Nutritional management of high-output ileostomies in paediatric patients is vital and more evidence-based guidelines are needed

Marijke Awouters1 | Tim Vanuytsel2 | Koen Huysentruyt3 | Pauline De Bruyne4 | Karen Van Hoeve5 | Ilse Hoffman5

INTRODUCTION

Ileostomies are created in children for diverse, age-related reasons. These include necrotising enterocolitis, intestinal atresia, meconium ileus, intestinal perforation, Hirschsprung’s disease, volvulus, abdominal trauma, polyposis and inflammatory bowel disease. Chronic intestinal failure with parenteral nutrition dependence is rare in ileostomy patients. A substantial length of the small intestine remains after the procedure so its absorptive capacity is retained. Nevertheless, medical complications can occur, such as...
as dehydration, electrolyte depletion, micronutrient deficiencies, osteopenia and malnutrition. These risks increase when there is a high-output ileostomy (HOI).\textsuperscript{1-3} Infants with an HOI are especially vulnerable to growth failure, with a decline in z-score for weight in the period between stoma formation and closure.\textsuperscript{3,4} Fortunately, the z-score generally recovers after stoma closure.\textsuperscript{5}

The colon is responsible for a substantial part of enteral fluid absorption.\textsuperscript{6} Interruption of its continuity therefore leads to an increase in enteral fluid losses. After ileostomy formation, an initial phase of postoperative ileus is followed by a gradual increase in ileostomy output in the first couple of days. Afterwards, enteric adaptation results in an increased absorptive capacity of the small bowel. This generally leads to decreasing output over the following weeks.\textsuperscript{6} Kanaghanis et al. reported a median faecal weight after adaptation of approximately 465 ± 219 grams per 24 h in adult ileostomy patients.\textsuperscript{7} No data for children are available. An HOI can emerge temporarily before adaptation or can be caused by intercurrent events such as infections. A small number of patients fail to adapt and develop a chronic HOI. The enteroendocrine L-cells normally optimise proximal gut absorption by secreting the adaptation promoting hormones peptide YY and glucagon-like-peptide 2. These cells are found in the terminal ileum and proximal colon. Therefore, the more the ileum is resected, the more the adaptive process can be disrupted.\textsuperscript{5,8}

When an HOI occurs, good nutritional management is vital to prevent the complications detailed above. However, the paediatric literature is scarce. There are no paediatric guidelines available on the nutritional management of an HOI and no universally agreed upon definition of paediatric HOI exists. The aim of this review was to summarise the available literature and to provide recommendations for the nutritional management of paediatric HOIs, including fluid and electrolyte management.

2 | METHODS

We conducted a thorough search of PubMed and Embase for papers published in English or French up to 31 June 2022. A variety of terms was used, including enterostomy, ileostomy, high output, management, nutrition, paediatric, neonatal, sodium, potassium, vitamin B12 and micronutrients. The reference lists of the selected papers were used to extend our search. Priority was given to papers including paediatric ileostomy patients. When these were lacking, insights were obtained from adult literature and other intestinal failure pathologies.

3 | RESULTS

In total 60 articles were reviewed, comprising 15 reviews, two systematic reviews, 17 retrospective studies, 20 prospective studies, two guidelines, one survey, one basic-science article, one case series and one case report. The papers we reviewed were published between 1962 and 2022. Only 16 papers addressed nutritional issues in paediatric ileostomy patients and 14 of them focused exclusively on neonates. The mean number of patients in these papers was 44.5 (range 1–190).\textsuperscript{2-5,9-20}

3.1 | Cut-offs for paediatric HOI

There is no universally agreed-upon definition of paediatric HOI, with significant differences in the cut-off values used in different paediatric papers. An overview of these values is provided in Table 1. Crealey et al. carried out the only retrospective study examining ostomy output, which was performed in 16 neonates. Half of the population were preterm infants. The authors reported a median stoma output of 5 mL/kg/day in the first 7 days following surgery, followed by a median of 17.5–20 mL/kg/day over the next 3 weeks. An HOI was considered as an output of >20 mL/kg/day, appeared in 10 of the 16 infants and was associated with poor weight gain. The exact ostomy output of these patients was not mentioned.\textsuperscript{9} Two more studies also used 20 mL/kg/day as the cut-off for HOI,\textsuperscript{10,11} but three others only considered >40–50 mL/kg/day as high-output.\textsuperscript{2,12,13} In the latter studies, no distinction was made between jejunostomies and ileostomies.\textsuperscript{2,12,13} In a study by Van Zoonen et al., three of the 10 infants with an output of >50 mL/kg/day died due to uncontrollable fluid and electrolyte losses.\textsuperscript{2}

