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Trends in use of specialised formula for managing cow's milk allergy in young children

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Key Messages

- Specialised formula prescriptions in England, Norway and Australia increased ≥ 2 -fold in the early 21st century
- Most infants prescribed specialised formula don't have milk allergy, with up to 10-fold excess prescription
- Unnecessary specialised formula use increases free sugars consumption so may promote dental decay and obesity.

Abstract

Background:

Excessive use of specialised formula for cow's milk allergy was reported in England, but complete analysis has not been undertaken and trends in other countries are unknown. Some specialised formula products, especially amino-acid formula, have high free sugars content. We evaluated specialised formula trends in countries with public databases documenting national prescription rates.

Methods:

Cross-sectional analysis of national prescription databases in United Kingdom, Norway and Australia. Outcomes were volume and cost of specialised formula, and proportion of infants prescribed specialised formula. Expected volumes assumed 1% cow's milk allergy incidence and similar formula feeding rates between infants with and without milk allergy.

Results:

Prescribed volumes of specialised formula for infants rose 2.8-fold in England from 2007-2018, with similar trends in other regions of the United Kingdom. Volumes rose 2.2-fold in Norway from 2009-2020 and 3.2-fold in Australia from 2001-2012. In 2020, total volumes were 9.7 to 12.6-fold greater than expected in England, 8.3 to 15.6-fold greater than expected in Norway and 3.3 to 4.5-fold greater than expected in Australia, where prescribing restrictions were introduced in 2012. In Norway the proportion of infants prescribed specialised formula increased from 2.2% in 2009 to 6.9% in 2020, or 11.2 to 13.3-fold greater than expected. In 2020, specialised formula for infants cost US\$117 (103 euro) per birth in England, US\$93 (82 euro) in Norway and US\$27 (23 euro) in Australia. Soya formula prescriptions exceeded expected volumes 5.5 to 6.4-fold in England in 1994 and subsequently declined, co-incident with public health concerns regarding soya formula safety. In 2020, 30-50% of prescribed specialised formula across the three countries was amino-acid formula.

Conclusions:

In England, Norway and Australia, specialised formula prescriptions increased in the early 21st century and exceeded expected levels. Unnecessary specialised formula use may make a significant contribution to free sugars consumption in young children.

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Introduction

Cow's milk allergy affects up to 1% of children before age two years.¹ Most infant formula is derived from cow's milk, so for infants with milk allergy who are not fully breastfed, specialised formula products have been developed as alternatives to cow's milk-based formula. Prescriptions for specialised formula are thought to have risen in England, and a 2006 report from Australia documented increasing prescriptions of amino-acid formula, but no comprehensive analysis of all specialised formula products across multiple countries has yet been undertaken.²⁻⁴

Increasing specialised formula use has been interpreted as evidence for milk allergy overdiagnosis, leading to use of specialised formula for managing common infant symptoms.^{2,3,5} This is because there is little evidence in high-income countries for a change in milk allergy incidence to explain rises in specialised formula prescription.² While specialised formula is reasonably well tolerated by most infants, and supports infant nutrition and growth, there are significant differences from standard cow's milk based infant formula or human breast milk.^{6,7} In specialised formula products, the lactose naturally present in breastmilk or cow's milk is partially or completely replaced by alternative carbohydrate sources, often free sugars such as glucose or sucrose.⁶ High free sugars intake is an important risk factor for obesity and dental decay, and a major public health issue.⁸ Thus, it is conceivable that unnecessary use of specialised formula may have important public health consequences that have not been studied to date.^{6,8-10}

We therefore undertook a cross-sectional survey of national prescription databases recording reimbursement of specialised formula for managing formula-fed infants with cow's milk allergy, to better understand recent trends in specialised formula use.

Methods

Study Design

We conducted a cross-sectional survey of national prescription databases to obtain reimbursement or sales data for specialised formula. Inclusion criteria were comprehensive prescription databases with complete national data for at least one type of specialised formula for at least one year. Exclusion criteria were databases without any complete national data, databases without a detailed breakdown of specialised formula brands and quantities reimbursed or sold, or regions where there is no public record of reimbursed or sold specialised formula volumes. We initially reviewed Euromonitor, an industry database of global and national infant milk formula sales data, but comprehensive data for specialised formula for managing milk allergy were not available. We then contacted colleagues from 23 countries covering over half of the world population to assess accessibility of national prescription records, of which three countries had publicly available national prescription data: United Kingdom, Norway and Australia, (Table S1). We reviewed breastmilk substitute products for infants with cow's milk allergy and excluded semi-solid or solid foods and specialised formula products specifically designed or reimbursed for use in infants with malabsorption or eosinophilic oesophagitis (Table S2). The primary outcome of interest was volume of specialised formula prescribed annually to children under 1-year old in each country. Secondary outcomes were annual cost of specialised formula reimbursement and the relationship between reimbursed volumes and expected volumes based on national feeding data and an estimated 1% incidence of milk allergy.¹

