Nutrition in Clinical Practice

Are Classic Bedside Exam Findings Required to Initiate Enteral Nutrition in Critically ill Patients: Emphasis on Bowel Sounds and Abdominal Distension

Journal:	*Nutrition in Clinical Practice*
Manuscript ID	NCP-2020-05-184.R1
Manuscript Type:	Invited Review
Keywords:	Nutrition, Enteral nutrition < Nutrition, Critical care < Research and Diseases, Nutrition assessment < Nutrition
Abstract:	The general physical examination of a patient is an axiom of critical care medicine but evidence to support this practice remains sparse. Given the lack of evidence for a comprehensive physical examination on admission to the intensive care unit, which most clinicians consider an essential part of care, should clinicians continue the practice of gastrointestinal system physical examination when commencing enteral nutrition in the critically ill? In this review of literature related to gastrointestinal system examination in the critically ill, the focus is on gastrointestinal sounds and abdominal distension. There is a summary of what these physical features represent, an evaluation of the evidence regarding use of these physical features in patients after abdominal surgery, exploration of the rationale for and against using the physical findings in routine practice, and detail regarding what is known about each feature in the critically ill. Based on the available evidence it is recommended that an isolated symptom, sign or bedside test does not provide meaningful information. However, it is submitted that a comprehensive assessment still has a role when initiating or administering enteral nutrition: specifically, when multiple features are present, clinicians should consider further investigation or intervention.

SCHOLARONE™
Manuscripts

ABSTRACT

The general physical examination of a patient is an axiom of critical care medicine but evidence to support this practice remains sparse. Given the lack of evidence for a comprehensive physical examination on admission to the intensive care unit, which most clinicians consider an essential part of care, should clinicians continue the practice of gastrointestinal system physical examination when commencing enteral nutrition in the critically ill?

In this review of literature related to gastrointestinal system examination in the critically ill, the focus is on gastrointestinal sounds and abdominal distension. There is a summary of what these physical features represent, an evaluation of the evidence regarding use of these physical features in patients after abdominal surgery, exploration of the rationale for and against using the physical findings in routine practice, and detail regarding what is known about each feature in the critically ill.

Based on the available evidence it is recommended that an isolated symptom, sign or bedside test does not provide meaningful information. However, it is submitted that a comprehensive assessment still has a role when initiating or administering enteral nutrition: specifically, when multiple features are present, clinicians should consider further investigation or intervention.

For Peer Review

INTRODUCTION

A physical examination of a patient complements information obtained from the history of presenting illness or injury, and assists with the formulation of potential diagnoses to inform further investigations [1-3]. Whilst a fundamental axiom of clinical medicine, there remains a lack of published data that the physical examination of the entire patient improves outcomes for critically ill patients [4]. Nonetheless, in addition to comprehensive examination on admission, a daily clinician examination of the patient is considered a cornerstone of caring for the critically ill [5].

In ambulant patients the focussed physical examination of the gastrointestinal system traditionally includes inspection, palpation, percussion and auscultation [6]. In the critically ill, interpretation of the gastrointestinal tract physical examination findings is more challenging because of limited patient feedback [7]. In the intensive care unit the gastrointestinal system examination relies on inspection and percussion to identify abdominal distension [8], palpation for focal tenderness to identify discrete pathologies such as acalculous cholecystitis or generalised tenderness for perforated viscus [9], and auscultation to identify the presence of sounds arising from the gastrointestinal tract - or so called 'bowel sounds' [10].

The provision of enteral nutrition is recommended for critically ill patients [11-13]. However, gastrointestinal dysmotility occurs frequently in critically ill patients [14], leading to enteral feed intolerance or other signs of gastrointestinal dysfunction in up to one third of patients [15-17]. How then should physical signs influence the decision to initiate, or continue, enteral nutrition in the critically ill?

In this review there is a focus on two physical signs – auscultation for gastrointestinal sounds and inspection and percussion to identify abdominal distension – as part of a comprehensive assessment of the gastrointestinal system (Figure 1). This review submits that such assessment should occur prior to initiating enteral nutrition and as part of ongoing daily assessment in the intensive care unit.

For Peer Review

However, there are gastrointestinal symptoms, such as vomiting, constipation (perhaps more precisely termed absence of defecation), and diarrhoea as well as simple bedside tests – including residual gastric volume, intra-abdominal pressure and blood lactate – that are not covered in this review. Whilst the details of these other clinical tools are beyond the scope of this review, updated literature reviews on these topics can be found elsewhere [18-22].

It should be recognised that performing a comprehensive assessment prior to initiation of enteral nutrition, as well as daily assessment whilst delivering enteral nutrition to the critically ill, may reduce the total 'dose' of nutrition delivered to a proportion of patients [23]. However, there remains uncertainty as to what comprises optimal nutrition therapy at the population level [24-27]. Accordingly, it seems improbable that reducing the dose of nutrition for an individual patient based on a comprehensive assessment will cause harm [28-30]. Furthermore, it is intuitively plausible that an approach to incorporate physical examination findings may be beneficial by optimising nutrient delivery to the individual and/or effecting early identification of ominous gut pathologies [31,32].

Gastrointestinal dysmotility during critical illness and postoperative ileus share many pathogenic features [33]. Given the greater number of studies evaluating the role of gastrointestinal examination in patents with postoperative ileus, a review of this pathology is included to provide relevant insights. For each physical examination feature, i.e. gastrointestinal sounds and abdominal distension, a summary is provided for:

(i) What the physical feature represents?

(ii) The use of the examination finding in patients after abdominal surgery.

(iii) The rationale for and against using the physical finding in routine practice.

(iv) What is known about the examination feature in the critically ill?

Gastrointestinal sounds

For Peer Review

What do gastrointestinal sounds represent?

Sound is produced when a force causes an object or substance to vibrate, with the energy transferred through sound waves. In 1905 Cannon first reported auscultation of gastrointestinal sounds [34]. Gastrointestinal sounds occur because of the transfer of energy arising from gastrointestinal tract motility.

In health, the motor function of the gastrointestinal tract is categorised in either the fasting or fed state. Fasting motility is divided into three phases; each phase having typical contractile features within the gastrointestinal tract. These three phases are termed the migratory motor complex and occur in a cyclical fashion; phase I is characterised by quiescent motor pattern, phase II by irregular motor contraction and phase III by periods of regular contractions [35].

In a series of elegant experiments, Tomomasa and colleagues established that, at least in health, gastrointestinal sounds represent the energy transferred during intraluminal propulsion that occurs during late fasting phase II of the migratory motor complex [36]. The duration of each phase of the migratory motor complex varies substantially between individuals; however in fasted healthy volunteers the mean (± SEM) duration of phase I (the quiescent phase) is reported to be 23 ± 4 minutes [37]. This prompted Tomomasa and colleagues to suggest that clinicians who want to precisely quantify gastrointestinal sounds should listen for 20 minutes, or for shorter periods at intervals of 20-25 minutes [36].

The use of gastrointestinal sounds as a clinical sign in patients after abdominal surgery

In patients presenting to hospital, auscultation of gastrointestinal sounds was traditionally thought to assist with diagnosing acute gastrointestinal pathologies [38,39]. However, the clinical utility of auscultating the abdomen has been challenged by a number of studies involving healthy volunteers or patients after major surgery [40-44]. Indeed, there is only weak agreement between clinicians when

For Peer Review

identifying whether gastrointestinal sound recordings are from healthy volunteers or patients with pathologies [42]. The weak inter-rater reliability of gastrointestinal auscultation may reflect the short period of observation [45].

Read and colleagues observed 124 patients after major abdominal surgery at a single centre [43]. In this study gastrointestinal sounds were detected in 40% of patients on postoperative day 0, increasing to 88% by day 4 [43]. However, the presence of gastrointestinal sounds was not associated with passing of flatus, bowel movement or tolerance of oral intake [43]. Recommendations that comprise the enhanced recovery after surgery (ERAS) program include early initiation of enteral nutrition without waiting for gastrointestinal sounds [46]. Moreover, even in patients who develop postoperative ileus, expert consensus opinion is that auscultation for gastrointestinal sounds is of limited to no use [47]. Finally, a recent systematic review of randomised clinical trials evaluating ileus post gastrointestinal surgery identified 217 randomised clinical trials, with only 21 (< 10%) reporting time to detect gastrointestinal sounds and no trials having time to detect gastrointestinal sounds as the primary outcome [48]. Taken together, these data suggest that as a single physical feature, auscultation for gastrointestinal sounds provides negligible meaningful information when caring for patients with postoperative ileus.

An inadequate duration of observation may explain why auscultation for gastrointestinal sounds is of limited value in identifying postoperative ileus [43]. Experts have suggested that technology could augment any benefits of auscultation by allowing prolonged recordings, signal enhancement to identify more sounds, and machine learning to interpret these sounds [49]. Using such technology, a study of 40 participants (25 with postoperative ileus, 7 patients tolerating enteral nutrition and 8 healthy controls) at a single centre reported that patients with postoperative ileus produced substantially less acoustic data than those without ileus, and those without ileus produced substantially less acoustic data than healthy volunteers during a 60 min period of monitoring [50]. This group then conducted a subsequent longitudinal study using the same technology in 28 patients at 2

For Peer Review

hospitals after major abdominal surgery and reported that acoustic data during prolonged monitoring was less in patients with postoperative ileus [51].

The rationale for auscultating for gastrointestinal sounds in the critically ill

The rationale for including abdominal auscultation in routine practice when caring for the critically ill includes that univariate analysis reveals associations between absence of gastrointestinal sounds and mortality [52,53]. However, severity of illness and other concomitant symptoms are confounding variables, with gastrointestinal sounds less likely to be heard in more severely ill patients. Within observational data sets researchers attempt to adjust for severity of illness using acute physiology scores, e.g. APACHE or SOFA, however these are crude adjustments that do not account for many additional factors such as sedation or analgesia. Fasting critically ill patients spend a greater proportion of time in phase I of the migrating motor complex, and late phase II and III motor activity is infrequent [54-56]. As described above, gastrointestinal sounds occur during intraluminal propulsion in late phase II. Accordingly, those auscultating for gastrointestinal sounds during critical illness should expect lesser periods of gastrointestinal sounds than in ambulant populations because many of the treatments administered in the intensive care unit, such as analgesic and sedative drugs, attenuate gastrointestinal motility [57,58].

