THE MELBOURNE STUDY OF DIET AND CANCER

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Summary

A prospective cohort study is being mounted in Melbourne to examine the links between diet and the incidence of certain cancers and non insulin dependent diabetes mellitus and mortality from ischaemic heart disease, stroke, and "all-causes" in both men and women. The study deliberately exploits the increased heterogeneity of dietary intakes in migrants as they become more or less acculturated with increasing residence in Australia. The first phase is to recruit 30,000 southern European migrants and 20,000 Australian-born volunteers. Information will be gathered by questionnaire about personal history, lifestyle and diet. Following a series of physical measurements, blood samples will be collected. Some key indicators will be analysed immediately and samples of plasma and white cells will be stored in liquid nitrogen. It will take four and a half years to recruit the cohort. Follow-up is planned for 20 years from commencement, with one third of the cohort being actively followed up each year. By collecting baseline measurements of medical history, blood pressure, anthropometry and biochemistry, it will be possible prospectively to identify disease-causing mechanisms relevant to different disease outcomes. As cohort members develop the diseases of interest, their data will be compared with those of unaffected "control" individuals selected from within the cohort.

I. INTRODUCTION

It is generally accepted that a large proportion of all cancer in developed countries such as Australia is caused by exogenous factors. Doll and Peto (1981) estimated that 10-70% of all cancers in the United States are related to diet with a "guestimate" of 35%. This is in accordance with previous estimates (Higginson and Muir 1979; Wynder and Gori 1977). The width of this estimate testifies to the limited knowledge that exists at present of the relationship between diet, nutrition and cancer.

Dietary components, nutrients or nutritional status have been associated with cancers at a large number of sites in humans although no single food or nutrient has satisfied all of the epidemiological requirements for causality. Previous research has identified both apparent risk factors and protective factors in the diet. Some of these factors are site specific while others have a non-specific effect. Generally, vitamins C and E, beta-carotene and selenium are associated with a protective effect. A variety of mechanisms have been proposed e.g. via the scavenging of free radicals, the differentiation of healthy epithelium, and the production of essential enzymes. Meat and alcohol consumption, the proportion and type of fat in the diet, the level of energy intake (and the level of physical activity with which it is linked) are factors suspected of playing a role in cancer initiation and promotion. The roles of obesity and the distribution of body fat also need to be evaluated. From a cancer prevention point of view, the possible protective role of dietary fibre in colo-rectal cancer is also important.

If one applies the conventional criteria for causality in epidemiological studies to the published associations between diet and cancer, the state of knowledge is unimpressive. The strength of association

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is usually weak with relative risks between 1 and 2.5. The strong correlations shown in ecological studies comparing national rates are not reproduced in analytical studies within populations. The temporal relationship of cause and effect is difficult to establish. From case-control studies it is often impossible to know whether pre-existing disease had not changed dietary intake prior to diagnosis. Consistency of findings is not high from studies conducted in different populations using different methods and their interpretation is often controversial. Coherent biological models are often proposed but they tend to be conjectural. Specificity is not easy to demonstrate (and is possibly not appropriate) with universal and highly intercorrelated dietary exposures.

A substantial part of current evidence of an association between diet and cancer is based on international correlations (Armstrong and Doll 1975). Other investigators have undertaken detailed comparisons of populations with different incidence rates of specific cancers, e.g. comparative studies of males in Denmark and Finland in relation to colo-rectal cancer (Jensen et al. 1982). While such studies are very useful in indicating areas where additional research should be carried out, the associations found are not necessarily causal.

