

Advancing analytic methods to understand asthma control and disease morbidity

Madeleine Ullman Shalowitz, MD, MBA Evanston, Ill

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Best practices for asthma treatment are well established, and most individuals' asthma can be controlled with optimal therapy. Adherence to treatment plans has been more difficult to ensure, and a substantial literature has focused on interventions to increase adherence to prescribed treatments, particularly the controller medications. More recently, attempts to understand the determinants of nonadherence have broadened to include the patient perspective, including their understanding of asthma as a chronic illness, concern about long-term consequences of medication use, cultural influences, behavioral impediments, and neighborhood influences.

Pediatric asthma has an additional complexity because the parent is an interface between the child and the medical care system and instrumental in assuring adherence. Conceptually, this model is multilevel, multidimensional, and interactive, as shown in Fig 1, where the adhesive strip represents the health outcome—that is, asthma control—and the eye represents the parent perspective in reporting on the child.

In a contextual model (in contrast to a medical model), the child's illness is simply 1 attribute of the child. The parent's perception (and reporting) of the child's symptoms and function outside the treatment setting is influenced by many personal factors. These parent factors might include the parent's own physical and mental health, cognitive capacities, economic and other sources of stress and support, and the quality of the parent-child relationship (the intersection of the circles), among others. The child's asthma control may be affected by the larger family and community contexts directly and also indirectly via contextual effects on the parent. Finally, culture and society influence knowledge, attitudes, beliefs, and behavior of the parent and child; culture and society also affect those with whom they interact.

Bender and Zhang's article in the current issue, entitled "Negative affect, medication adherence, and asthma control in children,"¹ considers the interplay between affect and adherence on asthma control, showing that although important, adherence is not the sole determinant of control. In their sample, adherence

overall was poor, echoing many previous studies about the inadequate usage of daily inhaled corticosteroids (even when prescribed) in the population of individuals with asthma.^{2,3}

Parents' negative affect was not associated directly with adherence, even though one might have hypothesized that depression would affect parents' ability to encourage and enforce regular use of medication. On the other hand, symptom reports were related to both parent and child negative affect, which could be interpreted as worse symptoms being depressing or those with depressive symptoms interpreting symptoms more negatively. A third possibility was not explored: poor asthma control and negative affect may result, at least in part, from a common exposure outside the treatment setting and unrelated to asthma or asthma care per se.

In the asthma literature, *exposure* usually refers to an environmental antigen or irritant. *Psychosocial exposures* refer most typically to institutional, infrastructure, community, or interpersonal sources of stress. Examples include community violence, racism, and differential access to treatment and services (municipal services such as police protection or garbage pick-up in addition to health care itself).

The point is that health outcomes are a small part of a much larger context. If that is the case, then the context is shared across health conditions, not just asthma. Fig 2^{4,5} shows the covarying trends in asthma and obesity over a similar period. Are these coincidental, interdependent, or different reactions to a similar context?

We do not know the answer, of course. An intriguing hypothesis is that physiological inflammatory pathways are activated under conditions of insufficiently buffered stress, leading to multiple opportunities for poor outcomes, with genetics playing a role in the expression. Chen et al⁶ recently showed (1) lack of family support was related to increased asthma symptoms and decreased pulmonary function via allergic inflammation, and (2) more neighborhood problems led to increased morbidity via health behaviors (smoking). In other words, more richly defined predictive models encompass community variation and family and individual processes that lead to physiological change. With better precision about the social and physical environment, intervention strategies could be tailored for an impact on specific contextual influences.

There are a number of key elements to consider in the design and analysis of studies intending to model the social and physical context as predictors of health outcomes. Population-representative samples are most desirable, to have the representation of the range of outcomes given a common context, and to have the greatest generalizability. Short of being population-representative, well designed comparison groups will help explain how the context leads to poor outcomes for some but not others. For example, studies of clinical samples have suggested high rates of

From the Feinberg School of Medicine, Northwestern University; and the Department of Pediatrics, Evanston Northwestern Healthcare Research Institute.

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Reprint requests: Madeleine Ullman Shalowitz, MD, MBA, Department of Pediatrics, Northwestern University, Feinberg School of Medicine, Evanston Northwestern Healthcare Research Institute, 2650 Ridge Ave, Evanston, IL 60201. E-mail: m-shalowitz@northwestern.edu.

