

# Dietary assessment tools for developing countries for use in multi-centric, collaborative protocols

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## Abstract

In recent years, increasing interest in the format of multi-centric studies among different populations in developing nations has evolved in the field of health surveys and epidemiology. Dietary intake data are most often part of these cross-cultural and cross-national collaborative efforts. Various questions have been raised about the appropriate endeavours for dietetics and nutritional sciences in developing societies, the instruments available for application, and the pitfalls and caveats in their use. An important consideration is that studies be hypothesis-driven and not mere ‘fishing expeditions’ of unfocused data gathering. All known dietary intake measurement tools are within the purview of developing country research, but they often must be adapted individually and differentially to suit a given population. In a multi-centric context, this is complicated. The watchword should be collecting comparable information across sites, not using identical approaches. Choice of dietary intake measurement tools must be honed to the hypotheses and assumptions, on the one hand, and the exigencies and pitfalls of working in the developing country milieu, in which linguistics, seasonality, migration, uncommonness of food systems and ethical considerations present barriers and caveats, on the other. Within the hypotheses, the assumptions regarding the penetration of the measured exposures must be borne in mind. Multi-centre studies in developing countries have relevance and importance in the context of food security, diet and disease, eating behaviour and satiety regulation, and nutritional anthropology.

**Keywords**  
Dietary assessment  
Developing countries  
Multi-centre studies  
Nutritional epidemiology  
MesoAmerica

People eat foods, not nutrients (Doris Howes Calloway, 1975).

Although interest in diet and nutrition in low-income countries burgeoned after World War II, the specific topic addressed in this paper is relatively new. It would hardly have been considered more than 15 years ago, but is particularly relevant to the central theme of the Fourth International Conference on Dietary Assessment Methods. It really concerns two issues. First, how do we define what are the unique features of a ‘developing country’ that produce challenges to the conventional selection of and for the use of dietary intake assessment tools and approaches? Second, what is our understanding of the nature and purpose of multi-centric studies? The combination leads us to the points of interaction when the hypotheses that can and should be tested by recourse to multi-centric nutritional research are made.

## Nature of working in developing countries

The term ‘developing countries’ does not define a fixed sub-segment of the global political map. It has a very optimistic ring when stated as ‘developing’, implying

progress towards a better state of development, understood to be in the social and economic domains<sup>1</sup>. This term is, in fact, an early accession to ‘political correctness’, as the same zones were once called underdeveloped nations or less developed countries (LDCs).

In the routine and official parlance of the United Nations and its agencies, the terms ‘First World’ (for the democratic, industrialised countries), ‘Second World’ (for the socialistic, industrialised countries) and ‘Third World’ (for the rest – none of the above) reigned until the last decade. With the decline of Communism, the second category got ‘redistricted’ between the First and Third Worlds. ‘North and South’ or ‘Tropical and Non-Tropical’ are reasonable semantic proxies if two caveats are kept in mind: first, that some important nations such as China and North Korea in the Northern Hemisphere, and the nations of the southern zones of Africa (Zambia, Lesotho, Namibia) and Latin America (Argentina, Chile), are temperate in climate but developing in nature; and second, that ethnic subgroups such as Eskimos and Native Americans in the USA, Inuits in Canada, Aborigines in Australia and the Maori in New Zealand (called by some the ‘Fourth World’) often represent deprived and marginalised groups that are

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the original inhabitants of regions populated by European migrants.

Some generalities can be made about developing countries that are relevant to the discussion. The countries of interest are largely tropical in their location (exceptions noted above). That geographic fact, in and of itself, defines factors about rainfall and precipitation cycles and lowland temperatures. It also defines what the various staple food crops might be, what the quality of soil is, and what foods complementary to the agricultural production might be. Chances are greater that some of the dietary intake of the populace will come from foraging and gathering in the wild and from hunting and fishing wild fauna<sup>2,3</sup>. The rural, agricultural population (peasants) will be at least partially self-dependent for foods (subsistence farming). High rates of illiteracy may be found, especially among women, and the populations may be traditional and traditionalist in their cultural evolution and outlook. Finally, populations will be short-lived in terms of median life expectancy, with relatively low numbers having survived to the ages when chronic disease incidences become prevalent<sup>4</sup>. All of these 'functional' characteristics are probably more relevant to the issues of dietary assessment in 'developing countries' than any geopolitical ones. These characteristics of developing countries – and their contrasts from developed, Westernised countries – present both advantages and disadvantages for dietary research. These contrasts are outlined in Table 1.

### Multi-centre and multi-site studies

The motivation for multi-centric trials has come initially and primarily from situations in which there is a presumption of commonality. They have sought to find the common thread or the common truth, so to speak. The original multi-centre or multi-site studies were about sameness, and about parallel, if not strictly identical, protocols and procedures. At least in the medical realm, multi-centre studies evolved because there were not enough 'cases' available at any given location to produce a 'series' large enough for analysis. In establishing the validity of coronary by-pass surgery in the 1970s, the conglomerate of hospitals in the Veterans Administration

of the USA was enrolled. In this format, to all intents and purposes, the populations are the same, the interventions or observers are identical, and a single, 'convergence' results. Other examples include vaccine trials; the assumption was that polio immunisation was protective, but no single centre or area provided enough subjects to get to the critical number rapidly. A multi-site study that we are all familiar with is the National Health and Nutrition Examination Survey (NHANES) of the USA.

The arena of diet, nutrition and health is now a forum for multi-centric collaborative research embracing countries of the tropics. The Internet and email, supplemented by telefacsimile and rapid courier services, have facilitated the globalisation of interest. These are among the factors that have allowed this format for simultaneous protocol projects to go forth.

### *Multi-centre dietary comparative studies about similarities*

However, there are other motivations, which tend to demonstrate similarities. The Food Habits in Later Life: A Cross-Cultural Study (FHILL)<sup>5</sup> was about both similarities and differences. The epidemiological and actuarial evidence for demographic transition was documenting that longevity was increasing around the world, in Sweden and Japan and in Italy and Greece. On the face of it, there is little in common about the traditional cuisines of these four countries; nevertheless, the FHILL hypothesis was that a number of different ways of eating would have a common compatibility with longer and healthy life<sup>5</sup>.

