

overestimate the number of factors to retain (3). So, our methods were actually more thorough than using Kaiser's criterion on its own. Ultimately, our decision to choose two principal components was clear when we considered the scree plot, in which the first component was the vegetable–fruit–soyfood pattern and the second component was the dim sum–meat pattern, and interpretability of the components.

The second issue raised suggests that our findings lack “statistical rigor,” because we did not adjust for multiple comparisons. Ironically, we chose to use the principal components method, because it is a solution to the multiple comparisons problem that can occur in conventional analyses of nutritional epidemiologic data. For example, by using principal components analysis, we reduced the extensive dataset of 165 food and beverage items to only two components representing dietary patterns. This is hardly an example of multiple comparisons even when looking at five outcomes. The conventional method would have been to examine each of the items individually in relation to each of the outcomes. In that setting it might have made sense to adjust for multiple comparisons even though it would not be standard in our field when evaluating observational (e.g., nonrandom) data (4, 5). Teo and Chong also suggest that our examination of several outcomes contributes to the problem of multiple comparisons. As we indicated in the introduction to our article (2), we examined dietary patterns in relation to cough with phlegm to follow up on our previous finding of an inverse association between fiber intake and that outcome. We included all of the other respiratory outcomes for completeness and based on requests during the review process. In summary, we incorporated the suggested Kaiser's criterion to decide on the number of components, and we avoided multiple comparisons by using principal components analysis.

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Does Most Asthma Really Begin during the Preschool Years?

To the Editor:

Prospective population-based studies, such as that of Morgan and colleagues (1) describing the natural history of asthma to age 16, are important to avoid bias from (1) studies of referred patient populations that are prone to sampling bias (“referral” bias) and bias from (2) retrospective medical record reviews that are prone to ascertainment and “diagnostic” bias.

In their Introduction, Morgan and coworkers stated: “It now seems established that, in the majority of cases of persistent asthma, symptoms begin during the preschool years....” (1) However, their data indicate that less than half of adolescent asthma was present at age 3. At all ages up to 16, “late-onset wheeze” (at age 6 but not at age 3) was numerically greater than “persistent wheeze” (present at age 3) (Table 1). At ages 13 and 16, there were more infrequent and frequent wheezers in the two “preschool phenotypes” labeled “non-wheezers” (at ages 3 and 6) and late-onset wheezers combined than in the “transient early wheezers” (at age 3) and persistent wheezers (Figure 2). These data suggest that the majority of adolescent asthma was not present in children whose first symptoms began in the preschool years (age 3, as compared with age 6 or later).

Morgan and coworkers cited an editorial (2) referencing Yunginger and colleagues (3) to support the statement that “most persons of any age who have chronic, persistent asthma have their first symptoms during their preschool years (2).” However, Yunginger and coworkers (3) performed a medical record review that is inherently subject to ascertainment bias. They also excluded asthma in any subject with an FEV₁ less than 50% (this “diagnostic bias” will exclude adult asthma associated with fixed obstruction [4]). In the absence of a physician diagnosis, they accepted nonsmoking and several markers of clinical atopy as adjunctive criteria to classify “definite” asthma. A meta-analysis casts doubt that asthma is predominantly an atopic disease (5). Hence, including atopy (and, I would add, nonsmoking) as a “tie-breaker” to identify asthma also introduces diagnostic bias against adult asthma, the majority of which is clinically non-atopic. On the other hand, a more rigorously designed, prospective, population-based study documented a stable incidence of asthma (0.30–0.35 per 100 subject years) throughout adulthood (6). My conclusion is that it may not be so well established that most asthma begins in the preschool years, or even in childhood. What do the authors think?

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From the Authors:

Dr. Hahn raises an important point regarding our recent article (1), which deserves clarification. As he notes, we state in the introduction that it now seems established that the majority of cases of persistent asthma begin during the preschool years. Perhaps better would have been "by the age of six" or "by the first grade," which our data strongly support. Indeed, our conclusion was more precise in stating that both lung function characteristics in early infancy and events occurring during the first six years of life determine the expression of asthma and the level of lung function that will be achieved during childhood and into early adult life.

We agree that of those children with current wheeze at age 16, only 40% wheezed in the first three years of life; however, 68% were wheezing by age 6. Further, of those with frequent wheezing at age 16, 79% were transient, persistent or late onset wheezers. Some of these children likely began wheezing in their fourth or fifth year of life, but certainly all had wheezed by the first grade.

In our paper, we did not address the prevalence or immune or physiologic characteristics of asthma in adulthood. We recognize that there is a continued low stable incidence of asthma during the adult years as reported by our colleagues (2). We are continuing to follow our cohort and will evaluate the nature of incident asthma in adulthood as we have done in relation to obesity and puberty (3, 4). Nonetheless, our data clearly demonstrate that the majority of wheeze occurring during adolescence began by age 6. More importantly, we have been able to demonstrate that deficits in lung function related to asthma, as described in other longitudinal population studies (5, 6), appear to occur prior to age 6 and remain stable through adolescence. As noted in our paper, we are concerned that even the transient wheeze group, demonstrating diminished lung function, but rates of atopy similar to the never-wheeze group, may be at risk for later pulmonary disease (7).

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expenses, totaling \$8,482. In August 2005, he traveled to South Africa for the Allergy Society of South Africa Annual Meeting, which was partially sponsored by Merck South Africa. For this, his airline ticket was purchased by Merck directly and he received a small honorarium totaling \$2,500. In September 2005, he participated in a Pfizer Advisory Board and received honorarium payment of \$3,000. In 2005 he provided consultation services for Genentech teleconference. For these services, he was compensated \$300. Although he is a member of the Pulmonary Advisory Board for Xolair, he has not yet participated in any meetings and has not received any financial support related to this board. Similar to his participation in the Genentech Advisory Board, he is a member of the AltanaPharma Global Advisory Board for Roflumilast but has not yet attended any meetings or provided any services related to this board. No monies have been received from AltanaPharma. He has not participated in any events or received any financial contribution from AstraZeneca since 2003. In 2003, he presented a talk in Phoenix, AZ at an event sponsored by GlaxoSmithKline. For his lecture, he received an honorarium of \$1,500. No additional participation or financial relationship has existed in the years following. The small grants received from commercial entities in the name of Dr. Martinez are deposited directly into University Foundation accounts used for the sole purpose of continuing education at the University of Arizona, Arizona Respiratory Center. These are listed on Dr. Martinez's disclosure because he is the Director of the Center, and therefore, the responsible party. There is no direct financial relationship between Dr. Martinez and the financial sponsors of the recipient education programs. The pending patent is in direct relation to a grant funded by the National Institutes of Health. No commercial entity is currently associated.

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