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Taste, Hunger, and Satiety in Critical Illness: A Scoping Review

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Abstract

This review aims to explore the relationship between taste, hunger, and satiety and their influence on outcomes for patients in intensive care units (ICUs). A literature search was conducted using MeSH (Medical Subject Headings) and key terms across PubMed Online, Google Scholar, the Cochrane Library, Embase, and UpToDate between February 28, 2003 and May 19, 2023, following guidance from the EQUATOR (Enhancing the Quality and Transparency of Health Research) network. Inclusion criteria comprised English-language articles reporting outcome studies of ICU patients related to taste, hunger, or satiety, stratified by acute or recovery phases. The search yielded 943 citations. After reviewing abstracts, 10 full-text articles were retrieved and included, though the quality of evidence was limited to observational studies. Findings indicate that patients commonly experience early satiety and decreased appetite during the acute phase of critical illness, which typically improves by three months post-ICU. However, appetite dysregulation may persist beyond this period. Reduced appetite, a common feature of Post-Intensive Care Syndrome (PICS), was associated with long-term low mood. While taste alterations were reported, no studies addressed their restoration or impact. These findings highlight the need for further primary research into taste alterations and their effects on the patient experience among critical illness survivors. This review underscores the limited research available on how changes in taste, hunger, and satiety affect ICU survivors and suggests that additional studies are necessary to further explore these aspects.

Keywords: Critical care; Hunger; Intensive care; Intensive care nursing; Nil by mouth; Nutrition in intensive care; Post-intensive care syndrome; Recovery; Rehabilitation; Satiety; Sensory deprivation; Taste.

Introduction

Admission to an intensive care unit (ICU) poses a substantial challenge to individuals that extends beyond survival. Patients not only face severe physical illness, but also find themselves in an unfamiliar, isolated, and sterile environment. This can disrupt the body's natural

equilibrium and expose patients to both physical and psychological sequelae.

While a wealth of research exists on ICU rehabilitation,^[1] there is a lack of focus on the patient experience and the influence of the clinical environment. One article examining the impact of an ICU stay on patients drew parallels with criteria published by Amnesty International for psy-

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chological torture,^[2] citing deprivation of food, water, sensory input, and sleep, alongside prolonged exposure to noise.^[3] Many of these factors are commonly experienced by critically ill ICU patients.

Post-Intensive Care Syndrome (PICS) has become associated with prolonged exposure to these stressors. It encompasses a range of holistic symptoms experienced during the acute admission that persist into the recovery phase. These include acquired weakness, cognitive or brain dysfunction, and mental illness. Among those who experience PICS, only 50% return to work within a year, reflecting a significant burden of morbidity.^[4] The ABCDE bundle (Awakening and Breathing Coordination, Delirium monitoring/management, and Early exercise/mobility) was introduced to support the identification of this syndrome, with a particular focus on the prevention and detection of delirium.^[5] Sensory stimulation and re-orientation are recognized as protective factors against ICU delirium.^[6] Furthermore, maintaining optimal nutritional status has been recommended for managing both PICS and delirium.^[5]

As a result, there may be an opportunity to enhance patient satisfaction, orientation, and physical optimization by understanding their experiences of hunger and satiety, as well as their interaction with taste, an often-overlooked sense. This narrative literature review aims to evaluate the existing clinical research on this topic and to provide recommendations for future studies. Definitions of key terms such as critical illness, intensive care unit, acute, and recovery periods are presented in the supplementary section of the appendix [Supplementary Table 1].

Aim

The aim of this research was to enhance our understanding of the relationship between taste, hunger, satiety, and critical illness, and to inform clinical practice and guide future research.

Objectives

- To systematically evaluate the literature addressing taste alterations during critical illness and the recovery period, and to present the findings narratively.
- To systematically evaluate the literature addressing hunger and satiety during critical illness and the recovery period, and to present the findings narratively.

Materials and Methods

Data Sources and Searches

Searches utilizing MESH (Medical Subject Headings) and key terms were conducted using PubMed Online, Google Scholar, the Cochrane Library, Embase, and UpToDate, between 28 February 2003 and 19 May 2023 (Fig. 1).

Study Selection

Inclusion Criteria

- Primary research of any hierarchical level.
- Research conducted in either level 2 or level 3 care settings (high dependency and intensive care units).^[7]
- Inclusion of at least one of the following as outcomes (or related terms with equivalent meaning). These did not have to be primary outcomes:
 - Taste
 - Hunger
 - Satiety

Exclusion Criteria

- Articles or reviews lacking primary research.
- Insufficient detail to ascertain intervention via open-access platforms.
- Studies conducted in level 1 care settings.
- Failure to meet inclusion criteria.

Data Extraction

Data were collected using a standardized form, including study design, country of origin, setting, selection criteria, participant characteristics, and outcome measures. A total of ten papers were included in the original review. One additional paper was identified during journal review and subsequently added, resulting in a total of eleven papers.

Taste and Critical Illness

Taste is one of the five human senses that allows us to interact with and interpret the world around us. While it is inherently linked to the food we consume for survival, for many, taste also represents pleasure, emotion, and memory. As such, the deprivation of this sense can be profoundly distressing.

