The burden of asthma: weighing the community risk against individual risk

Ahmad von Schlegell, Evalyn N Grant, Kevin B Weiss

During the past few years findings from two studies—the International Study of Asthma and Allergies in Childhood (ISAAC)\(^1\) and the European Community Respiratory Health Survey (ECRHS)\(^2\)—seem to have dominated much of the thinking about the geographical variations in the prevalence of asthma. These studies suggest important variations by geographical site in different countries and, to a lesser extent, in study centres within countries. However, these studies only raise new questions as to how geographical factors contribute to the aetiology of asthma. For example, are the geographical variations in the prevalence of asthma caused by unique exposures to disease causing agents found only in local environments? Do differences in geographical location in some way alter host susceptibility? Do local environmental conditions, either physical or sociocultural, alter the host/agent interactions in ways that are critical to the expression of this condition?

In this issue of *Thorax* Duran-Tauleria and Rona\(^3\) further elucidate how social and physical environmental factors may explain some of the geographical expression of asthma prevalence. Their study focuses on the differences in asthma and respiratory symptoms among three populations—two nationally representative samples of English and Scottish children and a third sample of children living within the inner cities of England. The authors found a higher prevalence of children with persistent (as opposed to occasional) wheeze within the inner city population than in the other two sampled populations. They also found that the prevalence of asthma attacks was higher in the non-inner city sample of English children than in the other two groups. Social and physical environmental factors—mainly social deprivation (as measured by the Townsend score)—seemed to explain much of the geographical variation in children with persistent wheezing. This finding held even after adjusting the analysis for many of the well known risk factors that might otherwise have explained these differences such as age, sex, parental atopy, and maternal smoking.

The importance of social and physical environmental factors in disease expression is well known and has been studied extensively for many health conditions, including asthma. A number of studies suggest an association between higher asthma morbidity/mortality rates and geographical areas of lower socioeconomic standing. The literature on the effects of social environmental factors on the prevalence of asthma is less definitive, but there have been several studies that suggest findings similar to those of Duran-Tauleria and Rona. Yet this current study also provides new insights into the possible mechanisms by which poverty may influence the development of asthma based on its impact on communities independent of its effect on individuals.

The results of this study suggest that individual measures of social and physical environmental risk (specifically, measures of socioeconomic status) may be less important to the prevalence of asthma than geographical ecological measures (specifically, the Townsend deprivation score of the area of residence). The finding that an ecological measure may explain risk better than individual measures is perhaps at first disconcerting. On further reflection, however, it would be expected that the relative deprivation index (Townsend score) may be acting as a surrogate for other sociocultural or physical environmental exposures common to parochial experience—for example, it is possible that high levels of outdoor pollutants such as ozone, small particulate matter, and sulphur dioxide might be disproportionately represented in areas of poverty. It is also possible that any one or more of these exposures may be more closely associated with geographical ecology than individual socioeconomic status.

Similarly, allergens, cigarette smoke, inadequate ventilation, dampness, and lack of air conditioning have all been cited as possible indoor environmental risk factors for the expression of asthma.\(^4\) Areas of increased poverty may be associated with risks of exposure that are less amenable to individual risk avoidance than population risk avoidance. For example, areas of poverty tend to have a higher density of population with more persons sharing residences—either more persons per household or more households per building. In shared living arrangements many exposures such as moulds, cockroaches, and cats are more likely to be community problems, requiring community based solutions, and are less under the control of any one individual, regardless of individual attitudes or behaviours towards changing these exposures.

Furthermore, these two examples of how poverty may impact asthma at the community level focus on asthma specific risk factors. Other literature on social and physical environmental deprivation suggests that more generic factors may be significant—for example, local community social and cultural practices may alter the general perception of disease within a community either through basic health beliefs, through susceptibility to disease, or by likelihood of contact with health care providers that would in some way influence awareness of clinical symptoms.\(^5\)

While it is interesting to ponder the possible differences as to how geographical community factors (compared with individual factors) affect the risk of asthma, Duran-Tauleria and Rona caution us about some of the key limitations of their findings. Most noteworthy is the fact that there was variable reporting of socioeconomic measures for the populations with the father’s occupation more likely to be missing from the inner city population. The authors state that the lack of willingness to disclose
the father’s occupation may be due to a higher frequency of single parent families headed by the mother. The effect of this loss of information on the analysis of socioeconomic status is not clear. In addition, one must question whether measures of individual socioeconomic status, based on constructs developed in the mid 1900s—for example, father’s occupation—are still valid and reliable in today’s society. Finally, the overall limitations of self-reported compared with observed health experience need to be considered.

