Analysis of Value-Based Costs of Undesignated School Stock Epinephrine Policies for Peanut Anaphylaxis

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IMPORTANCE Children experiencing anaphylaxis at school may lack access to a personal epinephrine device, prompting recent legislation permitting undesignated (eg, non–student specific) stock epinephrine autoinjector units at school. However, epinephrine device costs vary, and the cost-effectiveness of undesignated school stock epinephrine is uncharacterized to date.

OBJECTIVE To define value-based strategies for undesignated school stock epinephrine programs.

DESIGN, SETTING, AND PARTICIPANTS Markov simulations of the Chicago Public Schools system were used over extended time horizons to model 2 school stock epinephrine autoinjector policies to provide access for at-risk students. The dates of the data used in the analysis were September 2017 to June 2018 (the 2017-2018 school year).

MAIN OUTCOMES AND MEASURES This study compared the following 3 strategies: no school undesignated epinephrine supply, school undesignated supplemental epinephrine supply (supplemental model), and school undesignated universal epinephrine supply (universal model). The base-case model assumed a 10-fold reduced fatality risk with having undesignated stock epinephrine units available vs not having undesignated stock epinephrine units available. Costs of school stock epinephrine units available for acquisition by schools were evaluated from a societal perspective. Quality-adjusted life-years (QALYs) and total epinephrine acquisition expenses were calculated.

RESULTS Based on Markov simulations of the Chicago Public Schools system (371,382 students), the cost was $107,816 (95% CI, $107,382-$108,250) for no school undesignated epinephrine supply compared with $108,160 (95% CI, $107,725-$108,595) for the supplemental model and $100,397 (95% CI, $99,979-$100,815) for the universal model. Undesignated stock epinephrine improved outcomes, with 26.869 (95% CI, 26.841-26.897) QALYs accrued as the model concluded compared with 26.867 (95% CI, 26.839-26.896) QALYs for the strategy without undesignated stock epinephrine. When comparing supplemental model stock epinephrine to the strategy without undesignated devices, the incremental cost-effectiveness ratio was high at $268,811 per QALY in the base-case simulation. However, the cost of the supplemental model fell below $100,000 per QALY when the annual undesignated epinephrine acquisition costs did not exceed $338 per school (compared with stock epinephrine unavailability). The universal model dominated all others and was associated with significant cost savings ($7419 per student at risk who would otherwise be prescribed an individual school epinephrine supply).

CONCLUSIONS AND RELEVANCE Undesignated school stock epinephrine is cost-effective at device acquisition costs not exceeding $338 per school per year, although a universal model vs a supplemental model is associated with superior health and economic outcomes.
Legislation to either permit or mandate school-based stock epinephrine programs has emerged to provide timely access to epinephrine for children with known anaphylaxis risk and for children without documented risk given that as many as 25% of first-time anaphylactic reactions occur in school (inclusive of both adults and children at the school). Because food allergy is estimated to affect up to 8% of US children (approximately 5.9 million children younger than 18 years and 3.3 million children aged 6 to 17 years) and because not all allergic children have a personal epinephrine device available at school at all times (although this is recommended), these programs can enable access to an epinephrine device and facilitate appropriate anaphylaxis management in the school setting. In a study of the Chicago Public Schools system voluntary stock epinephrine policy and outcomes, DeSantiago-Cardenas and colleagues reported that 38 stock autoinjectors were administered in the first year of the program. Students received 92.1% (35 of 38) of the epinephrine administrations, while 7.9% (3 of 38) of the epinephrine units were administered to nonstock epinephrine administrations, while 7.9% (3 of 38) of the epinephrine units were administered to reported first-time anaphylactic reactions, including 21 of 38 cases for reactions attributable to food, 2 of 38 cases for venom, 2 of 38 cases for an inhalant allergen, and 13 of 38 cases for undocumented triggers.

Recent controversies have emerged around the cost escalation of epinephrine autoinjectors, and ongoing and future cost inflation could pose a barrier to epinephrine access in some settings, as could interruption to supply (experienced for Auvi-Q [Kaléo] and more recently for EpiPen [Mylan N.V.]). Evidence suggests that significant variability exists in epinephrine autoinjector cost in relation to brand, insurance coverage, and discount coupon availability. Because wide variation in epinephrine autoinjector device costs exists, we undertook Markov simulations of the Chicago Public Schools system to further characterize the value-based costing of undesignated school supplies of emergency epinephrine and to explore an optimal stock epinephrine policy. The objective of this study was to define value-based strategies for undesignated school stock epinephrine programs.