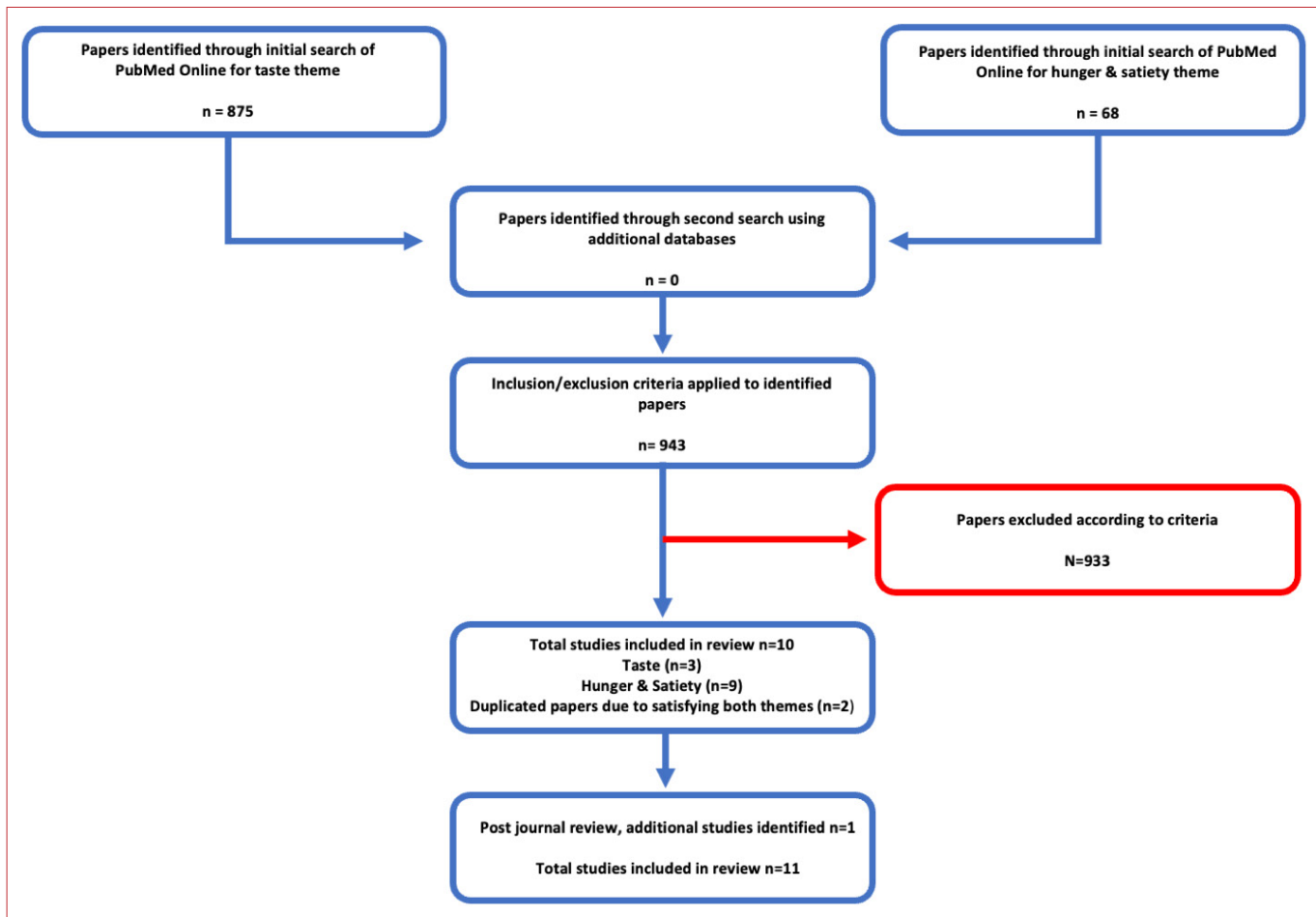


Figure 1. Flow diagram illustrating the study selection process.

The literature search identified three papers that included taste as an outcome during either the acute or recovery phases of critical illness. Although all three studies considered taste as an outcome, none identified it as a primary focus.

Acute Phase

The earliest study, conducted in 1999 by Tanimoto et al.,^[8] utilized a pre/post study design alongside qualitative interviews. Ten healthy volunteers were admitted to an ICU for four days to examine the psychological and physiological effects of the environment. The study found that participants experienced significantly increased fatigue and confusion ($p < 0.05$), and most reported periods of depression ($p < 0.01$). Taste was described as being “altered” among participants. The authors concluded that in order to improve the patient experience, interventions should target the five senses, particularly sight, sound, and taste.

A prospective observational study by Moisey et al.^[9] assessing the adequacy of nutritional intake in 19 critically ill adults over 125 days following liberation from mechanical ventilation, and explored barriers to eating among those receiving an oral diet. A total of 102 barriers were reported, of which 11% were related to changes in taste. The identification of taste alteration as a barrier supports Tanimoto’s^[8] assertions, suggesting that disruption of this sense may negatively impact both acute illness and recovery by reducing nutritional intake.

However, there are limitations to the conclusions that can be drawn. Both studies had small sample sizes ($n=10$ and $n=19$, respectively) and were conducted in single-center settings,^[8,9] which limits the generalizability of the findings. Furthermore, the study by Moisey et al.^[9] was a feasibility study and lacked a comparison group. In Tanimoto et al.’s study,^[8] although the pre/post design offered a basic indication of trajectory and its significance, the frequency of taste alteration was not measured; instead,

it was extrapolated from qualitative data. As a result, the prevalence of taste changes was not determined. Finally, although taste changes were noted as a barrier in both studies, they did not provide detail on how patients' taste was altered.^[8,9] This information is crucial to guide future research and the development of targeted interventions.