Information from studies of individuals is more persuasive in demonstrating possible cause-effect relationships. Diet-cancer relationships have been investigated by means of case-control studies for a number of cancers but these studies are subject to several sources of bias. They are dependent on the sensitivity of the dietary questionnaire or biochemical marker to measure dietary habits of the distant past (Byers et al. 1985; Van Leeuwen et al. 1983; Jensen et al. 1984). Cancer itself, or another pre-existing condition, may lead to dietary changes and result in spurious associations because the measured exposure at the time of disease onset may be quite different from the exposure at the time of diagnosis. Problems of misclassification of exposure become more serious for past than for present habits. It is difficult to know whether weak associations demonstrated in case-control studies are due only to artifacts of reporting biases, or whether they are indicative of much stronger associations which have been attenuated by random misclassification arising from imprecise dietary assessments.

Cohort studies avoid some of these problems by comparing groups that have and do not have the dietary patterns of interest. Exposure is known at a given point so there is no need to attempt retrospective measures of diet and there is less concern about the possibility of biased recall. Greater control over measurement techniques can be afforded and exposure is known to occur before the onset of disease. Still a sufficient difference in exposure must exist between the two groups for a potential effect to be noticed (Wynder and Herbert 1987).

Few prospective cohort studies have been conducted with the aim of relating diet to subsequent cancer development (Hirayama, 1978; Heuch et al. 1983; Phillips and Snowdon, 1983; Jones et al. 1987; Willett et al. 1987). Together with intervention trials, such studies are likely to provide substantive evidence on associations between diet and cancer, but they are expensive to conduct and in most populations of the world, follow-up of cohort members represents a major difficulty.

In summary, studies of diet and cancer generally reveal three design problems; namely, poor measurement of both the current amount and past history of dietary intake, lack of range in dietary exposures in study populations, and bias arising from retrospective studies of diet and disease.

These can be overcome by selecting a study population to be followed prospectively, by measuring dietary exposures long before disease presents and by enrolling subjects with a wide range of dietary intakes. It is the latter aspect that the Melbourne study addresses in a novel way.

II. RESEARCH OPPORTUNITIES PRESENTED BY MIGRANTS

As already noted, many studies of diet and cancer have given only modest and inconsistent measures of association. Apart from the measurement of dietary intake, which is notoriously difficult, studies have been criticised for the selection of study populations which lack range in dietary exposures. In populations where everyone eats similar foods and nutrient intakes are homogeneous, it is difficult to detect differences in disease outcomes related to differences in food intake and, therefore, the risks that can be detected will tend to be associated with non diet related variables. This will inevitably lead to the rejection of diet related hypotheses, when in reality the study would never have been able to accept them. In addition, it will be impossible to detect a change in risk with increasing dietary intake in studies which are restricted to either "safe" or "saturated" ranges of exposure. Studies of diet and cancer, therefore, need to survey populations with as wide a range of food and nutrient intakes as possible in order to capture a biologically relevant range of exposures.

Australia has enjoyed a considerable influx of migrants since World War II and has one of the largest concentrated populations of migrants to be found in the world. The mortality experience of migrant groups has been examined by several authors (Armstrong et al. 1983; McMichael et al. 1980; Young 1986; McMichael and Bonnet 1981). The largest migrant group, people from the British Isles, demonstrate elevated cancer mortality compared with the Australian-born, particularly for tobacco associated causes of death. Conversely, the second largest group of migrants to Australia, people from southern Europe, enjoy lower mortality than the Australian-born population. The mortality benefits are particularly evident for cancers of the bowel, breast and prostate. It has been shown that migrants from southern Europe maintain a lower mortality from these cancers some decades after arrival in Australia, and it is reasonable to suggest that this is substantially a result of their diet and other lifestyle factors (McMichael and Giles 1988).

The initially low mortality rates from cancer in southern European migrants increase with increasing duration of residence. As early as five years after migration, change is apparent in cancer mortality. Nevertheless, after 20 years or more of Australian residence a 30% mortality benefit remains and seems to be stable. The early increase in cancer mortality would suggest that the changes that occur on migration have a late stage effect, promoting rather than initiating cancer. The increase in mortality rates after arrival in Australia points to an environmental effect. It is suggested that the residual mortality benefit may well be due to beneficial elements that remain in the southern European cuisine/lifestyle and resist acculturation. It is assumed that individual migrants at any point in time will be somewhere on a dietary scale between eating very much as they did in their native country and eating close to the Australian norm. Theoretically therefore, migrants should demonstrate a wider range of dietary intake than the indigenous population.

