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Commentary: Reaching a milestone in diagnosing coeliac disease

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Clinical prediction rules for diagnosis seek to optimise the sensitivity and specificity of our diagnostic approach to a given problem. In this issue of the *BMJ*, Hopper and colleagues report a rare accomplishment in this regard—a decision rule that achieved 100% sensitivity in disease detection, in this case for coeliac disease.¹ The rule is simple—a positive serological test for IgA antibody to tissue transglutaminase combined with being at “high risk” (having weight loss, diarrhoea, or anaemia). The rule identified every patient with the disease in a cohort of 2000 patients, all of whom underwent intestinal biopsy as the gold standard and the final diagnostic step. This is a welcome advance. As the authors emphasise, coeliac disease may affect up to one in a 100 people, only one case in seven is ever diagnosed, and an appreciable diagnostic delay of many years often occurs.^{2,3}

This result will probably not change clinical practice, however, as current algorithms for coeliac disease already incorporate these factors. Rather, this study strongly validates this approach and allows us to estimate with some confidence the probabilities of success or failure at each step of the process. The results support the current practice of forgoing endoscopic biopsy in low risk patients with negative serology, as none of the 1170 patients meeting these criteria was found to have coeliac disease on biopsy. The study confirms that biopsy has an important role in high risk patients with positive serology. It has been suggested that this combination provides adequate evidence to diagnose coeliac disease without the need for biopsy, and a substantial proportion of patients given the diagnosis (up to 25% in one survey) have never been biopsied.³ However, 40% of high risk patients with positive serology in Hopper and colleagues' study did not have coeliac disease when biopsied. Even acknowledging the possibility that coeliac disease can be missed on

biopsy, we agree with the authors that biopsy is essential in this cohort, given the daunting prospect of lifelong adherence to a gluten-free diet.

The wisdom of biopsy in high risk patients who are tissue transglutaminase antibody negative is debatable. Although Hopper and colleagues recommend biopsy in this group, this approach identified only seven additional cases out of the 585 patients biopsied, and at least some of these cases could be predicted by testing for IgA deficiency.

This decision rule now needs to be tested in other settings,⁴ and the rule may fare less well because:

- The population studied was a referral cohort; the base rate of disease will probably be lower in primary care cohorts
- Variability in assigning patients at high risk will increase if subsequent clinicians use their own definitions of weight loss, diarrhoea, or anaemia
- The results of tissue transglutaminase antibody testing will vary more as many different laboratories will be used
- The interpretation of biopsies will be less uniform, given the inherent variability between pathologists and differences in the quality of biopsy samples, which will come from multiple endoscopists.

The decision rule might be improved by incorporating a panel of serological markers. In particular, almost all patients with coeliac disease carry the HLA markers DQ2 or sometimes DQ8. The absence of DQ2 and DQ8 would therefore be reassuring in patients who are at high risk but are tissue transglutaminase antibody negative. Until a better rule is developed and validated, the decision rule of Hopper and colleagues seems to be the most cost effective and efficient way to assess coeliac disease.

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Operational implications of using 2006 World Health Organization growth standards in nutrition programmes: secondary data analysis

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ABSTRACT

Objective To assess the implications of adopting the World Health Organization 2006 growth standards in combination with current diagnostic criteria in emergency and non-emergency child feeding programmes.

Design Secondary analysis of data from three standardised nutrition surveys (n=2555) for prevalence of acute malnutrition, using weight for height z score (<-2 and <-3) and percentage of the median (<80% and <70%) cut-offs for moderate and severe acute malnutrition from the National Center for Health Statistics/WHO growth reference (NCHS reference) and the new WHO 2006 growth standards (WHO standards).

Setting Refugee camps in Algeria, Kenya, and Bangladesh.

Population Children aged 6-59 months.

Results Important differences exist in the weight for height cut-offs used for defining acute malnutrition obtained from the WHO standards and NCHS reference data. These vary according to a child's height and according to whether z score or percentage of the median cut-offs are used. If applied and used according to current practice in nutrition programmes, the WHO standards will result in a higher measured prevalence of severe acute malnutrition during surveys but, paradoxically, a decrease in the admission of children to emergency feeding programmes and earlier discharge of recovering patients. The expected impact on case fatality rates of applying the new standards in conjunction with current diagnostic criteria is unknown.

Conclusions A full assessment of the appropriate use of the new WHO standards in the diagnosis of acute malnutrition is urgently needed. This should be completed before the standards are adopted by organisations that run nutrition programmes targeting acute malnutrition.

INTRODUCTION

The World Health Organization's child growth standards (WHO standards) are based on data from a multicentre international study and reflect how children

grow under optimal conditions. They are designed as a standard rather than just a reference and can be used for individual diagnoses and international comparisons.^{1,2} The standards were released in April 2006, and WHO is advocating their adoption as a replacement for the currently used international growth reference, produced by the National Center for Health Statistics, Centers for Disease Control and Prevention, and WHO in 1978 (NCHS reference).³ Many unanswered questions remain, however, relating to the practical implementation and monitoring of nutrition programmes with the new WHO standards.

The prevalences of global acute malnutrition and severe acute malnutrition are key indicators calculated from the weight for height index of a sample of children. They are used to monitor high risk or food insecure situations and to trigger alerts and leverage resources for interventions.⁴ Nutritional status can be expressed by the zscores method, which corresponds to standard deviations from the mean value, or as percentages of the median value.

Global acute malnutrition includes all cases with a weight for height index below a z score of -2 or 80% of the median, plus cases with oedema, whereas severe acute malnutrition includes those cases with a weight for height index below a z score of -3 or 70% of the median, plus cases with oedema. Whereas z score cut-offs are routinely used to assess the need for an intervention, admissions to and discharges from feeding programmes are often based on the more easily calculated percentage of the median cut-offs.

In this paper, we use z score cut-offs and calculated percentage of the median cut-offs to compare retrospectively the prevalence of malnutrition obtained in nutritional assessments in three refugee food aid operations. We then calculate the potential impact on the numbers of children treated in selective feeding programmes.

METHODS

We used the two methods commonly used for describing the anthropometric status of children—z scores and the percentage of the median—for the

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