Auscultation may have some negative predictive value, i.e. hearing gastrointestinal sounds means that the critically ill patient is less likely to have dysmotility. However, retrograde peristalsis or bowel movement proximally from obstructed bowel also produce sounds [42,44,59,60].

What do we know about gastrointestinal sounds as a clinical sign in the critically ill?

For Peer Review

Survey data suggest auscultatation of the abdomen is far from a universal examination technique with ≈80% of the surveyed 2298 critical care nurses in the United States reporting that they used this method [61,62]. Observational studies also indicate that wide variation in practice remains even when the abdomen is auscultated, with no single methodology regularly implemented [63-65].

The European Society of Intensive Care Medicine (ESICM) Working Group on Abdominal Problems (2012) has provided recommendations on gastrointestinal auscultation and the implications of gastrointestinal sounds as one component of physical examination [10]. It should be emphasised that these recommendations are based solely on expert opinion. The expert opinion was that clinicians listen for at least one minute in two quadrants repeated once [10] and that the absence of gastrointestinal sounds was considered abnormal [10]. However, the "*presence of bowel sounds does not confirm normal motility, and reoccurrence of bowel sounds does not correlate with improvement of paralysis. There are no special management suggestions for absent/abnormal bowel sounds [10].*" Indeed, it is plausible that the absence of gastrointestinal sounds does not represent pathology. Indeed, because a period of quiescence is normal, particularly in the critically ill, an absence of gastrointestinal sounds during a short period of observation without any additional symptoms, signs or abnormal bedside tests, should not identify gastrointestinal dysfunction, nor trigger any management decisions.

Given that a greater duration of observation in postoperative ileus is more informative than a shorter period, there is face validity in assuming auscultation for longer periods may be more beneficial. It is possible that technology could assist with prolonged monitoring [66]. A small proof of concept study evaluating the feasibility of prolonged monitoring was recently published [67]. Gunto and colleagues attached 4 acoustic sensors to the abdomen of 5 critically ill patients who required mechanical ventilation and were able to record gastrointestinal sounds for more than 24 hours in each patient [67].

Abdominal distension

For Peer Review

What does abdominal distension represent?

Abdominal distension has been defined as a sagittal abdominal diameter that is greater than the rib cage or hip height [68]. However, this definition only refers to volume with no consideration of pressure generated by the change in volume [69]. This is important as abdominal distension is pathognomonic when increased pressure is present but is of lesser importance when the volume increase occurs without any pressure change.

Traditional teaching is that causes of distension begin with the letter 'F'; i.e. fat (obesity), fluid (ascites), foetus, flatus (gaseous distension), faeces or 'filthy' big tumour [70]. Whether, and to which extent, a certain increase in volume causes augmentation of pressure is dependent on abdominal compliance [71]. In ambulant patients a rapid increase in intra-abdominal volume is usually due to fermentation of dietary or endogenous substrates within the large bowel lumen, which are the major sources of gas production [72]. Several factors related to critical illness contribute to rapid increase in intra-abdominal volume and increased pressure. These include tissue oedema, ascites and intraluminal gas or fluid due to motility disturbances, maldigestion and malabsorption.

The use of abdominal distension as a clinical sign in patients after abdominal surgery

Inspection of the abdomen in the immediate postoperative period is important to detect complications (e.g. bleeding). Identification of abdominal distension in this phase should prompt investigations to exclude bleeding (e.g. measurement of haemoglobin and/or imaging). However, palpation and percussion is more challenging in the immediate postoperative phase, is observer-dependent and does not afford quantification for repeat comparison. Measurement of intra-abdominal pressure may allow quantification and comparison over time and can be considered in patients developing abdominal distension after major abdominal surgery or trauma [73,74]. Intra-

For Peer Review

abdominal pressure measurement can assist with identification of abdominal compartment syndrome, a life-threatening consequence of abdominal distension of any aetiology, that requires definitive intervention rather than just increasing organ support within the intensive care unit [75,76]. However, interpretation of dynamics of intra-abdominal pressure requires adaption for abdominal compliance and any pressure value must be considered relative to the patient, the surgery completed and other organ dysfunction [71,77].

In the later postoperative course, bowel distension, commonly along with bowel paralysis, is the main cause of abdominal distension. For some institutions that are familiar with intra-abdominal pressure monitoring (Figure 2), repeat intra-abdominal pressure monitoring over time can provide dynamic information and trigger further imaging. Importantly, imaging may only reveal dimensions of the bowel without quantifying the internal pressure applied to the bowel wall. Therefore, radiology findings commonly refer to bowel dilatation, whereas distension is a clinical diagnosis (pressure being commonly associated with discomfort/pain/tenderness) [69].

The rationale for abdominal distension as a clinical sign in the critically ill

Gastrointestinal dysmotility is frequently associated with abdominal distension [14]. Clinical examination to differentiate increased volume from pathognomic distension (increased volume and pressure) is challenging in the ICU, particularly in patients receiving sedation, analgesia and muscle relaxant. However, clinically identified abdominal distension is associated with intra-abdominal hypertension [65].

Digestion and absorption of carbohydrates and lipids can be impaired in the critically ill [78-81]. Accordingly, this may result in modest increases in abdominal girth without symptoms – i.e. increase in volume without additional symptoms, signs or tests that suggest corresponding increase in pressure – that may be initially treated with variation in supply of carbohydrate or lipid to the colon

For Peer Review

[81-83]. Fermentation of an endogenous substrate may also be due to slow colonic transit or changes in the microbiome, which may respond to specific intervention to stimulate defecation or increasing the diversity in the microbiome [83-88].

However, an increase in volume with additional symptoms, signs or bedside tests indicative of an increase in pressure – e.g. pain, absence of bowel motions, profuse diarrhoea, tenderness, hyperlactatemia and increased gastric residual volume – should trigger further investigations, monitoring or intervention.

What is known about using abdominal distension as a clinical sign in the critically ill?

In several cohort studies conducted in the critically ill abdominal distension has been included as a sign of pathology in several cohort studies [52,65]. However, in previous studies abdominal distension was identified either with a subjective clinical assessment, where pressure was also present, or by an enlargement of bowel identified radiologically. Whilst intra-abdominal pressure was measured in many of the patients, intra-abdominal hypertension was included as an additional and separate physical feature. The majority of patients with 3 or more concomitant gastrointestinal symptoms had intra-abdominal hypertension [64]. None of these studies report an association between an isolated physical feature of abdominal or bowel distension and death. However, when distension was incorporated with other features, then the presence of 3 or more gastrointestinal symptoms was independently associated with increased mortality [64]. Accordingly, abdominal distension may provide important information as part of a comprehensive clinical assessment until reliable bedside monitoring tools become available.

ADVICE FOR CLINICIANS AND FUTURE DIRECTIONS

For Peer Review

Enteral nutrition remains a component of routine care [11,29] and the authors recommend against waiting for gastrointestinal sounds prior to starting enteral nutrition. Similarly there are no data to suggest daily cursory auscultation *per se* to decide whether enteral nutrition will be of benefit. However, when auscultation is a component of a more comprehensive assessment of gastrointestinal function, and the presence or absence of gastrointestinal sounds is incorporated with other examination features and simple bedside tests auscultation probably has an additive role.

If an increase in abdominal volume occurs without additional features, clinicians can consider a reduction in carbohydrate load, strategies to increase the diversity of the microbiome or measurement of intra-abdominal pressure. None of these interventions are, however, supported by unequivocal data from randomised clinical trials. Intra-abdominal pressure may be useful when there is uncertainty about the need for additional investigation/s that require transport out of the intensive care unit or an intervention that is associated with more than negligible risk.

Whether decisions based on such complex assessment of a constellation of imprecise symptoms, signs and test results improve outcomes remains untested. However, without a proven alternative, it is the opinion of the authors that the use of minimally-invasive and inexpensive assessment methodologies is better than abandoning routine assessment of gastrointestinal function. Because excessively aggressive administration of enteral nutrition may cause harm [31], a daily evaluation with early identification of serious events such as non-obstructive bowel ischemia and critical bowel distension with life-threatening perforation should continue as part of routine care.

Given this, the use of technology to allow prolonged periods of minimally invasive observation, with presence and characteristics of gastrointestinal sounds validated using objective criteria, warrants further evaluation. This technology may be particularly useful in cohorts of patients for whom clinicians remain uncertain about whether to initiate or increase enteral nutrition, such as those with hypotension requiring considerable vasopressor support or profound hypoxia or acidosis [11,13,31,32,89].

For Peer Review

Future studies should also produce data that informs when to initiate intra-abdominal pressure monitoring and what interventions are effective once intra-abdominal hypertension is identified.

For Peer Review

Figure captions:

Figure 1. Bedside assessment of the gastrointestinal tract

Figure 2. Intra-abdominal pressure is measured in the supine, paralysed patient at end-expiration via a transducer in continuity with the bladder, zeroed at the mid-axillary line. 25ml of fluid is instilled in the empty bladder and the pressure taken after 60 seconds.