The majority of southern European migrants to Australia were born in Italy and Greece. Previous research on migrants from Greece has shown that some dietary changes occur quickly on arrival characterised by an increased

consumption of preferred foods such as beef. Largely, however, the native cuisine is preserved (Powles 1988). Little information has been available on current dietary intake in individual Australians. Mean values taken from the 1983 survey of the nation's nutrition (Cashel et al. 1986) showed some differences between the southern European migrants and the Australian-born population but were not informative as to the range of food intake by individuals. In this 24 hour recall survey, the southern European migrants were fairly stereotyped as they ate more pasta, green leafy vegetables and fruit and drank more red wine than the Australian-born.

III. THE MELBOURNE COLLABORATIVE COHORT STUDY

a) Overview

The conception of the cohort study was determined by two requirements; first, to make a significant contribution to the understanding of the relationship between diet and cancer and second, to develop a research program that would take advantage of some unique opportunities that exist in Victoria. These two imperatives were met by the large migrant groups resident in Melbourne and by their diversity in disease patterns shown by mortality studies, and their diversity of dietary intake and other lifestyle factors demonstrated in previous surveys and pilot studies.

The principal aim of the study is to measure the effect(s) of dietary intake on a broad spectrum of health and disease endpoints. Its major objective is to build a research resource capable of testing prospectively the current hypotheses linking dietary and lifestyle factors with the incidence of and mortality from certain cancers, with mortality from all causes, with the incidence of non insulin dependent diabetes mellitus, and with mortality from acute myocardial infarction and atherothrombotic brain infarction.

To this end, a large cohort is being assembled of at least 30,000 Greek-born and Italian-born migrants and 20,000 Australian-born residents of Melbourne aged beetween 40 and 69 at recruitment. From each individual at recruitment, dietary and other lifestyle information, physical measurements, and a blood sample are being collected. Some blood analyses are performed immediately and aliquots of plasma and lymphocytes are being stored in liquid nitrogen against future requirements to examine plasma components, biochemical markers of dietary intake, DNA adducts and DNA itself. The cohort will be followed for up to twenty years and as sufficient numbers of endpoints are detected, specified hypotheses will be tested usually by conducting case control studies within the cohort. It is intended that the resource will also facilitate many allied research projects in its lifetime.

b) Recruitment

It is necessary to recruit 1 in 4 of the Greek and Italian born migrants into the study. This is being accomplished in a number of ways as there is no available sampling frame which enables a random sample of this proportion of these target populations and it is considered that 25% is the maximum practicable recruitment proportion. Voluntary participation is the only feasible method of recruiting in these populations. As continuity of follow up is most important to longitudinal studies, volunteers are preferred in that they are more likely to maintain their interest than random recruits. The strategy for Australian-born subjects is different.

Recruitment will be restricted to residents of randomly selected census collectors' districts recruited by a combination of letter drops, phone ins and door to door canvassing. It is intended to recruit similar proportions (25%) of the Australian-born residents of these areas to help control for any differential selection bias between the migrants and the native Australians.

A survey centre has been established in the municipality of Coburg in the heart of the migrant community and close to major transportation routes. It is anticipated that to reach the target of 50,000 subjects it will be necessary to supplement recruitment at this centre by using a mobile unit. A caravan has been fitted for this purpose and it will be used to attract enrolments at large shopping centres and other public venues.

