<td>216</td>
<td>2.35</td>
<td>0.015</td>
<td></td>
</tr>
</tbody>
</table>

b) Digoxin ($x$) within three weeks

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
<th>$\Omega$</th>
<th>$X^2_1$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$x$</td>
<td>35</td>
<td>23</td>
<td>2.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\bar{x}$</td>
<td>143</td>
<td>228</td>
<td>8.94</td>
<td>0.005</td>
<td></td>
</tr>
</tbody>
</table>

c) Frusemide ($x$) within three weeks

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
<th>$\Omega$</th>
<th>$X^2_1$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$x$</td>
<td>23</td>
<td>12</td>
<td>2.81</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\bar{x}$</td>
<td>155</td>
<td>277</td>
<td>7.29</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

d) Prodromal New Angina ($x$)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
<th>$\Omega$</th>
<th>$X^2_1$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$x$</td>
<td>13</td>
<td>44</td>
<td>0.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\bar{x}$</td>
<td>164</td>
<td>206</td>
<td>8.56</td>
<td>0.005</td>
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</tr>
</tbody>
</table>

e) Prodromal Increased Angina ($x$)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
<th>$\Omega$</th>
<th>$X^2_1$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$x$</td>
<td>31</td>
<td>65</td>
<td>0.63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\bar{x}$</td>
<td>139</td>
<td>183</td>
<td>3.18</td>
<td>0.10</td>
<td></td>
</tr>
</tbody>
</table>
f) Prodromal New Acute Coronary Insufficiency (x)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
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</thead>
<tbody>
<tr>
<td>x</td>
<td>18</td>
<td>60</td>
</tr>
<tr>
<td>\bar{x}</td>
<td>152</td>
<td>189</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 11.29 \quad p < 0.001 \]

\[ \Omega = 0.37 \]

---

g) Prodromal Lethargy (x)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
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<tbody>
<tr>
<td>x</td>
<td>77</td>
<td>93</td>
</tr>
<tr>
<td>\bar{x}</td>
<td>93</td>
<td>153</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 2.03 \quad p < 0.15 \]

\[ \Omega = 1.36 \]

---

h) Time of Year of Onset (x is the six cooler months)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
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</thead>
<tbody>
<tr>
<td>x</td>
<td>105</td>
<td>112</td>
</tr>
<tr>
<td>\bar{x}</td>
<td>73</td>
<td>139</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 8.03 \quad p < 0.005 \]

\[ \Omega = 1.79 \]

---

i) Post-Mortem Fibrosis and/or Old Myocardial Infarction (x)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
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</thead>
<tbody>
<tr>
<td>x</td>
<td>76</td>
<td>5</td>
</tr>
<tr>
<td>\bar{x}</td>
<td>23</td>
<td>12</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 13.3 \quad p < 0.001 \]

\[ \Omega = 7.93 \]

---

j) Post-mortem Left Ventricular Hypertrophy (x)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>40</td>
<td>4</td>
</tr>
<tr>
<td>\bar{x}</td>
<td>59</td>
<td>13</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 1.11 \quad p < 0.30 \]

\[ \Omega = 2.20 \]

---

k) Total Alcohol (x)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drinkers</td>
<td>89</td>
<td>135</td>
</tr>
<tr>
<td>\bar{x}</td>
<td>52</td>
<td>75</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 0.01 \quad NS \]

\[ \Omega = 0.975 \]
Spirits

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
<th>( \Omega )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drinkers</td>
<td>40</td>
<td>68</td>
<td>0.83</td>
</tr>
<tr>
<td>Non-Drinkers</td>
<td>101</td>
<td>142</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Wine & Sherry

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
<th>( \Omega )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drinkers</td>
<td>40</td>
<td>61</td>
<td>0.96</td>
</tr>
<tr>
<td>Non-Drinkers</td>
<td>102</td>
<td>149</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Beer

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>M.I.</th>
<th>( \Omega )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drinkers</td>
<td>65</td>
<td>84</td>
<td>1.26</td>
</tr>
<tr>
<td>Non-Drinkers</td>
<td>78</td>
<td>127</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Further Analysis of Possible Effect of Alcohol

Divide total alcohol consumption to four groups 0 grams/week, 1-50 grams/week, 51-300 grams/week, >300 grams/week. Take the category 1-50 grams/week to be the reference group for the odd ratio computations.

Teetotallers

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>S.D.</th>
<th>M.I.</th>
<th>( \Omega )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>50</td>
<td>65</td>
<td>1.57</td>
</tr>
<tr>
<td>1-50</td>
<td>25</td>
<td>51</td>
<td>1.73</td>
</tr>
<tr>
<td>1-50 grams/week</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
These findings form the basis for a graphical representation (Figure 35).

**Figure 35. Alcohol Consumption versus Ratio of Relative Risks of Sudden Death to Myocardial Infarction (and No Sudden Death)**
The only clearly significant difference in this categorical univariate analysis is that between the 1-50 gram/week and the >300 gram/week categories. This remains significant at the $\alpha = 0.05$ level even when adjustment is made for the fact that here the data is split and so several comparisons are made.

The question immediately arises as to whether the dip in the ratio of relative risks at low alcohol doses is real or may represent random variation. It is noted that neither of the categories zero, 51-300, show ratios significantly different from unity in comparison to the 1-50 category, applying the usual $X^2_1$ test. This is even before adjusting for the fact that the tests were suggested by the data and are multiple (e.g. by Bonferroni's method). Using a components of $X^2$ tests as suggested by Armitage (178) the total $X^2_2$ from the 4 x 2 table is significant $p < 0.03$, (implying an overall difference), $X^2$ (linear) is significant $p < 0.02$ and $X^2$ (departure from linearity) is not significant ($p > 0.15$). Consequently this data does not give good evidence that there is a relative decrease in risk of S.D. compared with the risk of M.I. at low alcohol doses. It does support the increasing risk of S.D. compared to the risk of MI as alcohol dose increases.

The role of alcohol consumption as a discriminant between sudden death and non-sudden death myocardial infarction was investigated by use of the logistic function. This assumes that the probability of sudden death among the combined group of these two groups of cases can be expressed as

$$\frac{1}{1 + e^{-(\alpha + \beta \cdot \text{Alcohol})}}$$

It can be shown then that $\beta$ describes an 'exponential' gradient of the ratio of relative risks of sudden death and non-sudden death myocardial infarction between the situations where alcohol = $x$ grams per week and zero grams per week, i.e. $e^{\beta x}$ describes this ratio for any given value of $x$. It can be shown that the
dependent variable of this analysis is the ratio of incidences of sudden death and
definite MI (non sudden death) as: - Let \( N \) = Total number of coronary cases
in combined group of both syndromes and let \( P \) be the proportion of sudden
deaths in this combined group. Let \( X \) be the number of sudden deaths and \( Y \) be
the number of definite MI's (non-sudden deaths). Let \( T \) be the number of persons
in the population from which both sets of cases were drawn.

\[
\text{Odds} = \frac{P}{1-P} = \frac{X}{N} \cdot \frac{(N-X)}{N} = \frac{X}{T} \cdot \frac{Y}{N} = \frac{X}{T} \cdot \frac{Y}{T} =
\]

Incidences of sudden death \( \quad \) incidence of definite MI (non-sudden death).

A. (All Sudden Death Cases). The equation found, (using a Walker-Duncan
routine) is Probability of Sudden Death \( = \frac{1}{\text{-(-0.487 + 0.0015 Alcohol)}} \)

alcohol coefficient is significant \( p < 0.007 \). This implies that the ratio of incidences at alcohol =

- 100 g/wk compared to alcohol = 0 g/wk is 1.06
- 300 g/wk compared to alcohol = 0 g/wk is 1.57
- 500 g/wk compared to alcohol = 0 g/wk is 2.12
- 1000 g/wk compared to alcohol = 0 g/wk is 4.49

The same analyses were applied to the two subgroups of the sudden death
cases, i.e. first those associated with diagnosed myocardial infarction and
secondly those not associated with diagnosed myocardial infarction. In both
cases the comparison was with cases of definite myocardial infarction not
associated with sudden death (B & C below).

B. (Sudden death and coexistent definite MI versus definite MI with no
sudden death)

The first case gave the following equation:

\[
\text{Probability of sudden death} = \frac{1}{\text{-(-2.16 + 0.0021 Alcohol)}}
\]

1 + e
The coefficient for alcohol was significant \( p < 0.025 \). There were only 29 cases (with alcohol data) who died suddenly in association with definite infarction. With only one independent variable, this is still an adequate number of cases for discriminant analysis (179), but probably explains the reduced significance of the result as compared to analysis A. Notice, however, that \( \beta \) is increased and this corresponds to an increased estimated gradient of the odds (or ratio of incidences) with change in alcohol dose.

For alcohol = 100 grams/week compared to zero grams/week, ratio = 1.23
For alcohol = 300 grams/week compared to zero grams/week, ratio = 1.88
For alcohol = 500 grams/week compared to zero grams/week, ratio = 2.85
For alcohol = 1000 grams/week compared to zero grams/week, ratio = 8.18

C. (Sudden death and no diagnosed acute MI versus MI with no sudden death)

The second case gave the following equation:

\[
\text{Probability of sudden death} = \frac{1}{1 + e^{-(0.70 + 0.0014 \text{ Alcohol})}}
\]

The coefficient for alcohol was significant \( p < 0.05 \). For this regression, numbers were much greater, there being 113 in the sudden death group. Despite this, significance is somewhat reduced over Case B and the magnitude of the estimated coefficient is decreased, with the coefficient for Case B being 50% greater than that for Case C. It should be remembered that in Case C the subjects described by the dependent variable are inevitably contaminated with cases that in fact had myocardial infarction, but this was undiagnosed. This may well account for about 50% of supposedly non-infarct sudden deaths (Cobb (159)) but overall Case C sudden deaths differ from Case B sudden deaths in having included a group of sudden deaths due to a primary arrhythmia. Consequently,
if all diagnoses had been correctly made, one may expect the coefficient for alcohol in the true Case C to be much further reduced and possibly to lose significance. It is assumed that alcohol has effect to promote sudden death in only those cases also having suffered MI and that the coefficient for them is 0.0020 (see Case B), then if \( x = \) number of cases of sudden death associated with definite MI and \( n \) is the total number of sudden deaths, the observed \( \beta \) in Case B may be a weighted average thus: 
\[
\frac{x \times 0.0020 + (n-x) \times 0}{n} = 0.0015
\]

(i.e. the coefficient from Case A where all sudden deaths are combined). Thus \( x = 0.75 \times n \), then \( x = 107 \). This can be further checked using Case C
\[
\frac{(x-29) \times 0.0020 + (n - 29 - (x-29)) \times 0}{n - 29} = 0.0014
\]

as there were 29 cases of known definite infarction associated with sudden death excluded from this group. Then \( x = 108 \) is in close agreement with the first estimate. This is based on assumptions and 'soft data' but it implies that about 3/4 of sudden deaths are associated with infarction.

Liberthson's study of resuscitated 'would-be sudden deaths', suggests that only about one-third of the true myocardial infarctions associated with sudden deaths are being diagnosed (128). This is consistent with the analysis just completed and the Auckland findings that 23% of sudden death cases have also diagnosable MI. For many cases the lack of MI diagnosis would be because no postmortem was conducted and for others because death occurred before postmortem changes were manifested.

D. A further comparison related to alcohol will be discussed later in the Discussion of Intersyndromal Comparisons section, but the basic calculation is given here. This is between sudden death cases associated with diagnosed infarction and those in whom definite infarction was not diagnosed. The estimated
equation is:

\[
\text{Probability of sudden death in association with definite MI} = \frac{1}{1 + e^{(-1.413 + 0.0003 \text{ Alcohol})}}
\]

The coefficient for alcohol did not approach significance (\( p \sim 0.70 \)).

b) Univariate Comparisons Between Possible Myocardial Infarction Cases (Who Did Not Die Suddenly) And Definite Myocardial Infarction Cases.

