

We feel strongly that public policy is the key to eradicating the HPV epidemic. Legislation and official recommendations are crucial to determining HPV vaccination rates, and are areas where otolaryngologists currently lack voice. We can and should take part in the national conversation. The CDC's Advisory Committee on Immunization Practices (ACIP) is responsible for all national vaccination guidelines, and currently lacks representation from all surgical fields except obstetrics and gynecology.⁵ Representation by the American Academy of Otolaryngology-Head and Neck Surgery or the American Head and Neck Society on committees like ACIP are necessary to providing surgical insight into vaccine prophylaxis of this preventable disease. There is still much work to be done in the fight against HPV. Nevertheless, if otolaryngologists begin to tackle the problem at all levels, we have the potential to greatly reduce HPV-associated OPSCC in the United States.

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Limitations to the Association of Risk of Airway Disease With Removal of Adenoids and Tonsils in Children

To the Editor The conclusion by Byars et al¹ that the children who have had adenoidectomy and/or tonsillectomy are at a greater lifetime risk of airway disease may be supported by their data; however, their implication that surgery is causally related to this incidence is unfounded.

Baseline characteristics of the control and intervention groups in this study are likely significantly different. A significant proportion of children undergoing adenotonsillectomy have a predisposition to airway diseases (asthma, allergy, and

sinusitis) and recent publications point to a shared etiology with sleep-disordered breathing.² Owing to difficulties identifying asthma under the age of 5, most national guidelines do not allow for diagnosis³—invalidating any estimates of incidence prior to this age. Because the surgical arm of this cohort had an underlying predisposition to airway diseases (visible as the extra disease burden of around 1-in-5 identified in the study), the so-called causality is incorrect. The appropriate control group would be patients meeting criteria for surgery but not having it, so both groups are exposed to the same predisposition.

The statement “participants in the case and control groups were selected such that their health did not differ significantly prior to surgery”^{1(e1)} is misguided, and may have arisen from a lack of clinical involvement in design and publication of this study. The authors “only included those not diagnosed with the outcome diseases prior to surgery in the first 9 years,”^{1(e2)} which both nullifies the assessment of benefit of surgery in those already diagnosed with reactive airway diseases and misses those with reactive airway disease not formally diagnosed (at a likely greater rate in the intervention groups).

Diagnosis of atopic disease has increased since the study period (1979-1999) owing to contemporary practices of skin prick or RAST testing in children presenting with sleep-related breathing disorders.⁴ The findings of an increased incidence of airway diseases is contradicted by level 1 evidence demonstrating improved asthma outcomes after adenotonsillectomy.⁵

Additional concerns regarding the authors' conclusions, include:

- Chronic obstructive pulmonary disease and conjunctivitis risk without plausible mechanism or parental smoking history.
- “Abnormal breathing” is neither a clinically useful term nor relatable to a disease.
- “Current research suggests that tonsils and adenoids play specialized roles in immune system development and function” (reference from 1934, not current).^{1(e2)}
- “Improvements in sleep apnea of children may be less than hoped for”^{1(e2)} (reference actually states adenotonsillectomy “still offers significant improvements in AHI, making it a valuable first-line treatment for pediatric OSAHS”).⁶⁽⁸⁰⁰⁾

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1. Byars SG, Stearns SC, Boomsma JJ. Association of long-term risk of respiratory, allergic, and infectious diseases with removal of adenoids and tonsils in childhood. *JAMA Otolaryngol Head Neck Surg.* 2018;144(7):594-603.
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To the Editor Byars et al¹ recently published a large case-control study based on data from Danish health registries. We believe that several important limitations in the study need to be addressed.

In Denmark, all information, including diagnoses, related to hospital visits, is registered in the Danish National Patient Registry (DNPR).² Information on patient contacts and medicine use in the primary sector (general practice and specialist care) is recorded in the National Health Security Registry (NHSR) and National Prescription Registry (NPS), respectively.²⁻⁵

In the article by Byars et al,¹ it is stated that the information on diagnoses and operations was obtained from the DNPR. However, the DNPR has limitations. Most cases of rhinitis, otitis media, upper airway infections, less severe cases of allergy and asthma, etc, are treated successfully in the primary sector by general practitioners and specialist physicians (eg, ear, nose, throat [ENT]) without referral to hospitals. Hence, these patients do not appear in the DNPR, but only in the NHSR and NPR. Based on the information obtained from the article by Byars et al,¹ these registries have not been explored. This will result in a substantial risk of selection bias (most likely causing reverse causality) in the preoperative analysis of morbidity, as well as in the diagnoses made in the observation period postoperatively.

