

## Scoping Review

# A Scoping Review of Evidence to Develop an Evidenced-Based Protocol on the Prevention and Treatment of Constipation in the Critically Ill

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### ABSTRACT

**Aims and objectives:** To define constipation and review and synthesize evidence for how critical care nurses and physicians can prevent and treat constipation in critically ill patients admitted to the ICU.

**Background:** Constipation is a common complication amongst critically ill patients. The rate of constipation is reported from 15-83%. Basic nursing tasks in a high-tech environment might get low priority and lead to care left undone. Constipation increases both morbidity and mortality and is associated with worse functional outcomes in these patients. Management of constipation is therefore of medical and health economic interest and is an area where significant improvement is possible.

**Design:** A scoping review with a systematic search of the literature was conducted to perform a synthesis of the evidence.

**Methods:** A total of 19 studies investigating preventative and management measures of constipation in the critically ill admitted to the ICU were included. Appraisal of Guidelines for Research and Evaluation (AGREE II) was followed. Critical Appraisal Skills Program (CASP) was applied to assess the quality of the included studies.

**Conclusion:** A systematic interprofessional approach to preventing and treating constipation is important to evaluate and improve continuously in an evidence-based manner. More research is needed. Studies investigating non-pharmacological measures are scarce.

**Relevance to clinical practice:** This interprofessional approach may ensure a better quality of advanced nursing care in the ICU. The evidence-based protocol must be implemented in the education of advanced nursing and physician programs.

**Keywords:** Bowel care, constipation, critical care, critically ill, evidence-based nursing.

### INTRODUCTION

Constipation is an underestimated complication for the critically ill patient, which is often untreated until it leads to symptoms (Lat et al., 2010). Nursing staff in intensive care units (ICUs) play an important part in monitoring and evaluating bowel movements. This is significant in preventing complications related to constipation (Perez-Sanchez et al., 2017). The reported incidence of constipation in the ICU varies between 15% and 83% (Aikawa et al., 2022; Habeeb et al., 2022; Mostafa et al., 2003). This range could be due to incomplete documentation (McKenna

et al., 2001). Perez-Sanchez et al. (2017) reported that 63% of critically ill patients experienced constipation. They found that there was a lack of agreement in defining constipation in critically ill patients among experts. Studies demonstrated that constipation is associated with length of ICU stay, as well as increased morbidity and mortality (Azevedo et al., 2009, Guerra et al., 2013, Gacouin et al., 2010). Complications related to constipation may include higher abdominal pressure, bacterial translocation, feeding intolerance, discomfort, higher morbidity, and increased mortality (Wanik et al., 2019).

An evidence-based bowel management protocol resulted in improved daily defecation in mechanically ventilated patients and a reduction in the sequential organ failure assessment score (SOFA) (Azevedo et al., 2009). Inter-professional team discussions and plans are platforms for learning and research dissemination in the ICU (Hansen & Severinsson, 2009); thus, research studies on constipation and its consequences are important for higher prioritization of this problem.

In the holistic care of critically ill patients, the area of bowel care is often overlooked. The dominant care delivery model within nursing and acute care has been the disease-focused model of diagnosis and treatment, according to Vollman (2013). The prevention of complications has unfortunately received less priority. Within critical care nursing, the fundamentals of care and evidence-based practice are essential in high-quality treatment and care. With the primary concern of treating and caring for the patients to preserve life, less priority has been given to the problem of bowel care (Dorman et al., 2004). Constipation has been paid scant attention, and issues of failure to defecate in critically ill patients are difficult to determine (Mostafa et al., 2003). Patients' experiences from post-intensive care follow-up clinics have described constipation as a distressing part of their stay (Hill et al., 1998). Critically ill patients are in a situation of limited autonomy, and constipation can be an unnecessary strain. Preventing and treating constipation might be one of many tasks in missed nursing care, defined as care that nurses regard as necessary but leave undone due to lack of time (Ball et al., 2014).

The shortage of CCNs worldwide has already led to a recruitment problem for ICUs (Endacott et al., 2015). Strong evidence shows that lower nursing staff levels in hospitals are associated with worse patient outcomes (Ball et al., 2014). Kalisch and Xie (2014) found that patient-identified missed nursing care predicts adverse events. Errors that are committed and care that is omitted need attention. In a busy ward, essential nursing tasks that request documentation often receive priority, and preventive activities are overlooked. The prevention of constipation in ICUs is one such preventive activity.

### **Background**

Constipation may lead to severe complications. Mechanical consequences of constipation may arise, abdominal pressure will increase and lead to reduced lung

compliance and high intrathoracic pressure (Azevedo et al., 2009, Fukuda et al., 2016, Mostafa et al., 2003). Bacterial translocation in critically ill patients may lead to higher risk for infection as a direct complication of constipation (Azevedo et al., 2009, Gacouin et al., 2010). Critically ill patients that had bowel movements after 6 days had a high risk of sepsis with a high SOFA score (Gacouin et al., 2010). Mechanically ventilated patients have a significant risk of delirium if they are constipated (Smonig et al., 2016). Constipation leads to prolonged stay in the ICU (van der Spoel et al., 2007, van der Spoel et al., 2006). Bowel movements after 6 days have furthermore a negative impact on the critically ill patients' outcome (Prat et al., 2016). Two randomized, controlled trials (RCTs) have shown that severity of morbidity and time before first bowel movement had a significant association with mortality in the patients admitted in ICU (de Azevedo et al., 2015, van der Spoel et al., 2007).

The aetiology of constipation in critically ill patients is multifactorial. Maintenance of normal fluid and electrolyte balance is important in such patients (Btaiche et al., 2010). Adequate hydration and encouraging mobilization when possible are also essential (Vincent & Preiser 2015). Early enteral nutrition is significantly effective for occurrence of bowel movement and is recommended for critically ill patients (Nassar et al., 2009). However, limited research has been performed on non-pharmacological prevention strategies and treatment of constipation in the critically ill patients.

### **The authors' pre-understanding**

As CCNs in a general ICU in a Norwegian university hospital, we have experienced that constipation is an under-estimated problem and that prevention of constipation receives low priority, is not discussed inter-professionally in a daily manner and there is no protocol for its management. We observed a high rate of constipated patients in the local ICU and conducted baseline measures that indicated a constipation rate of 66–80% after application of the following criterion: 3 days with no bowel movement (Reintam et al., 2012). We experienced that prevention and treatment were often assigned randomly and without a plan. Documentation of the patients' bowel function was at a minimum, with limited description of volume, consistency, and frequency. Prevention and treatment of constipation were not included in the inter-professional daily plan. In addition, constipation is hardly mentioned in the local CCN post-graduate/master educational curriculum. Pilot telephone interviews with other Norwegian and Danish ICUs revealed uncertainty in prevention and treatment of constipation.

### **Aim**

The aim of this scoping review is therefore to obtain an overview of existing evidence on constipation definitions, prevention, and treatment of constipation in critically ill patients. The review was guided by the following review questions:

1. How is constipation in the critically ill patients defined?
2. What are the prevention and treatment recommendations regarding constipation in critically ill patients?

Based on this review and consensus from an inter-professional expert group, we also wanted to provide recommendations for prevention and treatment of constipation in critically ill patients in ICUs. The recommendations were made for physicians and nurses because constipation prevention and treatment are a shared responsibility.

## **METHODS**

A scoping review design was used due to the absence of published reviews and on the topic of prevention and treatment of constipation in critically ill ICU patients.

### **Search methods**

The review was approved by the head of the Research Department of the hospital where it was conducted. Together with an expert librarian, we performed a systematic literature search structured after the S-pyramid (Dicenso et al., 2009) to provide the best scientific recommendations. The search was limited to studies in Nordic and English languages. The first systematic literature search was conducted in November 2016–February 2017. The final updated systematic literature search was conducted in May 2023. All studies including mechanically ventilated and non-mechanically ventilated critically ill adults over 18 years old admitted in medical or surgical ICUs were included in this scoping review.