By definition there is no overlap between these two categories of cases. As previously, any comparisons which were significant or approached significance are shown. The odds ratio, which is here equivalent to the ratio of the relative risks of definite infarction and possible MI, with factor x present, as compared to the same ratio with factor x absent, is also given. The \( X^2_1 \) statistic includes a continuity correction. Missing data can be calculated by recalling that there were 293 definite MI cases and 99 possible MI cases (who did not die suddenly).

a) Sex

<table>
<thead>
<tr>
<th></th>
<th>Def. MI</th>
<th>Poss. MI</th>
<th>( \Omega )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>224</td>
<td>63</td>
<td>1.86</td>
</tr>
<tr>
<td>Female</td>
<td>69</td>
<td>36</td>
<td></td>
</tr>
</tbody>
</table>

b) Past Acute Coronary Insufficiency (x)

<table>
<thead>
<tr>
<th></th>
<th>Def. MI</th>
<th>Poss. MI</th>
<th>( \Omega )</th>
<th>( X^2_1 )</th>
<th>( p &lt; 0.05 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>39</td>
<td>26</td>
<td>0.44</td>
<td>7.65</td>
<td>( p &lt; 0.01 )</td>
</tr>
<tr>
<td>( \bar{x} )</td>
<td>249</td>
<td>73</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
c) **Use of β-Blockers Within 3 Weeks (x)**

<table>
<thead>
<tr>
<th></th>
<th>Def. MI</th>
<th>Poss. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>39</td>
<td>24</td>
</tr>
<tr>
<td>̅x</td>
<td>253</td>
<td>75</td>
</tr>
</tbody>
</table>

d) **Use of Lasix/Edecrin within 3 Weeks (x)**

<table>
<thead>
<tr>
<th></th>
<th>Def. MI</th>
<th>Poss. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>̅x</td>
<td>278</td>
<td>86</td>
</tr>
</tbody>
</table>

e) **Lack of Energy in the Prodrome (x)**

<table>
<thead>
<tr>
<th></th>
<th>Def. MI</th>
<th>Poss. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>108</td>
<td>50</td>
</tr>
<tr>
<td>̅x</td>
<td>176</td>
<td>48</td>
</tr>
</tbody>
</table>

f) **Sweating During the Acute Phase Reported by Patient (x)**

<table>
<thead>
<tr>
<th></th>
<th>Def. MI</th>
<th>Poss. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>193</td>
<td>55</td>
</tr>
<tr>
<td>̅x</td>
<td>72</td>
<td>40</td>
</tr>
</tbody>
</table>

g) **Pallor and/or Sweating Noted by Observer Post-Event (x)**

<table>
<thead>
<tr>
<th></th>
<th>Def. MI</th>
<th>Poss. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>97</td>
<td>16</td>
</tr>
<tr>
<td>̅x</td>
<td>130</td>
<td>66</td>
</tr>
</tbody>
</table>

A further difference related to outcome. As by definition no deaths in the possible infarcts could occur in less than 24 hours, a comparison of deaths from 1 day to 30 days was made. The following table results:
h) Death after the first 24 hours (x) (252 definite MI's remain after the first 24 hours)

<table>
<thead>
<tr>
<th></th>
<th>Def. MI</th>
<th>Poss. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>31</td>
<td>2</td>
</tr>
<tr>
<td>\bar{x}</td>
<td>221</td>
<td>97</td>
</tr>
<tr>
<td>\Omega</td>
<td>6.80</td>
<td></td>
</tr>
<tr>
<td>X^2</td>
<td>7.30</td>
<td>p &lt; 0.01</td>
</tr>
</tbody>
</table>

i) Methyldopa (x)

<table>
<thead>
<tr>
<th></th>
<th>Def. MI</th>
<th>Poss. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>\bar{x}</td>
<td>276</td>
<td>87</td>
</tr>
<tr>
<td>\Omega</td>
<td>0.42</td>
<td></td>
</tr>
<tr>
<td>X^2</td>
<td>4.05</td>
<td>p &lt; 0.05</td>
</tr>
</tbody>
</table>

No significant differences were noted for smoking, digoxin use, most previous prodromal symptoms including frequency of previous infarction, time of onset of the acute event, alcohol consumption, acute pulse rate and blood pressure.

c) Univariate Comparisons Between All Sudden Deaths and Possible Myocardial Infarction Cases (Who Did Not Die Suddenly).

There was no overlap between these two groups, by definition. As previously, any comparisons which were significant or approached significance are shown. The odds ratio which is here equivalent to the ratio of the relative risks of sudden death and possible MI, with factor x present, as compared to the same ratio with factor x absent, is also given. The $X^2_1$ statistic includes a continuity correction. Missing data can be calculated by recalling that there was a total of 178 sudden deaths and 99 possible MI's (who did not die suddenly).

a) Age

The mean age for sudden death cases was 58.6 years and for possible MI cases 55.4 years. Using a students t test and the observed variances this difference is significant $p < 0.005$. 
b) Sex (x)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>Poss. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>137</td>
<td>63</td>
</tr>
<tr>
<td>Female</td>
<td>41</td>
<td>36</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 4.99, \ p < 0.005 \]
\[ \Omega = 1.91 \]

c) Previous or Present Hypertension (x)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>Poss. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>52</td>
<td>42</td>
</tr>
<tr>
<td>\bar{x}</td>
<td>84</td>
<td>38</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 3.61, \ p < 0.06 \]
\[ \Omega = 0.56 \]

d) Painful Prodromal Symptoms (new of Increased Chest Pain) (x)

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>Poss. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>44</td>
<td>40</td>
</tr>
<tr>
<td>\bar{x}</td>
<td>133</td>
<td>59</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 6.53, \ p < 0.02 \]
\[ \Omega = 0.49 \]

e) Time of Day of Onset (Night = x, Day = \bar{x})

<table>
<thead>
<tr>
<th></th>
<th>S.D.</th>
<th>Poss. MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>68</td>
<td>53</td>
</tr>
<tr>
<td>\bar{x}</td>
<td>95</td>
<td>45</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 3.28, \ p < 0.07 \]
\[ \Omega = 0.61 \]

There were no significant or suggestive differences in previous symptoms, recent medications, smoking history, time of year of onset, or alcohol consumption.

Clinical shock, increased pulse rate, decreased blood pressure were all quite dramatic differences in the post onset examination of sudden death cases. However as so few sudden death cases survived to such an examination, the data is unrepresentative of the total group in all probability.
Section 7.6: MULTIVARIATE INTERSYNDROMAL COMPARISONS

a) Multivariate Comparison Between Persons Dying Suddenly and Those Suffering Definite Myocardial Infarction but Not Dying Suddenly

A multivariate logistic analysis (67) was performed stepwise to try to select those variables significantly and independently contributing towards the discrimination of these two types of cases. The following independent variables were given for selection from: sex, age, height, weight, Quetelet's index, previous angina, previous acute coronary insufficiency, previous myocardial infarction, previous dyspnea, use of digoxin, β blockers, frusemide, thiazides, methyldopa, cigarettes, prodromal angina, prodromal acute coronary insufficiency, prodromal breathlessness, prodromal lethargy, beer, wine, spirits, total alcohol consumption, season of year. (Cases with no missing data = 328).

The following 5 variables were selected as independent significant discriminators. (Table 72)

<table>
<thead>
<tr>
<th>Variable</th>
<th>t statistic</th>
<th>p value</th>
<th>standardized logistic coefficient</th>
<th>logistic coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prodromal New Acute Coronary Insufficiency</td>
<td>2.83</td>
<td>&lt;0.005</td>
<td>-0.39</td>
<td>-0.988</td>
</tr>
<tr>
<td>Prodromal New Angina</td>
<td>2.61</td>
<td>&lt;0.01</td>
<td>-0.36</td>
<td>-0.971</td>
</tr>
<tr>
<td>Digoxin Use</td>
<td>2.49</td>
<td>&lt;0.02</td>
<td>0.30</td>
<td>0.872</td>
</tr>
<tr>
<td>Total Alcohol</td>
<td>3.22</td>
<td>&lt;0.002</td>
<td>0.42</td>
<td>0.00195</td>
</tr>
<tr>
<td>Season of Year</td>
<td>3.53</td>
<td>&lt;0.0005</td>
<td>0.43</td>
<td>0.888</td>
</tr>
</tbody>
</table>

Intercept = -0.72

(Positive coefficients imply that the variable is associated with sudden death)

Table 72. Logistic Discriminant Analysis Separating Persons Dying Suddenly and Those Suffering Definite Myocardial Infarction (but Not Dying Suddenly)
The fit of the data to the model is depicted in Fig. 36. The fit is excellent except for the first two points. These two points result in a highly significant goodness of fit $X^2$ test. This implies that there are cases who have a low predicted risk of sudden death who nevertheless do die suddenly. Probably then there are discriminants (risk factors) operative in these cases that have not been documented in this study.

![Figure 36. Observed versus Predicted Probabilities of Sudden Death from amongst a Population of Definite Myocardial Infarction Cases and Sudden Death Cases.](image-url)
b) Multivariate Comparison of Possible Myocardial Infarction Cases (who did not die suddenly) and Cases of Definite Myocardial Infarction

A multivariate logistic analysis was used. The variables included were based on a stepwise linear discriminant analysis. All antecedent variables shown in the univariate comparison section were included for selection in the linear analysis. Any variables approaching significance were included in the logistic analysis. Although there are some potential hazards in this sequence of steps, it was reassuring to note that there were only small changes in t values between the linear and logistic analyses. It seems unlikely that any highly significant variables have been missed by this procedure. Only variables that were significant at the 5% level in the logistic equation are reported below. Fortunately, only one variable needed exclusion as nonsignificant following the initial logistic analysis, after selection of variables from the linear procedure. (Cases with no missing data = 316). Table 73 shows the analysis result.

<table>
<thead>
<tr>
<th>Variable</th>
<th>t statistic</th>
<th>P value</th>
<th>Standardized Logistic Coefficient</th>
<th>Logistic Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of frusemide/ethacrynic acid within 3 weeks</td>
<td>2.82</td>
<td>&lt;0.005</td>
<td>-0.34</td>
<td>-1.275</td>
</tr>
<tr>
<td>Sex*</td>
<td>3.99</td>
<td>&lt;0.001</td>
<td>-0.73</td>
<td>-1.640</td>
</tr>
<tr>
<td>Height (cms.)</td>
<td>2.88</td>
<td>&lt;0.005</td>
<td>-0.54</td>
<td>-0.058</td>
</tr>
<tr>
<td>Total Alcohol</td>
<td>2.67</td>
<td>&lt;0.01</td>
<td>-0.34</td>
<td>-0.00188</td>
</tr>
</tbody>
</table>

Intercept = 13.2

*Male = 1, Female = 2

Negative coefficients imply that the variable is associated with possible myocardial infarction.

Age came very close to achieving significance (p<0.06).

Table 73. Logistic Discriminant Analysis Separating Persons Experiencing Definite Myocardial Infarction From Those Experiencing Possible Myocardial Infarction.
Figure 37 shows the predicted versus the observed fit of roughly decile groups (according to predicted values). The fit, although showing some scatter is adequate according to a chi-squared goodness of fit test, which is not significant.

![Graph showing fitted versus observed probabilities](image)

**Figure 37.** Observed versus Predicted Probabilities of Definite Myocardial Infarction from amongst a Population of Definite Myocardial Infarction Cases and Possible Myocardial Infarction Cases.

c) Multivariate Comparison of Possible Myocardial Infarction Cases (who did not die suddenly) and Cases of Sudden Death.

A multivariate logistic analysis was performed. The variables included were based on a stepwise linear discriminant analysis. All antecedent variables when in the univariate comparison section were presented for selection in the stepwise analysis. Any variables approaching significance were included in the logistic analysis. Although there are some potential hazards in this sequence of steps we were reassured by the small changes in t values between the linear and logistic analyses. It seems unlikely that any highly significant variables have been missed by this procedure. Only variables that were significant were included in the logistic equation reported below. As before, only one variable needed exclusion as nonsignificant once logistic analysis was started, after the
selection of variables from the linear procedure. (Cases with no missing data = 275). Table 74 shows the analysis result.

<table>
<thead>
<tr>
<th>Variable</th>
<th>t statistic</th>
<th>P value</th>
<th>Standardized Logistic Coefficient</th>
<th>Logistic Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year of Birth*</td>
<td>3.78</td>
<td>&lt;0.0005</td>
<td>-0.50</td>
<td>-0.0582</td>
</tr>
<tr>
<td>Sex†</td>
<td>2.59</td>
<td>&lt;0.01</td>
<td>-0.33</td>
<td>-0.739</td>
</tr>
</tbody>
</table>

Intercept is 2.52 Negative coefficients imply that the variable is associated possible myocardial infarction.

Table 74. Logistic Discriminant Analysis Separating Cases Dying Suddenly from Persons Experiencing Possible Myocardial Infarction.

Figure 39 shows the predicted versus the observed fit of roughly decile groups (according to predicted values). The fit appears excellent and the chi-squared goodness of fit test does not approach significance.

