The impact of weight and weight loss on clinical outcomes of hospital inpatients

A thesis by

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THESIS ABSTRACT

An increase in worldwide obesity has led to much research into the health of the overweight and obese human population. Obesity is caused by many factors including poor dietary intake, stress and an increase in physical inactivity and has been found to cause multiple complications including cardiovascular diseases, some cancers, kidney diseases and musculoskeletal issues. Research involving hospital admissions of overweight and obese individuals has shown that there are uncertainties as to whether poorer hospital outcomes occur. The obesity paradox has also been demonstrated with lower mortality rates observed in patients who are obese or overweight with conditions including cardiovascular disease, diabetes and chronic obstructive pulmonary disease.

The primary aims of this thesis were to determine whether morbid obesity ($\geq$40kg/m^2) was associated with a longer inpatient length of stay and whether weight loss between hospital admissions (more than 30 days from discharge to readmission) showed altered health outcomes from those who did not have any significant weight change.

This research has demonstrated an increased length of stay in the morbidly obese which remained after adjusting for confounders including comorbidity, socioeconomic status and ethnicity. Weight loss was associated with poorer hospital outcomes (longer length of stay, longer length of stay in the intensive care unit (if admitted) and higher mortality) regardless of initial body mass index both during and after an unplanned hospital readmission.

DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint award of this degree. The author acknowledges that copyright of published works contained within the thesis resides with the copyright holder(s) of those works. I give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time. I acknowledge the support I have received for my research through the provision of an Australian Government Research Training Program Scholarship.

Kellie Fusco

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PUBLICATIONS ARISING FROM THESIS

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LIST OF ABBREVIATIONS

ANOVA	One-way Analysis of Variance
ATSI	Aboriginal and/or Torres Strait Islander
BMI	Body Mass Index
CAD	Chronic Artery Disease
CCI	Charlson Comorbidity Index
CI	Confidence Interval
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CVD	Cardiovascular Disease
eMUST	Malnutrition Universal Screening Tool
FMC	Flinders Medical Centre
HF	Heart Failure
ICU	Intensive Care Unit
IQR	Inter Quartile Range
IRR	Incidence Risk Ratio
IRSD	Index of Relative Social Disadvantage
IWL	Intentional Weight Loss
LOS	Length of Stay
NSQIP	National Surgical Quality Improvement Program
PIR	Poverty Income Ratio

RAH	Royal Adelaide Hospital
RCTs	Randomised Control Trials
RR30	Readmission within 30 days
RSI	Relative Stay Index
SAHREC	Southern Adelaide Human Clinical Research Ethics Committee
T2DM	Type 2 Diabetes Mellitus
UHR	Unplanned Hospital Readmission
US	United States
UWL	Unintentional Weight Loss
WHO	World Health Organization

CHAPTER ONE: INTRODUCTION AND LITERATURE REVIEW

Introduction

Weight is an important factor in the health of all humans because obesity and being overweight have a negative impact on the human population. Both conditions are defined by the World Health Organization (WHO) as an accumulation of excess body fat (WHO, 2021) which may impair health. The WHO defines an overweight person as one having a body mass index (BMI) of 25-29.9kg/m^2 and a person with obesity as one having a BMI greater than 30.0kg/m^2. BMI is calculated as a person's weight in kilograms divided by the square of their height expressed in metres (WHO, 2021). Altered BMI cut off levels for Asian populations are recommended due to their health risks occurring at lower BMI levels (Consultation, 2004). For many years, there has been conjecture related to the validity of using BMI as a tool for investigating, describing and managing overweight and obesity. BMI is recommended for use at a population level rather than an individual level as it does not account for race, muscle mass or distribution of body fat (Nuttall, 2015, Goh et al., 2004, AIHW, 2022). However, BMI continues to remain a useful tool for research studies (Cereda et al., 2017, Dennis et al., 2018, Woolley et al., 2019, Fusco et al., 2017, Akinyemiju et al., 2016).

World-wide, obesity has increased 3 fold in the past 50 years (WHO, 2021) and the state of being overweight or obese is now commonplace. In Australia, during 2017-2018, these two conditions affected 67% of adults (i.e., those aged 18 years and older), with 36% being overweight and 31% obese. Men had higher rates of being overweight or obese than women with 75% of men affected compared to 60% of women. According to the Australian Institute of Health and Welfare (Health and

Welfare, 2023), obesity was more common in older age groups, with 42% of adult men and 39% of adult women aged 65-74 years being obese, compared to 18% of men and 14% of women aged between 18 and 24 years.

Complications of obesity include cardiovascular disease, chronic kidney disease, musculoskeletal issues, diabetes mellitus and some cancers (AIHW, 2017). All these co-morbidities can either be prevented or improved by diet, exercise and intentionally changing behaviour with an aim of up to 10% weight loss (Goldstein, 1992, Poirier et al., 2006, Williamson et al., 2015, Ryan and Yockey, 2017). If one assumes that obesity carries health implications for hospital inpatients as well as community living populations, weight loss would be considered an obvious strategy to reduce levels of obesity both in the community and in hospitals. Disappointingly, widespread implementation of weight loss strategies is absent. In the primary health care setting only about 20% of subjects with obesity were diagnosed with obesity and only 22% of these patients (i.e. <5% of all subjects with obesity) were given an obesity management plan (Jarolimova et al., 2013). New technologies offer cause for optimism. The use of digital food diaries and weight loss applications is increasing and either method may be useful for encouraging weight loss to occur (Hanson et al., 2021, Cheng et al., 2022). If weight loss does not occur, pharmacological therapy and/or bariatric surgery may be considered as a strategy to induce weight loss and reduce the increased cost of obesity in hospitals (Jarolimova et al., 2013, Kent et al., 2017). When a patient with obesity is admitted to hospital, the admission can be an opportunity to address this condition. Not only can hospitals encourage weight loss and prevent complications of obesity by providing the resources for bariatric surgery to inpatients (Tsui et al., 2021, Bleich et al., 2012), they can also facilitate ambulatory care in outpatient clinics (Lantz et al., 2003). These strategies are not always prevalent and may not be the primary consideration for treatment for inpatients with obesity whilst in hospital. It is also unknown whether the community living patient with obesity or who is overweight and without a history of recent hospital admission may differ significantly in regard to comorbidities and potential weight loss interventions from the acutely unwell hospitalised patient with the same BMI.

Inpatient obesity prevalence mirrors that observed in the community. One study measured the height and weight of all inpatients in one hospital on one day and found 22.3% were obese (Dennis et al., 2018). Regardless of their admission reason, inpatients with obesity tend to experience a longer length of stay (LOS) than similar patients with the same presentation who were within the normal weight range or overweight (Ram et al., 2021). A study of BMI and LOS in patients with gall bladder disease showed that higher BMI was associated with a longer LOS for patients who underwent cholecystectomy (Liu et al., 2008). Similarly, another study, involving 3,399 chronic obstructive pulmonary disease (COPD) patients, also found that obesity was associated with a longer LOS for inpatients when compared to their non-obese counterparts (Inabnit et al., 2018). However, this situation is not clear cut and needs further clarification. This clarification is crucial because any patient experiencing an avoidable or manageable condition contributing to a prolonged LOS may be a target for an intervention. Such interventions can enhance safety, efficiency and the overall cost-effectiveness of health care.

Hospitals are under pressure to accommodate large numbers of patients (both elective and emergency admissions). Measures to reduce the inpatient LOS of any admission and measures to prevent admissions altogether are significant for hospitals (Ragavan et al., 2017). These measures would assist not only with hospitals' financial burdens of care delivery but also would assist with creating hospital capacity (Ragavan et al., 2017, Rojas-Garcia et al., 2018). LOS of an index admission is, amongst other factors, an important predictor of readmission rates (Table 1.1) (Ram et al., 2021, (Braet et al., 2015, Sharma et al., 2018, Maali et al., 2018, Hua et al., 2015). The avoidance or shortening of the duration of any readmission to hospital is also a target for health care improvement because these actions will also improve hospital congestion (Wong et al., 2010).

Table 1.1. Factors that increase the risk of readmission

Risk Factors	
Malnutrition	Multiple visits to emergency departments in the 6 months prior
Corticosteroid use	Charlson comorbidity index
Age > 50 years	Self-discharge against medical advice
Use of illicit substances	Poly pharmacy (use of >6 different medications)
Socioeconomic status	Living alone
Longer inpatient length of stay	Obesity
Premature discharge	

(Allaudeen et al., 2011, Mudge et al., 2011, Ram et al., 2021, Braet et al., 2015, Caughey et al., 2017, Maali et al., 2018, Cruz et al., 2022, Sharma et al., 2018, Graham et al., 2015, Jepma et al., 2019, Kong and Wilkinson, 2020, Fernandez-Garcia et al., 2020, Jensen et al., 2021)

It is not just the hospital that benefits from shorter and fewer admissions and readmissions. Patient outcomes are also affected by inpatient LOS. Increased LOS can impact upon patients’ mental health, mobility and ability to perform activities of daily living safely (Rojas-Garcia et al., 2018, Ram et al., 2021). Being able to minimise LOS is therefore of advantage to both the hospital and the patient. Minimisation of LOS needs to be done carefully because premature discharge can increase the risk of hospital readmission (Rojas-Garcia et al., 2018). It therefore warrants the questions: Is the inpatient with obesity a potential target for a weight loss intervention? Does the association of BMI with LOS mean that lowering BMI by weight loss will subsequently produce a shorter inpatient LOS and thus reduce health care utilisation?

Within this complex array of competing demands for health care delivery, it is difficult to piece together the best strategy to optimise care of the patient with obesity and to optimise hospital function. How is the LOS of an admitted or readmitted patient with obesity to be shortened safely and efficiently? Is weight loss the answer? Is the hospital inpatient with obesity better or worse off than the inpatient who is not obese? Should weight loss be encouraged in the patient with obesity, recently hospitalised for acute illness, whether old or young, of slightly or significantly increased BMI? Is an inpatient who has lost weight to achieve a BMI of $30kg/m^2$ in a similar situation to an inpatient with a BMI of $30kg/m^2$ who has not lost weight? The literature on these questions is absent or divided.

Literature review

The impact of weight on the clinical outcomes of hospital inpatients.

This literature review identifies research addressing whether weight, weight change between hospital admissions and obesity have an impact on clinical outcomes during hospitalisation. Table 1.2 indicates the definitions of weight used for the purpose of this thesis.

Patients who are underweight have been excluded from this review due to significant research previously completed in this area (Finkielman et al., 2004, Woolley et al., 2019, Potter et al., 1988, Mullen et al., 2009) which consistently indicated adverse health outcomes for this underweight population compared to those of normal weight.