For Peer Review

REFERENCES

1. Verghese A. Culture shock--patient as icon, icon as patient. *N Engl J Med.* 2008;359(26):2748-2751.
2. Metkus TS, Kim BS. Bedside Diagnosis in the Intensive Care Unit. Is Looking Overlooked? *Ann Am Thorac Soc.* 2015;12(10):1447-1450.
3. Verghese A, Charlton B, Kassirer JP, Ramsey M, Ioannidis JP. Inadequacies of Physical Examination as a Cause of Medical Errors and Adverse Events: A Collection of Vignettes. *The American journal of medicine.* 2015;128(12):1322-1324.e1323.
4. Hiemstra B, Koster G, Wiersema R, et al. The diagnostic accuracy of clinical examination for estimating cardiac index in critically ill patients: the Simple Intensive Care Studies-I. *Intensive Care Med.* 2019;45(2):190-200.
5. Schneiderman H. Toward a Renascence of Physical Diagnosis in the Intensive Care Unit. *Ann Am Thorac Soc.* 2015;12(10):1423-1424.
6. Pichetshote N, Pimentel M. An Approach to the Patient With Chronic Undiagnosed Abdominal Pain. *Am J Gastroenterol.* 2019;114(5):726-732.
7. Plummer MP, Reintam Blaser A, Deane AM. Gut dysmotility in the ICU: diagnosis and therapeutic options. *Curr Opin Crit Care.* 2019;25(2):138-144.
8. Nguyen T, Frenette AJ, Johanson C, et al. Impaired gastrointestinal transit and its associated morbidity in the intensive care unit. *J Crit Care.* 2013;28(4):537 e511-537.
9. Plummer MP, Kar P, Cousins CE, et al. Critical Illness Is Associated With Impaired Gallbladder Emptying as Assessed by 3D Ultrasound. *Crit Care Med.* 2016;44(9):e790-796.
10. Reintam Blaser A, Malbrain ML, Starkopf J, et al. Gastrointestinal function in intensive care patients: terminology, definitions and management. Recommendations of the ESICM Working Group on Abdominal Problems. *Intensive Care Med.* 2012;38(3):384-394.

For Peer Review

11. Reintam Blaser A, Starkopf J, Alhazzani W, et al. Early enteral nutrition in critically ill patients: ESICM clinical practice guidelines. *Intensive Care Med.* 2017;43(3):380-398.

12. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr.* 2016;40(2):159-211.

13. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr.* 2018.

14. Deane AM, Chapman MJ, Reintam Blaser A, McClave SA, Emmanuel A. Pathophysiology and Treatment of Gastrointestinal Motility Disorders in the Acutely Ill. *Nutr Clin Pract.* 2019;34(1):23-36.

15. Gungabissoon U, Hacquoil K, Bains C, et al. Prevalence, risk factors, clinical consequences, and treatment of enteral feed intolerance during critical illness. *JPEN J Parenter Enteral Nutr.* 2015;39(4):441-448.

16. Reintam Blaser A, Starkopf L, Deane AM, Poeze M, Starkopf J. Comparison of different definitions of feeding intolerance: A retrospective observational study. *Clin Nutr.* 2015;34(5):956-961.

17. McClave SA, Gualdoni J, Nagengast A, Marsano LS, Bandy K, Martindale RG. Gastrointestinal Dysfunction and Feeding Intolerance in Critical Illness: Do We Need an Objective Scoring System? *Curr Gastroenterol Rep.* 2020;22(1):1.

18. Adike A, Quigley EM. Gastrointestinal motility problems in critical care: a clinical perspective. *J Dig Dis.* 2014;15(7):335-344.

19. Kar P, Jones KL, Horowitz M, Chapman MJ, Deane AM. Measurement of gastric emptying in the critically ill. *Clin Nutr.* 2015;34(4):557-564.

20. Elke G, Felbinger TW, Heyland DK. Gastric residual volume in critically ill patients: a dead marker or still alive? *Nutr Clin Pract.* 2015;30(1):59-71.

For Peer Review

21. Moonen PJ, Reintam Blaser A, Starkopf J, et al. The black box revelation: monitoring gastrointestinal function. *Anaesthesiol Intensive Ther.* 2018;50(1):72-81.

22. Hay T, Bellomo R, Rechnitzer T, See E, Ali Abdelhamid Y, Deane AM. Constipation, diarrhea, and prophylactic laxative bowel regimens in the critically ill: A systematic review and meta-analysis. *J Crit Care.* 2019;52:242-250.

23. Reignier J, Mercier E, Le Gouge A, et al. Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial. *JAMA.* 2013;309(3):249-256.

24. Rice TW, Wheeler AP, Thompson BT, et al. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. *Jama.* 2012;307(8):795-803.

25. Arabi YM, Aldawood AS, Haddad SH, et al. Permissive Underfeeding or Standard Enteral Feeding in Critically Ill Adults. *N Engl J Med.* 2015;372(25):2398-2408.

26. Chapman M, Peake SL, Bellomo R, et al. Energy-Dense versus Routine Enteral Nutrition in the Critically Ill. *N Engl J Med.* 2018;379(19):1823-1834.

27. Fetterplace K, Gill BMT, Chapple LS, Presneill JJ, MacIsaac C, Deane AM. Systematic Review With Meta-Analysis of Patient-Centered Outcomes, Comparing International Guideline-Recommended Enteral Protein Delivery With Usual Care. *JPEN J Parenter Enteral Nutr.* 2019.

28. Patel JJ, Codner P. Controversies in Critical Care Nutrition Support. *Crit Care Clin.* 2016;32(2):173-189.

29. Patel JJ, Martindale RG, McClave SA. Controversies Surrounding Critical Care Nutrition: An Appraisal of Permissive Underfeeding, Protein, and Outcomes. *JPEN J Parenter Enteral Nutr.* 2018;42(3):508-515.

30. Wernerman J, Christopher KB, Annane D, et al. Metabolic support in the critically ill: a consensus of 19. *Crit Care.* 2019;23(1):318.

For Peer Review

31. Reignier J, Boisrame-Helms J, Brisard L, et al. Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2). *Lancet.* 2018;391(10116):133-143.

32. Patel JJ, Rice T, Heyland DK. Safety and Outcomes of Early Enteral Nutrition in Circulatory Shock. *JPEN J Parenter Enteral Nutr.* 2020.

33. Caddell KA, Martindale R, McClave SA, Miller K. Can the intestinal dysmotility of critical illness be differentiated from postoperative ileus? *Curr Gastroenterol Rep.* 2011;13(4):358-367.

34. Cannon WB. AUSCULTATION OF THE RHYTHMIC SOUNDS PRODUCED BY THE STOMACH AND INTESTINES. *American Journal of Physiology-Legacy Content.* 1905;14(4):339-353.

35. Deane A, Chapman MJ, Fraser RJ, Bryant LK, Burgstad C, Nguyen NQ. Mechanisms underlying feed intolerance in the critically ill: Implications for treatment. *World J Gastroenterol.* 2007;13(29):3909-3917.

36. Tomomasa T, Morikawa A, Sandler RH, et al. Gastrointestinal sounds and migrating motor complex in fasted humans. *Am J Gastroenterol.* 1999;94(2):374-381.

37. Luiking YC, Reijden ACvd, Henegouwen GPvB, Akkermans LMA. Migrating motor complex cycle duration is determined by gastric or duodenal origin of phase III. *American Journal of Physiology-Gastrointestinal and Liver Physiology.* 1998;275(6):G1246-G1251.

38. Cullen PT, Storey BE, Cuschieri A, Campbell FC. Detection of clustered gastrointestinal contractions in partial intestinal obstruction by surface vibration analysis. *Ann Surg.* 1989;210(2):234-238.

39. Mansy HA, Sandler RH. Detection and analysis of gastrointestinal sounds in normal and small bowel obstructed rats. *Med Biol Eng Comput.* 2000;38(1):42-48.

40. Ross JT, Matthay MA, Harris HW. Secondary peritonitis: principles of diagnosis and intervention. *BMJ.* 2018;361:k1407.

41. West M, Klein MD. Is abdominal auscultation important? *Lancet.* 1982;2(8310):1279.

For Peer Review

42. Felder S, Margel D, Murrell Z, Fleshner P. Usefulness of bowel sound auscultation: a prospective evaluation. *J Surg Educ.* 2014;71(5):768-773.

43. Read TE, Brozovich M, Andujar JE, Ricciardi R, Caushaj PF. Bowel Sounds Are Not Associated With Flatus, Bowel Movement, or Tolerance of Oral Intake in Patients After Major Abdominal Surgery. *Dis Colon Rectum.* 2017;60(6):608-613.

44. Breum BM, Rud B, Kirkegaard T, Nordentoft T. Accuracy of abdominal auscultation for bowel obstruction. *World J Gastroenterol.* 2015;21(34):10018-10024.

45. Du X, Allwood G, Webberley KM, Osseiran A, Marshall BJ. Bowel Sounds Identification and Migrating Motor Complex Detection with Low-Cost Piezoelectric Acoustic Sensing Device. *Sensors (Basel).* 2018;18(12).

46. Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. *JAMA Surg.* 2017;152(3):292-298.

47. Hedrick TL, McEvoy MD, Mythen MMG, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Postoperative Gastrointestinal Dysfunction Within an Enhanced Recovery Pathway for Elective Colorectal Surgery. *Anesth Analg.* 2018;126(6):1896-1907.

48. Chapman SJ, Thorpe G, Vallance AE, et al. Systematic review of definitions and outcome measures for return of bowel function after gastrointestinal surgery. *BJS Open.* 2019;3(1):1-10.

49. Allwood G, Du X, Webberley KM, Osseiran A, Marshall BJ. Advances in Acoustic Signal Processing Techniques for Enhanced Bowel Sound Analysis. *IEEE Rev Biomed Eng.* 2019;12:240-253.

50. Spiegel BM, Kaneshiro M, Russell MM, et al. Validation of an acoustic gastrointestinal surveillance biosensor for postoperative ileus. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract.* 2014;18(10):1795-1803.

For Peer Review

51. Kaneshiro M, Kaiser W, Pourmorady J, et al. Postoperative Gastrointestinal Telemetry with an Acoustic Biosensor Predicts Ileus vs. Uneventful GI Recovery. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract.* 2016;20(1):132-139; discussion 139.

52. Reintam Blaser A, Poeze M, Malbrain ML, et al. Gastrointestinal symptoms during the first week of intensive care are associated with poor outcome: a prospective multicentre study. *Intensive Care Med.* 2013;39(5):899-909.