### *Multi-centre dietary comparative studies about differences*

However, it may be a fair generalisation to say that – either consciously or unconsciously – the multi-centric imperative in the dietary realm is more about contrasts and differences than about similarities. In this respect, having different ecological and cultural settings examined provides a range of variation, and allows one to perceive different exposures (diet, lifestyle and environment) associated with different outcomes (nutritional status, health and function). It is the contrast and variety sought in the sample that allow the capture of a 'range' of variation,

**Table 1** Comparative advantages and disadvantages of performing multi-centric studies in developed and developing countries

Developed	Developing
<i>Advantage</i>	<i>Disadvantage</i>
Easy contact of subjects by remote access, post, telephone, beeper, Internet	Populations often of difficult or dangerous access, but direct contact required
Literate and can fill in self-scored questionnaires	Often illiterate and require direct interviewer intervention
Toxic and microbiological contamination generally low and documentable	Contamination, toxins, mycotoxins and food-borne microbiota frequent, but poorly documented
<i>Disadvantage</i>	<i>Advantage</i>
Recipes often unknown or not carefully observed; meals often prepared away from home	Informants often have first-hand knowledge and recall of exact ingredients and recipes

which not only describes and embraces the variety but also seems to define the 'limits' of commonality. The multi-centre study in European elderly<sup>6</sup>, Survey in Europe on Nutrition and the Elderly, a Concerted Action of the European Concerted Action in Nutrition and Health (SENECA–EURONUT), exemplifies this purpose well, and it is revisited in another contribution in this supplement<sup>7</sup>.

### **Multi-centre vs. multi-site studies**

These two terms are not strictly synonymous. A multi-centre study is one in which a number of different research entities collaborate to address a collective, common research protocol at geographically distinct sites. A multi-site study is one in which different population groups at dispersed locations are evaluated. The Veterans Administration and NHANES studies alluded to above are examples of multi-site interactions as they are technically run out of a single 'centre'. One can have studies in which many centres collaborate with one another involving collection of data at one centre and analysis of samples at another. These are not multi-centric in our parlance. These would be settings of a multi-centre 'consortium' that operates 'in series' in the electrical circuit analogy. A true multi-centre study has a number of different study sites and are wired 'in parallel' on the circuit board.

The possible configurations of multi-centre studies are illustrated in Table 2. The various centres can be all of the industrialised, developed-country temperate zone that is a North–North liaison. This is the one variant of collaboration that is not the focus of this paper. The remaining three configurations do interest us, however, including those in which countries in both industrialised and tropical regions are involved (North–South), as well as those strictly in developing countries with sites in several countries or several distinct geographical sites within a given nation. As a caveat to the North–North issue, however, there has been introduced the term 'Fourth World', referring to the indigenous and indigent populations of a developed country; for example, the reservation-based Native Americans in the USA or the Aborigines in the Northwest Territory of Australia. Clearly a comparative study of the white residents of Durban (developed South African) and the Zulu (developing South Africans) in the Natal Province would be a perfectly relevant example of the present topic.

**Table 2** Type of multi-centre studies of interest

Developed–developed (North–North)	[0]
Developed–developing (North–South)	[X]
Developing–developing (South–South)	[X]
Within developing (South–South)	[X]

### *Examples of multi-centre, multi-site studies of diet*

For whatever reason, studies on ageing populations can be mobilised to best illustrate a range of multi-centre studies in the area of nutrition and diet (Table 3). The first member of this genre was a cross-national and cross-cultural study of health and health-protective and risk factors for older residents of four Pacific locations: Fiji, the Philippines, Malaysia and the Republic of South Korea, led by Dr Gary Andrews of Flinders University in Australia. This is basically a South–South configuration<sup>8</sup>. This was followed by the creation of SENECA–EURONUT, which began its work by studying diet and health in 19 middle-sized towns in 12 European nations<sup>6,7</sup>. Historically, the Center for Studies of Sensory Impairment, Aging and Metabolism (CeSSIAM) in Guatemala was to have been the only non-European site in this otherwise European collaboration. These plans ran into a demographic limitation: namely, that, because only 5.5% of Guatemalans are over 60 years of age, finding sufficient subjects within a small radius of population proved to be impossible. As a result, the final configuration was a North–North multi-centre study.

FHILL<sup>5</sup> represents the broadest selection of multi-centric collaboration in the North–South axis. It was originated within Committee II/4 on Nutrition and Ageing of the International Union of Nutritional Sciences (IUNS). It was led by Professor Mark Wahlqvist of Monash University in Melbourne, Australia, and his comments in this supplement<sup>9</sup> derive their experience and vitality from FHILL. The concentration of the study was on food, food systems, food habits and food intake, but it bore important homology with the SENECA study in the other questions. The original sites included Australia, Sweden, Greece and Japan among the developed countries and China and the Philippines among the emerging nations. Within Australia, sub-populations of Anglo-Celts, immigrant Greeks and immigrant Chinese were enrolled, the latter two for comparison with their age-peers in the nations of origin<sup>10</sup>. Historically, FHILL ran into the same demographic imperative in its headquarters country, Australia, that Guatemala had experienced approaching the SENECA task. It sought to enrol elderly among the Aboriginal

**Table 3** Examples of multi-centre diet studies in gerontological nutrition

Study	Investigators
Ageing in the Western Pacific Survey in Europe on Nutrition and the Elderly, a Concerted Action of the European Concerted Action in Nutrition and Health (SENECA–EURONUT)	Andrews de Groot, van Staveren, Hautvast
Food Habits in Later Life (FHILL)	Wahlqvist, Hsu-Hage
Cross-Cultural Research on Nutrition in Older Subjects (CRONOS)	Gross, Solomons, Hautvast

(Fourth World) population of its Northwest Territory. This was thwarted completely by finding that the oldest survivors available for enrolment were in their late forties.

Guatemala and South Africa were not among the original participating sites for FHILL and do not form part of the pooled data<sup>5</sup>, but in a 'second wave' of protocol studies, both have contributed their information to the literature<sup>11–13</sup>. Thus, a broader balance of industrialised and pre-industrialised societies was embraced by this multi-centric, IUNS-committee protocol.

