

Benefits and Risks of Live Attenuated Influenza Vaccine in Young Children

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The burden of influenza is substantial in young children. During the 2003-2004 influenza season, the influenza-attributable hospitalization rate for children younger than 2 years was 3 per 1000, or approximately the same as that of persons aged 65 years and older, for whom annual vaccination has long been recommended.¹⁻³ Young children (ie, those younger than 5 years) also have very high rates of outpatient visits for influenza—10 to 250 times their rate of hospitalization.³ In light of this burden, the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention (CDC) recommended routine annual vaccination of all children aged 6 to 23 months with trivalent inactivated influenza vaccine (TIV), beginning in the 2004-2005 winter season.⁴ This recommendation was expanded in 2006 to include children aged 24 to 59 months, and again in 2008 to include children aged 5 to 18 years.^{1,5}

Although the safety of TIV in young children has been demonstrated in several studies, its efficacy in this age group appears to be less than that in older children and adults.⁶ A review of randomized trials reported a pooled efficacy estimate of 63% for children younger than 9 years,⁷ as contrasted with the generally accepted efficacy range of 70% to 90% among healthy adults younger than 65 years.⁸ In 2003, a live attenuated influenza vaccine (LAIV) was approved for use in healthy persons aged 5 to 49 years. Although data available at the time of approval indicated that LAIV was efficacious against influenza in children younger than 5 years, approval for this age group was withheld at that time due to uncertainty regarding safety.^{9,10}

To shed additional light on the comparative efficacy and safety of LAIV versus TIV in young children, a large phase III clinical trial was undertaken in 8475 children aged 6 to 59 months.¹¹ Although children randomized to LAIV had a significantly lower rate of culture-confirmed influenza compared with those receiving TIV (55% relative efficacy), and risks of medically significant wheezing (MSW) and hospitalization were comparable for the 2 vaccines in selected (especially older) children, potential safety concerns were noted. In particular, among children aged 6 to 11 months, LAIV was associated with a higher risk of MSW in the 42-day postvaccination period (3.8% vs 2.1% for TIV, $P = .08$). A higher risk of hospitalization—mostly for common pediatric (eg, respiratory, gastrointestinal) disorder—also was noted for LAIV among children

Objective: To examine the benefit-risk profile of live attenuated influenza vaccine (LAIV) across a range of clinical scenarios in which we varied assumptions regarding both the percentage of children who would receive LAIV in lieu of trivalent inactivated influenza virus (TIV) and the extent of off-label use.

Study Design: Model of expected benefits and risks of immunization of young children against influenza.

Methods: We estimated expected numbers of cases of influenza illness (FLU), medically significant wheezing (MSW), and hospitalization in a single influenza season under alternative assumptions regarding use of LAIV in lieu of TIV, based on projections from a large phase III trial.

Results: Assuming no use of LAIV in nonindicated children (aged <24 months and those with history of recurrent wheezing or asthma), and 50% use in lieu of TIV among children in the indicated population, there would be 2099 fewer FLU cases per 100,000 children aged 12 to 59 months, and no change in MSW or hospitalization. If LAIV also were used in lieu of TIV among 20% of children aged 12 to 23 months and 20% of children aged 24 to 59 months with a history of recurrent wheezing or asthma, there would be a further reduction of 397 FLU cases and 12 hospitalizations per 100,000 children aged 12 to 59 months, but 51 additional MSW cases.

Conclusions: Our study suggests that even if LAIV were sometimes used inadvertently in clinical practice in young children for whom it is not indicated, the overall balance of expected benefits and risks would remain favorable.

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Take-Away Points

Live-attenuated influenza vaccine (LAIV) is not recommended for use in children aged 24 to 59 months with a history of recurrent wheezing or asthma, or approved for use in children aged 12 to 23 months. In clinical practice, however, some of these children may inadvertently receive LAIV.

■ If LAIV were used inadvertently in lieu of TIV among 20% of vaccinees aged 12 to 23 months, and 20% of vaccinees aged 24 to 59 months with a history of recurrent wheezing or asthma, the number of cases of influenza and hospitalization would decline below levels otherwise expected, but the number of cases of medically significant wheezing would increase.

■ Even if LAIV were sometimes used inadvertently in clinical practice among young children for whom it is not indicated, the overall balance of expected benefits and risks would remain favorable.

aged 6 to 11 months over the period beginning with the first vaccine dose and ending 180 days after the last vaccination (6.1% vs 2.6% for TIV, $P = .002$). Children aged 12 to 23, 24 to 35, and 36 to 47 months with a history of wheezing or asthma who received LAIV also had nominally (but not significantly) higher risks of hospitalization.

In 2007, the US Food and Drug Administration (FDA) expanded its approval of LAIV to include children aged 24 to 59 months.¹² Approval came with several warnings and precautions, however, including one against its use in children younger than 24 months (because of increased risks of hospitalization and wheezing) and another against its use in those with asthma or recurrent wheezing. Notwithstanding the product labeling, LAIV may be used inadvertently in clinical practice in children for whom it is not currently indicated. Although it is unknown whether—and to what extent—use of LAIV may deviate from labeled indications and recommendations, off-label use of vaccines among children does not appear to be uncommon. For example, in a recent study of rotavirus immunization in Philadelphia, Pennsylvania, 23% of children who received rotavirus vaccine were reported to have been given their first dose when they were outside the recommended age range.^{13,14} We therefore undertook a study to examine the potential benefits and risks associated with approval of LAIV for use in children aged 24 to 59 months, considering the potential impact of possible off-label use.