Hospital staffing issues, outpatient clinics and most community obesity research has also been excluded from this review.

Table 1.2. BMI definitions

BMI (kg/m^2)	WHO definition	This thesis
<18.5	Underweight	Underweight (Excluded)
18.5 - 24.9	Healthy weight	Normal weight
25.0 – 29.9	Overweight	Overweight
30.0 – 34.9	Obese	Mild Obesity
35.0 - 39.9	Obese	Moderate Obesity
40.0 +	Obese	Morbid obesity

As stated earlier, a significant burden of disease in the population at large is caused by overweight- and obesity-induced comorbidity (Must et al., 1999). Being overweight and/or obese has been linked to numerous diseases with resulting impact upon clinical outcomes. As mentioned earlier, these outcomes include an increase in the LOS of the patient with obesity (Chen et al., 2007, Akinyemiju et al., 2016, Liu et al., 2008). Patients with morbid obesity (i.e. BMI ≥ 40kg/m^2) experience increased complications after cardiac surgery, while those who are overweight or mildly obese may experience fewer adverse outcomes (Gao et al., 2016). In this study, 4,740 patients underwent cardiac surgery at two different hospitals, with 5.8% falling into the category of morbid obesity. Interestingly, patients with mild obesity or those who were overweight (BMI 25.0 – 34.9kg/m^2) had improved post-surgery outcomes when compared to underweight patients and those with morbid obesity (Gao et al., 2016). This observed benefit of obesity has been described as the obesity paradox (Curtis et al., 2005, Mullen et al., 2009, Amundson et al., 2010, Iozzo et al., 2013, Gruberg et al., 2002).

Considering the established association of obesity with various other co-morbidities, it might be safe to assume that all patients who are overweight or obese are at risk of experiencing poorer health outcomes compared to those with a normal body weight (Wilson et al., 2002, Calle et al., 1999). However, the sporadic observation of the obesity paradox challenges this assumption. Recent evidence (Doehner et al., 2012) suggests that patients with several comorbidities and an elevated BMI (BMI 25.0 – 34.9kg/m^2), may exhibit a lower mortality rate when compared to similarly co-morbid patients with a normal BMI. This observed mortality benefit of being obese or overweight (i.e. the obesity paradox), has been noted in patients with one or more of a range of conditions, including diabetes, cardiovascular disease, COPD, and cancer (Carnethon et al., 2012, Tobias et al., 2014, Elagizi et al., 2018, Landbo et al., 1999, Yoon et al., 2011). These findings conflict with the studies previously cited herein, as well as other research demonstrating the disadvantages of increasing BMI on clinical outcomes (McEwen et al., 2012, Chaturvedi and Fuller, 1995, Liu et al., 2008, Inabnit et al., 2018, Chen et al., 2007, Akinyemiju et al., 2016, Calle et al., 1999, Wilson et al., 2002, Fusco et al., 2017).

In contrast to prevailing evidence highlighting the deleterious effect of increased BMI on health outcomes (Calle et al., 1999, Wilson et al., 2002, Fusco et al., 2017), the term obesity paradox was coined in the early 2000s. This term is used to describe improved mortality rates observed in patients with a higher BMI (≥25.0kg/m^2) when compared to those with a normal BMI (Curtis et al., 2005, Amundson et al., 2010, Gruberg et al., 2002).

The pathophysiology of the paradox remains unclear. It has been hypothesised that people with obesity have persistent low-grade inflammation present which allows macrophages to secrete adipocytes and cytokines, resulting in increased levels of tumour necrosis factors and interleukins 1 and 6. In the context of inpatient care among individuals with obesity, this heightened inflammatory response may allow for an augmented response to injury and improved tissue repair (Curtis et al., 2005, Mullen et al., 2009).

Interestingly, the obesity paradox is not consistently present, and factors such as the degree of obesity and the patient's age may influence its manifestation. In a prospective study conducted in the United States, comprising 118,707 patients who underwent non-bariatric surgery, lower mortality risk was observed in patients with a BMI between 25.1kg/m^2 and 40.0kg/m^2 compared to those with a normal BMI (Mullen et al., 2009). Conversely, a higher mortality risk was found in morbidly obese patients (BMI>40kg/m^2) when compared to patients with a normal BMI (Mullen et al., 2009). To illustrate the impact of age on these paradoxical effects of obesity on health outcomes, a study of 10,466 consecutive patients hospitalised for cardiovascular disease in Italy revealed that patients aged 65 years of age and under had a higher mortality risk with a higher BMI (Iozzo et al., 2013). However, for patients aged over 65years, this study found a protective effect associated with increasing BMI (≥25kg/m^2) against death from cardiac disease. This protective effect of increasing BMI in the older subjects was also seen in a retrospective study of 22,903 hospitalised patients (Woolley et al., 2019). In the age group of 60-79 years, overweight patients had a lower risk of prolonged LOS and adverse outcomes after discharge compared to normal weight patients. Similarly, in the same age matched group, patients with obesity also had a lower risk of adverse outcomes after discharge when compared to patients with a normal weight (Woolley et al., 2019).

The obesity paradox seems particularly noteworthy in those with a BMI under 40kg/m^2 who are aged over 60 years. An observational study of 24,699 elective hospital admissions found that patients with morbid obesity did not have an increased Charlson comorbidity index when compared to electively-admitted patients without morbid obesity (Fusco et al., 2017). This implies that patients with morbid obesity were less likely to be admitted to hospital for an elective admission if they were deemed at high risk perioperatively. The paradox in electively admitted populations may arise, in part, from careful selection of subjects for therapy, potentially leading to biased results.

Setting aside any obesity paradox, the inconsistent evidence regarding clinical outcomes of patients with obesity may, in part, be attributed to different cut-off values of BMI used to classify obesity in various studies (Despres, 2011). Alternatively, it could stem from the adverse effects of low BMI on outcomes or may relate to deficiencies in the BMI's ability to accurately reflect fat mass. In addition, published studies vary on the basis of methodological issues such as the source of BMI data (self-reported or objective evidence), patient selection bias, and the presence of residual confounding (Nazare et al., 2015, Akinyemiju et al., 2016). Very few studies have explored clinical outcomes in patients with morbid obesity (BMI ≥40kg/m^2) among hospitalised patients. It might be the case that older patients with mild obesity exhibit the obesity paradox and the heavier patient with more severe obesity does not (Table 1.3).

Table 1.3. Differing degrees of obesity on health outcomes

Paper/Author	Age range in years Mean ± SD	Number of participants	Study site	Comparator	Level of obesity	Outcomes
Finkelman et al (Finkielman et al., 2004)	64.2 ± 15.9 post operative 60.9 ± 19.1 non operative	19,699	Hospital	Normal	Mild and moderate	Decreased mortality in post operative patients admitted to the ICU
					Morbid	Increased ICU LOS in post operative patients admitted to the intensive care unit
Liu et al (Liu et al., 2008)	Mean age 56 years	1,282,547	Hospital	Normal	Mild, moderate and morbid	Increased risk of first hospital admission for gallbladder disease Increasing LOS with increasing BMI
Mullen, et al (Mullen et al., 2009)	Mean age 53.1	118,707	Hospital	Normal	Mild	Lower LOS, sepsis and mortality Increased superficial wound occurrence post operatively Increased morbidity with adjustments for age, gender and operation type and with further adjustments for significant NSQIP risk factors
					Moderate	Increased superficial wound occurrence post operatively Increased morbidity Lower mortality with adjustments for significant NSQIP risk factors
					Morbid	Increased superficial wound occurrence post operatively Increased mortality when adjusted for age, gender and operation type Increased morbidity
Reeves, et al (Reeves et al., 2014)	56.2 ± 4.9 women	1,251,619	Hospital	BMI 22.5-24.9	Mild, moderate and morbid	Increase in hospital admissions as BMI increases Largest increases in knee replacements and diabetes as BMI increases
Johnson et al (Johnson et al., 2015)	64.99 ± 10.04	78,762	Hospital	Normal	Morbid	Significantly increased mortality
Akinyemiju, et al (Akinyemiju et al., 2016)	>=40 Not given as a total but mean age per BMI grouping ranges from 71.5 (for normal BMI) – 56.9 (for BMI ≥50)	578,589	Hospital	Normal	Mild and moderate	Lower LOS Increased mortality
					Morbid	Increased LOS Increased mortality Increased complications in cancer patients
Gao et al (Gao et al., 2016)	63.6 ± 12.4	4,740	Hospital	Normal	Mild	Decreased in-hospital mortality Decreased surgical mortality Decreased ICU hours
					Moderate	Increased new atrial fibrillation/flutter
					Morbid	Increased deep sternal infection Prolonged ventilation Increased renal failure and renal dialysis requirement Increased RR30
Fusco et al (Fusco et al.,	Morbid obesity 54.4 ±	118,171	Hospital	Non-morbidly obese	Morbid	Increased LOS, ICU admission rate and RR28

2017)	15.4 Non-morbidly obese 56.7 ± 21.1					for emergency admissions Increased LOS, ICU hours and ICU admission rate for elective admissions
Jensen et al (Jensen et al., 2021)	66 ± 9.4 Range 26-97	3,897	Hospital	Normal	Mild, moderate, and morbid	No significant difference in LOS or RR90 when adjusted for other characteristics
Ram et al (Ram et al., 2021)	18+ 74 ± 13.7 Non-obese 67 ± 13.4 Mild + Moderate 62 ± 13.3 Morbid	578,213	Hospital	Normal/overweight	Mild and moderate	Decreased in-hospital mortality at readmission Increased hospital costs at readmission
					Morbid	Decreased in-hospital mortality at readmission, cardiovascular readmission as a reason for readmission Increased LOS and hospital costs at readmission and increased time to readmission
Evans et al (Evans et al., 2023)	Mild obesity: 45.7 ± 10.6 Moderate obesity: 45.8 ± 10.3 Morbid obesity: 45.3 ± 10.2	28,583	Hospital	Changes over an 8 year time period	Mild	Increased health care and health care costs Increased comorbidities including chronic kidney disease and HF
					Moderate	28% increase in health care costs compared to health care costs of mild obesity at 8 years Large increase in CKD
					Morbid	40% increase in health care costs compared to health care costs of mild obesity at 8 years Increased level of HF and CKD year 7-8
Must et al (Must et al., 1999)	25+	15,001	Community	Normal	Mild and moderate	No significant differences
					Morbid	Increased prevalence of T2DM, gallbladder disease, CVD, high blood cholesterol level (<55 years of age) and high blood pressure
Calle et al (Calle et al., 1999)	Mean age 57	1,184,657	Community	BMI 23.5-24.9 kg/m^2	Mild, moderate, and morbid	Increasing mortality with increasing BMI
Global BMI Mortality Collaboration (Global et al., 2016)		10,625,411	Community	Normal	Mild, moderate, and morbid	Increasing mortality with increasing BMI
Espallardo et al (Espallardo et al., 2017)	18+ No further information given	18,682	Community	Normal	Mild, moderate and morbid	Increased number of day admissions, hospital admissions, emergency visits and specialist/GP visits, all increasing with increasing BMI
Kent et al (Kent et al., 2017)	56.1 ± 4.8 Range 50-64	1,093,866	Community	BMI 20-22.5 kg/m^2	Mild, moderate and morbid	Increasing hospital costs as BMI increases
Khan, et al (Khan et al., 2018)	20-79 Grouped into 3 age groups 20-39, 40-59, 60-79	190,672	Community	Normal	Mild and moderate	Increased risk of CVD event Lower risk of death not caused by a CVD event (men) Increased risk of CVD death (men)