53. Reintam A, Parm P, Kitus R, Kern H, Starkopf J. Gastrointestinal symptoms in intensive care patients. *Acta Anaesthesiol Scand.* 2009;53(3):318-324.

54. Dive A, Moulart M, Jonard P, Jamart J, Mahieu P. Gastroduodenal motility in mechanically ventilated critically ill patients: a manometric study. *Crit Care Med.* 1994;22(3):441-447.

55. Chapman M, Fraser R, Vozzo R, et al. Antro-pyloro-duodenal motor responses to gastric and duodenal nutrient in critically ill patients. *Gut.* 2005;54(10):1384-1390.

56. Chapman MJ, Deane AM. Gastrointestinal dysfunction relating to the provision of nutrition in the critically ill. *Curr Opin Clin Nutr Metab Care.* 2015;18(2):207-212.

57. Heyland DK, Tougas G, King D, Cook DJ. Impaired gastric emptying in mechanically ventilated, critically ill patients. *Intensive Care Med.* 1996;22(12):1339-1344.

58. Chapple LA, Deane A. From dysmotility to virulent pathogens: implications of opioid use in the ICU. *Curr Opin Crit Care.* 2018;24(2):118-123.

59. Ching SS, Tan YK. Spectral analysis of bowel sounds in intestinal obstruction using an electronic stethoscope. *World J Gastroenterol.* 2012;18(33):4585-4592.

60. Gu Y, Lim HJ, Moser MA. How useful are bowel sounds in assessing the abdomen? *Dig Surg.* 2010;27(5):422-426.

61. Li B, Tang S, Ma YL, Tang J, Wang B, Wang JR. Analysis of bowel sounds application status for gastrointestinal function monitoring in the intensive care unit. *Critical care nursing quarterly.* 2014;37(2):199-206.

For Peer Review

62. Metheny NA, Mills AC, Stewart BJ. Monitoring for intolerance to gastric tube feedings: a national survey. *Am J Crit Care.* 2012;21(2):e33-40.

63. McClave SA, Snider HL, Lowen CC, et al. Use of residual volume as a marker for enteral feeding intolerance: prospective blinded comparison with physical examination and radiographic findings. *JPEN J Parenter Enteral Nutr.* 1992;16(2):99-105.

64. Padar M, Starkopf J, Uusvel G, Reintam Blaser A. Gastrointestinal failure affects outcome of intensive care. *J Crit Care.* 2019;52:103-108.

65. Reintam Blaser A, Regli A, De Keulenaer B, et al. Incidence, Risk Factors, and Outcomes of Intra-Abdominal Hypertension in Critically Ill Patients-A Prospective Multicenter Study (IROI Study). *Crit Care Med.* 2019;47(4):535-542.

66. Inderjeeth AJ, Webberley KM, Muir J, Marshall BJ. The potential of computerised analysis of bowel sounds for diagnosis of gastrointestinal conditions: a systematic review. *Syst Rev.* 2018;7(1):124.

67. Goto J, Matsuda K, Harii N, Moriguchi T, Yanagisawa M, Sakata O. Usefulness of a real-time bowel sound analysis system in patients with severe sepsis (pilot study). *J Artif Organs.* 2015;18(1):86-91.

68. Reintam Blaser A, Starkopf J, Malbrain ML. Abdominal signs and symptoms in intensive care patients. *Anaesthesiol Intensive Ther.* 2015;47(4):379-387.

69. Reintam Blaser A, Starkopf J, Moonen PJ, Malbrain M, Oudemans-van Straaten HM. Perioperative gastrointestinal problems in the ICU. *Anaesthesiol Intensive Ther.* 2018;50(1):59-71.

70. Talley NJ, O'Connor S. *Clinical examination : a systematic guide to physical diagnosi.* 6th International ed ed: Elsevier Australia; 2010.

71. Blaser AR, Bjorck M, De Keulenaer B, Regli A. Abdominal compliance: A bench-to-bedside review. *J Trauma Acute Care Surg.* 2015;78(5):1044-1053.

For Peer Review

72. Malagelada JR, Accarino A, Azpiroz F. Bloating and Abdominal Distension: Old Misconceptions and Current Knowledge. *Am J Gastroenterol.* 2017;112(8):1221-1231.

73. Kirkpatrick AW, Roberts DJ, De Waele J, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med.* 2013;39(7):1190-1206.

74. Sugrue M, Bauman A, Jones F, et al. Clinical examination is an inaccurate predictor of intraabdominal pressure. *World J Surg.* 2002;26(12):1428-1431.

75. De Waele JJ, Kimball E, Malbrain M, et al. Decompressive laparotomy for abdominal compartment syndrome. *Br J Surg.* 2016;103(6):709-715.

76. De Laet IE, Malbrain M, De Waele JJ. A Clinician's Guide to Management of Intra-abdominal Hypertension and Abdominal Compartment Syndrome in Critically Ill Patients. *Crit Care.* 2020;24(1):97.

77. Petro CC, Raigani S, Fayezizadeh M, et al. Permissible Intraabdominal Hypertension following Complex Abdominal Wall Reconstruction. *Plast Reconstr Surg.* 2015;136(4):868-881.

78. Burgstad CM, Besanko LK, Deane AM, et al. Sucrose malabsorption and impaired mucosal integrity in enterally fed critically ill patients: a prospective cohort observational study. *Crit Care Med.* 2013;41(5):1221-1228.

79. Deane AM, Rayner CK, Keeshan A, et al. The effects of critical illness on intestinal glucose sensing, transporters, and absorption. *Crit Care Med.* 2014;42(1):57-65.

80. Ali Abdelhamid Y, Cousins CE, Sim JA, et al. Effect of Critical Illness on Triglyceride Absorption. *JPEN J Parenter Enteral Nutr.* 2015;39(8):966-972.

81. Savino P. Knowledge of Constituent Ingredients in Enteral Nutrition Formulas Can Make a Difference in Patient Response to Enteral Feeding. *Nutr Clin Pract.* 2018;33(1):90-98.

For Peer Review

82. Qiu C, Chen C, Zhang W, et al. Fat-Modified Enteral Formula Improves Feeding Tolerance in Critically Ill Patients: A Multicenter, Single-Blind, Randomized Controlled Trial. *JPEN J Parenter Enteral Nutr.* 2017;41(5):785-795.

83. de Brito-Ashurst I, Preiser JC. Diarrhea in Critically Ill Patients: The Role of Enteral Feeding. *JPEN J Parenter Enteral Nutr.* 2016;40(7):913-923.

84. Shimizu K, Yamada T, Ogura H, et al. Synbiotics modulate gut microbiota and reduce enteritis and ventilator-associated pneumonia in patients with sepsis: a randomized controlled trial. *Crit Care.* 2018;22(1):239.

85. Oami T, Chihade DB, Coopersmith CM. The microbiome and nutrition in critical illness. *Curr Opin Crit Care.* 2019;25(2):145-149.

86. McClave SA, Martindale RG. Why do current strategies for optimal nutritional therapy neglect the microbiome? *Nutrition (Burbank, Los Angeles County, Calif).* 2019;60:100-105.

87. Hay T, Deane AM, Rechnitzer T, et al. The hospital-based evaluation of laxative prophylaxis in ICU (HELP-ICU): A pilot cluster-crossover randomized clinical trial. *J Crit Care.* 2019;52:86-91.

88. Heinonen T, Ferrie S, Ferguson C. Gut function in the intensive care unit - What is 'normal'? *Aust Crit Care.* 2020;33(2):151-154.

89. Patel JJ, Kozeniecki M, Peppard WJ, et al. Phase 3 Pilot Randomized Controlled Trial Comparing Early Trophic Enteral Nutrition With "No Enteral Nutrition" in Mechanically Ventilated Patients With Septic Shock. *JPEN J Parenter Enteral Nutr.* 2019.

For Peer Review

ABSTRACT

The ~~evidence to support any~~ general physical examination of a ~~critically ill~~ patient is an axiom of critical care medicine but evidence to support this practice remains sparse. Given the lack of evidence for a comprehensive physical examination on admission to the intensive care unit, which most clinicians consider an essential part of care~~Should, therefore~~, should clinicians continue the practice of gastrointestinal system physical examination when commencing enteral nutrition in the critically ill?

In this review of literature related to gastrointestinal system examination in the critically ill, the focus is on gastrointestinal sounds and abdominal distension. There is a summary of what these physical features represent, an evaluation of the evidence regarding use of these physical features in patients after abdominal surgery, exploration of the rationale for and against using the physical findings in routine practice, and detail regarding what is known about each feature in the critically ill.

Based on the available evidence it is recommended that an isolated symptom, sign or bedside test does not provide meaningful information. However, it is submitted that a comprehensive assessment still has a role when initiating or administering enteral nutrition: specifically, when multiple features are present, clinicians should consider further investigation or intervention.

For Peer Review

INTRODUCTION

A physical examination of a patient complements information obtained from the history of presenting illness or injury, and assists with the formulation of potential diagnoses to inform further investigations [1-3]. Whilst a fundamental axiom of clinical medicine, there remains a lack of published data that the physical examination of the entire patient improves outcomes for critically ill patients [4]. Nonetheless, in addition to comprehensive examination on admission, a daily clinician examination of the patient is considered a cornerstone of caring for the critically ill [5].

In ambulant patients the focussed physical examination of the gastrointestinal system traditionally includes inspection, palpation, percussion and auscultation [6]. In the critically ill, interpretation of the gastrointestinal tract physical examination findings is more challenging because of limited patient feedback [7]. In the intensive care unit the gastrointestinal system examination relies on inspection and percussion to identify abdominal distension [8], palpation for focal tenderness to identify discrete pathologies such as acalculous cholecystitis or generalised tenderness for perforated viscus [9], and auscultation to identify the presence of sounds arising from the gastrointestinal tract - or so called 'bowel sounds' [10].