Even in adults, there is no consensus about the definition of HOI. In general, the output from an ileostomy has been considered to be clinically significant when it exceeded 2000 mL a day on two consecutive days,\textsuperscript{3,4,15} but other studies have used a lower cut-off of 1500 mL.\textsuperscript{16}

3.2 | Identifying organic causes

Organic causes need to be sought when an HOI appears (Table 2). Possibilities include infections such as sepsis, enteritis and intra-abdominal collections. Also small intestinal bacterial overgrowth, intestinal obstruction or sub-obstruction, enteric fistulae, lactose intolerance, prokinetic drugs and recurrent inflammatory bowel disease should be considered. Endocrine causes hypothyroidism and adrenal insufficiency. In addition, mild forms of coeliac disease can become symptomatic once a part of the gastro-intestinal tract is excluded.\textsuperscript{6,15}
Lastly, general feeding intolerance and cows’ milk intolerance can contribute to HOIs in preterms, neonates and infants. When a cause is found, it should be managed appropriately. However, most of the time HOI is idiopathic and empiric treatment should be started.

3.3 | Fluid management

Regulation of enteral fluid ingestion is one of the most important interventions for HOI in toddlers and older children. In general, internal consumption of both hypotonic and hypertonic fluids should be avoided. Hypotonic fluids with an osmolarity of <200 mmol/L, such as still water and most light or zero-sugar soft drinks, elicit a sodium efflux to the intestinal lumen. This results in a net ostomy sodium loss which increases ostomy volumes. The combination of salt and fluid loss can increase thirst, leading to a vicious circle that puts the patient at risk for severe dehydration and electrolyte disturbances. Ingestion of hyperosmolar drinks, such as regular soft drinks and fruit juices, elicits a net water efflux in the duodenum and jejunum, which also leads to increased ostomy output and dehydration.17

Optimal luminal water absorption occurs with isotonic drinks, with an osmolarity around 240 mmol/L was used. A Cochrane review compared the use of reduced osmolarity World Health Organisation (WHO) oral rehydration solution (ORS) (245 mmol/L) with the standard WHO ORS (311 mmol/L) in children with acute diarrhea. The authors found less need for unscheduled intravenous fluid infusions and a decreased stool output when the reduced osmolarity WHO ORS was used. Other studies have also found that optimal absorption of water, electrolytes and glucose occurred when a solution with an osmolarity around 240 mmol/L was used. Therefore, the use of glucose-electrolyte solutions such as St Mark’s electrolyte mix or the reduced osmolarity WHO ORS should be encouraged (Table 3). Some commercially available sport drinks are also suitable, but many of them are too hypotonic or hyperosmolar with too little salt and too much simple carbohydrates. Alcohol and caffeinated drinks should be discouraged in adolescents since both increase ileostomy output.21

An initial oral fluid restriction of 500–1000 mL daily has been
advised in adults with HOI, accompanied by rehydration with intravenous fluids. No recommendations have been formulated for children.

At the onset of HOI, most patients need rehydration with intravenous fluids. No studies have examined the ideal schedule for ad hoc fluid supplementation.

3.4 Electrolyte management

3.4.1 Sodium

Sodium losses are greater in ileostomy effluent than in the stools of healthy individuals, at a mean concentration of 120 mmol/L. This can lead to total body sodium depletion, which has been linked to poor weight gain in neonates and infants. This association was also described in a case series of four children and adolescents. Bower et al. showed that neonates with a higher average ileostomy output of 31 mL/kg/day were more at risk of sodium depletion than infants with a normal average output of 16 mL/kg/day. Sodium depletion was defined as a urinary spot sodium level of <10mmol/L. Zarraga et al. reported growth failure due to sodium depletion in a neonate with an ileostomy output fluctuating between 20 and 30 mL/kg/day.

