The supplement which accompanies this edition of the Journal explores the methodological issues which face all those who are interested in the subject of early intervention in childhood asthma (and other wheezing disorders) [1]. This has become a topical issue as evidence has increased that a number of factors which can affect the development of the foetus and young child may determine respiratory health for the rest of an individual’s lifetime.

Interventions early in childhood or early in the course of the disease itself can have a number of objectives. It may be important to distinguish these in considering the development of intervention programmes. Their pragmatic value is of course in their potential to reduce morbidity both for individuals and, of course, for populations. However, the theoretical basis for many interventions is weak. Another purpose is therefore to improve our understanding of important disease processes in asthma by examining the outcome of controlled interventions in groups of subjects. Clinical research always contains an element of conflict between these two approaches, since it is natural for those involved in patient-care to wish to find the solution to the health-needs of their patients as quickly as possible, even if this sometimes means bypassing the more laborious aspects of scientific research into the mechanisms of disease. However, by means of carefully designed studies, both decreased morbidity and improved scientific knowledge can be achieved.

While the distinction between primary and secondary intervention may seem to be somewhat arcane, it does have very important implications. By its nature, until we have reliable predictors of subsequent disease, primary prevention has to be a public health measure applied to a large and poorly characterized proportion of the population. Secondary intervention is simply a therapeutic intervention of some sort within a clinically defined population. Whilst it is likely to be a primary-care responsibility, the element of individual patient-care is more obvious and the ethical issues less controversial. The issue of primary and secondary preventive interventions also has major implications for the design of studies. The motivation of both the health professionals and parents participating in interventions is likely to depend on the degree to which participating children can be expected to benefit, as well as the complexity of the intervention itself. At one extreme, for instance, it is improbable that the parents of asymptomatic children will agree to the administration of aerosol therapy on a daily basis for many years in the expectation of reducing the risk of subsequent asthma. On the other hand, a single-shot immunization programme which reduced the risk of respiratory syncytial virus early in infancy, with possible long-term benefits, is by analogy with other immunization programmes likely to be quite acceptable.

With increasing awareness that asthma consists of a number of more-or-less well defined phenotypes, each of which is likely to have its own genetic and environmental causes, the recognition of predictably high-risk groups at an early stage is important. At the moment, risk-prediction is poor even for specific phenotypes, such as atopic asthma at school-age. The recognition of other phenotypes such as recurrent viral wheeze in preschool children, may depend on technically demanding procedures, such as neonatal lung-function measurement, which are only available in a few centres worldwide. Progress on genotyping is likely to provide the solution to the problem of subject selection.

There are numerous potential interventions. The importance of some, such as smoking cessation, has been recognized for many years. Achieving a successful outcome has been difficult because of our failure initially to understand the deep social (and psychological) impact of smoking in Western society. Wherever major environmental change is demanded, similar impediments are likely to be found. However, by focusing on critical stages in the development of atopic sensitization or in the evolution of lung damage from repeated infection, relatively brief and therefore more acceptable interventions more akin to immunization procedures may be developed.

Surprisingly little thought has been given to measuring the outcome of early interventions. Problems arise not only because of the limited number of validated clinical measures of outcome but also because, by their nature, early intervention studies demand prolonged follow-up. For instance, in order to determine whether antigen-avoidance in infancy alters the likelihood of adult-onset atopic asthma, lifelong follow-up would be required. This presents enormous organizational problems, as well as statistical and design difficulties.

One of the critical issues in early intervention is the effect on the growing child. Airway modelling takes place actively over the first few years of life, and much alveolization is postnatal. There are no effective tools for measuring these processes in childhood. With a paucity of data on experimental animals, the absence of developmental ill-effects from early therapeutic interventions remains a step of faith.

The accompanying supplement explores these and many other issues in depth. It is the result of a workshop.
which was modelled on previously successful exercises [2, 3]. The resulting papers represent mainly the work of the authors, tempered and modified by discussion and debate involving the whole group. In effect, each paper represents a view which has been peer-reviewed in the process of writing. We hope that the supplement represents a considered account of the methodological issues involved in every important aspect of early intervention in childhood asthma.

References