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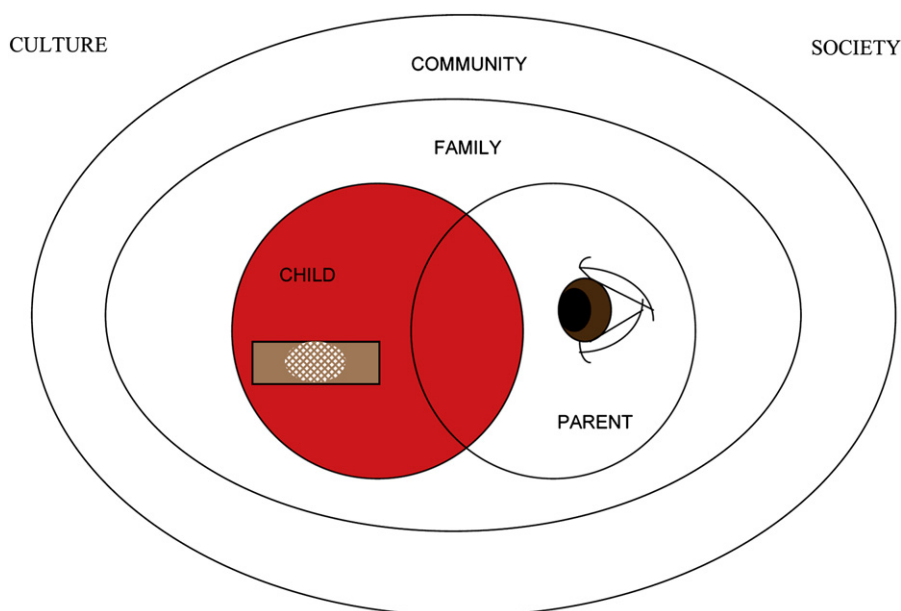


FIG 1. A contextual model of childhood chronic illness illustrates how a disorder such as asthma is an attribute of the child nested in increasingly larger, mutually interactive systems that influence the burden of illness.

maternal depression in women whose children have asthma. In a recent community-based study of asthma and maternal depression, Shalowitz et al⁷ showed that maternal depression was high in the population as a whole, but it was the mother's child's poor health, not the diagnosis of asthma per se, that was associated with symptoms of depression.

Reliability in measurement can be improved by using observable and quantifiable phenomena, not just the respondent's interpretation based on their feelings or recall. In a recent review, Gossec et al⁸ demonstrated the range of methods for measuring adherence in chronic illnesses, including asthma. Bender and Zhang¹ used an electronic tracking device on the metered-dose inhalers. Studies evaluating psychosocial outcomes in asthma often use ordinal scales to measure such constructs as affective states, perceptions, or quality of life. Frequently one instrument is a predictor and the other an outcome. An item-by-item comparison often reveals that the questions are very similar across instruments, and this creates problems interpreting whether there is clinical meaning when associations are statistically significant. Furthermore, there is the potential for respondent bias. For example, a depressed mother may perceive that her child's quality of life is lower, or that symptoms are more serious than they actually are.

Teasing out these relationships can be managed analytically, although not perfectly. For example, in cross-sectional studies, one might choose simply to control for maternal mental health in predictive models. Others have used structural equation modeling to sort through the interrelationships. Structural equation modeling requires a hypothetical model that specifies the anticipated relationships and the order in which they have influence, typically on the basis of history or the degree to which they can be modified. Thus, because sex and other genetic determinants are predetermined and unmodifiable, they are "upstream" in the model. Mood changes from moment to moment are more "downstream," and the outcome, in this case, asthma control, is the furthest downstream. Structural equation modeling analyses test the

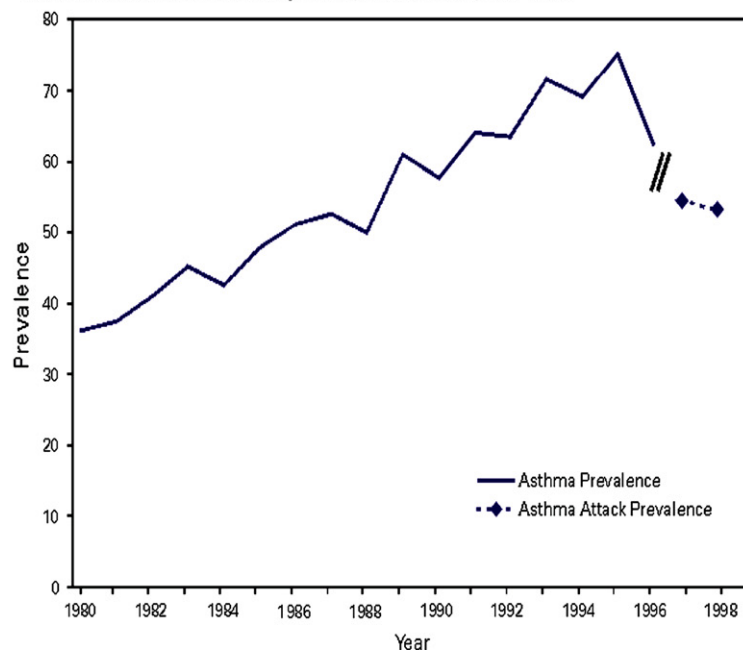
interrelationships among the predictors in the order in which the model specifies, and then the strength of the model as a whole is calculated. In 2 recent articles, Lim et al⁹ and Wood et al¹⁰ demonstrated in a cross-sectional sample that maternal depression does not have a relationship to children's asthma disease activity through adherence. Rather, maternal depression relates to the children's disease activity by having a direct and indirect relationship to children's internalizing symptoms, which then has a relationship to their disease activity.