After a deliberate slow start and settling period, an advertising campaign will be launched in early 1991 with successive media promotions calling for volunteers throughout the recruitment period. Newspaper articles outlining the study and calling for eligible volunteers will be published in Greek, Italian and local newspapers. Several interviews will be aired on both ethnic and non ethnic radio stations and the study will be advertised on SBS television. Once the target population has been made aware of the study, it is planned to accept spontaneous self enrolments by phone, supplemented by active enrolment at ethnic social nodes and networks e.g. clubs, societies and churches. Perhaps the most important strategy is recruitment by those subjects already in the cohort. It is considered that word of mouth is an important advertisement for the study. All subjects are encouraged to ask any eligible family and friends to enrol. When the supply of new subjects from the initial promotion is exhausted then a more direct approach will be undertaken. Comprehensive lists of Italian and Greek surnames will be used to focus the target population of southern European migrants in the phone book and Electoral Rolls. Television exposure will be sought through current affairs programs and concentrated publicity campaigns will be mounted in suburbs known to have higher numbers of people in the target population.

c) Measurement of dietary intake

The measurement of dietary intakes in epidemiological studies needs careful consideration. Accurate ordinal classification of individuals with respect to their dietary intakes is important. This requirement can economically be met in a prospective study only by the use of a food frequency questionnaire (FFQ) which will allow ranking of individual's usual food/nutrient intakes into broad quantiles of exposure. FFQs are typically developed from detailed studies of actual food consumption in the study population e.g. a number of days of weighed food records. However, certain foods which are suspected to be of aetiological importance are extremely difficult to estimate in a FFQ e.g. edible oils and alcohol. In this case special supplementary questions are asked to aid correct classification of individual exposures. The study population has been selected to maximise the range of the dietary intakes of interest. The lack of replication of the findings from ecological studies in population based studies has been ascribed partly to the narrow range of dietary intake in some study populations reducing the power to detect meaningful differences in effect, and exposure-risk relationships may differ outside the ranges of exposures studied. Individuals in the study population may change their dietary intake over time for a variety of reasons, one of which is the effect of being in

the study itself. Dietary information will, therefore, be collected at regular intervals. Finally, as the estimates of dietary intake are based on FFQs, some information will be collected from a sample of subjects to validate the FFQ classification e.g. food diaries or weighed food records.

Little information is available on the distribution of usual dietary intakes in individual Australians and particularly in migrant groups (Baghurst 1987; English et al. 1987). In order to obtain distributions of dietary intake for various nutrient and other dietary components, not only to demonstrate range in intake but also to use in power estimations for the sample sizes required to answer various hypotheses, it was necessary to collect food intake data from samples of individuals in the several target populations. Samples of about 300 each of Greek born, Italian born and Australian born men and women aged 40 to 69 were used to pilot questionnaires, a prototype FFQ, anthropometric measurements and blood collection. In addition, each subject recorded at least two sessions of 4 day weighed food records (WFR). The FFQ used in the cohort study has been developed using data from these WFRs along the principles suggested by Byers et al., (1985), Willett et al., (1985), Haile et al., (1986) and Block et al., (1986). Quantitative data are available ranking the contribution of foods to nutrient intake in the American (Block et al. 1986) and English (Cade and Margetts 1988) diets and similar analyses have been completed on the pilot data. A major finding from the pilot test was that the subjects generally had difficulty estimating portion sizes in the FFQ. For this reason, portion sizes are not asked in the FFQ, but are estimated from the WFRs obtained in the pilot studies by age, sex and ethnicity.