The optimal methods to assess sodium status are 24-h urine collection and calculating the fractional sodium excretion. Regrettably, both methods are not always easily attained in clinical practice. No correlation has been found between plasma sodium and growth failure, making it an unsuitable marker for sodium depletion. On the other hand, two studies found a positive correlation between the sodium levels in a spot urine sample and the evolution of the z-score for weight. Butterworth et al. considered a urinary sodium level of <10mmol/L as a severe deficiency and 10–30mmol/L as a moderate deficiency. They proposed a target value between 30 and 50 mmol/L and recommended weekly urinary sodium measurements until a stable level is reached. Very variable individual daily sodium needs have been reported in paediatric patients, with an average of 4–10 mmol/kg/day. Supplements need to be adapted to individual ostomy losses and urinary- and plasma sodium levels.

3.4.2 Potassium

A wide range of potassium content has been reported in the ileostomy fluid of adult patients. On average, the potassium loss ranged from 7 to 20 mmol/L in new ileostomies and 3–13 mmol/L in established ones. No data on children are available. In healthy adults, losses up to 22.5 mmol/24h have been described, with a mean range of 6.2–8.1 mmol/24h. The daily potassium loss in the stools of an adult with an HOI of 1.5 L/24h is thus similar to healthy adults. Moreover, renal compensation was observed in patients with normal kidney function when excessive gastro-intestinal losses developed. No correlation was found between urinary potassium levels and growth in neonates.

3.4.3 Metabolic acidosis

One paediatric study reported a large number of ileostomy patients developing a metabolic acidosis. This was due to the excessive loss of bicarbonate in the ileostomy fluid and the inability of the kidneys to secrete an acid load in the context of sodium depletion. Sodium chloride supplements enabled the majority of these neonates to achieve normal bicarbonate levels. Sodium bicarbonate supplements were recommended otherwise.

3.4.4 Magnesium

Magnesium deficiency is common in ileostomy patients, because it is largely absorbed in the terminal ileum and colon. Furthermore, secondary hyperaldosteronism can develop in response to sodium depletion and can increase renal magnesium excretion. Symptoms of hypomagnesaemia include muscle weakness and spasms, tremors and cardiac arrhythmia. A link with decreased bone mineral density in ileostomy patients has also been suggested. Supplements are often necessary, but intestinal absorption is saturable and very limited in this patient group. Moreover, oral supplements can further aggravate diarrhea and should be used with caution. Parenteral administration might therefore be needed. An oral dose of 10–20 mg elemental magnesium/kg/dose up to four times a day has been proposed. Magnesium oxide is the most frequently used oral form. Magnesium sulphate in 0.9% sodium chloride has been recommended for intravenous suppletion and should be administered through a slow infusion at a maximal rate of 25 mg/kg/h. The suggested dose was 25–50 mg/kg/dose, which equals 2.5–5 mg/kg of elemental magnesium.

3.5 Vitamins and minerals

Vitamin B12 is mainly absorbed in the terminal ileum after being bound to an intrinsic factor in the stomach and deficiencies often

<table>
<thead>
<tr>
<th>Reduced osmolarity</th>
<th>WHO ORS g/L</th>
<th>Saint-Mark’s g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>13.5 g</td>
<td>Glucose 20 g</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>2.6 g</td>
<td>Sodium chloride 3.5 g</td>
</tr>
<tr>
<td>Potassium chloride</td>
<td>1.5 g</td>
<td>Sodium bicarbonate or sodium citrate 2.5 g</td>
</tr>
<tr>
<td>Trisodium citrate, dihydrate</td>
<td>2.9 g</td>
<td>Osmolarity 245 mmol/L Osmolarity 290 mmol/L</td>
</tr>
</tbody>
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TABLE 3 Composition of WHO ORS and Saint-Mark’s solution.
develop after ileal resection. Because oral supplements cannot be used for this patient group, vitamin B12 is classically administered through intramuscular injections. These are painful and may cause stress in children. Sublingual administration has been studied in children at a dose of 1000 μg daily for a week, followed by every other day for 3 weeks. In addition, different dosing schedules of intranasal administration at a dose of 2 mg/puff have been validated in paediatric patients. These administration routes bypass intestinal absorption and are valuable alternatives to intramuscular injections.33,34

Other micronutrient deficiencies are also common. In particular vitamin A, D, E and K and the oligo-elements selenium and zinc should be monitored.15 There are no guidelines available about the frequency of testing. Prothrombin time can be used as an indirect measure to estimate vitamin K levels. Plasma zinc levels were found to be inversely correlated with stoma output in a French study of 30 infants with an ileostomy or jejunostomy.35 A poor enteral zinc absorption of 10% was equally demonstrated in a small study by Balay et al.36 that included 10 infants with an ostomy on nearly full enteral feeds. Low plasma zinc levels were observed in half of the infants.

