Diarrhoea in the critically ill

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Purpose of review
To summarize existing evidence on definition, epidemiology, mechanisms, risk factors, consequences, outcome and management of diarrhoea in the critically ill.

Recent findings
In health, diarrhoea is defined as the passage of three or more loose or liquid stools per day. In the critically ill, the diagnosis is yet to be formalized and reported prevalence of diarrhoea varies according to the definition used. Recent studies estimate the prevalence between 14 and 21% and describe risk factors for diarrhoea in critically ill patients. The precipitant of diarrhoea always needs to be identified, as targeted therapies are important for several causes. Although the majority of patients with diarrhoea require only supportive care, it is always essential to exclude, or confirm and treat infectious diarrhoea. There is little evidence to support delaying or withdrawing provision of enteral nutrition in patients with diarrhoea, and we recommend continuing enteral nutrition whenever possible. However, the consequences of diarrhoea – hypovolaemia, electrolyte disturbances, malnutrition, skin lesions and contamination of wounds – should be avoided or at least recognized promptly.

Summary
A definition of diarrhoea and a practical approach to identify the precipitant and to manage diarrhoea in critically ill patients are proposed.

Keywords
Clostridium difficile, diarrhoea, enteral nutrition, infectious diarrhoea

INTRODUCTION

Our review summarizes existing evidence regarding the definition, epidemiology, mechanisms, risk factors, consequences and outcomes of diarrhoea. We propose a practical approach to identify the cause and thereby treat patients with diarrhoea.

DEFINITION

The World Health Organization definition of diarrhoea is the passage of three or more loose or liquid stools per day [1]. However, other experts recommend that rather three criteria must be met: stool frequency, stool weight and stool consistency [2–4].

Stool frequency three stools or more per day, or a more frequent passage than is normal for the individual, defines this component of the diagnosis [4]. Normal gastrointestinal transit times are considered to be around 48 h [4].

Stool weight 200 g/day or above or volume 250 ml/day or above is considered abnormally high [4]. The average stool weight of healthy meat-eating adults is 105–140 g/24 h, being greater in vegetarians [4].

The Bristol Stool Chart is probably the most widely used description of stool consistency [5], with loose or watery stools (Bristol Stool Chart type 5–7) required to constitute diarrhoea [5].

In a survey, nursing staff found faecal frequency more important than consistency and quantity, whereas agreeing that diarrhoea was present in only three-fourths of cases, suggesting moderate

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KEY POINTS

- Definition of diarrhoea comprises stool frequency, stool weight and stool consistency.
- Prevalence of diarrhoea in unselected ICU population is between 14 and 21%.
- Infectious diarrhoea should always be identified and treated.
- Risk factors for *C. difficile* infection-associated diarrhoea are antimicrobials, age above 60 years, PPI, exposure to other patients with CDI, residence in a chronic care facility and severe underlying disease.
- Standardized approach to differential diagnosis and management is recommended.

reliability between observers when it comes to making the diagnosis [6].

For patients with colostomy, grading of chemotherapy-induced diarrhoea but not other forms has been proposed [7].

Extrapolating from data in health, we suggest that diarrhoea in the critically ill be defined as the simultaneous presence of stool frequencies three stools per day or more, with stool weights 200 g/day or higher and consistency of stools categorized as 5–7 on the Bristol Stool Chart.

EPIDEMIOLOGY

Recent studies have estimated the prevalence of diarrhoea in critically ill patients as between 14 and 21% [8,9,10▪], slightly higher when only patients with enteral nutrition were studied [11] (Table 1) [8,9,10▪,11], with the median onset of symptoms occurring 6 days after ICU admission [10▪]. However, none of these studies used a strict definition such as the one proposed above. Moreover, selected patients were studied and/or a limited period of observation used. Taken together, the true overall prevalence of diarrhoea in ICU population is unknown.

Diarrhoea is frequently occurring in critically ill patients during enteral nutrition, with prevalences reported varying from 10 to 78% [11–14]. Importantly, Ferrie and East [11] recently reported a reduction in the prevalence of diarrhoea from 36 to 23% ($P = 0.0002$) in severely ill tube-fed patients with the introduction of a bowel management protocol. However, the mean APACHE II score was significantly lower during the second phase of the study (22 vs. 29%. $P < 0.001$), and this raises the possibility that diarrhoea occurred more frequently in those patients that were more severely ill and represents a type I error. Such a hypothesis is supported by recent observational data in which patients with diarrhoea had greater illness severity scores [10▪].