The analysis of over 7,000 days of weighed food records has been completed for the purposes of describing ranges of dietary intake, the average portion sizes of foods consumed by age, sex and ethnicity, and for the development of food frequency questionnaires. The composition of the diets was determined from the records of weighed food intake using matrix multiplication (Ireland et al., 1990). The nutrient database consisted of McCance and Widdowson's "The Composition of Foods" (Paul and Southgate 1978; Paul et al. 1980; Tan et al. 1985). The composition of local foods not included in the database was added and used in the calculation of dietary composition (Department of Community Services and Health, 1989). The composition of some Greek composite dishes was obtained from Professor A. Trichopoulos, the author of the Greek Food CompositionTable (1982).

d) Data collection

Data are to be collected when (typically fasting) subjects attend either the cohort centre or the mobile unit. This will be done by two questionnaires and by physical measurements. The first questionnaire is a food frequency questionnaire (FFQ) and the second includes questions on medical history, demographic, occupational and reproductive variables and dietary and personal habits including physical activity. Both questionnaires have been designed to be interviewer administered and optically scanned with a minimal amount of free entries and subsequent post coding. Versions are available in English, Italian and Greek.

Each subject first attempts to complete the FFQ. Combined with the FFQ are several questions on eating habits and dietary supplementation. These questions relate to the way people eat and their eating and food preparation habits rather than the foods that they eat. Some foods are asked about which are difficult to estimate in a food frequency format e.g. oil

consumption. Questions include the use of fat spreads, the use of fats and oils in cooking, beverage consumption, use of milk in beverages, use of sugar in hot beverages, a history of drinking alcoholic beverages, questions on bran consumption and a vitamin supplement inventory.

e) Physical measurements

Once the FFQ is completed, the subject is directed to an examination room where the FFQ is checked and other questions are administered. Then a number of anthropometric measurements are taken and recorded on a data sheet. A standard sequence is followed in order to minimise any variability from minor anxiety that any procedure may cause. Blood pressure is measured first, then body impedance and then height, weight and waist and hips circumferences. On completing all measurements the subject is directed to a waiting area outside the phlebotomy rooms. A nurse then records their drug inventory and takes a blood sample. After these procedures, the subject returns their questionnaire to reception where it is electronically scanned to make sure all questions have been answered within range and consistency checks. Any queries regarding their questionnaire are resolved before they depart or take refreshment.

f) Blood collection, analysis and storage

Nurses take a total of 20ml of blood into 2 vacutainers (EDTA). A laboratory assistant collects the blood samples as soon as possible and takes them to the laboratory for immediate processing. After measuring total cholesterol and glucose immediately using only a few microlitres of blood, the remaining sample is processed to extract 2 aliquots of lymphoctyes and two aliquots of plasma for storage in liquid nitrogen. On all fasting subjects a third aliquot of plasma is stored for the eventual analysis of insulin and triglycerides.

g) Follow up and detection of endpoints

It is intended to re-survey each study subject by telephone and mail once every three years to collect further health and dietary information. It is not intended at this time to recontact subjects physically or to take any more blood. Non-fatal, non-cancer outcomes will primarily be indentified via this active follow-up using a short questionnaire. Cancer incidence information will be supplied by the Victorian Cancer Registry and all causes of mortality will be identified via regular death certificate data received by the Registry. All outcomes will be verified with the individual's medical care givers and institutions.

h) Analysis

For each specific hypothesis, for a predetermined strength of association there will exist a minimum number of cases for detecting effects with a given level of significance (say $P<0.05$) with a given power (say 80%). Given an hypothesised risk ratio based on literature survey, and an appropriate misclassification rate, when it is considered that a sufficient number of cases is acquired, statistical assessment of the specific hypothesis will be carried out (providing for the exclusion of early disease onsets). In testing each specific hypothesis, multivariate analyses will be

performed to assess to what extent the risk due to the specified factor depends on the modifying effects of other factors. In addition, tests will be performed of the consistency of risk estimates across sex, age and ethnic categories, and interactions between risk factors will be explored.

For every factor specified in an hypothesis, the effect on all cause mortality will be assessed through univariate and multivariate analyses, following a similar analytical procedure as for testing specific disease hypotheses. Specified and new hypotheses on disease causation will be tested using the questionnaire data on dietary and non-dietary exposures from the entire study cohort, i.e. the classical cohort analysis technique (Breslow and Day 1987). Rates of disease will be compared between exposure categories to examine dose-response relationships. Time-response or latency periods will be examined where applicable. In this way, control groups will be constructed within the study cohort. Case-control analyses will be conducted according to the principals described by Breslow and Day (1980, 1987).