Figure 38. Observed versus Predicted Probabilities of Sudden Death from amongst a Population of Sudden Death Cases and Possible Myocardial Infarction Cases.

*Year of birth is recorded as the last two digits of the year e.g. 1924 becomes 24.

†Male = 1, Female = 2.
Section 7.7: DISCUSSION OF INTERSYNDROMAL COMPARISONS

(230)

a) The variables significantly separating definite MI without sudden death from sudden death cases can be divided into three types:

i) Those relating to prodromal painful symptoms

ii) Those relating to heart failure probably

iii) Others, including time of year and alcohol.

The observation that painful prodromal symptoms are less likely to be found in sudden death cases is probably related to the silent infarctions missed in accumulating definite MI cases but included in the sudden death cases. This has been discussed more fully in the 'Discussion of definite MI results' earlier in this chapter.

Several variables are significant discriminants that may act through their association with heart failure. In every case, the implication is that heart failure is found more frequently in sudden death cases. This includes variables such as digoxin and frusemide, post-mortem fibrosis and/or old myocardial infarction and possibly also alcohol could be included in this group. These variables are summarized by the inclusion of digoxin in the multivariate regression, as the variable most strongly discriminating. It is important to note that alcohol is in the equation independently. It is conceivable that digoxin and frusemide do not just reflect heart failure but could have some toxic effect promoting sudden death. These data cannot distinguish these possibilities. Others have also noted the tendency for sudden death cases to be predicted by heart failure (180, 141).

The tendency for sudden deaths, to occur particularly in the cooler months
is well known but unexplained. The tendency for angina to be precipitated by cold may be invoking the same mechanism as that contributing to sudden death. It is known that blood pressure and serum cholesterol are higher in the winter months (181, 182). It may be significant that respiratory virus infection is more common in the cooler months.

The ability of alcohol consumption to discriminate between these two groups of cases is of great interest. Much data (183, 184, 185) now suggests that small or moderate alcohol consumption raises HDL cholesterol levels and possibly also decreases some coronary disease events (186, 187). However, such evidence has usually not been related specifically to sudden death. Other sources of evidence have indicated that high alcohol consumption is positively associated with cardiac death (141, 142, 188, 189, 190).

The present data suggest firstly that the ratio of risk of sudden death to the risk of definite MI without sudden death, increases with increase in alcohol consumption. This could be due either to an increase in the risk of sudden death with alcohol consumption or a decrease in risk of definite MI with alcohol consumption or both. That it is the first, is strongly suggested by the analyses of the section in this chapter entitled 'Univariate Comparisons Between Persons Dying Suddenly and Those Suffering Definite MI (But Not Sudden Death)'. Alcohol analysis B in this section, compared two groups of cases, both of whom had proven definite myocardial infarction but only one of which consisted of cases who also died suddenly. Despite the small number of cases (29 patients) in this second group, alcohol significantly discriminated between those two groups with the largest coefficient of any of the univariate alcohol analyses. As the difference between these two groups of cases was 'sudden death', alcohol would seem to
be associated with this phenomenon, either independent of definite MI, or as part of an interaction process whereby alcohol is associated with sudden death in the presence of acute MI.

Alcohol analysis D tested the comparison between sudden deaths with coexisting acute MI and sudden deaths having no diagnosed acute MI. This comparison is difficult to interpret. On the basis of the work of Baum et al (133) it would seem likely that a minimum of 35% of the cases with no diagnosed MI in fact do have an acute MI. The true figure may be nearer 75% if most of the 60% of Baum's cases who could not be resuscitated, could not, on account of massive infarction. If this latter figure is close to the truth, it is not surprising that discrimination is difficult as both groups of cases are very similar. The rather conjectural weighted analysis of the regression coefficients performed on page of this chapter, would support this latter figure.

Various mechanisms can be proposed to explain the postulated relationship between alcohol and sudden death, if it is causal. i) Chronic alcohol consumption promotes electrical instability and ventricular fibrillation, ii) chronic alcohol consumption causes heart failure which may then promote death through ventricular fibrillation and/or severe acute heart failure, iii) in the presence of a fresh or impeding myocardial infarction chronic alcohol ingestion leads to death through severe acute heart failure.

The author favours the latter two possibilities, particularly the last, for the following reasons: data from the myocardial infarction discussion earlier in this chapter gives no evidence that persons having definite MI and proven ventricular fibrillation as a complication consume any more alcohol than those definite MI cases not suffering ventricular fibrillation.
Secondly, the coefficient for alcohol in 'alcohol-analysis B' was greater and more significant (despite the low numbers) than that from 'alcohol-analysis C'. As the sudden death cases without diagnosed MI in the analysis C would include a higher proportion of persons suffering primary ventricular fibrillation, this argues against hypothesis (i).

Thirdly, while heavy consumers of alcohol are known to have an excess of arrhythmias (191), these are most usually supraventricular and nonfatal. However, ventricular arrhythmias are not unknown (192). Most work has related to the acute effects of alcohol. In this study the chronic effects are being considered.

Fourthly, there is accumulating evidence of subclinical cardiomyopathy in persons consuming large quantities of alcohol chronically. Using systolic time intervals and other measures there is evidence of decreased cardiac performance in such persons (191, 192, 193, 194, 195). The data of Barboriak et al (196) suggest that persons with chest pain undergoing angiography have less coronary disease if they consume more than 180 g ethanol per week. Consequently their symptoms have come on earlier or are due to a separate pathology.

A recent publication (161) has reported a decrease in sudden death in persons consuming alcohol compared with teetotallers. There are however several problems with this study. Only 56% of the ascertained cases were finally included in the study. Biases relating to this selection are not discussed by Hennekens et al. Secondly, alcohol consumption was documented only for the three months before death and may well have been very atypical of normal habits due to increasing symptoms. Thirdly, the relationship grew weaker with higher alcohol doses. The lack of power of alcohol to discriminate when it was considered just as a binary variable (teetotaller/nonteetotaller), is due to the
preponderance of cases that had zero alcohol intake. A random fluctuation (possibly), here involving slightly more teetotallers than expected being in the sudden death group, nullifies the significant differences shown amongst the smaller numbers of drinkers. Alternatively the dip in the odds ratio shown for low intakes could be real, but no good evidence could be found for this.

It seems possible that any real effect of alcohol to promote sudden death would be the cumulative result of years of alcohol consumption. It should be remembered that in this study, the habits of only the last one year were documented. On many occasions the author was told that cases who had died suddenly, had a few years back had a much higher intake, but since becoming symptomatic (often symptoms of heart failure) had markedly reduced their consumption. Also, it seems likely that intakes ascertained from wives and friends would usually be rather less than the truth. On many occasions the wife seemed to have a rather hazy notion of the husband's intake at the bar i.e. outside the home. She nearly always knew the consumption at home, but if she could comment concerning the bar, it was usually from an occasion when she had accompanied her husband. He may well have consumed less than usual on such an occasion. Consequently, for both of these reasons, the author believes it quite likely that the effect of alcohol as a discriminant has been underestimated in this study.

It is probable that the relationship between coronary disease and alcohol is complex. There is little doubt that alcohol consumption can increase levels of HDL cholesterol to a modest extent (183, 184, 185).

However, this benefit may well be substantially or completely undermined (depending on the population's habitual alcohol intake) by a subclinical alcohol-induced cardiomyopathy which becomes clinical and rapidly fatal in the event of
a myocardial infarction further decreasing left ventricular function.

b) The variables significantly separating possible myocardial infarction cases (who did not die suddenly) from definite myocardial infarction cases included sex, indices of chest pain or treatment for this (past acute coronary insufficiency and the use of \( \beta \) blockers), indices of heart failure (use of frusemide or ethacrynic acid and lack of energy in the prodromal period), indications perhaps of adrenergic discharge (sweating and pallor) in the acute phase, and fatal outcome between one and 30 days after the acute event. The multivariate equation was made to include only variables that could be conceived as predictors. Thus variables relating to the time after the acute event were excluded (sweating at first assessment, death withing 30 days). The multivariate approach has unconfounded two more complex interrelations of the variables. Height considered univariately was not close to significance. However once the difference in sex ratio was taken into account, the univariate similarity in heights was shown to be unexpected as the excess females in the possible myocardial group should have made this group shorter. Secondly, alcohol becomes significant after being nearly so in a univariate test. This again was related to the sex ratio difference and the different average intakes of men and women. Past acute coronary insufficiency and prodromal lethargy became nonsignificant in the multivariate equation due to relatively small but significant correlations between those variables and the use of frusemide or ethacrynic acid. Thus the typical possible infarct (who did not die suddenly) differed from the typical definite myocardial infarction case by being more likely a female, having more chronic chest pain, probably more heart failure, consuming more alcohol, being taller, manifesting less clinical shock in the acute phase and dying much less frequently
between one and 30 days after the acute event.

It is interesting to note that several similarities exist between this comparison and that considered in the last section. Alcohol, heart failure and chest pain discriminated in both comparisons, suggesting similarities perhaps between the sudden death cases and the possible myocardial infarction cases who did not die suddenly.

These considerations suggest that possible myocardial infarction is a separate syndrome or group of syndromes. A distinct, recurrent pathological process may be involved resulting in small areas of necrosis, associated with chest pain, and finally precipitating heart failure. Alcohol could be one aetiological agent as it is well known to be associated with a rather diffuse myocardial fibrosis (197). The female preponderance may represent also a peculiar response of females to ischaemia. Mitchell et al (132) found women who died in association with myocardial infarction to have a considerable excess of fine fibrotic lesions (unrelated to coronary lesions), compared to normal women. This was not so for males. The present study shows female definite myocardial infarction cases to have more antecedent indices of heart failure than males. Perhaps the possible myocardial infarction syndrome represents symptoms associated with the formation of these lesions.

c) The variables significantly separating possible myocardial infarction cases (who did not die suddenly) from cases who died suddenly were few in number. In fact only three were statistically significant, sex ratio, painful prodromal symptoms and age. Two other variables that came close to significance were previous or present hypertension more common in the possible myocardial
infarction cases ($p<0.06$), and time of day of onset with the possible myocardial infarction cases being more common between 6 P.M. and 6 A.M. ($p<0.07$).

The multivariate analysis showed only two factors as significant, with the painful prodromal symptoms losing significance due to other weak correlations and also in the change from linear to logistic model. In particular, alcohol does not come close to achieving significance.

One interpretation would be that the possible myocardial infarctions represent patients who would subsequently proceed to sudden death, differing mainly in being younger by about 4 years on average. The difference in sex ratio could be a result of relative female resistance to sudden death despite having developed ischaemic disease or perhaps the fine fibrotic pattern whether or not due to ischaemia. This could result in lower age specific sudden death rate in females than males despite the relative excess of the postulated predisposing lesions (132). That such relative 'resistance to sudden death' may exist among females with coronary disease is indicated by the following analysis from the present study, which was alluded to in the 'Discussion of Sudden Death Results' section.

It was observed that 7 females and 50 males, who had died suddenly, had a past history of old myocardial infarction. Then as the total populations of males and females in the community are roughly equal: \[ \frac{\Pr(\text{Old MI and sudden death|female})}{\Pr(\text{Old MI and sudden death|male})} \leq \frac{7}{50} \leq \frac{\Pr(\text{old MI|sudden death, female}) \times \Pr(\text{sudden death|female})}{\Pr(\text{old MI|sudden death, male}) \times \Pr(\text{sudden death|male})}. \]

As \( \Pr(\text{sudden death|male}) / \Pr(\text{sudden death|female}) \geq 3 \), then \( \Pr(\text{old MI|sudden death, female}) / \Pr(\text{old MI|sudden death, male}) = \frac{3 \times 7}{50} = 0.42. \) This difference between the sexes is
statistically significant (p<0.03). This implies that amongst female sudden deaths, old infarctions are less common. Thus there seems to be a sex-dependent dissociation here between myocardial infarction and sudden death. Perhaps this implies a second sudden death promoting process in females operating in the absence of the clinical expression of coronary disease.

An alternative analysis can be performed. As before,

$$\frac{\Pr(Sudden \ death \ and \ old \ MI | female)}{\Pr(sudden \ death \ and \ old \ MI | male)} = \frac{\frac{7}{50}}{(\Pr(Sudden \ death | old \ MI, \ female) \times \Pr(Old \ MI | female)} / (\Pr(Sudden \ death | old \ MI, \ male) \times \Pr(Old \ MI | male)).$$

The quantity $\frac{\Pr(Old \ MI | male)}{\Pr(Old \ MI | female)}$ is somewhat conjectural but one would expect this to be similar to the ratio of fresh MI's in a given time i.e. about 3. In this case we find that $\frac{\Pr(Sudden \ death | old \ MI, female)}{\Pr(Sudden \ death | old \ MI, male)}$ is again about 0.42.

