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Original article

# Observed appetite and nutrient intake three months after ICU discharge

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SUMMARY

*Background & aims:* Oral intake is diminished immediately after ICU discharge, yet factors affecting nutritional intake after hospital discharge have not been evaluated. The aim of this study was to evaluate dietary intake and factors which may influence intake - appetite and gastric emptying - 3-months after ICU discharge.

*Methods:* Inception cohort study with ICU survivors compared to healthy subjects. Following an overnight fast, all participants consumed a standardized carbohydrate drink, containing $^{13}$C-octanoic acid, to measure gastric emptying. Dietary intake was assessed by recall of the preceding day and a standard weighed buffet meal 4-h post-drink. Appetite was assessed pre-drink (fasting) and pre- and post-buffet using visual analogue scales.

*Results:* Fifty-one ICU survivors (82% male; 70 ± 9 y; BMI 28 ± 6 kg/m$^2$) and 25 healthy subjects (60% male; 67 ± 12 y; BMI 27 ± 4 kg/m$^2$) were evaluated. From the 24-h recall ICU survivors consumed less calories (ICU 1876 (708) vs. healthy subjects 2291 (834) kcal; $p = 0.025$) with no difference in macronutrient intake, however reported a lower preference for fat ($p < 0.001$). Calorie and macronutrient intake from the weighed buffet was similar between groups: calories (ICU: 658 (301) vs. healthy subjects: 736 (325) kcal; $p = 0.149$); protein (ICU: 37 (19) vs. healthy subjects: 40 (17) g; $p = 0.275$); fat (ICU: 23 (12) vs healthy subjects: 26 (13) g; $p = 0.261$); and carbohydrates (ICU: 69 (35) vs. healthy subjects: 79 (42) g; $p = 0.141$). ICU survivors reported feeling less full regardless of time-point ($p = 0.041$). There was no difference in the rate of gastric emptying between the two groups ($p = 0.216$).

*Conclusions:* ICU survivors reported less preference for fat and less calorie consumption than healthy subjects. However, intake of calories and macronutrients at a weighed meal was similar in the two groups, as was the rate of gastric emptying. ICU survivors reported being less full after the test meal, suggesting factors other than appetite may influence intake.



## 1. Background and aims

Approximately 50% of critically ill patients develop marked calorie and protein deficits during their intensive care unit (ICU) admission and these deficits contribute to substantial weight loss [1,2]. Nutritional deficits are associated with increased mortality and considerable morbidity including greater duration of ventilatory support and longer length of stay [3,4]. Survivors of critical illness report persistent functional impairments, which are due, at least in part, to muscle wasting [5,6].

The transition from artificial nutrition support to oral intake has been shown to exacerbate calorie and protein deficits, both after extubation in ICU and later during the hospital admission after ICU discharge [7,8]. There are a number of reasons for the nutritional

*Abbreviations:* APACHE II, Acute Physiology and Chronic Health Evaluation II score; BMI, Body Mass Index; ICU, Intensive Care Unit; GEC, Gastric Emptying Coefficient; LOS, Length of Stay; VAS, Visual Analogue Scale.

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deficits seen in ICU and following ICU discharge. Delayed gastric emptying occurs frequently during critical illness [9,10], but it is unknown whether, and when, dysmotility resolves as patients recover. In other hospital populations appetite is acutely affected resulting in decreased intake [11]. However, appetite, and subsequent oral intake, post-hospitalization in survivors of ICU has not been quantified.

The primary objective of this study was to evaluate oral nutritional intake in survivors of critical illness 3-months after discharge from ICU using a standard weighed buffet meal. Secondary objectives were to evaluate the effect of critical illness on reported appetite and nutritional intake, appetite during the fasting and post-prandial phase of the buffet meal, and gastric emptying.

## 2. Methods

This was an inception cohort study of ICU survivors, with healthy subjects acting as a control group. The Royal Adelaide Hospital Human Research Ethics Committee approved the study protocol and the study was conducted in accordance with the Helsinki Declaration of 1975 as revised in 1983. The protocol was registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12616000702415).