METHODS

Model Description

We developed a model to characterize expected benefits and risks of immunization of young children (aged 12-59 months) against influenza in a given season. Children aged 6 to 11 months were not considered in the model because they are at least 1 full year removed from the lower age limit reflected in the revised indication for LAIV, and thus were assumed highly unlikely to receive LAIV in clinical practice. In the model, we conservatively assumed that children would

receive either LAIV or TIV, and, therefore, that LAIV would be used exclusively in lieu of TIV during that influenza season. For children who were vaccine-naïve, we allowed vaccination to be either partial (1 dose only) or complete (2 doses). To reflect differential benefits and risks, we stratified the model population into 4 subgroups based on age (12-23 months vs 24-59 months) and risk profile (with or without a history of recurrent wheezing or asthma). Outcomes of interest included expected numbers of cases of influenza illness and MSW, and hospitalizations. Risk of these events was assumed to depend on age, risk status, vaccine received, and whether vaccination was partial or complete. We estimated our model using data from a large phase III clinical trial of LAIV versus TIV in young children and other sources, as described below. We examined expected benefits and risks under various scenarios regarding the extent of use of LAIV among children in the above-defined subgroups. The time frame of interest was a single influenza season.

Model Population

Estimation of model parameters was based primarily on data from the safety population (all children who received at least 1 dose of study vaccine with any follow-up data) in the phase III clinical trial (Table). The design of this randomized, double-blind, active-controlled trial has been described in detail elsewhere.¹¹ Briefly, 8475 children aged 6 to 59 months (primarily from the United States, Europe, and the Middle East) were randomized 1:1 to receive either LAIV or TIV before the beginning of the 2004 influenza season. Randomization was stratified by age at first dose, previous influenza vaccination, history of recurrent wheezing (prospectively defined as ≥ 3 medically attended wheezing illnesses), and country of residence. Exclusion criteria included a history of hypersensitivity to any component of LAIV or TIV, immunosuppressive condition, medically diagnosed/treated wheezing within 42 days before study enrollment, history of severe asthma (as assessed by the investigator), acute febrile illness within 3 days before enrollment, and recent use of aspirin or salicylate-containing products. Children not previously vaccinated against influenza received 2 doses of study vaccine; all others received 1 dose. Each dose of LAIV and TIV contained the three 2004-2005 influenza virus strains recommended by the FDA.

The proportions of the model population in the 4 age and risk subgroups (ie, vaccinated children aged 12-23 and 24-59 months, respectively, with and without a history of recur-

Benefits and Risks of LAIV in Children

Table. Estimated Values for Model Parameters

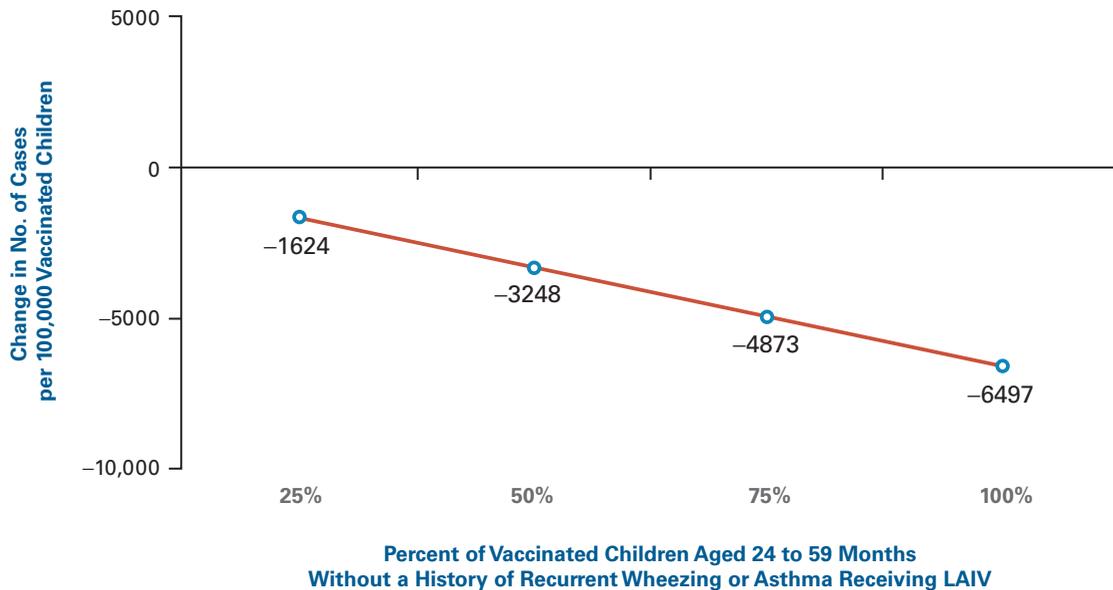
Model Parameter	Age			
	12-23 mo		24-59 mo	
	History of Asthma/Recurrent Wheezing	No History of Asthma/Recurrent Wheezing	History of Asthma/Recurrent Wheezing	No History of Asthma/Recurrent Wheezing
US vaccinated population aged 12-59 mo, %	1	24	10	65
Completeness of vaccination^a				
Partial, %	33	33	23	23
Full, %	67	67	77	77
Rate of model outcomes per 100 children				
Modified CDC-ILI through 180 days PLD				
LAIV				
Partial	5.8	4.2	6.2	6.7
Full	4.6	3.3	4.8	5.2
TIV				
Partial	18.8	10.8	16.4	16.2
Full	12.5	7.2	10.9	10.8
MSW through 84 days PFD				
LAIV				
Partial	20.0	3.7	10.1	2.0
Full	22.6	4.2	10.1	2.0
TIV				
Partial	17.2	3.2	10.1	2.0
Full	17.2	3.2	10.1	2.0
All-cause hospitalization through 180 days PLD				
LAIV				
Partial	6.1	3.1	2.2	2.2
Full	6.1	3.1	2.2	2.2
TIV				
Partial	3.3	3.5	2.2	2.2
Full	3.1	3.5	2.2	2.2