Data Collection

Quantity and cost of specialised formula reimbursements were collected from national databases. Annual live birth rates and national formula-feeding rates were collated from

relevant public databases to estimate expected quantity of specialised formula consumption (Tables S3 to S5). In England, prescription data for specialised formula reimbursed by the National Health Service (NHS) were obtained from Prescription Cost Analysis reports held at the British Library in hard copy (1991-1997), and digital reports held at the National Archives (1998-2003), and NHS Digital Prescription Cost Analysis website (2003-2020). In Scotland, prescription data were obtained from Public Health Scotland Community Dispensing Prescription Cost Analysis website (2001-2019), in Northern Ireland from the Health and Social Care Business Services Organization Prescription Cost Analysis website (2000-2020), and in Wales from NHS Wales Prescription Cost Analysis website (2017-2020). Where relevant, quantities reimbursed were multiplied by the product size to yield the total grams of powdered formula reimbursed. Annual live birth rates were obtained from birth characteristics datasets on the relevant national statistics website for each country. In Norway, prescription data for reimbursed specialised formula for both 0-to 11-month and 12-to 23-month-old infants were obtained on request from the Norwegian Directorate for Health along with the unique number of users of this group of products. The quantities reimbursed were multiplied by the product size to yield the total grams of powdered formula reimbursed. Annual live birth rates were obtained from Statistics Norway. In Australia, prescription data for specialised formula reimbursed under the Pharmaceutical Benefits Scheme (PBS) and Repatriation PBS were obtained from the Services Australia website, multiplying the number of prescriptions by the number of items claimed per prescription to yield the total grams of powdered formula reimbursed. Annual live birth rates dataset was retrieved from the Australian Bureau of Statistics website.

Data Analysis

Specialised formula quantities were standardized to volume, using the British National Formulary for Children online version (United Kingdom) or manufacturer (Norway and Australia) recommended weight-to-volume for preparation of liquid formula feeds, in grams per litre. Total reimbursement costs were summarised in the local currency and converted to United States Dollars (\$US) and euros using mid-2020 currency conversion rates.

The number of infants expected to be diagnosed with milk allergy was estimated as 1% of annual live births.¹ The proportion of milk-allergic infants expected to use formula milk was estimated using national infant feeding survey data. The volume of specialised formula expected to be consumed was estimated using reference daily formula consumption values of 780ml for 0- to 5.9-month-old and 600ml for 6- to 11.9-month-old infants.¹¹

Results

Community prescription data were available from England (1991-2020), Norway (2009-2020) and Australia for years 1992 to 2020, Data were available for other regions of the United Kingdom for shorter periods of time and are summarised separately. Data for extensively hydrolysed formulas (EHF) and amino-acid formulas (AAF) were available from all three countries and data for soya formula from England and Norway only. Data for the number of infants prescribed a specialised formula were only available from Norway. The specific eligible products available for public reimbursement in each country are summarised in Table 1, and products excluded from analysis are listed in Table S2.

Trends in volume of reimbursed specialised formula

Data for specialised formula products marketed for infants less than one year in England are shown in Figure 1. Prescribed volumes rose 2.8-fold between 2007 and 2018 without any subsequent rise. This represents a 4.9-fold increase in EHF and a 6.7-fold increase in AAF for those years, accompanied by a decline in soya formula. There was an earlier rise in volumes of reimbursed soya formula, peaking in 1994 at 5.5 to 6.4 times greater than expected volume. In 2020, soya represented less than 1% of reimbursed specialised formula volumes, but the total volume of reimbursed specialised formula was 9.7 to 12.6-fold greater than expected. Data for other regions of the United Kingdom showed similar trends (Figures S1 to 3). Volumes of reimbursed specialised formula marketed for children over one year in England increased to 2019, mainly AAF, without a further rise in 2020, at less than one-tenth the volumes for infants under one year (Figure S4).

Data for specialised formula products marketed for infants less than one year in Norway are shown in Figure 2. Prescribed volumes rose 2.2-fold between 2009 and 2020. This represents a 1.7-fold increase in EHF and 30.8-fold increase in AAF for those years, with cessation of

soya prescription from 2010 onwards. In 2020 the total volume of reimbursed specialised formula was 8.3 to 15.6-fold greater than expected. Volumes of reimbursed specialised formula marketed for children over one year in Norway increased to 2019, mainly EHF, without a further rise in 2020, at approximately one-quarter the volumes for infants under one year (Figure S5). For Norway, data were available on the number and age of children who had received at least one prescription of at least one of the included specialised formula products. These data in relation to total number of live births are shown in Figure 3. The proportion of infants prescribed specialised formula rose from 2.2% in 2009 to 6.9% in 2020. In 2020, the proportion of Norwegian infants less than one year prescribed a specialised formula was 11.2- to 13.3-fold greater than expected. In 2020, 69.7% of specialised formula marketed for infants under one year was prescribed for this age group, but 30.3% was prescribed for older children (Figure S6). Similarly, 60.4% of specialised formula marketed for children over one year was prescribed for this age group, but 39.6% was prescribed for infants under one (Figure S7).

Data for specialised formula products marketed for infants less than one year in Australia are shown in Figure 4. Prescribed volumes rose 3.2-fold between 2001 and 2012. This represents a 1.8-fold increase in EHF and a 5.0-fold increase in AAF for those years. Prescribing restrictions were introduced in late 2012 which mandated specialist consultation for prescription of AAF. Direct sale of EHF and rice-based formula to the public was introduced in 2013 which may also have limited any further rise in reimbursed specialised formula volumes after 2012. Despite increased availability of EHF outside of the PBS system, reimbursed volumes of EHF continued to increase from 2013 to 2020. In 2012, the last year where data are likely to be complete, the total volume of reimbursed specialised formula was 3.2 to 4.4-fold greater than expected. In 2020, where data are likely to be incomplete due to availability of EHF and rice infant formula without prescription (i.e. over the counter), the

total volume of reimbursed specialised formula was 3.3 to 4.5-fold greater than expected. Volumes of reimbursed specialised formula marketed for children over one year in Australia increased to 2012, exclusively AAF, but were also stable between 2013 and 2020 at approximately one-tenth the volumes for infants less than one year (Figure S8). In 2020, AAF accounted for 33.7% of prescribed specialised formula in England, 30.6% in Norway and 53.5% in Australia.