### 2.1. Patients

Patients were eligible if they were aged >30 years and alive three-months after discharge from the Royal Adelaide Hospital ICU. Patients were excluded if they: were pregnant during the ICU admission; were unable to provide informed consent; or were unable to attend an appointment at the hospital.

Patients were identified through screening of consecutive intensive care admissions. Following hospital discharge, eligible patients were sent a letter with a participant information sheet and opt-out consent form in English. A study investigator then contacted eligible patients to ascertain their willingness to participate in the study. Consort diagram shown in Fig. 1.

### 2.2. Healthy participants

Healthy subjects were recruited through advertisements at the study centre or from a pool of study volunteers from previous studies conducted in our department. Eligible subjects included those aged >30 years, who were able to attend an appointment in person, and able to provide informed consent. Subjects were excluded if they: were pregnant or breastfeeding; were taking medications known to affect gastrointestinal motility (e.g. prokinetics, antidepressants, sedatives, opiates, anticonvulsant agents); had previous gastrointestinal surgery (apart from appendectomy); had current or previous gastrointestinal disease or major dysfunction; or regularly consumed >20 g alcohol or >10 cigarettes per day. Subjects were offered honorarium for their time.

### 2.3. Study procedures

Study procedures are shown in Fig. 2. On the study day, all study participants presented to the hospital following a 12-h overnight fast (solids and liquids).

### 2.4. Gastric emptying

At t = 0 min, all participants consumed a standardized carbohydrate drink of 350 ml water containing 75 g glucose (Glucaid 75 g/300 ml, Thermo Fisher) and 100 mg of $^{13}$C-octanoic acid. Breath samples were taken at t = −10 and −5 min, every 5 min for the first hour after the carbohydrate drink, and subsequently every 15 min for the duration of the study period [12]. The concentration of $CO_2$ and the percentage of $^{13}CO_2$ was measured in each sample with an isotope ratio mass spectrometer (Europa Scientific, ABCA model 20\20, Crewe UK). Correct end-expiratory sampling was assessed as a $CO_2$ concentration of greater than 1% in all samples [13].

### 2.5. Appetite

ICU patients were asked to report whether they had experienced a change, either an increase or decrease, in appetite from the time-point before they were admitted to ICU.

A set of Visual Analogue Scales (VAS), compiled based on previous studies [14,15], were completed by all participants at three time-points during their study visit: in the fasted state (t = −10 min); at completion of gastric emptying measurement (t = 180 min − delayed post-prandial phase); and immediately following the standard meal buffet (immediate post-prandial

