This issue of *International Journal of Epidemiology* includes ten papers on cancer: two breast,1,2 two colorectal,3,4 three brain,5–7 one pancreatic,8 one lung,9 and one overall cancer.10 The very large cohort study in Denmark found that women with higher educational attainment had the highest incidence of, and mortality from, breast cancer. The authors concluded that the time trends in social distribution will result in increasing incidence.1 A Sino-US study found that in both American and Chinese women, their babies’ birthweight was positively associated with maternal height, pre-pregnancy body mass index, and weight gain during pregnancy, and most remarkably that the differences in the three maternal variables between women in the two samples fully explained the birthweight difference between the two samples of babies.2 As Chinese women who migrate to the US tend to grow taller and heavier and will have heavier offsprings, the authors predict an increasing incidence of breast cancer in successive generations of Chinese migrants. Future research needs to confirm whether this observation was a result of the authors’ longstanding hypothesis that hormone-dependent malignancies have their origin in intrauterine life where higher levels of pregnancy hormones favor the generation of more susceptible stem cells with compromised genomic stability. There should also be more work examining lifestyle or other environmental determinants of pregnancy hormone levels and possible mechanisms by which they may influence carcinogenesis.

These associations of improving socioeconomic status and changing maternal anthropometry with concomitant increases in breast cancer in developed countries are likely to be applicable to the rapidly developing economies of the world. Hong Kong, which has the most urbanized and westernized Chinese population, has already shown clearly increasing breast cancer incidence in the past quarter-century.11 Whereas the evidence shows that lifestyle and environmental factors are responsible for most of the increase, the majority of research resources are currently devoted to genetic factors, and the main strategy for prevention is screening. For primary prevention, some factors have been shown to be clearly protective and should be recommended for public health action and can be practised by individuals, such as breastfeeding.12 Other factors will need intervention trials to confirm their causative role and the effectiveness of intervention programmes, such as early menarche; and whether it can be delayed by increased physical activity in childhood. Another issue is the additional risk posed by the worldwide epidemic of childhood and adolescent obesity. The relative contributions from overnutrition and physical inactivity need to be further dissected, and cross-cultural studies are needed.

Screening by mammography and breast self-examination has spread rapidly from the West to the East. Notwithstanding the controversies about efficacy (for mammography), or the lack thereof (for breast self-examination) of such secondary preventive measures, a lower prevalence of breast cancer should warrant a careful review of the local epidemiology and the costs, benefits, and harms. Although Hong Kong’s breast cancer incidence has increased on average by 1.2% annually during the last 27 years to being the highest in Asia, the absolute risk of breast cancer is still less than half those in the UK and US. In addition, the increase is non-uniform among different age groups: those 50–79 years (the age group that might benefit from mammography screening) recorded the smallest rises, with even a decrease in 60–69 year olds (Figure). A recent review shows that mass screening is not justified in the East.13 This example illustrates the potential danger of accepting epidemiological findings wholesale from a different population without careful reappraisal, taking into account geoethnic characteristics.

Both colorectal cancer studies and the pancreatic cancer study in this issue relate to dietary factors. For colorectal cancer, the

Figure Average annual percentage change (AAPC) and associated 95% CI for breast cancer incidence by age groups, Hong Kong 1973–1999
large US cohort study found no association with total dietary fibre intake. The French-Canadian case-control study found that arachidonic acid (from poultry products) increased risk and butyric acid (from dairy and egg products) and alpha-linolenic acid reduced risk. The Japanese nested case-control study found that regular physical exercise, a regular bowel habit, and frequent consumption of raw vegetables were protective for pancreatic cancer but smoking had only a modest adverse effect. Whereas the US authors caution that fibre intake was low in their cohort (as in other Western cohorts which found no association between fibre and colorectal cancer), it is not clear how typical the nature and level of fatty acid intake in French-Canadians and the raw vegetable consumption in Japanese was, as compared with other Western and non-Western populations. With increasing urbanization and socioeconomic development, the diet of different populations, particularly the rapidly developing populations, will tend to become more homogeneously westernized, followed by increasing incidence of various Western diet-related cancer. In epidemiological research, this Western diet and other lifestyle transitions will provide a golden opportunity for cross-cultural collaborative studies on how different behavioural factors interact among themselves and with genetic factors in cancer aetiology.

