Journal of the Royal Society of New Zealand

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/tnzr20

A review of chyme reinfusion: new tech solutions for age old problems

Chen Liu, Sameer Bhat, Ian Bissett & Gregory O'Grady

To cite this article: Chen Liu, Sameer Bhat, Ian Bissett & Gregory O'Grady (2022): A review of chyme reinfusion: new tech solutions for age old problems, Journal of the Royal Society of New Zealand, DOI: 10.1080/03036758.2022.2117832

To link to this article: https://doi.org/10.1080/03036758.2022.2117832

Published online: 07 Sep 2022.

JOURNAL OF THE ROYAL SOCIETY OF NEW ZEALAND
https://doi.org/10.1080/03036758.2022.2117832

Taylor & Francis
Taylor & Francis Group

REVIEW ARTICLE

OPEN ACCESS Check for updates

A review of chyme reinfusion: new tech solutions for age old problems

Chen Liu [a], Sameer Bhat[a], Ian Bissett [a,b,c] and Gregory O'Grady[a,b,c,d]

[a]Department of Surgery, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand; [b]The Insides Company Ltd, Auckland, New Zealand; [c]Auckland City Hospital, Te Whatu Ora (Te Toka Tumai Auckland), Auckland, New Zealand; [d]Auckland Bioengineering Institute, The University of Auckland, Auckland, New Zealand

ABSTRACT

High-output double enterostomies (DES) and enteroatmospheric fistulae (EAF) are associated with significant morbidity, including infection, malnutrition, and prolonged hospital admissions. Management is complex and has remained a challenging surgical problem for many decades in both adult and paediatric patient populations. Chyme reinfusion (CR) from the proximal to distal DES or EAF limb is a potential therapeutic solution which has been shown to be safe and beneficial; however, early methods have involved the manual handling of chyme, which is labour intensive and poorly tolerated by both patients and staff. Over the past four decades, there has been growing interest in the application and development of medical device technology to improve the effectiveness and user-friendliness of CR. New Zealand (NZ) has been at the forefront of innovation in this field, with exciting translational research projects in both adults and neonates (funded and enabled by the NZ MedTech CORE). This narrative review provides a summary of the evolution of CR technology globally, synthesises the extant clinical evidence and highlights future directions.

ARTICLE HISTORY
Received 7 May 2022
Accepted 18 August 2022

HANDLING EDITOR
Julie Choisne

KEYWORDS
Chyme; reinfusion; intestinal failure; high output enterostomy; medical devices; colorectal

Introduction

The first descriptions of surgical stoma formation were based in the sixteenth century. These early procedures carried high morbidity and mortality risks with patients surviving only a few days (Kaidar-Person et al. 2005; Doughty 2008). Ever since, the morbidity of stomas, and particularly small bowel double enterostomies (DES) and enteroatmospheric fistulae (EAF), has been well documented in both the adult and paediatric populations, although quoted morbidity and mortality rates have varied due to the low incidence of EAF and high heterogeneity among patients in the literature (Gutierrez et al. 2011; Bafford and Irani 2013). High output of intestinal contents is a common sequela of both DES and EAF of the small bowel, preceding multiple complications including dehydration, renal impairment, malnutrition, electrolyte abnormalities and intestinal failure (Evenson and Fischer 2006; Martinez et al. 2008).

CONTACT Chen Liu chenliu818@gmail.com

Given that this morbidity arises from excessive intestinal losses through the proximal DES or EAF limb, chyme reinfusion (CR) into the distal small bowel logically presents as a therapeutic solution when the distal limb is accessible (Wong et al. 2004; Lau et al. 2016). Despite this, CR has not gained widespread popularity, principally due to the lack of specialised equipment, unpleasant workflows and poor tolerance among both patients and staff (Bhat, Cameron, et al. 2020; Bhat, Sharma, et al. 2020). Over the past four decades, medical device technology in this field has advanced significantly, producing progressively more user-friendly and effective CR options, with New Zealand (NZ) having been at the forefront of recent innovations.

In this narrative review of CR technology, we present a summary of the CR techniques developed thus far for adult and paediatric patient populations, the evidence of their efficacy and clinical benefits, the key technological limitations, and directions for further work in this field.

History of chyme reinfusion technology in adults

The earliest known English-language publication related to CR was authored by Levy and colleagues in 1983 (Levy et al. 1983). The prospective cohort study reported on the clinical outcomes of 30 patients with peritonitis and subsequent temporary enterostomy or enterocutaneous fistula (ECF). The CR method used was built for purpose and named the Enteromate Systeme (Soci'et'e Labodial, Les Clayes-sous-Bois, France). The system featured a roller pump set-up that aspirated effluent into a sterile 50 ml disposable plastic container. The container measured both volume and weight electronically. A servo-controlled roller pump was then used to reinfuse the liquid at a continuous rate via a silicone rubber balloon catheter which was inserted into the distal intestine (Levy et al. 1983).

A summary timeline of subsequent publications related to CR methodologies and innovations in adults is detailed in Table 1. The core components involved during CR are: (a) A method of collecting the chyme from the proximal DES or EAF limb, (b) An intermediate method of processing the chyme (if required) and (c) A method of delivering the chyme into the downstream small or large intestine through an accessible distal DES or EAF limb. The more novel technologies comprise closed loop systems whereby stoma effluent is collected, processed and delivered without manual intervention (Bhat, Sharma, et al. 2020). Historically, the most basic method of collecting chyme has been manual, using urinary Foley catheters of various sizes. As our knowledge and understanding has advanced, more sophisticated technologies have since been developed, involving aspiration roller pumps or temporary storage of the chyme within the patient's own stoma appliance (Levy et al. 1983; Picot et al. 2020; Sharma et al. 2020; Liu et al. 2021). Intermediate processing most commonly involves filtering the chyme to remove solid particles, which minimises or prevents blockages of the reinfusion tubing. This has been achieved through a variety of methods, ranging from the use of porous cloth and gauze to household food mesh strainers (Rinsema et al. 1988; Cresci and Martindale 1997; Kittscha 2016; Nagar et al. 2018). One research group refrigerated the collected effluent at 4°C prior to reinfusion (Calicis et al. 2002). Another group used a dedicated blender to blend chyme output to reduce the risk of distal intestinal obstruction when reinfused (Kwun 1999). Chyme delivery techniques range from the use of

Table 1. Summary timeline of chyme reinfusion methodologies in adults.