This implies that in females with coronary disease, despite having this disease die suddenly, less. Thus there seems to be a factor that protects females from sudden death, even in the presence of coronary disease. Then the similar male/female sex ratio in the sudden death and definite myocardial infarction cases could be due to two opposing influences 1) A factor protecting women from sudden death even in the presence of coronary disease, tending to increase the ratio, 2) A relatively higher proportion of women dying suddenly having some other process operative, tending to decrease this ratio.

It seems possible that part of the explanation could be related to alcohol consumption. Women drink less alcohol and therefore their coronary disease is less often expressed as sudden death. Also there is some evidence that women are resistant to the cardiac effects of alcohol (198).
In as much as it is finally impossible to prove two variables to be related as cause and effect, this section must be considered as hypothetical. However the evidence linking some variables is quite strong. Other relationships are largely conjectural.

**Mechanisms**

The development of the diseased state to such an extent as to manifest itself in one of the common clinical syndromes is usually a process occurring over many years. In this discussion the aetiological mechanisms will be considered to usually act in two phases a) a chronic preparatory phase, b) a precipitating phase. While it seems possible that a clinical event may occur under the influence of only a precipitating aetiological agent the evidence suggests that this is uncommon. Probably a preparation by means of the accumulation of atheromatous deposits in the walls of the coronary arteries is followed by a precipitating mechanism acting more acutely to trigger the clinical event. Conceptually it is also possible that some acute events may be the result solely of the 'preparative' process having reached a advanced stage.

On reviewing the times of onset of prodromal and previous symptoms and the probability density histograms in the present study, a pattern seems to emerge for painful symptoms at least. This implies a gradual increase in probability before the prodromal period and a more rapid increase in probability of the symptoms within the prodromal period. Usually the histograms give an appearance similar to an exponential function, once the changing time scale is taken into account along the x axis. There does not seem to be evidence for any acute deviation from this pattern at any particular time before the prodromal
period or within the prodromal period except for the 24 hours immediately preceding the acute event. In this period there appears to be a disproportionate increase in prodromal symptoms.

This suggests the interposition of some precipitating factor at this time. Of the precipitating factors to be considered, the most likely would seem to be coronary spasm, accumulating coronary mural thrombosis or perhaps acute focal necrosis in the case of sudden death (if this pathology is painful). Alternatively these time observations may imply that the gradual progression of the preparative factors has at this point resulted in a threshold being passed leading to a disturbance of myocardial metabolic homeostasis and finally an acute coronary episode. However, there are some populations that appear to have little atheroma, but more than expected clinical events (199, 200) and presumably these events may be due to some precipitating factors. Prinzmetal angina (201) and occasionally infarction due to spasm (202) is another example of a situation where there may be very little coronary atheroma (usually some (201)), but clinical events do occur.

The evidence seems clear that a high prevalence of coronary atheroma within a population is associated with clinical coronary disease and vice versa (203). Animal work also supports the idea that accumulation of atheroma leads to an increased frequency of myocardial infarction (204). The atheromatous hypothesis has considerable intellectual appeal, as the mechanism seems straightforward, that of chronic or acute ischaemia leading to symptoms and/or muscle damage. It is also common knowledge experimentally, that ischaemia is associated with an increased frequency of severe arrhythmia and sudden death (205). Similarly the coronary-care unit experience has demonstrated the
association between acute myocardial infarction, arrhythmia and sudden death (206).

Consideration will now be given to the aetiology of each of the coronary syndromes separately.

a) Chronic stress-invoked angina appears to be a reversible situation as compared to myocardial infarction or sudden death. This suggests a 'supply and demand' problem. Perhaps this syndrome represents the effects of the preparative atheromatous phase having reached a relatively severe degree. The capacity for the development of collateral arterial supply in the human coronary tree seems limited (207), but probably important in cases of long standing angina.

b) Prinzmetal Angina: Not all angina need be explained on the above basis. The concept of temporary spasm usually occurring at a small focus of sclerosis or atheroma (201) is clearly important in a few people. Spasm could here be viewed as a reversible precipitating factor.

c) Definite Myocardial Infarction: Infarction with 'normal' coronary arteries has been described several times (208). Various mechanisms have been postulated such as thrombosis. A spectrum of possible but rare causes is discussed by Chetlin et al (209). Variation in the clotting potential of the blood may on occasion produce hypercoagulability or platelet hyperaggregability, leading to occlusion, even in normal arteries (21). The possible importance of this factor is shown by the report of Gertler et al (211) significantly relating a coagulation profile score to risk of coronary heart disease, with highest values of this score in post MI and acute MI groups.

Because the human coronary tree has even fewer collaterals than that of
the dog (212), the infarction almost always resulting from acute occlusion in the dog (205), would seem likely in the human also.

Despite some of the above considerations, for the vast majority of cases of myocardial infarctions, significant atheromatous damage is usually present in two or three of the major coronary arteries (169). While it is conceptually possible that under the influence of atheromatous deposition, the walls of the coronary arteries could slowly 'grow' together and finally occlude, recent pathological evidence seems to suggest that often the terminal occlusion follows rupture of an atheromatous plaque and subsequent coronary arterial mural thrombosis progresses to occlusion of the narrowed lumen (213). This last process may involve precipitating factors in the rupture or could conceivably be a final natural stage of the accumulation of poorly supported friable atheromatous material.

There are several sources of evidence suggesting that precipitating factors are often involved in acute myocardial infarction. 1) In 31% of cases in the present study there were no prodromal symptoms to suggest the development of critical stenosis and impending occlusion. This result is similar to that of others. This could of course be consistent with a ruptured plaque and thrombotic occlusion before the development of critical atheromatous stenosis. 2) The apparently quite sudden decline in risk after cessation of smoking (111, 214). This would seem perhaps too sudden to be accounted for by regression of atheroma and may imply the removal of other effects associated with smoking. 3) The apparently quite sudden changes in death rates ascribed to coronary disease in countries influenced by the privations of the second world war (215). It could be also, that atheroma can regress more rapidly than usually thought
under the influence of a quite severely restricted diet. The anecdotal results from the Longevity Centre, Santa Monica, California (216) may represent a similar sequence of events. 4) The lack of postmortem acute occlusion in many fatal infarctions (217), suggests that an acute occlusion is not the only cause of infarction. This seems particularly so with subendocardial infarction, whereas with transmural infarction an acute occlusion can usually be demonstrated (129). 5) The pattern of times of onset of previous and prodromal symptoms as discussed above.

The subendocardial infarction would seem to differ from transmural infarction in several ways apart from the obvious one, possibly suggesting a different aetiology. Erhardt (218) has investigated the differences with a small number of fatal cases. Several quite striking differences emerged.

The subendocardial infarction patient was much more likely to give a history of previous angina or acute coronary insufficiency, and to give a history of heart failure. Admission to hospital was often delayed, but sudden unexpected death in hospital was more frequent. At postmortem, coronary thrombosis was much less frequent and previous infarction somewhat more common (usually also subendocardial). Infarction was much more likely to be diffusely scattered, with the lesions often showing a varying age. The heart usually showed a high degree of myocardial fibrosis.

Erhardt's pathological and symptomatic findings are in complete agreement with those of this study reported in the Discussion of Definite Myocardial Infarction section. The pathological findings suggest perhaps an affinity between those subendocardial cases and the sudden death and possible myocardial infarction cases.
d) Sudden Cardiac Death

Sudden cardiac death is due to cardiac arrest. This may be due to asystole or ventricular fibrillation (although an ineffective ventricular tachycardia may progress to ventricular fibrillation). Liberthson's work (128) suggests that the terminal arrhythmia is ventricular fibrillation in about 70% of cases. These arrhythmias may be primary, or secondary to myocardial infarction and/or severe cardiac failure due to other cause. In this study cases suffering severe cardiac failure due to other cause, causing the patient to be bedridden within 24 hours prior to the onset of acute symptoms, were specifically excluded as non-sudden deaths.

Recognizable lesions involving the conducting system of the heart seem to be uncommon in persons dying suddenly (173). Myocardial infarction may cause sudden severe cardiac failure which could conceptually bring about almost instantaneous death. Myocardial infarction is also well-known to be associated with ventricular fibrillation.

In western societies, it is true that persons dying suddenly, almost always have moderate or severe coronary atheroma and usually areas of myocardial fibrosis, either discrete or diffuse. The presence of coronary atheroma is not compelling evidence for a causal relationship, as the general population also has much coronary atheroma. In particular, it would seem necessary to demonstrate that in populations with very little coronary atheroma, sudden death is rare. Some data is available for instance for Bantus where atherosclerosis is uncommon and death signed as due to coronary disease is also rare. How reliable the stated causes of death are, is uncertain. Another factor may be the 'pyramidal' age structure of the population, as age is correlated with both athero-
sclerosis and sudden death.

Of interest also would be to know the frequency of sudden death of the type seen clinically in western countries and usually ascribed to coronary disease but perhaps due to other factors. The usually observed coronary disease in western populations may sometimes be an innocent bystander or at most a facilitating factor rather than the prime aetiological factor. However the similarity of risk factors for sudden death and other manifestations of coronary disease, would make it seem likely that the same processes are at work here, in many cases at least. That probably about 50% of sudden deaths are associated with myocardial infarction also would lend support to this.

A fatal arrhythmia on the basis of some other pathology would however seem likely to be the sequence in a proportion of cases, a so-called primary arrhythmia. McGill in his book *The Geographic Pathology of Atherosclerosis* (219) presents data suggesting rather low rates of atherosclerosis in coronary deaths from some Inter American and South American countries. He then suggests that this observation may be due to misdiagnosis with 'myocardial necrosis and fibrosis due to infections or nutritional disorders' possibly accounting for the discrepancy.

Clinicians are well aware of arrhythmias, often potentially serious, in many diverse cardiac disorders, such as rheumatic fever, haemochromatosis, connective tissue disorders, viral myopericarditis and metabolic disorders particularly hypokalaemia. Schwartz and Walsh (150) discuss these factors in more detail, as they relate to sudden death. Baroldi (169) describes a lesion he calls coagulative myocytolysis - a focal necrosis - in 67% of sudden deaths, but only in 40% of acute infarctions studied within 2 days of the acute event.
Frink et al (220) observed a non-obstructive mural coronary thrombosis in 6 out of 6 postmortems of men who died suddenly with no history of coronary disease. He postulated that distal microthrombi may have caused scattered areas of ischaemia and electrical instability. He was able to demonstrate such microthrombi in 4 out of 6 hearts.

Others (221) have considered the evidence for psychogenic mechanisms inducing ventricular fibrillation.

A fairly consistent observation in several studies has been the association between indices of heart failure and sudden death. It is not clear whether this association implies 1) the physiological situation of heart failure - (increased left ventricular volume, and wall tension and so possibly aggravated ischaemia due to decreased cardiac efficiency) - causes the fatal arrhythmia. The increased catecholamine levels in association with this disorder may be important. It is notable that the best predictor of 'primary' cardiac arrest after a proven infarction in the present study, was pulse rate which probably also indicates catecholamine levels and heart failure; or 2) the pathology producing the heart failure may also lower the threshold for arrhythmias. As many such pathologies involve areas of fibrosis this is quite likely, invoking the re-entry mechanism; or 3) one metabolic consequence of acute ischaemia is elevated levels of free fatty acids and these may be toxic to the myocardium stimulating arrhythmias (222). This may be important when the failure is due to ischaemic pathology. 4) The treatment of heart failure with digoxin and diuretics may result in toxic mechanisms or metabolic imbalance, particularly hypokalaemia. 5) Interactions between some of the above factors, in particular superadded acute ischaemia may drop cardiac output below a critical level.
e) Possible Myocardial Infarction: Little is known of this syndrome in comparison to definite myocardial infarction or sudden death. Consequently much of the following is conjectural, but supported by some evidence. Pathological data is not available as the condition is generally not rapidly and dramatically fatal about the time of the acute event.

It is very likely that this also is not a 'pure' syndrome pathologically or aetiologically. As commented previously, probably some cases of chronic stress induced angina could have been included. However the author endeavoured to exclude such cases by definition. Small subendocardial infarctions may not show clearly positive enzyme elevation. A proportion of possible myocardial infarctions may reflect this pathology. There seem to be some similarities between cases suffering subendocardial infarction and possible myocardial infarction cases.