In spite of these limitations, this study provides additional evidence that there is still much to be learned about the phenotypic expression of the syndrome called “asthma” through the study of small area variations. While studies such as the ISAAC and ECRHS are essential for understanding the global burden of asthma, studies of variations in the prevalence of asthma and morbidity in small areas within communities are more likely to elucidate some of the key interrelations between host, agent, and environment for this disease.

Screening older patients for obstructive airways disease

Antony Crockett

Many studies have shown an increase in the number of cases of obstructive airways disease (asthma and chronic obstructive airways disease) in all age groups over the last few decades.1 2 In the elderly, breathlessness is a common symptom3 and is increasingly common with age.4 A large number of patients with this symptom will have obstructive airways disease5 6 and estimates of the proportion of the elderly population who have evidence of chronic airways obstruction range from 20%5 7 to 30%.8 Some elderly subjects with objective evidence of obstructive airways disease will not have received a formal diagnosis9 and will not be receiving any specific treatments.10 Many patients may be untroubled by their symptoms10 or have adapted to them.11 In response to these findings, several authors have recommended screening for obstructive airways disease in elderly patients.12 13 The premise is that the prevalence of respiratory symptoms in the elderly is high and therefore a considerable proportion of elderly subjects will have obstructive airways disease. Screening in primary care will identify those with obstructive airways disease, allowing therapeutic intervention to be applied which will lead to reduced morbidity and mortality in the treated subjects. However, before general practices invest the resources into screening for obstructive airways disease in the elderly, there must be good evidence for their doing so.

As there are no cures for obstructive airways disease, much attention has been focused on whether early detection and subsequent suitable interventions will prevent worsening of the condition and will lead to improved quality and quantity of patients’ lives. The earliest detection will be screening of previously undiagnosed individuals who are asymptomatic or whose symptoms are insufficient for the patient to seek medical attention. Effective screening requires the early detection of disease for which safe treatment is available but which, if left untreated, progresses to disability and death.

There is increasing evidence that early intervention with treatments for asthma, especially inhaled corticosteroids, has a substantial impact on later morbidity and may lead to long term remission.14 15 In chronic obstructive pulmonary disease (COPD), however, the delayed introduction of inhaled corticosteroids does not appear to be harmful.16 17 Moreover, patients with the mildest COPD do not seem to benefit at all from taking inhaled corticosteroids18 19 nor from any other intervention except stopping smoking.20 21 There are great benefits from early interventions in younger people with obstructive airways disease but the benefits of early diagnosis and intervention in the elderly are less clear.

In this issue of Thorax, Dickinson et al22 report the results of a study of screening older patients with obstructive airways disease and concluded that screening asymptomatic elderly patients in a semi-rural practice was not worthwhile. The study screened a random sample of 353 patients aged 60–75 years using peak flow diaries, symptom questionnaires, and respiratory function tests. Thirty newly diagnosed patients were identified (8% of the screened population), eight of whom had asthma and the remainder COPD. No patient had severe disease. Six patients accepted treatment (1.2% of the screened population), five with asthma and one with COPD.

These results fail to confirm the large burden of unmet need described in other UK studies15 that concur with the findings of a large Dutch study23 that no evidence of significant untreated disease could be found. Dickinson et al24 also identified far fewer patients than a two year Dutch study undertaken by Van den Boom et al on 1155 subjects aged 25–70 years.25 Like the study by Dickinson et al, patients with known obstructive airways disease were excluded. Extrapolation of the Dutch study showed that 7.7% of the population had persistent increased bronchial hyperreactivity (BHR) and decreased lung function, another 12.5% had signs of BHR and a rapid decline in lung function, and a further 19.4% had mild objective signs of obstructive airways disease.