Iron absorption occurs primarily at the duodenum and proximal jejunum, so ileostomy formation should not significantly affect intestinal iron transport.37 Most iron deficits in ileostomy patients result from their underlying illness.38 Also folic acid and copper are mostly absorbed in the stomach and duodenum, so no deficiencies would be expected after ileostomy formation.39 Nevertheless, Balay et al.36 found low copper levels in half of the infants on enteral nutrition. If there are high stoma losses, the accelerated transit time may compromise intestinal absorption of micronutrients even if they are absorbed proximally. Therefore, follow-up of all micronutrients is warranted.

3.6 Dietary management

3.6.1 Neonates and infants

There are no studies available on the dietary management of ileostomies in neonates or infants. The literature is also scarce in the broader group of intestinal failure patients and mostly focussed on patients with short bowel syndrome. Moreover, recommendations are often more experience based than evidence based.

One study reported that the strongest correlation with shorter duration of parenteral nutrition needs in neonates with short bowel syndrome was seen with breast milk.40 This is thought to be modulated by the presence of immunological factors such as immunoglobulin A, leucocytes and nucleotides, anti-inflammatory cytokines, growth-factors, human milk oligosaccharides and microbiota.41,42 Pasteurised donor breast milk has been increasingly used for preterm infants when maternal breast milk was not available. Its use has not been reported in patients with intestinal failure. Pasteurisation does not significantly affect saccharides, lipids and some growth factors and cytokines. However, it reduces the immunoglobulin A levels, certain other growth-factors and microbiota.43 This could limit the benefits of using donor breast milk in ileostomy patients. When breast milk is not available, extensively hydrolysed or amino-acid formulas have often been recommended.41,44 However, a blind crossover study by Ksiazyk et al.45 in 10 infants with short bowel syndrome did not show a difference in weight gain or nitrogen balance between extensively hydrolysed and standard polymeric infant formula. It should be noted though that all patients still had up to 70% of parenteral nutrition. Amino acid formulas have shown a possible advantage in some children with short bowel syndrome and persistent feeding intolerance with extensively hydrolysed formula. They improved feeding tolerance and reduced parenteral nutrition needs.40,46 Studies that compare standard polymeric infant formula, extensively hydrolysed formula and amino acid formula in enterostomy patients are lacking.

There have not been any studies that compared formulas with different long-chain triglyceride (LCT) and medium-chain triglycerides (MCT) ratios in infants with intestinal failure. LCTs were shown to stimulate the secretion of peptide YY and glucagon-like-peptide 2, promoting bowel adaptation and mediating the ileal brake.47 Supplementation of 50 mL of infant formula with 1 mL of Microlipid, a 50% LCT emulsion (Nestle Health Science, Vaud, Switzerland) improved weight gain and decreased ileostomy output in 10 premature infants with an entostomy.48 A randomised controlled trial found that enteral LCT supplementation with a combination of Microlipid and fish oil allowed a decrease in parenteral lipid administration without affecting weight gain in premature infants with an entostomy. However no decrease in ostomy output was seen.49 The absorption of LCTs is bile-dependent, whereas MCTs are directly absorbed through the enterocyte in a bile and pancreatic independent fashion. They were shown to increase total energy absorption during a high-fat LCT and MCT diet in adult patients with a short bowel syndrome who had a colon in continuity.50 However, adding MCTs to the high-fat diet increased the overall fat absorption in the ostomy patients, but decreased carbohydrate and protein absorption. Therefore, the total energy uptake did not change. Moreover, there was a tendency towards a higher ostomy output. Hence, a colon in continuity seemed necessary for MCT suppletion to be beneficial.50 MCT suppletion has not been reported in neonatal enterostomy patients.