Recovery Phase

Merriweather et al.'s^[10] 2016 qualitative study addresses some of the gaps identified in the previous research. It explored patients' experiences of eating during the recovery period, using observations and semi-structured interviews analyzed through grounded theory methodology. Patients reported that taste changes became particularly pronounced in the first few days following transfer from the ICU to the ward. Some described food as too bland or too salty, while others noted a metallic taste. Many simply felt that food no longer tasted the same as it had before admission. This was especially distressing when patients attempted to eat foods they had previously enjoyed, often resulting in "food aversions" that reduced access to desirable foods and flavors.^[10] The study concluded that, for many patients, eating ceased to be a pleasurable experience and instead became a chore, something necessary to fuel the body. The authors criticized the medical system's focus on treating physical illness while neglecting the principles of holistic care. They also emphasized the importance of incorporating patient-led outcomes, such as taste, to support effective rehabilitation. These findings align with the recommendations of both Tanimoto and Moisey et al.^[8-10]

Hunger and Satiety in Critical Illness

Ten studies were identified that included hunger and/or satiety as outcomes during either the acute or recovery phases of critical illness.

Acute Phase

Moisey et al.^[9] in 2021 concluded that the most frequently reported barrier to eating in recently extubated patients was a reduction in appetite (24%, n=77). Additionally, 15% of patients reported experiencing early satiety, further limiting their intake. Supporting these findings, Li et al.^[11] examined patient-reported symptoms in individuals who had previously undergone mechanical ventilation. They found that moderate-intensity thirst, tiredness, hunger, generalized discomfort, and depressed mood were reported by approximately 30% of patients after extubation (n=15). Hunger was the fifth most commonly

reported symptom out of the nine analyzed. Moreover, hunger was significantly associated with thirst, with a moderate strength of correlation ($r=0.58$). The authors suggested that more attention should be paid to managing the wide range of symptoms ICU patients experience, including hunger, in order to improve patient comfort, especially as many of these symptoms are interrelated but not often measured together in research.

To support more accurate quantification and identification of these symptoms, Baumstarck et al.^[12] in 2019 developed an 18-item questionnaire, the IPREA (Inconforts des Patients de REAnimation) tool. This instrument includes hunger as one of the 18 symptoms assessed. A multicenter, cluster-randomized, parallel-group validation study was conducted (n=944), which found the questionnaire to be both statistically valid and user-friendly. Notably, the three greatest discomforts reported by patients were sleep deprivation, thirst, and perfusion lines/devices. The least frequently reported discomforts were visiting hours, hunger, and isolation. This reduced reporting of hunger supports the findings of Moisey^[9] and, to some extent, Li et al.,^[11] with hunger being a less commonly reported symptom compared to others measured.

In contrast, a 2001 study using the Edmonton Symptom Assessment Scale (ESAS) found that 55% of patients (n=100) experienced unsatisfied hunger, with nearly half of these reporting it to a severe degree.^[13] Hunger was reported almost as frequently as pain (56%). The three most frequently reported symptoms were discomfort, thirst, and difficulty sleeping, remarkably similar to the findings of the IPREA study.^[12,13] This conflicting evidence suggests that further research is needed to clarify the significance of this trend and that patients' experiences may be subject to a high degree of variability.

The cause of reduced appetite during an ICU stay is believed to be multifactorial. Critical illness itself presents a compelling explanation. A study by Nematy et al.^[14] in 2006 investigated the concentrations of appetite-regulating hormones (ghrelin and pancreatic peptide YY (PYY)) in ICU patients. Additionally, they measured patients' self-reported appetite levels alongside their actual food intake. They found that ghrelin levels, an appetite-inducing hormone, were significantly reduced. Furthermore, levels of PYY, which has an inhibitory effect on appetite, was significantly increased. Notably, these hormone levels were observed to trend back toward normal within

the final three weeks of ICU admission. A further study by Karaca et al.^[15] in 2022 which examined ghrelin trends over the course of ICU stays, also showed a decline over time; however, this finding was not statistically significant. Together, these studies support the concept that critical illness leads to appetite dysregulation, contributing to reduced nutritional intake. These findings also raise the question of whether the variability seen in hunger-related outcomes may stem from a failure to stratify results by illness severity. However, environmental factors have also been identified as contributing barriers. Patients reported increased nausea and vomiting, dislike of hospital food, uncomfortable eating positions, the presence of lines and devices, and strict mealtimes as additional obstacles to adequate intake.^[9,10]

Recovery Phase

The findings of Nematy et al.^[14] in 2006 suggested that as a person recovers from their ICU stay, appetite should return to baseline as physiological systems undergo allostasis. However, this is not always consistent with patient experiences.

From patient interviews, Merriweather et al.^[10] in 2016 found that loss of appetite was the most frequently reported physiological symptom at three months post-ICU discharge. Additionally, patients reported that early satiety continued to negatively impact their nutritional intake. These findings are consistent with several acute-phase studies.^[9,11] and they suggest that appetite dysregulation may be prolonged in this patient population.