Another IUNS committee, this one Committee II/3 on Nutrition and Urbanization, under the chairmanship of Dr Rainer Gross, did not take a back seat to its sibling on ageing. As an initiative arising in a confederation of Southeast Asian nations, the Reconnaissance Study (as it was originally known) emerged from collaboration in Indonesia, Malaysia, the Philippines and Thailand. It merged with collaborators in Brazil, Guatemala and Mexico in Latin America, with the final addition from East Asia, China, into an eight-nation multi-centre research team. The protocol had a sampling frame that called for 600 subjects per site in balanced samples of older (60–75 years) and younger (35–45 years) men and women in each of three internal geographic niches in each country: urban elite, urban poor and rural agrarian (Table 4). Coming after SENECA and FHILL in its genesis, it consciously sought to create homology with the fore-runner multi-centre studies. Circumstances in its funding efforts within the European Commission, moreover, allowed only for enough money to produce pilot data on 24 individuals from each projected site<sup>14</sup>. The investigators met in Wageningen, The Netherlands, to review the experience. Hence, it became the first of the four collaborations not to flow directly from blueprint to the field. Preliminary experience from the eight different cultural domains identified the need to re-work the protocol towards streamlining and generalising its questions. A definitive name for a definitive protocol emerged in the Wageningen meeting: Cross-Cultural Research on Nutrition in Older Subjects<sup>15</sup>. The acronym, CRONOS, symbolises the ancient Greeks' god of time. The 600-person sampling frame proved to be a challenge both to funding and to execution. As Masters student projects, various 'hemi-CRONOS' studies – involving part, but not all, of the 12-cell configuration – were conducted in two of

the original Southeast Asian nations<sup>16,17</sup> and in Vietnam<sup>18</sup>. Most recently, in Guatemala at CeSSIAM, the full panel of age and geographic subgroups were enrolled within 80% of the target number<sup>19</sup>. The process to involve centres into the CRONOS multi-centre protocol consortium is ongoing, embraced now by both IUNS Committees II/3 and II/4.

A study involving CeSSIAM in Guatemala and the National Perinatology Institute in Mexico, in collaboration with European centres, is trying to blaze new trails in the understanding of this multi-centric imperative. Many of the insights gathered here, however, come from a study that is emerging at the present time, and is of the North–South configuration involving four nations and five centres. It is a project entitled 'Concordance with the Provision of the WCRF/AICR Guidelines on Prevention of Cancer in Northern Europe and MesoAmerica: Comparative Insights for Cancer Risk and Its Reduction', funded by the World Cancer Research Fund (WCRF) and its base centre in the University of Dundee, Scotland. The populations of interest come from four regions: (1) south-west Scotland; (2) the whole of The Netherlands; (3) the Yucatan Province in southern Mexico; and (4) the Central Highlands of Guatemala. The corresponding participating centres are: (1) the University of Glasgow; (2) RIVM, the Netherlands National Institute on Public Health and the Environment; (3) the Instituto in Mexico; and (4) CeSSIAM. The hypotheses relate to greater levels of concordance with the precepts of the cancer prevention goals and guidelines<sup>20</sup> in those living in more rural and traditional settings within countries and in the lower-income countries of MesoAmerica, compared with the more affluent nations of Northern Europe. It is also hypothesised that, within the ongoing personal experience of each setting, dietary profiles and cuisines will be identified that satisfy all of the principles of lowering cancer risk while providing adequate micronutrient intakes.

### The role of hypotheses in multi-centric dietary research

We have already mentioned the term 'hypotheses' on several occasions. The appropriate application of dietary assessment tools is closely linked to the hypotheses being tested, and success in the genre of multi-centric research is linked to the nature and existence of hypotheses. For the traditionally trained scientist, the configuration of a transnational multi-centre study can evoke the reaction that this is a 'fishing expedition': 'These researchers will enrol a lot of people, collect a ton of data, make a myriad of correlations, and report something.' This is a biting – but a fair – pre-emptive criticism. The best advice is to ablate it pre-emptively with a mind-set that seeks hypothesis-driven research in the multi-centre context.

The consequences of a sharply focused, parsimonious approach will be that instruments will be brief, reducing involvement in both self-administered formats and

**Table 4** Enrolment matrix for a generic national study in the Cross-Cultural Research on Nutrition in Older Subjects (CRONOS), with 50 subjects in each of 12 social stratum–sex–age-group cells

Age (years)	Urban elite (1)		Urban poor (2)		Rural poor (3)	
	M	F	M	F	M	F
60–75	50	50	50	50	50	50
35–45	50	50	50	50	50	50

face-to-face interviews. Enrolling a large cross-sectional sample or cohort will be less time-consuming. The data-bytes generated will be modest and intrinsically manageable. There will be less collateral information cluttering the files. One is seen to be going after one species of fish in a specific niche.

The temptation to 'go fishing' after more diverse quarry, however, often cannot be resisted. Besides the criticism voiced above, one must examine the consequences. Instruments will be more expansive and it will take longer to administer them in terms of subject time and length of interviews. The management of data will become more complex as variables increase in number. The 'efficiency' in logistic effort and cost, however, will often increase as one makes the scope more expansive. Compromises can be made, especially in the direction of seeking information that has proved useful in previous dietary research. *Post-hoc* hypotheses can often be formulated around the archival data, and serve as hypothesis-generating 'preliminary findings' around which to formulate future multi-centric research efforts.

### **The tools of dietary assessment in multi-centric developing-country research**

#### ***What are the tools?***

Perhaps, too much has been written on the pros and cons of applying different dietary assessment tools in different circumstances<sup>21</sup>. These proceedings will further update and refine the nuances of this theme. For those who attended the Fourth International Conference on Dietary Assessment Methods, the 'standard fare' of instruments will be familiar: (1) 24-hour recalls; (2) multiple-day food records; (3) direct weighing; and (4) food-frequency questionnaires (FFQs). To this, we can add some techniques more related to the anthropological domain such as focus groups, interviews with key informants and direct intra-household observation<sup>22</sup>. Finally, some futuristic ideas, heralded by modern computer and analytical technology, could be applied, especially in the context of unacculturated and pre-literate populations in rural areas of the developing world.

The 24-hour recall is the sovereign of all dietary instruments, and it is the technique most emphasised and venerated in the training of nutritionists and dietitians, especially in developing nations<sup>23,24</sup>. Insofar as the paradigm of undernutrition and deficient nutrient intake have dominated public health and research concern in the low-income populations of the tropics, the 24-hour recall has been a worthy 'unit of currency' of traditional dietetics. For purposes of quantification of intake, the application of single 24-hour recalls should be applied only at the group level, until proved otherwise. It takes from three to 20 different days of recording to produce within-individual stable estimates of individual nutrients.