Trends in expenditure on reimbursed specialised formula

Data for expenditure on specialised formula products marketed for infants less than one year in England are shown in Figure S9. Prescription costs rose from £4.6 million per annum in 1991 to £59.8 million in 2018 with a fall to £53.5 million in 2020. At the peak of soya formula reimbursement in 1994, the total cost of specialised formula was £7.1 million. AAF accounted for 55% of expenditure in 2020. In 2020 England's public expenditure on specialised formula for managing milk allergy equated to £91 (US\$117; €103 euros) per infant born in that year.

Data for expenditure on specialised formula products marketed for infants less than one year in Norway are shown in Figure S10. Prescription costs rose from Kr15.9 million per annum in 2009 to Kr46.4 million per annum in 2020. AAF accounted for 54% of expenditure in 2020. In 2020 Norway's public expenditure on specialised formula for managing milk allergy equated to Kr880 (US\$93; €82 euros) per infant born in that year.

Data for expenditure on specialised formula products marketed for infants less than one year in Australia are shown in Figure S11. Prescription costs rose from AU\$1.1 million per annum in 1992 to AU\$16.2 million in 2012. Following prescribing restrictions introduced in late 2012, costs fell to AU\$10.0 million by 2020. AAF accounted for the majority of specialised formula expenditure from 1996 onwards and 86% in 2020. In 2020, Australia's public

expenditure on specialised formula for managing milk allergy equated to AU\$39 (US\$27; €23 euros) per infant born in that year.

Discussion

In this international survey we identified three countries with comprehensive, publicly available databases of specialised formula prescription for infants with cow's milk allergy. In all three countries, there was a marked rise in volumes of specialised formula reimbursed by public health systems in the early 21st century, in the absence of any concurrent evidence for a rise in milk allergy.¹²⁻¹⁵ The data suggest that by 2020 there was 10-fold excess use of specialised formula for managing milk allergy in the United Kingdom and Norway and at least three-fold excess use in Australia, where non-recorded specialised formula use is likely to be greater than in the United Kingdom and Norway. In Norway, the proportion of infants prescribed specialised formula was at least 10 times expected levels. These data suggest high levels of milk allergy overdiagnosis and mark an important shift in early child nutrition. The findings fit within a wider picture of global increases in per capita consumption of infant formula, which itself represents an important shift in early child nutrition.¹⁶ Rapid increases in AAF reimbursement were first noted in Australia in 2006 and an increase in specialised formula prescriptions in England was reported in 2018 and 2020.²⁻⁴ However, this is the first comprehensive evaluation of trends in either country and the first report of trends in Norway. The lack of further increase in AAF prescription in Australia since 2013 is likely due to prescribing restrictions put in place at that time. AAF prescriptions were 2.2-3.0 fold higher than expected total specialised infant formula prescriptions in Australia in 2012, compared with 1.4-1.9 fold for England and 0.7-1.4 fold for Norway; whereas by 2020 AAF rates were up to 4-fold higher than expected in England and Norway, but only up to 2.4-fold higher in Australia. Although EHF has been available since the 1940s, soya formula appears to have been the dominant specialised formula in the late 20th century, at least in England. In the late 1990s, concerns were raised about phytoestrogens in soya formula affecting endocrine development, especially thyroid and reproductive functions.¹⁷ These concerns led national

governments to recommend against use of soya formula in the early years of the 21st century, which likely accounts for the decline in soya formula prescriptions and replacement with EHF and AAF.¹⁸

Levels of specialised formula prescription now significantly exceed expected levels in these countries. The long-term consequences of this change in early nutrition for a significant minority of the population are unknown. Standard infant formula products derive most of their sugar content from lactose naturally present in cow's milk, which is not considered a free sugar. Although free sugars are added to standard formula products, especially those marketed for children aged over one year, free sugars are present in higher quantities in specialised formula products, especially AAF, than in standard infant formula.⁶ A young infant drinking 780mls per day of AAF might consume up to 55g of dried glucose syrup per day, which compares to United Kingdom Department of Health and Social Care recommended upper limits of 14g free sugars per day for children aged 2 to 3 years and 30g per day for adults.⁸ Free sugars intake has been linked with dental decay and obesity, which has led the World Health Organization (WHO) and others to recommend limiting total free sugars consumption for both children and adults.^{6,8,19-21} Excessive specialised formula use has been interpreted as a consequence of cow's milk allergy overdiagnosis, which in turn has been associated with adverse effects on maternal quality of life and breastfeeding confidence.²⁻⁴ Patient charities, healthcare professionals and the formula industry have all been implicated in contributing to milk allergy overdiagnosis.³ Milk allergy diagnosis and management guidelines may also have played a role in promoting overdiagnosis.⁵

Limitations

This study is limited to data analysis of reimbursements from community prescriptions only and does not include direct to consumer, non-reimbursed sales. In Australia, these are likely