IV. SIGNIFICANCE OF THE STUDY

An estimated proportion of over one third of all cancers attributable to dietary factors (Doll and Peto 1981) makes diet the most important public health issue in cancer apart from smoking. Nonetheless, the lack of firm evidence for the role of most dietary factors in cancer aetiology makes it important to obtain such evidence as a basis for the recommendations of specific dietary changes that would decrease cancer morbidity. Such recommendations must be designed not only to reduce the incidence of cancer at most or several sites, but to prevent adverse changes in the rates of all cancers (Miller et al. 1989). The results of a cohort study of migrant and Australian-born men and women will contribute significantly to the knowledge of diet-cancer associations. As the study will include information on non-dietary risk factors for cancer, it will provide a significant contribution to our knowledge of the qualitative and quantitative role of such factors for a number of cancers. It will be possible to examine major interactions between various lifestyle factors including diet, personal habits and other risks.

The southern European migrants are currently enjoying a mortality benefit equivalent to an extension of life expectancy from age 20 years, compared with Australian-born, of 4 to 5 years (Young 1986). This is a consequence of mortality ratios between Australian-born and southern European migrants being between 1.5 and 2.0 in the cohort target age range. The identification of modifiable risk factors and their relative contribution to this substantial difference will have major ramifications for public health. With increasing person years of follow up, both main effects and their interactions with other risk factors will be estimated with statistical precision as a consequence of the large number of deaths that will be accrued in the first decade of the study.

The establishment of a large bank of plasma, lymphoctyes and other biological material is integral to modern cohort studies. The increasing awareness of the genetic basis of disease predispositon, the importance of DNA adducts as measures of biologically meaningful exposures to carcinogens, and the increasing availability of genetic probes will make such material valuable for future studies. Although banks of biological material exist in some parts of the world, few have the size of the one proposed in this study. The combination of questionnaire-based information and biological material

from individuals who can be followed-up completely for cancer and other major causes of death, will constitute a unique resource for research that will combine population and molecular sciences and permit further exploration of the genetic and environmental contributions to cancer incidence and premature mortality.

REFERENCES

ARMSTRONG, B.K., and DOLL, R. (1975). Int. J. Cancer. 15: 617.

BAGHURST, K., CRAWFORD, D., RECORD, S., WORSLEY, A., BAGHURST P., SYRETTE, J., (1987). 'The Victoiran Nutrition Survey' (CSIRO Division of Human Nutrition: Adelaide).

BLOCK, G., HARTMAN, A.M., DRESSER, C.M., CARROLL, M.D., GANNON, J., GARDNER, L., (1986). Am. J. Epidemiol. 124: 453.

BRESLOW, N.E. and DAY, N.E. (1987). 'Statistical methods in cancer research. Vol II. The design and analysis of cohort studies' (I.A.R.C.:Lyon).

BYERS, T., MARSHALL, J., FIEDLER, R., ZIELEZNY, M., GRAHAM, S. (1985). Am. J. Epidemiol. 122: 41.

CADE, J.E. and MARGETTS, B.M. (1988). Int. J. Epidemiol. 17(4): 844.

CASHEL, K., ENGLISH, R., BENNETT, S., BERZINS, J., BROWN, G., MAGNUS, P., (1986). 'National Dietary Survey of Adults: 1983, No. 1 - Foods consumed'. (AGPS: Canberra).

Department of Community Services and Health. (1989). 'Composition of foods Australia (COFA)' (AGPS: Canberra).

DOLL, R. and PETO, R. (1981). J. Natl. Cancer Inst. 66: 1192.