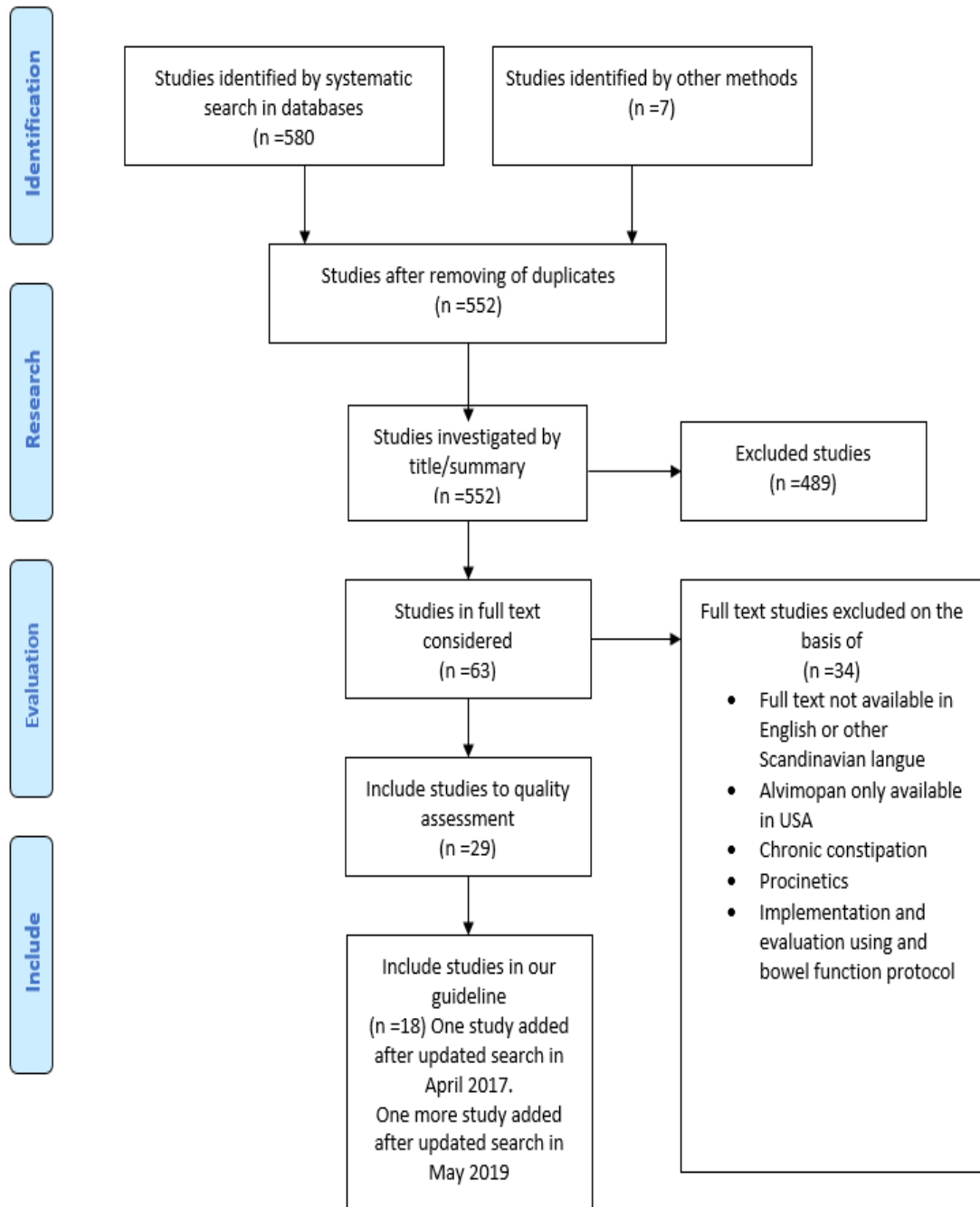
The search was conducted together with an expert librarian in the following databases: UpToDate, BMJ Best Practice, National Guideline Clearinghouse, NICE guidance, Norwegian, Swedish, and Danish networks for Procedures, Joanna Briggs Institute, MEDLINE, Embase, CINAHL, The Cochrane Library, Epistemonikos, Clinical Evidence, PEDro (Physiotherapy Evidence Database), OTSeeker Clinical Queries in PubMed. Search terms used was “obstipation”, “constipation”, “colonic inertia”, “dyschezia”, “intensiv\*”, “critical care”, “intensive care”, “intensive care units/ICU”, “intensive care nursing”, “critical care nursing” and “practice guideline”

### **Search outcome**

A total of 552 studies were investigated by the title and article summary. Of these, 489 studies were excluded due to the lack of relevance for this review. Most of the studies identified did not investigate constipation in the critically ill patients admitted in ICU, but other patient categories. There were 63 studies consider based on full text, and 29 were included for quality assessment which will be thoroughly described in the next section. Some of the studies were excluded because they scoped a bowel movement protocol being implemented, but with no scientific methodology or description of the measures recommended. After the first

systematic search in 2017 18 studies were included. Two updated systematically searches (2019 and 2023) revealed five more studies. 23 studies were included (figure 1 PRISMA flow chart)

**Figure 1.**  
PRISMA Flowchart for Literature Review



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009;6(7):e1000097. doi:10.1371/journal.pmed1000097

### Quality appraisal

To assess quality of the included studies, the Appraisal of Guidelines for Research & Evaluation (AGREE II) was adopted. In development of evidence-based guidelines the tool provides a rigorous methodology (Brouwers et al., 2010). The first and second authors performed the quality appraisal using the Critical Appraisal Skills Programme (CASP) checklist (Tables 1, 2 and 3) (CASP, 2023). A local interdisciplinary group consisting of an experienced intensivist, gastric surgeon, advanced practitioner, nutritionist and two CCNs (the first and second authors) were invited to review the quality of the research and discuss the research findings as experts. There were no economical or personal interests involved in the interdisciplinary group. This local expert group discussed the relevance of including research on constipation in cancer patients. Consensus was established that the situation of critically ill patients is unique because they are often in a comatose condition, which is affected by several physiological factors. Therefore, their situation is not comparable with that of other patient groups.

The quality-appraisal process was initially performed by the first and second authors individually and then together using the CASP checklists (CASP, 2023). Critical appraisal of the included studies' strengths of recommendations was difficult to conclude on due to varying aims, methods, measures, analyses, and conflicting recommendations.

**Table 1.**

*Critical Appraisal Skills Programme Scores for Randomized Clinical Trials*

| RCT | Authors                                 | Q 1 | Q 2 | Q 3 | Q 4 | Q 5 | Q 6 | Q 7 | Q 8 | Q 9 | Q 10 | Q 11 | Total |
|-----|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|-------|
| 1   | Azevedo et al 2015, England             | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2    | 2    | 22    |
| 2   | Masri et al, 2010, United Arab Emirates | 2   | 2   | 2   | 2   | 2   | 0   | 2   | 2   | 2   | 1    | 1    | 18    |
| 3   | Van der Spoel et al, 2007, Netherlands  | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2    | 2    | 18    |
| 4   | Dehghan et al, 2018, Iran               | 2   | 2   | 2   | 2   | 1   | 2   | 2   | 2   | 2   | 2    | 2    | 21    |
| 5   | Patel et al, 2020, USA                  | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2    | 2    | 22    |

**Table 2.**

*Critical Appraisal Skills Programme Scores for Case Control Studies*

| Case Control | Authors                        | Q 1 | Q 2 | Q 3 | Q 4 | Q 5 | Q 6a | Q 6b | Q 7 | Q 8 | Q 9 | Q 10 | Q 11 | Total |
|--------------|--------------------------------|-----|-----|-----|-----|-----|------|------|-----|-----|-----|------|------|-------|
| 1            | Guardiola et al, 2016, Spain   | 2   | 2   | 2   | 2   | 2   | 2    | 2    | 2   | 2   | 2   | 2    | 2    | 24    |
| 2            | Knowles et al, 2014, Australia | 2   | 2   | 2   | 2   | 2   | 2    | 2    | 2   | 1   | 2   | 2    | 2    | 23    |
| 3            | McKenna et al, 2001, Australia | 2   | 2   | 2   | 2   | 2   | 2    | 2    | 2   | 2   | 2   | 2    | 2    | 24    |
| 4            | McPeake et al, 2011, Scotland  | 2   | 2   | 2   | 2   | 2   | 2    | 2    | 2   | 2   | 2   | 2    | 2    | 24    |
| 5            | Patanwala et al, 2006, USA     | 2   | 2   | 2   | 2   | 2   | 1    | 2    | 2   | 2   | 2   | 2    | 2    | 23    |
| 6            | Sawh et al, 2012, England      | 2   | 2   | 2   | 2   | 2   | 2    | 2    | 2   | 2   | 1   | 2    | 2    | 23    |

