

Clinical & Experimental Allergy / Early View

RESEARCH LETTER | [Full Access](#)

Milk allergy guidelines for infants in England promote over-diagnosis: A cross-sectional survey

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First published: 15 November 2021

<https://doi-org.bibliosan.clas.cineca.it/10.1111/cea.14053>

Key Messages

In 2019, we identified 70 English primary care guidelines for milk allergy diagnosis and management.

All guidelines promoted overdiagnosis by suggesting milk allergy diagnosis for common symptoms such as constipation.

All guidelines recommended maternal dietary restriction, only half indicated breastfeeding is best for milk-allergic infants.

To the Editor,

Diagnosis of cow's milk allergy (CMA) in infants is based on reproducible symptoms and absence of symptoms on elimination of cow's milk protein.^{1,2} Previous research has raised concerns that CMA guidelines published by national or international organizations could be driving CMA overdiagnosis.¹ Personal testimonies by mothers suggest that a diagnosis of suspected CMA may reduce breastfeeding confidence, especially when maternal dietary restrictions are advised,² and the potential for this to lead to cessation of breastfeeding has been suggested by earlier comments by experts in the fields of breastfeeding and CMA.^{2,3} Dietary restrictions are not likely to be needed for most breastfed infants with CMA, since

quantities of cow's milk protein transferred to the infant via breastmilk are much smaller than thresholds of reactivity in children with CMA.¹⁻³ Data from England show that specialized formula prescriptions have been steadily rising, with a 5- to sixfold increase in prescription costs in England between 2008 and 2018.^{4,5} There is no sign of a change in CMA prevalence in the UK, Australia or the United States over the past 30 years to explain this trend.⁶⁻⁸

We sought to explore the role that local guidelines play in CMA overdiagnosis, by performing a cross-sectional survey of all available local primary care guidelines endorsed or co-authored by the 191 clinical commissioning groups (CCGs) in England. CCGs are overseen by health commissioners who look after local health needs and manage the health budget for regions of England, each with a population of between a hundred thousand and a million people. Between April and September 2019, we searched all 191 CCG websites for guidelines on the diagnosis or management of infants with suspected CMA. TS and RT extracted data independently from each guideline using a bespoke data extraction proforma. There was excellent agreement between the data extractors (eg $\kappa = 0.779$ for stating breast milk is best for infants with CMA), but in the small number of cases where there was a discrepancy in data extraction, this was resolved by direct discussion, or arbitration by a third researcher, HSH. Data were analysed using Microsoft Excel 2016, and graphs developed within the package. Statistical analysis using the independent t test was performed in SPSS version 27 (IBM).

One hundred and sixty (84%) health regions in England had accessible CMA guidelines during the study period. There were 70 different guidelines, with 38 (54%) guidelines unique to a region, and 32 (46%) used across more than one region. Out of 67 guidelines identifying the date of authorship, 45 (67%) were from 2017 or later, with only 10 (15%) from 2015 or earlier. Fifty of 70 (71%) reported an updated due date, with 18/50 (36%) having expired on or before the previous year.

Sixty-three (90%) guidelines addressed CMA diagnosis, of which 43 (68%) reported separate criteria for non-IgE-mediated CMA, and 20 (32%) reported a single set of diagnostic criteria without discriminating non-IgE- and IgE-mediated CMA signs and symptoms. As shown in Figure 1, a wide range of signs and symptoms were included in diagnostic criteria specific for non-IgE-mediated CMA, covering the most common signs and symptoms that occur in healthy infants. Only four symptoms (constipation, diarrhoea, colic and eczema) were consistently reported by all 43 guidelines as suggestive of non-IgE-mediated CMA. Other symptoms commonly cited were reflux (98%), blood in stools and food refusal (both 95%), and mucus in stools, pruritus and erythema (each 88%). Symptoms and signs that were only rarely cited as indicators of non-IgE-mediated CMA included nausea (2%) and breathlessness (9%).