Intermittent bolus feeding is the most physiological way of providing nutrition. It promotes the cyclic secretion of gut hormones, with a trophic effect on the mucosa.51 Even so, continuous tube feeding has been shown to decrease faecal losses by 31–62% and improve weight gain in a small group of infants with protracted diarrhoea or short bowel syndrome.52 However, it should be kept in mind that continuous feeding decreases intestinal motility and might contribute to small intestinal bacterial overgrowth, which can in turn induce an HOI.53 Moreover, ceasing oral feeds completely can cause oral aversion.53 We did not find any controlled studies of infants and children with an ileostomy that compared bolus and continuous feeding.
3.6.2 Toddlers and older children

We did not find any literature that provides dietary advice for pediatric ileostomy patients. In adult ileostomy patients a high-calorie intake was often necessary to provide adequate intestinal energy absorption. The primary advice has been to provide a low insoluble fibre diet, as these fibres increased ileostomy output by 20–25%. On the other hand, soluble fibres have been reported to increase stool consistency and intestinal transit time. Partially hydrolysed guar gum decreased ostomy output and increased stool consistency in 29 adult patients with an ileostomy. The use of 2–6 g of guar gum in each meal has also been reported in paediatric patients with short bowel syndrome. Other soluble fibres sources used were liquid pectin, wheat dextrin and pectin-rich foods such as green beans, sweet potatoes and bananas. Lastly psyllium fibre also decreased ileostomy output in a comparative study of 38 adult ileostomy patients.

A four-day LCT diet with a high fat percentage of 56% did not decrease ostomy output in adults. Both a general high-fat diet and MCT suppletion have even been linked to increased ostomy output and are therefore not recommended. Complex carbohydrates, found in white bread, pasta, potatoes and rice should be encouraged. However, simple carbohydrates should be avoided due to the osmotic effect in the intestinal lumen. A low fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) diet decreased stoma output by a mean of 95 mL/day in adult ileostomy patients with normal baseline output and increased its consistency. However, the diet is difficult to adhere to in the long term. Lastly, eating three marshmallows three times a day had a positive effect on ileostomy output and consistency in a crossover trial with 28 ileostomy patients, due to the gelatine content. A mean decrease in ileostomy output of 75 mL/day was seen in 20/28 patients.

General consumption advice (Figure 2) includes eating multiple small portions during the day and primarily drinking fluids between meals. Patients should be encouraged to chew well and eat slowly. Chewing gum should be discouraged, as it increases ostomy output.

There have not been any studies on elemental diets or continuous enteral tube feeding in older children or adults with ileostomies.

4 DISCUSSION

In general, the non-surgical complications and management of pediatric ileostomies have been very poorly studied. Even the normal evolution of ileostomy output in children after ostomy formation is unknown and there is no agreed-upon definition for paediatric HOI. Very divergent cut-offs from 20 up to 50 mL/kg/day have been used empirically. The limited evidence available does not support a safe paediatric HOI threshold of more than 20 mL/kg/day on two consecutive days, with an upper limit of 1500 mL/day. A study in 16 neonates described growth deficit above this level, but exact ostomy

**FIGURE 1** Clinical and biological follow-up of paediatric ileostomy patients. HOI, high-output ileostomy; PN, parenteral nutrition.
outputs were not mentioned. In another study, sodium depletion was seen at a mean output of 31 mL/kg/day. Clinical research is needed to be able to define a more validated cut-off point, but it is important to recognise that this cut-off is only an auxiliary in ileostomy management. Clinical parameters, such as adequate growth, hydration status and electrolyte and micronutrient balances remain the most important outcomes.

An organic cause for an HOI should always be eliminated and treated correctly if found (Table 2). General advice for the fluid, electrolyte and micronutrient management of these patients is summarised in Figure 1. When ileostomy output surpasses 20 mL/kg/day, we recommend starting intravenous fluid suppletion. There is a lack of studies on this subject, but we suggest to start with an assessment of the initial fluid deficit and a correction over 24–48 h. Ad hoc supplementation needs should initially be evaluated every 8 h, compensating 1:1 all losses surpassing 7 mL/kg/8 h. Compensations should be administered slowly over 2–3 h to avoid rapid fluid shifts. We recommend using isotonic 0.9% sodium chloride. If metabolic acidosis persists despite adequate sodium suppletion, an alkalisising solution such as Ringer’s Lactate or Hartmann solution can be used instead. The supplementation interval can be increased to every 12 h when the patient is stable. On the other hand, compensations should be administered more frequently if the ileostomy output is very high.