PATHOPHYSIOLOGICAL MECHANISMS OF DIARRHOEA

Four different pathophysiological mechanisms underlying diarrhoea have been described: motoric, osmotic, secretory and exudative [3]. According to a more recent review [15], we suggest narrowing the focus to distinguish only between two pathophysiological processes: osmotic, reduced water absorption because of osmotically active substances intraluminally or short passage time; and secretory, imbalance between absorption and secretion of electrolytes leading to increased water secretion.

RISK FACTORS

Enteral nutrition may be mistakenly considered a common precipitant of diarrhoea. Interestingly, a meta-analysis suggested that the risk of developing diarrhoea was similar in patients receiving enteral or parenteral nutrition [16]. In contrast, a recent study reported that the enteral delivery of more than 60% of energy targets increased the risk of diarrhoea by 1.75 (1.02–3.01), whereas just the presence of enteral nutrition had no impact [10▪]. These latter data suggest that there may be a small intestinal threshold of nutrient absorption [17] and beyond such a level, malabsorption and diarrhoea occur. Another factor that appears to be associated with the risk of diarrhoea is exposure to antimicrobial drugs [10▪].

Proven risk factors for diarrhoea in general ICU population are enteral nutrition more than 60% of energy target and exposure to antimicrobial drugs.

CLASSIFICATIONS OF DIARRHOEA

Diarrhoea can be described by its severity, duration and cause.

Severity

Severe diarrhoea requires treatment (e.g. fluids), whereas mild is self-limiting (Fig. 1). However, the term ‘mild’ does not exclude the need for interventions, as mild diarrhoea might be infectious and therefore require treatment.

Duration

Acute diarrhoea lasts for less than 2 weeks and chronic diarrhoea more than 4 weeks. The majority

Table 1. Summary of recent larger studies reporting prevalence of diarrhoea in critically ill patients

Author and year	Definition	Design	Study patients	Main inclusion criteria	Main exclusion criteria	Prevalence	Association with outcome
Ferrie and East, 2007 [11]	Bowel activity exceeding three stools of any consistency per day, or at least three unformed stools (or 300 ml) per day, for two consecutive days	Prospective, single-centre, before and after introduction of bowel management protocol	656	Length of stay >3 days + enteral nutrition	No enteral nutrition	36% before, 23% after the introduction of a bowel management protocol	No
Reintam *et al.*, 2009 [8]	Not formed stools at least three times per day	Prospective, single-centre	1312	All patients admitted to the ICU	None	14%	No
Reintam Blaser *et al.*, 2013 [9]	Not formed stools at least three times per day	Prospective, multicentre	377	Mechanical ventilation at admission continued for >6 h	Spontaneous breathing at admission, no bladder catheter (for IAP measurements)	21.5	No
Thibault *et al.*, 2013 [10▪]	At least three liquid stools per day	Prospective, single-centre	278	All patients staying for >24 h	No admission diagnosis of gastrointestinal bleeding, and without enterostomy or colostomy	14%	NA