Modified CDC-ILI indicates culture-confirmed influenza-like illness, as defined by Centers for Disease Control and Prevention, caused by any strain; LAIV, live attenuated influenza vaccine; MSW, medically significant wheezing; PFD, post first dose; PLD, post last dose; TIV, trivalent inactivated influenza vaccine.
^aFull: receipt of 2 doses if vaccine-naïve; 1 dose otherwise.

rent wheezing/asthma) were estimated based on the size of each subgroup in the total US population and corresponding vaccine coverage levels. The size of each subgroup was estimated by multiplying the number of children aged 12 to 23 months and 24 to 59 months, respectively, in the United States (based on 2005 US Census data)¹⁵ and the age-specific percentage of children with a history of recurrent wheezing or asthma (based on unpublished data from the phase III trial, MedImmune, 2007). Because the age distribution of children in the phase III trial was different from that in the United

States (ie, children aged 6-23 months were overrepresented in the trial), percentages from the trial were standardized to the US population. Vaccine coverage levels were assumed to be the same in all subgroups, based on the recent Advisory Committee on Immunization Practices recommendation of annual influenza vaccination for older children and a recent survey suggesting comparable coverage levels among children aged 12 to 23 months and those aged 24 to 59 months with asthma, groups for whom annual vaccination was recommended at the time.^{16,17} Among vaccine-naïve children, the proportion re-

■ **Figure 1.** Change in Number of Cases of Modified CDC-ILI per 100,000 Vaccinated Children Aged 24 to 59 Months Without a History of Recurrent Wheezing or Asthma Under Alternative Assumptions Regarding Substitution of LAIV for TIV^a



Modified CDC-ILI indicates culture-confirmed influenza-like illness, as defined by Centers for Disease Control and Prevention, caused by any strain; LAIV, live attenuated influenza vaccine; TIV, trivalent inactivated influenza vaccine.
^aChange versus scenario in which all vaccinated children were assumed to receive TIV.

ceiving only 1 dose was estimated based on data from the National Immunization Survey, the National Health Interview Survey, and other sources.^{1,8,17,18} Due to the greater likelihood of prior vaccination, fewer older children were estimated to be vaccine-naïve.