The provision of enteral nutrition is recommended for critically ill patients [11-13]. However, gastrointestinal dysmotility occurs frequently in critically ill patients [14], leading to enteral feed intolerance or other signs of gastrointestinal dysfunction in up to one third of patients [15-17]. How then should physical signs influence the decision to initiate, or continue, enteral nutrition in the critically ill?

In this review there is a focus on two physical signs – auscultation for gastrointestinal sounds and inspection and percussion to identify abdominal distension – as part of a comprehensive assessment of the gastrointestinal system (Figure 1). This review submits that such assessment should occur prior to initiating enteral nutrition and as part of ongoing daily assessment in the intensive care unit.

For Peer Review

However, there are gastrointestinal symptoms, such as vomiting, constipation (perhaps more precisely termed absence of defecation), and diarrhoea as well as simple bedside tests – including residual gastric volume, intra-abdominal pressure and blood lactate – that are not covered in this review. Whilst the details of these other clinical tools are beyond the scope of this review, updated literature reviews on these topics can be found elsewhere [18-22].

It should be recognised that performing a comprehensive assessment prior to initiation of enteral nutrition, as well as daily assessment whilst delivering enteral nutrition to the critically ill, may reduce the total 'dose' of nutrition delivered to a proportion of patients [23]. However, there remains uncertainty as to what comprises optimal nutrition therapy at the population level [24-27]. Accordingly, it seems improbable that reducing the dose of nutrition for an individual patient based on a comprehensive assessment will cause harm [28-30]. Furthermore, it is intuitively plausible that an approach to incorporate physical examination findings may be beneficial by optimising nutrient delivery to the individual and/or effecting early identification of ominous gut pathologies [31,32].

Gastrointestinal dysmotility during critical illness and postoperative ileus share many pathogenic features [33]. Given the greater number of studies evaluating the role of gastrointestinal examination in patents with postoperative ileus, a review of this pathology is included to provide relevant insights. For each physical examination feature, i.e. gastrointestinal sounds and abdominal distension, a summary is provided for:

(i) What the physical feature represents?

(ii) The use of the examination finding in patients after abdominal surgery.

(iii) The rationale for and against using the physical finding in routine practice.

(iv) What is known about the examination feature in the critically ill?

Gastrointestinal sounds

What do gastrointestinal sounds represent?

Sound is produced when a force causes an object or substance to vibrate, with the energy transferred through sound waves. In 1905 Cannon first reported auscultation of gastrointestinal sounds [34]. Gastrointestinal sounds occur because of the transfer of energy arising from gastrointestinal tract motility.

In health, the motor function of the gastrointestinal tract is categorised in either the fasting or fed state. Fasting motility is divided into three phases; each phase having typical contractile features within the gastrointestinal tract. These three phases are termed the migratory motor complex and occur in a cyclical fashion; phase I is characterised by quiescent motor pattern, phase II by irregular motor contraction and phase III by periods of regular contractions [35].

In a series of elegant experiments, Tomomasa and colleagues established that, at least in health, gastrointestinal sounds represent the energy transferred during intraluminal propulsion that occurs during late fasting phase II of the migratory motor complex [36]. The duration of each phase of the migratory motor complex varies substantially between individuals; however in fasted healthy volunteers the mean (± SEM) duration of phase I (the quiescent phase) is reported to be 23 ± 4 minutes [37]. This prompted Tomomasa and colleagues to suggest that clinicians who want to precisely quantify gastrointestinal sounds should listen for 20 minutes, or for shorter periods at intervals of 20-25 minutes [36].

The use of gastrointestinal sounds as a clinical sign in patients after abdominal surgery

In patients presenting to hospital, auscultation of gastrointestinal sounds was traditionally thought to assist with diagnosing acute gastrointestinal pathologies [38,39]. However, the clinical utility of auscultating the abdomen has been challenged by a number of studies involving healthy volunteers or patients after major surgery [40-44]. Indeed, there is only weak agreement between clinicians when

For Peer Review

identifying whether gastrointestinal sound recordings are from healthy volunteers or patients with pathologies [42]. The weak inter-rater reliability of gastrointestinal auscultation may reflect the short period of observation [45].

Read and colleagues observed 124 patients after major abdominal surgery at a single centre [43]. In this study gastrointestinal sounds were detected in 40% of patients on postoperative day 0, increasing to 88% by day 4 [43]. However, the presence of gastrointestinal sounds was not associated with passing of flatus, bowel movement or tolerance of oral intake [43]. Recommendations that comprise the enhanced recovery after surgery (ERAS) program include early initiation of enteral nutrition without waiting for gastrointestinal sounds [46]. Moreover, even in patients who develop postoperative ileus, expert consensus opinion is that auscultation for gastrointestinal sounds is of limited to no use [47]. Finally, a recent systematic review of randomised clinical trials evaluating ileus post gastrointestinal surgery identified 217 randomised clinical trials, with only 21 (< 10%) reporting time to detect gastrointestinal sounds and no trials having time to detect gastrointestinal sounds as the primary outcome [48]. Taken together, these data suggest that as a single physical feature, auscultation for gastrointestinal sounds provides negligible meaningful information when caring for patients with postoperative ileus.

An inadequate duration of observation may explain why auscultation for gastrointestinal sounds is of limited value in identifying postoperative ileus [43]. Experts have suggested that technology could augment any benefits of auscultation by allowing prolonged recordings, signal enhancement to identify more sounds, and machine learning to interpret these sounds [49]. Using such technology, a study of 40 participants (25 with postoperative ileus, 7 patients tolerating enteral nutrition and 8 healthy controls) at a single centre reported that patients with postoperative ileus produced substantially less acoustic data than those without ileus, and those without ileus produced substantially less acoustic data than healthy volunteers during a 60 min period of monitoring [50]. This group then conducted a subsequent longitudinal study using the same technology in 28 patients at 2

For Peer Review

hospitals after major abdominal surgery and reported that acoustic data during prolonged monitoring was less in patients with postoperative ileus [51].

The rationale for auscultating for gastrointestinal sounds in the critically ill

The rationale for including abdominal auscultation in routine practice when caring for the critically ill includes that univariate analysis reveals associations between absence of gastrointestinal sounds and mortality [52,53]. However, severity of illness and other concomitant symptoms are confounding variables, with gastrointestinal sounds less likely to be heard in more severely ill patients. Within observational data sets researchers attempt to adjust for severity of illness using acute physiology scores, e.g. APACHE or SOFA, however these are crude adjustments that do not account for many additional factors such as sedation or analgesia. Fasting critically ill patients spend a greater proportion of time in phase I of the migrating motor complex, and late phase II and III motor activity is infrequent [54-56]. As described above, gastrointestinal sounds occur during intraluminal propulsion in late phase II. Accordingly, those auscultating for gastrointestinal sounds during critical illness should expect lesser periods of gastrointestinal sounds than in ambulant populations because many of the treatments administered in the intensive care unit, such as analgesic and sedative drugs, attenuate gastrointestinal motility [57,58].

Auscultation may have some negative predictive value, i.e. hearing gastrointestinal sounds means that the critically ill patient is less likely to have dysmotility. However, retrograde peristalsis or bowel movement proximally from obstructed bowel also produce sounds [42,44,59,60].

What do we know about gastrointestinal sounds as a clinical sign in the critically ill?

For Peer Review

Survey data suggest ~~wide variation between clinicians as to whether they~~ auscultatation of the abdomen is far from a universal examination technique with ≈80% of the surveyed 2298 critical care nurses in the United States reporting that they used this method [61,62]. Observational studies also indicate that wide variation in practice remains even when the abdomen is auscultated, with no single methodology regularly implemented [63-65].

The European Society of Intensive Care Medicine (ESICM) Working Group on Abdominal Problems (2012) has provided recommendations on gastrointestinal auscultation and the implications of gastrointestinal sounds as one component of physical examination [10]. It should be emphasised that these recommendations are based solely on expert opinion. The expert opinion was that clinicians listen for at least one minute in two quadrants repeated once [10] and that the absence of gastrointestinal sounds was considered abnormal [10]. However, the "*presence of bowel sounds does not confirm normal motility, and reoccurrence of bowel sounds does not correlate with improvement of paralysis. There are no special management suggestions for absent/abnormal bowel sounds [10].*" Indeed, it is plausible that the absence of gastrointestinal sounds does not represent pathology. Indeed, because a period of quiescence is normal, particularly in the critically ill, an absence of gastrointestinal sounds during a short period of observation without any additional symptoms, signs or abnormal bedside tests, should not identify gastrointestinal dysfunction, nor trigger any management decisions.

Given that a greater duration of observation in postoperative ileus is more informative than a shorter period, there is face validity in assuming auscultation for longer periods may be more beneficial. It is possible that technology could assist with prolonged monitoring [66]. A small proof of concept study evaluating the feasibility of prolonged monitoring was recently published [67]. Gunto and colleagues attached 4 acoustic sensors to the abdomen of 5 critically ill patients who required mechanical ventilation and were able to record gastrointestinal sounds for more than 24 hours in each patient [67].

For Peer Review

Abdominal distension

What does abdominal distension represent?

Abdominal distension has been defined as a sagittal abdominal diameter that is greater than the rib cage or hip height [68]. However, this definition only refers to volume with no consideration of pressure generated by the change in volume [69]. This is important as abdominal distension is pathognomonic when increased pressure is present but is of lesser importance when the volume increase occurs without any pressure change.

Traditional teaching is that causes of distension begin with the letter 'F'; i.e. fat (obesity), fluid (ascites), foetus, flatus (gaseous distension), faeces or 'filthy' big tumour [70]. Whether, and to which extent, a certain increase in volume causes augmentation of pressure is dependent on abdominal compliance [71]. In ~~the community~~ ambulant patients a rapid increase in intra-abdominal volume is usually due to fermentation of dietary or endogenous substrates within the large bowel lumen, which are the major sources of gas production [72]. Several factors related to critical illness contribute to rapid increase in intra-abdominal volume and increased pressure. These include tissue oedema, ascites and intraluminal gas or fluid due to motility disturbances, maldigestion and malabsorption.