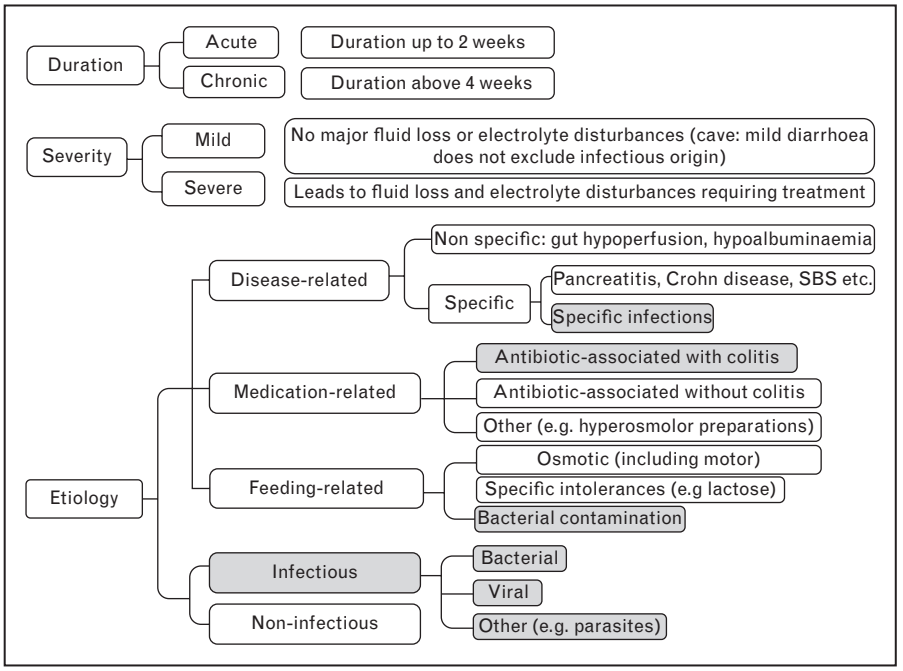

FIGURE 1. Classifications of diarrhoea. Different forms of infectious diarrhoea are marked in grey. SBS, short bowel syndrome.

of critically ill patients have acute diarrhoea, with 89% of diarrhoea episodes in critically ill patients lasting for 4 days or less [10▪,18].

Cause

It is our opinion that differentiation between disease-related, medication-related and diet-related diarrhoea is useful.

Infectious vs. noninfectious

Because of differences in management, it is very important to distinguish additionally between infectious and noninfectious diarrhoea. Causes and management of noninfectious diarrhoea are presented in Table 2 [15,19] and of infectious diarrhoea in Table 3 [20▪▪,21–23].

We wish to emphasize that diarrhoea is a symptom. Accordingly, only diagnosing and then treating the underlying cause may solve the problem.

DISEASE-RELATED DIARRHOEA

Underlying or concomitant disease or acute condition can cause disease-related diarrhoea. Assessment of specific intolerances, like lactose or sorbitol intolerance and fructose malabsorption, requires accurate anamnesis.

Pancreatic exocrine insufficiency and bile salt malabsorption-associated diarrhoea may occur without preexisting diagnosis and stops immediately when pancreatic enzymes or cholestyramin are added [24–26]. Wang *et al.* [24] reported moderate steatorrhoea in more than half of the patients in the ICU. Steatorrhoea was graded severe in almost 20% and the occurrence of steatorrhoea was closely associated with shock, sepsis, diabetes, cardiac arrest, hyperlactacidemia, invasive mechanical ventilation and haemodialysis. Although the assessment of duodenal enzyme output is complicated and not applicable at bedside, a sophisticated study of a small cohort reported that the content of amylase, chymotrypsin and trypsin in aspirated duodenal fluid was significantly reduced in patients with septic shock when compared with nonseptic patients as well as healthy subjects ($P < 0.01$) [25], consistent with the concept that pancreatic insufficiency is likely to contribute to diarrhoea in a proportion of ICU patients.

It has been proposed that hypoalbuminaemia (<2.5 g/dl), leading to reduced oncotic pressure, can be associated with reduced reabsorption of water from the gut lumen [2].

Severe infections, organ rejections after transplantation, endocrine disorders (thyroid diseases, diabetes among others), gastrointestinal tumours and malassimilation, for example, in short bowel syndrome or chronic inflammatory bowel disease are also associated with diarrhoea.

Disease-related diarrhoea resolves only when the trigger is eliminated.