					Morbid	Larger increased risk of CVD event Increased risk of CVD death (men and women) Lower again risk of death not caused by a CVD event (men)

LOS = length of stay, BMI = body mass index, NSQIP = National Surgical Quality Improvement Program, HF = heart failure, CKD = chronic kidney disease, CVD = cardiovascular disease, ICU = intensive care unit, RR90 = readmission within 90 days, T2DM = type 2 diabetes mellitus, RR30 = readmission within 30 days. Green = indicates improved outcomes when compared to the comparator. Red = indicates worse outcomes when compared to the comparator. Blue = indicates no significant differences when compared to the comparator

A major limitation of existing studies is the lack of detailed data on associated co-morbidities, patients' socio-economic status and ethnicity–all of which have been identified as factors contributing to both obesity and patients' clinical outcomes. A systematic review examining the risk of obesity in relation to socioeconomic status revealed that lower socioeconomic status is associated with a higher risk of obesity (El-Sayed et al., 2012). A cross-sectional study involving 17,238 male participants found that Non-Hispanic Whites and Non-Hispanic Blacks with a higher poverty income ratio (PIR; defined as the ratio of family income to the poverty threshold) were more likely to be obese than those with a low PIR (Zare et al., 2022). Notably, the PIR did not impact whether Mexican Americans were obese or not (Zare et al., 2022). In a 20 year prospective study of 121,700 female participants, encompassing 1,294,799 person-years of follow up, ethnicity including blacks, Asians and Hispanics, was identified as a significant risk factor for type 2 diabetes mellitus (T2DM) compared to whites, with a changing BMI highlighted as a significant contributing risk factor (Shai et al., 2006). This study demonstrated that for a 5-point increase in BMI, the relative risk of developing T2DM differed between ethnic groups and was highest in the Asian population, followed by Hispanics, whites and blacks.

Being mindful of the likely different effects of differing degrees of obesity on health outcomes and acknowledging the past oversight of confounders such as the comorbidity burden, socioeconomic status, and participants' ethnicity, the second chapter in this thesis aims to investigate the association between morbid obesity

(BMI ≥40kg/m^2) and clinical outcomes in hospitalised patients, incorporating these crucial confounders. It is important to note that in this study, ethnicity data was only collected for patients who were identified as Aboriginal and/or Torres Strait Islander (ATSI), without further differentiation based on other ethnicities such as white, black, Asian, or Hispanic.

However, there is little information on the effects of weight loss (as opposed to no weight loss) on health outcomes for the patient with obesity recently hospitalised for an acute illness. A prospective presented by Williamson (Williamson et al., 2015) indicated an average weight loss of 5.5% lowered the incidence of type 2 diabetes mellitus and improved risk factors for cardiovascular disease. However, it is reasonable to anticipate that even more substantial weight loss could lead to even greater improvements in individuals with obesity. Another review (Ryan and Yockey, 2017) suggested that glycaemic improvement occurred after as little as 2.5% weight loss and health-related and quality of life improved after a 5% weight loss. This latter study looked at other factors including knee pain, mobility, sexual function and urinary incontinence. All of these issues improved after 5% weight loss. Non-alcoholic steatotic hepatitis activity score, however required 10% weight loss before significant pathological improvement could be seen (Ryan and Yockey, 2017).

No studies have investigated weight loss after hospital admission for acute illness, nor have studies addressed the association of any weight loss with clinical outcomes following future admissions. Consequently, it is challenging to determine whether weight loss is advisable for every acutely unwell inpatient with any degree of obesity.

While there are data suggesting improved health outcomes following 2.5-10% weight loss (Williamson et al., 2015, Ryan and Yockey, 2017), there is no evidence in the literature demonstrating that this degree of weight loss correlates with reduced health care costs. A literature search failed to uncover any published studies examining the health care costs of patients who are readmitted to hospital for an acute illness following weight loss. In fact, weight loss may not necessarily result in cost-savings. Community based studies, including one involving 2,083 women in the United States with a mean age of 80.2 years, found that those who lost ≥5% of their initial weight incurred a 35% increase in total healthcare costs after adjusting for age and current BMI (Schousboe et al., 2018) when compared to those who did not show any significant weight change. This increase in health care costs occurred irrespective of initial BMI. However, when patient comorbidity and the ability to achieve activities of daily living were included in an adjusted statistic model, this increase in healthcare costs was no longer significant (Schousboe et al., 2018). This suggests that the loss of lean body mass as well as fat mass might have occurred, potentially leading to poorer health outcomes. Another community-based study involving 3,199 participants observed that employee attendance at a workplace wellness centre was associated with an improvement in BMI. The improvement was seen in 46% of participants who visited the wellness centre 180-360 times over a four-year period and in 72% who visited the wellness centre more than 360 times over the same period, compared to those who visited 1-60 times (both $p<0.05$). There was also a significant decrease in healthcare costs (28.1% for those who visited the wellness centre 61-180 times, 29.7% for those who visited 180-360 times and 37.5% for those who visited more than 360 times) when compared to those who only attended the wellness centre between 1 and 60 times (Borah et al., 2015). These varying results may be related to age and gender of participants: Schousboe studied women with a mean age of 80.2 years, while Borah had employed participants with a mean age of 44.4 years. Studies have also been published predicting higher costs will be incurred by patients with obesity as the incidence of obesity increases (Kent et al., 2017, Wang et al.,

2011) in the absence of any work detailing whether weight loss might improve these projections.

The impact of weight loss on the clinical outcomes of hospital inpatients.

In certain scenarios, a patient with a lower BMI may experience better health outcomes when compared to a patient with a higher BMI. That patient's lower BMI may either be the result of weight loss or be present without prior weight loss. While weight loss undeniably reduces BMI, the relevance of previous weight loss is of uncertain importance in the recently acutely unwell patient and is challenging to assess. Limited research has compared the outcomes of groups of patients with obesity who have undergone weight loss with the outcomes of patients with that lower BMI already (i.e. without previous weight loss). Consequently, it is challenging to confidently determine whether weight loss in itself, carries a significant impact. Beyond assessing the impact of 'previous weight loss' vs 'no weight loss' on BMI's influence on health outcomes, addressing weight loss itself is complicated. Any weight loss that occurs may be intentional weight loss (IWL) or unintentional weight loss (UWL). While there is ample evidence supporting the beneficial effects of weight loss on health outcomes (Williamson et al., 2015, Tabucanon et al., 2020, Clausen et al., 2018), distinguishing IWL in hospitalised patients with obesity from the UWL of the chronically co-morbid is a challenging task.

In a study conducted in the United States of America, 9,144 people aged 45 years and older were examined through self-reporting to assess whether they had experienced any weight loss and to determine whether weight loss was intentional or unintentional (Meltzer and Everhart, 1995). This study found that UWL was associated with an elevated risk of mortality among the participants. This finding aligns with another study addressing UWL, which reported an increased mortality risk following UWL in patients with heart failure and also in older adults, even after adjusting for factors such as smoking, lack of physical activity and comorbidities (Perera et al., 2021). A prospective study of 2,677 patients attending an outpatient clinic identified an association between UWL and a diagnosis of malignancy. The increased mortality rate among these patients was primarily attributed to the high prevalence of those who had high stage or metastasised cancers (Bosch et al., 2017). A systematic review and meta-analysis published in 2018 (De Stefani et al., 2018) corroborated these findings, revealing a significant increase in overall mortality among patients with UWL. Importantly, this analysis indicated that obese patients experiencing UWL did not show benefit in terms of an improved cardiovascular mortality, contrary to the occasionally observed phenomenon reported as the obesity paradox.

IWL on the other hand has been associated with lower overall mortality rates for both men (Williamson et al., 1999) and women (Williamson et al., 1995) but only under certain conditions. A study involving 49,337 overweight and obese white men aged 40-64 years revealed an increase in diabetes-associated mortality for those who experienced a weight loss of 20 pounds (~8kg) or more, particularly when they had no known comorbidities. Interestingly, men with known comorbidities demonstrated a decrease in diabetes-associated mortality following this degree of weight loss (Williamson et al., 1999). The significance of comorbidities in influencing the benefits of weight loss was further underscored in another study by Williamson, focusing on females. In this investigation of 43,457 women aged 40-64 years, a reduction in mortality was observed with IWL, specifically in the context of pre-existing obesity related conditions. Those women without pre-existing obesity related conditions observed a smaller (but significant) reduction in mortality following IWL compared to those with pre-existing obesity related conditions. (Williamson et al., 1995). However, a recent narrative review into IWL in individuals aged 50 years and older found that IWL produced no change in mortality rates, regardless of pre-existing BMI (Yannakoulia et al., 2022).

While weight loss has been recognised for its potential to optimise general health and well-being, it can also be a reaction to, or a manifestation of an underlying illness or declining health. In one study involving 31,680 participants, individuals who intentionally, or otherwise, lost more than 10% of their body weight were found to have a higher likelihood of being diagnosed with conditions such as arthritis, diabetes, cancer, liver or respiratory diseases in the preceding 12 months compared to those who did not experience such significant weight loss.

The weight loss observed in large epidemiological studies is commonly categorised as IWL or UWL. However, the accuracy of this categorisation is subject to questioning, because categorisation can be determined by the clinician or the individual. The associated ill-health implications of correct classification are significant. For instance, in a study examining individuals who lost >10% of their weight in the previous twelve months, those categorised as experiencing UWL had a cancer diagnosis in 11.3% of cases, while those with IWL, were commonly diagnosed with diabetes (12.3%) (Vierboom et al., 2018). IWL can improve long term prognosis in patients with coronary artery disease, whereas UWL may be associated with a poorer prognosis in the same patient population (Pack et al., 2014). A prospective study of 4869 older men (aged 56-75 years) found that IWL was associated with a reduction in non-cardiovascular disease (CVD) mortality but there was no significant difference in CVD mortality (Wannamethee et al., 2005). A meta-analysis of 15 randomised control trials (RCTs) also found a significant improvement in all-cause mortality (15% reduction) among participants randomly assigned to the weight loss interventions compared to control arms (Kritchevsky et al., 2015). The

RCTs included in the analysis incorporated lifestyle-based weight loss interventions and classified weight loss as intentional, supporting the theory that IWL reduces mortality.