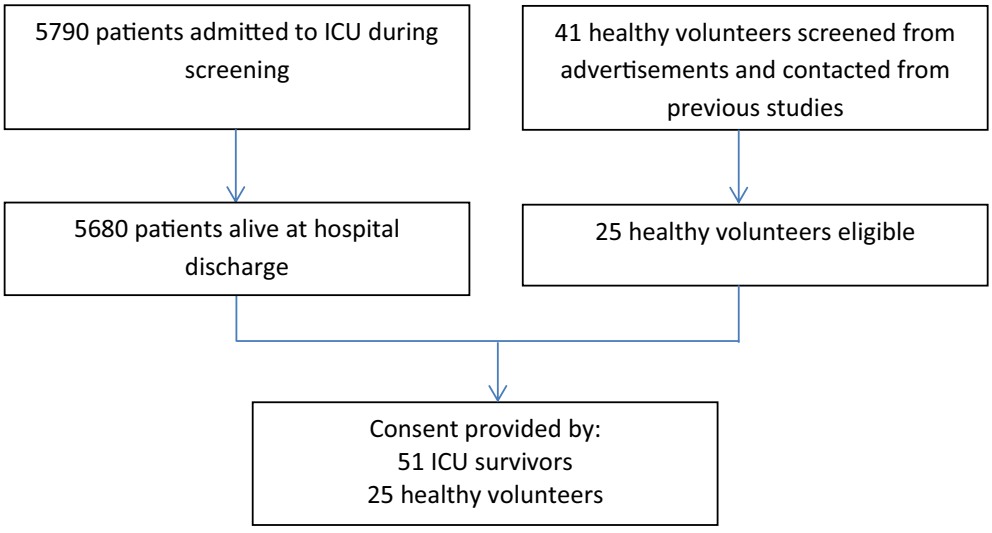


**Fig. 1.** Consort diagram. Note: All consented participants completed the study.

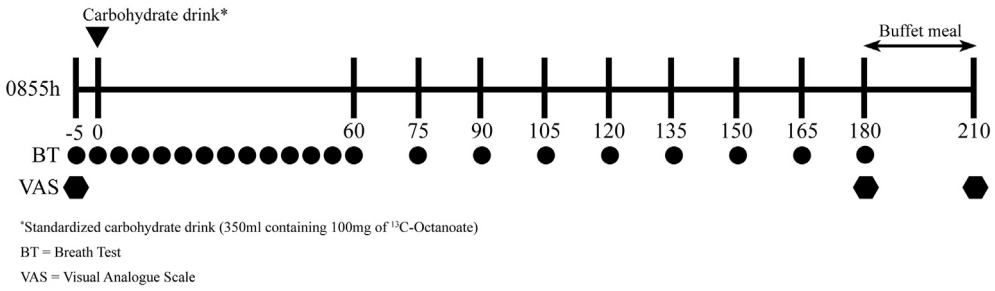


**Fig. 2.** Study procedures timeline.

phase). Each VAS consisted of a 100 mm horizontal line, where 0 mm represented 'sensation not felt at all' and 100 mm 'sensation felt the greatest'. The participant was required to place a vertical mark along the line to indicate the strength of each sensation.

### 2.6. Standard weighed meal buffet

Three hours after the carbohydrate drink (t = 180 min), participants were provided with a standard buffet meal, which has previously been validated to assess nutrient intake [16]. The buffet meal comprised four slices (125 g) of wholemeal bread, four slices (125 g) of white bread, 100 g sliced ham, 100 g sliced chicken, 85 g sliced cheddar cheese, 100 g lettuce, 100 g sliced tomato, 100 g sliced cucumber, 20 g mayonnaise, 20 g margarine, 170 g apple, 190 g banana, 175 g strawberry yoghurt, 150 g chocolate custard, 140 g fruit salad, 375 ml iced coffee, 350 ml orange juice, 600 ml water, and a 12 g chocolate bar. The entire buffet meal contained 2666 kcal, 123 g protein, 81 g fat, and 342 g carbohydrate. Participants were unaware of the purpose of the weighed food buffet and were instructed to consume as much of this meal as required to make them comfortably full [16]. The amount of calories and macronutrients consumed at this meal was quantified using Foodworks dietary analysis software (Xyris, Brisbane, Australia).

### 2.7. 24-h dietary recall

During the study appointment a trained dietician (LSC or MJS) recorded the participant's dietary intake from the day prior to the study day as a measure of 'usual' intake. To ensure consistency between dieticians a standard 24-h recall data form was used, with consensus on interview and portion estimate techniques. All food items were entered into Foodworks dietary analysis software by a single investigator to quantify the amount of calories and macronutrients consumed.

### 2.8. Anthropometrics

At the study appointment, participants' height, weight, weight history and circumferences (hip, waist, neck) were measured. For ICU survivors, their self-reported weight from prior to ICU admission was compared to their measured weight at three-month follow-up.

### 2.9. Activity

Participants were asked to report the average total hours per week they currently spend participating in 'mild' (walking), 'moderate' (e.g. golf, gentle swimming), or 'vigorous' (e.g. jogging, cycling, tennis) physical activity.

### 2.10. Statistical analysis

Based on previously collected pooled data from 10 studies on healthy subjects conducted by investigators from the Centre for Research Excellence in Translating Nutritional Science to Good Health the mean calorie intake from the standard buffet meal was 431 kcal. Based on this value, a sample size of 50 ICU patients with a 2:1 recruitment for healthy subjects (n = 25), provided 80% power at the 0.05 significance level, to detect a difference in calorie intake of 300 kcal. This was chosen *a priori* to be of clinical relevance and likely to lead to a meaningful effect on nutritional status.