Classification of individuals' customary diets as 'adequacy' of nutrients or as 'exposing' to various dietary non-nutrients of recent interest requires within-individual stability. For the purposes of developing other instruments, it is a valuable screening device to provide a sketch of the variety of edible items in a region or population. But for prospective studies, this needs to be consolidated by other methods. The FFQ has assumed the role of classifying intake and exposures of individuals. The instrument developed by Willett and colleagues for the Nurses' Health Study<sup>25</sup> is a prototype of the FFQ, and one that has been used in a number of Spanish-speaking nations across the world from Spain<sup>26</sup>, to Costa Rica<sup>27</sup>, Mexico<sup>28,29</sup> and Guatemala<sup>30,31</sup>.

The years have revealed problems with the FFQ approach that must be recognised and, where possible, addressed. A number of sources of variability are recognised<sup>32</sup>, and within-individual reproducibility is of the order of 0.7 to 0.6 at best. The data from FFQ may be most robust for macronutrients and, as micronutrient intakes and phytochemical exposures have emerged in the context of cancer epidemiology, the framing of food groups has been recognised as a limiting factor to the validity of the information<sup>33</sup>. A botanical approach to grouping foods has been tried in Morocco and New Zealand to overcome the weaknesses at the vitamin, mineral and phytochemical level.

How does one gain inferences for new knowledge about risk of chronic (or even acute) disease? It is generally to contrast incidence (or prevalence) across the extremes of levels of intake, lowest versus highest, as grouped into thirds (tertiles), fourths (quartiles) or fifths (quintiles)<sup>34,35</sup>. What determines differences in intakes? This varies depending on cultural contexts. In industrialised countries, the variety of different foods and their combination separates individuals. The original Willett food-frequency instrument in the Nurses' Health Study had 61 different foods<sup>34</sup>. The contemporary one contains 161 items (WC Willett, personal communication, 2000).

Portion size can be relatively insignificant when variance is driving the relationship. In rural populations, the menu is limited. We found in a coffee-growing region of Guatemala that only 29 food items were mentioned by plantation dwelling populations, whereas this rose to 44 among those living in the county-seat that served these coffee-growing preserves<sup>36</sup>. Hence, having higher intakes of calcium would not be determined by whether one ate milk and cheese or not, but by how many lime-treated corn tortillas one consumed. Portion size among the same items, rather than variety among different items, is the key.

Energy distortion by aggregate number of options on the list is another generic FFQ problem. The more options offered, the more overreporting of cumulative energy will be scored. The fewer options, the less overreporting of cumulative energy; with the concomitant weaknesses of

not reaching the micronutrients and chemicals that are found only in selected and specific edible items.

***The quality of the information should match the purposes of the collection***

It can fairly be said that learning the craft of 24-hour recall interviews became a rite of passage for the training of nutritionists/dietitians and its professional use became a ritual. It has really only been in the recent two decades that a closer examination of the other, aforementioned tools has emerged. Dietary assessment has no idols or icons. There are many ways to skin the cat of dietary intake, some more appropriate than others. It is really an *a priori* evaluation and judgement of what the hypothesis is, what the population characteristics are, and what personnel and resources are available that should guide the design of a multi-centre study. The same approach need not be followed in every land. What must be ensured is that the purpose of the collection is in harmony with the quality of the information sought, and that the information sought from each site is mutually compatible one with another.

***Futuristic potential***

With microchip technology, one can envision forms of surveillance by multiple video cameras that would allow observation of the cooking and dining areas of a household on a continuous basis, like *The Truman Show* movie or the *Big Brother* television series. Within the ethical dictates of informed consent and anonymity of data, such a form of obtaining multiple food records of whole families could be calibrated and used. It is hard to see, however, any way in which data reduction could be done other than the laborious method of viewing the tapes and scoring the spoonfuls (or handfuls). Apropos of the latter, for common-pot settings, the video camera approach might provide better quantitative data than verbal recall.

Various futuristic possibilities can be based on faecal analyses. In excess of 96% of dietary protein is digested and absorbed during the passage through the digestive system of a healthy individual. Each proteinaceous food we eat has species-specific proteins. Highly sensitive and specific chemical or immunological examination of subjects' stools could theoretically reconstruct the dietary intake by using a protein fingerprint, at least in a qualitative manner. Such a co-proantigen analysis merits evaluation for development. If a more quantitative gauge of intake of specific foods is needed – and if the study situation allows control of the food supply to the study subjects – non-absorbable rare-earth metals could be added to the foods. Quantitative faecal collection could provide estimates of quantities consumed.

The custom of using a common family pot, rather than plate servings, confounds recording of individual intakes. Observer participation has been used to assess intra-household distribution<sup>22</sup>, but this is obtrusive, and two

eyes and two hands provide limited recording capacity. Multiple video cameras could provide visual data that can scan and cover all of the household members and their serving and feeding motions throughout home-based meals. The advance of technology will undoubtedly present numerous additional ideas. Organisers of multi-centre studies should be eager to embrace and explore their possible applications.

***Dietary intake of the breast-fed child***

The food that is most resistant to commercialisation and is the essence of 'subsistence' production is human milk fed to infants. This population and this food are not excluded from a multi-centre consideration. With exclusive breast-feeding, all of the questions relate to differential volumes and to variation in the nutrient (and non-nutrient) constituents of the milk. The new frontier of comparative study involves heretofore ignored constituents such as phytochemicals<sup>37</sup> and, unfortunately, toxic substances passed from the environment to the infant via the milk<sup>38</sup>.

When partial breast-feeding is the paradigm, a very complex set of considerations emerges, including all of those related to milk volumes as well as valid approaches to measure exposures, and all of this in the context of caretakers' reporting of the frequency, variety and amounts of complementary foods and beverages administered. Given that the health and vigour of the infant determine his or her appetite and intake<sup>39</sup>, comparative dietetics for children less than one year of age represents one of the most intricate challenges to multi-centre research on diet in developing nations.