**Methods**

**Study Design**

Computer-based mathematical microsimulations (TreeAge Pro 2018; TreeAge Software, Inc) were used to evaluate hypothetical cohorts of children with peanut allergy from kindergarten through high school graduation, with a continued horizon to age 80 years (eFigure in the Supplement). Markov models are well suited to health care simulations and were used because they can account for the annual costs and recurrent risks of peanut exposure and reactions, allowing transitions between different health states. The dates of the data used in the analysis were September 2017 to June 2018 (the 2017-2018 school year). According to the criteria of the Colorado Multiple Institutional Review Board, this study was exempt from institutional review board review.

**Undesignated School-Based Epinephrine Strategies Compared**

We compared different approaches to undesignated school-based epinephrine policies. Because many children who experience anaphylaxis in the school setting are treated with school devices, we chose to compare supplemental and universal stocking practices. The study compared the following 3 strategies: (1) no school undesignated epinephrine supply, in which the only devices available are personal autoinjectors provided by students with an allergic condition; (2) school undesignated supplemental epinephrine supply, in addition to student-supplied devices (supplemental model); and (3) school undesignated universal epinephrine supply, in which school-based devices supplant the need for student-supplied devices (universal model). In the supplemental model, in addition to the school receiving an annual supply of 2 twin packs of undesignated stock epinephrine, children with peanut allergy attending school also received an annual prescription of an epinephrine twin pack dedicated for exclusive use at school (which is not available for at-home use and requires that an extra unit be dispensed as part of the prescription) per the current policy; after high school graduation, they received an annual prescription for a single twin pack (because colleges and universities do not have stock policies and because this is the typical management for peanut-allergic adults). The current practice in the 49 states with stock epinephrine law is the supplemental model; before the first stock legislation in 2011, no stock epinephrine was available, and allergic individuals provided their own units for school in every state. We are unaware of any state or school district using the universal model. Because individual epinephrine prescriptions are often not available or carried when needed for anaphylaxis, it was assumed that having undesignated stock epinephrine units available would be associated with a 10-fold overall risk reduction in fatality among school-age children compared with not having undesignated stock epinephrine units available. This assumption is based on prior publications, intended to be deliberately conservative, and represents an estimate of a plausible range given that no study to date has defined the fatality risk reduction attributable to having epinephrine available (or could ethically do so). Home epinephrine autoinjector twin packs were prescribed to every allergic child in all strategies compared because this is the standard...
of care independent of any stock epinephrine strategy modeled. We assumed that all schools assigned to each strategy compared adopted their assigned approach to stocking epinephrine.

**Assumptions**

Base-case assumptions and probabilities were derived from similar prior cost-effectiveness analyses of peanut-allergic children (Table 1). In all strategies, children who received epinephrine at school were transported to and seen in an emergency department for evaluation and management per current guideline recommendations. The incidence of pediatric food allergy fatality was modeled at 3.25 cases per 1 million at-risk person-years for school-age children without school-based epinephrine and at 3.25 cases per 10 million at-risk person-years for school-age children with access to undesignated school-based epinephrine. We modeled a high rate of children at risk for anaphylaxis (prevalence rate, 8%; range, 5%-11%) to account for other children without peanut allergy who may also experience anaphylaxis in the school setting. Costs of school stock epinephrine units available for acquisition by schools were evaluated from a societal perspective among this population, and it was assumed that all students would have the stock epinephrine device administered for treatment of a reaction occurring at school, irrespective of that student also having supplied his or her own personally designated unit at school (to achieve model parsimony). For these calculations, 2 epinephrine twin packs costing $715 (95% CI, $685-$743) per package were procured annually for each school per year based on the Chicago Public Schools system (646 schools, 371382 students, 30622 school-based emergency department at-risk person-years (sensitivity, 3.25 to 33)).