The question arises: Is it the influence of comorbidity or the intentionality of the weight loss that is important? The field is complex. In a prospective study of 2, 677 patients referred to an outpatient clinic in Spain to investigate UWL, 33% of patients were deemed to have their weight loss caused by a malignant process, 37% caused by non-malignant disorders (including digestive disorders, endocrine disorders, infectious diseases, neurological diseases, respiratory and renal diseases), 16% caused by psychosocial disorders and 14% were unexplained (Bosch et al., 2017). Other studies have also found similar strong associations of UWL with comorbidity (Bouras et al., 2001, Perera et al., 2021).

Both IWL and UWL are linked to ill health, and both may contribute to heightened mortality risks (Wannamethee et al AIM 2005). If anything, UWL and not IWL is associated with a significant increase in all-cause mortality risk in older men (Wannamethee et al AIM 2005), although it is noteworthy that IWL driven by health reasons can also be associated with elevated mortality. A systematic review and meta- analysis published in 2014, encompassing 12 studies and 35,335 patients with coronary artery disease (CAD), aimed to determine whether weight loss was correlated with increased cardiovascular events while taking into account the reason for the weight loss (Pack et al., 2014). The authors found that patients with CAD who unintentionally lost weight faced an increased risk of cardiovascular events, while those who intentionally lost weight demonstrated a decreased risk of cardiovascular events (Pack et al., 2014).

Thus, when confronted with the possibilities that obesity and weight loss might both adversely affect health outcomes in some inpatient populations, it is inviting to clarify whether some inpatients with obesity should be advised to lose weight in order to expedite, if not optimise, their care upon potential readmission to hospital. This prompted a study involving 576 young adults at risk of CVD who experienced a weight loss of equal to, or exceeding 5% of their initial body weight. Out of this cohort, over half, (293; 51%) were identified as having IWL, while 283 (49%) had UWL (Cui et al., 2019). Both groups exhibited changes in CVD risk factors. Notably, when UWL occurred and exceeded 6% within one year, the improvements in CVD risk factors were more pronounced than if IWL occurred and was greater than 6% within the same timeframe (Cui et al., 2019). On average, the IWL group started with a higher BMI than the UWL group (IWL starting mean BMI 33.7kg/m^2 compared to UWL (26.7kg/m^2)). The cause of the weight loss was not determined in the study. It is possible there may have been disease processes which may be associated with changes in CVD risk factors. This study showed unexpected results and older adults have not been studied to determine whether this remains true.

In summary, a patient's age, comorbidity burden, degree of obesity, amount of any recent weight lost, duration of that weight loss (see below), and its intentionality are relevant factors that complicate weight management of the acutely unwell inpatients. Importantly, the relevance of acuity of illness remains relatively unexplored across populations of emergency-admitted hospital inpatients with obesity, electively admitted inpatients with obesity, and relatively healthy individuals living in the community with obesity. This raises fundamental questions: Should weight loss advice be universally offered to all inpatients? If so, how much weight loss is advisable and what method should be employed? Does a patient (possibly older or more obese) with IWL fare better post- discharge than a similar patient with UWL? Can a patient entering a lower

BMI category achieve outcomes comparable to an inpatient residing in the same BMI category with no prior weight loss? Answering these questions requires a careful strategic approach. Initially, as demonstrated in this thesis, an observational study can be conducted, examining patients admitted to hospital twice and weighed on both occasions. Subsequently, interventional studies can be performed using precise definitions of significant weight loss, distinguishing patients with IWL from those with UWL, and applying differing strategies for weight loss. These patients can be compared with BMI-matched patients who experience no weight loss.

Weight loss and Readmission

Flares in chronic conditions are frequently the cause of an unplanned hospital admission (Brunner-La Rocca et al., 2020, Allaudeen et al., 2011, Mudge et al., 2011, Ram et al., 2021, Braet et al., 2015, Graham et al., 2015) and admitted patients with chronic conditions are often subsequently readmitted following their index admission (Brunner-La Rocca et al., 2020, Ram et al., 2021). These chronic conditions include, but are not limited to, chronic heart failure, chronic kidney disease, depression, metastatic cancer, bacterial pneumonia, COPD, hypertension and stroke. Notably, these chronic conditions not only elevate the risk of readmission but can also be associated with weight loss. In addition to factors previously presented in Table 1.1, weight loss has also been identified as a risk factor increasing the likelihood of an early readmission (within 30 days of discharge) (Allaudeen et al., 2011, Friedmann et al., 1997, Cruz et al., 2022, Sharma et al., 2017). However, none of the above-mentioned studies explicitly addresses whether the weight change observed was deliberate or unintentional.

The period of time over which weight loss occurs may also impact readmission risk. Studies suggest that rapid weight loss after discharge carries with it an increased risk of early readmission (i.e., within 30 days of discharge) (Allaudeen et al., 2011). If weight loss occurs more slowly following discharge, is there any evidence regarding the clinical impact of weight loss? While unplanned hospital readmission is typically studied within 30 days following discharge, several studies have explored unplanned but delayed readmissions occurring more than 30 days after hospital discharge (Maali et al., 2018, Jepma et al., 2019, Ram et al., 2021, Friedmann et al., 1997, Hua et al., 2015, Mudge et al., 2011, Sharma et al., 2018). Unfortunately, none of these studies has examined the impact of weight loss prior to that delayed readmission and its impact on patient outcomes. While distinguishing IWL from UWL may be crucial, the impact of protracted weight loss, regardless of its aetiology, on health outcomes remains unknown.

Typically, health outcomes measured after weight loss include LOS and readmission risk. As previously mentioned, readmission and a prolonged LOS during readmission impose a significant burden on already congested hospitals (Berenson et al., 2012, Hansen et al., 2011). If the associations of BMI and weight loss with these outcomes are better understood and if a patient's outcomes are modifiable by altering their weight, then significant benefits might arise to the care of the inpatient with or without obesity.

Aims

Recognising the deficiencies, complexities and contradictions in the existing literature, this thesis addressed two primary issues. Firstly, we sought to determine in greater detail whether morbid obesity (BMI ≥ 40kg/m^2) was associated with a prolonged inpatient LOS. Secondly, we aimed to understand whether weight loss before a readmission produces any differences in health outcomes during and following an unplanned hospital readmission (UHR). These were observational studies that addressed specific inpatient populations such as older patients and patients with morbid obesity. These studies lay groundwork for the design and timing of future interventional studies discriminating IWL from UWL.

To meet these aims, in the second chapter, we examined the association between morbid obesity and clinical outcomes in hospitalised patients (aged < 80 years), including important confounders such as comorbidity burden, socioeconomic status and ethnicity (ATSI) of participants. The hypothesis for this study was that hospitalised patients with morbid obesity would experience worse clinical outcomes than patients without morbid obesity after adjustment for these confounders. The primary outcome measure for this study was inpatient LOS. The secondary outcomes were in-hospital mortality, the number of hospital-acquired complications during admission, ICU length of stay, and 30 day readmissions. Patients were categorised into those with and without morbid obesity.

Given the indication from the second chapter that patients with morbid obesity are more likely to experience a longer inpatient LOS, we explored whether weight loss after a hospital admission would result in a favourable outcome for the patient's readmission. Therefore, the aims of the third chapter were several. The first aim was to determine whether any characteristics or outcomes of an index admission could identify patients who were more likely to change weight prior to a readmission. The second aim was to determine whether this weight change produces any differences in health outcomes during or following that readmission. This was studied in the population as a whole, in the older patients, and in the patients with morbid obesity. The hypothesis of this study was that weight loss before readmission predicts that readmission but also carries improved clinical outcomes when compared to those who remained weight stable. This allows future work to explore the concepts and consequences of healthy and unhealthy weight loss; weight loss that may be deliberate or unintentional.

Bibliography

AIHW 2017. Impact of overweight and obesity as a risk factor for chronic conditions: Australian Burden of Disease Study.

AIHW 2022. Australia's health 2022: data insights. Australia's health series number 18 ed. www.aihw.gov.au/reports-data/australias-health.

AKINYEMIJU, T., MENG, Q. & VIN-RAVIV, N. 2016. Association between body mass index and in-hospital outcomes: Analysis of the nationwide inpatient database. *Medicine (Baltimore),* 95**,** e4189.

ALLAUDEEN, N., VIDYARTHI, A., MASELLI, J. & AUERBACH, A. 2011. Redefining readmission risk factors for general medicine patients. *J Hosp Med,* 6**,** 54-60.

AMUNDSON, D. E., DJURKOVIC, S. & MATWIYOFF, G. N. 2010. The obesity paradox. *Crit Care Clin,* 26**,** 583-96.

BERENSON, R. A., PAULUS, R. A. & KALMAN, N. S. 2012. Medicare's readmissions-reduction program--a positive alternative. *N Engl J Med,* 366**,** 1364-6.

BLEICH, S. N., CHANG, H. Y., LAU, B., STEELE, K., CLARK, J. M., RICHARDS, T., WEINER, J. P., WU, A. W. & SEGAL, J. B. 2012. Impact of bariatric surgery on health care utilization and costs among patients with diabetes. *Med Care,* 50**,** 58-65.

BORAH, B. J., EGGINTON, J. S., SHAH, N. D., WAGIE, A. E., OLSEN, K. D., YAO, X. & LOPEZ-JIMENEZ, F. 2015. Association of worksite wellness center attendance with weight loss and health care cost savings: Mayo Clinic's experience. *J Occup Environ Med,* 57**,** 229-34.

BOSCH, X., MONCLUS, E., ESCODA, O., GUERRA-GARCIA, M., MORENO, P., GUASCH, N. & LOPEZ-SOTO, A. 2017. Unintentional weight loss: Clinical characteristics and outcomes in a prospective cohort of 2677 patients. *PLoS One,* 12**,** e0175125.

BOURAS, E. P., LANGE, S. M. & SCOLAPIO, J. S. 2001. Rational approach to patients with unintentional weight loss. *Mayo Clin Proc,* 76**,** 923-9.

BRAET, A., WELTENS, C., SERMEUS, W. & VLEUGELS, A. 2015. Risk factors for unplanned hospital re-admissions: a secondary data analysis of hospital discharge summaries. *J Eval Clin Pract,* 21**,** 560-6.