The use of abdominal distension as a clinical sign in patients after abdominal surgery

Inspection of the abdomen in the immediate postoperative period is important to detect complications (e.g. bleeding). Identification of abdominal distension in this phase should prompt investigations to exclude bleeding (e.g. measurement of haemoglobin and/or imaging). However, palpation and percussion is more challenging in the immediate postoperative phase, is observer-dependent and does not afford quantification for repeat comparison. Measurement of intra-

For Peer Review

abdominal pressure may allow quantification and comparison over time and can be considered in patients developing abdominal distension after major abdominal surgery or trauma [73,74]. Intra-abdominal pressure measurement can assist with identification of abdominal compartment syndrome, a life-threatening consequence of abdominal distension of any aetiology, that requires definitive intervention rather than just increasing organ support within the intensive care unit [75,76]. However, interpretation of dynamics of intra-abdominal pressure requires adaption for abdominal compliance and any pressure value must be considered relative to the patient, the surgery completed and other organ dysfunction [71,77].

In the later postoperative course, bowel distension, commonly along with bowel paralysis, is the main cause of abdominal distension. For some institutions that are familiar with intra-abdominal pressure monitoring (Figure 2), repeat intra-abdominal pressure monitoring over time can provide dynamic information and trigger further imaging. Importantly, imaging may only reveal dimensions of the bowel without quantifying the internal pressure applied to the bowel wall. Therefore, radiology findings commonly refer to bowel dilatation, whereas distension is a clinical diagnosis (pressure being commonly associated with discomfort/pain/tenderness) [69].

The rationale for abdominal distension as a clinical sign in the critically ill

Gastrointestinal dysmotility is frequently associated with abdominal distension [14]. Clinical examination to differentiate increased volume from pathognomic distension (increased volume and pressure) is challenging in the ICU, particularly in patients receiving sedation, analgesia and muscle relaxant. However, clinically identified abdominal distension is associated with intra-abdominal hypertension [65].

Digestion and absorption of carbohydrates and lipids can be impaired in the critically ill [78-81]. Accordingly, this may result in modest increases in abdominal girth without symptoms – i.e. increase

in volume without additional symptoms, signs or tests that suggest corresponding increase in pressure – that may be initially treated with variation in supply of carbohydrate or lipid to the colon [81-83]. Fermentation of an endogenous substrate may also be due to slow colonic transit or changes in the microbiome, which may respond to specific intervention to stimulate defecation or increasing the diversity in the microbiome [83-88].

However, an increase in volume with additional symptoms, signs or bedside tests indicative of an increase in pressure – e.g. pain, absence of bowel motions, profuse diarrhoea, tenderness, hyperlactatemia and increased gastric residual volume – should trigger further investigations, monitoring or intervention.

What is known about using abdominal distension as a clinical sign in the critically ill?

In several cohort studies conducted in the critically ill abdominal distension ~~or bowel distension in the critically ill~~ has been included as ~~one~~ a sign of pathology ~~/symptom~~ in several cohort studies [52,65]. However, in previous studies abdominal distension was identified either with a subjective clinical assessment, where pressure was also present, or by an enlargement of bowel identified radiologically. Whilst intra-abdominal pressure was measured in many of the patients, intra-abdominal hypertension was included as an additional and separate physical feature. The majority of patients with 3 or more concomitant gastrointestinal symptoms had intra-abdominal hypertension [64]. None of these studies report an association between an isolated physical feature of abdominal or bowel distension and death. However, when distension was incorporated with other features, then the presence of 3 or more gastrointestinal symptoms was independently associated with increased mortality [64]. Accordingly, abdominal distension may provide important information as part of a comprehensive clinical assessment until reliable bedside monitoring tools become available.

For Peer Review

ADVICE FOR CLINICIANS AND FUTURE DIRECTIONS

Enteral nutrition remains a component of routine care [11,29] and the authors recommend against waiting for gastrointestinal sounds prior to starting enteral nutrition. Similarly there are no data to suggest daily cursory auscultation *per se* to decide whether enteral nutrition will be of benefit. However, when auscultation is a component of a more comprehensive assessment of gastrointestinal function, and the presence or absence of gastrointestinal sounds is incorporated with other examination features and simple bedside tests auscultation probably has an additive role.

If an increase in abdominal volume occurs without additional features, clinicians can consider a reduction in carbohydrate load, strategies to increase the diversity of the microbiome or measurement of intra-abdominal pressure. None of these interventions are, however, supported by unequivocal data from randomised clinical trials. Intra-abdominal pressure may be useful when there is uncertainty about the need for additional investigation/s that require transport out of the intensive care unit or an intervention that is associated with more than negligible risk.

Whether decisions based on such complex assessment of a constellation of imprecise symptoms, signs and test results improve outcomes remains untested. However, without a proven alternative, it is the opinion of the authors that the use of minimally-invasive and inexpensive assessment methodologies is better than abandoning routine assessment of gastrointestinal function. Because excessively aggressive administration of enteral nutrition may cause harm [31], a daily evaluation with early identification of serious events such as non-obstructive bowel ischemia and critical bowel distension with life-threatening perforation should continue as part of routine care.

Given this, the use of technology to allow prolonged periods of minimally invasive observation, with presence and characteristics of gastrointestinal sounds validated using objective criteria, warrants further evaluation. This technology may be particularly useful in cohorts of patients for whom clinicians remain uncertain about whether to initiate or increase enteral nutrition, such as those with

For Peer Review

hypotension requiring considerable vasopressor support or profound hypoxia or acidosis [11,13,31,32,89]. Future studies should also produce data that informs when to initiate intra-abdominal pressure monitoring and what interventions are effective once intra-abdominal hypertension is identified.

For Peer Review

Figure captions:

Figure 1. Bedside assessment of the gastrointestinal tract

Figure 2. Intra-abdominal pressure is measured in the supine, paralysed patient at end-expiration via a transducer in continuity with the bladder, zeroed at the mid-axillary line. 25ml of fluid is instilled in the empty bladder and the pressure taken after 60 seconds.

For Peer Review

REFERENCES

1. Verghese A. Culture shock--patient as icon, icon as patient. *N Engl J Med.* 2008;359(26):2748-2751.
2. Metkus TS, Kim BS. Bedside Diagnosis in the Intensive Care Unit. Is Looking Overlooked? *Ann Am Thorac Soc.* 2015;12(10):1447-1450.
3. Verghese A, Charlton B, Kassirer JP, Ramsey M, Ioannidis JP. Inadequacies of Physical Examination as a Cause of Medical Errors and Adverse Events: A Collection of Vignettes. *The American journal of medicine.* 2015;128(12):1322-1324.e1323.
4. Hiemstra B, Koster G, Wiersema R, et al. The diagnostic accuracy of clinical examination for estimating cardiac index in critically ill patients: the Simple Intensive Care Studies-I. *Intensive Care Med.* 2019;45(2):190-200.
5. Schneiderman H. Toward a Renascence of Physical Diagnosis in the Intensive Care Unit. *Ann Am Thorac Soc.* 2015;12(10):1423-1424.
6. Pichetshote N, Pimentel M. An Approach to the Patient With Chronic Undiagnosed Abdominal Pain. *Am J Gastroenterol.* 2019;114(5):726-732.
7. Plummer MP, Reintam Blaser A, Deane AM. Gut dysmotility in the ICU: diagnosis and therapeutic options. *Curr Opin Crit Care.* 2019;25(2):138-144.
8. Nguyen T, Frenette AJ, Johanson C, et al. Impaired gastrointestinal transit and its associated morbidity in the intensive care unit. *J Crit Care.* 2013;28(4):537 e511-537.
9. Plummer MP, Kar P, Cousins CE, et al. Critical Illness Is Associated With Impaired Gallbladder Emptying as Assessed by 3D Ultrasound. *Crit Care Med.* 2016;44(9):e790-796.
10. Reintam Blaser A, Malbrain ML, Starkopf J, et al. Gastrointestinal function in intensive care patients: terminology, definitions and management. Recommendations of the ESICM Working Group on Abdominal Problems. *Intensive Care Med.* 2012;38(3):384-394.

For Peer Review

11. Reintam Blaser A, Starkopf J, Alhazzani W, et al. Early enteral nutrition in critically ill patients: ESICM clinical practice guidelines. *Intensive Care Med.* 2017;43(3):380-398.

12. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr.* 2016;40(2):159-211.

13. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr.* 2018.

14. Deane AM, Chapman MJ, Reintam Blaser A, McClave SA, Emmanuel A. Pathophysiology and Treatment of Gastrointestinal Motility Disorders in the Acutely Ill. *Nutr Clin Pract.* 2019;34(1):23-36.

15. Gungabissoon U, Hacquoil K, Bains C, et al. Prevalence, risk factors, clinical consequences, and treatment of enteral feed intolerance during critical illness. *JPEN J Parenter Enteral Nutr.* 2015;39(4):441-448.

16. Reintam Blaser A, Starkopf L, Deane AM, Poeze M, Starkopf J. Comparison of different definitions of feeding intolerance: A retrospective observational study. *Clin Nutr.* 2015;34(5):956-961.

17. McClave SA, Gualdoni J, Nagengast A, Marsano LS, Bandy K, Martindale RG. Gastrointestinal Dysfunction and Feeding Intolerance in Critical Illness: Do We Need an Objective Scoring System? *Curr Gastroenterol Rep.* 2020;22(1):1.

18. Adike A, Quigley EM. Gastrointestinal motility problems in critical care: a clinical perspective. *J Dig Dis.* 2014;15(7):335-344.

19. Kar P, Jones KL, Horowitz M, Chapman MJ, Deane AM. Measurement of gastric emptying in the critically ill. *Clin Nutr.* 2015;34(4):557-564.

20. Elke G, Felbinger TW, Heyland DK. Gastric residual volume in critically ill patients: a dead marker or still alive? *Nutr Clin Pract.* 2015;30(1):59-71.

For Peer Review

21. Moonen PJ, Reintam Blaser A, Starkopf J, et al. The black box revelation: monitoring gastrointestinal function. *Anaesthesiol Intensive Ther.* 2018;50(1):72-81.