Table 2. Causes and specific management of noninfectious diarrhoea

Etiologic classification group	Specific pathology/condition/drug	Management	Remarks
Disease-related	Specific intolerances (lactose, sorbitol, fructose, celiac disease)	Avoiding the trigger	Anamnesis is essential
	Pancreatic exocrine insufficiency	Pancreatic enzymes (cave different administration rules via gastric and postpyloric tube) [19]	Can also occur in critically ill patients without previous pancreatic disease
	Endocrine disorders (thyroid disease, diabetes, Zollinger-Ellison syndrome)	Treating the trigger	
	Tumours (gastrointestinal, pheochromocytoma)	Treating the trigger	
	Chronic malassimilation states (short bowel syndrome, chronic inflammatory bowel disease)	Treating the trigger where possible	
	Bile acid malabsorption (cholestasis, postcholecystectomy)	Cholestyramine can be considered	
	Intoxications (heavy metal poisoning)	Gastrointestinal decontamination and chelation therapy	
Medication-related	Laxatives	Stop when no indication any more	
	Prokinetics	Stop when no indication any more	
	Hyperosmolar oral liquid preparations	Alternative preparations where possible	Detailed list elsewhere [15] Cave oral preparations via tube, especially postpyloric
	Preparations with significant amount of poorly absorbed large carbohydrates (sorbitol, xylitol)	Alternative preparations where possible	Detailed list elsewhere [15]
	Antibiotics		Antibiotic-associated diarrhoea with colitis is addressed under infectious diarrhoea
	Chemotherapy	In case of neutropenic colitis broad-spectrum antibiotics are recommended, rarely surgery may be needed	Cell fragments and membranes in stool support the diagnosis
	Radiotherapy		Cell fragments and membranes in stool support the diagnosis
Diet-related	Tube-feeding	Iso-osmolar formula with fibres, continuous administration. If severe diarrhoea persists after excluding other causes, changing formula and excluding contamination of the feeds, rate of enteral nutrition could be reduced.	Enteral nutrition should not be stopped because of diarrhoea
	Oral diet	Isotonic fluids, frequent small meals, avoidance of hypo- or hyperosmolaric fluids, gradual return to normal diet	

MEDICATION-RELATED DIARRHOEA

Laxatives are frequently administered to critically ill patients, and their prophylactic use is thought to reduce the occurrence of gastrointestinal paralysis/paralytic ileus [27]. The implementation of a bowel management protocol should alert clinicians to promptly cease laxatives if diarrhoea occurs. Diarrhoea resolves in about 25% of all cases when laxatives are ceased [11].

Prokinetics are frequently implicated as causing diarrhoea with motor effects reducing gastrointestinal transit time. However, in the critically ill, the

Table 3. Miscellaneous pathogens causing infectious diarrhoea [20▪▪,21–23]

Pathogen	Characteristics	Special aspects	Diagnostics	Antimicrobial treatment options
Bacteria				
Clostridium difficile	Large bowel, toxin-producing, dysentery, antibiotic-associated, recurrence-prone	Offending antibiotic should be withdrawn if possible. Unfavourable prognostic factors: WBC count >15 000 cells/μl or albumin <30 g/l or ≥50% rise in baseline creatinine [20▪▪]. Risk of toxic megacolon.	Fecal test for toxin A and B. Search in all ICU patients with diarrhoea	Choice of regimen depending on severity and recurrence. Metronidazol. Vancomycin enterally. Fidaxomicin. Rifaximin enterally
Escherichia coli-producing Shiga-like toxin (EHEC s. *E. coli* O157:H7)	Large bowel, toxin-producing, consider when nonfebrile bloody diarrhoea	Sporadic diarrhoea, 5–10% develop haemolytic uremic syndrome	Stool culture, test for Shiga toxin	No treatment with antimicrobials
Escherichia coli (ETEC, EPEC, EAggEC, EIEC)	Small bowel (EIEC in large bowel), toxin-producing	Sporadic diarrhoea, traveller's diarrhoea	Stool culture	Fluoroquinolone
Salmonella typhus	Small and large bowel, toxin-producing, dysentery, sometimes bloody diarrhoea	Food poisoning, sporadic diarrhoea, traveller's diarrhoea. Risk of intestinal perforation, osteomyelitis, septic arthritis and mycotic aneurysm	Stool culture, blood culture if high fever	Fluoroquinolone. Ceftriaxone if acquired in Asia. Longer treatment in immunocompromised patients
Salmonella nontyphoidal	Small and large bowel, dysentery, sometimes bloody diarrhoea	Sporadic diarrhoea, traveller's diarrhoea	Stool culture, blood culture if high fever (bacteraemia in 2–4%)	Antibiotics only if age >50 y, bacteraemic, severely ill or immunocompromised patient, vascular graft, prosthetic joints or haemoglobinopathy. Fluoroquinolone
Shigella	Large bowel, toxin-producing. dysentery, sometimes bloody diarrhoea	Sporadic diarrhoea, traveller's diarrhoea	Stool culture	Fluoroquinolone in immunocompromised
Campylobacter species	Large and small bowel, dysentery, bloody diarrhoea	Sporadic diarrhoea, traveller's diarrhoea, self-limited in normal host, associated with Guillain-Barré Syndrome (in 15% of cases) or reactive arthritis	Stool culture	Azithromycin, for *Campylobacter fetus* gentamicin
Staphylococcus aureus	Small bowel, toxin-producing	Food poisoning	None	None
Bacillus cereus	Small bowel, toxin-producing	Food poisoning	None	None
Klebsiella oxytoca	Large bowel, toxin-producing, bloody diarrhoea, antibiotic-associated	Rare		Responds to stopping offending antibiotic
Yersinia enterocolitica	Large bowel, dysentery			Antibiotics only if severe, doxycycline plus aminoglycoside
Vibrio cholerae	Large bowel, toxin-producing	Food poisoning, traveller's diarrhoea. Rehydration is essential.	Stool culture	Doxycycline, azithromycin, tetracycline