In Denmark, most adenoidectomies and, to a lesser extent tonsillectomies and/or tonsillotomies, are performed in an ENT specialist office, which means that these procedures are not reported to the DNPR, but only to the NHSR.^{2,4} We estimate that during the 30-year period from 1979 to 2009, ENT specialist offices performed at least 200 000 to 250 000 adenoidectomies in children aged 9 years or older, which are not registered in the DNPR. We suspect that the most patients who underwent surgery in an ENT specialist office are to be found in the group that Byars et al¹ have defined as controls.

In addition, children referred to and who underwent surgery in hospitals are most likely selected according to comorbidities. A frequent reason for having adenoidectomy performed in a hospital is higher risk of complications, owing to either the surgical procedure itself or the anesthesia. This also introduces a high risk of systematic selection bias in the study.

We believe that using the DNPR as the only source of outcome diagnoses and operations has introduced substantial and unpredictable bias into the study by Byars et al. The conclusions made by the authors may therefore not be valid.

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In Reply Four main issues were raised by Kitipornchai and Mackay and Lüscher et al. All of them appear invalid as challenges of our main results.¹

1. Our study¹ rigorously accounted for the biases mentioned by Mackay and Kitipornchai. We tested for differences in baseline characteristics ensuring that control/intervention groups did not differ presurgery, which protected our analyses against pre-existing differences in health burden, ie, selection bias. Denmark comprehensively tracks individual health/disease from birth to death because free health care requires registration for all hospital-related diagnoses. The validity of these records is therefore unaffected by socioeconomic status as in most other countries, particularly the United States. These circumstances enabled us to employ multiple controls¹ protecting considerably against confounding, reverse causality and measurement bias.

2. There is good independent support for the risk associations that we uncovered. Two short-term observational studies show positive associations between these surgeries and later airway diseases, including asthma.^{2,3} Two additional larger, longer-term national cohort studies⁴ (and Janzsky et al, 2011; cited in our study) also tend to support our conclusions. Our study shows that benefits of surgery are ambiguous for otherwise healthy children; Mackay and Kitipornchai refer to cases where health is already compromised before surgery.

3. The Danish National Patient Registry (DNPR) has sufficient identification and classification of diagnoses. Extensive reviews of DNPR performance—across all ICD diagnosis groups including more than 380 estimates from Table S1 in Schmidt et al, 2015 (reference 2 cited by Lüscher et al)—allowed us to estimate mean positive predictive value (PPV), 76 (95% CI, 73%-78%); sensitiv-

ity, 65 (95% CI, 58%-71%); and specificity, 98 (95% CI, 97%-99%) for all public health analyses. The 79 estimates across surgeries yielded means that were even higher (PPV, 87; 95% CI, 80%-93%; sensitivity, 82; 95% CI, 73%-91%; specificity, 98; 95% CI, 97%-100%), protecting against missing/misclassified data.

Another DNPR study estimated that asthma risk associations only become inaccurate when low sensitivity (<20%) and low specificity (<85%) occur jointly.⁵ Because our study considerably surpassed that threshold, we had more than adequate capture/classification of diagnoses to avoid data inaccuracies or biases to an extent that would have changed our overall conclusions based on reported risk magnitudes and *P* values.

4. Lüscher et al extrapolate backward without mentioning that we captured most surgery data in the years examined. Vestergaard et al⁶ (who accessed all Danish registries—DNPR and National Health Security Registry [NHSR]—containing surgery data) document that few (adeno)tonsillectomies were performed as hospital-based outpatient surgeries or privately between 1970-2000. We compared their complete surgery data with our (adeno)tonsillectomy numbers, which showed that we captured 144 104 of those 153 212 surgeries, a sensitivity of 94%. There are also 87 834 DNPR-recorded adenolectomies between 1979-1999—converting Lüscher et al's unreferenced 30-year estimate to these 20 years gave a sensitivity of 53%-66% and a specificity of 97%-98% for DNPR-recorded adenolectomies included in our study,¹ giving no reason for concern.

Our study,¹ and the clarifications above, thus indicate that our conclusions are both robust and sufficiently supported by previous studies to suggest that rethinking long-term risks of surgical removal of immune organs, whose functional importance has substantial recent support (ie, Brandtzaeg 2003, citation 1 in our study), is warranted.

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CORRECTION

Misspelled Surname in Byline and Author Contributions: In the article titled "Opioid Prescribing Practice and Needs in Thyroid and Parathyroid Surgery,"¹ an author's surname was misspelled in the initial online publication. "Quintanilla-Diek" has been corrected to "Quintanilla-Dieck" in both the article byline and author contributions. This article was corrected online.

1. Shindo M, Lim J, Leon E, Moneta L, Li R, Quintanilla-Dieck L. Opioid prescribing practice and needs in thyroid and parathyroid surgery [published online October 25, 2018]. *JAMA Otolaryngol Head Neck Surg*. doi:[10.1001/jamaoto.2018.2427](https://doi.org/10.1001/jamaoto.2018.2427)