**Table 3.**

*Critical Appraisal Skills Programme Scores for Cohort Studies*

| Co-hort | Authors                       | Q 1 | Q 2 | Q 3 | Q 4 | Q 5a | Q 5b | Q 6a | Q 6b | Q 7 | Q 8 | Q 9 | Q 10 | Q 11 | Q 12 | Total |
|---------|-------------------------------|-----|-----|-----|-----|------|------|------|------|-----|-----|-----|------|------|------|-------|
| 1       | Arpino et al, 2009, USA       | 2   | 2   | 1   | 1   | 1    | 2    | 2    | 2    | 1   | 1   | 1   | 2    | 2    | 2    | 22    |
| 2       | Bishop et al, 2010, Australia | 2   | 2   | 1   | 2   | 2    | 2    | 2    | 2    | 2   | 2   | 2   | 2    | 2    | 2    | 27    |
| 3       | Dorman et al, 2004, England   | 2   | 1   | 1   | 2   | 0    | 0    | 2    | 2    | 2   | 2   | 2   | 2    | 2    | 2    | 22    |
| 4       | Gibson et al, 2014, USA       | 2   | 1   | 1   | 2   | 1    | 2    | 2    | 2    | 2   | 2   | 2   | 2    | 2    | 2    | 25    |
| 5       | Merchan et al, 2017, USA      | 2   | 2   | 1   | 2   | 2    | 2    | 2    | 2    | 2   | 1   | 1   | 2    | 2    | 2    | 25    |
| 6       | Ring et al, 2011, Australia   | 2   | 2   | 1   | 2   | 0    | 0    | 2    | 2    | 2   | 2   | 2   | 2    | 2    | 2    | 23    |
| 7       | Ritchie et al, 2008, England  | 2   | 2   | 1   | 2   | 2    | 2    | 2    | 2    | 2   | 1   | 1   | 2    | 2    | 2    | 25    |
| 8       | Habeeb, et al, 2022, USA      | 2   | 2   | 1   | 2   | 1    | 1    | 2    | 2    | 2   | 1   | 2   | 2    | 2    | 2    | 24    |

Reference: Critical Appraisal Skills Programme (2018). CASP Checklist. Available at: [https://casp-uk.net/wp-content/uploads/2018/01/CASP-Systematic-Review-Checklist\\_2018.pdf](https://casp-uk.net/wp-content/uploads/2018/01/CASP-Systematic-Review-Checklist_2018.pdf) Accessed: 22/6-2019.

Disagreements were discussed in the inter-professional expert group. Two included reviews (Btaiche et al., 2010; Lat et al., 2010) were not critically appraised due to limited description of methodology; however, they were discussed as expert statements by the interdisciplinary expert group.

#### **Data abstraction and synthesis**

Data were abstracted, visualised in a matrix after the process of quality appraisal with CASP checklists. The data were compiled in a summary of findings, which is the fundament for the evidence presented in the results. The results were then put in a schematic protocol presented as a flow chart model. After completion, the synthesis with recommendations were sent out to an official hearing from key stakeholders, both internal and external. After the feedback was included, the synthesis was finished and ready for implementation.

## **RESULTS**

The results are presented to align with the research questions with individual articles summarized in the summary table (Appendix 1) and are reflected in the Protocol for the Prevention and Treatment of Constipation in the Critically Ill Based on a this Scoping Literature Review (Figure 2).

#### **Research question 1:** How is constipation defined in critically ill patients?

The definition of constipation found in most included studies was no bowel movement within 3 ICU days (72 hours) (Azevedo et al., 2009, Bishop et al., 2010, Dorman et al., 2004, Nassar et al., 2009, Sawh et al., 2012, van der Spoel et al., 2007). The European Society of Intensive Care Medicine (Blaser, 2012) defines constipation in the ICU as 3 days without bowel movement.

The interdisciplinary expert group's conclusion was that the definition of constipation is no bowel movement within 3 ICU days.

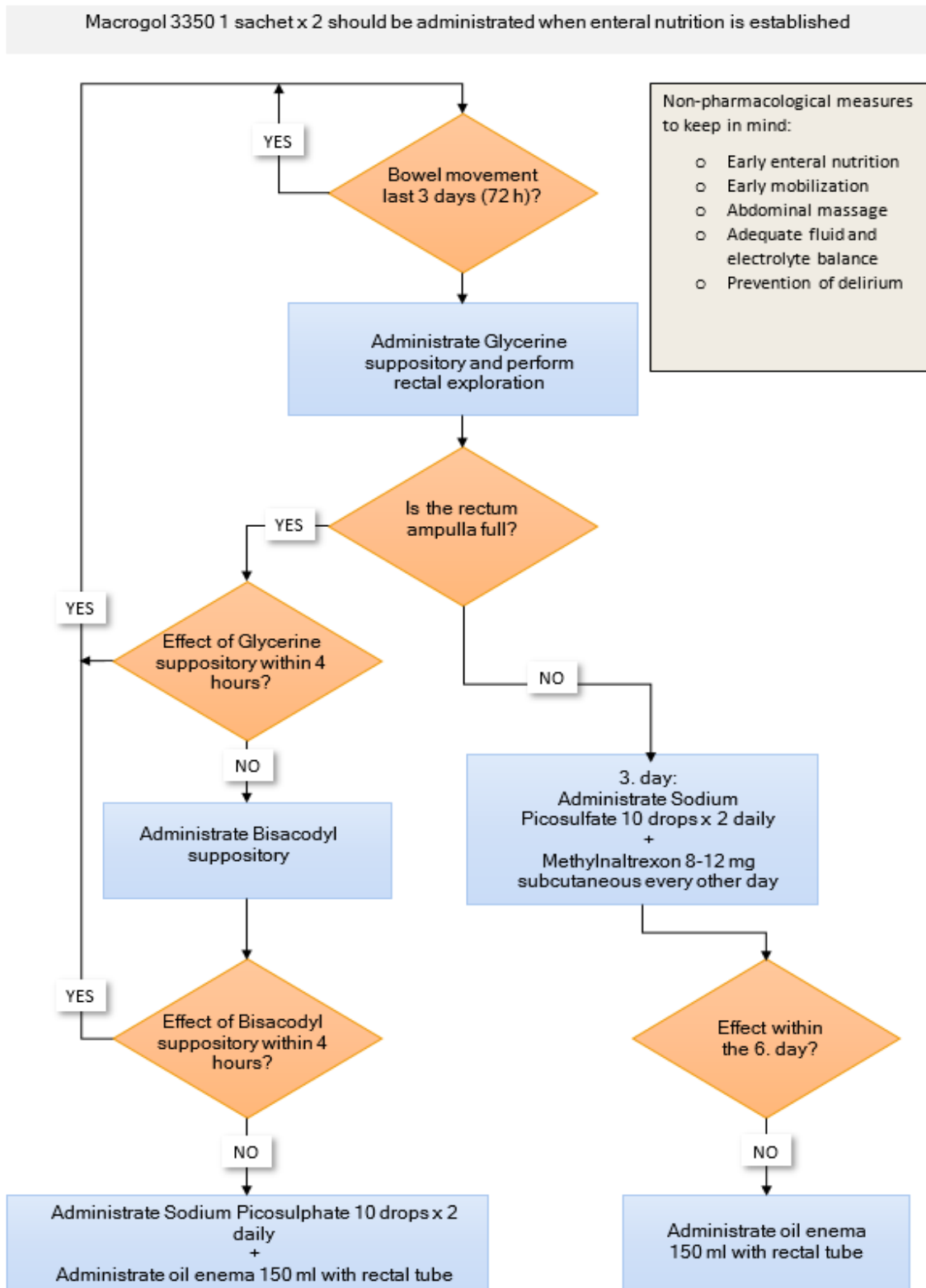
#### **Research question 2:** What are the prevention and treatment recommendations regarding constipation in critically ill patients?

##### ***Non-pharmacological prevention and treatment***

An Australian cohort study with 16 critically ill patients conducted by Ring (2011) included prune juice as a prophylactic intervention in the bowel management protocol, without effect. Dehghan et al. (2018) found in a RCT performed in Iran that abdominal massage had an effect on constipation in the critically ill patients. By providing an abdominal massage for 15 minutes twice a day for 3 days, time to first defecation was significantly reduced. The proportion of constipated patients in the intervention group was 37% versus 68% in the control group (Dehghan et al., 2018).