***Concerning comparative assumptions in hypothesis testing***

We labour, as scientists, under the watchwords of 'objective' and 'verifiable' and within the confines of the scientific method. Even the most precise chemical and molecular biological issues in research, however, are full of assumptions. They can be either spoken or unspoken. Working across cultures and across nations brings out the existence of 'buried' assumptions. The prudent recommendation is to confront and understand the underlying assumptions, and understand the consequences of following them. One should have discussions not only about the procedures, but also about the assumptions in their application and interpretation. Table 5 outlines a series of assumptions that are likely to operate in multi-centre research studies.

Testing of hypotheses around multiple-site data fundamentally involves comparisons across localities and their populations. The validity of this exercise begins with the reasonableness and construct validity of the hypotheses. It then requires two additional features: (1) the comparability of information; and (2) the comparability of populations.

**Table 5** Assumptions related to the degree of influence of certain factors on specific host outcomes, with a consideration of often-unrecognised modifiers

Food's nutrients → Nutritional status
• growth requirements
• absorption
• health
Protective substance → Disease protection
• genetics
• noxious exposures
• collateral protective exposures
Promoting agent → Disease progression
• genetics
• collateral noxious exposures
• protective exposures

### ***The role and limits of inter-site standardisation***

Inter-site standardisation is important for anthropometry, and round-robin assay exercises are important for biological analyses to ensure that a measurement and value from one site corresponds to that of another. Three different levels of increasing logistic complexity have been used in the past to achieve equivalent measurements: (1) common training and standardisation via a common instruction manual; (2) common training and standardisation via convening the investigators; and (3) standardisation via exchanges of personnel across sites. For dietary purposes, however, the possibilities are different because a common questionnaire or approach may not be used across centres and across sites to gather dietary information. The goal is getting comparable information, not utilising a uniform measurement approach.

The solution to the dilemma of standardisation and comparability across sites for dietary issues is to maximise the internal validity and accuracy for any given site. If the information is correct for any given site, it will be valid across sites. How does one recognise distortions? There exists neither a science nor an art for making adjustments, and the potential of having differential measurement of the same exposure variables in the different populations ever looms over the endeavour.

### ***The comparability of populations***

Population contrasts have a series of caveats. Of a more generic concern to multi-centric studies in developing countries is the caveat related to the selection of populations. If we are interested in the comparison of nationally representative samples, there is little need to design prospective multi-centre studies. Such a sampling frame would be prohibitively expensive, and it is the custom (and obligation) of governments to perform such surveys. Hypothesis-driven multi-centric studies on a manageable scale of cost and scope will seek to compare and contrast some population types as 'archetype', as in the elderly 'burghers' of SENECA<sup>6</sup> or the urban middle-class of CRONOS<sup>14</sup>. The problem arises in the innate comparability (equivalency) of the archetypal populations

across settings and the comparability of contrasts within nations.

An example of how multi-centric protocols lock onto situations in which assumptions about universality can be misleading comes from the design of the CRONOS project<sup>15</sup> (Fig. 1). Within each country, 'A', 'B' and 'C', in a CRONOS multi-centre collaboration, the procedures call for selecting an urban middle class, an urban underclass and a rural agrarian population. The intrinsic contrasts among social strata within country, and among similar social strata across countries, are inherent in hypotheses about urbanisation and ageing. There are potential flaws or distortions in the assumptions related to the comparability of data from common protocols across nations. This is illustrated schematically in Fig. 1. The vertical axis, 'Status', represents a composite of social, economic and educational indices on a common, absolute scale. Each of the letters across the horizontal 'Countries' axis – 'A', 'B' and 'C' – designates a different nation's population and their three sub-samples by social class. In country 'A', there are minor status gaps among the three social settings, whereas in country 'B' these intra-group status distances are profound. Nevertheless, the urban elite of both countries is roughly equivalent. The situation posed by country 'C' is that there is a generous separation of status among the three sub-segments of the population, but the urban middle class and the urban poor are both inferior in absolute status to those in the former two nations. These theoretical considerations would serve to admonish those who would make too simplistic assumptions in the analysis of a CRONOS collaboration; interpretations must incorporate considerations about parallel or non-parallel status differentiation both within and across the national sites.

	COUNTRIES		
	A	B	C
S	a1	b1	
T	a2		c1
A	a3	b2	
T			c2
U			
S		b3	c3

**Fig. 1** Schematic conceptual model of the caveats and foibles of making strict, absolute comparisons within nations across social-class sites and across nations within the same social-class categories. The 'Status' (vertical) axis is a theoretical composite of social, economic and educational indices. The 'Countries' (horizontal) axis depicts three participating nations, identified by letters. The postscript 1 represents an urban middle-class population; the postscript 2, urban lower class; and the postscript 3, rural peasantry in a given country (see text for fuller explanation)

### Biological tenets of comparative assumptions regarding exposures

Dietary assessment is basically about foods. In designing studies and interpreting the data, certain assumptions about the biological effects of food consumption are inherent. All of these can be viewed within the paradigm of 'exposures' and the consequences of misclassification of exposures<sup>40,41</sup>. The most basic is that the nutrients in food support the nutritional status of the consumer. This would have a variance and distribution in a normative population. However, beyond the precision of the exposure estimate are all of the biological assumptions about what the exposure to a food subtends (Table 5).

When superficially equivalent individuals in different population settings ingest the same amount of nutrient from foods, it has widely different biological impacts. This can be explained in part by the variance that exists beforehand in the nutrient reserves of the individual. Requirements for growth are different depending upon tissue accretion rates of different individuals. The intestinal health of the populace would dictate the absorption of the nutrient(s). Different rates of recurrent gastroenteritis, tropical enteropathy and parasitoses would produce variance in the efficiency of absorption of the same nutrients from the same foods. Similarly, underlying health conditions in the population can produce distinct utilisation.

A variation on these caveats operates for the paradigm of protective substances in foods and protection from diseases. Caution is recommended in assuming that these relations are universal. The genetic make-up of a population will modify this by presenting populations in which individuals are constitutionally very resistant to the disease or overly susceptible. One cannot protect when no protection is needed, and one may not be able to protect when the propensity is overwhelming. As diet is rarely the only factor in pathogenesis, associated noxious exposures are likely to vary depending on customs and environment. Similarly, protective factors work in concert, and by focusing like a laser beam on one single food or chemical, one may lose the perspective of this collaterality and synergism of dietary effects.