(*Continued*)

Table 3 (*Continued*)

Pathogen	Characteristics	Special aspects	Diagnostics	Antimicrobial treatment options
Vibrio parahaemolyticus and *vulnificus*	Large bowel, toxin-producing	Food poisoning, traveller's diarrhoea. *V. vulnificus*: skin lesions and bacteraemia, life-threatening	Stool culture	*V. parahaemolyitcus*: treat if severe disease. Fluoroquinolone *V. vulnificus*: treat early. Ceftazidime plus doxycycline
Aeromonas/Plesiomonas	Small bowel	Food poisoning, traveller's diarrhoea	Stool culture	Fluoroquinolone
Virus				
Norovirus	Small bowel, nausea and vomiting	Highly contagious, majority of outbreaks of nonbacterial gastroenteritis.	Stool or emesis for PCR	None
Rotavirus	Small bowel, nausea	Mainly in small children	Stool for rapid antigen test	None
Adenovirus	Small bowel		Stool for rapid antigen test	None
Cytomegalovirus	Large bowel, dysentery	Search in case of immunosuppression	Mucosal biopsy for histology, plasma PCR	Ganciclovir
Herpes simplex virus	Large bowel	Search in case of immunosuppression	Mucosal biopsy for histology and PCR	Valacyclovir
Protozoa				
Entamoeba histolytica	Large bowel, dysentery, bloody diarrhoea	Risk factors: anoreceptive intercourse and colonic irrigation	Stool for enzyme immunoassay or PCR	Metronidazole
Cryptosporidium parvum	Small bowel	Search if HIV-infected (with immunodeficiency) and diarrhoea >10 days	Stool for enzyme immunoassay	Nitazoxanide
Microsporidium species	Small bowel	Search if HIV-infected (with immunodeficiency) and diarrhoea >10 days	Stool for enzyme immunoassay	Albendazole
Isospora belli	Small bowel	Search if HIV-infected (with immunodeficiency) and diarrhoea >10 days	Stool for enzyme immunoassay	Trimethoprim/sulfamethoxazole
Cyclosporacayatanensis	Small bowel	Search if HIV-infected (with immunodeficiency) and diarrhoea >10 days	Stool for enzyme immunoassay	Trimethoprim/sulfamethoxazole
Giardia lamblia	Small bowel	Search if chronic traveller's diarrhoea	Stool for microscopy or enzyme immunoassay	Tinidazole, nitazonaxide, albendazole

EAggEC, enteroaggregative *Escherichia coli*; EHEC, enterohemorrhagic *Escherichia coli*; EIEC, enteroinvasive enteroaggregative *Escherichia coli;* EPEC, enteropathogenic *Escherichia coli*; ETEC, enterotoxicogenic *Escherichia coli*; WBC, white blood cell.

motilin agonist erythromycin at a dose of 200 mg acutely slows rather than accelerating small intestinal transit time [28]. When prokinetic drugs are used during intragastric feeding in the critically ill, metoclopramide was associated with diarrhoea in 32%, erythromycin in 30% and their combination in 49% [29]. In all patients included in the latter study, diarrhoea was mild and stopped immediately after discontinuing prokinetic therapy.