The lung cancer case-control study in women in Germany found a reduction in risk with use of oral contraceptives and hormone replacement therapy but there was no association with age at menarche, length of menstrual cycle, and number of children. The authors suggested a possible protective role of hormonal factors in the aetiology which is in contrast to that for tumours of the female reproductive system (such as breast cancer). As the primary aim of this study focused on residential radon, the results need to be confirmed by studies designed specifically to collect detailed information on hormones.

All the three brain tumour studies are case-control studies, which are the only practicable study design given the rarity of the disease. The California childhood study is based on vital records and should have eliminated the major problems of recall bias and participation bias. The finding that high birthweight was associated with increased risk of astrocytomas but not primitive neuroectodermal tumours is robust. As noted above, the US authors caution that fibre intake was low in their cohort (as in other Western cohorts which found no association between fibre and colorectal cancer), it is not clear how typical the nature and level of fatty acid intake in French-Canadians and the raw vegetable consumption in Japanese was, as compared with other Western and non-Western populations. With increasing urbanization and socioeconomic development, the diet of different populations, particularly the rapidly developing populations, will tend to become more homogeneously westernized, followed by increasing incidence of various Western diet-related cancer. In epidemiological research, this Western diet and other lifestyle transitions will provide a golden opportunity for cross-cultural collaborative studies on how different behavioural factors interact among themselves and with genetic factors in cancer aetiology.

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Another US West Coast childhood case-control study found no association between maternal use of nitrosatable drugs during pregnancy and brain tumour risk in the offspring, even though nitrosamines have been shown to be potent neurocarcinogens in animal studies. The third brain tumour study concerns US adults. Higher income and education levels were associated with increased risk of low-grade glioma and acoustic neuroma but not for high-grade (more malignant) glioma.

The three studies above together suggest that different types of brain tumours in childhood or adults probably differ aetologically. Cross-culture multi-centre collaboration is needed to provide sufficient statistical power to detect small risks for individual subtypes of brain tumour and to better delineate the aetiological mechanisms.

The Greek retrospective cohort study on pilots and cabin crew, who were occupationally exposed to cosmic radiation, found low standardized mortality ratios for all causes, all cancer, and lung cancer. This study is limited by the healthy worker effect and the small number of events due to a small sample size, although the duration of follow-up was over 20 years. Again, a cross-culture study with aircrew from many countries appears feasible and could give definitive answers on cosmic radiation and mortality.

Our advocacy for cross-culture collaborative epidemiological (CCCE) studies applies not only to studies on cancer but also to other diseases and health conditions. When different research teams from individual studies which have been independently planned and executed make available their data for pooled analysis, the synergistic strengths are well illustrated by some recent publications. Although such examples are still uncommon, their successes are strong justifications for more. Better still, CCCE studies should be planned among different researchers in different populations using comparable methods, and should be prioritized for funding. Funding organizations can call for such grant applications and this will be the first and critical step forward. The most practicable and efficient approach is a mega case-control study that can accommodate many aetiological hypotheses to meet the needs of different researchers or funding agencies. The diseases we have reviewed above (e.g. breast cancer, colorectal cancer, and brain tumour) are good examples for such studies. Collaborative cohort studies under one protocol are rarely feasible but nested case-control studies based on the collaboration of several bio-banks with blood samples can be a major breakthrough for disentangling the relative contributions of genetic, lifestyle, and environmental risk factors if researchers are prepared to work together for the common good.

There are many more successful examples of multi-centre collaboration in mega-randomized controlled trials, and epidemiologists have much to learn from the experiences of multi-centre trials. Let us start to break down the barriers.

**References**


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