Similarly, if the disease-promoting agent leading to initiation or progression of the pathological process rests with diet, a similar syllogism emerges. Once again the genetic predisposition – resistant or susceptible – defines the risk context. Other noxious exposures, from the diet or from the environment, work in concert, although they may not be measured in a given protocol. Protective factors that oppose and counteract the pathogenic potential of the adverse food or food constituent vary from setting to setting, and within setting among individuals. To the extent that the modifying and mediating factors differ from population to population in a multi-centric comparison, less will be the 'purity' in any hypotheses about foods.

Finally, for some important aspects of social and behavioural research related to diet, the exactitude of the exposure of the organism is not as important as the intention to consume. Obviously, if one measures the amount of oil or salt purchased for a home, one cannot predict accurately the exposures of each individual that would contribute to vascular disease or hypertension. This is because much of the oil stays in the pan and much of the salt rolls off as fast as it is sprinkled on<sup>42</sup>. However, a multi-centre inquiry concerned with the efficacy of public health education campaigns to reduce consumption of these two items, might usefully test a hypothesis using information on the purchase or household supply level, whereas these would be insufficient for individual classification.

### Intrinsic limitations of dietary intake assessment in developing countries

The cultural traditions and ecological circumstances of developing countries are not only about intrinsic diversity but also present features that are at odds with the basic tenets and experience of dietary intake assessment in developed nations. Table 6 lists some of the intrinsic limitations for this endeavour in developing nations. This begins with communication. In this case, it is a servomechanism by which a set of instructions and inquiries go out from investigator to study population, and a set of responses comes back. For this to succeed both parties must, in the final analysis, 'be on the same page' and be 'speaking the same language'. Both linguistics and cultural dimensions intercede. For any common protocol, there will be a prototype on file, and this might be in English. It then might be translated for discussion and data management into the official language of each country, Spanish for Mexico and Guatemala. The fidelity of forward translation and back translation between English and Spanish must be checked. Then, under certain circumstances, an indigenous dialect will be the final language of questioning and responding in MesoAmerica. In this case,

**Table 6** Synopsis of unique concerns for dietary assessment in multi-centre contexts in developing countries

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Linguistic
• back-translation fidelity
Seasonality
• tropical agriculture
• hunter-gatherers
Migration
• nomadic pastors
• male work cycles (to cities, to harvests)
Uncommon foods
• interviewer repulsion
• lack of food composition data
Ethical consideration
• report consumption of endangered or protected species
• consumption of unsafe or toxin-bearing items

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the additional forward- and back-translation fidelity needs to be probed.

Linguistics goes beyond the encounter of interviewer and subject, however. With international multi-centric studies care must also be taken with regard to the basic botanical taxonomic classification of foods and their relation to the food composition values. A case example from MesoAmerica will serve as an illustration. For the tree squash, *Sechium edule*, the common name differs across localities. It is *chayote* in the USA and Mexico, but referred to as *güisquil* in Guatemala. Even within the same country, common names differ. The green herb, *Solanum nigrum*, is known variously as *macuy* and *quilete*. With respect to food composition tables in relation to common names, things take on more complexity. The food known as *chayote* (*S. edule*) in the INCAP food table<sup>43</sup> gives the nutrient values for the green-coloured *güisquil*, and it is to serve as a proxy for the white-fleshed *perolero*, presumably a variant of the same species.

With crop and ripening sequencing, greenhouse production and importation, fruits and vegetables have year-round availability in industrialised nations. However, seasonality is a major factor in determining the foods that are observed to be eaten, or are recalled in a proximal food recall or record, in developing societies. Tropical agriculture is highly dependent on temperature and rainfall variation. This is true of forage plants as well. Mangoes, for instance, ripen over a five-month period in the early months of each year, with each individual variety having a much narrower commercialisation niche.

With respect to hunting and fishing, as a basis for – or a supplement to – the diet<sup>4</sup>, the migration of wild fowl and the spawning or migration of fish determine a seasonality for wild game. Even settled hunter–gatherers will have a varied diet throughout the year as various species swim or fly by the encampments.

Migration is not only an issue for what we eat, but for the consumers themselves. The nomadic pastoralist lifestyle arose in the Mediterranean regions some 40 000 years ago<sup>44</sup>. It provided food security in terms of having tight control on the animal protein in the diet. It also introduced milk as a life-long dietary staple. A consequence for dietetics, however, is that the accessory foods to meat and dairy products will vary not only by season but also by the terrain that the herds are passing through at any given phase of the journey.

In contemporary developing country societies, workers – especially male workers – often have migratory work cycles. These vary from a weekly cycle, in which the men might leave the village from Monday to Friday for construction work in a city, only to return to the family at weekends (as was recorded in the Solis Valley of Mexico<sup>45</sup>), to a seasonal cycle, in which they leave their hamlet to earn money in the sugar harvest in the Guatemalan lowlands in autumn and the coffee harvest on the mountain slopes in spring. The consequence for the

migrant worker is an equally cyclical pattern of food service, and possibly diet. That for the researcher is the inability to interview men in association with studies of a pre-selected geographical habitat.

Uncommon foods are ‘uncommon’ precisely because we, the acculturated scribes of dietetics, have not used them or heard of them. In this respect, ‘uncommon’ is very much in the eyes of the beholder. Interviewer cultural bias can adversely affect scientific inquiry to the extent that interviewer repulsion at the foods in a local food system may prejudice frank and accurate recording. Consumption of insect grubs (‘maggots’ to us) or rodents (‘rats’ to us), not to mention assorted serpents and arachnids, among the Orang Asli forest people of Malaysia may be more than the Westernised nutritionist can endure. They may bias the research by instituting a unilateral ‘don’t ask–don’t tell’ policy.

Another limitation is that even when there are food composition data, they are inconsistent or variable across geography. The systems of reference used for determining nutrient contents of the foods consumed in different regions, and for assessing the adequacy of micronutrient intakes across sites, are not intuitively obvious. Suppose that we have information on the intake of white potato (*Solanum tuberosum*) from diet records from the Peruvian highlands and the Irish countryside. And further suppose that when we compare the ascorbic acid content in a food composition table published in Lima with another published in Dublin, we find a discrepancy of 300 mg of vitamin C per 100 g edible portion. What should be done? Should we use the respective values for the respective sites? Should we decide to use one of the values – the Irish or the Peruvian – for the study’s food composition software? Should we make an average? Or should we use a ‘third source’, say the USDA Handbook No. 8?