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to have been higher than in England or Norway since 2013, which may partly explain the lower rates of specialised formula use in Australia. There is some uncertainty about the assumptions underlying our calculations. Although the most robust estimate of challenge-proven milk allergy incidence in the first two years is less than 1%,¹ studies using less stringent criteria for diagnosing milk allergy tend to report higher rates.²² We also assumed that formula feeding rates and volumes would be similar in infants with milk allergy to the general population, and there is little empirical evidence for or against this assumption. However, the Norwegian data on number of infants prescribed a specialised formula show a similar level of overtreatment to the data for prescribed volumes, suggesting that formula consumption may be similar to population norms in those using specialised formula. We have assumed that milk allergy overdiagnosis is mainly responsible for this observed increase in use of specialised formula. It is possible that there has been an increase in milk allergy incidence, as recently reported in one Chinese study.²³ However, epidemiological studies do not suggest any increase in milk allergy in England or Australia in recent decades.¹²⁻¹⁵ Finally, data are limited to three, high-income countries and trends in specialised formula consumption may differ in other settings - other methodologies may be needed to develop a complete understanding of global patterns of specialised formula use.

Conclusions

This study provides evidence of increased and excessive prescription of specialised formula for managing cow's milk allergy in formula-fed infants in three countries. The data show an important shift in early childhood nutrition which is likely to increase early years free sugars consumption and may promote the development of non-communicable disease.

Author contributions

Dr Boyle had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Boyle, Mehta, Allen.

Acquisition, analysis or interpretation of data: All authors.

Drafting of the manuscript: Mehta, Allen, Boyle.

Critical revision of the manuscript for important intellectual content: All authors

Statistical analysis: Mehta, Allen, Boyle.

Administrative, technical or material support: All authors

Supervision: Boyle.

Declaration of interests

DEC declares grant funding unrelated to this work from the National Health and Medical Research Council of Australia, part time employment at DBV technologies who develop food allergy treatments, and advisory board payments from Allergenis and Westmead Fertility Centre. RJB declares consultancy payment from Cochrane, John Wiley and sons and the British Society for Allergy and Clinical Immunology for editorial work, and payment for expert witness work in cases involving food anaphylaxis and a disputed infant formula health claim. All other authors declare they have no competing interests.

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1998 in England; and to Rebecca S Jones, library manager and liaison librarian at Imperial College London for assistance sourcing historic Prescription Cost Analysis data.

Data sharing:

Detailed summary data are presented in the supplementary material. Requests for access to this information should be directed to the corresponding author, and reasonable requests for data sharing will be considered.

Table 1. Specialised formula products included in analyses

	Australia	England	Norway
Soya Formula			
Farley's OsterSoy Formula	-	1991 – 1993	-
Farley's Soya	-	1998 – 2015	-
Infasoy	-	1998 – 2019	-
ProSobee	-	1998 – 2008	2009 – 2010
ProSobee Concentrated Liquid	-	1991 – 1999	-
SMA Wysoy	-	1998 - 2019	-
Extensively Hydrolysed Formula			
Alfaré	1992 – 2020	2001	2009 – 2020
Althéra	-	2013	2009 – 2020
Alimentum	-	2013 – 2019	-
Aptamil Gold+ Pepti-Junior	1998 – 2020	-	-
Aptamil Pepti/ Cow and Gate Pepti	-	2010	-
Aptamil Pepti 1	-	2011 – 2019	-
Aptamil Pepti 2	-	2011 – 2019	-
Milupa Prejomin	-	1991 - 2010	-
Nutramigen ^a	1992 – 2001	1998 – 2016	2009 – 2018
Nutramigen 1 Lipil	-	2004 – 2019	2009 – 2020
Nutramigen 1 with LGG	-	2015 – 2019	-
Nutramigen 2 Lipil ^a	-	2003 – 2019	2009 – 2020

Nutramigen 2 with LGG	-	2015 – 2019	2009 – 2010
Nutramigen 3 ^b	-	2018 – 2020	-
Pepticate	-	-	2013 – 2020
Pepticate Plus ^b	-	-	2016 – 2020
Profylac	-	-	2009 – 2017
Amino Acid Formula			
Alfamino	2014 – 2020	2014 – 2019	2014 – 2020
Elecare	2002 – 2020	-	-
Elecare LCP	2010 – 2020	-	-
Neocate	1994 – 2012	1998 – 2019	-
Neocate Active ^b	-	2007 – 2020	2009 – 2020
Neocate Advance ^b	2004 – 2020	1999 – 2020	2009 – 2020
Neocate Advance Tropical Flavour ^b	2007 – 2015	-	-
Neocate Gold	2011 – 2020	-	-
Neocate Junior ^b	2017 – 2020	2017 – 2020	2019 – 2020
Neocate Junior Vanilla ^b	2012 – 2020	2017 – 2020	-
Neocate LCP	2007 – 2020	2008 – 2019	2009 – 2020
Neocate Nøytral Pulv ^b	-	-	2009 – 2011
Neocate Syneo	2018 – 2020	2018 – 2019	-
Nutramigen AA Lipil	-	2008 – 2014	2009 – 2016
Nutramigen PurAmino	-	2014 – 2020	2015 – 2020

^aIn Norway, these include Nutramigen Farmag Nøytral Pulv, Nutramigen Pulv, Nutramigen Pulver Nøytral ('Nutramigen'); and Nutramigen 2 Farmag Pulv,

Nutramigen 2 DHA Pulv, Nutramigen 2 Lipil Farmag, Nutramigen 2 Pulv ('Nutramigen 2 Lipil') ^bMarketed for children age over one year.