BRUNNER-LA ROCCA, H. P., PEDEN, C. J., SOONG, J., HOLMAN, P. A., BOGDANOVSKAYA, M. & BARCLAY, L. 2020. Reasons for readmission after hospital discharge in patients with chronic diseases-Information from an international dataset. *PLoS One,* 15**,** e0233457.

CALLE, E. E., THUN, M. J., PETRELLI, J. M., RODRIGUEZ, C. & HEATH, C. W., JR. 1999. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med,* 341**,** 1097-105.

CARNETHON, M. R., DE CHAVEZ, P. J., BIGGS, M. L., LEWIS, C. E., PANKOW, J. S., BERTONI, A. G., GOLDEN, S. H., LIU, K., MUKAMAL, K. J., CAMPBELL-JENKINS, B. & DYER, A. R. 2012. Association of weight status with mortality in adults with incident diabetes. *JAMA,* 308**,** 581-90.

CAUGHEY, G. E., PRATT, N. L., BARRATT, J. D., SHAKIB, S., KEMP-CASEY, A. R. & ROUGHEAD, E. E. 2017. Understanding 30-day re-admission after hospitalisation of older patients for diabetes: identifying those at greatest risk. *Med J Aust,* 206**,** 170-175.

CEREDA, E., KLERSY, C., HIESMAYR, M., SCHINDLER, K., SINGER, P., LAVIANO, A., CACCIALANZA, R. & NUTRITIONDAY SURVEY, C. 2017. Body mass index, age and in-hospital mortality: The NutritionDay multinational survey. *Clin Nutr,* 36**,** 839-847.

CHATURVEDI, N. & FULLER, J. H. 1995. Mortality risk by body weight and weight change in people with NIDDM. The WHO Multinational Study of Vascular Disease in Diabetes. *Diabetes Care,* 18**,** 766-74.

CHEN, Y., JIANG, Y. & MAO, Y. 2007. Hospital admissions associated with body mass index in Canadian adults. *Int J Obes (Lond),* 31**,** 962-7.

CHENG, Y. C., LIU, H. C., HSU, C. Y. & LEE, I. T. 2022. Duration of Treatment in a Weight Loss Program Using a Mobile App is Associated with Successful Weight Loss During the COVID-19 Pandemic. *Diabetes Metab Syndr Obes,* 15**,** 1737-1747.

CLAUSEN, E. S., FRANKEL, C., PALMER, S. M., SNYDER, L. D. & SMITH, P. J. 2018. Pre-transplant weight loss and clinical outcomes after lung transplantation. *J Heart Lung Transplant,* 37**,** 1443-1447.

CONSULTATION, W. H. O. E. 2004. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet,* 363**,** 157-63.

CRUZ, P. L. M., SOARES, B. L. M., DA SILVA, J. E. & LIMA, E. S. R. R. 2022. Clinical and nutritional predictors of hospital readmission within 30 days. *Eur J Clin Nutr,* 76**,** 244-250.

CUI, Z., CAI, J., LEWIS, C. E. & STEVENS, J. 2019. Changes in Cardiovascular Disease Risk Factors with Unintentional Versus Intentional Weight Loss: The Coronary Artery Risk Development in Young Adults Study. *Metab Syndr Relat Disord,* 17**,** 143-148.

CURTIS, J. P., SELTER, J. G., WANG, Y., RATHORE, S. S., JOVIN, I. S., JADBABAIE, F., KOSIBOROD, M., PORTNAY, E. L., SOKOL, S. I., BADER, F. & KRUMHOLZ, H. M. 2005. The obesity paradox: body mass index and outcomes in patients with heart failure. *Arch Intern Med,* 165**,** 55-61.

DE STEFANI, F. D. C., PIETRAROIA, P. S., FERNANDES-SILVA, M. M., FARIA-NETO, J. & BAENA, C. P. 2018. Observational Evidence for Unintentional Weight Loss in All-Cause Mortality and Major Cardiovascular Events: A Systematic Review and Meta-Analysis. *Sci Rep,* 8**,** 15447.

DENNIS, D. M., CARTER, V., TREVENEN, M., TYLER, J., PERRELLA, L., LORI, E. & COOPER, I. 2018. Do acute hospitalised patients in Australia have a different body mass index to the general Australian population: a point prevalence study? *Aust Health Rev,* 42**,** 121-129.

DESPRES, J. P. 2011. Excess visceral adipose tissue/ectopic fat the missing link in the obesity paradox? *J Am Coll Cardiol,* 57**,** 1887-9.

DOEHNER, W., ERDMANN, E., CAIRNS, R., CLARK, A. L., DORMANDY, J. A., FERRANNINI, E. & ANKER, S. D. 2012. Inverse relation of body weight and weight change with mortality and morbidity in patients with type 2 diabetes and cardiovascular co-morbidity: an analysis of the PROactive study population. *Int J Cardiol,* 162**,** 20-6.

EL-SAYED, A. M., SCARBOROUGH, P. & GALEA, S. 2012. Unevenly distributed: a systematic review of the health literature about socioeconomic inequalities in adult obesity in the United Kingdom. *BMC Public Health,* 12**,** 18.

ELAGIZI, A., KACHUR, S., LAVIE, C. J., CARBONE, S., PANDEY, A., ORTEGA, F. B. & MILANI, R. V. 2018. An Overview and Update on Obesity and the Obesity Paradox in Cardiovascular Diseases. *Prog Cardiovasc Dis,* 61**,** 142-150.

ESPALLARDO, O., BUSUTIL, R., TORRES, A., ZOZAYA, N., VILLORO, R. & HIDALGO-VEGA, A. 2017. The Impact of Severe Obesity on Healthcare Resource Utilisation in Spain. *Obes Surg,* 27**,** 2058-2066.

EVANS, M., ANUPINDI, V. R., DEKOVEN, M., DE LAGUICHE, E., DIVINO, V., FAURBY, M. D., HAASE, C. L., SOMMER MATTHIESSEN, K. & PEARSON-STUTTARD, J. 2023. Eight-year trends in obesity-related complications and health care cost progression in a US population with obesity: A retrospective cohort study. *Diabetes Obes Metab,* 25**,** 536-544.

FERNANDEZ-GARCIA, S., REPRESAS-REPRESAS, C., RUANO-RAVINA, A., MOURONTE-ROIBAS, C., BOTANA-RIAL, M., RAMOS-HERNANDEZ, C. & FERNANDEZ-VILLAR, A. 2020. Social and clinical predictors of short- and long-term readmission after a severe exacerbation of copd. *PLoS One,* 15**,** e0229257.

FINKIELMAN, J. D., GAJIC, O. & AFESSA, B. 2004. Underweight is independently associated with mortality in post-operative and non-operative patients admitted to the intensive care unit: a retrospective study. *BMC Emerg Med,* 4**,** 3.

FRIEDMANN, J. M., JENSEN, G. L., SMICIKLAS-WRIGHT, H. & MCCAMISH, M. A. 1997. Predicting early nonelective hospital readmission in nutritionally compromised older adults. *Am J Clin Nutr,* 65**,** 1714-20.

FUSCO, K. L., ROBERTSON, H. C., GALINDO, H., HAKENDORF, P. H. & THOMPSON, C. H. 2017. Clinical outcomes for the obese hospital inpatient: An observational study. *SAGE Open Med,* 5**,** 2050312117700065.

GAO, M., SUN, J., YOUNG, N., BOYD, D., ATKINS, Z., LI, Z., DING, Q., DIEHL, J. & LIU, H. 2016. Impact of Body Mass Index on Outcomes in Cardiac Surgery. *J Cardiothorac Vasc Anesth,* 30**,** 1308-16.

GLOBAL, B. M. I. M. C., DI ANGELANTONIO, E., BHUPATHIRAJU SH, N., WORMSER, D., GAO, P., KAPTOGE, S., BERRINGTON DE GONZALEZ, A., CAIRNS, B. J., HUXLEY, R., JACKSON CH, L., JOSHY, G., LEWINGTON, S., MANSON, J. E., MURPHY, N., PATEL, A. V., SAMET, J. M., WOODWARD, M., ZHENG, W., ZHOU, M., BANSAL, N., BARRICARTE, A., CARTER, B., CERHAN, J. R., SMITH, G. D., FANG, X., FRANCO, O. H., GREEN, J., HALSEY, J., HILDEBRAND, J. S., JUNG, K. J., KORDA, R. J., MCLERRAN, D. F., MOORE, S. C., O'KEEFFE, L. M., PAIGE, E., RAMOND, A., REEVES, G. K., ROLLAND, B., SACERDOTE, C., SATTAR, N., SOFIANOPOULOU, E.,

STEVENS, J., THUN, M., UESHIMA, H., YANG, L., YUN, Y. D., WILLEIT, P., BANKS, E., BERAL, V., CHEN, Z., GAPSTUR, S. M., GUNTER, M. J., HARTGE, P., JEE, S. H., LAM, T. H., PETO, R., POTTER, J. D., WILLETT, W. C., THOMPSON, S. G., DANESH, J. & HU, F. B. 2016. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet,* 388**,** 776-86.

GOH, V. H., TAIN, C. F., TONG, T. Y., MOK, H. P. & WONG, M. T. 2004. Are BMI and other anthropometric measures appropriate as indices for obesity? A study in an Asian population. *J Lipid Res,* 45**,** 1892-8.

GOLDSTEIN, D. J. 1992. Beneficial health effects of modest weight loss. *Int J Obes Relat Metab Disord,* 16**,** 397-415.

GRAHAM, K. L., WILKER, E. H., HOWELL, M. D., DAVIS, R. B. & MARCANTONIO, E. R. 2015. Differences between early and late readmissions among patients: a cohort study. *Ann Intern Med,* 162**,** 741-9.

GRUBERG, L., WEISSMAN, N. J., WAKSMAN, R., FUCHS, S., DEIBLE, R., PINNOW, E. E., AHMED, L. M., KENT, K. M., PICHARD, A. D., SUDDATH, W. O., SATLER, L. F. & LINDSAY, J., JR. 2002. The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: the obesity paradox? *J Am Coll Cardiol,* 39**,** 578-84.

HANSEN, L. O., YOUNG, R. S., HINAMI, K., LEUNG, A. & WILLIAMS, M. V. 2011. Interventions to reduce 30-day rehospitalization: a systematic review. *Ann Intern Med,* 155**,** 520-8.

HANSON, P., SUMMERS, C., PANESAR, A., ODURO-DONKOR, D., LANGE, M., MENON, V. & BARBER, T. M. 2021. Low Carb Program Health App Within a Hospital-Based Obesity Setting: Observational Service Evaluation. *JMIR Form Res,* 5**,** e29110.