*Protocol for the Prevention and Treatment of Constipation in the Critically Ill Based on a Scoping Review of the Literature*



## ***Pharmacological prevention and treatment***

### **Laxatives**

In a RCT from the Netherlands van der Spoel et al. (2007), compared the effect of lactulose with macrogol (PEG4000) on 308 critically ill patients. The results showed that both lactulose and macrogol had the same effect on bowel movement versus the placebo. The study also revealed that macrogol had a better effect on opioid-induced constipation than lactulose (van der Spoel et al., 2007). Masri et al. (2010) studied the effect of lactulose on bowel movement in a RCT of 100 critically ill patients from the United Arab Emirates. Lactulose was administered every 12 hours for the first 72 hours in the ICU. They found that 18% patients in the lactulose group versus 4% in the control group had bowel movements within 72 hours. An Australian pilot cohort study on 44 ICU patients, showed significant association with lactulose administration and bowel movement and stool volume (Bishop et al., 2010). Guardiola et al. (2016) found in a Spanish case control study that macrogol administered to 197 critically ill patients had a better effect when administered prophylactic the first day of admission versus administered as a treatment. The same study also found less administration of other laxatives to patients who were administered macrogol (Guardiola et al., 2016). Furthermore, an American review conducted by Lat et al. (2010) describes the use of osmotic and stimulant laxatives alone or in combination with a stool softener with a positive effect on opioid-induced constipation in patients receiving ICU treatment (Lat et al., 2010).

### **Opioid receptor antagonists**

In five of the included studies, medication-induced constipation in ICUs was explored. The safety of enterally administered naloxone as prophylactic or treatment of opioid-induced constipation in critically ill patient was assessed by Arpino and Thompson (2009). They found no association with alteration in sedation score, dose administered of fentanyl and midazolam or in vital measurements, but the number of bowel movements within 24 hours increased after naloxone administration (Arpino and Thompson, 2009). A small pilot study, however, does not support this finding (Duprey et al., 2022)

A study conducted by Sawh et al. (2012) sought to assess the efficiency of methylnaltrexone compared with other conventional laxatives. Methylnaltrexone was very effective to produce defecation, and furthermore the drug was well tolerated and did not demonstrate any change or reversed effect of fentanyl (Sawh et al., 2012). However, this was not supported by Patel (2020), who found no significant difference between methylnaltrexone and regular laxatives (Patel et al., 2020). Methylnaltrexone can be administered for a short duration to critically ill patients and leads to reduced time to bowel movement (Lat et al., 2010).

Naloxegol and methylnaltrexone were administered to 100 critically ill patients in a medical ICU ward where 48 patients received methylnaltrexone and 52 patients received naloxegol. Bowel movement occurred within 30 hours in the naloxegol group and 24 hours in the methylnaltrexone group (Merchan et al., 2017). However, Habeeb (2022) studied effect of enteral naloxone versus methylnaltrexone on time to first bowel movement in ICU patients, and found that naloxone was a significant predictor of bowel movement within 48 hours, with 18 hours to first bowel movement in the naloxone group versus 41 hours in the methylnaltrexone group (Habeeb et al., 2022).

### Enemas

The effect of enemas on constipation were not discussed in any of the included studies. However, bowel management protocols from the included studies and Nordic hospitals recommended the use of enemas in critically ill ICU patients. We found that none of the Nordic protocols were evidence based.

### *Synthesis of the evidence*

Based on these findings and consensus from the inter-professional expert group, we performed a synthesis of the evidence.

## **DISCUSSION**

The aim of this systematic review was to obtain an overview of existing evidence on definitions, prevention and treatment of constipation in critically ill patients. We found conflicting or unclear definitions of constipation even among researchers and members of the inter-professional expert group established for this study. We also found a variety of prevention and treatment suggestions/strategies underlining the importance of an evidence-based bowel management protocol to promote a shared understanding based on evidence on this important matter. To succeed with prevention and treatment of constipation in critically ill patients, shared interdisciplinary understanding of what constipation is, how important prevention and treatment are, as well as systematic evidence-based recommendations on how to deal with it, are crucial.

Implementation of an evidence-based definition of constipation and an inter-professional bowel management plan based on evidence-based recommendations, may change the way nurses and physicians prioritize prevention and treatment of constipation in their daily work (Dorman et al., 2004, McKenna et al., 2001, Hansen & Severinsson, 2009). As CCNs, we must be aware of our responsibilities concerning prevention, observation, documentation, and reporting of constipation in the ICUs. Some of the included studies (Dorman et al., 2004, McKenna et al., 2001) based their findings on documentation from patients' journals and found that this kind of documentation was often incomplete or missing and represented a possible confounder. Systematic and correct documentation is crucial to patient safety

(McKenna et al., 2001, Dorman et al., 2004).

The establishment of an interprofessional understanding and plan for bowel management with guidelines for prevention and management of constipation in the ICU, will hopefully provide a more structured approach to bowel function, as well as promotion of awareness of constipation as an important issue for the critically ill patient (Lat et al., 2010; Perez-Sanchez et al., 2017). Dorman et al. (2004) concluded that a new guideline and algorithm for bowel care in the ICU involving the inter-professional team in daily discussions on ward rounds was successful. Documentation rate and quality increased when bowel management protocols were implemented and followed (McKenna et al., 2001, Dorman et al., 2004).

Evidence-based recommendations also brings along new knowledge of the severity of constipation in critically ill patients that CCNs and physicians might lack. Knowledge about the importance of rectum exploration every third day might reduce the barrier to performing the technique among nurses (McPeake et al., 2011) and thereby reduce the constipation and mortality rate in critically ill patients (de Azevedo et al., 2015, van der Spoel et al., 2007). Making constipation prevention and treatment a nurse-sensitive quality indicator might influence the status of bowel management. Nurses' preventative observational function is crucial. Most complications due to reduced gastrointestinal motility are not treated before they lead to symptoms such as constipation (Lat et al., 2010). Knowles et al. (2014) showed that initiating clinicians decision-making process in deciding to follow protocols is difficult to achieve. Despite thorough implementation nurses and physicians did not use the bowel management protocols developed. Factors such as knowledge, attitudes and beliefs can assist in targeting implementation strategies to positively affect clinician behaviour change (Knowles et al., 2015). Implementation strategies is there for crucial. Ritchie et al. (2008) measured the effect of a standardized protocol in the ICU, and after implementation the rate of constipation went down from 83% to 40%.

There are spread evidence for prophylactic use and effect of laxatives in the ICU. Hay et al. (2019) did not find support for prophylactic effect of laxatives to the critically ill patients. Osmotic laxatives are recommended for successful bowel movement (Lat et al., 2010). Early administration of macrogol as a prophylactic to critically ill patients had a better effect than its administration as a treatment for constipation; critically ill patients receiving macrogol were less likely to need other types of laxatives (Guardiola et al., 2016). Routine use of both stimulants and osmotic agents should be considered for all critically ill patients (Patanwala et al., 2006).

Based on experience, the expert group recommended macrogol due to reduced side effects compared to lactulose. Van der Spoel et al. (2007) found that lactulose and macrogol had the same effect on bowel movement as placebo and that

macrogol had a better effect on opioid-induced constipation than lactulose.

Research indicates that there is a lack of priority among nursing staff regarding bowel care (McPeake et al., 2011, Dorman et al., 2004) because constipation is a stigmatic subject that leads to a negative impact on nurses, such as feeling embarrassed in performing rectal exploration (McPeake et al., 2011). Henderson (1997) described the unique function of the nurse in assisting the individual in activities contributing to health or its recovery, or a peaceful death, and that she or he would perform them unaided if they had the necessary strength, knowledge or will.

In a high-tech medical environment, it is important to consider basic nursing as essential to positive patient outcomes. CCNs play an important role in non-pharmacological constipation prevention through abdominal massage (Dehghan et al., 2018), mobilization of the critically ill patients (Vincent and Preiser, 2015), administration of fluid and nutrition (Btaiche et al., 2010), pain prevention and treatment prevention of intensive delirium (Smonig et al., 2016). There is a need to provide high priority attention to these areas of care. To improve the clinical outcome it is essential that evidence-based nursing care strategies are implemented to reduce the errors that are avoidable (Vollman, 2013). Evidence-based nursing practice is considered useful amongst nurses in their clinical work, but they lack the knowledge on implementation in practice. Therefore it is of high importance to increase the skills and knowledge and encourage nurses in activism and professional values, and this connected with the nurses competencies can lead to nursing development (Skela-Savič et al., 2017). There is a need for a systematic approach for research that evaluates basic nursing care interventions (prevention of constipation) as well as effective relationships within the wider health-care context (Kitson et al., 2014).