Figure legends

Figure 1. Volume of reimbursed specialised infant formulas for under 1 year olds with milk allergy in England. Data on the number of community prescriptions of reimbursed powdered amino acid formulas (AAF), extensively hydrolysed formulas (EHF) and soya formula products were obtained from the annual England National Health Service Prescription Cost Analysis reports. Volumes were calculated using product details in the British National Formulary for Children. Predicted volumes are the lower to upper bound range of expected total specialised formula consumption, based on 1% of live births each year with milk allergy, population-based formula feeding rates from the 2005 and 2010 United Kingdom National Infant Feeding Survey and estimated daily formula consumption of 780ml at 0-5.9 months and 600ml at 6-11.9 months.

Figure 2. Volume of reimbursed specialised infant formulas for under 1 year olds with milk allergy in Norway. Data on the number of tins of all amino acid formulas (AAF), extensively hydrolysed formulas (EHF) and soya formulas were obtained from the Norwegian Directorate of Health. Volumes were calculated using product details from manufacturer websites. Predicted volumes are the lower to upper bound range of expected total specialised formula consumption, based on 1% of live births each year with milk allergy, population-based formula feeding rates from the 2007 and 2019 Norwegian National Dietary Surveys among 6 and 12-month-old infants and the 2013 Norwegian National Survey and estimated daily formula consumption of 780ml at 0-5.9 months and 600ml at 6-11.9 months.

Figure 3. Percentage of infants under 1 year old prescribed a specialised infant formula in Norway. Data on the number of infants under 1 year prescribed a specialised formula for infants were obtained from the Norwegian Directorate of Health. Data are expressed as %

annual live births for the same calendar year, obtained from Statistics Norway. Predicted lower and upper bound estimates for % of infants who have milk allergy and are formula-fed is based on 1% of live births each year with milk allergy, population-based formula feeding rates from the 2007 and 2019 Norwegian National Dietary Surveys among 6 and 12-month-old infants and the 2013 Norwegian National Survey.

Figure 4. Volume of reimbursed specialised infant formulas for under 1 year olds with milk allergy in Australia. Data on the number of community prescriptions reimbursed by the Pharmaceutical Benefits Schedule and Repatriation Pharmaceutical Benefits Schedule for powdered amino acid formula (AAF) and extensively hydrolysed formula (EHF) products were obtained from Services Australia. Volumes were calculated using product details from manufacturer websites. Predicted volumes are the lower and upper bound range of expected total specialised formula consumption, based on 1% of live births each year with milk allergy, population-based formula feeding rates from the 2010 Australian National Infant Feeding Survey and estimated daily formula consumption of 780ml at 0-5.9 months and 600ml at 6-11.9 months. The Pharmaceutical Benefits Advisory Committee mandated specialist consultations prior to approval of AAF prescriptions products from July 2012 onwards (red arrow) and direct to customer sales of EHF and rice-protein-based formulas were introduced from 2013. Direct to customer sales data and sales of soya formula could not be included in this analysis.