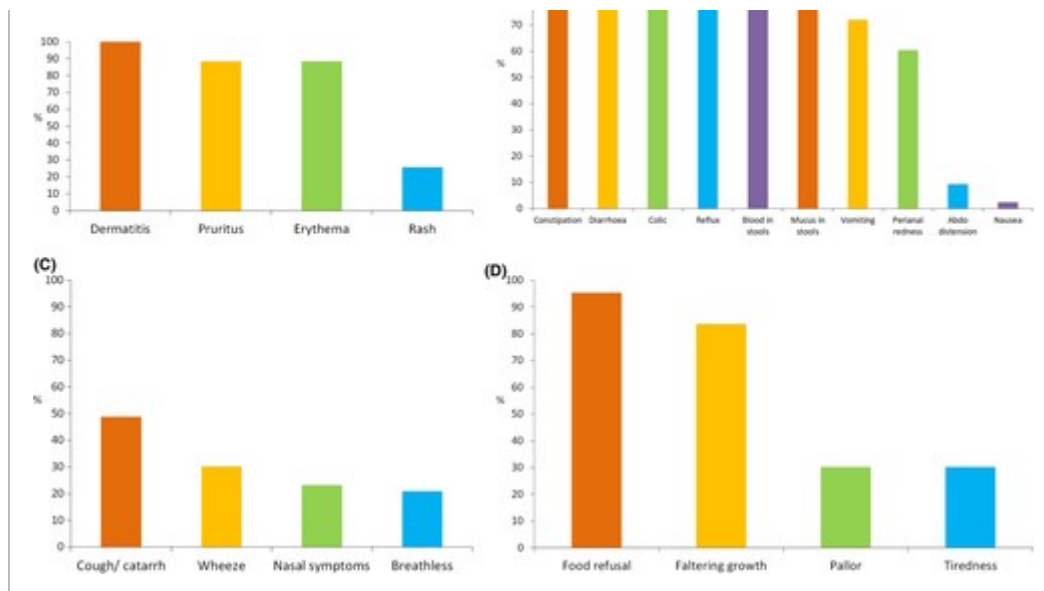


FIGURE 1

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Guideline recommendations for diagnosis of non-IgE-mediated milk allergy. Data shown are the frequency with which specific skin (A), gastrointestinal (B), respiratory (C) or general (D) symptoms or signs were cited as indicators of possible non-IgE-mediated milk allergy, in the 43 community infant milk allergy guidelines in England which specifically addressed symptoms and signs of non-IgE-mediated milk allergy in 2019

The commonest symptoms and signs used as diagnostic criteria by the 20 guidelines not separating non-IgE- from IgE-mediated CMA were eczema, reflux and constipation (all 100%), diarrhoea (95%), colic, vomiting and blood in stools (90%). Anaphylaxis was cited as an indicator of CMA in 16 (80%) of these guidelines. Out of all 63 guidelines on diagnosis of suspected CMA, 15 (24%) stated that there were usually a few or several symptoms present, and 55 (87%) mentioned that in order to reach a definite diagnosis, infants need to be rechallenged with cow's milk protein after a period of two to six weeks to see whether symptoms return.

The management of suspected CMA was addressed by all 70 guidelines. Sixty-four (91%) addressed management in breastfed infants, summarized in Figure 2. They all advised exclusion of cow's milk products from the maternal diet; the remaining six guidelines only addressed management in formula-fed infants and did not address breastfeeding a child with CMA. Very few (4/64, 6%) stated that a switch from breast to specialist formula milk may be indicated. A possible need to avoid other mammalian milk was suggested by 11/64 (17%), and non-milk products by 12/64 (19%). Out of the 64 guidelines for the management of breastfed infants with suspected CMA, 32 (50%) stated that breast milk is the best milk for infants with suspected CMA, with further 12 (19%) advising encouragement to continue breastfeeding without stating any reason for this. Only 5 (8%) suggested referral to a breastfeeding support advisor. No guidelines suggested that there should be any differences in diagnostic criteria for CMA (eg types or numbers of symptoms/signs) between

breastfed and bottle-fed infants. Only 9 (13%) stated more generally that CMA was less common in breastfed infants or required a different diagnostic approach.