### ***Methodological limitations***

The evidence-based practice methodology guided us through the process together with the AGREE II instrument (Brouwers et al., 2010). The quality of the included studies was at the lowest levels of the S-pyramid. This raises a question about the quality of the evidence informing the recommendations. The available literature regarding constipation in critically ill patients is limited and 13 of the included studies were single studies. Therefore, the interdisciplinary expert group's opinion was important. Besides being an interdisciplinary expert group designed for this study, the group represented an inter-professional platform in the ICU for inter-professional discussions. The participants articulated their experiences and skills regarding constipation prevention and treatment to improve patient treatment and care, reducing professional boundaries. Knowledge integration like this, involves discipline-specific knowledge exchange and creation of common language and knowledge for treatment and care of better quality (Godemann, 2008).

Nurses tend to rely on social interaction and experiences instead of evidence-based resources as sources of information for their clinical decision making, when they are faced with uncertainty (McCaughan et al., 2005, Estabrooks et al., 2005, Marshall et al., 2011, Thompson et al., 2008). However, in the field of knowledge utilization within nursing, there has been a significant growth (Scott et al., 2010).

We believe that a collaborative team approach will provide higher priority for prevention and treatment of constipation because both CCNs and physicians are responsible for the prevention and treatment of constipation in critically ill patients. This shared responsibility needs a shared understanding of how constipation is defined and its consequences. Inter-professional discussions on a daily basis about prevention, documentation and treatment are crucial, and evidence-based knowledge and guidelines are important guides for inter-professional discussions and plans (Hansen & Severinsson, 2009).

The discussion and consensus statements in the interdisciplinary expert group strengthen the validity and reliability of the recommendations and are themselves a resource of evidence.

## CONCLUSION

Constipation in critically ill ICU patients can influence the rate of patient mortality, morbidity, and discomfort. We found that most included studies used the evidence-based definition of constipation in ICU as no bowel movement within 3 days. We believe it is of vital importance that the interprofessional ICU team agrees to, as well as document and act in accordance with the same definition and treatment plan.

We found few studies on non-pharmacological constipation prevention and treatment. Further research is needed. A structured inter-professional approach towards evidence-based prevention and treatment of constipation can influence the rate of mortality, morbidity and discomfort.

A team approach to severity, documentation and planning for prevention and treatment of constipation is crucial and may provide higher priority to constipation among CCNs and physicians. CCNs must be aware of their responsibility to prevent, observe, document and report signs of constipation to the inter-professional team. Constipation can be prevented and treated effectively.

It is important that CCNs have academic competence to understand research and undertake their own research and influence the interprofessional team. Evaluation and constantly improvement of treatment and care are essential. Prevention and treatment of constipation through nursing measures may increase the survival rate. Further research is needed on this topic.

Overall, further research on prevention and treatment of constipation in the critically ill patients is required. Few studies on non-pharmacological prevention and treatment of constipation and the involvement of CCNs were found. There is



also a need for more research on further development of inter-professional bowel management protocols, evaluation of effect and how to succeed with implementation in the professional team. An interdisciplinary team with international expert on this approach would strengthen the evidence even further.

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**Appendix 1.**

*Summary Table for Articles Targeting the Prevention and Treatment of Constipation in the Critically Ill*

| Methods           |              |   |  |   | Results  |  |   |
|-------------------|--------------|---|--|---|--|--|---|
| Author /Year      | Study design | Sample size   | Intervention   | Comments/ Risk of bias  | Findings   | Conclusion   | Relevance/ transferability  |
| Arpino, 2009. USA | Cohort study | n= 24<br>Critical care patients. Cohort of patients who received at least one dosage of naloxone. | Enteral naloxone administrated in various dose from 0.9-3.6 mg | Small sample. Poor documentation of the range of bowel movements. No control group. The intervention group was compared to baseline measurements. No use of confidence intervals. | They measured how naloxone affected RASS, vital parameters, and the amounts of opioids and sedatives administrated. They measured total number of bowel movements before and after naloxone. | Naloxone enterally was not associated with change of RASS level, vital parameters, nor fentanyl, midazolam or propofol dosages. More patients had bowel movement in the intervention group compared to baseline, (26% vs 11%). | Providers may consider naloxone enterally for constipated critical care patients. |

|                                    |                           |  |  |   |  |  |  |
|------------------------------------|---------------------------|--|--|---|--|--|--|
| <p>Azevedo, 2015.<br/>England</p>  | <p>RCT</p>                | <p>n= 88<br/>Adult mechanically ventilated patients, both surgical and medical.<br/>44= intervention group<br/>44= control group</p> | <p>Investigate if daily defecation with lactulose had an impact on SOFA scores (Sequential Organ Failure Assessment Scores).</p> | <p>The two groups were comparable.<br/>Results included p-values and confidence interval.</p> | <p>The patients in the intervention group had more frequent bowel movements than the control group.</p>                                  | <p>Daily defecation led to significant reduction in SOFA scores.<br/>The results of this study pointed in direction (p-value 0,08) of lower morbidity with daily defecation.</p> | <p>Daily bowel movement is associated with improved SOFA scores.<br/>However, caution is required as the intervention group also had longer lengths of stay and more frequent cases of pneumonia than the control group.</p> |
| <p>Bishop, 2010.<br/>Australia</p> | <p>Cohort pilot study</p> | <p>n= 44<br/>Critical care patients were observed for 274 days on mechanical ventilation.</p>  | <p>Investigate bowel function and patterns of defecation in critically ill mechanical ventilated patients.</p>                   | <p>Patients received lactulose until first defecation.</p>                                    | <p>Constipation rates were common.<br/>Laxatives were effective.<br/>Opioids were associated with lower frequency of bowel movement.</p> | <p>Lactulose and ondansetron were significant in effect of defecation.<br/>Lactulose had a significant relationship with stool volume.</p>                                       | <p>This study revealed that there is a high incidence of constipation in the ICU.<br/>Lactulose is effective in the prevention or treatment constipation.</p>  |



|                    |        |   |  |  |  |   |   |
|--------------------|--------|---|--|--|--|---|---|
| Btaiche, 2010      | Review | Search history is described and documented.                             | Investigate critical illness, gastrointestinal complications and medication administrated while enteral nutrition was given to the critical care patients. | This paper presents existing evidence for naloxone, methyl naltrexone and alvimopan to restore bowel function. | Review over how medication and enteral nutrition effects the gastrointestinal tract.                             | Early and adequate enteral nutrition are important for critical care patients. Constipation can be prevented through different strategies, such as adequate fluid balance, opioid antagonists, and laxatives. | A higher volume of aspirate (500 ml) leads to a higher frequency of patients being fed enterally. In the national guideline for nutrition, the aspirate level is set to 300 ml. |
| Dehgan, 2018, Iran | RCT    | N=70. 35 patients in the intervention group and 35 in the control group | In the intervention group the patients received abdominal massage for 15 minutes twice a day, for 3 days. The control group received basic nursing,        | Small sample size  | There was a lower number of constipated patients in the intervention group (37%) versus the control group (68%). | Abdominal massage decreases the time to the first bowel movement.   | Non-pharmacological measures to prevent constipation in the critically ill patients are effective.  |

|                       |              |  |  |   |  |  |  |
|-----------------------|--------------|--|--|---|--|--|--|
| Dorman, 2004, England | Cohort study | n= 9 pre-intervention<br>n= 10 post-intervention | Implementa-tion of a bowel movement protocol.  | Older study with a small sample. Confidence intervals are not presented.  | This study focuses on bowel and bowel function. The health care professional had improved documentation after protocol implementation. They also started laxatives earlier than before the intervention. Laxatives were started coordinately with enteral nutrition. | The implementation of the bowel movement protocol led to focus on bowel care as a daily routine. | The audit identified constipation as a problem. Their bowel movement protocol will be relevant for this study. |
| Gibson, 2014, USA     | Cohort study | n= 16 Adult male patients in MICU                | Measure safety and effectiveness of enteral naloxone for opioid-induced constipation in a medical ICU. | Study period was 5 years – and only 16 male patients. No control for historical changes in practice. Individual doses of naloxone were given. 75% received other additional laxatives. No documentation of level of sedation. | The average daily dose of naloxone was 4.7 mg. 15 of 16 had bowel movement within 24 hours after administration.   | Naloxone administration is associated with bowel movements.                                      | Administering enterally naloxone can prevent and help the patients to defecate.                                |