			Chyme reinfusion method	
Year	First Author	Country	Collection method	Reinfusion method
1983	Levy	France	'Automate Systeme': Roller pump	Servo-controlled roller pump via silicone rubber balloon catheter (size not specified)
1987	Gouma	Netherlands	Infusion set (every 4 h)	Roller pump via urinary bladder catheter
1990	Prior	UK	Urinary catheter bag	Peristaltic pump via 20 F foley catheter
1995	Maeda	Japan	Stoma connector device	Stoma connector device
1997	Cresci	USA	Manual collection	Manual reinfusion via feeding tube (size not specified)
2000	Bissett	Nepal	Manual collection	Manual reinfusion via catheter syringe and foley catheter (size not specified)
2002	Calicis	France	Aspiration pump	Continuous reinfusion via silicone rubber balloon catheter (size not specified)
2010	Picot	France	'Enteromate II': Roller pump	Roller pump via silicone rubber balloon catheter (size not specified)
2011	Yuan	China	Aspiration pump	Reinfusion at specific rate via triple lumen foley catheter (size not specified)
2013	Pflug	Brazil	Water seal system	Diet infusion pump via triple lumen foley catheter (size not specified)
2013	Ye	China	Self-designed precision drainage bag	Enteral nutrition infusion pump via foley urinary or PEJ catheter
2014	Coetzee	South Africa	Manual collection	APPLIX feeding pump via 16 F foley catheter
2016	Kittscha	Australia	Manual collection	Kangaroo pump continuous infusion via 12 F foley silicone balloon catheter
2016	Thibault	France	'Enteromate II System': Peristaltic pump	Peristaltic pump via polyurethane nasogastric 14–16 F Levine-typed tube without balloon
2016	Sanchez Guillen	Spain	Ileostomy bag via closed drainage system	Intestinal reinfusion pump via 24 F gastrostomy feeding tube
2020	Duan	China	Unclear	Peristaltic pump ('Link-2008 Device') via feeding tube (size not specified)
2020	Picot	France	Aspiration pump	Portable pump via 15–16 F Levine-typed tube without balloon
2020	Sharma	NZ	Ostomy bag	Portable centrifugal pump via gastrostomy feeding tube ('The Active Link™')
2021	Liu	NZ	Ostomy bag	Portable centrifugal pump via custom enteral feeding tube ('The Insides System™')

Notes: F, French; NZ, New Zealand; PEJ, Percutaneous Endoscopic Jejunostomy; UK, United Kingdom; USA, United States of America.

basic, manual syringe reinfusion through a Foley catheter, to more advanced peristaltic pumps which enable patients to be reinfused continuously or via intermittent bolus dosing (Bissett 2000). Thus far, only one CR system utilises a custom enteral feeding tube (discussed below) (Liu et al. 2021). Some researchers have also stated dietary restrictions to facilitate CR which include low residue, pureed, or soft food and/or restriction of oral fluid intake to 1.5 litres per day (Liu et al. 2016; Picot et al. 2020).

Enteroclysis or fistuloclysis are also enteral nutrition techniques that are often sited amongst the CR literature. However, it is important to note that these techniques are not equivalent. Enteroclysis describes the administration of enteral nutrition or hydration solutions into the downstream bowel through the efferent orifice of an enterostomy or ECF (Thibault and Picot 2016). Fistuloclysis comprises a subset of enteroclysis, whereby enteral nutrition is administered specifically into the efferent limb of a small bowel fistula (Layec et al. 2020). During these processes, chyme from the afferent bowel is, in fact, discarded. These terms have sometimes been incorrectly used interchangeably with CR (Du Toit 2014; Wu et al. 2014). Future research in this field should be clear in this distinction to avoid confusion.

History of chyme reinfusion technology in neonates and paediatrics

Puppala et al. first demonstrated CR in a series of two neonates (mean gestational age: 37 weeks) with short bowel syndrome due to distal jejunal atresia in 1985 (Puppala et al. 1985). Proximal stomal losses were manually collected and infused into the distal stoma limb every four hours through an 8 French nasogastric tube (Argyle Labs, Argyle, NY, USA) that was passed 2 cm into the distal ileostomy via a Holter (peristaltic) pump (Critikon, Tampa, FL, USA).

Several different CR methods have since been published and are summarised in Table 2. Collection of intestinal contents from the proximal DES or EAF limb has been entirely manual, using luer lock syringes and/or standard stoma bags of varying sizes. However, a mixture of manual and automated methods has been used for CR when the distal DES or

Table 2. Summary timeline of chyme reinfusion methodologies in neonatal and paediatric patients.

				Chyme reinfusion method	
Year	First author	Country	Population	Collection method	Reinfusion method
1985	Puppala	USA	Neonatal	Manual collection	Holter Infusion Pump
1987	Riggs	USA	Neonatal	Gusseted pouch (manual collection)	Syringe feeding pump via rubber catheter (10 Fr)
1997	Schafer	Germany	Neonatal	CEST technique using silicone tube connected to adhesive stoma bag	Automatic Roller (Kangaroo) Pump
1999	Al-Harbi	Canada	Neonatal	Standard stoma bag (manual collection using luer lock syringe)	Syringe infusion pump via foley or urinary bladder catheter (8 Fr)
2000	Schafer	Germany	Neonatal	CEST technique	Electric roller pump system
2003	Gardner	Canada	Neonatal	Standard stoma bag (manual collection using luer lock syringe)	Syringe pump with mini-infuser extension set via urinary foley catheter (8 Fr) or nasogastric tube (8 Fr)
2004	Wong	Hong Kong	Neonatal	Manual collection	Syringe pump via nasogastric tube (8 Fr)
2010	Corbett	UK	Neonatal	Not reported	Not reported
2010	Sidebotham	USA	Paediatric	Manual collection	Via catheter (16 Fr); CR appliance not reported
2012	Drenckpohl	USA	Neonatal	Syringe (manual collection)	Enteral (Kangaroo) Pump & Feeding Syringe via catheter tube (size not specified)
2014	Annibali	Italy	Paediatric	Not reported	Not reported
2015	Federici	Italy	Neonatal	Not reported	Not reported
2015	Haddock	Canada	Neonatal	Not reported	Via silastic feeding tube (5–6.5 Fr), foley catheter (5 Fr) or gastrostomy tube (12 Fr); CR appliance not reported
2016	Gause	USA	Neonatal	Not reported	Electronic syringe pump via foley catheter (6 Fr) with balloon
2016	Koike	Japan	Neonatal	Standard stoma bag (manual collection)	Syringe pump via an enteral feeding tube (5–6.5 Fr)
2016	Lau	Hong Kong	Neonatal	Not reported	Syringe pump via infant feeding tube (8 Fr)
2017	Inoue	Japan	Neonatal	Sealed cylinder (manual collection)	Not reported
2017	Tanaka	Japan	Neonatal	Not reported	Manual injection; CR appliance not specified
2019	Elliot	Canada	Neonatal	Manual collection using luer lock syringe	Syringe pump via urinary foley catheter
2019	Sancar	Austria	Neonatal	Not reported	Manual injection via feeding probe (5–8 Fr) or self-controlling rectal catheter

Notes: CEST, continuous extracorporeal stool transport; CR, chyme reinfusion; Fr, French catheter sizing; UK; United Kingdom; USA, United States of America.

EAF limb was accessible. Automated methods have more recently involved the use of either electronic syringe or peristaltic (roller) pumps, with CR occurring through Foley catheter tubes, urinary bladder catheters, or enteral (gastrostomy or nasogastric) feeding tubes, ranging from 5 to 16 French in size (Drenckpohl et al. 2012; Gause et al. 2016; Koike et al. 2016; Lau et al. 2016; Elliott and Walton 2019).