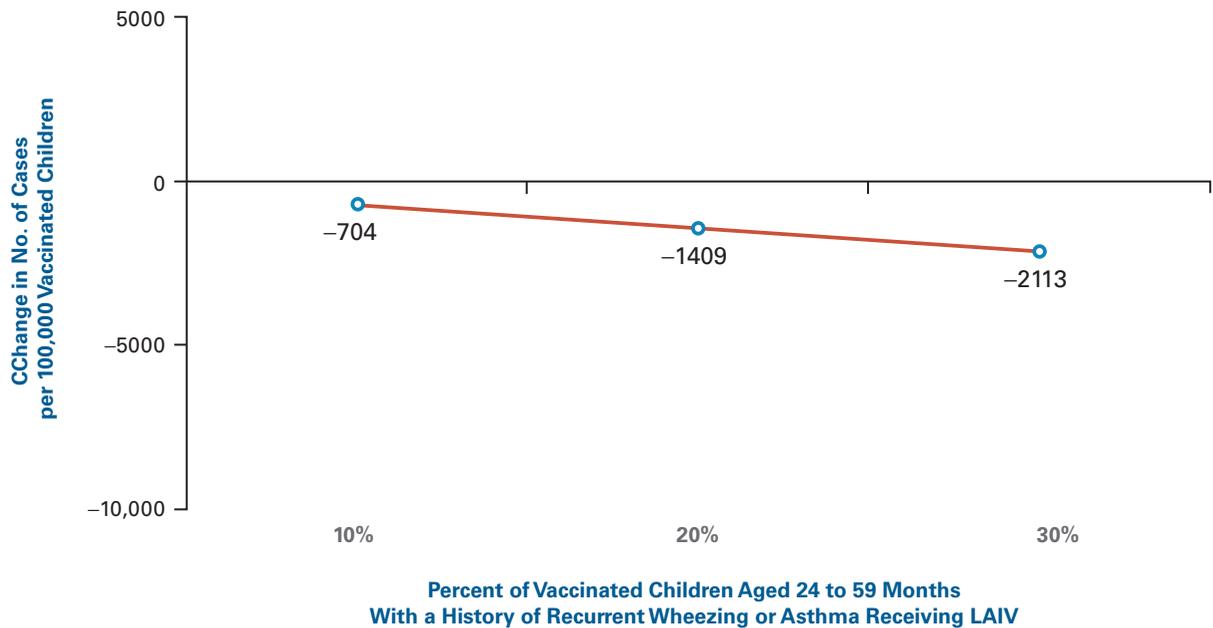
Outcomes

Influenza illness was defined, per the phase III clinical trial protocol, as body temperature $\geq 100^{\circ}\text{F}$ oral or equivalent plus cough, sore throat, or runny nose/nasal congestion occurring on the same day or consecutive days, in association with a positive nasal swab culture for wild-type influenza (modified CDC-ILI [culture-confirmed influenza-like illness, as defined by the CDC, caused by any strain]). Rates for children fully vaccinated with TIV and LAIV were based on data from the phase III trial, with age standardization to the US population, and included disease caused by both matched (ie, included in the vaccine) and unmatched strains occurring up to 180 days after the last dose of vaccine. For children receiving only partial vaccination with LAIV, the rate of modified CDC-ILI was conservatively assumed to be 28% higher than the risk with full vaccination, based on results of another phase III study.¹⁹ For partial vaccination with TIV, the rate of modified CDC-ILI was assumed to be 50% higher than that for full vaccination with TIV.²⁰

Medically significant wheezing was defined as wheezing documented by a healthcare provider and accompanied by (1) tachypnea, retractions, or dyspnea; (2) O_2 saturation $< 95\%$; or (3) a new prescription for daily bronchodilators.¹¹ Rates of MSW for children aged 12 to 23 months who were assumed to be vaccinated with LAIV (full or partial) were based on age-adjusted data from the phase III trial; all such events through 84 days after first dose of vaccine were considered (which corresponds to the prespecified maximum follow-up period for evaluating the occurrence of MSW in the trial—ie, 42 days after receipt of last dose of vaccine, which for vaccine-naïve children was specified to occur 28-42 days after receipt of first dose). Rates of MSW for children of this age assumed to receive TIV were based on trial data and were assumed to be the same for full and partial vaccination. For children aged 24 to 59 months, rates of MSW in the phase III trial were, in fact, slightly lower for LAIV than for TIV, but they were conservatively assumed to be the same in our analysis, irrespective of risk status.

Hospitalization was defined as an inpatient admission for any reason lasting 24 hours or more. Hospitalization rates for fully vaccinated children were based on age-standardized trial data (through 180 days after the last dose). Rates for partially vaccinated children aged 12 to 23 months were assumed to be higher than those for fully vaccinated children in this age

■ Figure 2. Change in Number of Cases of Modified CDC-ILI per 100,000 Vaccinated Children Aged 24 to 59 Months With a History of Recurrent Wheezing or Asthma Under Alternative Assumptions Regarding Substitution of LAIV for TIV^a



Modified CDC-ILI indicates culture-confirmed influenza-like illness, as defined by Centers for Disease Control and Prevention, caused by any strain; LAIV, live attenuated influenza vaccine; TIV, trivalent inactivated influenza vaccine.

^aChange versus scenario in which all vaccinated children were assumed to receive TIV.

group, based on higher modified CDC-ILI rates and the conditional probability of influenza-related hospitalization.²¹ Rates for children aged 24 to 59 months receiving TIV and LAIV were again conservatively assumed to be the same, despite a slightly lower rate for LAIV in the trial.

Analyses

We first conducted analyses to compare expected benefits and risks in each of the 4 subgroups of children assumed to receive either LAIV or TIV: (1) aged 24 to 59 months without a history of recurrent wheezing or asthma (ie, those not covered by warnings and precautions); (2) aged 24 to 59 months with a history of recurrent wheezing or asthma; (3) aged 12 to 23 months without a history of recurrent wheezing or asthma; and (4) aged 12 to 23 months with a history of recurrent wheezing or asthma. For the first group (ie, those not covered by warnings and precautions), substitution of LAIV for TIV was allowed to vary from 25% to 100%. In analyses focusing on the other 3 groups, substitution of LAIV for TIV was varied from 10% to 30% (lower rates were assumed, due to the warnings and precautions).