|                        |                    |   |   |  |   |   |  |
|------------------------|--------------------|---|---|--|---|---|--|
| Guardiola, 2016, Spain | Case control study | N=197<br>Adult critical care patients<br>63= observational phase<br>64= treatment phase<br>70= prophylactic phase | Measure the prevalence of lower gastrointestinal tract paralysis (GI-paralysis). Compare laxative treatments and prophylactic measures, for stimulating defecation. | In the observational phase, the occurrence of GI-paralysis was documented. In the treatment-phase they were given treatment starting on day 4. In the prophylactic-phase they got prophylactic treatment from day 1. The patients got administrated PEG 4000 (polyethylene glycol [macrogol]) every 6 hours until defecation occurred. If no defecation within 5 days they got administrated an enema (1 liter of paraffin, glycerin, and sodium phosphate) and/or neostigmine in 24 hours. If still no defecation, the patients received high-dose PEG over 12 hours by feeding tube. | 90% in the observational group had GI paralysis. In the treatment group 25% had GI -paralysis, and in the prophylactic group 8,6% had GI-paralysis. There was a shorter length of stay and shorter length on ventilator for the prophylactic group. | PEG4000 gives best outcome for critically ill patients if it is administrated on day 1. | Presents a new type of definition of constipation. Beside 3 days without bowel movements, dilatation of the colon and presence and frequency of bowel sounds should be measured. |
|------------------------|--------------------|---|---|--|---|---|--|

|                          |                    |   |   |  |   |   |  |
|--------------------------|--------------------|---|---|--|---|---|--|
| Hay, 2019, Australia     | Systematic review  | Limited to critical care  | To review if prophylactic laxative bowel regimen prevent constipation           | Studies included in the review had low evidence level, and few studies to compare.   | Prophylactic laxative bowel regimen increases the risk of diarrhea and did not reduce the risk of constipation.   | Low data about prophylactic laxative bowel regimen and do not support their use   | None.  |
| Knowles, 2014, Australia | Case control study | N= 101 preimplementation group<br>N= 107 postimplementation group | Measure if a bowel movement protocol had effect                                 | Evidence based protocols were developed for preventing constipation, rectal exploration and treatment of constipation and diarrhea | No significant findings in cases of constipation before and after the intervention  | Nurses and doctors did not use the protocols, regardless of thorough implementation in the ward.  | Usefulness of the protocols developed. Barriers in implementation of change. |
| Lat, 2010, USA           | Review             | Search strategy was not documented.                               | Medicine induced acute hepatitis and gastrointestinal complications in the ICU. | Relevant because they present a section on constipation in critically ill patients   | Stimulant agents and osmotic agents have effect on constipation in critically ill patients. Methylnaltrexone abbreviated time to first bowel movement for patients with opioid induced constipation | Regarding to this review article stimulant and osmotic agents have a positive impact on constipation. Metylnaltrexone and alvimopan decreased the time to the first bowel movement. | Presents existing evidence for laxatives and opioid antagonists              |

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|--|---------------------------|---|---|---|--|--|---|
| <p>Masri, 2010, United Arab Emirates</p> | <p>RCT</p>                | <p>N=100<br/>Control group= 50<br/>Intervention group= 50<br/>Adult mechanical ventilated patients, mostly males</p>            | <p>Early versus late defecation in context with patient outcome. Evaluate use of laxative in prophylaxis of constipation in critical ill patients.</p>                                    | <p>Intervention group got administrated lactulose 20 ml x 2 the first three days (started within 4-6 hours after admission to the ICU). Control group received no laxatives the first three days. After three days treatment was cared for individually by doctor's order. They measured severity of constipation after 5 days.</p> | <p>In the intervention group 18% had bowel movement within 76 hours. In the control group 4% had bowel movement within 76 hours<br/>Early bowel movement within 5 days gave shorter time on ventilator versus late bowel movement.</p> | <p>Lactulose can prevent constipation</p>  | <p>Gives evidence for use of lactulose to prevent constipation in the ICU.</p>  |
| <p>McKenna, 2001, Australia</p>          | <p>Case control study</p> | <p>N= 120<br/>60= pre intervention group<br/>60= post intervention group.<br/>Critically ill patients, 75 men and 45 women.</p> | <p>Nurse led bowel movement protocol were developed based on a review of literature. They measured frequency of constipation and diarrhea before and after implementing the protocol.</p> | <p>Constipation was defined as 3 days with no bowel movement. First measure after 3 days by rectal exploration.</p>   | <p>Implementation of bowel movement protocol led to better documentation and evaluation of bowel function by the nurses.</p>   | <p>Bowel movement protocol can be a helpful tool for critical care nurses and can increase and improve both documentation and evaluation of bowel movement in the ICU.</p> | <p>The results are based on the documentation of bowel activity. They are dependent on the documentation being done sufficiently. Uncertainty if the protocol had the desired effect.</p> |

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|-------------------------|--|---|--|--|--|--|---|
| McPeake, 2011, Scotland | Case control study                             | Total N= 55.<br>26= intervention group<br>27= control group | Measure effect of implementation of a bowel movement protocol.   | No measure of continued or sustained use at 6-month.                                     | After implementation of the protocol the occurrence of constipation was reduced to 37% from 58%.<br>Diarrhea was reduced by 15% (from 20% to 5%). Days of documentation of bowel movement rose to 100%.          | Occurrence of constipation and diarrhea can improve by education of health care professionals and with use of bowel movement protocol. | This study gives evidence for use of protocol in preventing and treatment of constipation |
| Merchan, 2017, USA      | Cohort. Pilot study with retrospective design. | Sample N=100.<br>Methylnaltrexone: 48<br>Naloxegol: 52      | Measure how long before first bowel movement after 72 hours with fentanyl infusion, followed by the number of bowel movements within 24 hours. | Patients were given from 0 to 4 different laxatives additionally to the survey medicine. | Time before first bowel movement were 30 hours for the naloxegol group vs 24 hours for the methylnaltrexone group.<br>None of the groups had a change in sedation niveau, dosage of opioids or vital parameters. | Methylnaltrexone and naloxegol was both effective for the bowel movement to occurrence.  | Strengthens the use of opioid antagonists for bowel movement in ICU patients.             |

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|------------------------|--------------------|---|--|--|---|---|--|
| Patanwala, 2006, USA   | Case control study | N=50<br>25= group who had bowel movement within 96 hours<br>25= group who did not have bowel movement within 96 hours | Compare effect of regular laxatives in a medical ICU       | Few participants. Some received more laxatives than others. Dependent on sufficient documentation of bowel function when results audited by audit. | Stimulant (senna) was associated with bowel movement. Stool softeners can have impaired effect on constipation because of reduced gastrointestinal motility. Bisacodyl (toilax) had a trend towards being significant in effect. Opioids increases risk of constipation. Use of vasopressin gives increased number of constipated patients. Critically ill patients have high incidence of constipation. Main side effect from laxatives includes abdominal cramps. | Routine use of stimulant and osmotic agents should be considered for all critical care patients.      | Routine use of stimulant and osmotic agents should be considered for all critical care patients. |
| Ritchie, 2008, England | Cohort study       | N= 48<br>Critical care patients   | Audit the effect of bowel movement protocol over 12 months | Follow up study after Mostafa revealed that the constipation incidence was 83%   | The rate of constipation was 40% after implementing the bowel movement protocol   | Constipation was still a problem, but less patients suffered from it after implementing the protocol. | Protocol use decreased the impact of constipation.   |