Growth should be strictly monitored and levels of electrolytes, minerals and vitamins should be closely followed in patients with an HOI (Figure 1). The need for sodium suppletion can be assessed based on serum and urinary sodium levels. We aim for a urinary sodium of 30–50 mmol/L in a spot urine sample. A mean daily sodium need of 4–10 mmol/kg/day was reported in infants and children with an ileostomy and was highly dependent on individual losses. Potassium losses in most adult ileostomy patients did not surpass the upper limit of the loss in stools of healthy individuals. Moreover, no link was seen between urinary potassium and growth in neonates. Therefore, additional potassium suppletion should only be provided when hypokalaemia develops. Hypomagnesaemia should be supplemented, especially when the patient is symptomatic. Parenteral suppletion is often necessary in this case. Micronutrient deficiencies should be supplemented accordingly.

The next step comprises initiation of an optimal age-dependent dietary management (Figure 2). We did not identify any papers on the dietary management of paediatric ileostomy patients. We recommend bolus feeds with breast milk as the primary choice for infants. The presence of immunological factors and the promotion of cyclic gut hormone secretion can improve bowel adaptation. The use of pasteurised breast milk has not been reported in neonates with intestinal failure. In short bowel syndrome patients, an extensively hydrolysated formula was generally recommended when breast milk was not available. When this was not tolerated, changing to an amino acid formula and/or continuous feeds showed beneficial effects on stool output. However even in short bowel syndrome patients, there is little evidence supporting these recommendations. Moreover, in neonatal ileostomy patients, osmolarity might outweigh protein hydrolysates in its impact on ostomy output, as seen in adult patients. LCT suppletion can facilitate weight gain and might decrease ileostomy output in infants. MCT suppletion on the other hand, is not recommended. Older children should be encouraged to primarily drink an isotonic or slightly hypotonic glucose-electrolyte solution, such as St Mark’s or reduced osmolarity WHO ORS (Table 3). Some sport drinks are also suitable, depending on the osmolarity and the glucose and sodium content. An enteral fluid

**FIGURE 2** Dietary advices for neonates and toddlers/older children with high-output ileostomies. HOI, high-output ileostomy; LCT, long chain triglycerides; ORS, oral rehydration solution.
restriction of 500–1000 mL/day in combination with parenteral fluid suppletion was advised in adults. This roughly equates to an initial restriction at 50% of normal enteral fluid intake for children. Dietary advice should promote a diet that is high in calories and proteins, low in insoluble fibres, moderate in fat, rich in complex carbohydrates and low in simple carbohydrates. To increase stool consistency and decrease ostomy output, marshmallows and/or soluble fibres can be added to the diet. Soluble fibres include partially hydrolysed guar gum, pectin, pectin-rich foods such as green beans, sweet potatoes and bananas and wheat dextrin. If all of this is insufficient, a low FODMAP diet can be tried. Lastly, general advice regarding eating behaviour should be given (Figure 2). If none of this works and enteral feeds are not tolerated or high-output persists with the appearance of complications, partial parenteral nutrition should be considered.

5 Conclusion

Even though it is important to prevent complications in paediatric patients with HOIs by providing correct nutritional management, very little evidence is available on the subject. Even the normal output of an ileostomy in paediatric patients is unknown. This paper proposes a cut-off for paediatric HOI of 20 mL/kg/day on two consecutive days, with an upper limit of 1500 mL/day. We have tried to provide clinicians with tools to help them with the nutritional management of paediatric HOIs. However, clinical research is needed to be able to provide more evidence-based guidelines and uniform, high-quality care for paediatric HOI patients.

Author Contributions

Marijke Awouters: Investigation; conceptualization; methodology; writing – original draft; project administration; visualization.
Tim Vanuytsel: Writing – review and editing; visualization. Koen Huysentruyt: Writing – review and editing; visualization. Pauline De Bruyne: Writing – review and editing; visualization. Karen van Hoeve: Writing – review and editing; visualization. Ilse Hoffman: Conceptualization; writing – review and editing; supervision; visualization.

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