We then pooled results from these separate analyses, weighting estimates for each subgroup by its respective proportion of the total vaccinated population aged 12 to 59

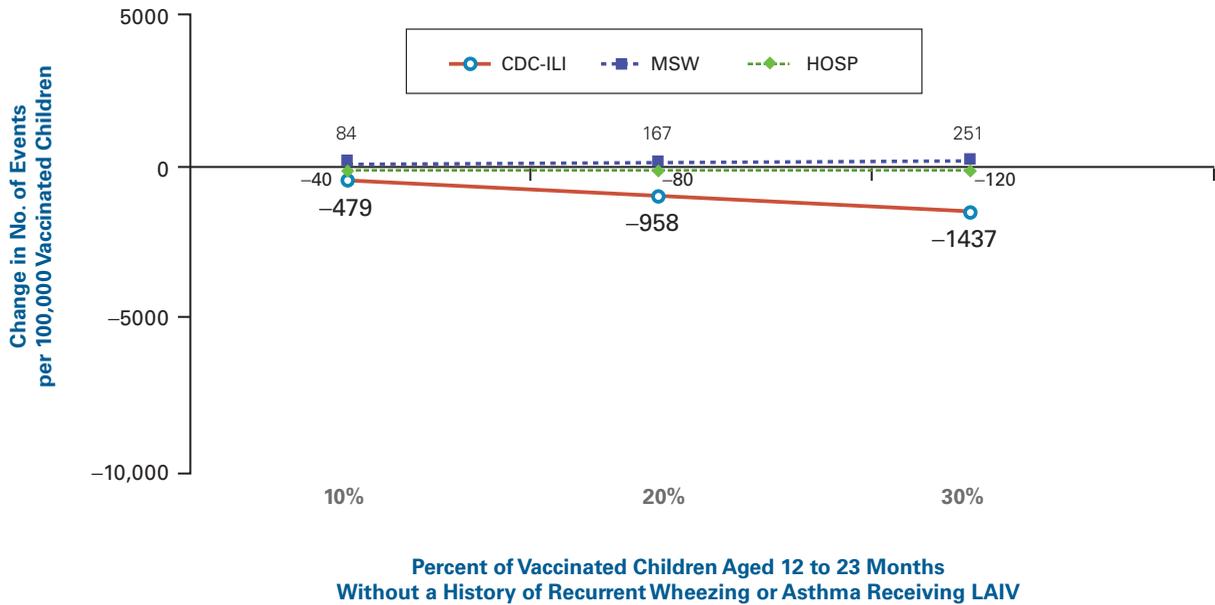
months, to yield expected changes in the outcomes of interest at various assumed levels of use of LAIV. In these pooled analyses, rates of use of LAIV in children covered by warnings and precautions were assumed never to exceed LAIV coverage rates among children aged 24 to 59 months without a history of recurrent wheezing or asthma (ie, those not covered by the warnings and precautions). We expressed our results on a standardized basis, per 100,000 children vaccinated.

RESULTS

Change in Expected Cases of Influenza

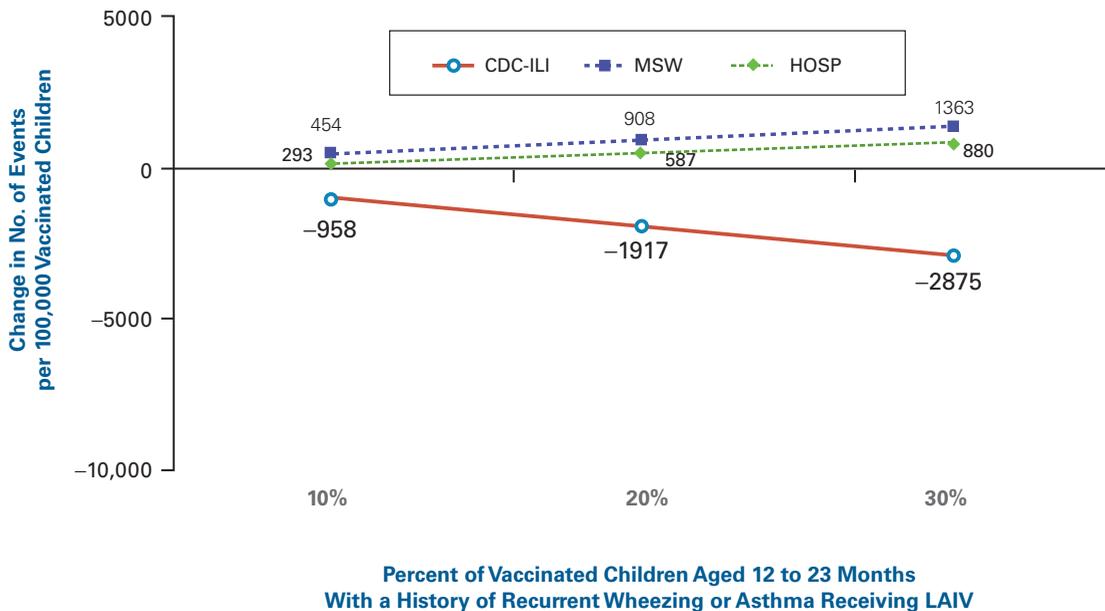
Use of LAIV in lieu of TIV among children aged 24 to 59 months without a history of recurrent wheezing or asthma would result in 650 fewer cases of influenza illness per 100,000 vaccinated in this group for every 10% increase in share (Figure 1). Thus, for example, if 50% of these children received LAIV rather than TIV, cases of influenza illness would be expected to decrease by 3248 per 100,000 vaccinated in this subgroup. Similar reductions in the number of cases of influenza illness (per 100,000 vaccinated) would be expected with 10% increases in share in the other 3 groups: 704 fewer cases among children aged 24 to 59 months with a history of recurrent wheezing or asthma (Figure 2), 479 fewer