The concentration of $^{13}CO_2$ in each breath sample was plotted over time. Using the resulting curves, the gastric emptying coefficient (GEC) – a measure of the rate of appearance and disappearance of tracer in the breath sample with a greater number indicating more rapid emptying; and the half emptying time ($t_{50}$) – the time taken for half of the stomach's contents to empty – were calculated [13].

Data are presented as mean (SD) or median (IQR). Independent samples *t*-tests were used to compare data between ICU survivors and healthy subjects. Intake data were adjusted to account for differences in sex between the two groups. P-values of <0.05 were considered significant.

VAS outcomes were analysed using repeated measures analysis of variance (RM ANOVA) with effects for group, time (baseline, delayed post-prandial, immediate post-prandial), and the group by time interaction. Significant interactions were followed by pairwise post-hoc tests comparing between groups.

## 3. Results

ICU patients were screened for eligibility from November 2016 to January 2017. Participant demographic data and characteristics are listed in Table 1. The mean (SD) APACHE II on admission was 16 (6). The average weight change from reported weight at ICU admission to actual weight at three-month follow-up, was a loss of 3.3 (7.7) kg. Seventy-three percent of patients lost weight with a mean loss of 6.5 (6.1) kg or 9.1 (11.0) % body weight, and 27% gained weight with a mean gain of 5.5 (4.0) kg or 7.0 (5.3) % body weight.

### 3.1. Dietary intake

ICU survivors reported consuming significantly less calories compared to healthy subjects on the day prior to the study (Table 2). In terms of the primary outcome, there were no significant differences in intake of any macronutrient at the standard weighed buffet between ICU survivors and healthy subjects (Table 2). On average, ICU survivors took significantly longer to consume the standard weighed buffet to reach the point of satisfaction compared to healthy subjects: 34 (11) vs. 24 (9) minutes (p = 0.001).

**Table 1**
Participant demographic data on study day.

| | ICU survivors n = 51 | Healthy subjects n = 25 | *p* |
|---|---|---|---|
| Age on study day (yrs), mean (SD) | 69.7 (9.0) | 66.6 (12.4) | 0.211 |
| Sex (male), n (%) | 42 (82) | 15 (60) | **0.035** |
| Pre-ICU reported weight (kg), mean (SD) | 85.4 (20.7) | | |
| Pre-ICU BMI (kg/m$^2$), mean (SD) | 29.4 (6.3) | | |
| Measured weight (kg), mean (SD) | 83.1 (20.4) | 79.8 (15.3) | 0.469 |
| Height (m), mean (SD) | 1.7 (0.1) | 1.7 (0.1) | 0.788 |
| BMI (kg/m$^2$), mean (SD) | 28.3 (6.1) | 27.3 (4.2) | 0.470 |
| Circumferences (cm), mean (SD) | | | |
| Waist | 105.2 (17.4) | 98.6 (13.2) | 0.101 |
| Hip | 109.5 (17.8) | 102.2 (13.2) | 0.077 |
| Neck | 41.7 (6.6) | 38.9 (4.2) | 0.062 |
| Exercise (hours/week), mean (SD) | | | |
| Mild | 6.9 (10.3) | 7.7 (7.0) | 0.744 |
| Moderate | 7.2 (39.8) | 4.5 (4.5) | 0.737 |
| Heavy | 0.4 (1.7) | 0.4 (1.4) | 0.940 |
| ICU admission reason, n (%) | | | |
| Cardiac | 21 (41) | | |
| Sepsis/Infection | 8 (16) | | |
| Trauma | 7 (14) | | |
| Gastrointestinal | 4 (7) | | |
| Other | 11 (22) | | |
| APACHE II on admission, mean (SD) | 16 (6) | | |
| ICU LOS, days: median (IQR) | 3.1 (1.7–5.9) | | |
| Hospital LOS, days: median (IQR) | 13.9 (8.4–21.9) | | |
| Length of mechanical ventilation, hours: median (IQR) | 15 (10.3–50.3) | | |
| Number ventilated: n (%) | 18 (35) | | |
| Discharge location: n (%) | | | |
| Home | 35 (69) | | |
| Other acute care hospital | 10 (20) | | |
| Chronic care hospital | 6 (12) | | |

APACHE II: Acute Physiology and Chronic Health Evaluation II score, BMI: Body Mass Index, ICU: Intensive Care Unit, LOS: Length Of Stay. *p*-values <0.05 are shown in bold.