Dickinson et al estimated that finding 30 new patients with obstructive airways disease, six of whom were willing to accept treatment, required 331 hours of nurse time and 18 hours of doctor time. No estimations of staff and prac-
tice organisation costs, equipment, transportation, and patient costs were made but, assuming that nurse time costs £10 an hour and doctor time £50 an hour, each newly diagnosed patient cost at least £140 (US$225) and each newly treated patient cost £700 (US$1120). It is possible that some of the relatively high initial costs may be offset by long term health outcomes.24 25

The question remains, then, whether general practices should screen their elderly patients for obstructive airways disease. On the available evidence the answer must be no, or at least not yet. Screening for any disorder carries with it ethical considerations as well as those of resource allocation and utilisation. If we wish to screen patients who have no symptoms, or symptoms insufficient for them to seek medical attention, we must be sure that there are effective and safe treatment options that will prevent or slow down the progress of their condition. For elderly patients with mild obstructive airways disease there is no convincing evidence that any therapeutic intervention will lead to long term benefit. Screening large sections of a population in primary care will require a great deal of a practice's financial, personnel and organisational resources, for all of which there are already many competing demands. Finding patients and giving them a diagnosis is not necessarily the same as providing effective treatment.

Screening for obstructive airways disease in other age groups may be more worthwhile. Most of the evidence supporting early therapeutic intervention is from studies in childhood asthma and screening for obstructive airways disease in children may be more cost effective and beneficial to our patients. In the prevention of COPD, or early intervention, the single most important factor is stopping cigarette smoking, and the resources of the primary health care team may be better spent preventing patients from smoking and helping those who smoke to stop. The methods used by Dickinson et al and in the Dutch studies involved questionnaires and respiratory function testing. These methods are time consuming and expensive and may need repeating at intervals of up to two years. However, screening by symptom scores alone,26 peak flow variability,26 or reversibility of airflow obstruction in response to a bronchodilator27–29 have all been shown to lack sensitivity. Measuring BHR may be a more reliable and discriminatory test for obstructive airways disease,30 especially in the elderly,31 but it is impractical for use in a primary care setting.

The study by Dickinson et al is evidence that screening for obstructive airways disease in elderly patients in primary care is probably a poor use of scarce practice resources. Those resources are better allocated to screening for obstructive airways disease in younger age groups, to smoking prevention and cessation or, in the absence of practical tests for BHR, to adding spirometric tests to the other checks carried out at opportunistic or planned health screening.

ANTONY CROCKETT

Elm Tree Surgery,
Shrivenham,
Swindon SN6 8KG, UK

A quagmire for clinicians: when technological advances exceed clinical knowledge

Susan Redline, Mark Sanders

Obstructive sleep apnoea hypopnoea syndrome (SAHS) is currently estimated to affect between 2% and 25% of the adult population. Increasingly, data indicate that obstructive SAHS, if untreated, may result in both short and long term sequelae including daytime sleepiness, poor quality of life, neuropsychological impairment, hypertension, and cardio-cerebrovascular diseases. Its high prevalence and potentially substantial morbidity present challenges to the health care system and to individual care providers to diagnose and identify those individuals at greatest risk of obstructive SAHS related complications and those most likely to benefit from specific interventions. On the one hand, the costs associated with evaluation with the “gold standard” (overnight laboratory based multi-channel polysomnography) could exceed $1500/patient. In the USA this cost alone could result in annual health care expenditures of >$18 billion if all adults with suspected SAHS were tested. On the other hand, the economic costs of untreated SAHS are substantial. These, however, are more difficult to estimate since they may include the costs associated with loss of work productivity, occupational and vehicular accidents, and potentially preventable hypertension and cardio-cerebrovascular diseases. Regarding the latter alone, it has been estimated that between $3 million and $2 billion spent on treatment of hypertension and cardiovascular diseases annually in the USA may be reduced by effective treatment of SAHS (estimates varying according to the estimated attributable risk). In times of escalating aggregate health care costs, how should the appropriate balance between costs and benefits be achieved?