■ **Figure 3.** Change in Number of Events per 100,000 Vaccinated Children Aged 12 to 23 Months Without a History of Recurrent Wheezing or Asthma Under Alternative Scenarios Regarding Substitution of LAIV for TIV^a



Modified CDC-ILI indicates culture-confirmed influenza-like illness, as defined by Centers for Disease Control and Prevention, caused by any strain; HOSP, all-cause hospitalization; LAIV, live attenuated influenza vaccine; MSW, medically significant wheezing; TIV, trivalent inactivated influenza vaccine. ^aChange versus scenario in which all vaccinated children were assumed to receive TIV.

■ **Figure 4.** Change in Number of Events per 100,000 Vaccinated Children Aged 12 to 23 Months With a History of Recurrent Wheezing or Asthma Under Alternative Scenarios Regarding Substitution of LAIV for TIV^a



Modified CDC-ILI indicates culture-confirmed influenza-like illness, as defined by Centers for Disease Control and Prevention, caused by any strain; HOSP, all-cause hospitalization; LAIV, live attenuated influenza vaccine; MSW, medically significant wheezing; TIV, trivalent inactivated influenza vaccine. ^aChange versus scenario in which all vaccinated children were assumed to receive TIV.

cases among children aged 12 to 23 months without a history of recurrent wheezing or asthma (Figure 3), and 958 fewer cases among children aged 12 to 23 months with a history of recurrent wheezing or asthma (Figure 4).

Change in Expected Cases of Medically Significant Wheezing and Hospitalization

In the 2 groups of children aged 12 to 23 months, however, there would be offsetting increases in MSW: an additional 84 cases per 100,000 vaccinated among those without a history of recurrent wheezing or asthma, and an additional 454 cases per 100,000 vaccinated among those with such a history. Changes in rates of hospitalization also would be expected among children aged 12 to 23 months: a decrease of 40 admissions per 100,000 vaccinated children without a history of recurrent wheezing or asthma, but an additional 293 admissions per 100,000 vaccinated children with such a history. (Because rates of MSW and hospitalization [ie, the values for corresponding model inputs set forth in the Table] were assumed to be the same for LAIV and TIV among all children aged 24 to 59 months, projections do not differ by the assumed use of LAIV in lieu of TIV.)

Populationwide Changes

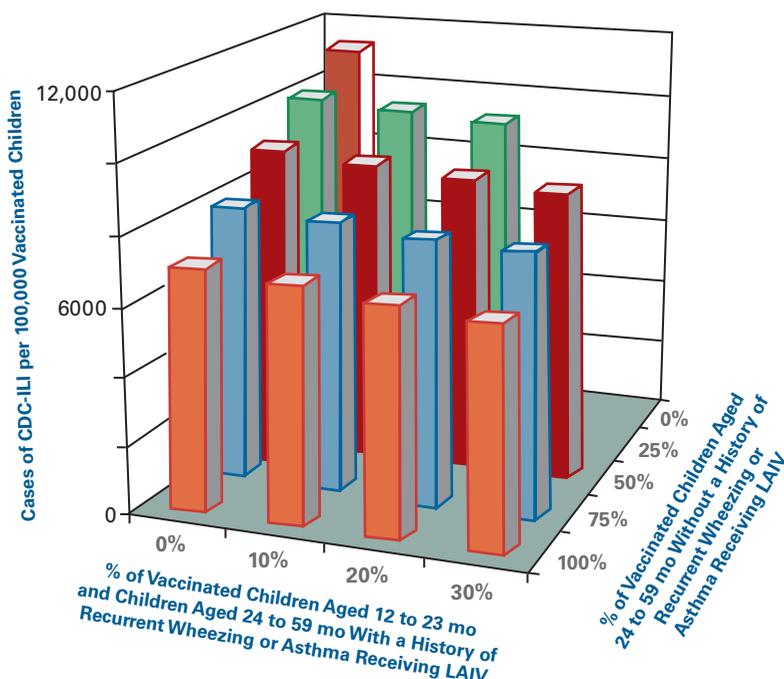
With aggregation across the 4 age and risk subgroups based on population weights, if 50% of vaccinated children in the indicated population receive LAIV in lieu of TIV—and assuming no use among children aged 12 to 23 months or those with a history of recurrent wheezing or asthma—the rate of influenza illness among vaccinated children aged 12 to 59 months would decline by 2099 cases per 100,000 (Figure 5), while rates of MSW and hospitalization would remain unchanged (Figure 6 and Figure 7, respectively). If LAIV also was used in lieu of TIV by 20% of vaccinated children age 12 to 23 months and 20% of those with a history of recurrent wheezing or asthma, the expected rate of influenza illness among vaccinated children aged 12 to 59 months would decline by an additional 397 cases per 100,000, and the expected rate of hospitalization would decline by 12 cases per 100,000. Such use, however, would result in an additional 51 cases of MSW per 100,000 vaccinated.

