

Letter to the Editor

Calculating the effect of population-level implementation of the Learning Early About Peanut Allergy (LEAP) protocol to prevent peanut allergy

To the Editor:

The Learning Early About Peanut Allergy (LEAP) study demonstrated a 70% to 86% relative reduction in the incidence of peanut allergy (PA) in high-risk infants (with severe atopic dermatitis [AD] or egg allergy) if peanut was introduced between 4 and 11 months of age.¹ Using data about AD and egg sensitization collected from BASELINE, Ireland's first unselected prospective birth cohort study,²⁻⁵ we calculated the effect of implementing the LEAP protocol in our population.

BASELINE shows the point prevalence of both AD overall and of severe AD (SCORAD score >40) at 6 months of age and the point prevalence of both egg sensitization at 12 months of age and challenge-proved PA at 24 months of age in Ireland.^{4,5} Egg is typically not introduced to the infant's diet in Ireland until after 6 months,^{2,3} and therefore it is typically later in the second 6 months of life that Irish children are evaluated for egg allergy. National data were accessed for the number of births in Ireland in 2013.⁶ For the calculations below, we have used data from the LEAP study's intention-to-treat analysis with worst case imputation.¹

There were 68,684 births in Ireland in 2013.⁶ The prevalence of challenge-proved PA in Ireland is 1.75% at 2 years.⁵ These figures suggest 1,202 ($68,684 \times 0.0175$) cases of PA in 2-year-old Irish infants.

Of Irish children, 18.7% have AD at 6 months of age, of whom 13.5% (2.4% overall) have severe AD (SCORAD score >40).⁴ One thousand six hundred forty-eight ($68,684 \times 0.024$) Irish children would meet the LEAP study's SCORAD-based criterion.

Fifty-three (3.0%) of 1745 BASELINE children were sensitized to egg with skin prick test (SPT) responses of 3 mm or greater before 12 months of age.⁵ At formal review at 6 months, 11 (20.8%) of these 53 patients had a SCORAD score of greater than 40. Therefore the total number of 12-month-old children with egg allergy in Ireland can be calculated at 2,061 ($68,684 \times 0.03$). The 429 (20.8%) with egg allergy and SCORAD scores of greater than 40 must be eliminated from the egg allergy group to avoid them being counted twice. Therefore 1,632 ($2,061 - 429$) Irish children would meet the LEAP study's egg allergy-related criterion.

Three thousand two hundred eighty ($1,648 + 1,632$) Irish children born in 2013 would meet the 2 most objective LEAP inclusion criteria. Of LEAP study participants, 10.6% were excluded because of a "strongly positive" SPT response (>4 mm). Three hundred forty-eight ($3,280 \times 0.106$) LEAP-eligible Irish children would be excluded, leaving 2,932 ($3,280 - 348$) suitable for peanut consumption (see Table E1 in this article's Online Repository at www.jacionline.org). Of children randomized in the LEAP study, 84.7% had a negative (0 mm) SPT response.⁵

Two thousand four hundred eighty-three ($2,932 \times 0.847$) LEAP-eligible Irish children would have a negative SPT response. The remaining 449 ($2,932 \times 0.153$) LEAP-eligible Irish children would have a positive SPT response (1-4 mm). Of children with negative SPT responses in the LEAP study's peanut

consumption group, 3.7% had PA compared with 13.3% in the avoidance group.

Of the projected group with negative SPT responses ($n = 2,483$), 92 ($2,483 \times 0.037$) LEAP-eligible Irish children would still have PA despite consumption. If peanuts were avoided, 330 cases of PA would have developed ($2,483 \times 0.133$). Therefore 238 cases ($330 - 92$) of PA would be avoided with peanut consumption in the group with negative SPT responses. This is a 9.6% absolute reduction.

Of children with positive SPT responses in the LEAP study's consumption group, 10.6% still had PA versus 35.3% in the peanut avoidance group. Forty-eight (449×0.106) LEAP-eligible Irish children with positive SPT responses would still have PA despite peanut consumption versus 158 cases of PA (449×0.353) if peanuts were avoided. One hundred ten cases ($158 - 48$) of PA would be prevented by peanut consumption in the group with positive SPT responses. This is a 24.7% absolute reduction.

The projected incidence of PA in LEAP-eligible children with SCORAD scores of greater than 40 or egg allergy who, before the LEAP study, would have routinely avoided peanut would be 488 cases (330 in the group with negative SPT responses and 158 in the group with positive SPT responses). The total number of cases of PA that could be avoided in Ireland using the LEAP protocol per annum would be 348 (238 LEAP-eligible Irish children with negative SPT negative responses and 110 LEAP-eligible Irish children with positive SPT responses) (see Table E2 in this article's Online Repository at www.jacionline.org). This represents a relative reduction of 71% in the defined high-risk groups of infants.

There would be a substantial effect on the incidence of PA in the 2,932 Irish children who meet the 2 most objective LEAP criteria of severe AD with SCORAD scores of greater than 40 or existing egg allergy at 6 months, with a relative reduction in the incidence of PA of 71%. The population-level effect is less dramatic (29% relative reduction) because LEAP-defined high-risk children are only a minority of cases (488/1202 cases per annum).

Our report has limitations relating mainly to the use of a slightly different case definition for egg allergy to those used in the LEAP study. However, all Irish cases were in infants with challenge-proved egg allergy rather than merely egg-sensitized infants. The only national data for PA relate to challenge-proved PA at 2 years compared with the LEAP definition of PA at 5 years (60 months). Although PA can resolve, this is in only a minority of cases (20%), and therefore we have not made any specific estimates of the likely rate of PA in Ireland at 6 years of age to make a direct comparison with LEAP data. Our calculations presume full implementation of the LEAP protocols. However, these limitations are offset by the robustness of the existing LEAP data and published BASELINE data, by the similarity of the estimates of Irish and British rates of PA and by the broad socioeconomic similarities of the 2 countries.

The LEAP study has shown that peanut consumption is safe and well tolerated. However, community implementation would demand huge additional resources at all levels of health care. Further studies need to be performed to assess many unresolved aspects of peanut introduction.

The LEAP study has already prompted international organizations to reexamine their allergy prevention advice.⁷ Exercises such as we report here could be done with the data of any country that has reliable national prevalence data for allergic conditions in infancy to better inform pragmatic national policy changes and appropriate resource allocation in countries with different prevalences of PA.

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TABLE E1. Calculation of the number of Irish children suitable to be offered the LEAP protocol

No. of children born in Ireland (2013) ⁶	68,684
No. of Irish children with AD and SCORAD scores >40 at 6 mo of age (2.4%) ⁴	1,648
No. of Irish children with egg allergy at 12 mo of age (3%) ⁵	2,061
Subtotal of eligible children	3,709
Excluded children with SCORAD scores >40 and egg allergy	429
Subtotal	3,280
SPT response >4 mm to peanut (10.6%) ¹	348
No. of Irish children suitable for LEAP-based peanut introduction	2,932

TABLE E2. Calculation of the effect of implementation of the LEAP protocol in 2932 LEAP-eligible Irish children

	SPT response, 0 mm (84.7%)	SPT response, 1-4 mm (15.3%)	Total
No.	2,483	449	2,932
Avoidance group: cases (%) of PA (A)	330 (13.3)	158 (35.3)	488
Consumption group: cases (%) of PA (B)	92 (3.7)	48 (10.6)	140
No. of cases of PA prevented (A – B)	238	110	348