In one study, Schafer et al. suggested a novel CR method occurring within a custom closed system ('continuous extracorporeal stool transport (CEST)') in 1997 (Schäfer et al. 1997). An adhesive stoma bag was connected to a silicon tube in series, through which proximal DES output was collected. A Kangaroo Pump was then used to undertake CR, whereby the silicon tube was compressed to propel intestinal contents into the distal DES limb. This method was noted to be well-tolerated by both parents and staff, although it is of interest that CEST was not examined in any other studies.

Of note, one group filtered the proximal DES output using a dry gauze prior to CR, so that contents were less likely to lead to obstruction in the distal small bowel (Koike et al. 2016). Continuous rather than bolus CR has been more frequently employed, although in one study, CR was initially bolused and later advanced to continuous reinfusion in a single patient (Koike et al. 2016; Bhat, Cameron, et al. 2020). Interestingly, patients' parents were educated about and provided aid for the CR process in five studies (Schäfer et al. 1997; Al-Harbi et al. 1999; Gardner et al. 2003; Sidebotham et al. 2010; Annibali et al. 2014).

Clinical benefits of chyme reinfusion in adults

Patients with DES or EAF of the small bowel are frequently troubled by high outputs, which often result in serious complications for adults (Gutierrez et al. 2011; Bafford and Irani 2013). These include fluid and electrolyte disturbances such as dehydration, renal impairment, metabolic acidosis, hypokalaemia, hyponatraemia and hypomagnesaemia, which often culminate in prolonged hospital stays or recurrent readmissions (Dudrick and Panait 2011; Hayden et al. 2013; Justiniano et al. 2018; Assaf et al. 2021). Malnutrition in the form of weight loss, hypoalbuminaemia and anaemia as well as vitamin and trace element deficiencies are also common (Dudrick and Panait 2011). In addition, EAF patients often initially present with sepsis requiring immediate and careful source control of an underlying infection comprising broad-spectrum antibiotics, percutaneous drainage or surgery before reaching a stable clinical state sufficient for safely undertaking CR (Bhama 2019). Cumulatively, these sequelae can result in intestinal failure (IF), which is defined as the inability of the gut to absorb sufficient macronutrients, micronutrients or fluid, resulting in the need for intravenous nutrition to maintain health or facilitate growth (Couper et al. 2021). Inpatient management of IF patients is expensive, with one cohort study estimating the daily cost per patient to range from £360 to £1102 (Saunders et al. 2013). Total parental nutrition (TPN) is used in to mitigate the risks associated with IF in these instances, but such therapy is not curative and merely compensates for fluid and nutritional losses without improving bowel function. In addition, TPN is accompanied by risks such as catheter-related complications (e.g. thrombosis and infection), gut dysfunction (e.g. microbiome dysbiosis or inflammation), hepatobiliary dysfunction (e.g. derangement of liver function tests (LFTs) or cholestasis) and metabolic complications such as

hyperglycaemia (Abu-Wasel and Molinari 2014; Madnawat et al. 2020; Shafiekhani et al. 2022). Prolonged diversion of intestinal contents from the distal small bowel and colon can also have a detrimental effect on intestinal motility, leading to an increased risk of prolonged post-operative ileus following stoma reversal and impaired distal bowel function (Garfinkle et al. 2019; Keane et al. 2019).

CR has been advocated as a complete solution to this range of clinical problems and complications. Up to 86% reduction in the volume of intestinal losses has been demonstrated when CR has been optimally implemented, with significant reductions in the number of patients with DES or EAF outputs exceeding 1000 ml per day, from 97% to just under 8% in one prominent cohort (Layec et al. 2020; Picot et al. 2020). Normalisation of electrolyte abnormalities, reduced need for intravenous fluids, and significant improvements in the creatinine clearance have also been found (Rinsema et al. 1988; Cresci and Martindale 1997; Picot et al. 2010). This is hypothesised to be due to restoration of the ileal break, causing inhibition of gastric emptying and reduction in gastric secretions, resulting in slower gut motility which allows for increased absorption and reduced outputs (Wu et al. 2014; Thibault and Picot 2016).

CR also leads to improvement in a range of nutritional biomarkers. This includes significant increases in serum albumin, net nitrogen absorption (89% increase), net fat absorption (91% increase), body mass index (BMI), and in the plasma citrulline concentration (a biomarker of intestinal function which parallels enterocyte mass) (Picot et al. 2010, 2013; 2020). These findings facilitate earlier cessation of TPN, and, thus, avoidance of the TPN associated risks detailed above. Layec et al. found that all 37 patients admitted to hospital with EAF were weaned from their TPN within 3 days (interquartile range: 0–14) of CR initiation (Layec et al. 2020). This reduced dependence on TPN appears long-lasting, with no patients from one study cohort requiring TPN after a median follow-up period of 25 months (Nagar et al. 2018).

The impact of CR on recovery of bowel function following DES reversal or EAF repair has been less well investigated. Two publications to-date have shed light on this aspect and produced promising results. The first is a retrospective study conducted in China by Duan et al. that included 117 Crohn disease patients (33 who underwent CR and 84 without) and assessed the impact of CR on rates of post-operative ileus and post-operative diarrhoea (defined as three or more loose or liquid stools per day) (Duan et al. 2020). They found a significant reduction in the incidence of post-operative ileus within the CR group, which was maintained after propensity-score matching (11.5% *vs.* 42.3%, $p = 0.012$). The significantly lower rate of post-operative diarrhoea found on initial analysis, however, did not persist following propensity-score matching (7.7% *vs.* 23.1%, $p = 0.191$). The second is a retrospective cohort study of 159 EAF patients who underwent definitive surgical repair and assessed the impact of CR on post-operative complications (Tian et al. 2022). They found CR to be an independent significant protective factor against post-operative complications, recurrent fistula and ileus (multivariate odds ratios of 0.161, 0.382, and 0.209, respectively).

Clinical benefits of chyme reinfusion in neonates and paediatrics

CR is also associated with improvements in numerous nutritional biomarkers in the neonatal and paediatric populations. Positive rate of weight gain has been observed following

the period of CR, of which two studies showed this increase in weight to be statistically significant when compared to patients who did not undergo CR (Schäfer et al. 1997; Al-Harbi et al. 1999; Wong et al. 2004; Drenckpohl et al. 2012; Haddock et al. 2015; Koike et al. 2016; Tanaka et al. 2017). TPN was also completely ceased in an average of ~60% of neonatal and paediatric patients who underwent CR (Bhat, Cameron, et al. 2020). Relative to those who did not receive CR, a shorter duration of TPN was exhibited among CR cohorts (Gause et al. 2016; Lau et al. 2016; Inoue et al. 2017). In addition, fewer incidences of stomal prolapse were noted by Inoue et al. in patients receiving CR (0% vs. 100% in those not undergoing CR). This was thought to be due to the improved nutritional status of patients, likely resulting in increased tissue tensile strength (Inoue et al. 2017).