Merriweather^[16] expanded on this research in 2018 through a cohort study (n=193), aiming to examine appetite scores during the recovery phase of critical illness and their association with systemic inflammation, a theory previously explored by Nematy et al.^[14] The study concluded that a greater number of days spent in an acute hospital following ICU admission was associated with poorer appetite scores ($p=0.03$). Furthermore, patients' visual analogue scale (VAS) scores for appetite showed significant improvement at three months post-discharge compared to one week ($p<0.01$). Regarding the potential impact of inflammation, the study found that elevated levels of C-reactive protein (CRP), an acute-phase reactant protein in the blood, were significantly associated with reduced appetite one week post-ICU discharge ($p=0.01$), but not at three months.^[16] Although CRP is a non-specific inflammatory marker and can be elevated for various reasons, these findings strongly support the

hypothesis proposed by Nematy et al.^[14] in 2006 that inflammation impairs appetite regulation.^[16]

However, the hypothesis that appetite and early satiety improve by three months post-discharge is challenged by other studies, which suggest that significant dysregulation persists beyond this timeframe. For example, Chapple et al.^[17] in 2019 found that ICU survivors consumed significantly fewer calories compared to healthy individuals during a 24-hour dietary recall conducted three months post-admission. Additionally, ICU survivors reported experiencing reduced satiety compared to healthy controls after consuming the same quantity of food ($p=0.041$). These findings contradict earlier studies that reported increased appetite with recovery time and suggested that patients tended to experience increased satiety with reduced intake.^[14,16] While recall bias may have contributed to some discrepancies, this explanation alone seems insufficient and raises the possibility of differing sample population characteristics or other unmeasured factors.^[17] Furthermore, the results prompt consideration of whether additional, unidentified variables are influencing patients' reduced caloric intake despite the presence of strong hunger cues.

Kitayama et al.'s^[18] work supports the idea of prolonged appetite dysregulation that persists after ICU discharge. They examined the relationship between appetite reduction and depression using validated questionnaires (the Short Nutritional Assessment Questionnaire and the Hospital Anxiety Depression Scale) in 648 Japanese patients up to 12 months post-ICU discharge. This was a secondary analysis from the previously reported SMAP-HoPe study (Survey of Multicenter Assessment with Post-Intensive Care Syndrome for Home Living Patients). They found that the prevalence of appetite loss at 12 months was 25.4%, and that greater severity of depression was associated with a higher probability of appetite loss ($p\leq0.001$). This could be interpreted as patients being more susceptible to long-term appetite loss following an ICU stay. However, it is unclear whether this reduction in appetite is a consequence of low mood (as appetite loss is a recognized symptom of depression), or whether prolonged dysregulation of physiological appetite mechanisms leads to reduced intake, which in turn contributes to low mood^[14,16]—a classic “chicken or the egg” conundrum. Most likely, it is a combination of these factors. Nevertheless, this research presents compelling evidence that impaired appetite is relatively common 12 months after ICU discharge and is associated with de-

pression. Mental health disturbances are a recognized component of PICS,^[5] and this research suggests that focusing on appetite and pleasurable food experiences could aid in the management of this syndrome and help reduce morbidity.

Discussion

This literature review identified ten primary research studies that included taste, hunger, or satiety as outcomes in critically ill patients, either during the acute or recovery phase of their illness.

Taste

Although there is a lack of evidence on taste, some common findings emerged among the three studies identified. There was a consensus that taste can be altered during critical illness; however, the studies varied in the level of insight they provided. Taste changes appeared to be most prominent during the acute phase of illness and in the initial days following step-down to ward care.^[8–10] Only one study offered detailed insight into how taste may change in these patients.^[10] Taste alteration varies considerably: some patients reported food as too bland, others as overly flavorful, and some described a metallic aftertaste, potentially linked to medication side effects or other unmeasured factors present in the ICU environment. Without the measurement of these crucial confounding variables, it is difficult to fully interpret the significance of these findings.

The number of factors that may influence a patient's taste while admitted to the ICU is extensive; however, it is crucial to consider these when interpreting the evidence presented. A significant variable is the underlying medical condition leading to admission. Numerous disease states can result in critical illness, but certain conditions are more commonly associated with dysgeusia than others. Neurological conditions that disrupt the gustatory pathway, both in the brain and the peripheral nervous system, can lead to taste alteration or loss. Examples include stroke, traumatic brain injury, and delirium, to name a few.^[19–21] Cancer patients also experience higher rates of dysgeusia, both due to the cancer itself and the treatments administered.^[19,20,22–24] The ability of viral illnesses to disrupt taste perception came to public attention during the Coronavirus Disease 2019 (COVID-19) pandemic.^[19–21,25] Other disease states associated with taste disturbances include endocrine disorders, nutri-

ent deficiencies, liver and renal failure, rheumatological conditions, and major affective disorders.^[19–21] While this list is not exhaustive, it highlights the diverse causes of critical illness, and their respective treatments, which can influence the data collected.