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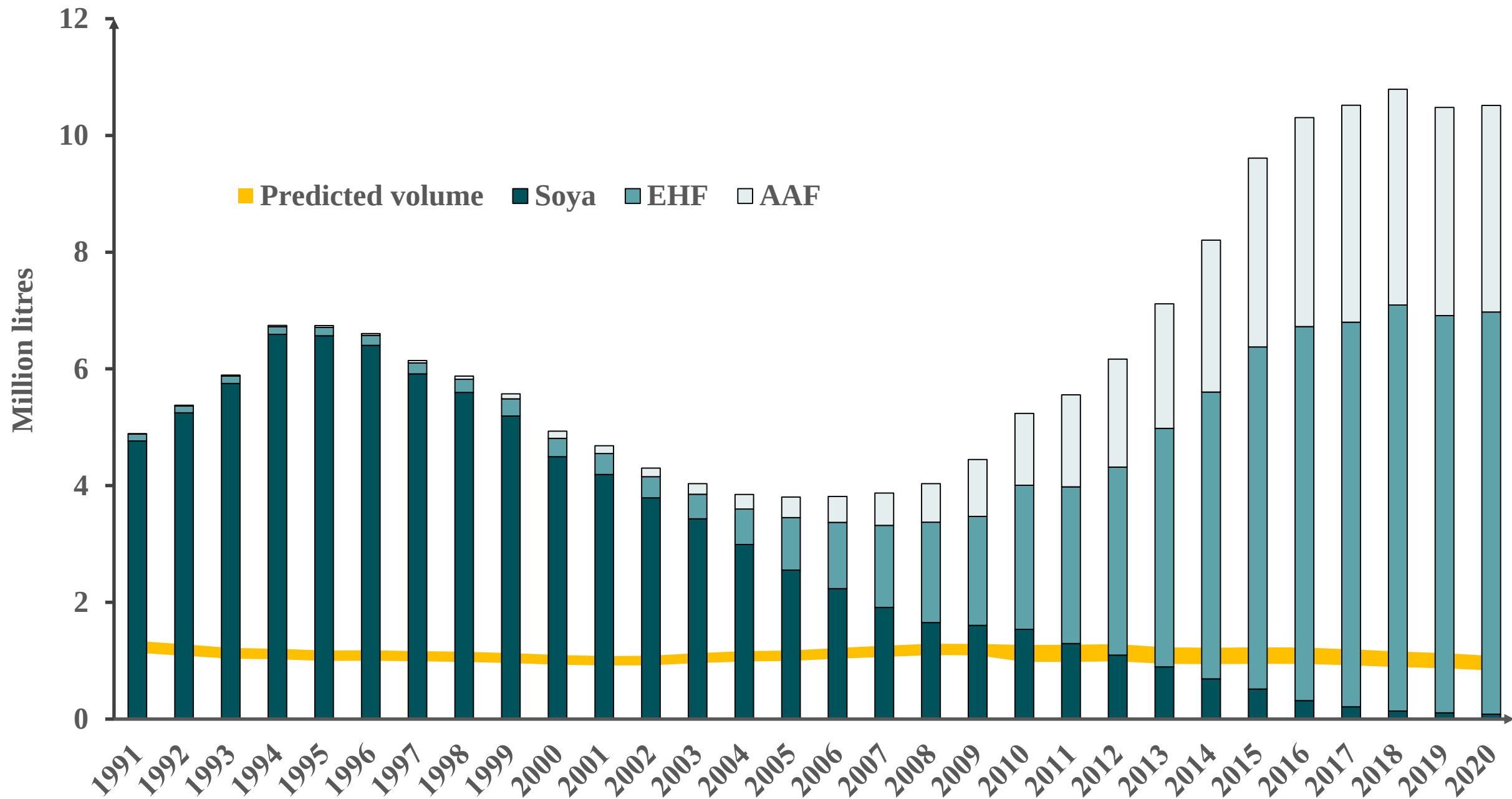
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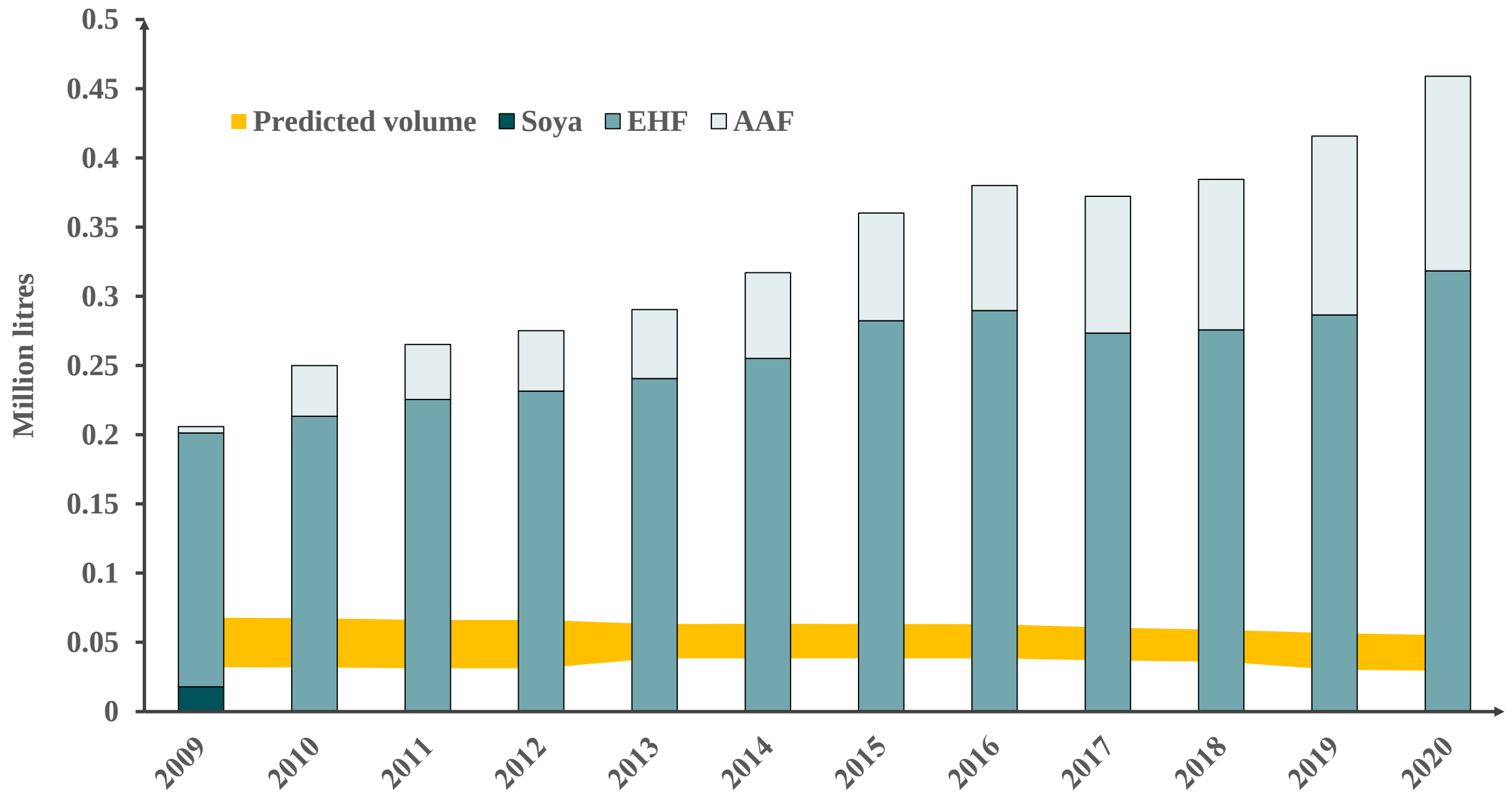