Another group of cases could be persons with fine fibrotic lesions (possibly the stress-strain ? catecholamine-induced lesion described by Baroldi (169) which may be the same lesion described by Mitchell and Schwartz (172)).

Also it is notable that several reports suggest a poor prognosis on follow-up of cases similar to those defined here as possible myocardial infarction (151, 156, 223, 224). This could be further evidence that these cases are sudden deaths 'in preparation'. The multivariate analysis showed few differences from sudden death cases.

Coronary angiography on patients with unstable angina has been performed, revealing single vessel disease in approximately 30%, two vessel disease in 30% three vessel disease in 30% and normal coronary arteries in the remaining 10% (225). Consequently coronary disease in probably implicated in some cases at least, as these frequencies are higher than those found in persons dying by
accident or due to disease unrelated to atherosclerosis, in these age groups (226).

Figure 39 summarizes some of these postulated relationships.
Figure 39. Possible Mechanisms Involved In The Production of Several Coronary Syndromes.
Section 7.9: THE ROLE OF LIFE STYLE AND RISK FACTORS IN THE PRODUCTION OF THE CORONARY SYNDROMES

This section is not intended as a comprehensive review of the very large literature relating to these topics. Rather, the author will try, briefly, to relate partially alterable life style factors to the production of the pathological mechanisms discussed in the last section.

Foremost in these considerations must be diet. Although still controversial to some (227), most epidemiologists now accept the bulk of population and experimental data relating saturated and polyunsaturated fats and dietary cholesterol to the level of serum cholesterol (228, 229, 230). Polyunsaturates probably increase cholesterol excretion transiently (231). In turn there is clear evidence of the relationship of serum cholesterol to clinical coronary disease.

That the effect of serum cholesterol is specifically on coronary atheroma is not so well established, but population comparisons certainly suggest this, with those populations consuming diets high in fats having greater amounts of coronary atheroma (232). Animal work also supports this hypothesis (233). However, the International Atherosclerosis Project report (234), while somewhat supportive also included other nutrients as importantly predicting raised coronary lesions. The techniques of data collection in this last study of a necessity make conclusions suggestive only. As stated by Stamler (235), perhaps a high fat diet is a necessary (and sufficient) factor in the production of coronary disease.

Increasing evidence suggests that dietary fibre also can reduce serum cholesterol. The fibre components particularly associated with this effect seem to be pectin (236), some gums and mucilages (236) and possibly lignin. Wheat bran is not active in this respect (237). There is some evidence that diets high
in vegetable content may be associated with lower serum cholesterols than
that accounted for by the triglyceride fat and cholesterol differences alone
(238, 239). This could be due to some of these fiber components, phytosterols (240), silicon (241) or unidentified factors.

Interestingly, there are several other possible mechanisms through
which a diet high in polyunsaturates may be beneficial. Linoleic acid is the
prominent fatty acid component of such diets. This fatty acid has been demon-
strated to decrease the thrombotic tendency of platelets, in contradistinction
to the action of several of the common saturated fatty acids (242).

Secondly, linoleic and linolenic acids are involved in the formation of
the prostaglandin group of metabolically active chemicals. This may explain
their effect of platelet adhesiveness. In addition it could explain the evidence
that vegetarians may have lower blood pressures (243, 244), as many of the
prostaglandins induce arterial dilatation and water and sodium diuresis.

Some high fibre diets and high linoleic acid diets have been observed to
decrease plasma insulin and fasting glucose levels (245, 246, 247). This may
be important in decreasing cardiovascular disease. Linoleic acid in animal
experiments has been found to increase cardiac contractility, perhaps without
increased oxygen consumption. Many of these aspects are summarized, with
references, in the review article by Vergroesen (242).

It may be significant that linoleic acid forms a usual part of the lecithin-
cholesterol-acyl transferase reaction (LACT) which is involved in the trans-
port of cholesterol away from the arterial wall to the liver. Linoleic is the
fatty acid usually utilized in the conversion of lysolecithin to lecithin.

Although familial LCAT deficiency is associated with worsened athero-
sclerosis, within the 'normal' range for the LCAT enzyme, higher values of the enzyme are correlated with hyper-B lipoproteinaemia and low levels of HDL cholesterol (248). It has been found both in rats and humans that the feeding of polyunsaturated fats lower the level of LCAT (249).

Russian researchers have demonstrated the effect of gastrointestinal reflexes on the electrocardiogram both in animal and human experiments. The observed effects are usually confined to persons with ischaemic disease. These data are summarized by Simonson (250). Possibly gastrointestinal disease, stimulatory foods eaten (e.g. mustard) may act as precipitating factors.

An interesting observation by Davies et al (251) was that patients suffering myocardial infarction in a coronary care unit showed significantly higher titres of antibodies directed against eggs and cows milk. The implications of this are not clear. It could be that this reflects an increased intake of these dietary articles over time, which has also led to coronary atherosclerosis. Another perhaps less likely hypothesis would be that immunologic reactions are involved in the production of the fine fibrotic lesions which are possibly associated with sub-endocardial infarction. It is noteworthy that Baroldi (169) describes a lymphocytic infiltration about these lesions in the acute phase.

The role of alcohol has already been extensively discussed in previous sections of this chapter. It seems likely that alcohol raises HDL to a modest extent, decreases cardiac performance acutely (252, 253) and chronically (193, 194, 195) and is associated with the production of fibrotic myocardial lesions. Triglycerides are also elevated by alcohol acutely and chronically (254) but the relevance of this to clinical coronary disease is debatable. Chronic alcohol consumption may be associated with higher blood pressure and this may be
important (see below) (255, 256).

Epidemiological and experimental evidence (257, 258) suggests that dietary sodium (and perhaps potassium) affect the risk of developing hypertension. As hypertension is an established risk factor for atherosclerosis and clinical coronary disease (259), these are important observations.

Hypertension will also likely increase the cardiac work/available myocardial O\textsubscript{2} ratio. Hypertension is also often associated with left ventricular hypertrophy. It seems quite likely that the combination of left ventricular hypertrophy and increased wall tension may be associated with subendocardial ischaemia and/or the production of interstitial myocardial lesions (172).

Smoking cigarettes is clearly associated with coronary disease. There is evidence implicating several mechanisms. Postmortem studies show smokers to have increased arterial atherosclerosis (260). Smokers have higher levels of carboxyhaemoglobin which will increase the cardiac work/available myocardial O\textsubscript{2} ratio. This has been demonstrated to lower the threshold for angina (261). Recent analyses (262, 263) have shown that smokers have lower levels of HDL 'good' cholesterol, although causality is not yet established. This may be why smokers have more atherosclerosis.

It is also known that smokers' blood shows decreased platelet survival in vivo and in vitro (264). As thrombosis figures prominently as a mechanism, smoking may be a precipitating factor also.

Exercise and physical fitness relate to several matters already discussed. Some evidence exists that increased cardiac fitness reduces the risk of death following infarction (265). Also it seems likely that clinical coronary disease as a whole is less frequent in persons who habitually have a higher level of
activity. There are still conflicts in the literature, which have been summarized well by Leon and Blackburn (266).

Exercise affects several other risk factors in a salutary fashion to decrease risk. Exercise increases HDL cholesterol (267, 268) (specifically HDL\(_2\) (269), and reduces the level of serum triglycerides (270). Exercise reduces blood pressure - perhaps by weight reduction (271). Exercise may decrease the tendency to smoke cigarettes (272). It also reduces serum glucose and insulin levels, in obese individuals at least (267).

Of the various psychosocial factors that have been investigated, only Type A (coronary prone) behavior has emerged as a significant predictor (273). Other variables studied have not given consistent results (273). Various mechanisms have been postulated, with some evidence linking these psychological factors to disease mechanisms. There is some inconsistent evidence that stress alters platelet aggregation (274), but as pointed out in a British Medical Journal Editorial (275), these in vitro findings with respect to platelets are not easy to interpret. Friedman and Rosenman (276) have some evidence that Type A personality is associated with higher serum cholesterols, shorter blood clotting time and increased cigarettes smoked.

Nevertheless the available evidence does suggest an effect independent of associations with established risk factors (277). Behavioral therapy to change Type A behaviour is being investigated (278).

Occasional reports suggest that acute psychological influences may promote primary ventricular fibrillation. Lown has described cases and postulated mechanisms (221). However, most sudden deaths seem to have no clear stressful precipitation (35). There do seem to be socioeconomic differences with
respect to persons dying suddenly. Presumably this factor operates through some associated environmental or psychological variables. Holme et al (279) reports changes in various risk factors with social class in Oslo. In this population overall risk scores increasing with lower social class (i.e. lowest education and income). It seems possible that alcohol consumption could also be implicated to explain the results of the present study; i.e., high alcohol consumption results in lower social class and also sudden death.

Many studies now report an increased risk of cardiovascular death in localities with soft water compared to those with hard water (280, 281, 282). Not all reports are consistent (283, 284), but probably sufficient are to make this a serious contender as a risk factor. It seems that the increased mortality particularly affects those sudden deaths occurring within 1 hour of onset (285). Several theories may explain this association. Although other associated confounding variables have been looked for, none have been found.

Hard water contains much more calcium than soft and there is some evidence that dietary calcium lowers serum cholesterol (286). Stitt, Crawford, et al have compared the characteristics of persons in hard and soft water areas (287) and indeed found both serum cholesterol and blood pressures significantly higher in the soft water areas. The gross differences in sodium contents of these waters could well be expected to increase blood pressure in hard water areas, however the opposite was found. Soft water corrodes piping and there are differences in manganese, magnesium, aluminium, boron, iodide, fluoride, and silica contents of these waters consistently (280). No consistent differences were found in cadmium concentrations despite the report that high renal cadmium/zinc ratios are associated with arterial hypertension (288).
The reduction in silica in soft water has been suggested as the important factor as atherosclerotic arteries have low silicon concentrations compared to normal arteries (241).

A common (although undocumented) observation in the present study was the frequency with which the spouse of a sudden death case, reported the deceased as having had the "flu" in the few weeks or days before death. This was usually interpreted by the author as incipient pulmonary oedema. However, it may have been a viral illness as implied historically.

Many common viruses are well known to cause a myo-pericarditis (289, 290). Transient ECG changes are also quite frequent during viral illness. It has been observed that patients suffering myocardial infarction have significantly higher antibody titres against some common viruses, than controls (291). Thus viruses could conceivably cause primary necrotic damage, probably of a focal type. Epidemiological evidence is also consistent with this hypothesis (292).

Alternatively it has been suggested that a viral induced arteritis may cause a secondary infarction in some instances (293).

In summary the evidence suggests the following life-style changes to reduce the risk of coronary disease.

i) consume a diet largely composed of natural vegetables and grains

ii) restrict sodium intake

iii) do not smoke cigarettes

iv) avoid high or probably even moderate intake of alcohol

v) maintain a good level of physical fitness by regular moderate exercise

vi) do not consume soft drinking water for long periods

vii) if you have a Type A personality, it may in the future be possible to
obtain effective psychotherapy.
CHAPTER 8

CONCLUSIONS
CONCLUSIONS

The following conclusions are drawn on the basis of the data and discussion in previous chapters. The evidence is circumstantial in some instances and this will be mentioned. In view of the complexity of the interrelationships which analysis of the data revealed, the conclusions are presented essentially as a series of statements. The discussion relating to the points tabulated in the following paragraphs has been included in the relevant chapters.