Medications commonly administered in the ICU have also been associated with taste disturbances. These include antibiotics, muscle relaxants, antihypertensives, diuretics, anti-arrhythmics, hypnotics, antipsychotics, chemotherapy agents, anti-epileptics, antivirals, and bronchodilators.^[19–21,25–29] Another influencing factor is the presence of associated patient symptoms such as thirst, pain, and nausea, which are often inextricably linked to taste perception.^[30–32] A separate literature search was conducted on olfaction and thirst in critical illness, given their close relationship with taste. However no new studies meeting the inclusion criteria were identified. We do, however, recognize the growing body of research focusing on thirst as a primary outcome in ICU patients.^[33] Finally, increased age is also a risk factor, due to factors such as loss of taste buds, endocrinological changes, a higher risk of neurodegenerative disease, and polypharmacy.^[19–21,29,34] As the population ages, the average age of ICU patients is rising, with individuals aged 70 to 74 currently being the most represented group.^[35] It is important to consider all of these factors, which collectively shape the ICU environment and the experience of the critically ill patient. Future studies should aim to measure these variables to allow for greater accuracy of results.

Ultimately, it is difficult to draw any substantial conclusions from this research. Although the studies were prospective in nature, reducing historical bias, all three featured small sample sizes and were conducted at single centers, limiting the generalizability of the findings. Furthermore, only one of the papers included a control group,^[8] making it impossible to confirm whether the findings reflect a broader trend or are isolated, non-reproducible results. Additionally, because taste was not the primary outcome measured, the level of detail in the published results is limited. The studies focused on barriers to caloric intake rather than taking a patient-centered approach that considers how taste might satisfy cravings and enhance the pleasure of eating.

Primary research that includes patient-reported outcomes would provide a deeper understanding of patients' needs, enabling the development of targeted interventions. These could involve eliminating potential

causative factors, such as specific medications, associated symptoms, or commonly aversive flavors. This could also involve introducing agents that stimulate taste to aid in rehabilitation and recovery, such as flavored gels, foams, or orodispersible films. If found to positively influence taste, hunger, and satiety, such interventions could lead to improved physical and mental health outcomes, particularly during the extended recovery period.

Finally, Moisey et al.^[9] in 2021 excluded patients receiving enteral or parenteral nutrition from their study. We therefore do not have sufficient evidence to determine whether nil by mouth patients experience food cravings or specific flavor desires during their illness. This patient group is unexplored in the literature and may present opportunities for innovative, safe interventions to stimulate taste. Such interventions would align with the early recommendations of Tanimoto et al.^[8] in 1999, who emphasized that the senses should be prioritized to enhance patient mood, increase vigor, and potentially reduce the prevalence of PICS and ICU delirium.

Hunger and Satiety

When considering hunger, there is a trend suggesting that many patients experience reduced appetite during both the acute and recovery phases of critical illness. Furthermore, data indicate that appetite tends to increase as patients move further from the acute phase. This may be attributable to a decrease in inflammatory mediators and the re-regulation of hormones, such as ghrelin and PYY.^[14,16] However, there is disagreement regarding the duration of appetite dysregulation, with some evidence suggesting it may persist well beyond three months after ICU discharge.^[17,18] Additionally, there is compelling evidence that appetite dysregulation is significantly associated with mood disturbances, a recognized feature of PICS.^[18]

Satiety is less frequently studied, with fewer research papers including it as a measured outcome. Among those that did, the majority suggest that patients experience early satiety, particularly during the initial reintroduction of oral intake and the step-down to ward care.^[9,10] However, similar to hunger, the effect of critical illness on satiety during the recovery period has not been thoroughly assessed. An important observation is that symptoms reported by patients often appear to be interrelated. Pain, thirst, and discomfort may all contribute to reduced appetite and early satiety. Identifying these symptoms, potentially through the use of validated questionnaires,

could help improve understanding of the patient experience and guide strategies to enhance long-term outcomes.^[8,11–13]

There are apparent gaps in the literature. Firstly, although a link between symptoms experienced in the ICU has been suggested by many, Li et al.^[11] in 2006 was the only study to statistically assess the strength of these correlations.^[17] Secondly, as highlighted in the discussion on taste, further qualitative research is needed to explore how hunger and appetite are affected during both the acute and recovery phases. This would provide valuable context to support existing quantitative findings. Thirdly, patient-reported outcome questionnaires have been shown to be both easy to administer and effective in identifying distressing symptoms.^[12,13] Experimental research involving patients, beyond these initial feasibility studies, would be beneficial, perhaps in the form of a pre/post cohort study, to examine the impact on patient outcomes. Depending on the findings, this approach could be incorporated into standard practice with minimal institutional effort.

Finally, as previously alluded to, a neglected patient group consists of those with mandated oral restrictions, i.e. nil by mouth. It should be considered whether their experience of hunger and satiety is independent of the route of nutrient delivery (enteral vs. parenteral feeding). This could help determine whether patients experience discomfort due to unmet physiological cues, despite receiving their prescribed nutritional intake through alternative routes (Table 1).

Study Limitations

This review followed a systematic process, adhering to the EQUATOR (Enhancing the Quality and Transparency of Health Research) and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to identify studies, and the methodology is reported to allow for reproducibility. We have surveyed and synthesized the key areas of research, presenting them in a logical structure with critical analysis of the available evidence. However, there are certain limitations. Despite the detailed approach, this review may not be fully comprehensive of all studies conducted in this area, as some papers may not have been identified by the search strategy.

The purpose of this review was to evaluate the effects of critical illness and the ICU environment on taste, hunger, and satiety. While we acknowledge that many additional

factors can influence these outcomes, several of which have been explored in the discussion, a comprehensive literature search focused on these factors was beyond the scope of this review.