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| <p>Ring, 2011, Australia</p> | <p>Cohort study</p> | <p>N= 16<br/>7= Baseline<br/>9= Post implementation</p> | <p>Investigate if a bowel movement protocol could reduce number of days before first bowel movement in the ICU. All patients got prune juice. At day 3 macrogol was administrated. The patients received enemas if rectum ampulla was full when rectum exploration was performed on day 7.</p> | <p>Search of literature is not described. The bowel movement protocol is based on 5 articles and experiences from a multidisciplinary group</p> | <p>Time before first bowel movement went down from 9 to 5,3 days</p> | <p>Use of the protocol can help shorten the time to first bowel movement for critical care patients.</p> | <p>This study shows how important focus on bowel function is.</p> |
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| <p>Sawh, 2012, England</p> | <p>Case control study</p> | <p>N= 15<br/>Critical care patients.<br/>All treated with sodium docusate and senna the first 72 hours.<br/>7= Methylnaltrexone bromide<br/>8= Sodium picosulfate glycerin suppository</p> | <p>Investigate the effect of methylnaltrexone versus conventional laxatives on opioid induced constipation on the critically ill patients</p> | <p>Patients treated with senna/docusate in 72 hours. Thereafter the groups received either methylnaltrexone or sodium picosulfate and glycerol suppository.</p> | <p>6 of 7 in the methylnaltrexone group had bowel movement within 24 hours. Of the sodium picosulfate/glycerol supp group none of the participants had bowel movement<br/>The methylnaltrexone group was fully enterally fed and had smaller residual volumes than the other group.</p> | <p>Methylnaltrexone has significant better effect on opioid induced constipation</p> | <p>Methylnaltrexone is a consideration for preventing constipation in the hose on opioid medications.</p> |
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| Van der Spoel, 2007, Netherlands | RCT                        | N= 308<br>Adult critical care patients from 2 hospitals | Compare effect of PEG, lactulose, and placebo. And if any of the three was better in stimulating to bowel movement and improving outcomes. | Pharmacists mixed study medicine which were mixed in alike bottles containing 100 ml sterile water and medicine/placebo. The study was blinded. | Lactulose and PEG had the same effect on stimulate bowel movement versus placebo. PEG had slightly better effect on opioid induced constipation. Lactulose was associated with shorter length of stay. If defecation did not occur within 3 days, neostigmine was most effective. Defecation within 6 days was related to a shorter stay in the ICU, regardless of use of laxatives | Both PEG and lactulose was effective on stimulation of bowel movement.                                    | Study suggest PEG to prevent constipation. |
| Habeeb, E et al, 2022, USA       | Retrospective cohorts tudy | N= 160<br>Patients from 2015-2020                       | Compare naloxone enterally given vs methylnaltrexone.  | The two groups are not equal, more medical ICU patients in one of the groups.   | Time to first bowel movements was shorter in the naloxone group.  | Time to first bowel movement was shorter in the naloxone group 18 hours vs 41 hours for methylnaltrexone. | Supports use of naloxone.                  |

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| Duprey, M et al, 2022, USA | A Rando mized Double -Blind Placebo - Control led Pilot Trial | N= 12   | Measure effectiveness of naloxone versus methylnaltrexone.  | Small sample   | Time to first bowel movements was the same compare naloxone vs placebo.                               | The findings in this study do not give evidence because of small size sample  | N/A   |
| Patel, et al, 2020, USA    | RCT   | N= 84   | Methylnaltrexone vs placebo, measure rescue-free laxation (hours), to first bowel movement.                             | Wild confidence intervals. A clinically important difference cannot be excluded.             | The was no difference in time to rescue-free laxation (hours), compared methylnaltrexone and placebo. | No evidence to support methylnaltrexone compared to conventional laxative.  |   |
| Azevedo, 2015. England     | RCT   | n= 88 Adult mechanically ventilated patients, both surgical and medical. 44= intervention group 44= control group | Investigate if daily defecation with lactulose had impact on the SOFA score (Sequential Organ Failure Assessment score) | The two groups are alike and comparable. The p-values and confidence interval are presented. | The patients in the intervention group had more frequent bowel movements than the control group       | Daily defecation led to significant reduction in SOFA score. The results of this study pointed in direction (p-value 0,08) of lower mortality were daily defecation occurred. | Daily bowel movement is proven to give better outcomes in SOFA score regarding this study, but the intervention group had longer length of stay and more frequent cases of pneumonia than the control group |

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| Bishop, 2010. Australia | Cohort study – pilot observational | n= 44<br>Critical care patients were observed for 274 days on mechanical ventilation | Investigate bowel function and patterns of defecation in critically ill mechanical ventilated patients.   | Patients received lactulose until first defecation                                  | Constipation was common. Laxatives given had effect and opioids given was associated with lower frequency of bowel movement. | Lactulose and ondansetron were significant in effect of defecation. Lactulose had a significant relationship with stool volume .  | This study revealed that there is a high incidence of constipation in the ICU. It gives evidence for lactulose to prevent or treat constipation  |
| Btaiche, 2010           | Review                             | Search history is described and documented for                                       | Investigate critical illness, gastrointestinal complications and medication administered while enteral nutrition was given to the critical care patients. | This paper presents existing evidence for naloxone, methylnaltrexone and alvimopan. | Review over how medication and enteral nutrition effects the gastrointestinal tract  | Early and adequate enteral nutrition are important for critical care patients. Constipation can be prevented through different strategies, such as adequate fluid balance, opioid antagonists, and laxatives. | According to this study acceptance of a higher volume of aspirat (500 ml) could be relevant for our guideline leading to higher frequens of patients being fed enterally. In the national guideline for nutrition, the aspirat level is set to 300 ml. |

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| Dehghan, 2018, Iran   | RCT          | 70 35 patients in the intervention group and 35 in the control group | In the intervention group the patients received abdominal massage for 15 minutes twice a day, for 3 days. The control group did only receive basic nursing, | Low number of patients included   | It was lower number of constipated patients in the intervention group vs the control group 37% vs 68%   | Abdominal massage does decrease the time for first bowel movement.                              | Non-pharmacological measure to prevent constipation in the critically ill patients.  |
| Dorman, 2004, England | Cohort study | n= 9 pre-intervention n= 10 post-intervention                        | Implementation of bowel movement protocol   | Old study. The ward inspected had an unstructured approach to constipation. They wanted a change. Confidence intervals are not presented.                 | This study focuses on bowel and bowel function. Health care professional documentation improved after implementation. They also started laxatives earlier than before the intervention. Laxatives were started concurrently with enteral nutrition. | The implementation of the bowel movement protocol led to focus on bowel care as a daily routine | This study presents same issues that we had in our ward. The audit identified constipation as a problem. Their bowel movement protocol will be relevant for this study |
| Gibson, 2014, USA     | Cohort study | n= 16 Adult male patients in MICU                                    | Measure safety and effectiveness of enteral naloxone for opioid-induced constipation in a medical ICU   | 16 males included over 5 years. Individual doses of naloxone were given. 75% received other laxatives additionally. No documentation of level of sedation | Average daily dose of naloxone was 4.7 mg. 15 of 16 had bowel movement within 24 hours after administration.  | Naloxone gives bowel movement   | Administering enterally naloxone can prevent and help the patients to defecate.  |

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| Guardiola, 2016, Spain | Case control study | N=197<br>Adult critical care patients<br>63= observational phase<br>64= treatment phase<br>70= prophylactic phase | Measure the prevalence of lower gastrointestinal tract paralysis (GI-paralysis). Compare laxative treatments and prophylactic measures, for stimulating defecation | In the observational phase, the occurrence of GI-paralysis. In the treatment-phase they were given treatment from day 4. In the prophylactic-phase they got prophylactic treatment from day 1. The patients got administrated PEG 4000 (polyethylene glycol [macrogol]) every 6 hours until defecation occurred. If no defecation within 5 days they got administrated an enema (1 liter of paraffin, glycerin, and sodium phosphate and/or neostigmine in 24 hours. If still no defecation the patients received high-doses of PEG over 12 hours by feeding tube | 90% in the observational group had GI paralysis. In the treatment group 25% had GI -paralysis, and in the prophylactic group 8,6% had GI-paralysis. There was shorter length of stay and shorter length on ventilator for the prophylactic group. | PEG4000 gives best outcome for critically ill patients if it is administrated on day 1. | Presents a new type of definition of constipation. Beside 3 days without bowel movements, dilatation of the colon and presence and frequency of bowel sounds should be measured |
| Hay, 2019, Australia   | Systematic review  | The search Included patients how was in critical care   | To review if prophylactic laxative bowel regimen prevent constipation  | Studies included I the SR have low evidence level and its few studies to compare  | Prophylactic laxative bowel regimen increases the risk of diarrhea and did not reduce the risk of constipation  | Low data about prophylactic laxative bowel regimen and do not support their use         |   |

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| Knowles, 2014, Australia | Cas control study | N= 101 pre-implementation group<br>N= 107 postimplementation group | Measure if a bowel movement protocol had effect   | Evidence based protocols were developed for preventing constipation, rectal exploration and treatment of constipation and diarrhea. | No significant findings in cases of constipation before and after the intervention  | Nurses and doctors did not use the protocols, regardless of thorough implementation n the ward  | Effective evidenced based protocols despite poor adoption. |
| Lat, 2010, USA           | Review            | Search strategy is not documented                                  | Approach medicine induced acute hepatitis and gastrointestinal complications in the ICU | Relevant because they present a chapter about constipation in critically ill patients.  | Stimulant agents and osmotic agents have effect on constipation in critically ill patients. Methylnaltrexone abbreviated time to first bowel movement for patients with opioid induced constipation | Regarding to this review article Stimulant and osmotic agents have good effect on constipation. Methylnaltrexone and alvimopan abbreviated time for first bowel movement. | Presents evidence for laxatives and opioid antagonists.    |