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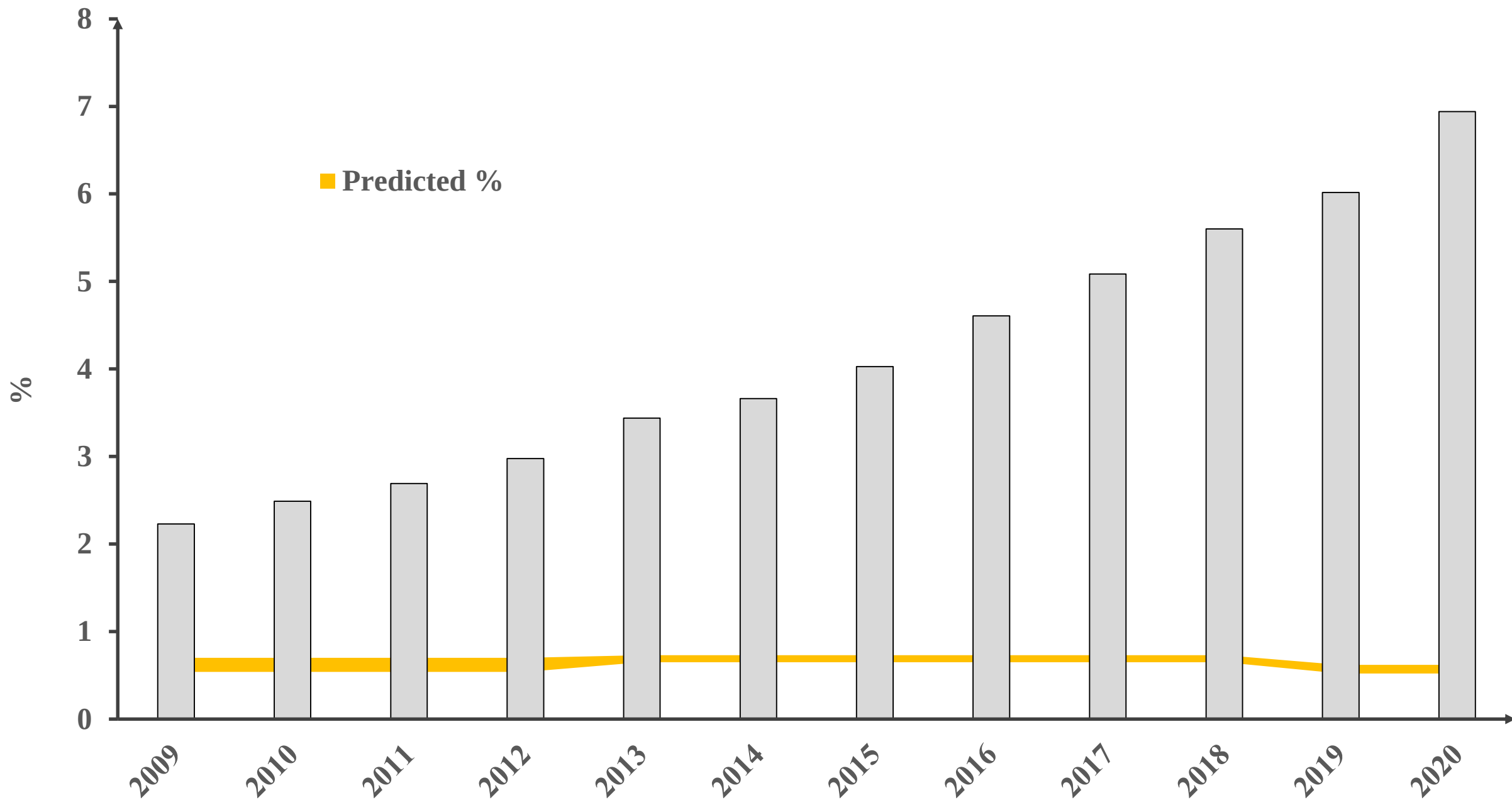
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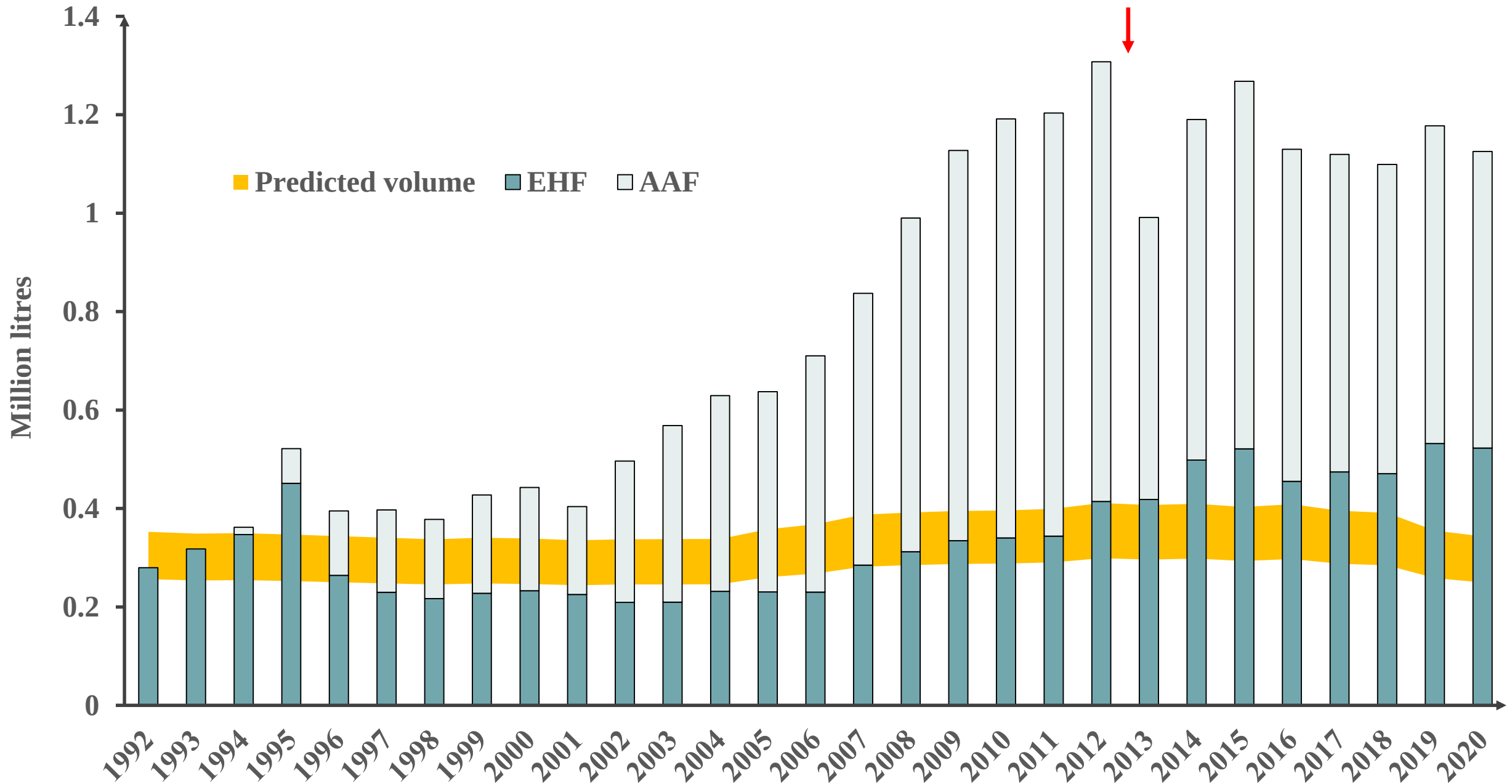