Normalisation of derangements in liver function and enzyme profiles, serum electrolytes, and fluid balance have also observed during periods of CR. Specifically, this included improvements in alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT) and serum bilirubin levels, with one study showing a statistically significant reduction in the mean peak bilirubin level after CR (155 vs. 275 μmol/L; $p < 0.001$) (Al-Harbi et al. 1999; Wong et al. 2004; Gause et al. 2016; Lau et al. 2016). Inoue et al. also demonstrated a significant recovery from anaemia in patients who underwent CR, through improvements in serum haematocrit (37.8% vs. 29.7%; $p = 0.0227$), and haemoglobin (12.2 vs. 9.65 g/dL; $p = 0.0282$) levels (Inoue et al. 2017). Furthermore, a consistent reduction in output from the proximal DES limb was noted in a 6-month-old with chronic intestinal pseudo-obstruction (CIPO), albeit this was not seen in any other studies (Annibali et al. 2014).

CR also resulted in rehabilitation and maturation of the distal bowel following DES reversal surgery. In particular, a reduction in the size discrepancy between the proximal and distal intestine has been seen, facilitating a technically easier DES reversal operation (Corbett and Turnock 2010; Lau et al. 2016; Elliott and Walton 2019; Sancar et al. 2020). This reduction in size was statistically significant in one study (25 vs. 53%; $p = 0.034$), which ascribed this to the trophic effect of CR (Lau et al. 2016). A significant reduction in the rates of postoperative anastomotic leakage (3 vs. 20%; $p = 0.029$) after DES reversal was also seen in this study. The distal ileum villus length, crypt width and depth was also significantly increased in one study following CR (Tanaka et al. 2017).

Limitations of chyme reinfusion technology in adults

Advancement of CR technology has been impeded by several limitations. Firstly, CR can be associated with some adverse effects (AEs), particularly when initiated after a significant period of defunctioning of the distal gut. Studies have reported dull or spasmodic abdominal discomfort and pain, nausea and vomiting, which may be attributable to excessively rapid or bolus (as opposed to continuous) CR, or the reinfusion of cooled chyme (Wu et al. 2014; Kittscha 2016; Nagar et al. 2018; Picot et al. 2020). Both constipation and diarrhoea have also been described but are often mild in severity (Wu et al. 2014; Kittscha 2016).

Patient tolerability of CR can be affected by these symptoms. Abdominal pain was severe enough to cause one patient in a cohort of 21 with small bowel stomas to cease CR early (Calicis et al. 2002). In a retrospective cohort of 95 high output upper gastrointestinal fistula patients, 13.9% withdrew after no more than 10 days of CR due to intolerable

symptoms such as diarrhoea, abdominal pain, nausea and vomiting (Wu et al. 2014). Some CR systems demanded a significant modification to a patient's diet whilst being reinfused, which has further reduced patient tolerability (Kwun 1999; Picot et al. 2010; Kittscha 2016; Liu et al. 2016; Picot et al. 2017). The need to only consume pureed meals led to < 5% of one cohort prematurely stopping CR in a study by Picot et al. (2020)

Despite development of novel CR solutions spanning some 40 years, technical challenges remain (Bhat, Sharma, et al. 2020). Purpose-built equipment has been lacking, with most previous methods utilising existing enteral nutrition pumps, Foley catheters, or even dialysis material (Thibault and Picot 2016). As such, technical problems including backflow or loss of intestinal contents, tube blockage, tube dislodgement and even tube migration into the distal stoma or EAF limb have arisen (Du Toit 2014; Wu et al. 2014; Picot et al. 2017; Nagar et al. 2018). Balloon-tipped tubes may also cause obstruction of the bowel wall preventing reflux of chyme and leading to intolerable high pressures in the downstream bowel. Excessive volumes within these balloons could also create ischaemic lesions of the mucosa and subsequent scar stenosis (Layec et al. 2020).

Of importance, the financial costs associated with CR may limit its use, particularly in lower income healthcare settings. The use of specialised, purpose-built devices may not be covered by insurance providers, and there may be recurring costs associated with consumable device components, such as tubes and filters (Somashekar and Sharma 2020). Furthermore, dietary modifications to ensure a liquid stoma effluent consistency which is compatible with the aforementioned methods and devices may require special feeds that are expensive for patients and their families to acquire. However, the discussion of costs associated with CR should take into account the economic burden of the alternative management options which may involve prolonged inpatient admissions, home IV nutrition, and protracted stoma appliance durations (Bissett et al. 2020).

Unpleasant and laborious workflow has been perhaps the paramount factor limiting the widespread uptake of CR. Current methods of CR require manual processing of the chyme prior to reinfusion, such as collection in a separate bag, refrigeration, sieving to remove large food particles, and regular transfer to a reinfusion system (Thibault and Picot 2016). After processing, the chyme may then need to be manually reinfused. This can be time consuming, labour-intensive and demanding for hospital staff and patients. Also, almost all staff and patients agree that manual handling of chyme is odorous and associated with feelings of disgust (Bhat, Sharma, et al. 2020). Lack of adequate training of patients and their caregivers and resistance from clinicians and nursing staff have also been identified by dieticians as obstacles to CR. All of those surveyed (100%) expressed willingness to attempt CR if more information was available and guidance provided by protocols (Blaauw et al. 2018). The combination of these factors has resulted in CR previously failing to gain widespread popularity in the adult population over the past four decades.

Limitations of chyme reinfusion technology in neonates and paediatrics

Progress in the field of CR technology among neonatal and paediatric patients has been hindered by similar technical concerns as well as more specific limitations. These include dislodgement of the distal catheter tube and reflux or leakage of intestinal contents after distal reinfusion, causing peristomal skin irritation, amplified by the increased challenges of fitting stoma appliances in the neonatal population (Bhat, Cameron, et al. 2020). The

lack of standardised sizing for Foley or urinary catheters and enteral feeding tubes, may have contributed to these findings.

The current methods of CR, which are mostly manual and involve the manual collection of proximal DES or EAF output into a stoma bag using luer lock syringes, are also very demanding and resource intensive, requiring input and expertise from specialist stomal nurses as well as multidisciplinary team members (Bhat, Cameron, et al. 2020).

AEs related to CR in neonatal and paediatric populations vary in their severity and are most commonly gastrointestinal. CR was associated with the development of mild diarrhoea and prolapse of the distal DES limb in two studies (Corbett and Turnock 2010; Federici et al. 2015). This was hypothesised to result from reinfusion in bolus rather than continuous doses (Riggs 1987). Some serious AEs have been infrequently noted and include intestinal perforation as well as recurrent haemorrhage around the distal EAF site necessitating multiple blood transfusions (Haddock et al. 2015). Haddock and colleagues reported three cases of intestinal perforation among the 23 neonates (mean gestational age: 35 weeks) undergoing CR in their retrospective cohort study (Haddock et al. 2015). Among these, mortality was the final result in one patient, arising from a combination of septic shock, abdominal compartment syndrome, abdominal wall necrosis, recurrent bacteraemia and multiple episodes of gastrointestinal bleeding and multiple organ failure, despite undergoing reoperation (Haddock et al. 2015). Collectively, these limitations associated with CR methodologies have slowed progress and technological advancements in this patient group.