HEALTH, A. I. O. & WELFARE 2023. Overweight and obesity. Canberra: AIHW.

HUA, M., GONG, M. N., BRADY, J. & WUNSCH, H. 2015. Early and late unplanned rehospitalizations for survivors of critical illness*. *Crit Care Med,* 43**,** 430-8.

INABNIT, L. S., BLANCHETTE, C. & RUBAN, C. 2018. Comorbidities and length of stay in chronic obstructive pulmonary disease patients. *COPD,* 15**,** 355-360.

IOZZO, P., ROSSI, G., MICHELASSI, C., LANDI, P. & CARPEGGIANI, C. 2013. Interpretation of the "obesity paradox": a 30-year study in patients with cardiovascular disease. *Int J Cardiol,* 168**,** 112-6.

JAROLIMOVA, J., TAGONI, J. & STERN, T. A. 2013. Obesity: its epidemiology, comorbidities, and management. *Prim Care Companion CNS Disord,* 15.

JENSEN, C. B., TROELSEN, A., PETERSEN, P. B., CC, J. O., KEHLET, H., GROMOV, K., CENTRE FOR FAST-TRACK, H. & KNEE REPLACEMENT COLLABORATIVE, G. 2021. Influence of body mass index and age on day-of-surgery discharge, prolonged admission, and 90-day readmission after fast-track unicompartmental knee arthroplasty. *Acta Orthop,* 92**,** 722-727.

JEPMA, P., TER RIET, G., VAN RIJN, M., LATOUR, C. H. M., PETERS, R. J. G., SCHOLTE OP REIMER, W. J. M. & BUURMAN, B. M. 2019. Readmission and mortality in patients >/=70 years with acute myocardial infarction or heart failure in the Netherlands: a retrospective cohort study of incidences and changes in risk factors over time. *Neth Heart J,* 27**,** 134-141.

JOHNSON, A. P., PARLOW, J. L., WHITEHEAD, M., XU, J., ROHLAND, S. & MILNE, B. 2015. Body Mass Index, Outcomes, and Mortality Following Cardiac Surgery in Ontario, Canada. *J Am Heart Assoc,* 4.

KENT, S., GREEN, J., REEVES, G., BERAL, V., GRAY, A., JEBB, S. A., CAIRNS, B. J., MIHAYLOVA, B. & MILLION WOMEN STUDY, C. 2017. Hospital costs in relation to body-mass index in 1.1 million women in England: a prospective cohort study. *Lancet Public Health,* 2**,** e214-e222.

KHAN, S. S., NING, H., WILKINS, J. T., ALLEN, N., CARNETHON, M., BERRY, J. D., SWEIS, R. N. & LLOYD-JONES, D. M. 2018. Association of Body Mass Index With Lifetime Risk of Cardiovascular Disease and Compression of Morbidity. *JAMA Cardiol,* 3**,** 280-287.

KONG, C. W. & WILKINSON, T. M. A. 2020. Predicting and preventing hospital readmission for exacerbations of COPD. *ERJ Open Res,* 6.

KRITCHEVSKY, S. B., BEAVERS, K. M., MILLER, M. E., SHEA, M. K., HOUSTON, D. K., KITZMAN, D. W. & NICKLAS, B. J. 2015. Intentional weight loss and all-cause mortality: a meta-analysis of randomized clinical trials. *PLoS One,* 10**,** e0121993.

LANDBO, C., PRESCOTT, E., LANGE, P., VESTBO, J. & ALMDAL, T. P. 1999. Prognostic value of nutritional status in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med,* 160**,** 1856-61.

LANTZ, H., PELTONEN, M., AGREN, L. & TORGERSON, J. S. 2003. A dietary and behavioural programme for the treatment of obesity. A 4-year clinical trial and a long-term posttreatment follow-up. *J Intern Med,* 254**,** 272-9.

LIU, B., BALKWILL, A., SPENCER, E., BERAL, V. & MILLION WOMEN STUDY, C. 2008. Relationship between body mass index and length of hospital stay for gallbladder disease. *J Public Health (Oxf),* 30**,** 161-6.

MAALI, Y., PEREZ-CONCHA, O., COIERA, E., ROFFE, D., DAY, R. O. & GALLEGO, B. 2018. Predicting 7-day, 30-day and 60-day all-cause unplanned readmission: a case study of a Sydney hospital. *BMC Med Inform Decis Mak,* 18**,** 1.

MCEWEN, L. N., KARTER, A. J., WAITZFELDER, B. E., CROSSON, J. C., MARRERO, D. G., MANGIONE, C. M. & HERMAN, W. H. 2012. Predictors of mortality over 8 years in type 2 diabetic patients: Translating Research Into Action for Diabetes (TRIAD). *Diabetes Care,* 35**,** 1301-9.

MELTZER, A. A. & EVERHART, J. E. 1995. Unintentional weight loss in the United States. *Am J Epidemiol,* 142**,** 1039-46.

MUDGE, A. M., KASPER, K., CLAIR, A., REDFERN, H., BELL, J. J., BARRAS, M. A., DIP, G. & PACHANA, N. A. 2011. Recurrent readmissions in medical patients: a prospective study. *J Hosp Med,* 6**,** 61-7.

MULLEN, J. T., MOORMAN, D. W. & DAVENPORT, D. L. 2009. The obesity paradox: body mass index and outcomes in patients undergoing nonbariatric general surgery. *Ann Surg,* 250**,** 166-72.

MUST, A., SPADANO, J., COAKLEY, E. H., FIELD, A. E., COLDITZ, G. & DIETZ, W. H. 1999. The disease burden associated with overweight and obesity. *JAMA,* 282**,** 1523-9.

NAZARE, J. A., SMITH, J., BOREL, A. L., ASCHNER, P., BARTER, P., VAN GAAL, L., TAN, C. E., WITTCHEN, H. U., MATSUZAWA, Y., KADOWAKI, T., ROSS, R., BRULLE-WOHLHUETER, C., ALMÉRAS, N., HAFFNER, S. M., BALKAU, B. & DESPRÉS, J. P. 2015. Usefulness of measuring both body mass index and waist circumference for the estimation of visceral adiposity and related cardiometabolic risk profile (from the INSPIRE ME IAA study). *Am J Cardiol,* 115**,** 307-15.

NUTTALL, F. Q. 2015. Body Mass Index: Obesity, BMI, and Health: A Critical Review. *Nutr Today,* 50**,** 117-128.

PACK, Q. R., RODRIGUEZ-ESCUDERO, J. P., THOMAS, R. J., ADES, P. A., WEST, C. P., SOMERS, V. K. & LOPEZ-JIMENEZ, F. 2014. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. *Mayo Clin Proc,* 89**,** 1368-77.

PERERA, L. A. M., CHOPRA, A. & SHAW, A. L. 2021. Approach to Patients with Unintentional Weight Loss. *Med Clin North Am,* 105**,** 175-186.

POIRIER, P., GILES, T. D., BRAY, G. A., HONG, Y., STERN, J. S., PI-SUNYER, F. X., ECKEL, R. H., AMERICAN HEART, A., OBESITY COMMITTEE OF THE COUNCIL ON NUTRITION, P. A. & METABOLISM 2006. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. *Circulation,* 113**,** 898-918.

POTTER, J. F., SCHAFER, D. F. & BOHI, R. L. 1988. In-hospital mortality as a function of body mass index: an age-dependent variable. *J Gerontol,* 43**,** M59-63.

RAGAVAN, M. V., SVEC, D. & SHIEH, L. 2017. Barriers to timely discharge from the general medicine service at an academic teaching hospital. *Postgrad Med J,* 93**,** 528-533.

RAM, P., SHAH, M., LO, K. B. U., AGARWAL, M., PATEL, B., TRIPATHI, B., ARORA, S., PATEL, N., JORDE, U. P. & BANERJI, S. 2021. Etiologies and predictors of readmission among obese and morbidly obese patients admitted with heart failure. *Heart Fail Rev,* 26**,** 829-838.

REEVES, G. K., BALKWILL, A., CAIRNS, B. J., GREEN, J., BERAL, V. & MILLION WOMEN STUDY, C. 2014. Hospital admissions in relation to body mass index in UK women: a prospective cohort study. *BMC Med,* 12**,** 45.

ROJAS-GARCIA, A., TURNER, S., PIZZO, E., HUDSON, E., THOMAS, J. & RAINE, R. 2018. Impact and experiences of delayed discharge: A mixed-studies systematic review. *Health Expect,* 21**,** 41-56.

RYAN, D. H. & YOCKEY, S. R. 2017. Weight Loss and Improvement in Comorbidity: Differences at 5%, 10%, 15%, and Over. *Curr Obes Rep,* 6**,** 187-194.

SCHOUSBOE, J. T., KATS, A. M., LANGSETMO, L., TAYLOR, B. C., VO, T. N., KADO, D. M., FINK, H. A. & ENSRUD, K. E. 2018. Associations of recent weight loss with health care costs and utilization among older women. *PLoS One,* 13**,** e0191642.

SHAI, I., JIANG, R., MANSON, J. E., STAMPFER, M. J., WILLETT, W. C., COLDITZ, G. A. & HU, F. B. 2006. Ethnicity, obesity, and risk of type 2 diabetes in women: a 20-year follow-up study. *Diabetes Care,* 29**,** 1585-90.

SHARMA, Y., MILLER, M., KAAMBWA, B., SHAHI, R., HAKENDORF, P., HORWOOD, C. & THOMPSON, C. 2017. Malnutrition and its association with readmission and death within 7 days and 8-180 days postdischarge in older patients: a prospective observational study. *BMJ Open,* 7**,** e018443.

SHARMA, Y., MILLER, M., KAAMBWA, B., SHAHI, R., HAKENDORF, P., HORWOOD, C. & THOMPSON, C. 2018. Factors influencing early and late readmissions in Australian hospitalised patients and investigating role of admission nutrition status as a predictor of hospital readmissions: a cohort study. *BMJ Open,* 8**,** e022246.

TABUCANON, T., WILCOX, J. & TANG, W. H. W. 2020. Does Weight Loss Improve Clinical Outcomes in Overweight and Obese Patients with Heart Failure? *Curr Diab Rep,* 20**,** 75.

TOBIAS, D. K., PAN, A., JACKSON, C. L., O'REILLY, E. J., DING, E. L., WILLETT, W. C., MANSON, J. E. & HU, F. B. 2014. Body-mass index and mortality among adults with incident type 2 diabetes. *N Engl J Med,* 370**,** 233-44.

