and INR. MELD scores can range from 6 to 40 (MELD scores greater than 40 are all grouped together and receive a score of 40)."

Despite the fact that it should be impossible to achieve a MELD score of >40, many of the online calculators do indeed generate numbers greater than this ceiling value. This is dependent upon numbers entered for the international normalised ratio (INR), bilirubin and creatinine. We would therefore caution all clinicians when using these or similar calculators to analyse retrospective data. MELD scores can easily and incorrectly be generated with values >40.

Calculation of the median score (with interquartile ranges) would not highlight this problem, but sample mean and SD may. These values may skew the data—for example, the 5-month survival probability with a MELD score of 40 should actually be lower than depicted on the graph, and the mean MELD score in table 1 should be <18.

This has potential ramifications for all large multicentre trials and systematic reviews utilising published MELD scores.

We would also like to add comment to the potential influence of sodium not meeting the fourth criterion of ‘stability’ in a scoring system for organ allocation. Sodium levels, like creatinine, can be easily manipulated through overzealous diuretic usage. Perhaps the measurement of variables not directly influenced by diuretic use would be of benefit.

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REFERENCE

Toxigenic and non-toxigenic Clostridium difficile: determinants of intestinal colonisation and role in childhood atopic manifestations

In a previous paper published in this journal, we reported on the role of the intestinal microbiota in the development of atopic manifestations, as examined in a prospective birth cohort (KOALA). 1 We showed that infants colonised with Clostridium difficile were at increased risk of developing eczema, wheeze and sensitisation. An association between C. difficile and atopic diseases has also been reported by others. 2, 3

A possible underlying mechanism could be through breaking oral tolerance, as C. difficile can cause inflammation in gut tissues, leading to increased permeability of the mucosal barrier and thus facilitating the penetration of allergens. 4 The enteropathogenicity of C. difficile is associated with the production of toxins A and B, encoded by the genes tcdA and tcdB. Both toxins disrupt epithelial cell tight junctions and thereby ablate epithelial barrier function. 5 According to the hypothesised mechanism, it is expected that especially infants colonised with toxin-producing strains are at increased risk of developing atopic diseases.

The aim of this study was to examine which factors influence (non)-toxigenic C. difficile colonisation and to examine the role of C. difficile toxigenicity on the development of atopic manifestations.

Faecal samples of 957 one-month-old infants, participating in the KOALA study, were available for analysis (for a detailed description of methods see Penders et al.). The samples have been subjected to real-time PCRs for the detection of C. difficile and its toxins A and B, according to the assays as described in Penders et al., Belanger et al. 6 and van den Berg et al. 7, respectively.

Information on potential determinants of (non)-toxigenic C. difficile colonisation, atopic symptoms and potential confounders was retrieved through repeated questionnaires. Specific immunoglobulin E (IgE) was measured in blood samples collected at the infant’s age of 1 and 2 years. A clinical diagnosis of eczema was made at 2 years. A total of 200 infants (20.9%) were colonised with non-toxigenic (A+B−), 36 (3. 8%) with toxigenic A+B+ and 4 (0.4%) with toxigenic A+B− C. difficile. Hospital delivery (especially caesarean section) and hospital admission following birth were associated with higher colonisation rates of both toxigenic and non-toxigenic C. difficile. Exclusively breastfed infants were less often colonised with (non)-toxigenic strains compared with their formula-fed counterparts. Boys were at increased risk of being colonised with toxigenic strains (fig 1). Maternal education, maternal organic and/or vegetarian diet, maternal probiotic and antibiotic use during pregnancy, birth season, number of siblings, fever in the first month of life and the presence of furry pets were not associated with colonisation by either non-toxigenic or toxigenic C. difficile.

Colonisation of infants with non-toxigenic, but not with toxigenic, C. difficile increased the risk of developing (parentally reported and clinically diagnosed) eczema and sensitisation to food allergens (tables 1 and 2). This implies that toxins A and B are not responsible for the increased risk of eczema and sensitisation among carriers of C. difficile. The different

Figure 1 Faecal counts of C. difficile in infants colonised with non-toxigenic (median 4.68 log10 colony-forming units (CFU)/g; 95% range 2.73–8.23) and toxigenic (median 7.55 log10 CFU/g; range 3.0–8.41) strains. *Reference category
assoc.