There is a variety of sophisticated regression techniques that enter sets of variables in steps, and also account for the loss of independence of the predictors from one another that occurs when there are shared characteristics in the sample that are either known or unknown. Some common terms are *fixed effects*, *random effects*, and *hierarchical linear models*.

Finally, although the holy grail in research is causality, proving causality with a larger social and physical context is difficult if not impossible, except with an intervention study and a longitudinal design. Social scientists have developed numerous statistical techniques to make predictions with a higher level of assurance. Establishing a statistically significant relationship with temporal precedence makes a stronger case for the relationship being more than coincidental. Bender and Zhang¹ use 1 of these techniques, lagged analysis, to evaluate depressive symptoms at baseline and adherence and control over the subsequent period. They also used regression techniques that may be less familiar to medical scientists because they take into account repeated measures in the same participant (the lagged analysis was repeated more than once in the same participant in sequential observation periods) as well as comparisons between participants.

To evaluate hypotheses that are more complex, more sophisticated methods are required. It is unlikely that individual scientists have all of the necessary expertise. As a manuscript reviewer, I commonly ask that social scientists enlist the aid of medical scientists and vice versa. Social scientists choose

Asthma
Prevalence* of childhood asthma among persons aged 0–17 years, by year —
National Health Interview Survey (NHIS), United States, 1980–1998†



* Per 1000 population.

† NHIS was redesigned in 1997, resulting in a discontinuation of the trend.

Overweight/Obesity

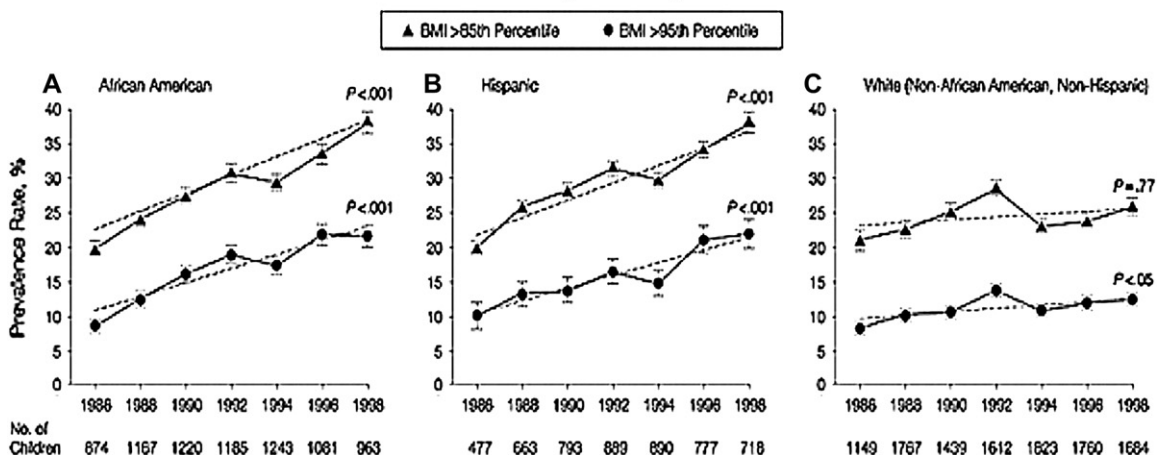


FIG 2. Trends in childhood asthma prevalence (1980–1998; Mannino DM, Homa DM, Akinbami LJ, Moorman JE, Gwynn C, Redd SC. Surveillance for asthma—United States, 1980–1999. *MMWR Surveill Summ* 2002;51:1–13⁴) and childhood obesity prevalence (1986–1998; Strauss RS, Pollack HA. Epidemic increase in childhood overweight, 1986–1998. *JAMA* 2001;286:2845–8⁵). Reproduced with permission. BMI, Body mass index.

statistical tools based on the characteristics of the sample and the variables, and the questions to be answered. They also may have preferences based on their statistical world view. Thus a biostatistician, an economist, and a policy analyst may develop somewhat different analytic plans.

Asthma is a chronic disorder that represents well the complexity of interactions among the biological, the psychosocial, and the physical environment. Advances in medicine and the social and statistical sciences offer the opportunity to build a more sophisticated understanding of these interactions and how they affect individuals clinically and the health of the population.

Interdisciplinary collaboration in asthma research shows great promise for synergy and will undoubtedly yield a richer, more sophisticated understanding of how to improve the lives of families with asthma.

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