Table 1. Simulation Model Inputs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model Reference</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of food allergy fatality</td>
<td>5 to 19 y: 3.25 (95% CI, 1.73 to 6.10) cases per 1 million at-risk person-years (sensitivity, 3.25 to 33); ≥20 y: 1.81 (95% CI, 0.94 to 3.45) cases per 1 million at-risk person-years (sensitivity, 1.81 to 18.1)</td>
<td>Umasanthar et al, 2013</td>
</tr>
<tr>
<td>Probabilities, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unintentional peanut exposure if allergic</td>
<td>11.7 Per year (sensitivity, 5 to 50)</td>
<td>Vander Leek et al, 2000</td>
</tr>
<tr>
<td>Moderate to severe reaction after peanut exposure</td>
<td>52 (sensitivity, 10 to 70)</td>
<td>Vander Leek et al, 2000</td>
</tr>
<tr>
<td>Hospitalization after severe food-allergic reaction</td>
<td>0.18 Per year after allergic reaction (sensitivity, 0.16 to 0.20)</td>
<td>Shaker, 2017</td>
</tr>
<tr>
<td>Outpatient visits for food allergy after allergic reaction</td>
<td>20.4 Per year after allergic reaction (sensitivity, 20.0 to 21.0)</td>
<td>Shaker, 2017</td>
</tr>
<tr>
<td>Spontaneous peanut tolerance</td>
<td>1.1 Per year (age range, 5 to 20 y) (sensitivity, 0.5 to 2)</td>
<td>Skonick et al, 2001</td>
</tr>
<tr>
<td>Students at risk for anaphylaxis</td>
<td>8 (range, 5 to 11)</td>
<td>Gupta et al, 2011</td>
</tr>
<tr>
<td>Costs, 2018 US $</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal epinephrine autoinjector (annual cost per twin pack)</td>
<td>715 (95% CI, 685 to 741)</td>
<td>Shaker et al, 2017</td>
</tr>
<tr>
<td>Undesignated school epinephrine</td>
<td>1430 Per school (shared by total No. of children at risk in each school)</td>
<td>Shaker et al, 2017; Gupta et al, 2011; Chicago Public Schools</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>5899 (95% CI, 5732 to 6066)</td>
<td>Patel et al, 2011; Bureau of Labor Statistics</td>
</tr>
<tr>
<td>ED visit</td>
<td>691 (95% CI, 689 to 693)</td>
<td>Patel et al, 2011; Bureau of Labor Statistics</td>
</tr>
<tr>
<td>Outpatient visit for food-allergic reactions</td>
<td>235 (sensitivity, 225 to 245)</td>
<td>Patel et al, 2011; Bureau of Labor Statistics</td>
</tr>
<tr>
<td>Ambulance runs for allergic reactions</td>
<td>573 (sensitivity, 512 to 632)</td>
<td>Patel et al, 2011; Bureau of Labor Statistics</td>
</tr>
<tr>
<td>Pediatrician visits (mean incremental annual cost for food allergy diagnosis)</td>
<td>100 (sensitivity, 94 to 105)</td>
<td>Bureau of Labor Statistics; Gupta et al, 2013</td>
</tr>
<tr>
<td>Allergist visits for food allergy (mean incremental annual cost for food allergy diagnosis)</td>
<td>149 (sensitivity, 143 to 155)</td>
<td>Bureau of Labor Statistics; Gupta et al, 2013</td>
</tr>
<tr>
<td>Nutritionist visits for food allergy (per year)</td>
<td>17 (sensitivity, 15 to 18)</td>
<td>Bureau of Labor Statistics; Gupta et al, 2013</td>
</tr>
<tr>
<td>Alternative health care professional visits for food allergy (per year)</td>
<td>25 (sensitivity, 22 to 27)</td>
<td>Bureau of Labor Statistics; Gupta et al, 2013</td>
</tr>
<tr>
<td>Incremental annual grocery costs (living with food allergy)</td>
<td>310 (sensitivity, 290 to 330)</td>
<td>Bureau of Labor Statistics; Gupta et al, 2013</td>
</tr>
<tr>
<td>Job-related opportunity costs from food allergy (per year)</td>
<td>2597 (sensitivity, 2450 to 2744)</td>
<td>Bureau of Labor Statistics; Gupta et al, 2013</td>
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<tr>
<td>Additional Assumptions</td>
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<td>Fatality reduction from undesignated school stock epinephrine</td>
<td>10-fold (sensitivity, 10-fold to 100-fold)</td>
<td>NA</td>
</tr>
<tr>
<td>Start age, y</td>
<td>5 (sensitivity, 3 to 7)</td>
<td>NA</td>
</tr>
<tr>
<td>Annual discount rate</td>
<td>0.03 (sensitivity, 0 to 0.03)</td>
<td>Bureau of Labor Statistics</td>
</tr>
<tr>
<td>Negative health state consequence for food allergy</td>
<td>−0.09 (sensitivity, −0.02 to −.11)</td>
<td>Mittman et al, 1999; Carroll and Downs, 2009</td>
</tr>
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Abbreviations: ED, emergency department; NA, not applicable (meaning that this was an assumption we made and there is no source).
Results

In the base-case simulation, the cost was $107,816 (95% CI, $107,382–$108,250) for no school undesignated epinephrine supply compared with $108,160 (95% CI, $107,725–$108,595) for the supplemental model and $100,397 (95% CI, $99,979–$100,815) for the universal model. Health outcomes were better with undesignated stock epinephrine, with $26,869 (95% CI, $26,841–$26,897) QALYs accrued as the model concluded compared with $26,867 (95% CI, $26,839–$26,896) QALYs for the strategy without undesignated stock epinephrine.