### 3.2. Appetite

Seventy-nine percent (n = 37/47) of ICU survivors reported their appetite was lower after being admitted to ICU than usual. The VAS for appetite sensations in the fasted state, delayed post-prandial phase, and immediate post-prandial phase are shown in Table 3. There was a significant group effect, with ICU survivors having a significantly lower preference for fat than healthy subjects ($p < 0.001$). ICU survivors reported feeling less full across all time-points when compared to healthy subjects ($p = 0.041$).

**Table 2**
Intake data from standard weighed buffet and 24-h recall.

| | ICU survivors n = 51 | Healthy subjects n = 25 | *p* | *p* (Adjusted for sex) |
|---|---|---|---|---|
| **From weighed buffet** | | | | |
| Calories, kcal | 658 (301) | 736 (325) | *0.304* | *0.149* |
| Protein, g | 37 (19) | 40 (17) | *0.574* | *0.275* |
| Fat, g | 23 (12) | 26 (13) | *0.346* | *0.261* |
| Carbohydrate, g | 69 (35) | 79 (42) | *0.298* | *0.141* |
| % calories from protein | 23 (5) | 22 (4) | *0.594* | *0.709* |
| % calories from fat | 31 (11) | 32 (9) | *0.748* | *0.930* |
| % calories from carbohydrate | 43 (14) | 43 (9) | *0.904* | *0.851* |
| **From 24-h recall** | | | | |
| Calories, kcal | 1876 (708) | 2291 (834) | ***0.021*** | ***0.025*** |
| Protein, g | 88 (37) | 95 (29) | *0.408* | *0.327* |
| Fat, g | 75 (49) | 104 (70) | ***0.035*** | *0.055* |
| Carbohydrate, g | 194 (93) | 211 (77) | *0.360* | *0.318* |
| Alcohol, g | 4 (13) | 10 (26) | *0.250* | *0.137* |
| % calories from protein | 19 (5) | 18 (4) | *0.154* | *0.193* |
| % calories from fat | 34 (12) | 38 (11) | *0.177* | *0.226* |
| % calories from carbohydrate | 43 (12) | 39 (12) | *0.236* | *0.261* |
| % calories from alcohol | 2 (6) | 3 (8) | *0.422* | *0.384* |

Data presented as mean (SD).

### 3.3. Gastric emptying

There were no differences in the gastric emptying coefficient (survivors 3.4 (0.3) vs. 3.3 (0.3); $p = 0.15$) or $t_{50}$ (95 (57) vs. 112 (52) minutes; $p = 0.22$).

## 4. Discussion

To our knowledge this is the first time that detailed assessment of nutritional intake, including evaluation of appetite (both quantified during weighed buffet and self-reported), dietary intake and gastric emptying have been measured in survivors of critical illness. Despite the majority of patients reporting weight loss since ICU admission, calorie intake at the test meal was similar in the ICU survivors when compared to healthy subjects and ICU survivors reported feeling less full at the end of their meal. However, reported appetite and caloric intake was less in the ICU survivors than in the healthy subjects, which could contribute to weight loss.