Hyperosmotic preparations containing lactose, sorbitol or other osmotically active components (e.g. magnesium) can induce osmotic diarrhoea [15], especially in patients with respective intolerance. Medications causing osmotic diarrhoea are listed elsewhere [15].

Laxatives and prokinetics should be stopped immediately when the indication is not present anymore. All prescribed substances need to be checked for their indication and ingredients, and alternative preparations need to be considered where possible.

Antibiotic-associated diarrhoea

Incidence of antibiotic-associated diarrhoea (AAD) is up to 25% and depends on the antibiotic drug used and can be classified as follows [30–32]:

AAD without colitis is usually mild and self-limiting with different underlying causes:

(1) Direct prokinetic effect of antibiotics on gastrointestinal motility (e.g. erythromycin, azithromycin)
(2) Microbial modification with unmetabolized carbohydrates causing osmotic diarrhoea [33,34].
(3) Unmetabolized dihydroxy bile acids owing to disturbed microbiota induce secretory diarrhoea [30,35].

AAD with colitis is induced by bacterial overgrowth of gut microbiota by *Clostridium difficile* or rarely *Klebsiella oxytoca* (see section INFECTIOUS DIARRHOEA).

Diarrhoea in the immunocompromised patient

Diarrhoea in immunocompromised and/or neutropenic patients (commonly both disease-related and medication-related diarrhoea) is severe in up to 10% and has a specific etiologic spectrum [36,37].

Neutropenic enterocolitis is a combination of pyrexia (>38.5°) and abdominal symptoms (pain in right iliac fosse, abdominal distension, diarrhoea) along with typical radiologic findings (gross thickening of ileal and caecal wall with surrounding inflammatory changes) in neutropenic patients (absolute neutrophil count <500 cells/mm^3) [38].

DIET-RELATED DIARRHOEA

Diarrhoea as a complication of enteral nutrition is often reported, whereas less associated with oral diet in hospitalized patients.

Enteral feeding

Long-time enteral nutrition, but also high-osmolality and/or low-fibre formula, bolus feeding and/or too fast increase to the target, and postpyloric enteral nutrition have been associated with increased prevalence of diarrhoea in stroke unit patients [39]. The latter is not confirmed in critically ill patients [40,41].

Bacterial contamination of the enteral formulas is rarely seen. More frequently, retrograde bacterial overgrowth of tube feeding systems with *Enterococcus, Enterobacter cloacae* and *Klebsiella oxytoca* was found, whereas bacterial count correlated directly with severity of illness, and the time the systems were used [42,43].

In case of diet-related diarrhoea, soluble fibres added to the meal exert positive effects; when being fermented by gut microbiota to gas and short-chain fatty acids they can increase transit time, reduce stool frequency and improve consistency [15].

Oral diet

A significantly increased amount of oral fluids, increased amounts of ingested fibres or nutrients with a high amount of fructose or sorbitol may induce diarrhoea. Extubated patients require a gradual return to normal diet using isotonic fluids, and frequent small meals, with hypoosmolaric or hyperosmolaric fluids avoided [44].

INFECTIOUS DIARRHOEA

To exclude infectious diarrhoea in all patients with severe diarrhoea, anamnesis is important, completed by a clinical examination and laboratory values. When infectious diarrhoea is presumed, determination of the pathogen - either via culture or PCR of toxin or antigen - is essential (Table 3).

Bacterial diarrhoea

Different strains of *Eschericia coli* (Table 3) cause diarrhoea, but most of them are not relevant for the ICU. Different is enterohemorrhagic *E. coli*

(EHEC), which in up to 10% leads to a haemolytic uremic syndrome (HUS), characterized by acute renal failure, haemolytic anaemia and thrombocytopaenia [45]. The EHEC toxins are similar to the toxins produced by *Shigella dysenteriae*. The incubation period ranges from 3 to 8 days, and symptoms include bloody diarrhoea, abdominal cramps, fever and vomiting. Antibiotics and antimotility drugs are contraindicated because they may enhance toxin release. In patients with HUS, plasma exchange is recommended, and immunosuppressive therapy with eculizumab can be considered [46▪,47].