Under base-case assumptions, the supplemental model was not cost-effective compared with no school undesignated epinephrine supply (base-case incremental cost-effectiveness ratio, $268,811 per QALY (Table 2). However, in sensitivity analyses for this comparison, if the annual undesignated epinephrine acquisition costs to the school did not exceed $338, the supplemental model was a cost-effective public health policy, assuming a willingness-to-pay threshold of $100,000 per QALY (Figure 1). Assuming a lower willingness-to-pay threshold of $50,000 per QALY, then the value-based annual undesignated epinephrine acquisition ceiling costs fell to $162. In addition to epinephrine acquisition costs, the base-case model was also sensitive to fatality rates from anaphylaxis. At a pediatric fatality incidence of 1.37 cases per 100,000 person-years, the supplemental model is cost-effective at base-case model epinephrine school acquisition costs (willingness-to-pay, $100,000 per QALY and quality-adjusted life-year). ICER indicates incremental cost-effectiveness ratio. The universal model dominated across all sensitivity ranges.

Figure 1. Sensitivity Analysis on Cost of School Epinephrine, Assuming a Willingness-to-Pay Threshold of $100,000 per Quality-Adjusted Life-Year

School undesignated supplemental epinephrine supply is cost-effective when the annual school epinephrine expenditures do not exceed $338 per school (dashed line). The vertical dashed line indicates the intersection of the 2 colored lines, representing the device price threshold at or below which the current policy is cost-effective.

Gray bars show values above the base-case assumptions, while blue bars show values below the base-case assumptions. When the pediatric fatality incidence exceeds 1.37 cases per 100,000 person-years, the supplemental model is cost-effective at base-case model epinephrine school acquisition costs (willingness-to-pay, $100,000 per QALY and quality-adjusted life-year). ICER indicates incremental cost-effectiveness ratio. The universal model dominated across all sensitivity ranges.
universal model epinephrine strategy to be optimal in 99.9% of iterations (Figure 3).

Discussion

Access to epinephrine is a critical issue for children at risk for anaphylaxis; because many allergic children may potentially attend school without having an available personal epinephrine auto-injector, a stock supply of school autoinjectors can potentially be a lifesaving intervention. At a value-based annual total school epinephrine acquisition expense not exceeding $338 per school per year, the supplemental model (school undesignated supplemental epinephrine supply) is a cost-effective societal intervention compared with no school undesignated epinephrine supply. However, the universal model (school undesignated universal epinephrine supply) available for any student at school with known or unknown allergy risk—that replaces having the allergic child bring a dedicated autoinjector twin pack for the school year (an additional prescription on top of their twin pack prescribed for home)—dominated the base-case scenario in terms of producing superior health benefit and cost savings within the Chicago Public Schools system, with cost savings of $7419 per student at risk. Our aims of this analysis were to model under what assumptions the current stock epinephrine policy in the 49 US states that have such laws (schools stock undesignated units, while allergic children provide a dedicated unit) could be cost-effective and to investigate if an optimal policy could be devised that would maximize the benefits and minimize the costs. The universal model for stock epinephrine described herein shows great potential cost savings.

The current school epinephrine policy is inconsistent. All states except Hawaii have stock epinephrine legislation, but most states “opt in,” meaning that the law provides individual districts the option to allow schools to stock epinephrine, as opposed to mandating that all schools must do so. While inconsistencies in device prescription, the rate of opting in per district, and funding to obtain devices are occurring in opt-in states (even within mandated states), there are similar difficulties. Few studies exist to help understand the benefits of the legislation, the barriers to its effective implementation, and the areas in need of improvement. The exact number of devices used per year in schools with either type of stock epinephrine law—a state law mandating that schools and districts stock epinephrine or a law providing the option for schools and districts to stock this if they so choose (and the circumstances prompting their use)—is unknown, and there is no mechanism in place to date to track this nationally, although there are limited programs in states with mandated policies. Differences in epinephrine use policies (eg, who is treated with an undesignated device or a designated device) also may contribute to this uncertainty surrounding the outcomes that stock laws may achieve.