Technological innovations in chyme reinfusion research in adults within New Zealand

A novel, purpose-built CR device was developed in Auckland through a collaboration between surgical and engineering teams in the Department of Surgery and the Auckland Bioengineering Institute at The University of Auckland (Auckland, NZ) during 2018. Following multiple iterations informed by extensive literature review, repeated clinician evaluation and patient feedback, the final design was a centrifugal bolus pump, initially called the 'Active-Link™' device and later renamed the Insides System™ (The Insides Company, Auckland, NZ) (Bhat, Sharma, et al. 2020). The system consisted of three components: (1) A hand-held, portable, battery-operated and rechargeable driver unit, (2) A compact impeller pump with a neodymium magnetic bar that is placed within a standard stoma appliance, and (3) An intestinal 24–30 French gastric feeding tube, such as the Entuit® (Cook Medical, Bloomington, Indiana, USA) or the MIC Gastrostomy tube (Avanos Medical, Alpharetta, Georgia, USA), that was inserted into the downstream stoma or fistula limb and connected proximally to the pump. To activate the pump, the driver unit was held adjacent, but external, to the stoma appliance. Magnetic coupling between the driver and the impeller allowed activation and subsequent intermittent CR in bolus doses as required, without physically contacting the chyme. The driver had five speed settings to facilitate patient control of the CR rate based on the DES or EAF output viscosity and individual comfort. The feeding tube remained in-situ for the duration of the reinfusion period and the impeller device was changed by the patient every three days. Microbiology safety studies of the stoma contents were conducted in parallel with device development and demonstrated no growth of pathogenic bacterial species

within the chyme despite seven hours of continuous testing. The driver and pump components are depicted in Figure 1.

The first-in-human data from a feasibility study have since been published by Sharma et al. (2020). The cohort consisted of 10 patients who had either a small bowel stoma, an ECF or an EAF and over 740 patient-days of device testing was captured in total, with a median duration of device installation and testing of 39.5 days (range: 1–234 days). Clinical benefits derived included cessation of TPN in four out of five patients (80%), median weight gain of 2.6 kg and improvement in LFTs over the reinfusion period. The device also allowed testing of distal bowel function prior to reversal, with only one out of seven patients (14%) developing post-operative ileus following ileostomy reversal.

The device was able to overcome several of the barriers associated with previous CR techniques. Patients were able to be fully mobile and independent whilst undergoing CR therapy, thereby leading to high device usability amongst patients. The final design scored a median of two on a ten-point Likert scale for patient usability, with one representing 'very easy to use' and ten indicating 'very difficult to use'. Staff acceptability was also high, with 11/12 nursing staff who interacted with the final device version reporting very low levels of disgust associated with device use. The most common technical

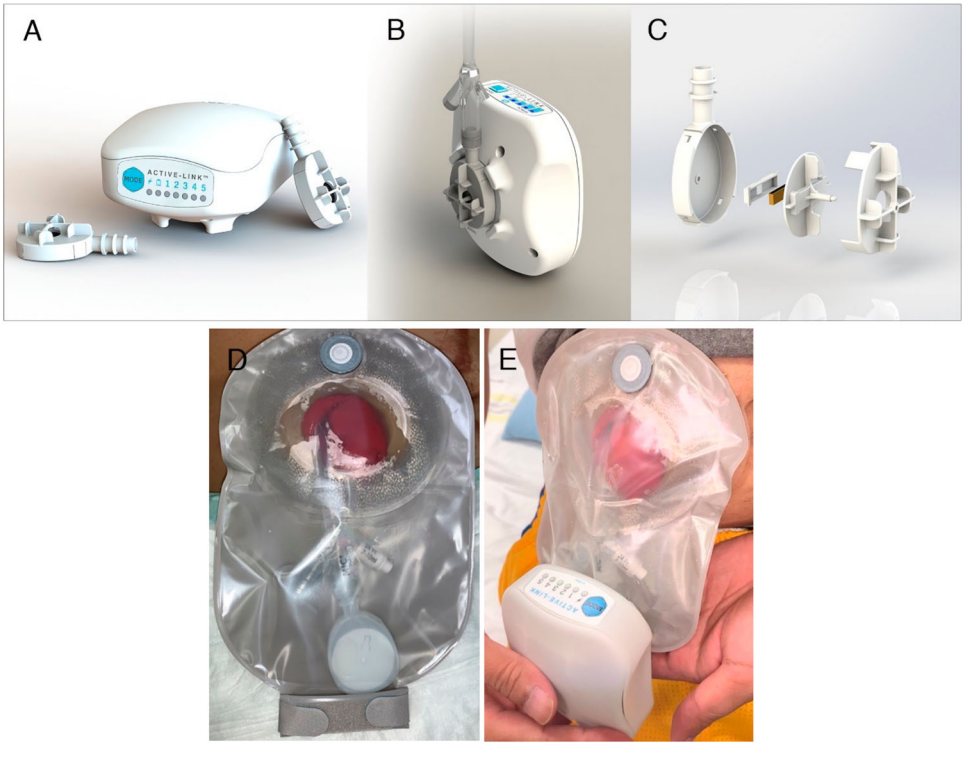

Figure 1. The Active-Link™ chyme reinfusion device driver unit and pump. **A,** Chyme reinfusion device with driver unit and centrifugal pump, **B,** Pump attached to feeding tube and magnetically couples to the base of the driver across the stoma appliance, **C,** Exploded view of impeller pump design, **D,** Example of pump and tube fitted within a stoma appliance, **E,** Front view of magnetic coupling between driver and pump across the stoma appliance. Reproduced with permission from Sharma et al. (2020) publication.

problem was pump blockages or congestion. This was mitigated by the addition of inlet shields and the advice to eliminate stringy or fibrous fruits and vegetables from their diet. Other technical issues included the feeding tube exacerbating peri-stomal skin irritation in three patients and tube dislodgement in a further three patients.

The device was also well tolerated. AEs included abdominal discomfort (occurring in seven patients), bloating (four patients), nausea (four patients), and constipation (three patients). These symptoms generally featured in the first week of reinfusion and subsequently subsided once reinfusion volumes and speeds were better titrated to each patient's individual comfort thresholds. There were no serious device-related AEs or microbiological complications.