Antibiotic-associated diarrhoea with colitis

C. difficile is a gram-positive spore-forming anaerobe that was identified as the leading course of toxin-positive AAD with pseudomembranous colitis in the late 1970s [48,49]. Severe colitis, toxic megacolon and death have all been reported. Recently, a considerable increase in the incidence of *C. difficile* infections (CDI) was reported [50]. The cause was a new *C. difficile* strain (NAP1/BI/027) that produces about 20 times the amount of the toxins A and B. The new strain is associated with a more severe course of disease, higher morbidity and mortality, a greater likelihood for ICU admission and higher healthcare costs [50]. Independent risk factors include antimicrobials (most notably quinolones, clindamycin, ampicillin and cephalosporines), age above 60 years, proton pump inhibitors (PPIs) [51▪], exposure to other patients with CDI, residence in a chronic care facility and severe underlying disease [52]. Relapses occur in up to 30% [53].

Klebsiella oxytoca AAD occurs after antibiotic treatment with penicillins, quinolones and cephalosporines and responds to cessation of antibiotic treatment [54]. Main symptoms are bloody diarrhoea and severe abdominal cramps; endoscopic findings are longish ulcers predominantly in the right colon [54].

Viral, fungal and parasitic diarrhoea

In patients who are immunocompromised, the presence of severe diarrhoea necessitates specific investigations for opportunistic pathogens (Table 3).

MANAGEMENT

Differential diagnosis and management algorithm is presented in Fig. 2.

Prevention is the desired management strategy of diarrhoea, but several factors that may promote diarrhoea (e.g. antibiotics) are unavoidable in critically ill patients. However, indication for each medication, including PPI [55], should be carefully considered.

To prevent feeding-associated diarrhoea, administration rules for enteral nutrition are important. Generally accepted options to reduce diarrhoea in enterally fed patients are iso-osmolar solutions and continuous infusion. In case of intolerances, lactose-free diets, and in patients with fat malabsorption, low fat or medium-chain triglyceride containing diets are recommended [56▪]. Some fibres (e.g. pectin and partially hydrolysed guar gum) have been reported to reduce the incidence of diarrhoea [56▪,57]. There are no data to support elemental diet for prevention or treatment of diarrhoea.

Specific treatment is available for pancreatic exocrine insufficiency and some forms of infectious diarrhoea (Table 3), whereas efforts to identify and treat the underlying cause and provision of supportive care are required for all patients with diarrhoea.

Supportive care with replacement of fluids and electrolytes and close monitoring of laboratory values and organ function are essential. Avoidance or early detection and treatment of consequences (skin lesions among others) is also important (see Fig. 2).

Isolation precautions to prevent nosocomial transmission are required for all symptomatic patients with infectious diarrhoea in the ICU because of their bedriddenness and to great extent incontinence.

Nonspecific treatment options

Opioids as antimotility drugs (loperamide) are not recommended as primary therapy and should be avoided in patients with acute dysentery characterized by blood in the stools and high fever, acute ulcerative colitis, bacterial enterocolitis caused by invasive organisms or AAD with colitis.

Cholestyramine may be considered in diarrhoea caused by bile acid malabsorption (patients with cholestasis, short bowel syndrome, terminal ileum resection and following cholecystectomy) [15]. It needs to be remembered that cholestyramine can reduce the absorption of enterally administered medications, including metronidazole used for CDI [15].

Probiotics and prebiotics can possibly reduce diarrhoea, but there are not enough data to recommend their routine use in critically ill patients [58,59]. Important is that in critically ill patients and immunocompromised patients, *Saccharomyces boulardii* is not recommended because of several reported cases of fungemia [60,61]. Faecal transplantation is recommended in case of multiple recurrent