The reason for the disparity between reported and measured intake is unclear. A number of psycho-social factors that affect nutritional intake, aside from appetite; such as chewing fatigue, taste aversions and financial stressors, may explain the difference. The ICU survivors took significantly longer to consume the weighed buffet than healthy subjects. This has been corroborated in an observational study of 22 general patients where fatigue at meals was reported two weeks after hospital discharge [17]. While this may not influence intake at a single meal, it may affect cumulative intake over a full day, particularly in 'real life' as opposed to 'artificial' laboratory conditions. Further, while this cohort of patients were able to participate in physical activity to the same degree as their healthy counterparts, in a more unwell group of patients other factors such as ability to shop and prepare meals may influence intake after hospital discharge, as has been shown to affect more than 50% of stroke survivors six months after injury [18]. Therefore, a greater understanding of the influence of psycho-social factors on intake in survivors of critical illness is required.

In this study, 79% of ICU survivors reported experiencing a reduced appetite in the three months from ICU admission. Similar observations have been made across a range of other hospitalized patient populations at differing time-points. In a study in elderly female patients 42% reported having a poor appetite in hospital [11]. Other studies have reported reduced appetite in 50% of mixed medical/surgical patients two weeks after hospital discharge [17] and 47% of cancer patients in the three months following gastrointestinal surgery [19].

In this study the reported appetite (VAS) on the study day did not differ between ICU survivors and healthy subjects. There may be several explanations for these findings. Firstly, other studies have quantified changes in appetite using simple yes/no responses rather than measurement using VAS, and hence reported appetite may be more sensitive to changes or more greatly influenced by respondent bias. Secondly, in this group of ICU survivors only 35% required ventilatory support, with a mean APACHE II score of 16, and they stayed in ICU for an average of four days, which may reflect a relatively low acuity group of patients whose appetite may have largely recovered by this time-point. For this group, improvements in appetite may have occurred earlier in their recovery. Exploration of changes in appetite in the early post-ICU and rehabilitation phase using prospective recruitment of patients during the ICU admission may deduce the stage at which appetite returns to usual levels.

**Table 3**
Mean visual analogue score out of 100 for appetite.

| | Fasted (t = 0) | | Delayed post-prandial (t = 180) | | Immediate post-prandial (t = 210) | | P group[a]time interaction | P group |
|---|---|---|---|---|---|---|---|---|
| | ICU survivors n = 51 | Healthy subjects n = 25 | ICU survivors n = 51 | Healthy subjects n = 25 | ICU survivors n = 51 | Healthy subjects n = 24[b] | | |
| How hungry do you feel? | 34 (30) | 40 (30) | 55 (29) | 61 (33) | 12 (24) | 5 (6) | *0.176* | *0.850* |
| How satisfied do you feel? | 22 (25) | 27 (23) | 25 (27) | 27 (26) | 75 (31) | 87 (13) | *0.502* | *0.117* |
| How full do you feel? | 16 (22) | 24 (23) | 19 (19) | 24 (27) | 74 (25) | 83 (14) | *0.885* | ***0.041*** |
| How much do you think you could eat now? | 46 (26) | 52 (21) | 57 (26) | 66 (19) | 12 (17) | 10 (11) | *0.316* | *0.239* |
| How strong is your desire to eat? | 36 (25) | 40 (25) | 52 (26) | 57 (28) | 16 (24) | 9 (11) | *0.238* | *0.926* |
| Would you like to eat something sweet? | 27 (30) | 27 (23) | 31 (31) | 23 (21) | 19 (31) | 11 (18) | *0.430* | *0.298* |
| Would you like to eat something salty? | 21 (23) | 27 (25) | 23 (27) | 34 (29) | 6 (12) | 11 (20) | *0.650* | *0.105* |
| Would you like to eat something savory? | 43 (30) | 40 (27) | 50 (32) | 55 (25) | 15 (23) | 12 (21) | *0.438* | *0.912* |
| Would you like to eat something fatty? | 10 (14) | 20 (22) [a] | 12 (17) | 30 (29) [a] | 6 (12) | 5 (7) | ***<0.001*** | *0.013* |
| Do you feel drowsy? | 16 (27) | 18 (21) | 27 (31) | 25 (22) | 12 (21) | 14 (17) | *0.437* | *0.979* |
| Do you feel calm? | 89 (16) | 80 (22) | 89 (15) | 75 (24) | 88 (20) | 84 (18) | *0.106* | ***0.020*** |

[a] Significant difference between groups in post-hoc pairwise tests (P < 0.05).
[b] Data missing for one participant at this time-point.