TSUI, S. T., YANG, J., ZHANG, X., DOCIMO, S., JR., SPANIOLAS, K. & PRYOR, A. D. 2021. Hospitalizations and emergency department visits in heart failure patients after bariatric surgery. *Surg Obes Relat Dis,* 17**,** 489-497.

VIERBOOM, Y. C., PRESTON, S. H. & STOKES, A. 2018. Patterns of weight change associated with disease diagnosis in a national sample. *PLoS One,* 13**,** e0207795.

WANG, Y. C., MCPHERSON, K., MARSH, T., GORTMAKER, S. L. & BROWN, M. 2011. Health and economic burden of the projected obesity trends in the USA and the UK. *Lancet,* 378**,** 815-25.

WANNAMETHEE, S. G., SHAPER, A. G. & LENNON, L. 2005. Reasons for intentional weight loss, unintentional weight loss, and mortality in older men. *Arch Intern Med,* 165**,** 1035-40.

WHO. 2021. *Obesity and Overweight Fact sheet* [Online]. Available: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight [Accessed 24/01/2023].

WILLIAMSON, D. A., BRAY, G. A. & RYAN, D. H. 2015. Is 5% weight loss a satisfactory criterion to define clinically significant weight loss? *Obesity (Silver Spring),* 23**,** 2319-20.

WILLIAMSON, D. F., PAMUK, E., THUN, M., FLANDERS, D., BYERS, T. & HEATH, C. 1995. Prospective study of intentional weight loss and mortality in never-smoking overweight US white women aged 40-64 years. *Am J Epidemiol,* 141**,** 1128-41.

WILLIAMSON, D. F., PAMUK, E., THUN, M., FLANDERS, D., BYERS, T. & HEATH, C. 1999. Prospective study of intentional weight loss and mortality in overweight white men aged 40-64 years. *Am J Epidemiol,* 149**,** 491-503.

WILSON, P. W., D'AGOSTINO, R. B., SULLIVAN, L., PARISE, H. & KANNEL, W. B. 2002. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. *Arch Intern Med,* 162**,** 1867-72.

WONG, H. J., MORRA, D., CAESAR, M., CARTER, M. W. & ABRAMS, H. 2010. Understanding hospital and emergency department congestion: an examination of inpatient admission trends and bed resources. *CJEM,* 12**,** 18-26.

WOOLLEY, C., THOMPSON, C., HAKENDORF, P. & HORWOOD, C. 2019. The Effect of Age upon the Interrelationship of BMI and Inpatient Health Outcomes. *J Nutr Health Aging,* 23**,** 558-563.

YANNAKOULIA, M., MAMALAKI, E. & POULIMENEAS, D. 2022. Intentional weight loss and mortality in middle-aged and older adults: A narrative review. *Maturitas,* 165**,** 100-103.

YOON, H. H., LEWIS, M. A., SHI, Q., KHAN, M., CASSIVI, S. D., DIASIO, R. B. & SINICROPE, F. A. 2011. Prognostic impact of body mass index stratified by smoking status in patients with esophageal adenocarcinoma. *J Clin Oncol,* 29**,** 4561-7.

ZARE, H., GILMORE, D. R., MEYERSON, N. S. & THORPE, R. J., JR. 2022. Income Inequality, Race/Ethnicity, and Obesity in U.S. Men 20 Years and Older: 1999 to 2016. *Am J Mens Health,* 16**,** 15579883221123852.

CHAPTER TWO

Chapter two consists of the published paper **'The Impact of Morbid Obesity on the Health Outcomes of Hospital Inpatients: An Observational Study'**

Chapter 2: Statement of Authorship

Statement of Authorship

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Principal Author

Name of Principal Author (Candidate)	Kellie Fusco		
Contribution to the Paper	Conceptualisation, methodology, statistical analysis, original draft preparation, critical review and editing		
Overall percentage (%)	80%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research Candidature and is not subject to any obligations or contractual agreement with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	25/01/24

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. The candidate's stated contribution to the publication is accurate (as detailed above)
ii. Permission is granted for the candidate in include the publication in the thesis; and
iii. The sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Article

The Impact of Morbid Obesity on the Health Outcomes of Hospital Inpatients: An Observational Study

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Abstract: Morbid obesity poses a significant burden on the health-care system. This study determined whether morbid obesity leads to worse health-outcomes in hospitalised patients. This retrospective-study examined nutritional data of all inpatients aged 18–79 years, with a body-mass-index (BMI) $\geq$ 18.5 kg/m^2 admitted over a period of 4 years at two major hospitals in Australia. Patients were divided into 3 groups for comparison: normal/overweight (BMI 18.5–29.9 kg/m^2), obese (BMI 30–39.9 kg/m^2) and morbidly-obese (BMI $\geq$ 40 kg/m^2). Outcome measures included length-of-hospital-stay (LOS), in-hospital mortality, and 30-day readmissions. Multilevel-mixed-effects regression was used to compare clinical outcomes between the groups after adjustment for potential confounders. Of 16,579 patients, 1004 (6.1%) were classified as morbidly-obese. Morbidly-obese patients had a significantly longer median (IQR) LOS than normal/overweight patients (5 (2, 12) vs. 5 (2, 11) days, p value = 0.012) and obese-patients (5 (2, 12) vs. 5 (2, 10) days, p value = 0.036). After adjusted-analysis, morbidly-obese patients had a higher incidence of a longer LOS than normal/overweight patients (IRR 1.04; 95% CI 1.02–1.07; p value < 0.001) and obese-patients (IRR 1.13; 95% CI 1.11–1.16; p value < 0.001). Other clinical outcomes were similar between the different groups. Morbid obesity leads to a longer LOS in hospitalised patients but does not adversely affect other clinical outcomes.

Keywords: morbid obesity; health outcomes; in-hospital mortality; length of hospital stay; readmissions

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1. Introduction

The prevalence of overweight and obesity has been increasing worldwide over the past 40 years [1]. It is estimated that in Australia, almost two thirds of adults are either overweight or obese [2]. Approximately 1 million adults in Australia have clinically severe obesity (defined as a body mass index (BMI) $\geq$ 40 kg/m^2 or $\geq$35 kg/m^2 with at least one complication) [3]. A significant burden of disease in the population at large is caused by overweight (and obesity) induced comorbidity [4]. Overweight and obesity have been linked to a number of diseases including diabetes, asthma, osteoarthritis, gout, cardiovascular disease, and certain types of cancers [2,5,6]. Obesity has long been considered as a major risk factor for mortality in both the general population and in hospitalised patients. The costs of obesity and overweight to the health care system are complex to calculate [7]. There is a burden of chronic disease reflected in higher costs for care of obese within the community but there is also a burden of acute and chronic disease reflected in higher costs for the care of obese individuals within hospitals such as may be seen due to longer and more frequent intensive care unit (ICU) admissions, longer lengths of hospital stay (LOS), and higher likelihood of readmission within 30 days [8,9].

Given the association of obesity with various other co-morbidities, it might be safe to assume that overweight and obese patients will have poorer health outcomes than those with a healthy body weight. However, recent evidence [10] suggests that older individuals with several comorbidities and an elevated BMI, may have a lower mortality when compared to patients with normal BMI. This mortality benefit of obesity has been termed as the 'obesity paradox' and has been observed in patients with diabetes, cardiovascular disease, chronic obstructive pulmonary disease (COPD) and cancer [11–15]. However, other studies have not confirmed the benefits of increasing BMI on clinical outcomes [16,17].

The inconsistent evidence regarding obese patients' clinical outcomes may be attributable to a number of factors including different cut-off values of BMI used to classify obesity in different studies [18]. In addition, studies may have methodological differences such as the source of BMI data (self-reported or objective evidence), patient selection bias and the presence of residual confounding [19,20]. In addition, very few studies have examined clinical outcomes in very severely obese patients, i.e., BMI $\geq$ 40kg/m^2, especially in hospitalised patients. A major limitation of the existing studies is the lack of detailed data on associated co-morbidities, socio-economic status of the patients and ethnicity, all of which have been identified as factors which can contribute to both obesity and clinical outcomes [21–23].

This study was therefore designed to examine the association between morbid obesity (BMI $\geq$ 40kg/m^2) and clinical outcomes in hospitalised patients after including important confounders such as the comorbidity burden, socioeconomic status and the ethnicity of the participants. The hypothesis for this study was that morbidly obese hospitalised patients will have worse clinical outcomes than non-morbidly obese patients. The primary outcome measure for this study was to determine whether morbid obesity was associated with a longer LOS. The secondary outcomes were to determine any differences in in-hospital mortality, number of complications during admission, ICU length of stay and 30-day readmissions between morbidly obese and non-morbidly obese patients.

2. Materials and Methods

Non-identifiable, routinely collected data from two of South Australia's tertiary-level teaching hospitals (Flinders Medical Centre (FMC) and Royal Adelaide Hospital (RAH)) were examined. These two hospitals in South Australia have adopted a nutritional screening tool (Malnutrition Universal Screening Tool (eMUST)) [24] which has allowed for the determination of each inpatient's BMI. These data, when linked to hospital inpatient databases, were used to determine the differences in outcomes for inpatients at these two hospitals using specific BMI groupings. The eMUST database was accessed and combined with data from the hospital inpatient database. The eMUST database includes information about the following variables: patient identification number, date of birth, date of hospital admission, date of performance of the MUST, height, weight, BMI, history of recent weight loss, impact of acute illness on nutritional status and the total MUST score. This study included information from all inpatients at FMC and RAH, who had an eMUST recorded between 1 January 2015 and 31 December 2018. The hospital inpatient dataset variables included: age, sex, Charlson comorbidity index, socio-economic category as determined by the Index of Relative Social Disadvantage (IRSD), indigenous status, LOS, admission to ICU, LOS in ICU, complications during index admission, readmissions within 7 and 30 days of discharge.

Patients with a BMI of 18.5–24.9 kg/m^2 were classified as normal, 25–29.9 kg/m^2 as overweight, 30–34.9 kg/m^2 as class 1 obesity, 35–39.9 kg/m^2 as class 2 obesity and $\geq$40 kg/m^2 as class 3 obesity or morbidly obese. For this study, patients were divided into 3 groups for comparison: normal/overweight (BMI 18.5–29.9 kg/m^2), obese (BMI 30–39.9 kg/m^2) and morbidly obese (BMI $\geq$ 40 kg/m^2). The ethical approval for this study was granted by the Southern Adelaide Human Clinical Research Ethics Committee (SAHREC) no 387.11.