Conclusion

The effect of critical illness on taste, hunger, and satiety is an under-researched area within intensive care medicine. While there is evidence to suggest that taste is altered during critical illness, the extent of these changes have not been systematically explored. Patients most commonly experience early satiety and decreased appetite during the acute phase of illness, which appears to improve by three months post-ICU discharge. However, appetite dysregulation may persist beyond this point. This reduction in appetite is associated with long-term low mood, a common feature of PICS. Further primary research is required, particularly in relation to taste, to better understand its relationship to the patient experience during ICU admission and recovery. Such research could inform the development of targeted interventions that not only enhance patient pleasure, motivation, nutritional intake but also reduce morbidity and promote long-term recovery.

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Table 1. Summary of evidence

Author(s)	Design	Population	Setting	Intervention	Comparison	Aim/Outcome(s)	Results	Quality of Evidence (GRADE/ GRADE-CERQual)
Acute Phase Studies Moisey et al. ^[9] in 2021	Prospective observational feasibility study	Adults on mechanical ventilation (MV) >72 hours, n=19	ICU Teaching hospital Ontario, Canada	None	None	(1) Quantify protein and energy intake and compare it to prescribed amounts in hospitalized, critically ill patients admitted to the intensive care unit (ICU) following liberation from mechanical ventilation (MV). (2) Evaluate the impact of different feeding modalities on intake relative to nutritional requirements. (3) Identify and describe patient-reported barriers to oral intake. (4) Assess the feasibility of recruiting participants for a larger-scale trial at a single center.	Most frequently reported barriers to eating included poor appetite (24%), early satiety (15%), taste changes (11%), nausea/ vomiting (10%), and disliking the food (10%). Protein and calorie intake were below prescribed amounts in patients whose enteral nutrition was discontinued and an oral diet prescribed as the sole source of nutrition following liberation from MV.	Å Very low
Tanimoto S et al. ^[8] in 1999	Single-arm pre/post study	Healthy volunteers, n=10	ICU Japan	Admission to ICU for 4 days and 3 nights	Comparison was made before and after the intervention using changes in validated questionnaires from baseline.	To investigate the psychological and physiological changes that occur in individuals placed in an inpatient ICU setting. (1) Change in Profile of Mood States scores.	Most healthy individuals developed feelings of depression at some point (p<0.05). Fatigue and confusion increased (p<0.05), while	ÅÅ Low

Table 1. Summary of evidence. (Cont.)

Author(s)	Design	Population	Setting	Intervention	Comparison	Aim/Outcome(s)	Results	Quality of Evidence (GRADE/ GRADE-CERQual)
Acute Phase Studies								
Li DT and Puntillo K. ^[11] in 2006	Prospective observational pilot study	Adults aged 21-80 who received mechanical ventilation (MV) for ≥12 hours, n=15	ICU Two large teaching hospitals California, USA	None	None	(2) Change in Zung Self-Rating Depression Scales scores. (3) Change in General Health Questionnaire scores. (4) Changes in physiological markers, including peripheral lymphocyte counts, natural killer cell activity, and urinary 17-ketosteroid and 17-hydroxycorticosteroid levels.	vigor decreased (p<0.01). General Health Questionnaire scores showed an increase (p<0.01). No significant changes were observed in physiological markers.	Å Very low
						To evaluate the self-reported symptoms of ICU patients receiving mechanical ventilation. (1) Document the prevalence and intensity of 9 symptoms: pain, dyspnea, thirst, nausea, hunger, tiredness, anxiety, generalized discomfort, and depressed feelings. (2) Examine the relationships among these symptoms.	All patients reported some degree of dyspnea. Nausea was the least prevalent symptom. Approximately 40% of patients experienced severe thirst and moderate to severe pain. More than 30% reported moderately intense thirst, tiredness, hunger, generalized discomfort, and depressed feelings. Several symptoms	

Table 1. Summary of evidence. (Cont.)

Author(s)	Design	Population	Setting	Intervention	Comparison	Aim/Outcome(s)	Results	Quality of Evidence (GRADE/ GRADE-CERQual)
Acute Phase Studies								
Baumstarck K et al. ^[12] 2019	Multicenter, cluster-randomized, two-parallel-group validation study	Patients >18 years old admitted to ICU for ≥3 days n=944	34 ICUs Tertiary care hospitals or community hospitals France	Application of the Identification of Discomforts questionnaire. Immediate feedback to bedside nurses and monthly feedback to the healthcare team, alongside tailored site-specific interventions.	Standard (usual) care	Validation of the 18-item version of the Inconforts des Patients de REAnimation (IPREA) questionnaire. 1) Collection of demographic data, type of admission, health status scores at admission (Knaus score and McCabe index), Simplified Acute Physiology Score, use of ventilation, vasopressors, or renal replacement therapy, and ICU stay duration. 2) Measurement and analysis of IPREA scores.	were found to be significantly correlated (p<0.05). The highest reported discomforts were sleep deprivation, thirst, and the presence of perfusion lines/ devices. The lowest reported discomforts were limited visiting hours, hunger, and isolation. The initial structure of the IPREA was confirmed using confirmatory factor analysis, which demonstrated a satisfactory fit. The overall discomfort score of the 18-item version of IPREA did not differ between men and women. Higher age was significantly correlated with a lower overall discomfort score. While MV was not linked to self-reported	AAAA High

Table 1. Summary of evidence. (Cont.)