Seventy-three percent of patients reported weight loss since their admission to ICU. This is comparable to data from a cohort follow-up study of 136 ICU survivors that reported 50% of patients weighed less 7–8 months after ICU discharge than before admission [20]. Additionally, in a group of ICU survivors admitted with acute respiratory distress syndrome, 30% had not returned to their baseline body weight two years after admission [21]. Malnutrition is associated with poor recovery [22] and hence effective interventions to ameliorate this weight loss are needed.

In the present study, gastric emptying did not differ between ICU survivors and healthy subjects. Around 50% of critically ill patients have slow gastric emptying while in the ICU but whether slow gastric emptying persists after hospital discharge is unknown. A limitation of this study is that gastric emptying was not measured in this cohort during their ICU stay, and so it cannot be conclusively determined whether at least a proportion of the patient group had slow gastric emptying when in ICU. Ott and colleagues have demonstrated in 12 head-injured patients admitted to ICU that delayed gastric emptying is common in the first week after injury and had not returned to normal three weeks later [23]. Further, a retrospective study reported delayed gastric emptying is associated with longer ICU stay, higher APACHE II scores, and admission diagnoses of trauma, head injury, burns, and sepsis [24]. The reported lower incidence of delayed gastric emptying with cardiac diagnoses and respiratory failure may be relevant to our cohort. Further research should deduce the time at which delayed gastric emptying resolves in patients admitted to ICU, and the effect this has on nutrient intake and functional recovery.

The strength of this study is that a comprehensive assessment of nutritional intake was performed, using validated techniques to measure gastric emptying, appetite and oral intake. In addition, dietary assessments, including 24-h recalls, were conducted by qualified dieticians. However, there are a number of limitations. Firstly, as the study required participants to attend an in-hospital appointment the included patients may not adequately reflect an ICU cohort of greater illness severity, and there may be selection bias towards those patients more interested in, or conscious of, nutrition. This is further highlighted by the participants' short length of ICU and hospital stay, minimal requirement for ventilator support, and primarily cardiac diagnoses. We also did not collect data on those patients that declined to participate. In addition, the physical activity levels of the patient group was similar to the healthy cohort; given numerous studies have reported impaired activity in ICU survivors [5,25], the interpretation is this cohort may have fewer co-existing illnesses or recovered better than other cohorts of survivors. Secondly, standard weighed buffets have been shown to reliably measure intake, however, they are usually used to measure intake after a given intervention in a cross-over study design, rather than comparing intake of two independent groups [14]. Therefore, it may be that influencers of nutritional intake in ICU survivors may not be adequately captured in the measurement of a single weighed meal. There are also limitations associated with the use of VAS to assess appetite, including relatively low reproducibility and methodological variation that cannot be accounted for, and potential recall bias for pre-ICU data and self-reported aspects.

Future research should aim to explore appetite and the influence on oral intake over the entire hospitalization and early after discharge, to determine the time-point at which these factors return to normal. Recruitment should be conducted prospectively to guarantee a cohort more reflective of a typical ICU cohort. In addition, an understanding of other factors that might influence nutritional intake and weight loss in ICU survivors should be determined qualitatively.

In conclusion, this study highlights that self-reported reductions in appetite, oral intake, and body weight are prevalent three-months after ICU discharge, yet this is not reflected in intake at a standard weighed buffet meal.

## Authors' contributions

LSC, MJC and AMD designed research; LSC, LMW, YAA, MJS, TN and PK conducted research; LSC, LMW, and KL analysed data; LSC, LMW, MJC, and AMD wrote the paper; and LSC had primary responsibility for final content. All authors read and approved the final manuscript.

## Statement of authorship

All authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript.

## Conflicts of interest

There are no conflicts of interest relevant to this research to disclose.

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Australian New Zealand Clinical Trials Registry: ACTRN12616000702415. http://www.anzctr.org.au/.

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