1. Coronary disease and its manifestations are not a development of the twentieth century. Based on largely anecdotal evidence it seems likely that it has existed from antiquity in select populations. (Refer Section 1.1)

2. It is possible to obtain useful data for epidemiological purposes using a population sample. The sample is random and therefore representative of the population. A Bayesian approach seems satisfactory and as usual a sampling technique results in an efficient procedure. (Refer Section 2.2)

3. Where collects are made from total populations, apparent differences between different places may be due to random fluctuations. In effect such a collect is a sample from a dynamic "superpopulation" with subpopulations entering and leaving the particular age range over N years (where N is arbitrary but >1). (Refer Section 2.2)

4. The incidence of definite myocardial infarction and sudden death in Auckland seems very similar to that of many western countries. Notable exceptions for the sum of all definite events are Helsinki, Sofia, Berlin,
Boden (Sweden), Gothenburg. It is difficult to compare the incidence of possible myocardial infarction with that of other places as so little data is available. (Refer Section 3.2)

5. Women with coronary disease differ from men in several ways. Those women suffering myocardial infarction are probably at a later stage of deterioration of cardiac function (as determined by symptoms). Despite this, women are less likely to die suddenly after a definite myocardial infarction (remote from the acute phase), when they presumably already have established coronary disease. Thus a protective factor for sudden death, as distinct from the factors protecting women from coronary disease, must be operating. Smoking as a risk factor seems of greater significance in women, as judged by the higher relative risk of MI in women. (Refer Sections 7.2 and 7.7)

6. Persons experiencing an attack of primary ventricular fibrillation (i.e., systolic blood pressure greater or equal to 100 mm Hg before the arrhythmia) in association with a definite myocardial infarction were distinguished by indices possibly reflecting the size and haemodynamic significance of the infarction, e.g., transmural infarction, clinical shock, tachycardia, dyspnea. Twenty-two percent of clinically shocked (i.e., pale, sweaty) persons developed primary ventricular fibrillation, but only 3% of non-clinically shocked patients did so. Twenty-three percent of persons with tachycardia > 100 beats/minute suffered primary ventricular fibrillation with their infarction, whereas only 6% of persons with pulse rates < 100 beats/minute did so. (Refer Section 7.2)
7. Persons experiencing transmural infarction were larger (but not more obese), experienced less chest pain in the past and prodrome preceding that infarction, had had fewer previous definite infarctions, showed more acute shock and had a poorer 28-day prognosis, than persons suffering a subendocardial infarction. At postmortem, old infarction and/or fibrosis were less common in patients experiencing transmural infarction. (Refer Section 7.2)

8. There appears to be a delay advantage for persons suffering myocardial infarction to call the ambulance directly, such cases having median delays to reach the coronary care unit over one hour shorter than those calling a doctor. These observations are perhaps even more significant for being made in an area in which there has been relatively little development of paramedical services. (Refer Chapter 4)

9. The clinical event of sudden death is usually all over before any help is sought (142/178 in this study). The event occurs infrequently at work, considering the proportion of time spent there, but also infrequently during the night hours 12 MN - 6 AM. (Refer Chapter 5)

10. In view of these findings and the spread-out character of Auckland city, it would seem that a rather large fleet of ambulances would be necessary to be effective in life saving. The long-term experience of such ambulances at other centres is not encouraging, despite initially enthusiastic reports more particularly from quite heavily built up areas. (Refer Chapter 5)
11. Overall, sudden deaths were only about two-thirds as frequent as definite myocardial infarctions. However, there was a pronounced seasonal swing with the sudden death frequency exceeding the definite myocardial infarction frequency by 20% in the cooler months. (Refer Chapter 5, Sections 7.5 and 7.7)

12. Sudden death occurred significantly more than expected in the lower social class areas of Auckland. This was so only for those cases dying more than 5 minutes after onset of symptoms. A possible explanation could be delay in seeking help for reasons such as finance, lack of transport, communication, or friends. Such deaths may in part be unnecessary. (Refer Chapter 5)

13. Proportionately more females experience possible myocardial infarction than is the case for the other two syndromes. This is particularly so for the Maoris and may imply that some special life styles or pathologies are operative here. (Refer Chapter 6)

14. Persons dying suddenly differed from persons experiencing definite myocardial infarction (but not dying suddenly). They experienced less prodromal chest pain, took digoxin and frusemide more frequently, consumed more alcohol, and the acute event occurred in the cooler months proportionately more often. At postmortem, they had significantly more myocardial scarring and/or fibrosis. (Refer Sections 7.5 and 7.6)

15. Persons experiencing definite myocardial infarction differed from persons experiencing possible myocardial infarction (who did not die suddenly).
They were more likely to be male, had less history of past acute coronary insufficiency, used less of beta-blocking drugs or frusemide/ethacrynic acid and described prodromal lethargy less frequently. Clinical shock was more common in the acute phase and death more common in the succeeding 30 days in the patients experiencing definite myocardial infarction. (Refer Sections 7.5 and 7.6)

16. Persons dying suddenly differed from those suffering possible myocardial infarction (but not dying suddenly) by being older, more likely to be male, and less likely to have had chest pain in the prodrome. (Refer Sections 7.5 and 7.6)

17. The comparison between cases dying suddenly and possible myocardial infarction cases (who did not die suddenly) was notable for the lack of difference between observed variables in these two groups of people. It is suggested that a sizable proportion of possible myocardial infarction cases are sudden deaths "in preparation." (Refer Sections 7.5, 7.6, 7.7, 7.8)

18. Certain symptomatic and pathologic variables seem similar between possible myocardial infarction cases and subendocardial definite infarction cases. (Refer Sections 7.2, 7.5, 7.6)

19. A second form of pathology, distinct from acute macroscopic infarction, may be operative in at least a proportion of cases of each of the coronary syndromes investigated. Either fine fibrosis or multiple areas of more confluent fibrosis are found in cases of sudden death, and fatal acute
subendocardial infarction. The apparent multivariate similarity between possible MI and sudden death cases perhaps implies this pathology exists also in possible MI cases. There was a relative deficit of such lesions in cases of fatal acute transmural infarction. Thus the data could be interpreted as suggesting that a primary myocardial process is present in some cases and that this may contribute towards sudden death.

One hypothesis would be that the observed excess of fibrotic tissue in the myocardium causes incipient chronic and/or frank acute heart failure and is associated with 1) an excess of arrhythmias, 2) a sudden reduction of cardiac output below a critical level in the presence of a coexistent acute infarction (or acute ischaemic episode). The present study lacks data to link any such phenomenon to the conducting tissues of the heart. (Refer Sections 7.2, 7.5, 7.7, 7.8)

20. Alcohol may be a risk factor for sudden death. Alcohol has a known toxic effect on the myocardium and may contribute on a long-term basis toward a cause of heart failure. However, the postulated effect is independent of other heart failure indices. A hypothesis which could be linked to that given in paragraph 19 would be that there is an interaction between a postulated alcohol effect and the process causing myocardial infarction, i.e., in the presence of acute infarction a history of chronic, moderate to high alcohol intake is associated with an increased likelihood of sudden death. (Refer Sections 7.2, 7.5, 7.6, 7.7, 7.8)
These conclusions suggest to this author several areas of potential value for future research.

a) A cluster analysis of the data of this study or similar data sets could be valuable. Multidimensional clusters of cases may emerge that suggest a quite different grouping of cases from those used in this study, i.e., those generally used. These new groupings may give aetiological insights.

b) It is probable that several risk factors have not been recognized. An intensive epidemiological study of "unlikely coronaries" could be productive. A group of 100 or so persons with documented infarction who have no recognizable risk factors could be evaluated in depth, both retrospectively and prospectively, with the aim of uncovering external environmental influences not currently recognized as having an association with coronary disease. Also, the reactions of this group to "normal" activities of daily life could be investigated.

c) Development of more effective lifestyle intervention techniques at a "neighborhood" and population-wide level, to hopefully reduce the high incidence of these disorders in the New Zealand population.

d) It will be important in future studies to verify the alcohol histories obtained from relatives of persons experiencing acute coronary events. It would be possible to use hospitalized acute MI patients to obtain a history and then unknown to them, interview the spouse, obtain collateral information through social or community agencies, and check the agreement.
e) A prospective study of the relationship between alcohol intake and sudden death is clearly indicated. Probably it would be most appropriate initially to undertake a stratified prospective study. After screening a large number of individuals, select a sample of teetotallers and a sample of persons having a high consumption of alcohol and follow these for N years.

f) It would be valuable to perform a follow-up study over 5-15 years of the possible myocardial infarction cases defined in this study. This could establish the main causes of death and so check the "sudden death in preparation" hypothesis. It would also fill in other aspects of the natural history of this condition.

g) Further studies should be established aimed at the question of whether coronary care units are an appropriate place of treatment for acute MI patients of all types. The place of home treatment should be carefully considered, particularly in view of the relationship between indices of possible adrenergic discharge and the likelihood of primary ventricular fibrillation. The present study design precluded analysis of this point in depth, but raises the possibility that current clinical practice may at least be associated with causes of sudden/later death. However, full extrapolation of the data has been resisted at this stage.

h) What is the factor apparently protecting females from sudden death in the presence of coronary disease? Such a factor could be related to sex dependent physiological differences or to differences in life style such as a lower alcohol intake. Such investigation could be related to (e) above.
i) What difference(s) in Maori wornen cause their apparent excess of possible myocardial infarction? Do they have an excess of the fine fibrotic lesions either for 1) all Maori women, 2) Maori women with coronary disease? A clinico-pathological study employing specialized histochemistry is indicated. Again, as in (b) above, a long-term prospective study of life style and life-events might yield new insights.

j) Further studies of the relationship, if any, between old or recent virus infection and coronary disease (particularly sudden death) should be undertaken. Serological studies on persons who die suddenly would be interesting, particularly as there is some evidence that viral myocarditis is often an accompaniment of the immune response rather than the original infection. Ultramicrohistology searching for evidence of old or recent viral involvement of myocardial tissue may prove profitable.

k) A major problem in the present study was the inability to distinguish between primary arrhythmic deaths and deaths associated with MI. The efforts of Raiskina et al. (294) and other groups to try to elucidate this problem using K+/Na+ distributions in postmortem tissues are important and further research in these areas would seem to be indicated.

* * * * * * * * * *

Finally, it is suggested that the results obtained and the analyses feasible on this data have in turn indicated that the epidemiological approach adopted for this study can produce conclusions which may serve as the basis for new hypotheses capable of being tested. Such testing
should be by further epidemiological research but also employing contributions from clinical medicine, pathology, sociology, psychology, and biochemistry. Cooperative endeavors would seem to offer the maximum promise for advancing our understanding of coronary heart disease.
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APPENDICES
Prior Distribution of $\theta$ and Estimation of $\sigma^2$

Definitions

Let:

$P'$ be a variable describing the number of persons in an individual doctor's practice,

$P^*$ be a variable describing the accumulated practice sizes of groups of D/G doctors (where $G \geq 10$),

$P$ be a variable describing the accumulated practice sizes of groups of $K$ doctors,

$Y'$ be a variable describing the number of letter replies naming a particular doctor,

$Y^*$ be a variable describing the number of letter replies naming a doctor from a group of D/G doctors.

The $P'$ will probably be distributed in some form of unimodal distribution not too dissimilar from the normal distribution in most societies (76).

Consider all possible selections of $K$ doctors from the total of $D$, then

$$\frac{\sum_{i=1}^{K} P_{ij}^*}{T}$$

is the proportion of the population served by the $i^{th}$ such group. By the central limit thereom, it would be expected that the $\theta (= \frac{P}{T})$ should be distributed normal $(\frac{K}{D}, \sigma^2)$ to a close approximation (provided $K \geq 20$) as $E(\frac{P'}{T}) = \frac{1}{D}$ and the expected value of the sum of $K$ such random selections is $\frac{K}{D}$.

$$\text{Var} \left( \frac{P'}{T} \right) = \text{Variance of the proportion of the community served by an individual doctor.}$$
\[ \text{Var}(P/T) = \text{Var}(\theta) = \sigma^2 = K(1 - h) \text{Var}(P'/T) = \frac{K}{T^2} \cdot (1 - h) \cdot \text{Var}(P') \]

(Eqn. 2) where \((1 - h) = (1 - \frac{K}{D})\) is a finite sampling correction factor.

It is possible to conveniently estimate \(\text{Var}(P')\) from the letter replies.

Divide the \(D\) doctors, randomly, to \(G\) groups of \(D/G\) doctors and estimate \(\text{Var}(Y^*)\) by the formula

\[
\sum_{j=1}^{G} (Y^*_j - \frac{N-j}{G})^2 , \quad j = 1, 2, \ldots, G.
\]

However this estimated variance contains a component due to binomially distributed random variation about the true value for each of the \(G\) groups.

This can be seen by consideration of a single doctor and his letter replies.

Using a well known formula (78), for the unconditional variance in terms of conditional variables,

\[
\text{Var}(Y^*) = \text{E}[\text{Var}(Y^*|P_1, P_2, \ldots, P_{D/G})] + \text{Var}(\text{E}(Y^*|P_1, P_2, \ldots, P_{D/G}))
\]

\[
= \text{E}[N \left(\frac{P_1 - 1}{T} + \cdots + \frac{P_{D/G} - 1}{T} \right)] + \text{Var}\left(\frac{N}{T} (P_1 + \cdots + P_{D/G})\right)
\]

\[
= N \left( \frac{P_1}{T} + \cdots + \frac{P_{D/G}}{T} \right) - N \left( \frac{P_1^2}{T^2} + \cdots + \frac{P_{D/G}^2}{T^2} \right) + \frac{N^2}{T^2} \cdot \text{Var}(P') \cdot (1-f)
\]

as the subscripts refer to order in the group of \(D/G\) practices, rather than specific practices. Note the necessity for the factor \((1-f) = (1 - \frac{1}{G})\)

due to finite sampling.

