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International collaborative clinical research: advantages are many, but we need to be cautious

Most health problems that confront the developing world can be attributed to poverty and ignorance. Poverty and ignorance complement each other as poverty is a hindrance to obtaining a good education which in turn makes people underestimate the importance of determinants of good health, such as, environmental sanitation and healthy life styles. As a consequence people in such countries have a disproportionate burden of communicable diseases. Developed countries having overcome most of the diseases caused by poverty have moved in a different direction. They are now saddled with non-communicable diseases caused by unhealthy and irresponsible life styles. Some developing countries, especially middle income countries like ours, are not too far behind in this respect; the global increase in diabetes is a good example [1].

The practice of medicine should be evidence based. Such evidence requires meticulously conducted clinical trials for which there needs to be an environment created within a sound scientific and ethical framework. Such trials also demand resources not easily available in developing countries. Developed countries have adequate resources, but not the abundance of clinical material seen in poorer countries. This imbalance encourages developed countries to seek opportunities to carry out collaborative clinical research in developing countries for purposes, such as, new drug development, therapeutic trials or novel and innovative interventions which can be of great benefit to patients.

New applications and advances in medical research are effecting slow but definitive changes in the developed world, which sooner or later will have a bearing on developing countries. In the USA the Methodology Committee of the Patient-Centred Outcomes Research Institute (PCORI) released for public comment a draft of its first report recommending selected standards for the conduct of research leading to evidence-based patient-centred health interventions [2]. Such documents should compel us to scrutinise our own understanding of methods underlying medical research. One may briefly consider the following as a basis for understanding the complexity of the issues involved. Aging of the population causes more people to suffer from co-morbid health conditions which affect research protocols and outcomes. Obesity in the developed world and malnutrition in the developing countries, especially in older people, are likely to produce different responses to one and the same treatment regimen. Similarly, the number of treatment options for common conditions such as diabetes and rheumatoid arthritis are so vast that determining the optimal treatment for people with both conditions becomes a complex exercise. The advent of individualized medicine presents further

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Association
Wijerama House
6, Wijerama Mawatha
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Tel: +94 11 2693324

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Tel: +94 11 2435975

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methodological challenges, since emphasis is placed on the individual rather than on the population. Further, the responses of an enlightened public through engagement and comment is certain to have a major impact on researchers planning investigations, policy makers weighing cost-effectiveness of health care interventions, and patients and clinicians who will be called upon to make informed decisions about the benefits and risks of interventions.

In the developing world many activities in industry, education and economic development are assisted by international cooperation or partnerships. Seeking such assistance is a pragmatic move, since developing countries do not have the resources, financial, technological or human, to carry out these activities by themselves. However, when getting involved in such partnerships an important condition needs to be fulfilled: a shift from the customary donor-driven agenda of the wealthier nations to a needs-driven approach with adequate safeguards for accountability and sustainability. In the field of collaborative research involving health care one has to be cautious, circumspect and wary, as there is potential for exploitation and manipulation. It is well known that 90% of world's health resources are spent on diseases that affect only 10% of humanity [3] who mainly live in rich countries. Spelt out another way, this means that the poor countries' health problems are poorly researched. International collaborative clinical research, especially drug trials, can also be a means of earning valuable foreign exchange for poor countries. This, however, should only be viewed as an incidental gain or by-product, and never the main objective. It is perhaps for these reasons that collaborative research remains a contentious subject with many stakeholders having doubts and concerns regarding motives, benefits and risks.

When seeking partners for collaborative research, the importance of protection for the patients cannot be over-emphasized. Most professionals are unaware that even the USA has not been able to adequately guarantee the protection of subjects (patients or healthy volunteers) who are involved in research activities in their own country [4]. In the USA ethical guidelines are designed more to protect the researchers than research subjects. It is also secretive and difficult for watchdog organizations or journalists to investigate potential wrong doing. Legal constraints may preclude subjects in foreign countries being compensated for injury, however serious they may be. In view of these deficiencies the US Congress, as recently as August 2012, introduced the Trials and Experimental Studies Transparency (TEST) Act [5]. This requires that trials conducted outside the USA be registered and be made available in a publicly accessible data base. This Act also means that characteristics of participants, the primary and secondary outcomes and adverse events need to be entered. This type of legislation will benefit poor-country research partners as well.

Medical researchers in Sri Lanka should seek the support of the state for the establishment of a comprehensive Act which governs clinical trials. The Ministry of Health should establish a regulatory division whose function would be to coordinate activities pertaining to clinical trials, including those which are conducted with foreign collaboration. Members of ethics committees (ECs) are the key personnel involved in determining whether or not research, especially clinical trials, should be allowed. It is important that they are made aware of their responsibilities towards both the research subjects as well as the researchers. 'Over regulation' by overly enthusiastic or excessively bureaucratic EC members could dampen the enthusiasm of researchers. Concentrating on trivia which have little bearing on the conduct of research may also frustrate patients waiting to take part in trials. Numerous instances have been quoted by researchers where a protocol approved by one EC has been turned down by another for completely different reasons [6,7]. ECs should function efficiently, expeditiously and professionally and be less

concerned with trivia, as delays can cost lives [6]. It is estimated that the lengthy consent procedures required by centres in the USA participating in the ISIS-2 trial on thrombolysis after myocardial infarction, probably cost 10,000 unnecessary deaths because patients could not be recruited as quickly as they were in the UK [8].

The potential benefits of collaborative research should also be placed before the public so as to dispel their fears and anxieties. They should be enlightened on the advantages of discovering new or innovative therapies or interventions, improvement to local infrastructure, expertise gained by local professionals, and the creation of collaborative partnerships with centres of excellence outside Sri Lanka. All the while taking whatever measures required to protect the participants from harm.

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N Amarasekera, Former Consultant Physician, National Hospital of Sri Lanka and Vice President of the Sri Lanka Medical Council.

Correspondence: NA, e-mail: <nanda_amar@hotmail.com>. Competing interests: none declared.