Table.E.1 Logistic regression's parameter estimates (individual threshold as dependent variable)

Milk (n=38)

Parameters	B	SE	p-value	OR	95% CI	
Age	-0.014	0.0447	0.752	0.986	0.903	1.076
Sex	-0.257	0.8093	0.751	0.773	0.158	3.777
Manifestation referred*	0.535	0.8809	0.544	1.707	0.304	9.594
Atopic Deases [#]	-0.732	0.4331	0.091	0.481	0.206	1.124
SPT Milk (PBP)	-0.047	0.1601	0.77	0.954	0.697	1.306
Casein	0.158	0.1871	0.398	1.171	0.812	1.690
Alpha Lactoalbumin	0.016	0.1547	0.915	1.017	0.751	1.377
Beta Lactoglobulin	-0.089	0.1554	0.568	0.915	0.675	1.241
sIgE Milk	-0.015	0.0147	0.291	0.985	0.957	1.013
Casein	-0.042	0.0546	0.437	0.958	0.861	1.067
Alpha Lactoalbumin	0.011	0.1456	0.937	1.012	0.76	1.346
Beta Lactoglobulin	-0.054	0.1359	0.691	0.947	0.726	1.237
Total IgE	0.000	0.0005	0.359	1	0.999	1.001
Sampson Score	-0.147	0.5403	0.785	0.863	0.299	2.489

Egg (n=49)

Parameters	B	SE	p-value	OR	95% CI	
Age	0.025	0.0248	0.322	1.025	0.976	1.076
Sex	1.257	0.6865	0.067	3.514	0.915	13.494
Manifestation referred*	0.458	0.7990	0.566	1.581	0.330	7.569
Atopic Deases [#]	0.298	0.3963	0.451	1.348	0.620	2.931
SPT Egg white (PBP)	-0.182	0.1084	0.093	0.833	0.674	1.031
Yolk (PBP)	0.288	0.1747	0.100	1.333	0.947	1.877
Egg white	-0.025	0.1371	0.855	0.975	0.746	1.276
Yolk	-0.164	0.1618	0.311	0.849	0.618	1.165
sIgE Egg white	-0.018	0.0486	0.716	0.983	0.893	1.081
Yolk	-0.243	0.1954	0.214	0.785	0.535	1.151
Ovoalbumin	0.065	0.0497	0.192	1.067	0.968	1.176
Ovomucoid	-0.038	0.0834	0.649	0.963	0.818	1.134
Total IgE	0.000	0.0013	0.812	1.000	0.998	1.003
Sampson Score	-0.111	0.3653	0.761	0.895	0.437	1.831

B, understandardized coefficient; SE, Standard Error; OR, Odds Ratio; CI, Confidence Intervals; SPT, Skin Prick Test; PBP, Prick By Prick; sIgE, specific IgE.

*Anaphylactic reaction, other reactions.

[#] Respiratory disease, cutaneous disease, both respiratory and cutaneous diseases, none.