Thus

\[
\text{Var}(Y^*) = \frac{N \cdot D}{T \cdot G} \cdot \text{E}[P'] - \frac{N \cdot D}{T^2 \cdot G} \{ \text{Var}(P') + (\text{E}[P'])^2 \} + \frac{D \cdot N^2 (1-f) \cdot \text{Var}(P')}{T^2 \cdot G} + \frac{D \cdot N^2 (1-f)}{T^2 \cdot G} \cdot \text{Var}(P') = \frac{N}{G} \cdot \frac{D}{G} + \frac{N}{G} \cdot \frac{D}{G} \cdot \text{Var}(P') \cdot \frac{D \cdot N^2 (1-f)}{T^2 \cdot G} - \frac{N \cdot D}{T^2} \cdot \text{Var}(P')
\]

\[
= \frac{N}{G} \cdot (D-1) + \frac{\text{Var}(P') \cdot N \cdot D}{T^2} \cdot \left( \frac{N(G-1)}{G} - 1 \right)
\]
Now substituting for $\text{Var}(P')$ in Eqn. 2 above

$$s^2 = \frac{(D-K) \cdot K \cdot G}{D^2 \cdot N \left( \frac{N(G-1)}{G} - 1 \right)} \left[ \text{Var}(Y^*) - \frac{N}{G} \cdot \frac{(D-1)}{D} \right] + \frac{(D-K) \cdot K \cdot G^2}{D^2 \cdot N^2 \cdot (G-1)} \left[ \text{Var}(Y^*) - \frac{N}{G} \right]$$

providing $N$ and $D$ are quite large and where $s^2$ estimates $\sigma^2$.

'Approximately zero' values can be caused by a randomly low estimate for $\text{Var}(Y^*)$ in a situation where $\text{Var}(\theta)$ is small (negative estimates are possible).
APPENDIX B

Bias When Poisson Variable Only Is Considered

Here, \( \hat{I} = \frac{X \cdot D}{T \cdot K} \), \( E(\hat{I}) = \frac{\lambda \cdot D}{T \cdot K} \). In fact \( I = \frac{\lambda}{\theta \cdot T} \)

\[
\text{Bias} = \frac{\lambda \cdot D}{K \cdot T} - \frac{\lambda}{\theta \cdot T} = \frac{\lambda}{\theta \cdot T} \cdot \frac{(D \cdot \theta - K)}{K} = D \cdot I \left( \frac{\theta - K/D}{K} \right)
\]

\[
\text{Var} (\text{Bias}) = E \left[ \left( \frac{D \cdot I \left( \frac{(\theta - K)}{D} \right)^2}{K} \right) \right] = \frac{D^2 \cdot I^2}{K^2} \sigma^2
\]

Thus standard deviation of bias = \( \frac{D \cdot I}{K} \cdot \sigma \). Thus when \( \sigma \) is large or \( K/D \) is small very significant biases can frequently be expected in the results of any particular investigation that are not compensated for in the credibility interval.
APPENDIX C

INITIAL VISIT DATA SHEET

Name of Doctor (and initial) : ______________________

Name of Patient. : ______________________

Time Visit Requested : ______________________

Time of Arrival. : ______________________

Time Rang Hospital. : ______________________

Time Rang Ambulance. (if applicable) : ______________________

Pulse Rate ______________________ /minute

Regular [ ] Irregular [ ]} Please tick correct box.

Blood Pressure ______________________

Respiratory Rate. ______________________ /minute

Crepitations (consistent with heart failure) at both lung bases. Yes/No

Shocked Appearance (irrespective of B.P.) Yes/No

Adm: 0661
APPENDIX D

DEPARTMENT OF COMMUNITY HEALTH
SCHOOL OF MEDICINE

The University of Auckland
Private Bag, Auckland, N.Z.

Telephone 33-105

AUCKLAND SUBURBS CORONARY AND SUDDEN DEATH PROJECT

Date ................................

Dr. ................................

................................

................................

Dear Dr ..........................

Your patient ................................
was recently included in this study. Could you please provide the following information, if it is available, within two weeks.

Reply to ticked boxes only.

a) Previous recordings

☐ 1. Last casual BP between .......... and ...........

☐ 2. Serum cholesterol & triglycerides (fasting) between ....

and ........ (Chol.....mg% Triglyc.....mg%)

☐ 3. Glucose Tolerance Test between ...... and ........

(..............mg%/1 hr..............mg%/2 hr.)

b) Relating to Acute Event

☐ 4. Time and date of call for aid .......... hrs. Date / /

☐ 5. Time of arrival ................. hrs.

☐ 6. Pulse rate ....................... Irreg/Reg. (Delete one)

☐ 7. Blood pressure ...................

☐ 8. Crepitations at both lung bases Yes/No

☐ 9. Shocked appearance (Irrespective of B.P.) Yes/No

☐ 10. Drugs within the last three weeks ................................

☐ 11. Other (specify) ..........................................

G.E. Fraser MB ChB MRACP
(Medical Research Fellow)
APPENDIX E.

QUESTIONNAIRE FOR
AUCKLAND SUBURBS CORONARY STUDY

<table>
<thead>
<tr>
<th>E.C.G.</th>
<th>ENZYMES</th>
<th>FIRST G.P. CALL</th>
<th>P.M. RESULT</th>
<th>2/12 Med Records</th>
<th>2/12 G.P. call</th>
</tr>
</thead>
</table>

Key: Yes = 1 if no other instructions
9(s) only---Unknown
0(s) only---Not Applicable

I. GENERAL

(Patient No. then Card No.)

(a) Full Name

(b) Address

(c) Telephone No.

(d) Date of Birth

(e) Sex M=1 F=2

(f) Race:

- European = 1
- Maori = 2
- Other Polynesian = 3
- Indian = 4
- Other = 5

Specify

(g) General Practitioner

(h) Date of Referral

(i) Height (cms)

(j) Weight (kgs)
(k) Place of treatment
Enter 1 if hospital
2 if home
3 if other (specify) ____________________________
If 2 or 3 included, enter:
1 if because of age
2 if because of patient request
3 if because of better treatment
4 if because of uncertainty of diagnosis (seen by doctor)
5 if because of no initial medical care
6 if because of some other reason (specify) ____________

(ii) Hospital
MM CCU Enter 3 GL CCU Enter 5 A CCU Enter 7
MM NonCCU Enter 4 GL NonCCU Enter 6 A NonCCU Enter 8

(m) Nationality
(a) New Zealander (in N.Z. 10 years) Enter 3
(b) English Enter 4
(c) Other Enter 5

II. PAST MEDICAL HISTORY

(i) Isch H.D. Symptoms before one month prior to present infarct.
(a) Angina
If yes, from
weeks to
weeks ago

(b) Acute "Coronary Insufficiency"
Enter 2 for No
Enter 3 for diagnosis aided by non-infarct E.C.G.
Enter 4 for clinical diagnosis--no E.C.G.
If 3 or 4, from
weeks to
weeks ago

(c) Diagnosed Previous Myocardial Infarcts (Records number)
(Confirm from G.P. or Hospital records)
If yes,
months ago (to first infarct)

(d) Breathlessness:
(a) only on exertion - enter 3
(b) during "normal" activities - enter 4
If 3 or 4, from
weeks ago, to
weeks ago
(i) Other Medical Illness of Significance

(a) stroke
(b) periph, vasc, disease (symptomatic)
(c) diabetes (at least fasting and two hour pp. sugar)
(d) hypertension--diagnosis from G.P.
(e) last recorded systolic blood pressure 58-60
   diastolic blood pressure within 1 year 61-63

(f) lipid abnormality

   Cholesterol
   If less than 220, enter 1
   If 220 to 300, enter 2
   If greater than 300, enter 3

   Triglyceride (fasting blood)
   If less than 100, enter 1
   If 100 to 150, enter 2
   If greater than 150, enter 3

(g) Other (specify)

Unknown if: never been tested or previous tests more than one year ago

(iii) Long-term Relevant Drugs

(Stopped < one week before)

Cardioactive Drugs and Diuretics

(a) Digoxin
(b) B Blockers
(c) Trinitrin
(d) Thiazides
(e) Lasix or Edecrin
(f) Aldactone
(g) Moduretic

Anti-hypertensives, Phenothiazines, Sulphonylureas, etc.

(a) Rauviloid
(b) Methyldopa
(c) Adrenergic neurone blockers
(d) Phenothiazine (specify)
(e) Sulphonylurea (specify)
(f) Atromid
(g) Tricyclic
(h) Others (specify)

(iv) Cigarette Smoking (Consider as "yes" if stopped < 6/12)

Enter 2 if never smoked
Enter 3 if stopped > 6/12, < 10 years
Enter 4 if 1-9 per day
Enter 5 if 10-19
Enter 6 if 20-39
Enter 7 if > 40
### III. HISTORY OF PRESENT ILLNESS

(i) Prodromal Symptoms (i.e., new or worsened symptoms within one month of infarct)

<table>
<thead>
<tr>
<th>Symptom Description</th>
<th>Yes/No</th>
<th>Onset</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) New angina</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If yes</td>
<td>onset</td>
<td>dys hrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1-5</td>
</tr>
<tr>
<td>(b) Increased or more severe angina</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If yes</td>
<td>onset</td>
<td>dys hrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1-5</td>
</tr>
<tr>
<td>(c) New acute &quot;coronary insufficiency&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Enter 2</td>
<td>for no</td>
<td>3 if supported by non-infarct ECG</td>
</tr>
<tr>
<td></td>
<td>If 3 or 4, onset</td>
<td>dys yrs</td>
<td>preinfarct</td>
</tr>
<tr>
<td>(d) Increased or &quot;more severe acute coronary insufficiency&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Enter 2</td>
<td>for no</td>
<td>3 if supported by non-infarct ECG</td>
</tr>
<tr>
<td></td>
<td>If 3 or 4 onset</td>
<td>dys hrs</td>
<td>preinfarct</td>
</tr>
<tr>
<td>(e) New or increased breathlessness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If yes</td>
<td>onset</td>
<td>dys hrs</td>
</tr>
<tr>
<td>(f) Lack of energy</td>
<td>If yes</td>
<td>onset</td>
<td>dys hrs</td>
</tr>
</tbody>
</table>

### IV. ACUTE PHASE SYMPTOMS

Enter 1 for classical pain
Enter 2 for atypical pain
(ii) Breathlessness at rest.
Enter 2 for No.
Enter 3 for SOB at rest.

(iii) Abnormal sweating

(iv) Other (specify)

V. MYOCARDIAL INFARCT TREATMENT DELAYS (Midnight coded as 2400)

(a) Date of onset of severest symptoms--day, month, and year
(b) Time of onset of severest symptoms
(c) Date of call for medical aid by patient--day and month
(d) Time of call for medical aid by patient
(e) Time of call for ambulance by patient
(f) Time of arrival of medical aid
(g) Time that doctor started to ring hospital
(h) Time that ambulance ordered by hospital
(i) Time that ambulance ordered by G.P.
(j) Time of arrival at hospital

(k) Time of arrival at CCU
(Where statement is not applicable, enter zeros.)

(l) *Time elapsed (hours, minutes)

(b) - (d) ........................................ 15-18
(b) - (e) ........................................ 19-22
(d) - (f) ........................................ 23-26
(f) - (g) ........................................ 27-30
(g) - (h) ........................................ 31-34
(e), (h) or (i) - (j) ......................... 35-38
(j) - (k) ........................................ 39-42
Other (specify) ................................ 43-46

If any unusual delay, specify cause:

Patient - 1
Medical - 2
Ambulance - 3

(f) - (g) ........................................ 47
(e), (h) or (i) - (j) ......................... 48
Other (specify) ................................ 49

*0000 does not mean zero time lapse, which will not occur in practice, rather it is the code for "Not Applicable."
VI. FIRST DOCTOR'S CLINICAL ASSESSMENT

<table>
<thead>
<tr>
<th>Hours after onset of acute symptoms</th>
<th>51-53</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) pulse rate per minute</td>
<td>54-56</td>
</tr>
<tr>
<td>If SR clinically, enter 1</td>
<td></td>
</tr>
<tr>
<td>If irregular, enter 2</td>
<td></td>
</tr>
<tr>
<td>(either AF or greater than 6 ectopics per minute)</td>
<td></td>
</tr>
<tr>
<td>(b) Systolic BP</td>
<td>58-60</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>61-63</td>
</tr>
<tr>
<td>(c) Creps. at lung bases</td>
<td>64</td>
</tr>
<tr>
<td>(d) Resp rate per minute</td>
<td>65-66</td>
</tr>
<tr>
<td>(d) &quot;Shock&quot;</td>
<td>67</td>
</tr>
</tbody>
</table>

(This section is always 'applicable', so repeated 0's record true values. If in cardiac arrest at first exam., enter 0's only, if dead.)