In situations where both the school has an undesignated stock epinephrine unit and the student also provides his or her own (how the current laws are implemented), it is unclear which unit is actually to be used: this is not specified in either the state law or the student’s individual plan. To our knowledge, there are no previous studies that have explored the outcomes of the 2 scenarios that we modeled (supplemental vs universal). Moreover, the value provided by currently recommended epinephrine use strategies—such as to immediately inject epinephrine for known or suspected allergen ingestion in the absence of symptoms and to call 911 and seek emergency care as a default policy after epinephrine use (vs a “wait and see” course of action if symptoms immediately resolve after initial treatment)—may have questionable health and economic value. Both of these management paths also influence the health and economic benefits stock epinephrine can provide given that their outcomes are compounded in any analysis of stock policies because the schools are instructed to do both per current anaphylaxis management plans.

Supply-side economics also factor into these scenarios. Epinephrine device cost has become a significant issue, stemming from a recent voluntary withdrawal of one branded device for almost 18 months, during which time the price of another branded autoinjector rose steeply, creating potential hardship and possible issues of access for some patients. Worse, the devices are subject to production shortages on top of such withdrawals. Multiple device products are available, including 2 generic options.
(generic EpiPen [Mylan N.V.] and generic Adrenaclick [Lineage Therapeutics]) and 3 branded options (EpiPen [Mylan N.V.], Auvi-Q [Kaléo], and Adrenaclick [Amneal Pharmaceutical]), allowing competition on price and patient preference. However, these devices are not necessarily similar in their use, despite the premise of value-based pricing for a device viewed as lifesaving is novel, although epinephrine autoinjectors fit an ideal description of a drug potentially subject to such pricing, particularly in the school environment, where current funding for the provision of stock devices is unclear. The EpiPen4Schools program has supplied a large number of districts with free devices and is tracking multiple aspects of the use of these devices among participating schools. For the 2014-2015 school year (12,275 schools), there were 2191 reported anaphylaxis cases, and 89.8% occurred in students (54% from food triggers), with the highest rate among students of high school age (40.1%). Epinephrine was administered on school property for 63.7% of the reactions, and the stock epinephrine supply was used in 631 of 1267 (49.8%). While few other data suggest how such devices are being used, this evidence underscores the importance of school stock epinephrine. There are limited data from other stock programs or states with stock epinephrine laws.

Limitations

This study has limitations and is based on multiple assumptions. The fatality risk differential between having and not having stock epinephrine is unknown, and we estimated this to conservatively be 10-fold, which we have published previously. We also assumed the current price for a single twin pack epinephrine device, which may be at a historical high level and could be subject to pricing and availability volatility. However, an advantage of simulations is that multiple sensitivity analyses can be conducted to create more robust models: we investigated other risk assumptions and sensitivity of the device acquisition price to find a common ground for both to show where stock epinephrine could be cost-effective. That said, data inputs for actual rates of use are limited, particularly in large school systems. In our model, we used the Chicago Public Schools system given its size and diverse sociodemographics, and it is one of the only large districts with available epinephrine use reporting statistics. Therefore, the Chicago Public Schools system was a good example for modeling in this simulation, although it may not generalize to other school districts. Fatality rates were obtained from the limited published data available, but they are difficult to track and estimate in the setting of food allergy and could also differ based on the source used. Overall, fatality from a food allergen or anaphylaxis is a rare event, but rates similar to ours have been used in other published analyses.

Conclusions

We show that a model of school-based stock epinephrine policy (with each allergic student bringing his or her own twin-pack device) is cost-effective when the annual acquisition price for undesignated school epinephrine does not exceed $338 per school, assuming a 10-fold reduction in fatality associated with stock epinephrine. However, a universal model approach where schools stock epinephrine for use by all students—but individual students are not asked to provide their own device for exclusive use at school—is cost saving and dominated other strategies. Under the right assumptions, school-based stock epinephrine can be a cost-effective strategy, and implementation of these programs should be encouraged and supported.
multi-state allergy societies, the American College of Allergy, Asthma, and Immunology, and the European Academy of Allergy and Clinical Immunology, reported being an associate editor for the Annals of Allergy, Asthma and Immunology; and reported being a member of the Joint Taskforce on Allergy Practice Parameters.

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REFERENCES