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| <p>Masri, 2010, United Arab Emirates</p> | <p>RCT</p>                | <p>N=100<br/>Control group= 50<br/>Intervention group= 50<br/>Adult mechanical ventilated patients, mostly males</p>          | <p>Early versus late defecation in context with patient outcome.<br/>Evaluate use of laxative in prophylaxis of constipation in critical ill patients.</p>                              | <p>Intervention group got administrated lactulose 20 ml x 2 the first three days (started within 4-6 hours after admission to the ICU).<br/>Control group received no laxatives the first three days.<br/>After three days treatment was cared for individually by doctor's order.<br/>They measured severity of constipation after 5 days.</p> | <p>In the intervention group 18% had bowel movement within 76 hours.<br/>In the control group 4% had bowel movement within 76 hours.<br/>Early bowel movement within 5 days gave shorter time on ventilator versus late bowel movement.</p> | <p>Lactulose can prevent constipation.</p>   | <p>Gives evidence for use of lactulose to prevent constipation in the ICU.</p>   |
| <p>McKenna, 2001, Australia</p>          | <p>Case control study</p> | <p>N= 120<br/>60= pre intervention group<br/>60= post intervention group<br/>Critically ill patients, 75 men and 45 women</p> | <p>Nurse led bowel movement protocol were developed based on a review of literature They measured frequency of constipation and diarrhea before and after implementing the protocol</p> | <p>Constipation was defined as 3 days with no bowel movement.<br/>First measure after 3 days was rectal exploration</p>   | <p>Implementation of bowel movement protocol led to better documentation and evaluation of bowel function by the nurses.</p>  | <p>Bowel movement protocol can be a helpful tool for critical care nurses, and can increase and improve both documentation and evaluation of bowel movement in the ICU</p> | <p>The results are based on the documentation of bowel activity. They are dependent on the documentation being done sufficiently.<br/>Uncertainty if the protocol had wanted effect.</p> |



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|-------------------------|---|--|---|---|---|---|---|
| McPeake, 2011, Scotland | Case control study                            | N= 55<br>26= intervention group<br>27= control group | Measure effect of implementation of a bowel movement protocol   | Would be of relevance to have a measure after 6 months to see if the protocol is used   | After implementation of the protocol the occurrence of constipation was reduced to 37% from 57,7%. Diarrhea was reduced with 15% from 20% to 5 %. Days of documentation of bowel movement rose to 100%        | Occurrence of constipation and diarrhea can improve by education of health care professionals and with use of bowel movement protocol | This study gives evidence for use of protocol in preventing and treatment of constipation |
| Merchan, 2017, USA      | Cohort. Pilot study with retrospective design | N=100<br>Methylnaltrexone: 48<br>Naloxegol: 52       | Measure how long before first bowel movement after 72 hours with fentanyl infusion. Thereafter measure how many bowel movements within 24 hours | Patients were given from 0 to 4 different laxatives additionally to the survey medicine | Time before first bowel movement were 30 hours for the naloxegol group vs 24 hours for the methylnaltrexone group. None of the groups had a change in sedation niveau, dosage of opioids or vital parameters. | Methylnaltrexone and naloxegol was both effective for stimulating bowel movement.   | Strengthens the use of opioid antagonists for bowel movement in ICU patients.             |

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| Patanwala, 2006, USA   | Case control study | N=50<br>25= group who had bowel movement within 96 hours<br>25= group who did not have bowel movement within 96 hours | Compare effect of regular laxatives in a medical ICU       | Few participants. Some received more laxatives than others. Dependent on sufficient documentation of bowel function when results are withdrawn by audit | Stimulant (senna) was associated with bowel movement. Stool softeners can have impaired effect on constipation because of reduced gastrointestinal motility. Bisocardyl (toilax) had a trend towards being significant in effect. Opioids increases risk of constipation. Use of vasopressin gives increased number of constipated patients. Critically ill patients have high incidence of constipation. Main side effect from laxatives is abdominal cramps. | Routine use of stimulant and osmotic agents should be considered for all critical care patients      | This study shows effect estimates relevant for our protocol |
| Ritchie, 2008, England | Cohort study       | N= 48<br>Critical care patients   | Audit the effect of bowel movement protocol over 12 months | Follow up study after Mostafa revealed that the constipation incidence was 83%  | The rate of constipation was 40% after implementing the bowel movement protocol  | Constipation was still a problem, but less patients suffered from it after implementing the protocol | Protocol is of relevance for this study                     |

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| <p>Ring, 2011, Australia</p> | <p>Cohort study</p> | <p>N= 16<br/>7= Baseline<br/>9= Post implementation</p> | <p>Investigate if a bowel movement protocol could reduce number of days before first bowel movement in the ICU.<br/>All patients got prune juice.<br/>At day 3 macrogol was administrated.<br/>The patients received enemas if rectum ampulla was full when rectum exploration was performed on day 7.</p> | <p>Search of literature is not described.<br/>The bowel movement protocol is based on 5 articles and experiences from a multidisciplinary group.</p> | <p>Time before first bowel movement went down from 9 to 5,3 days</p> | <p>Protocol can help shorten the time to first bowel movement for critical care patients</p> | <p>This study shows how important focus on bowel function is. Together with other studies it has a value for our study</p> |
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| Sawh, 2012, England              | Case control study | N= 15<br>Critical care patients.<br>All treated with sodium docusate and senna the first 72 hours.<br>7= Methylnaltrexone<br>8= Sodium picosulfate glycerin suppository | Investigate the effect of methylnaltrexone versus conventional laxatives on opioid induced constipation on the critically ill patients | Patients treated with senna/docusate in 72 hours. Thereafter the groups received either methylnaltrexone or sodium picosulphate and glycerol supp | 6 of 7 in the methylnaltrexone group had bowel movement within 24 hours. Of the sodium picosulphate/glycerol supp group none of the participants had bowel movement<br>The methylnaltrexone group was fully enterally fed and had smaller residual volumes than the other group.  | Methylnaltrexone has significant better effect on opioid induced constipation | Methylnaltrexone can possibly be a part of the protocol |
| van der Spoel, 2007, Netherlands | RCT                | N= 308<br>Adult critical care patients from 2 hospitals   | Compare effect of PEG, lactulose and placebo on stimulating a bowel movement along with patient outcomes.                              | Pharmacists mixed study medicine which were mixed in alike bottles containing 100 ml sterile water and medicine/placebo. The study was blinded.   | Lactulose and PEG had the same effect on stimulate bowel movement versus placebo. PEG had slightly better effect on opioid induced constipation. Lactulose was associated with shorter length of stay. If defecation did not occur within 3 days, neostigmine was most effective. Defecation within 6 days was connected with shorter stay in the ICU, regardless of use of laxatives | Both PEG and lactulose was effective on stimulation of bowel movement.        | Study suggest PEG to prevent constipation.              |

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|----------------------------|--|--------------------------------|---|---|---|--|--|
| Habeeb, et al, 2022, USA   | Retro-spective cohort study                                | N= 160 Patients from 2015-2020 | Compare naloxone enterally given vs methylnaltrexone  | The two groups are not equal, more medical ICU patients in one of the groups.               | Time to first bowel movements was shorter in the naloxone group.                                  | Time to first bowel movement was shorter in the naloxone group 18 hours vs 41 hours for methylnaltrexone |  |
| Duprey, M et al, 2022, USA | A Randomized Double-Blind Placebo - Controlled Pilot Trial | N= 12                          | Measure effectiveness of naloxone versus methylnaltrexone                                   | Small population of patients, the result is difficult to compare to other studies.          | Time to first bowel movements was the same compare naloxegol vs placebo.                          | The findings in this study do not give evidence because of small size sample.                            |  |
| Patel et al, 2020, USA     | RCT  | N= 84                          | Methylnaltrexone vs placebo, measure rescue-free laxation (hours), to first bowel movement. | The confidence interval was wide, and a clinically important difference cannot be excluded. | The was no different Time to rescue-free laxation (hours), compared methylnaltrexone and placebo. | No evidence to support methylnaltrexone compared to conventional laxative.                               |  |