ENGLISH, R., CASHEL, K., BENNETT, S., BERZINS, J., WATERS, A., MAGNUS, P., (1987). 'National Dietary Survey of Adults: 1983, No. 2 - Nutrient Intakes' (AGPS: Canberra).

HAILE, R.W.C., HUNT, I.F., BUCKLEY, J., BROWDY, B.L., MURPHY, N.J., ALPERS, D., (1986). J. Am. Diet. Assoc. 86 (5): 616-6.

HEUCH, I., KVALE, G., JACOBSEN, B.K. and BJELKE, E. (1983). Br. J. Cancer. 48: 637.

HIGGINSON, J. and MUIR, C.S. (1979). J. Natl. Cancer Inst. 63: 1291.

HIRAYAMA, T. (1978). Prev. Med. 7: 173.

IRELAND, P.D., JOLLEY, D.J. and GILES, G.G. (1990) Proc. Nutr. Soc. Aust. 15: (in press)

JENSEN, O.M., WAHRENDORF, J., ROSENQUIST, A. and GESER A. (1984). Am. J. Epidemiol. 120: 281.

JONES, D.Y., SCHATZKIN, A., GREEN, S.B., BLOCK, G., BRINTON, L.A., ZIEGLER, R.G., HOOVER, R., TAYLOR, P.R., (1987). J. Natl. Cancer Inst. 79: 465.

MCMICHAEL, A.J., MCCALL, M.G., HARTSHORNE, J.M., WOODINGS, T.L., (1980). Int. J. Cancer. 25: 431.

MCMICHAEL, A.J. and GILES, G.G. (1988). Cancer Res. 48: 751.

MILLER, A.B., BERRINO, F., HILL, M., JENSEN, O.M., RIBOLI, E., WAHRENDORF, J., (1989). In 'Diet and the aetiology of cancer'. P. 71 editor A.B. Miller (springer Verlag: Berlin).

PAUL, A.A. and SOUTHGATE, D.A.T. (1978). 'McCance and Widdowson's The Composition of foods'. 4th eds (HMSO: London).

PAUL, A.A., SOUTGATE, D.A.T. and RUSSELL, J. (1980). 'First supplement of McCance and Widdowson's The Composition of foods: Amino Acids Composition and Fatty Acid Composition' (HMSO: London).

PHILIPS, R.L. and SNOWDEN, D.A. (1983). Cancer Res. 43 (suppl) : 2403.

POWLES, J., KTENAS, D., SUTHERLAND, C., HAGE, B. In ' Food Habits in

Australia', p. 201, editors A.S., Truswell and M.L. Wahlquist (Rene Gordon: Melbourne).

TAN, S.P., WENLOCK, R.W. and BUSS, D.H. (1985). 'Second supplement of McCance and Widdowson's The Composition of foods: Immigrant foods'. (HMSO: London).

TRICHOPOULOS, A., (1982). 'Food composition table'. (Lenis: Athens).

VAN LEUWEN, F.E., DE VET, H.C.W., HAYES, R.B., VON STAVEREN, W.A., WEST, C.E., HAUTVAST, G.A.J. (1983). Am. J. Epidemiol. 118: 752.

WILLETT, W.C., SAMPSON, L., STAMPFER, M.J., ROSNER, B., BAIN, C., WITSCHI, J., HENNEKENS, C.M., SPEIZER, F.E., (1985). Am. J. Epidemiol. 122: 51.

WILLETT, W.C., STAMPFER, M.J., COLDITZ, G.A., ROSNER, B.A., HENNEKENS, C.H., SPEIZER, F.E., (1987). N. Engl. J. Med. 316: 22.

WYNDER, E.L. and GORI, G.B. (1977). J. Natl. Cancer Inst. 58: 825.

WYNDER, E.L. and HERBERT, J.R. (1987). J. Natl. Cancer Inst. 79: 605.

YOUNG, C. (1986). 'Selection and survival: immigrant mortality in Australia'. (AGPS: Canberra).