DISCUSSION

Three recent phase III randomized trials reported that the efficacy of LAIV was significantly better than that of TIV in preventing influenza in young children^{11,22} and in older children and adolescents with asthma.²³ There was evidence from one of these trials, however, that LAIV may increase risks (relative to TIV) of MSW and/or hospitalization in children aged 12 to 23 months and in those with a history of recurrent wheezing or asthma. Therefore, LAIV carries a warning/precaution against its use in persons with a history of recurrent wheezing or asthma, and it was not approved for use in children aged 12 to 23 months. Although it is unknown whether—and to what extent—use of LAIV may deviate from labeled indications and recommendations, off-label use of vaccines among children does not appear to be uncommon. Possible increased risks of MSW and hospitalization in children aged 12 to 23 months and those with a history of recurrent wheezing or asthma, therefore, make it essential that this issue be considered in any formal analysis of the benefits and risks of LAIV in young children.

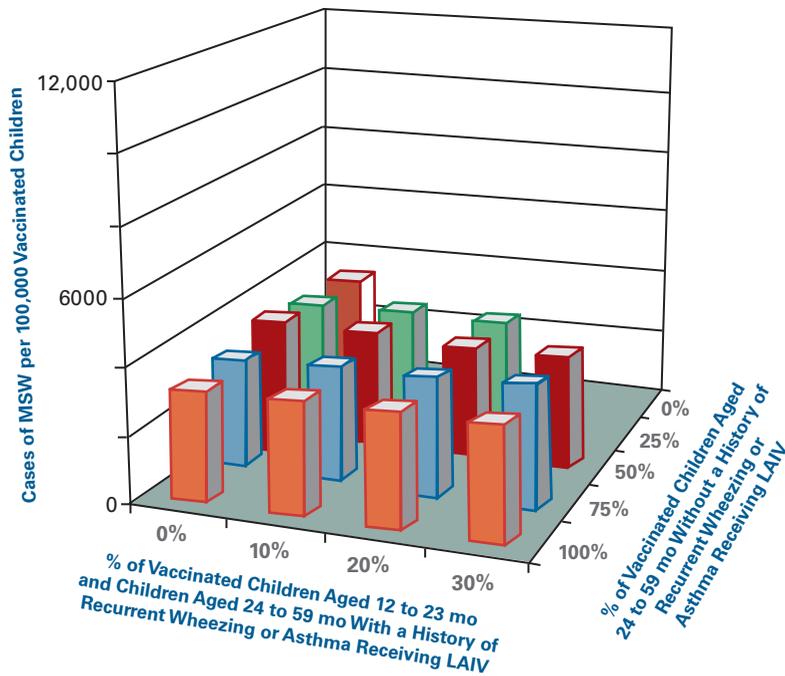
Our findings indicate that among children aged 24 to 59 months, irrespective of history of recurrent wheezing or

■ **Figure 5.** Cases of Modified CDC-ILI per 100,000 Vaccinated US Children Aged 12 to 59 Months



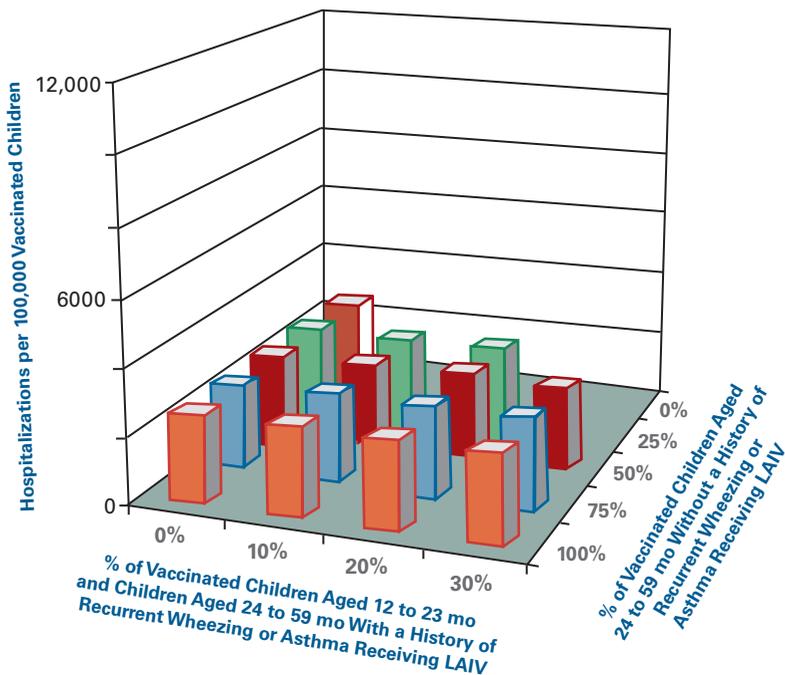
Modified CDC-ILI indicates culture-confirmed influenza-like illness, as defined by Centers for Disease Control and Prevention, caused by any strain; LAIV, live attenuated influenza vaccine.

■ **Figure 6.** Cases of MSW per 100,000 Vaccinated US Children Aged 12 to 59 Months



LAIV indicates live attenuated influenza vaccine; MSW, medically significant wheezing.