22. Hay T, Bellomo R, Rechnitzer T, See E, Ali Abdelhamid Y, Deane AM. Constipation, diarrhea, and prophylactic laxative bowel regimens in the critically ill: A systematic review and meta-analysis. *J Crit Care.* 2019;52:242-250.

23. Reignier J, Mercier E, Le Gouge A, et al. Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial. *JAMA.* 2013;309(3):249-256.

24. Rice TW, Wheeler AP, Thompson BT, et al. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. *Jama.* 2012;307(8):795-803.

25. Arabi YM, Aldawood AS, Haddad SH, et al. Permissive Underfeeding or Standard Enteral Feeding in Critically Ill Adults. *N Engl J Med.* 2015;372(25):2398-2408.

26. Chapman M, Peake SL, Bellomo R, et al. Energy-Dense versus Routine Enteral Nutrition in the Critically Ill. *N Engl J Med.* 2018;379(19):1823-1834.

27. Fetterplace K, Gill BMT, Chapple LS, Presneill JJ, MacIsaac C, Deane AM. Systematic Review With Meta-Analysis of Patient-Centered Outcomes, Comparing International Guideline-Recommended Enteral Protein Delivery With Usual Care. *JPEN J Parenter Enteral Nutr.* 2019.

28. Patel JJ, Codner P. Controversies in Critical Care Nutrition Support. *Crit Care Clin.* 2016;32(2):173-189.

29. Patel JJ, Martindale RG, McClave SA. Controversies Surrounding Critical Care Nutrition: An Appraisal of Permissive Underfeeding, Protein, and Outcomes. *JPEN J Parenter Enteral Nutr.* 2018;42(3):508-515.

30. Wernerman J, Christopher KB, Annane D, et al. Metabolic support in the critically ill: a consensus of 19. *Crit Care.* 2019;23(1):318.

For Peer Review

31. Reignier J, Boisrame-Helms J, Brisard L, et al. Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2). *Lancet.* 2018;391(10116):133-143.

32. Patel JJ, Rice T, Heyland DK. Safety and Outcomes of Early Enteral Nutrition in Circulatory Shock. *JPEN J Parenter Enteral Nutr.* 2020.

33. Caddell KA, Martindale R, McClave SA, Miller K. Can the intestinal dysmotility of critical illness be differentiated from postoperative ileus? *Curr Gastroenterol Rep.* 2011;13(4):358-367.

34. Cannon WB. AUSCULTATION OF THE RHYTHMIC SOUNDS PRODUCED BY THE STOMACH AND INTESTINES. *American Journal of Physiology-Legacy Content.* 1905;14(4):339-353.

35. Deane A, Chapman MJ, Fraser RJ, Bryant LK, Burgstad C, Nguyen NQ. Mechanisms underlying feed intolerance in the critically ill: Implications for treatment. *World J Gastroenterol.* 2007;13(29):3909-3917.

36. Tomomasa T, Morikawa A, Sandler RH, et al. Gastrointestinal sounds and migrating motor complex in fasted humans. *Am J Gastroenterol.* 1999;94(2):374-381.

37. Luiking YC, Reijden ACvd, Henegouwen GPvB, Akkermans LMA. Migrating motor complex cycle duration is determined by gastric or duodenal origin of phase III. *American Journal of Physiology-Gastrointestinal and Liver Physiology.* 1998;275(6):G1246-G1251.

38. Cullen PT, Storey BE, Cuschieri A, Campbell FC. Detection of clustered gastrointestinal contractions in partial intestinal obstruction by surface vibration analysis. *Ann Surg.* 1989;210(2):234-238.

39. Mansy HA, Sandler RH. Detection and analysis of gastrointestinal sounds in normal and small bowel obstructed rats. *Med Biol Eng Comput.* 2000;38(1):42-48.

40. Ross JT, Matthay MA, Harris HW. Secondary peritonitis: principles of diagnosis and intervention. *BMJ.* 2018;361:k1407.

41. West M, Klein MD. Is abdominal auscultation important? *Lancet.* 1982;2(8310):1279.

For Peer Review

42. Felder S, Margel D, Murrell Z, Fleshner P. Usefulness of bowel sound auscultation: a prospective evaluation. *J Surg Educ.* 2014;71(5):768-773.

43. Read TE, Brozovich M, Andujar JE, Ricciardi R, Caushaj PF. Bowel Sounds Are Not Associated With Flatus, Bowel Movement, or Tolerance of Oral Intake in Patients After Major Abdominal Surgery. *Dis Colon Rectum.* 2017;60(6):608-613.

44. Breum BM, Rud B, Kirkegaard T, Nordentoft T. Accuracy of abdominal auscultation for bowel obstruction. *World J Gastroenterol.* 2015;21(34):10018-10024.

45. Du X, Allwood G, Webberley KM, Osseiran A, Marshall BJ. Bowel Sounds Identification and Migrating Motor Complex Detection with Low-Cost Piezoelectric Acoustic Sensing Device. *Sensors (Basel).* 2018;18(12).

46. Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. *JAMA Surg.* 2017;152(3):292-298.

47. Hedrick TL, McEvoy MD, Mythen MMG, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Postoperative Gastrointestinal Dysfunction Within an Enhanced Recovery Pathway for Elective Colorectal Surgery. *Anesth Analg.* 2018;126(6):1896-1907.

48. Chapman SJ, Thorpe G, Vallance AE, et al. Systematic review of definitions and outcome measures for return of bowel function after gastrointestinal surgery. *BJS Open.* 2019;3(1):1-10.

49. Allwood G, Du X, Webberley KM, Osseiran A, Marshall BJ. Advances in Acoustic Signal Processing Techniques for Enhanced Bowel Sound Analysis. *IEEE Rev Biomed Eng.* 2019;12:240-253.

50. Spiegel BM, Kaneshiro M, Russell MM, et al. Validation of an acoustic gastrointestinal surveillance biosensor for postoperative ileus. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract.* 2014;18(10):1795-1803.

For Peer Review

51. Kaneshiro M, Kaiser W, Pourmorady J, et al. Postoperative Gastrointestinal Telemetry with an Acoustic Biosensor Predicts Ileus vs. Uneventful GI Recovery. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract.* 2016;20(1):132-139; discussion 139.

52. Reintam Blaser A, Poeze M, Malbrain ML, et al. Gastrointestinal symptoms during the first week of intensive care are associated with poor outcome: a prospective multicentre study. *Intensive Care Med.* 2013;39(5):899-909.

53. Reintam A, Parm P, Kitus R, Kern H, Starkopf J. Gastrointestinal symptoms in intensive care patients. *Acta Anaesthesiol Scand.* 2009;53(3):318-324.

54. Dive A, Moulart M, Jonard P, Jamart J, Mahieu P. Gastroduodenal motility in mechanically ventilated critically ill patients: a manometric study. *Crit Care Med.* 1994;22(3):441-447.

55. Chapman M, Fraser R, Vozzo R, et al. Antro-pyloro-duodenal motor responses to gastric and duodenal nutrient in critically ill patients. *Gut.* 2005;54(10):1384-1390.

56. Chapman MJ, Deane AM. Gastrointestinal dysfunction relating to the provision of nutrition in the critically ill. *Curr Opin Clin Nutr Metab Care.* 2015;18(2):207-212.

57. Heyland DK, Tougas G, King D, Cook DJ. Impaired gastric emptying in mechanically ventilated, critically ill patients. *Intensive Care Med.* 1996;22(12):1339-1344.

58. Chapple LA, Deane A. From dysmotility to virulent pathogens: implications of opioid use in the ICU. *Curr Opin Crit Care.* 2018;24(2):118-123.

59. Ching SS, Tan YK. Spectral analysis of bowel sounds in intestinal obstruction using an electronic stethoscope. *World J Gastroenterol.* 2012;18(33):4585-4592.

60. Gu Y, Lim HJ, Moser MA. How useful are bowel sounds in assessing the abdomen? *Dig Surg.* 2010;27(5):422-426.

61. Li B, Tang S, Ma YL, Tang J, Wang B, Wang JR. Analysis of bowel sounds application status for gastrointestinal function monitoring in the intensive care unit. *Critical care nursing quarterly.* 2014;37(2):199-206.

For Peer Review

62. Metheny NA, Mills AC, Stewart BJ. Monitoring for intolerance to gastric tube feedings: a national survey. *Am J Crit Care.* 2012;21(2):e33-40.

63. McClave SA, Snider HL, Lowen CC, et al. Use of residual volume as a marker for enteral feeding intolerance: prospective blinded comparison with physical examination and radiographic findings. *JPEN J Parenter Enteral Nutr.* 1992;16(2):99-105.

64. Padar M, Starkopf J, Uusvel G, Reintam Blaser A. Gastrointestinal failure affects outcome of intensive care. *J Crit Care.* 2019;52:103-108.

65. Reintam Blaser A, Regli A, De Keulenaer B, et al. Incidence, Risk Factors, and Outcomes of Intra-Abdominal Hypertension in Critically Ill Patients-A Prospective Multicenter Study (IROI Study). *Crit Care Med.* 2019;47(4):535-542.

66. Inderjeeth AJ, Webberley KM, Muir J, Marshall BJ. The potential of computerised analysis of bowel sounds for diagnosis of gastrointestinal conditions: a systematic review. *Syst Rev.* 2018;7(1):124.

67. Goto J, Matsuda K, Harii N, Moriguchi T, Yanagisawa M, Sakata O. Usefulness of a real-time bowel sound analysis system in patients with severe sepsis (pilot study). *J Artif Organs.* 2015;18(1):86-91.

68. Reintam Blaser A, Starkopf J, Malbrain ML. Abdominal signs and symptoms in intensive care patients. *Anaesthesiol Intensive Ther.* 2015;47(4):379-387.