This technology was further trialled and improved in a subsequent clinical study. The second study involved 19 adult ileostomy patients recruited between April 2019 and May 2020 (Liu et al. 2021). Patients were divided into three groups in chronological order. The first group used off-the-shelf gastrostomy tubes that were utilised in the Active-Link^{TM} device (Group One; $n = 7$ patients), the second group were involved in the iterative development phase where new tube designs were trialled (Development Group; $n = 7$) and the third group used a late iteration of the tube design (Group Two; $n = 5$). A total of 549 patient-days of device-use was captured. The gastrostomy feeding tubes used by patients from Group One exhibited multiple issues such as dislodgement ($n = 4$), localised abdominal pain ($n = 3$), inadequate fit of the tube/pump complex within the stoma appliance ($n = 1$) and bending of the tube leading to partial obstruction ($n = 1$). These problems led to the development of a custom enteral feeding tube specifically designed for use in a stoma, as depicted in Figure 2. Patients from Group Two experienced few tube-related issues, with no complaints relating to poor device fit. This is the first known instance of a built-for-purpose feeding tube for use in CR. The tube carries the following key features: (a) A plastic introducer that allows easy insertion of the device into the distal DES limb, (b) A long segment of the tube that can be cut at any length to allow customisation of tube size relative to a patient's stoma appliance, (c) A 90°

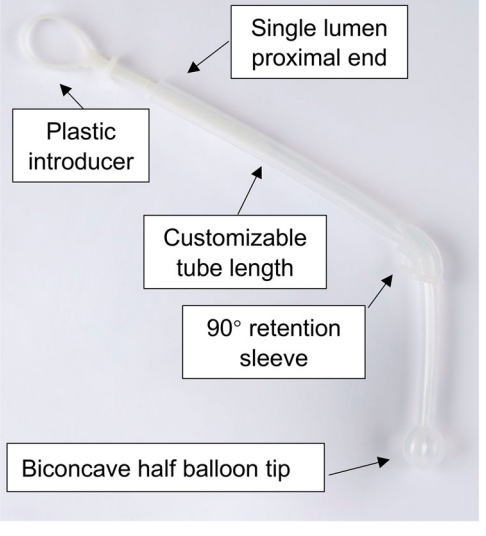

Figure 2. Custom enteral feeding tube (The Insides Company, Auckland, NZ).

retention sleeve to allow the tube to sit flat and parallel to the patient's abdominal wall and reduce device protrusion, and (d) A biconcave half-balloon tip that allows adequate tube retention within the abdomen without placing excessive pressure on the bowel wall. This tube design was incorporated into the Active-Link™ system, and following these modifications, the device was more recently renamed The Insides System™ (The Insides Company, Auckland, NZ), as depicted in Figure 3.

The clinical outcomes using The Insides System™ exclusively in ileostomy patients were encouraging. Eleven patients demonstrated a reduction in net stoma losses per day, with a median reduction of 452 mL. Five of the nine patients (56%) using loperamide at baseline ceased or reduced their dosages (Liu et al. 2021). Fourteen patients underwent ileostomy reversal with a median length of post-operative stay of 3.5 days (range: 1–28) and a 21% rate of prolonged post-operative ileus. Thirteen patients experienced at least one device-related minor AE prior to ileostomy reversal, with the most common being abdominal discomfort ($n = 10$). Two patients experienced serious device-related AEs which included a possible pressure ulcer in the distal ileal limb and in-growth of the bowel mucosa around the tube tip necessitating removal of the tube under a general anaesthetic. The minor AEs were often transient and the serious AEs led to device design changes preventing such events in future.

A case report from Australia in 2021 was the first published international application of the device in a high-output ECF patient (Solis et al. 2021). The patient underwent CR for 125 days prior to definitive surgical repair and was able to wean off TPN after just 2 days of reinfusion therapy.

Technological innovations in chyme reinfusion research in neonatal and paediatric populations within New Zealand

Following the successful design and implementation of a dedicated adult CR solution, innovation has also focused on improved solutions for paediatric cohorts, and in particular, neonates as the primary affected population (Bhat, Cameron, et al. 2020). At the time of writing, a novel device allowing a clean and user-friendly pathway for intermittent CR has been prototyped and is in first-in-human feasibility studies in NZ. Initial results are anticipated later in 2022.

Figure 3. The Insides System™ – chyme reinfusion device (The Insides Company, Auckland, NZ).

Conclusions and future research directions

Pre-operative stimulation of the distal small or large bowel prior to stoma reversal or fistula repair, via CR, is a promising therapy for minimising the high rates of morbidity associated with DES or EAF of the small bowel in both adult and paediatric patient populations (Rombey et al. 2019; Bhat, Cameron, et al. 2020; Bhat, Sharma, et al. 2020). However, as noted above CR has failed to gain traction globally because methods have traditionally been labour intensive, had unpleasant workflows, lacked purpose-built equipment, and ultimately have resulted in poor tolerability by both patients and staff (Bhat, Cameron, et al. 2020; Bhat, Sharma, et al. 2020).

The novel CR device, developed through a collaboration between surgeons and engineers in NZ, has significantly advanced the field of CR technology. First-in-human data have demonstrated that the device was able to overcome many of the earlier challenges faced when undertaking CR manually, such as its ease of use, and high tolerability amongst patients and acceptability by staff, whilst allowing patients to remain fully independent and mobile during its use (Sharma et al. 2020). Further clinical studies have shown benefits associated with The Insides System^{TM} device, including reduction of fluid losses and cessation or reduction of anti-diarrhoeal medication use (Liu et al. 2021). AEs associated were minimal and mostly transient, often leading to device design optimisation through repeated clinician evaluation and patient feedback (Sharma et al. 2020; Liu et al. 2021).

CR technological advancements, such as with The Insides System^{TM} device, have the potential to become the standard of care in adult and paediatric patients with high output DES or EAF of the small bowel, as well as for loop ileostomates in the community, when the distal limb is accessible and safe to use. To this end, a pivotal multi-center, randomised controlled trial, which aims to assess the impact of The Insides System^{TM} CR device on bowel function recovery following ileostomy reversal, is currently ongoing.

Disclosure statement

Prof Ian Bissett and Prof Gregory O'Grady are affiliated with The Insides Company Ltd and have ownership interests. Prof Bissett is the chief medical officer and a shareholder. Prof O'Grady is a director, and a shareholder.

Funding

Chen Liu was supported by the Health Research Council of New Zealand under the Clinical Research Training Fellowship Grant.

ORCID

Chen Liu http://orcid.org/0000-0002-9009-7154
Ian Bissett http://orcid.org/0000-0001-6530-2454

References

Abu-Wasel B, Molinari M. 2014. Liver disease secondary to intestinal failure. Biomed Res Int. 2014:968357.