■ **Figure 7.** All-Cause Hospitalizations per 100,000 Vaccinated US Children Aged 12 to 59 Months



LAIV indicates live attenuated influenza vaccine.

asthma, the benefit-risk profile of LAIV appears to be favorable; substantial reductions in influenza illness are likely to result from the use of LAIV (in lieu of TIV) without increased risks (ie, MSW, hospitalization). In children aged 12 to 23 months, however, the benefits of LAIV need to be weighed against an increased risk of MSW and an increased risk of hospitalization in those with a history of recurrent wheezing or asthma. For children of this age group without a history of recurrent wheezing or asthma, the substantial reduction in risk of influenza illness (479 fewer cases per 100,000 vaccinated with each 10% additional share) associated with LAIV must be weighed against a modest increase in the risk of MSW (84 events per 100,000 vaccinated); a small reduction in risk of hospitalization also was projected for this group (40 fewer admissions per 100,000 vaccinated). Among children aged 12 to 23 months with a history of recurrent wheezing or asthma, increases in the risks of both MSW (454 events per 100,000 vaccinated) and hospitalization (293 admissions per 100,000 vaccinated) must be weighed against the reduced risks of influenza illness (958 fewer cases per 100,000 vaccinated). We did not assign weights to the different outcomes and undertake a quantitative benefit-risk analysis because we felt that the balance of benefits and risks for each of the 4 subgroups of interest was clear.

Thus, from a public-health perspective, the overall benefit-risk balance associated with approval of LAIV depends largely on the extent of its use in children for whom it is indicated versus those included in label warnings and precautions. However, even when we assumed that LAIV would be widely used in this latter group, we found that benefits would likely accrue to the population as a whole in terms of decreased numbers of cases of influenza illness and a small decrease in the number of hospitalizations, counterbalanced by only a modest increase in the number of cases of MSW.

Benefits and Risks of LAIV in Children

Perhaps the most important limitation to our study is that it was based on the findings from a single randomized trial. Of note, the trial was not designed to have adequate statistical power for the stratified analyses that we undertook on a post hoc basis. Moreover, it is not certain that the relative benefits of LAIV would be the same in every influenza season, or that they would be as great in actual clinical practice, where children excluded from the trial might receive LAIV and vaccination might not occur in the optimal time window for maximum prophylactic effect. In influenza seasons with higher illness rates, the benefits of LAIV in absolute terms would undoubtedly be greater. Conversely, in seasons with lower illness rates, benefits would be reduced. Assuming a 50% lower influenza illness rate than that observed in the phase III clinical trial, for example, a 50% LAIV share in children aged 24 to 59 months without a history of wheezing or asthma and a 20% LAIV share in all other children aged 12 to 59 months would be expected to result in 1248 fewer cases of influenza illness and 11 fewer hospitalizations per 100,000 vaccinated children aged 12 to 59 months, offset by an additional 51 cases of MSW per 100,000. Even under this conservative assumption regarding influenza burden, however, the benefit-risk profile of LAIV appears to remain favorable.

Several additional limitations should be noted. Our subgroups of children with a history of recurrent wheezing or asthma did not include those with persistent or severe asthma, as they were excluded from the phase III clinical trial. The benefits and risks of LAIV in these children are accordingly unknown. We also did not consider vaccination of children age 6 to 11 months, even though they were included in the phase III clinical trial. (A significantly higher risk of hospitalization was reported for this youngest age group.) We reasoned, however, that it would be very unlikely for children of this age to receive LAIV in clinical practice, because they are at least a full year removed from the lower age limit (ie, 24 months) reflected in the revised indication. Any use of LAIV in children aged 6 to 11 months, however, would adversely impact the overall balance of benefits and risks. We also note that differences in the severity of outcomes between children receiving LAIV versus TIV were not taken into account due to sparse data, and that approximately one half of children in the phase III clinical trial resided outside the United States. The impact of these latter 2 limitations on our findings is unknown, although the observation of efficacy of LAIV versus TIV was robust across subgroups analyzed, including stratification by country of residence.¹¹

In conclusion, vaccination of children aged 24 to 59 months without a history of recurrent wheezing or asthma with LAIV rather than TIV was projected to have a favorable benefit-risk profile. Although use of LAIV also may be

favorable in children of this age group with a history of recurrent wheezing or asthma, its use in younger children (aged 12-23 months)—especially those with a history of recurrent wheezing or asthma—poses risks. However, under reasonable assumptions regarding use of LAIV in children for whom it is indicated versus those included in the warnings and precautions, the overall balance of benefits and risks indicates that approval of LAIV for use in younger children represents an advance in influenza prevention. Postmarketing studies in nonindicated populations that are currently under way will contribute further to our understanding of the overall benefit-risk balance of LAIV from a public-health perspective.

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Authorship Information: Concept and design (GO, DW, JE, KLN, JOK, RBB); acquisition of data (DW); analysis and interpretation of data (GO, DW, JE, KLN, JOK, RBB); drafting of the manuscript (GO, DW, JE, KLN, RBB); critical revision of the manuscript for important intellectual content (GO, DW, JE, KLN, JOK, RBB); statistical analysis (GO, DW); obtaining funding (GO); and supervision (GO).

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