Ethical considerations arise for the investigator exploring dietary habits in developing countries. As a ‘dietary detective’, the researchers place themselves in a position of getting information on activities prohibited and even criminalised by the larger, governing society. Interviewees may report consumption of endangered or protected species. In interviews with a Fourth-World population of coastal Indians, one might become privy to the hunting and consumption of a protected whale species. In Africa, ‘bush meat’ traffic, including chimpanzees and other dwindling fauna, may be the source of food in a dietary record. This places the investigator between respect for the authentic food-seeking behaviour, respect for the societal and cultural norms of the larger society, and respect for the greatest good for biodiversity as a whole. In the bush meat example, there is another ethical dilemma. What is the responsibility of investigative teams in the face of reports of consumption of unsafe or toxin-bearing items? It is widely suspected that the emerging viral diseases of tropical origin are transmitted and perpetuated as zoonoses from wild game, such as wild primates. Other

practices that Western science has implicated with adverse health consequences – chewing betel nuts, for instance – will be reported and recorded. The betel nut (*Areca catechu L.*) is known to be causal in oral cancers, and has recently been implicated in diabetogenesis as well<sup>46</sup>. Researchers entering these conflicting currents should have a previously considered plan as to how to navigate between anonymity of sources and advocacy for the 'greater good'.

### Applications of assessment tools

There is more about foods than just their nutrients. This is especially true and complex in developing countries. Foods are vectors of transmissible agents. Diarrhoeal pathogens such as *Vibrio cholerae*, protozoal organisms, *Giardia lamblia* and *Cryptosporidium parvum*, and the eggs of helminths such as roundworms and whipworms, come in food vectors. This has led health centres in Guatemala to place advisories on the walls against eating salads, with all of the implications for chronic disease risk that such entails. Foods are vectors of pre-formed toxins such as that from *Staphylococcus*. They also transmit the mycotoxins of *Aspergillus flavum* (aflatoxins) and *Fusarium moniliforme* (fumonisin)<sup>47</sup>. Even shellfish can be vehicles of the 'red tide' algae. Most recently, chemical correlates of disease risk and protection have placed the spotlight on noxious components of the diet (cholesterol, saturated fats, etc.) and protective agents such as phytochemicals including flavonoids<sup>48,49</sup> and carotenoids<sup>50</sup>.

The most exciting and important point of application of dietary assessment in developing countries is that it is not the monolithic concern for undernutrition that might be gathered from the priorities of the United Nations agencies' concerns. It is fecund territory for dietary assessment to be directed to all varieties of applications, and these can be consolidated into protocols for multi-centre studies whenever appropriate. This, however, also raises issues of the limitations of assessment tools to provide the relevant information in a reliable manner.

### Public health survey and surveillance

Ironically, but importantly, the most common application for dietary intake assessment in developing countries – namely, the domain of survey and surveillance for undernutrition and food insecurity – may be one of the least applicable areas for multi-centric studies. For most applications, representative national samples would be the focus, and routine national surveys would provide the flow of data, without the need for initiatives of academic centres. However, with specific hypotheses among sub-populations that would have needed oversampling in the national survey to provide comparative statistical power, a multi-centre study would be called for. The issues of urban poverty<sup>51</sup>, for instance, or of Chinese ethnic minorities in

Southeast Asian countries<sup>52</sup> would be ideal foci for multi-centre collaborations.

The assessment tools would be 24-hour recall, analysed by group for central tendencies, and possibly multiple 24-hour recalls within individuals or nutrient-of-interest (short list) FFQs to determine prevalences of inadequate intakes.

### Nutritional anthropology

The pattern of intake of different foods, rather than the level of nutrient intake, has generally been the concern of nutritional anthropology, dating to the era of Margaret Mead and Ruth Benedict. The questions are about cultural evolution and ecological adaptation. The number of different foods and beverages; their origins among cultivation, foraging and hunting and fishing; the nature of recipes; and the distribution within households are among the obvious foci of inquiry. Twenty-four-hour recall can be a tool, but it has obvious limitations. The symbolic meaning of foods, and even the partition of foods among the human population, the domestic animals and ceremonial offerings are of interest. Key informants and focus groups are probably the preliminary tools in a Rapid Assessment Procedure<sup>53</sup> format. Direct observations and food-frequency can complement the information for systematising the information. Obviously, it is relatively easy to generate hypotheses to be tested across cultures in multi-centre nutritional anthropology, but making a protocol for gathering comparable information is a largely unexplored challenge. Teufel<sup>54</sup> has delved into the concept of 'culturally competent' FFQs, which covers all aspects of the way the Western approach to knowing collides with non-Westernised ways of processing information. Multi-centre research in developing countries needs to be exquisitely sensitive to – and exploring of – this tension.

### Psychology and neuroscience

Dietary intake can be of interest in the area of psychology and neurosciences related to the behaviour of eating. This relevance includes regulation of appetite and so-called 'eating disorders', and neuroendocrine influences may be important co-factors in the obesity epidemiology<sup>55</sup>. What one eats plays at both ends of this equation. With dysregulated eating, energy intakes can be both too great and too slight for the needs to maintain weight and body composition at a given, habitual activity level.

The size and frequency of meals may influence satiation (the sensation of getting full at a meal) and satiety (the sensation of not being hungry after a meal). The partition of macronutrients among carbohydrates, fat, protein and ethanol can be regulatory on both consumption and energy metabolism. Even the propensity of a carbohydrate source to release its simple sugar more slowly or more rapidly, the so-called 'glycaemic index'<sup>56</sup>, governs the interval between meals before the urge to consume

returns<sup>57</sup>. For this kind of analysis, observations, food records or recent recall would be most appropriate, and it is not only the total number of items, but also their exact timing, sequence and combination. Because of the increase in the incidence of obesity, diabetes and metabolic syndrome X, even in the urbanising areas of developing nations, cross-cultural and multi-centric research on food habits that influence regulation of intake are urgently needed.