Al-Harbi K, Walton JM, Gardner V, Chessell L, Fitzgerald PG. 1999. Mucous fistula refeeding in neonates with short bowel syndrome. J Pediatr Surg. 34(7):1100–1103.
Annibali R, Gatti S, Rossi M, Tonelli L, Albano V, Catassi C. 2014. Case report: difficult management of chronic intestinal pseudo-obstruction (CIPO). Dig Liver Dis. 46:e125–e126.
Assaf D, Hazzan D, Ben-Yaacov A, Laks S, Zippel D, Segev L. 2021. Predisposing factors for high output stoma in patients with a diverting loop ileostomy after colorectal surgeries. Ann Coloproctol. Epub ahead of print. doi:10.3393/ac.2021.00241.0034.
Bafford AC, Irani JL. 2013. Management and complications of stomas. Surg Clin North Am. 93 (1):145–166.
Bhama AR. 2019. Evaluation and management of enterocutaneous fistula. Dis Colon Rectum. 62 (8):906–910.
Bhat S, Cameron NR, Sharma P, Bissett IP, O'Grady G. 2020. Chyme recycling in the management of small bowel double enterostomy in pediatric and neonatal populations: a systematic review. Clin Nutr ESPEN. 37:1–8.
Bhat S, Sharma P, Cameron NR, Bissett IP, O'Grady G. 2020. Chyme reinfusion for small bowel double enterostomies and enteroatmospheric fistulas in adult patients: a systematic review. Nutr Clin Pract. 35(2):254–264.
Bissett IP. 2000. Postoperative small bowel fistula: back to basics. Trop Doct. 30(3):138–140.
Bissett IP, Davidson J, Sutherland G, O'Grady G. 2020. Author response to: comment on: novel chyme reinfusion device for gastrointestinal fistulas and stomas: feasibility study. Br J Surg. 107(11):e557.
Blaauw R, Du Toit A, Boutall A. 2018. Opinions of South African dietitians on fistuloclysis as a treatment option for intestinal failure patients. South Afr J Clin Nutr. 31(2):6–11.
Calicis B, Parc Y, Caplin S, Frileux P, Dehni N, Ollivier JM, Parc R. 2002. Treatment of postoperative peritonitis of small-bowel origin with continuous enteral nutrition and Succus entericus reinfusion. Arch Surg. 137(3):296–300.
Corbett HJ, Turnock RR. 2010. An alternative management option for colonic atresia preventing loss of the ileocecal valve. J Pediatr Surg. 45(6):1380–1382.
Couper C, Doriot A, Siddiqui MTR, Steiger E. 2021. Nutrition management of the high-output fistulae. Nutr Clin Pract. 36(2):282–296.
Cresci GA, Martindale RG. 1997. Metabolic and nutritional management of a patient with multiple enterocutaneous fistulas. Nutrition. 13(5):446–448; discussion 448–449.
Doughty DB. 2008. History of ostomy surgery. Journal of Wound Ostomy & Continence Nursing. 35(1):34–38.
Drenckpohl D, Vegunta R, Knaub L, Holterman M, Wang H, Macwan K, Pearl R. 2012. Reinfusion of succus entericus into the mucous fistula decreases dependence on parenteral nutrition in neonates. ICAN: Infant, Child, & Adolescent Nutrition. 4(3):168–174.
Duan M, Cao L, Gao L, Gong J, Li Y, Zhu W. 2020. Chyme reinfusion is associated with lower rate of postoperative ileus in Crohn's disease patients after stoma closure. Dig Dis Sci. 65(1):243–249.
Dudrick SJ, Panait L. 2011. Metabolic consequences of patients with gastrointestinal fistulas. Eur J Trauma Emerg Surg. 37(3):215–225.
Du Toit A. 2014. Nutritional management of a complicated surgical patient by means of fistuloclysis. South Afr J Clin Nutr. 27(4):230–236.
Elliott T, Walton JM. 2019. Safety of mucous fistula refeeding in neonates with functional short bowel syndrome: a retrospective review. J Pediatr Surg. 54(5):989–992.
Evenson AR, Fischer JE. 2006. Current management of enterocutaneous fistula. J Gastrointest Surg. 10(3):455–464.
Federici S, Sabatino MD, Domenichelli V, Straziuso S. 2015. Worst prognosis in the 'complex' jejunoileal atresia: is it real? European J Pediatr Surg Rep. 3(1):7–11.
Gardner VA, Walton JM, Chessell L. 2003. A case study utilizing an enteral refeeding technique in a premature infant with short bowel syndrome. Adv Neonatal Care. 3(6):258–268; quiz 269–271.
Garfinkle R, Filion KB, Bhatnagar S, Sigler G, Banks A, Letarte F, Liberman S, Brown CJ, Boutros M. 2019. Prediction model and web-based risk calculator for postoperative ileus after loop ileostomy closure. Br J Surg. 106(12):1676–1684.

Gause CD, Hayashi M, Haney C, Rhee D, Karim O, Weir BW, Stewart D, Lukish J, Lau H, Abdullah F, et al. 2016. Mucous fistula refeeding decreases parenteral nutrition exposure in postsurgical premature neonates. J Pediatr Surg. 51(11):1759–1765.

Gutierrez IM, Kang KH, Jaksic T. 2011. Neonatal short bowel syndrome. Semin Fetal Neonatal Med. 16(3):157–163.

Haddock CA, Stanger JD, Albersheim SG, Casey LM, Butterworth SA. 2015. Mucous fistula refeeding in neonates with enterostomies. J Pediatr Surg. 50(5):779–782.

Hayden DM, Pinzon MC, Francescatti AB, Edquist SC, Malczewski MR, Jolley JM, Brand MI, Saclarides TJ. 2013. Hospital readmission for fluid and electrolyte abnormalities following ileostomy construction: preventable or unpredictable? J Gastrointest Surg. 17(2):298–303.

Inoue S, Odaka A, Muta Y, Beck Y, Sobajima H, Tamura M. 2017. Recycling small intestinal contents from proximal ileostomy in low-birth-weight infants with small bowel perforation. J Pediatr Gastroenterol Nutr. 64(1):e16–e18.

Justiniano CF, Temple LK, Swanger AA, Xu Z, Speranza JR, Cellini C, Salloum RM, Fleming FJ. 2018. Readmissions with dehydration after ileostomy creation: rethinking risk factors. Dis Colon Rectum. 61(11):1297–1305.

Kaidar-Person O, Person B, Wexner SD. 2005. Complications of construction and closure of temporary loop ileostomy. J Am Coll Surg. 201(5):759–773.

Keane C, Park J, Oberg S, Wedin A, Bock D, O'Grady G, Bissett I, Rosenberg J, Angenete E. 2019. Functional outcomes from a randomized trial of early closure of temporary ileostomy after rectal excision for cancer. Br J Surg. 106(5):645–652.

Kittscha J. 2016. Restoring gut continuity: reinfusion of effluent via distal limb of a loop jejunostomy. World Council of Enterostomal Therapists Journal. 36(4):28–31.

Koike Y, Uchida K, Nagano Y, Matsushita K, Otake K, Inoue M, Kusunoki M. 2016. Enteral refeeding is useful for promoting growth in neonates with enterostomy before stoma closure. J Pediatr Surg. 51(3):390–394.

Kwun H. 1999. Re-feeding of chymus into a high-output jejunostomy: a nursing care study. World Council Enterostomal Ther J. 19:20–21.

Lau EC, Fung AC, Wong KK, Tam PK. 2016. Beneficial effects of mucous fistula refeeding in necrotizing enterocolitis neonates with enterostomies. J Pediatr Surg. 51(12):1914–1916.