One strategy to reduce the costs associated with using complex expensive technology to diagnose a condition associated with common symptoms (snoring and daytime sleepiness, found in >50% to >20% of the population, respectively) is to use screening tests and/or diagnostic tests that are simpler and less costly than overnight laboratory based polysomnography. When using a highly sensitive screening test (high negative predictive value) only patients who test positive would proceed to the gold standard. On the other hand, use of a highly specific test (high positive predictive value) may require continued testing of those patients who screen negative, but might allow treatment to be applied only to those patients with positive results on the screening test without proceeding to further testing.

Evaluation of new technology and determination of test sensitivity and specificity has been performed predominantly by comparing the new tests with “conventional” laboratory based polysomnography. The premise of this work has been that obstructive SAHS is a disorder that is diagnosed specifically only after a critical threshold of apnoeas + hypopnoeas are exceeded by the “gold standard” polysomnographic evaluation. Evaluations of screening tests and new technology have therefore largely been based on comparing the number of “events” detected by overnight laboratory based polysomnography with the number of “events” detected by alternative tests. Indeed, third party payers who have required a specific apnoea + hypopnoea index (AHI) to justify reimbursement for specific treatments have endorsed this supposition.

Over the past 10 years a number of candidate tests/studies for screening and diagnostic purposes have been evaluated. These include limited channel and/or ambulatory polysomnography and single channel recordings, usually of oximetry. Evaluations of these studies have generally been encouraging, but use of these diagnostic modalities has not been widely endorsed because levels of prediction—when disease is defined on the basis of the number of “events”—while high, are imperfect. In addition, the overall economic benefit of such strategies has never been convincingly demonstrated.

In the current issue of Thorax Sériès and Marc report on the evaluation of a relatively new technology—namely, measurement of nasal pressure and flow from a simple nasal cannula, similar to that used to deliver oxygen, attached to a pressure transducer. Over the last five years this method of recording has gained much popularity because of its relative simplicity and because the signals obtained are generally clear and the changes in breathing pattern are easy to recognise. The method is intuitively appealing since the sensor detects patterns which reflect changes in flow and volume, parameters considered to be closely related to the underlying physiological disturbances of obstructive SAHS. This approach appears to be more physiologically grounded than the use of thermal sensors which measure changes in temperature at the nose and mouth.

Sériès and Marc first evaluated this technology by comparing the number of events detected by the sensor with the number of events detected by two more conventional approaches: scoring hypopnoeas by identifying breathing amplitude changes from (1) data obtained from inductance sensors and (2) data from a thermistor. Compared with each of the conventional approaches evaluated, a greater AHI was measured with the nasal cannula—4.5 h higher than the inductance method and 8.8 h higher than the thermistor method. In addition, 39% of events that appeared to be hypopnoeas by conventional methods appeared to be apnoeas by the nasal cannula method. When an AHI of >15/h was used to classify an individual as having obstructive SAHS, 22% of subjects who would have been classified as “normal” using the conventional (inductance) method were considered to have SAHS with the cannula method. Before interpreting these data it may be useful to consider other differences reported in the study.

Sériès and Marc also compared differences in the AHI determined by using the two other more conventional approaches. They found systematic differences of 4.3 h between the two more conventional methods, with more events being identified by the inductance method than by the thermistor method. Disease classification could therefore change significantly when a number of “events” is used to identify disease and when identification of such events, even in the context of a “gold standard” overnight polysomnographic study, has not been standardised because of variable use of different sensors for detecting breathing changes (as well as because of differences in
interpreting such signals, which also has not been standardised. Such differences in AHI that result from varying commonly used and divergent approaches has, in fact, been recognised by others and suggest the need to re-evaluate the concept of “gold standard” as applied to polysomnography.

The findings by Sériès and Marc highlight the problems in current approaches for evaluating new technology and in the application of such technology in a rational fashion to diagnose obstructive SAHS efficiently. Overnight laboratory based polysomnography is not a “gold standard” reference test; rather, it is a fairly general approach for the measurement and interpretation of sleep and breathing disturbances with substantial latitude for varying the use and interpretation of specific sensors. The latter, in turn, may result in discrepancies in AHI estimates between laboratories, each using the “gold standard”, that may exceed many discrepancies reported between “standard” polysomnography and alternative tests. If, indeed, the conventional approaches are not “gold standards”, how does one evaluate new technology? Accordingly, it is difficult to interpret the results of the study by Sériès and Marc which found more “events” detected by the newer technology. Are the additional events found with the nasal cannula “false positives” or is it a more sensitive technique that more accurately identifies individuals at short and/or long term risk of adverse health effects related to obstructive SAHS?