Author(s)	Design	Population	Setting	Intervention	Comparison	Aim/Outcome(s)	Results	Quality of Evidence (GRADE/ GRADE-CERQual)
Acute Phase Studies								
Nelson JE et al. ^[13] in 2001	Prospective single-group observational study	ICU patients with a current or past cancer diagnosis, consecutively admitted over 8 months n=100	ICU Tertiary-care urban medical center USA	None	None	To characterize the symptom experience of a cohort of intensive care unit patients at high risk for hospital death. (1) Patients' self-reports of symptoms using the Edmonton Symptom Assessment Scale (ESAS). (2) Ratings of pain or discomfort associated with ICU diagnostic/therapeutic procedures. (3) Stress associated with conditions in the ICU.	discomfort, patients treated with non-invasive ventilation (NIV) reported higher overall discomfort scores than those not treated with NIV. Between 55% and 75% of ESAS responders reported experiencing pain, discomfort, anxiety, sleep disturbance, or unsatisfied hunger or thirst, all rated as moderate to severe. Depression and dyspnea were reported at similar severity levels by approximately 40% and 33% of responders, respectively. Significant pain, discomfort, or both were associated with common ICU procedures, but most procedure-related symptoms were adequately controlled for the majority of patients. Inability to	À Very low

Table 1. Summary of evidence. (Cont.)

Author(s)	Design	Population	Setting	Intervention	Comparison	Aim/Outcome(s)	Results	Quality of Evidence (GRADE/ GRADE-CERQual)
Acute Phase Studies								
Nematy M et al. ^[14] in 2006	Prospective cohort study	Patients aged 18 to 85 years who were anticipated, in the opinion of the consultant, to stay in the ICU for more than three days, n=16	ICU Two tertiary-level teaching hospitals London	None	Healthy volunteers n=36	To assess the patterns of ghrelin and pancreatic peptide YY (PYY) levels during ICU stay in hospitalized patients. (1) Fasting blood samples were taken on days 1, 3, 5, 14, 21, and 28 of ICU stay or on the date of discharge. (2) Appetite was assessed using a visual analogue scale (VAS) on the same days as blood tests. (3) Food intake was measured using food charts and anthropometric data.	communicate, sleep disruption, and limitations on visiting were particularly stressful aspects of the ICU environment. ICU patients exhibited significantly lower levels of ghrelin on day 1 (297.8±76.3 versus 827.2±78.7 pmol/L, p<0.001). Ghrelin levels tended to rise towards normal during the final three weeks of hospital stay. PYY levels were significantly higher in ICU patients on day 1 (31.5±9.6 versus 11.3±1.0 pmol/L, p<0.05), with a downward trend toward normal levels during the last three weeks of hospitalization.	AA Low
Karaca et al. ^[15] in 2022	Prospective observational pilot study	Patients >18 years old admitted to the ICU for >48 hours n=60	ICU Single-center tertiary teaching hospital Türkiye	None	None	(1) To determine changes in serum total ghrelin and acylated ghrelin at baseline, and on days 2, 5, and 10 in ICU patients.	Total ghrelin levels decreased slightly, while acylated ghrelin levels increased significantly over time.	A Very low

Table 1. Summary of evidence. (Cont.)

Author(s)	Design	Population	Setting	Intervention	Comparison	Aim/Outcome(s)	Results	Quality of Evidence (GRADE/ GRADE-CERQual)
Acute Phase Studies								
Merriweather JL, et al. ^[16] in 2018	Post hoc analysis of the RECOVER randomized trial Intervention and control groups were combined for this analysis; therefore, it is a non-randomized study	Adult survivors of critical illness who received MV for more than 48 hours and were deemed fit for ICU discharge n=188	ICU Two major acute hospitals Scotland	None	None No baseline appetite measurements using VAS were taken	(2) To investigate the relationship between mortality and changes in serum total and acylated ghrelin levels in ICU patients. (1) To describe appetite scores in ICU survivors during the first 3 months after ICU discharge. (2) To explore the association between appetite and systemic inflammation. (3) To quantify appetite using visual analogue scales.	No relationship was found between total or acylated ghrelin levels and ICU mortality. Median VAS appetite score (scale 0-10) was 4.3 (2.0-6.5) at 1 week after ICU discharge, improving to 7.1 (4.6-8.9) at 3 months (mean difference 1.7 (0.9-2.4), $p<0.01$). The number of days spent in an acute hospital after ICU stay was associated with poorer appetite scores ($p=0.03$). C-reactive protein (CRP) levels and appetite were significantly associated at 1 week after ICU discharge ($p=0.01$), but not at 3 months ($p=0.67$).	AA Low
Merriweather JL, et al. ^[10] in 2016	Semi-structured interviews Grounded theory	Adult patients who received >48 hours of MV and were ready for	ICU and wards Teaching hospital Scotland	None	None	To explore the factors influencing nutritional recovery in	The core category identified was 'inter-	AAAA High

Table 1. Summary of evidence. (Cont.)