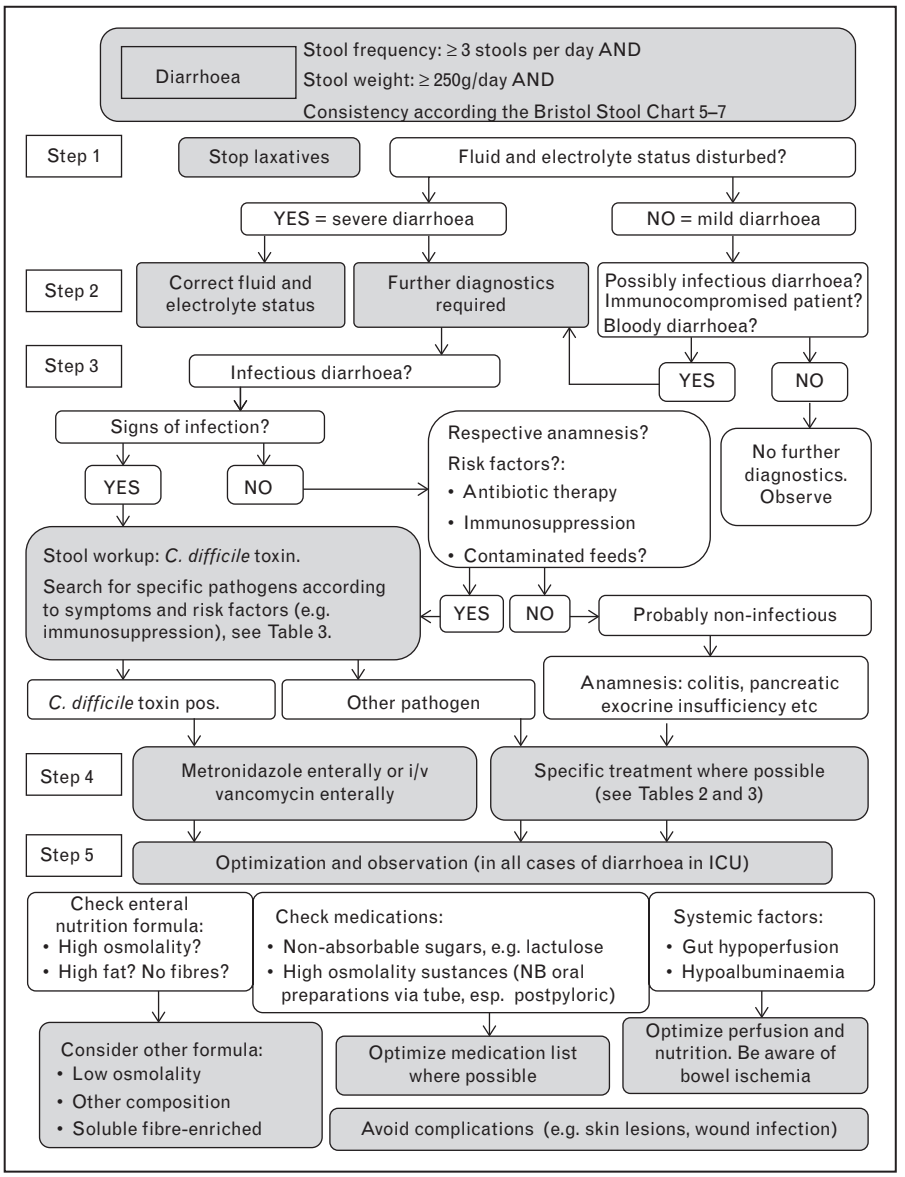

FIGURE 2. Differential diagnosis and management of diarrhoea.

CDI [20▪▪,62], but not studied in the critically ill patients.

CONSEQUENCES AND OUTCOME

There are several systemic (water and electrolyte dysbalance, haemodynamic instability, metabolic acidosis, malabsorption and malnutrition) and local (skin lesions and contamination of wounds) consequences of diarrhoea that need to be avoided or, at least, recognized early.

Higher disease severity scores at admission and longer ICU length of stay in patients with diarrhoea have been described [10▪,14], but it has not been demonstrated that diarrhoea itself is an independent risk factor for adverse outcome in critically ill patients [8,9,10▪]. Nonetheless, a greater incidence of bedsores occurs in patients with diarrhoea [63]. Although not definitively proven, it is very likely that diarrhoea has an impact on the risk of complications in ICU patients, as well as on the workload and costs [10▪].

CONCLUSION

We propose that diarrhoea in the critically ill patients be defined as the simultaneous presence of stool frequencies three or more stools per day, stool weights 200 g/day or more and consistency of stools categorized as 5–7 on the Bristol Stool Chart. We propose a practical approach for differential diagnosis and management of diarrhoea based on

existing evidence. However, further studies on epidemiology, risk factors, management and outcome of diarrhoea in critically ill patients are warranted.

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Conflicts of interest

None.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

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