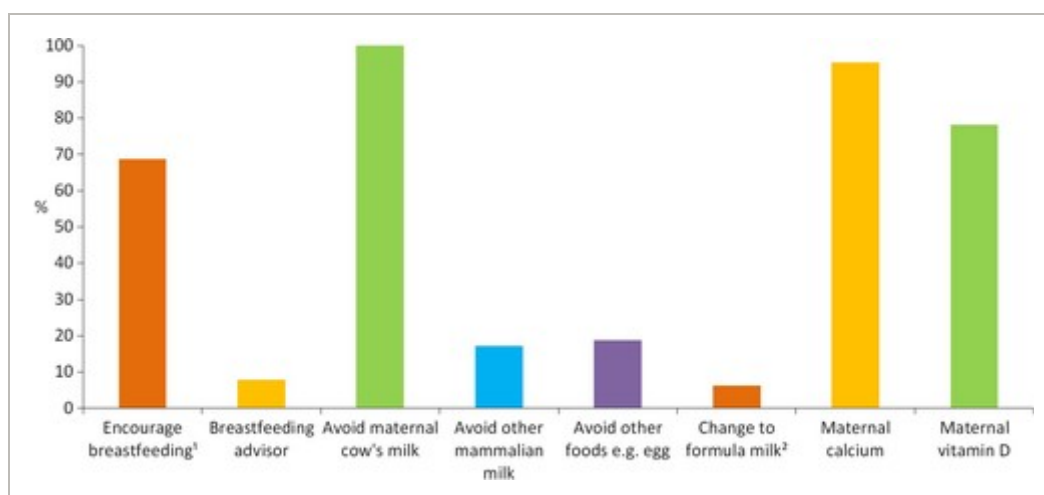


FIGURE 2

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Guideline recommendations for breastfed infants with suspected milk allergy. Data shown are the frequency of specific recommendations for managing breastfed infants with suspected milk allergy in the 64 community infant milk allergy guidelines in England which specifically addressed the management of breastfed infants. Data shown represent recommendations made for either all or a subset of breastfed infants with suspected milk allergy.¹Guidelines that contained a general statement about breast milk being best for infants with milk allergy were included ($n = 32$), along with those suggesting encouraging continuation of breastfeeding without a reason stated ($n = 12$).²Other than for reason of parental choice

All 70 guidelines recommended that the less expensive extensively hydrolysed formula (EHF) was used in uncomplicated mild/moderate cases of CMA in formula-fed infants and included recommendations for when to use the more expensive amino acid formula (AAF). The most common reasons for recommending AAF were severe IgE-mediated reaction to CMA such as anaphylaxis (64, 91%) and severe non-IgE-mediated CMA (59, 84%). Fifty-four (77%) guidelines suggested using AAF if EHF was unsuccessful, and further 6 (9%) stated AAF was indicated if at least two EHF were unsuccessful. Other stated indications for AAF were if infants had previously reacted to cow's milk protein in maternal breastmilk (34, 49%), multiple food allergies (20, 29%) and any IgE-mediated CMA, even if not severe (4, 6%).

This is the first cross-sectional survey of English milk allergy guidelines produced by regional commissioners for the diagnosis and management of CMA. We extracted and analysed data from 70 unique guidelines. The guidelines all appear to promote overdiagnosis of CMA, as they list multiple symptoms and signs that occur in many infants without underlying pathologies, and have little established relationship with CMA. Guidelines also fail to support breastfeeding, with universal recommendations to restrict maternal diets, a practice which is unlikely to be necessary in most breastfed infants with CMA,³ and a notable lack of advice is

that breastmilk is the best milk for infants with CMA in many guidelines. However, they were mostly consistent in not recommending that some women should switch from breastfeeding to using specialist formula.

A previous review of existing national and international guidelines raised concerns that they could lead to an overdiagnosis of CMA and a reduction in breastfeeding.³ Our findings suggest a similar risk arising from guidelines approved by local commissioners in England. Together, these two studies may help to explain the significant over-prescription of specialist formulas for managing CMA in England.⁴⁻⁶ The guidelines we reviewed also showed significant regional variations in recommendations for using AAF in place of EHF, which likely reflect a wider lack of consensus on this issue.⁹

Strengths of our study are that we reviewed guidelines from most health regions in England, and data were extracted consistently, with good agreement between the data extractors. A limitation of this work is that guidelines were only evaluated for one country, and local guidelines are not the only source of information that guides community practice in England. Thus, other guidelines, cultural norms, practices and patient expectations may also be relevant to the overdiagnosis and overtreatment of CMA.

CMA overdiagnosis is important, due to the impact on infants, families and healthcare services, and due to the potential for overdiagnosis to undermine breastfeeding.^{2,3} The diagnosis of CMA is predominantly made in primary care in England, and there is a need for greater support to reduce the current level of overdiagnosis and overtreatment. More evidence-based CMA guidelines would be the first step towards this, plus greater support for primary care, health visiting and community dietician services. Provision of help for families whose infants have common, self-limiting symptoms may be important in addressing dynamics that make incorrect diagnosis more likely.

CONFLICTS OF INTEREST

RB declares personal consultancy payments from Cochrane and Prota Therapeutics, expert witness fees for giving evidence in cases related to food anaphylaxis and infant formula health claims, and payments from Public Health England for membership of the UK Nutrition and Health Claims Committee and the UK Scientific Advisory Committee on Nutrition's Subgroup on Maternal and Child Nutrition. All other authors report no conflicts.

AUTHOR CONTRIBUTIONS

TS led and designed the study. MS and RB advised on study design and interpretation. TS, RT and HSH extracted data and performed initial delivery and interpretation of the findings. TS wrote the first draft of the research letter with assistance from RB and MS. All authors reviewed, commented and approved the final manuscript.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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