Author(s)	Design	Population	Setting	Intervention	Comparison	Aim/Outcome(s)	Results	Quality of Evidence (GRADE/ GRADE-CERQual)
Recovery Phase Studies	Qualitative	discharge from the ICU to the wards, n=17				patients after critical illness and to develop a model of care to improve current nutritional management for this patient group. (1) Interviews conducted at discharge from ICU and weekly thereafter until ward discharge. (2) Follow-up interview conducted at three months post-ICU discharge. (3) Observations of ward practice three times a week.	related system breakdowns during the nutritional recovery process. Three key themes emerged: experiencing a dysfunctional body, socio-cultural changes related to eating, and failures in organizational nutritional care delivery. Appetite, taste, and satiety were particularly affected, especially in the early days after transfer to the ward. Food was frequently described as bland, too salty, or having a metallic taste. These taste changes could lead to food aversions in some patients.	
Chapple LAS, et al. ^[17] in 2019	Prospective inception cohort study	Adult patients admitted to ICU who survived their admission n=51	ICU Australia	None	Healthy volunteers, n=25	To evaluate dietary intake and factors that may influence intake, appetite, and gastric emptying 3 months after ICU discharge.	From the 24-hour dietary recall, ICU survivors consumed fewer calories than healthy controls (ICU: 1876 (708) vs.	AA Low

Table 1. Summary of evidence. (Cont.)

Author(s)	Design	Population	Setting	Intervention	Comparison	Aim/Outcome(s)	Results	Quality of Evidence (GRADE/ GRADE-CERQual)
Recovery Phase Studies								
Kitayama M, et al. ^[16] in 2023	Secondary analysis of data obtained from a published ambidirectional cohort study (SMAP-HoPe study)	>Adults aged >65 years with an ICU stay of ≤3 nights, living at home 12 months post-discharge n=501	12 ICUs Japan	None	None	1) Dietary intake was assessed by recall of the preceding day and by consumption of a standard weighed buffet meal 4 hours post-drink. 2) Appetite was assessed while fasting and both pre- and post-buffet using visual analogue scales. 3) A standardized carbohydrate drink containing 13C-octanoic acid was used to measure gastric emptying. To describe the prevalence of appetite loss and examine the relationship between appetite loss and depression in patients living at home 12 months after ICU admission. 1) Hospital Anxiety and	healthy subjects: 2291 (834) kcal; p=0.025), with no differences in macronutrient intake. ICU survivors reported a lower preference for fat (p<0.001). Caloric and macronutrient intake from the weighed buffet meal was similar between groups. ICU survivors reported feeling less full regardless of the time point (p=0.041). There was no difference in the rate of gastric emptying between the two groups (p=0.216). The prevalence of appetite loss was 25.4% (95% confidence interval [CI], 21.5-29.4). High severity of depression was associated with increased likelihood of appetite loss (odds ratio, 1.2; 95% CI, 1.14-1.28; p=0.00).	AA Low

Table 1. Summary of evidence. (Cont.)								
Author(s)	Design	Population	Setting	Intervention	Comparison	Aim/Outcome(s)	Results	Quality of Evidence (GRADE/ GRADE-CERQual)
Recovery Phase Studies								
						Depression Scale (HADS) score at 12 months post-discharge. 2) Short Nutritional Assessment Questionnaire (SNAQ) score at 12 months post-discharge.		
Abbreviations: MV: Mechanical Ventilation; LMV: Liberation from Mechanical Ventilation; ICU: Intensive Care Unit; IPREA: Inconforts des Patients de REAnimation (Discomforts of ICU Patients); NIV: Non-Invasive Ventilation; VAS: Visual Analogue Scale; CRP: C-Reactive Protein; ESAS: Edmonton Symptom Assessment Scale; PYY: Pancreatic Peptide YY; HADS: Hospital Anxiety and Depression Scale; SNAQ: Short Nutritional Assessment Questionnaire; GRADE: Grading of Recommendations Assessment, Development, and Evaluation.								

Supplementary Table 1. Definitions of Key Terms**Critical Illness**

Despite being widely used throughout the literature, there is no consensus definition of critical illness, and the term is applied for varying purposes. A concept analysis study proposed the following definition: “*Critical illness is a state of ill health with vital organ dysfunction, a high risk of imminent death if care is not provided, and the potential for reversibility.*”^[36] The possibility of recovery distinguishes critical illness from terminal illness and the natural process of dying. Therefore, the potential for and process of recovery is a central element of intensive care medicine for critically ill patients.

Critical Care and the Intensive Care Unit

Critical care has been described as “*the identification, monitoring, and treatment of patients with critical illness through the initial and sustained support of vital organ functions.*”^[36] While this definition captures the aim of care, it does not specify the setting in which it occurs. The National Institute for Health and Care Excellence (NICE) further clarifies that critical care is typically delivered in either Intensive Care Units or High Dependency Units (HDUs).^[37] For the purposes of this review, we adopt an amalgamation of these definitions. Included studies involve patients admitted to an *Intensive Care Unit*, defined as a distinct geographical location within a hospital, encompassing level 2 to level 3 care (from high dependency to full invasive monitoring and life support).^[38]

Recovery Period

The *recovery period* is defined as the time following a patient’s discharge from the ICU. According to the UK National Institute for Health and Care Excellence (NICE) framework for rehabilitation after critical illness, patients with ICU stays longer than four days should receive follow-up assessments of morbidity within two to three months post-discharge.^[39] Consequently, a three-month post-discharge period is commonly used as a standardized benchmark across studies included in this review.

Acute Phase

The acute phase refers to the period during a patient’s admission to the ICU.