### **Nutritional epidemiology**

The term 'nutritional epidemiology' has very specific connotations regarding the diseases of interest. It is about diet and chronic disease risk<sup>32,33</sup>. It is widely agreed that early hunter–gatherer tribes suffered none of the chronic, degenerative diseases of modern Western societies<sup>58</sup>. However, few individuals survived acute disease, tribal warfare or predation to reach the age of susceptibility to chronic disease. The unfortunate characterisation by Trowell and Burkitt<sup>59</sup> of chronic degenerative maladies as 'diseases of Westernisation' deflected attention to this epidemic from tropical countries. They were poor, thought to be immune from obesity<sup>60</sup> and their dietary fibre intakes were high, which was presumed to take care of the rest. As more recent analyses of the patterns of epidemiological transition are showing<sup>61,62</sup>, these simplistic syllogisms were wrong. Cancer, stroke and cardiovascular disease are concerns for the populations of the tropical world.

Despite all the weaknesses of the 24-hour recall, what all forms of dietary intake method can ascertain, however, is the general pattern of consumption of foods and beverages. The 24-hour recall is instrumental in setting the stage for more 'durable' instruments. The FFQ has become the flagship of tools in nutritional epidemiology<sup>63</sup>. Its presumed within-individual stability allows for the determination of association with specific health outcomes<sup>25</sup>. On an individual basis, the FFQ can gauge diversity of intake, i.e. from how many different species one receives one's sustenance. Just diversity, without attention to portion sizes, can be quite informative – as in the case of associations of Kant *et al.*<sup>64</sup> with increased dietary variety and decreased all-cause mortality or in Drewnowski *et al.*'s<sup>65</sup> assessment of the 'French paradox'.

Given the set of assumptions operating on the health outcomes of food consumption in Table 5, the pattern of associations may vary from country to country, as genetic make-up, environmental influences, lifestyle, meal patterning and general diet vary. What we learn as prudent dietary advice for chronic disease prevention from US health professionals may not be relevant to developing countries. Ironically, however, it is in the traditional cuisines of rural agrarian populations where we might find keys to the practices to protect Western populations from Western diseases<sup>30</sup>. The dietary patterns that reduce risk of chronic disease have been codified in various national

dietary guidelines<sup>66</sup>. Our group is pioneering the application of multi-centric studies to examine how much spontaneous concordance with these recommendations<sup>30,31</sup> is to be found in the eating patterns and lifestyles in settings in which no overt promotion of guidelines is yet in operation. Hence, a product of nutritional epidemiological research is not only knowledge about what foods cause or prevent degenerative morbidity, but also can be so-called food-based dietary guidelines<sup>67</sup>.

### **Lessons learned and conclusions**

The SENECA–EURONUT study, although never encompassing any territory in a developing country, has important lessons for and contributions to developing country multi-centre studies. The obvious lesson relates to the population pyramid. If the total number of people surviving to older age is few, then enrolment of a sample of elderly will be difficult to impossible in less-developed, younger populations. This same lesson was repeated in the FHILL study in the instance of the Aborigines.

FHILL provided further insights into how huge, multiple datasets can be received, edited, cleaned, presented and analysed in a conjoint manner<sup>5</sup>. Having perspectives from China from both Beijing and sectors of Tianjin Province emphasise the contrasts that can be made within a developing country, itself. CRONOS has demonstrated how these protocols can serve as tools for graduate student research and how large datasets can be collected for minimal expenditures in a well-structured and frugal academic situation. The Philippines emerges, interestingly, as a cornerstone location. Segments of its population have been included in all of the ageing-related multi-centric studies<sup>5,8,17</sup>, with the exception of that based in Europe.

Urbanisation<sup>51,68,69</sup> is a major reality in developing countries, as half of the world will be urban by the year 2030. All of the populations in SENECA were to have been townships. FHILL had an eclectic mixture of rural and urban centres. Urbanisation became a strict coordinate of CRONOS<sup>15</sup> and is also part of the structure of our four-nation, multi-centre study on concordance with the WCRF's cancer prevention recommendations. One of the most available hypotheses is of rural–urban distinctions in diet and eating practices.

However, these same contrasts make it necessary to approach the obtaining of dietary information in distinct forms and with distinct rosters of food and beverage items even within nations, not to mention from MesoAmerica to Europe. This is in keeping with the admonition of Kohlmeier and Bellach<sup>40</sup> that 'these tools need to be designed for the population under study, based on prior information on the eating behavior of the population' in order to minimise misclassification errors of exposure. That the groups are culturally very distinct, in addition to

their diets, also affects the way that food-frequency instruments will elicit information. In the USA, validation correlation coefficients were variable and poorer in ethnic minorities, leading Coates and Monteilh<sup>70</sup> to suggest that FFQs 'performed less well in certain populations'. We feel the approach to this is not to despair, but to compensate for the lack of a common cultural appreciation with specialised and individualised strategies for clarifying the mission with each population.

This brief – and somewhat personal – review of the topic of multi-centre studies in developing countries tells us where we stand and where we are going. The advent of this modality is breaking new territory, and those of us performing them should enjoy the moment, before orthodoxy sets in and the genre becomes 'routine'. In fact, the complexity and assumptions are manifoldly greater than in single-centre studies and challenge the orthodoxy established in developed countries over the past five decades.

Setting up a multi-centre protocol across multiple tropical nations just to serve as a 'fishing expedition' to 'find what we can find', is not a reasonable enterprise. The protocols should be primarily hypothesis-driven, and without too many diverse hypotheses to address. One can be confident that they will be intrinsically hypothesis-generating and lead to insights outside the confines of the expressed objectives. In this regard, not only are biology and epidemiology the legitimate purview of multi-centric dietary research, but methodological research on assessment, itself, is always an opportunity.

When one has moved out of the conventional confines of a developed country, breaking with other conventions can easily follow. The bottom line is about producing new knowledge and new understanding. We recommend that researchers have no hesitancy in bringing the newest biological paradigms to the table. The importance of glycaemic index<sup>57,71</sup> of the diet and phytochemical consumptions may gain new insights from studying traditional human dietaries. And we need not be guilty if the outcomes benefit developed countries as well. With globalisation of the food supply, the tropical countries are at risk of losing their traditional food culture to new staples, which are more refined and more energy-dense. The only way that developing countries will hold onto the advantageous situation that their food legacy has left them is if the multinational export and food commercialisation industry reflects healthful food ways. Seeing that these are adopted in the exporting countries will characterise the chronic disease risk embodied in the foods that are thrust upon the world at large. It is these kinds of policy imperatives that should keep the academic community seeking to forge North–South collaborations.

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