VII. INVESTIGATIONS

(i) ECG (present)

<table>
<thead>
<tr>
<th>Type</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>If A enter 1 (full thickness--recent)</td>
<td>69-70</td>
</tr>
<tr>
<td>If B enter 2 (sub-endocardial--recent)</td>
<td></td>
</tr>
<tr>
<td>If C enter 3 (old Q waves, T wave change, LBBB., etc.)</td>
<td></td>
</tr>
<tr>
<td>If none of these, enter 4</td>
<td></td>
</tr>
</tbody>
</table>

For Type A (full thickness)

Specify changes:

For Type B (subendocardial)

Specify changes:

For Type C

Specify changes:

(continued)
Site
If anterior, enter 1
If post/inf, enter 2
If uncertain, enter 3

**LVH (by ECG criteria)**

(ii) **Antecedent Conduction Blocks**
- LBBB
- RBBB
- Hemiblock
- 1 HB
- 2 HB
- 3 HB

**Key**: NO if negative present or old (within 1 year) ECG
YES if positive old (within 1 year and at least 2 weeks after any infarct) ECG. Negative current ECG coded as unknown for LVH only.

(iii) Antecedent A.F.

(iv) Enzymes
For each enzyme, in first box enter no. of times estimated (if not estimated, enter zero) and in second box, the highest result according to:
- Type A, enter 1
- Type B, enter 2
- Normal, enter 3

SGOT
CPK
LDH
HBD

(v) Outcome
Cardiac arrest (1 or more)*
Death
If yes, Days
Hours after onset of acute symptoms
Minutes

*(Enter 3 if before decision on place of treatment made. Enter 4 if died at home. Enter 5 if in ambulance. Enter 6 if in CCU. Enter 7 if in hospital non-CCU. Enter 8 if other--specify: ______________________)
VIII. POST-MORTEM FINDINGS

(i) Enter zeros if no Post Mortem.
   If yes, for:
   (a) demonstrable infarct enter 1
   (b) LVH enter 2
   (c) diffuse myocardial fibroses enter 3
   (d) cardiac rupture enter 4
   (e) pulm. embolus enter 5
   (f) mural thrombus enter 6
   (g) cerebral infarct enter 7
   (h) old infarct (i.e., older than one month) enter 8
   (i) other (specify) enter 9

   24-27

   (Enter zero in unused boxes)

IX. CLASSIFICATION

(i) sudden death 29
(ii) myocardial infarction (definite) 30
(iii) myocardial infarction (probable) 31

X. ALCOHOL

(a) Average intake/week over last one year
   Beer, total ounces 33-35
   Wine, total ounces 36-38
   Spirits, total ounces 39-41

(b) Intake in 24 hours prior to infarct/death
   (Compare with the previous two drinking days)
   Normal or less than "Normal" enter 3
   Greater than "Normal" enter 4

   43
APPENDIX F

AUCKLAND SUBURBS CORONARY AND CARDIAC-RELATED SUDDEN DEATH PROJECT

AIMS

(a) To ascertain incidence of myocardial infarction and cardiac-related sudden death in persons under the age of 70 years.
(b) To find proportion treated at home and in hospital respectively.
(c) Assess delays in treatment.
(d) Assess prodromal symptoms and previous symptoms related to ischaemic heart disease.
(e) Document immediate and more long term previous drug therapy.
(f) The final outcome related to the various categories found in previous aims, ECG appearance, sex etc.

SIGNIFICANCE

(a) Information, of practical importance, for public health planning, hospital planning, rational treatment of myocardial infarction is lacking for New Zealand.
(b) Sudden deaths account for probably 200 deaths under the age of 70 each year in Auckland. Assessment of prodromal symptoms and other characteristics of these people may be of relevance in earlier detection of people at risk.
(c) The establishment of an incidence for both disorders at this stage will provide a baseline to assess change at some future date.

METHOD

You have been randomly selected along with about 40% of Auckland's doctors to participate in patient notification. Recognition of the high workload of most doctors, has prompted us to direct the questionnaire primarily at the patients, who will be individually seen either in hospital or at home, by a medically qualified investigator, preferably within 48 hours of the onset of acute symptoms.
Your co-operation is requested as follows:

(1) **PROMPT** notification of any person (up to 70 years of age) whom you suspect has had a coronary or has died suddenly probably from a cardiac cause. This is irrespective of whether the patient is hospitalised or not.

(2) If the diagnosis is made say by ECG, or by a specialist referral, days or weeks later, we should still be notified.

* Could your nurse ring 33-105, extension 613 with the names and addresses of cases.

(3) Where possible sudden deaths should be referred to the coroner. This is often awkward for social reasons, but would make our diagnostic accuracy much greater.

(4) Habits of hospitalisation and treatment must not be changed or the information gained will in part be valueless.

(5) Please inform locums of the aims and mechanics of the survey. If any of your patients are treated by a short term locum (e.g., Locum Emergency Services), please inform us of the patient as usual.

(6) At initial visit please note:

   (a) Pulse rate and regularity.
   (b) Blood pressure.
   (c) JVP.
   (d) Respiratory rate.
   (e) Time of your arrival. (see data sheet provided)

(7) You will be rung probably by the medical investigator, within 2-3 days for information concerning - brief particulars of patients past medical history, drug treatment, time of your arrival at patient, reason for place of treatment and results of your initial assessment of the patient.

(8) You will be rung routinely two months after the acute event to learn of any complications the patient has experienced post-infarct.

(9) Your nurse will also be routinely rung as a reminder of the survey, if we have had no contact with you in the preceding month. At this time please advise us of any patients who you may have overlooked notifying.

**NB**: The information gained by a short history and ECG on patients treated at home will not ordinarily be available to you, lest this in any way be construed as a consultative service.
26 March 1974

Dear Dr.,

You will remember being visited by myself within the last month concerning the "Auckland Suburbs Coronary and Cardiac-related Sudden Death Project", being run from the Medical School.

I would like to remind you that we start April 1, only six days away. We would like to be informed of any of your patients suffering either of these conditions from this date on, for two years.

Monthly reminder phone calls will be made to your nurse.

Thank you.

Yours sincerely,

G.E. Fraser MRACP
3 January 1975

Dear Doctor

The time seems appropriate for a progress report on my project - 'Epidemiology of Myocardial Infarction and Sudden Death in Auckland'.

Thank you for the support you have given, almost without exception, throughout 1974.

The major problem to date has been that of communication. The switchboard system and telephone operators used by the Medical School seem unable to cope with this sort of project and I apologise for the frustrations some of you have experienced in trying to make contact. At present I have an urgent request for a direct line to my office which should overcome this problem. I will let you know this alternative number as soon as possible.

You will have noticed that we are putting through telephone calls to you of two different types:

(a) my secretary routinely calls, monthly - if we have not recently heard from you, as a reminder.
(b) I call, instead of my secretary, if I have collected one of your patients recently, and require some further information - usually B.P., blood fats, or first assessment recordings at time of infarction.

Phone call type (a) I believe is important and should remain as it is. Whenever I phone for information I am very much aware that often I interrupt consultations. Also when you are busy, it is difficult to spare time to delve into case and pathology records that I request.

An alternative arrangement may be preferable to some of you, whereby I will have a small card printed, on this make my request, and mail it to you. At your leisure could you fill this in and return it to my office. If you would prefer this system, please return the 'tear-off' below.

Some results to date may be of some interest to you.

In the first eight months (i.e. 1/3 of total project time) we have collected 276 cases. Of these, 161 represent Definite Infarcts, 45 are Possible Infarcts (WHO criteria, 1969) and 70 were Sudden Deaths. It is possible to calculate from these figures that the total incidence of 'myocardial infarction' is close to 5 cases/1000 population at risk/year where I have defined 'population at risk' to be adults between the ages of 35 - 69 years. This figure is very close to that found in a similar project conducted in Perth, Australia some two years ago.

Thus about 25% of the total are represented by Sudden Deaths. About 28% of the total are female. I have defined 'treatment at home; to be where a patient is admitted to hospital more than 72 hours after acute symptoms begin or not at all. 'Treatment at home and hospital' if admission between 24 - 72 hours after symptoms begin.
Of the definite infarcts 10% were treated 'at home' and 8% were treated 'at home and hospital'. Of the possible infarcts, 36% were treated 'at home' and none, 'home and hospital'. Thus of all infarcts, 22% either did not get to hospital, or arrived 24 hours after acute symptoms began. Reasons for delay were assessed and were usually attributable to the patient.

Many other results will eventually be available, e.g.
(1) Pattern of deaths, post-infarct
(2) Prodromal symptoms of infarction and sudden death.
(3) Relate incidences at various times and parts of Auckland to geographic and climatic factors.
(4) Assess outcome in relation to smoking habits, alcohol intake, (Is V.F. more common in those with a higher alcohol intake?) and obesity in terms of 'ideal weight'?
(5) I hope some kind of non-rigorous comparison between cases (matched as closely as possible) treated at home and in hospital may be possible - Does the ambulance trip and CCU environment make cardiac arrest more likely?

I believe this project will give valuable information concerning the local scene and may also give some information of general interest.

In conclusion, two further points:
(a) The basis of referral of cases should be either: severe ischaemic-type pain of 20 minutes or more duration, or atypical symptoms, but supportive enzymes and/or ECG.
(b) Remember we are happy to organise enzyme studies on two consecutive days on any likely patient (with copy of result to you). Many possible infarcts had to be classified this way because appropriate enzyme studies were not done.

Best wishes for 1975

Yours sincerely

GE Fraser MB ChB MRACP
(Medical Research Fellow)

Name and Initial: Dr. ..................

I wish to substitute a card system for the gathering of additional information regarding patients. (This would include 'initial assessment information).
Dear Mrs. Gawith,

From the Medical School, we are conducting a major research project on coronary heart disease. This is supported and financed by the National Heart Foundation and the Medical Research Council of N.Z.

Coronary heart disease is a very common disorder in Auckland and seems to be increasingly afflicting middle-aged and even young adults.

About 130 of Auckland's doctors are co-operating in this project. We need to find out roughly what proportion of Auckland's population have one of these 130 doctors as their doctor. This is how you can help — even if, as in most cases, you have no known heart disease.

Two items of information as requested:

(a) Your usual local doctor's name and initial.
   (If you have no regular doctor, give the name of the doctor you would see if you became ill).

(b) Place a cross in the appropriate box below, regarding your age, as at the 15th of this month.

No appointments, or other information of any kind will be requested, but this much is vital. Your name was selected from the electoral roll, so we have no information about your health and of course are not suggesting that you have coronary disease.

The information will be treated as CONFIDENTIAL. Please return the whole page, with the boxes below completed in the stamped addressed envelope.

Thank you for your help.

Yours sincerely,

DR. G.E. FRASER, M.B.Ch.B, M.R.A.C.P.
(Medical Research Fellow)

Your Name: __________________________

Your Doctor's Name & Initial:  __________________________

Age: (place cross in correct box) Under 35 years [ ]

[ ] 35 - 49 years

[ ] 50 - 59 years

[ ] 60 - 69 years

[ ] Over 69 years
Dear (or present adult...occupant)

You will remember about ten days ago, receiving a request for your help in a medical research study on coronary heart disease. This is financed by the National Heart Foundation and the Medical Research Council of N.Z.

It seems you have not yet found time to give us the information requested.

At present, we have only about 40% of the replies needed to make this study successful. About 130 of Auckland's doctors are co-operating in this project. We need to find out roughly what proportion of Auckland's population have one of these 130 doctors as their local doctor. This is how you can help.

Please fill in the boxes and lines below. No further information will be requested, but this much is vital.

If you prefer not to use the stamped, addressed envelope, please phone the information to phone 33105, extension 613 (business hours).

Thank you for your help.

Yours sincerely,

Dr G.E. Fraser, M.B.Ch.B, M.R.A.C.P
(Medical Research Fellow)

Your Name: ________________________________

Your Doctor's Name & Initial: ________________

Age: (Place cross in correct box) Under 35 years [ ]

35 - 49 Years [ ]

50 - 59 Years [ ]

60 - 69 Years [ ]

Over 69 Years [ ]