69. Reintam Blaser A, Starkopf J, Moonen PJ, Malbrain M, Oudemans-van Straaten HM. Perioperative gastrointestinal problems in the ICU. *Anaesthesiol Intensive Ther.* 2018;50(1):59-71.

70. Talley NJ, O'Connor S. *Clinical examination : a systematic guide to physical diagnosi.* 6th International ed ed: Elsevier Australia; 2010.

71. Blaser AR, Bjorck M, De Keulenaer B, Regli A. Abdominal compliance: A bench-to-bedside review. *J Trauma Acute Care Surg.* 2015;78(5):1044-1053.

For Peer Review

72. Malagelada JR, Accarino A, Azpiroz F. Bloating and Abdominal Distension: Old Misconceptions and Current Knowledge. *Am J Gastroenterol.* 2017;112(8):1221-1231.

73. Kirkpatrick AW, Roberts DJ, De Waele J, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med.* 2013;39(7):1190-1206.

74. Sugrue M, Bauman A, Jones F, et al. Clinical examination is an inaccurate predictor of intraabdominal pressure. *World J Surg.* 2002;26(12):1428-1431.

75. De Waele JJ, Kimball E, Malbrain M, et al. Decompressive laparotomy for abdominal compartment syndrome. *Br J Surg.* 2016;103(6):709-715.

76. De Laet IE, Malbrain M, De Waele JJ. A Clinician's Guide to Management of Intra-abdominal Hypertension and Abdominal Compartment Syndrome in Critically Ill Patients. *Crit Care.* 2020;24(1):97.

77. Petro CC, Raigani S, Fayezizadeh M, et al. Permissible Intraabdominal Hypertension following Complex Abdominal Wall Reconstruction. *Plast Reconstr Surg.* 2015;136(4):868-881.

78. Burgstad CM, Besanko LK, Deane AM, et al. Sucrose malabsorption and impaired mucosal integrity in enterally fed critically ill patients: a prospective cohort observational study. *Crit Care Med.* 2013;41(5):1221-1228.

79. Deane AM, Rayner CK, Keeshan A, et al. The effects of critical illness on intestinal glucose sensing, transporters, and absorption. *Crit Care Med.* 2014;42(1):57-65.

80. Ali Abdelhamid Y, Cousins CE, Sim JA, et al. Effect of Critical Illness on Triglyceride Absorption. *JPEN J Parenter Enteral Nutr.* 2015;39(8):966-972.

81. Savino P. Knowledge of Constituent Ingredients in Enteral Nutrition Formulas Can Make a Difference in Patient Response to Enteral Feeding. *Nutr Clin Pract.* 2018;33(1):90-98.

For Peer Review

82. Qiu C, Chen C, Zhang W, et al. Fat-Modified Enteral Formula Improves Feeding Tolerance in Critically Ill Patients: A Multicenter, Single-Blind, Randomized Controlled Trial. *JPEN J Parenter Enteral Nutr.* 2017;41(5):785-795.

83. de Brito-Ashurst I, Preiser JC. Diarrhea in Critically Ill Patients: The Role of Enteral Feeding. *JPEN J Parenter Enteral Nutr.* 2016;40(7):913-923.

84. Shimizu K, Yamada T, Ogura H, et al. Synbiotics modulate gut microbiota and reduce enteritis and ventilator-associated pneumonia in patients with sepsis: a randomized controlled trial. *Crit Care.* 2018;22(1):239.

85. Oami T, Chihade DB, Coopersmith CM. The microbiome and nutrition in critical illness. *Curr Opin Crit Care.* 2019;25(2):145-149.

86. McClave SA, Martindale RG. Why do current strategies for optimal nutritional therapy neglect the microbiome? *Nutrition (Burbank, Los Angeles County, Calif).* 2019;60:100-105.

87. Hay T, Deane AM, Rechnitzer T, et al. The hospital-based evaluation of laxative prophylaxis in ICU (HELP-ICU): A pilot cluster-crossover randomized clinical trial. *J Crit Care.* 2019;52:86-91.

88. Heinonen T, Ferrie S, Ferguson C. Gut function in the intensive care unit - What is 'normal'? *Aust Crit Care.* 2020;33(2):151-154.

89. Patel JJ, Kozeniecki M, Peppard WJ, et al. Phase 3 Pilot Randomized Controlled Trial Comparing Early Trophic Enteral Nutrition With "No Enteral Nutrition" in Mechanically Ventilated Patients With Septic Shock. *JPEN J Parenter Enteral Nutr.* 2019.

For Peer Review

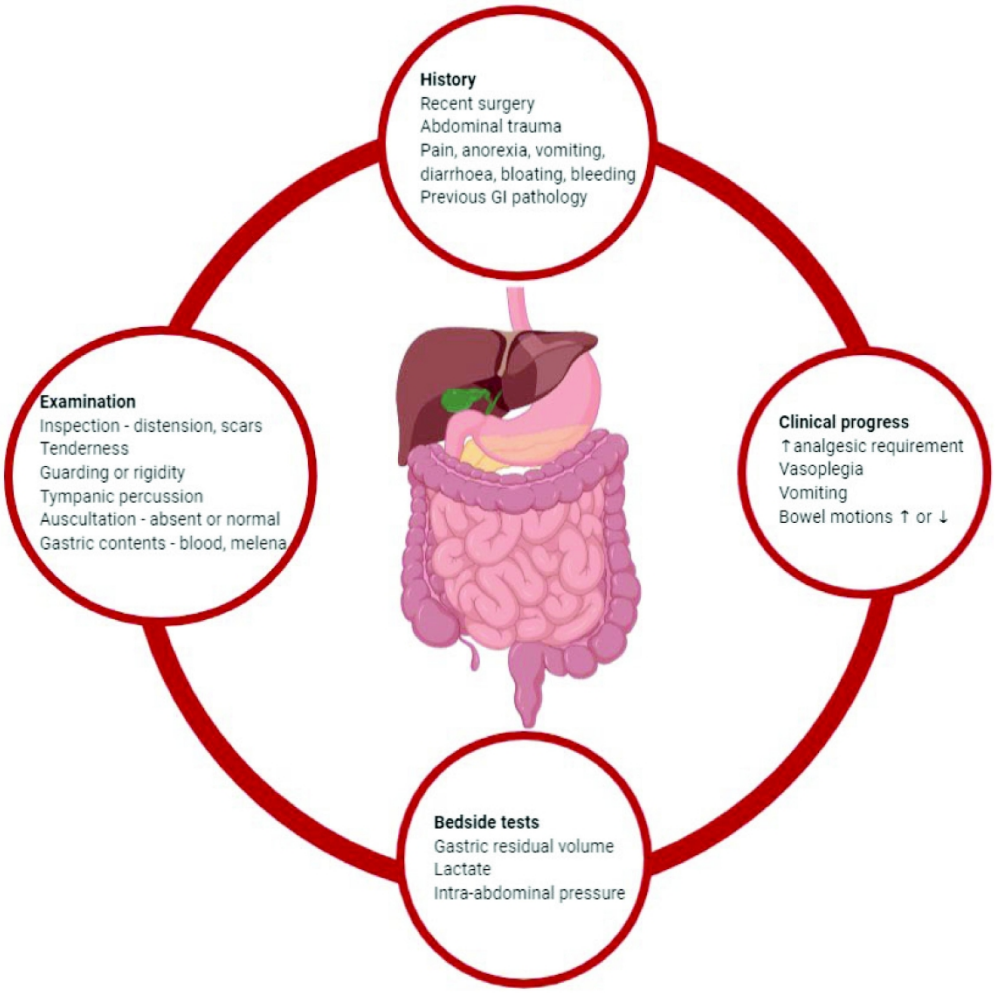

Figure 1. Bedside assessment of the gastrointestinal tract

179x178mm (600 x 600 DPI)

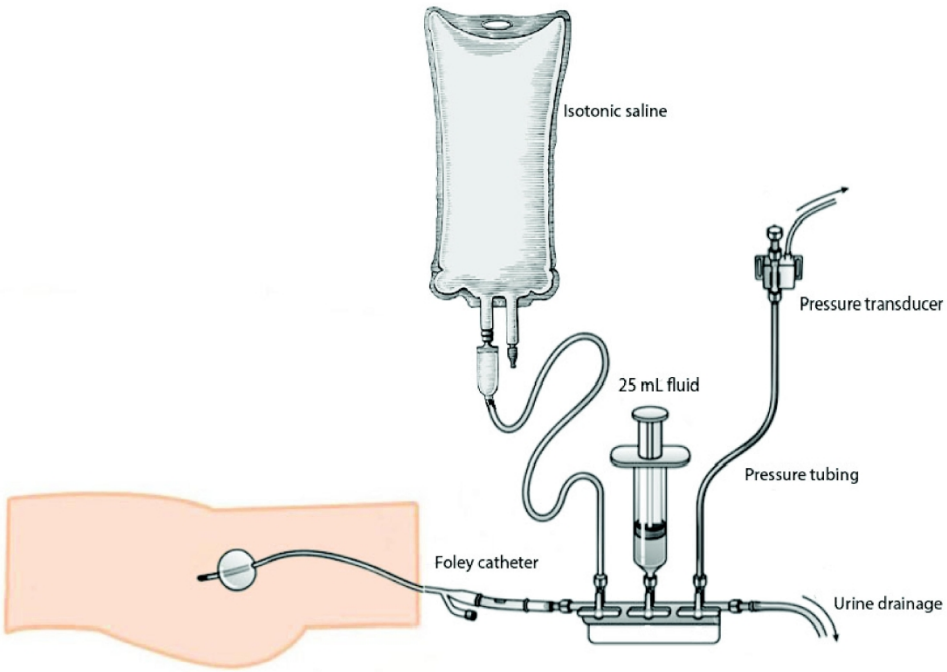

Figure 2. Intra-abdominal pressure is measured in the supine, paralysed patient at end-expiration via a transducer in continuity with the bladder, zeroed at the mid-axillary line. 25ml of fluid is instilled in the empty bladder and the pressure taken after 60 seconds.

174x127mm (600 x 600 DPI)