Using the number of detected events (apnoeas + hypopnoeas) as the benchmark for evaluation of new technology is a premise that should be questioned. It has not been validated by clinical data showing a clear cut dose-response relationship between the number of such events and the occurrence of adverse clinical consequences. The development of adverse cardiovascular and neuropsychological effects secondary to SAHS is, in fact, generally thought to be related to complex and related phenomena that include exposure to hypoxaemia, hypercapnia, sleep fragmentation, intrathoracic pressure swings, and autonomic nervous system activation. However, the AHI has not been convincingly shown to predict specific biological responses or clinical outcomes.

In an attempt to address the physiological significance of their findings, Sériès and Marc show that the arousal index, a marker of sleep fragmentation, was increased in the group of patients who tested negatively by the conventional approach and positively by the nasal cannula approach. Although this suggests that such individuals may be at risk of daytime sleepiness, little is really known regarding their overall increased health risks or likelihood of benefiting from specific treatment.

These gaps in our knowledge have not diminished the enthusiasm of many experts in sleep disorders for using this technology. Sensors and software for nasal pressure/measuring nasal flow/cannula are now being incorporated into ambulatory and simple sleep monitoring devices. This is occurring in the face of data, such as those reported by Sériès and Marc, that suggest that this technology may not be suitable for 9% of patients because of underlying nasal obstruction, and may require frequent repositioning of the nasal cannula that may be difficult to perform in an ambulatory setting. Although the advantages of such monitoring approaches may far exceed these limitations, it is incumbent on both sleep researchers and industry to work together to assure that the newest technology is most appropriately used for clinical decision making.

It seems that much of the emphasis over the past 10 years in evaluating new diagnostic or screening tests for obstructive SAHS has been misplaced. Industry appropriately has continued to press for the adoption of more sophisticated technology. However, most work has centred on evaluating both old and newly emerging technology against a gold standard that itself is poorly standardised and from which we have yet to derive a definitive metric of the disease process. Recording techniques and measurement approaches vary considerably within the rubric of laboratory based polysomnography. Of even more concern is the fact that the superiority of any given laboratory approach to identify short and long term morbidities or to predict responsiveness to treatment over other approaches, including clinical evaluation, simple single channel screening (oximetry), and multi-channel ambulatory recording, has not been established. The emergence of exciting and physiologically based approaches for measuring the stresses associated with obstructive SAHS—such as the nasal pressure flow techniques and other techniques such as pulse transit time (which measures blood pressure or subclinical arousals)—provides the challenge to evaluate systematically their abilities to identify efficiently, economically, and accurately clinically meaningful outcomes rather than to compare them with an imperfect gold standard. The work by Sériès and Marc and others working with the nasal pressure/cannula is important in delineating the comparability of data obtained with the newer sensors with more conventional approaches. However, future studies should also address the multiple lacunae that exist regarding the ability of new and old technologies to provide clinically and epidemiologically useful data. Sleep experts and industry need to form new partnerships that go beyond one dimensional assessments of “event” comparisons, and rather address the clinical usefulness of any given technique with regard to clinical predictive ability, patient acceptability, failure rates, and costs.

SUSAN REDLINE

Department of Pediatrics, Medicine, and Epidemiology,
Case Western Reserve University,
Rainbow Babies and Children’s Hospital,
11100 Euclid Avenue,
Cleveland,
Ohio 44106-6003,
USA

MARK SANDERS

Department of Medicine and Anesthesiology,
University of Pittsburgh School of Medicine,
Veterans Affairs Medical Center,
and Pulmonary Sleep Disorders Program,
University of Pittsburgh Medical Center,
Pittsburgh,
Pennsylvania,
USA

A quagmire for clinicians: when technological advances exceed clinical knowledge

SUSAN REDLINE and MARK SANDERS

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