Layec S, Seynhaeve E, Trivin F, Carsin-Mahé M, Dussaulx L, Picot D. 2020. Management of enteroatmospheric fistulas by chyme reinfusion: a retrospective study. Clin Nutr. 39:3695–3702.

Levy E, Palmer DL, Frileux P, Parc R, Huguet C, Loygue J. 1983. Inhibition of upper gastrointestinal secretions by reinfusion of succus entericus into the distal small bowel. A clinical study of 30 patients with peritonitis and temporary enterostomy. Ann Surg. 198(5):596–600.

Liu C, Ludlow E, Davidson RB, Davidson JB, Chu KS, O'Grady G, Bissett IP. 2021. Stoma-output reinfusion device for ileostomy patients: a feasibility study. Dis Colon Rectum. 64(11):e662–e668.

Liu MY, Tang HC, Yang HL, Chang SJ. 2016. Is jejunostomy output nutrient or waste in short bowel syndrome? Experience from six cases. Asia Pac J Clin Nutr. 25(2):430–435.

Madnawat H, Welu AL, Gilbert EJ, Taylor DB, Jain S, Manithody C, Blomenkamp K, Jain AK. 2020. Mechanisms of parenteral nutrition-associated liver and gut injury. Nutr Clin Pract. 35 (1):63–71.

Martinez JL, Luque-de-Leon E, Mier J, Blanco-Benavides R, Robledo F. 2008. Systematic management of postoperative enterocutaneous fistulas: factors related to outcomes. World J Surg. 32 (3):436–443; discussion 444.

Nagar A, Mehrotra S, Yadav A, Mangla V, Lalwani S, Mehta N, Nundy S. 2018. Distal bowel refeeding in patients with proximal jejunostomy. J Gastrointest Surg. 22(7):1251–1257.

Picot D, Garin L, Trivin F, Kossovsky MP, Darmaun D, Thibault R. 2010. Plasma citrulline is a marker of absorptive small bowel length in patients with transient enterostomy and acute intestinal failure. Clin Nutr. 29(2):235–242.

Picot D, Layec S, Dussaulx L, Trivin F, Thibault R. 2017. Chyme reinfusion in patients with intestinal failure due to temporary double enterostomy: a 15-year prospective cohort in a referral centre. Clin Nutr. 36(2):593–600.

Picot D, Layec S, Seynhaeve E, Dussaulx L, Trivin F, Carsin-Mahe M. 2020. Chyme reinfusion in intestinal failure related to temporary double enterostomies and enteroatmospheric fistulas. Nutrients. 12(5):1376.
Picot D, Layec S, Trivin F, Dussaulx-Garin L. 2013. PP058-SUN enterocutaneous fistulas of the small bowel: treatment by chyme reinfusion. Clin Nutr. 32:S43–S43.
Puppala BL, Mangurten HH, Kraut JR, Bassuk A, Shrock P, Benawra RS, Napier K. 1985. Distal ileostomy drip feedings in neonates with short bowel syndrome. J Pediatr Gastroenterol Nutr. 4(3):489–494.
Riggs RL. 1987. Pouching and refeeding system for infant with dual bilateral ostomies. J Enterostomal Ther. 14(1):35–38.
Rinsema W, Gouma DJ, von Meyenfeldt MF, Soeters PB. 1988. Reinfusion of secretions from high-output proximal stomas or fistulas. Surg Gynecol Obstet. 167(5):372–376.
Rombey T, Panagiotopoulou IG, Hind D, Fearnhead NS. 2019. Preoperative bowel stimulation prior to ileostomy closure to restore bowel function more quickly and improve postoperative outcomes: a systematic review. Colorectal Dis. 21(9):994–1003.
Sancar S, Sanal M, Renz O, Hechenleitner P. 2020. The feasibility of routine use of distal stoma refeeding method in newborns with enterostomy. J Matern Fetal Neonatal Med. 33 (17):2897–2901.
Saunders J, Parsons C, King A, Stroud M, Smith T. 2013. The financial cost of managing patients with type 2 intestinal failure; experience from a regional centre. e-SPEN Journal. 8(3):e80–e85.
Schäfer K, Zachariou Z, Löffler W, Daum R. 1997. Continuous extracorporeal stool-transport system: a new and economical procedure for transitory short-bowel syndrome in prematures and newborns. Pediatr Surg Int. 12(1):73–75.
Shafiekhani M, Nikoupour H, Mirjalili M. 2022. The experience and outcomes of multidisciplinary clinical pharmacist-led parenteral nutrition service for individuals with intestinal failure in a center without home parenteral nutrition. Eur J Clin Nutr. 76:841–847.
Sharma P, Davidson R, Davidson J, Keane C, Liu C, Ritchie SR, Chu K, Sutherland G, Bissett IP, O' Grady G. 2020. Novel chyme reinfusion device for gastrointestinal fistulas and stomas: feasibility study. Br J Surg. 107(9):1199–1210.
Sidebotham EL, Sepkowitz K, Price AP, Steinherz PG, La Quaglia MP, Kayton ML. 2010. Eradication of cryptosporidium from a defunctionalized colon limb by refeeding stoma effluent. J Pediatr Surg. 45(1):E33–E36.
Solis E, Wright DB, O'Grady G, Ctercteko G. 2021. Chyme reinfusion nutritional management for enterocutaneous fistula: first international application of a novel pump technique. Colorectal Dis. 23(7):1924–1929.
Somashekar U, Sharma D. 2020. Comment on: novel chyme reinfusion device for gastrointestinal fistulas and stomas: feasibility study. Br J Surg. 107(11):e556.
Tanaka A, Nakayama-Imaohji H, Shimono R, Suzuki M, Fujii T, Kubo H, Yasuda S, Koyano K, Nakamura S, Katsuki N, et al. 2017. Nutritional benefit of recycling of bowel content in an infant with short bowel syndrome. J Pediatr Gastroenterol Nutr. 65(3):e75–e76.
Thibault R, Picot D. 2016. Chyme reinfusion or enteroclysis in nutrition of patients with temporary double enterostomy or enterocutaneous fistula. Curr Opin Clin Nutr Metab Care. 19 (5):382–387.
Tian W, Zhao R, Xu X, Zhao Y, Luo S, Tao S, Yao Z. 2022. Chyme reinfusion reducing the postoperative complications after definitive surgery for small intestinal enteroatmospheric fistula: a cohort study. Front Nutr. 9:708534.
Wong KK, Lan LC, Lin SC, Chan AW, Tam PK. 2004. Mucous fistula refeeding in premature neonates with enterostomies. J Pediatr Gastroenterol Nutr. 39(1):43–45.
Wu Y, Ren J, Wang G, Zhou B, Ding C, Gu G, Chen J, Liu S, Li J. 2014. Fistuloclysis improves liver function and nutritional status in patients with high-output upper enteric fistula. Gastroenterol Res Pract. 2014:941514.