Statistics

Data were inspected for normality using histograms and differences between different groups were assessed using the one-way analysis of variance (ANOVA) or the Kruskal Wallis H test. Differences in categorical variables were analysed using the chi-squared statistics. We used the Dunn test for multiple comparisons and family wise error was adjusted by use of the Bonferroni correction. The relationships between morbid obesity and the outcome variables were examined using multilevel mixed-effect models with hospital outcomes as a random effect [25]. We used mixed-effects Poisson regression for LOS and incidence risk ratios (IRR) were determined, while in-hospital mortality, 7 and 30-day readmission rate were assessed by use of mixed-effects logistic regression models and odds ratios (OR) were determined. Patient-level factors, which have been identified as important in previous studies as potential confounders [23,26], were considered in the multilevel analysis as fixed effects. These included: age, sex, Charlson index, socio-economic status as determined by the IRSD, and indigenous status of the patients. An intercept-only model was also assessed in order to determine the intraclass correlation coefficient, which describes the proportion of the total variance that is attributable to clustering within-hospitals [27]. The appropriateness of the final model was confirmed by examining the distribution of the level 1 and level 2 residuals to check for normality. All statistical analyses were performed by of STATA version 17.0 (StataCorp LP, College Station, TX, USA). All outcomes were assessed using a 2-sided Type 1 error rate of alpha = 0.05.

3. Results

3.1. Data

The data included details of 28,907 inpatients who had an eMUST performed during hospital admission. After removal of the second and subsequent visits for any patient (n = 1631), underweight patients (BMI < 18.5 kg/m^2) (n = 1668), and those over the age of 80 years (n = 9029), 16,579 patients were available for inclusion in this study (Figure 1). When characterised according to the BMI, 34.6% of these patients had a normal BMI, 31.9% were overweight, 18.9% were in obese class 1, 8.5% in obese class 2 and 6.1% were morbidly obese (Table 1). For this study, we compared the clinical characteristics and outcomes between 3 groups: normal/overweight patients n = 11,028 (66.5%), obese patients (obesity class 1 and 2) n = 4547 (27.4%) and the morbidly obese group n = 1004 (6.1%).

3.2. Characteristics

Table 2 shows baseline characteristics of morbidly obese patients when compared to the other groups. Morbidly obese patients were more likely to be younger and female, with a higher comorbidity burden as reflected by the higher Charlson index, and they belonged to a lower socio-economic status as reflected by a lower IRSD score than those who were who were normal/overweight or those who were obese ($p < 0.05$). There was no significant difference in the number of patients who identified as indigenous or Torres Strait Islanders, who belonged to the morbidly obese category when compared to the other groups ($p < 0.05$).

Table 1. BMI categories of patients between 18–79 years excluding underweight patients.

BMI (kg/m^2)	Normal BMI BMI 18.5–24.9	Overweight BMI 25–29.9	Obese Class 1 BMI 30–34.9	Obese Class 2 BMI 35–35.9	Obese Class 3 BMI > 40
n = 16,579	5731	5297	3136	1411	1004
%	34.6	31.9	18.9	8.5	6.1

BMI, body mass index.

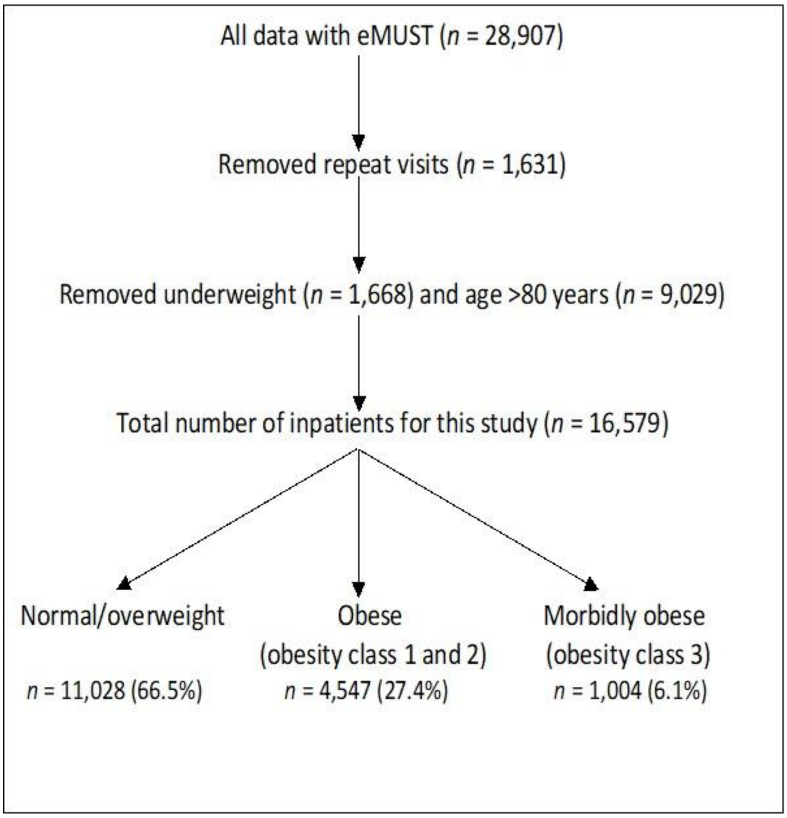

Figure 1. Study flow diagram.

Table 2. Baseline patient characteristics.

Variable	Normal/Overweight	Obese (Obesity Class 1 and 2)	Morbidly Obese (Obesity Class III)	*p* Value
Number of subjects (%)	*n* = 11,028 (66.5)	*n* = 4547 (27.4)	*n* = 1004 (6.1)	
Characteristics				
Age in years med (IQR)	60 (43,71)	61 (49,70)	56 (45,67)	<0.0001
Age categories (%)				
18–29	1346 (12.2)	272 (5.9)	71 (7.1)	<0.001
30–39	1030 (9.4)	383 (8.4)	81 (8.1)	
40–49	1270 (11.5)	553 (12.2)	193 (19.2)	
50–59	1783 (16.2)	901 (19.8)	230 (22.9)	
60–69	2397 (21.7)	1167 (25.8)	255 (25.4)	
70–79	3202 (29.0)	1271 (27.9)	174 (17.3)	
Charlson Index med (IQR)	0 (0,2)	1 (0,2)	1 (0,2)	<0.0001
Gender female *n* (%)	4455 (40.4)	2073 (45.6)	629 (62.7)	<0.001
Indigenous/Torres islander status *n* (%)	328 (2.9)	134 (2.9)	43 (4.3)	0.176
IRSD Quintile *n* (%)				
Q1 (most disadvantaged)	2505 (23.1)	1157 (25.8)	297 (30.0)	<0.001
Q2	2391 (22.2)	1105 (24.7)	259 (26.3)	
Q3	2147 (19.8)	866 (19.3)	183 (18.5)	
Q4	1844 (17.0)	717 (16.0)	128 (12.9)	
Q5 (least disadvantaged)	1942 (17.9)	634 (14.2)	122 (12.3)	

IQR, interquartile range; IRSD, index of relative socio-economic disadvantage.

3.3. Univariate Analysis

The median (IQR) overall hospital LOS was 5 (1, 9) days. Morbidly obese patients had a significantly longer median (IQR) LOS when compared to both normal/overweight patients (5 days (2, 12) vs. 5 days (2, 11), $p = 0.012$) and obese patients (5 days (2, 12) vs. 5 days (2, 10), p value = 0.036) (Table 3). The overall in-hospital mortality rate was 0.88% and there was no difference in mortality in different groups (0.51% vs. 0.93% vs. 0.90, $p = 0.439$), in morbidly obese, obese and normal/overweight patients, respectively (Table 3). Other outcomes including ICU admission, duration of ICU stay, number of complications during admission and readmission within 30-days of hospital discharge were similar between different groups of patients (Table 3).

Table 3. Clinical outcomes in morbidly obese compared to non-morbidly obese.

BMI	Normal/Overweight	Obese (Obesity Class 1 and 2)	Morbidly Obese (Obesity Class III)	*p* Value
Number of subjects	*n* = 11,028 (66.5)	*n* = 4547 (27.4)	*n* = 1004 (6.1)	
Outcomes				
*LOS days median (IQR)	5 (2, 11)	5 (2, 10)	5 (2, 12)	0.030
LOS *n* (%)				
≤2 days 3–14 days 15–28 days >28 days	3276 (29.7) 5801 (52.6) 1185 (10.8) 766 (6.9)	1266 (27.8) 2511 (55.2) 510 (11.3) 260 (5.7)	259 (25.8) 556 (55.4) 119 (11.9) 70 (6.9)	0.002
ICU admission rate	1041 (9.4)	400 (8.8)	98 (9.8)	0.393
ICU hours mean (SD)	14.3 (103.2)	10.2 (60.2)	11.9 (68.4)	0.051
In hospital mortality	95 (0.90)	41 (0.93)	5 (0.51)	0.205
No of complications mean (SD)	0.9 (2.1)	0.8 (2.0)	0.9 (1.9)	0.528
Readmissions within 7 days	531 (4.8)	196 (4.3)	53 (5.3)	0.271
Readmissions within 30 days	1332 (12.1)	538 (11.8)	127 (12.7)	0.759

*LOS adjusted for mortality. LOS, length of hospital stay; IQR, interquartile range; ICU, intensive care unit.

3.4. Adjusted Analysis

3.4.1. Comparison of Outcomes between Morbidly Obese and Normal/Overweight Patients

Tables 4 and 5 shows outcomes after multilevel mixed-effect regression models adjusted for various confounders in morbidly obese when compared to normal/overweight patients and obese patients, respectively. The proportion of total variance accounted for the two different hospitals as reflected by the intraclass correlation coefficient was small (0.001, SE 0.007, 95% CI 8.99–0.02). When compared to normal/overweight patients, the overall hospital LOS was significantly longer in morbidly obese patients (IRR 1.04; 95% CI 1.02–1.07; p value < 0.001) (Table 4). There was no significant difference in in-hospital mortality in morbidly obese patients when compared to the normal/overweight patients (aOR 0.65; 95% CI 0.26–1.62; $p = 0.354$) (Table 4). Similarly, other clinical outcomes such as ICU admission, length of ICU stay, complications and 30-day readmissions were also not significantly different between the two groups (Table 4).

Table 4. Multilevel mixed effects regression models comparing clinical outcomes in morbidly obese with normal/overweight patients.

Outcome	OR/IRR	95% CI	*p* Value
LOS			
Unadjusted model	1.04 *	1.02–1.06	<0.001
Adjusted model excluding Charlson index	1.05 *	1.03–1.07	<0.001
Adjusted model with Charlson index	1.04 *	1.02–1.07	<0.001
In-hospital mortality			
Unadjusted model	0.57	0.23–1.41	0.224
Adjusted model excluding Charlson index	0.67	0.27–1.67	0.392
Adjusted model with Charlson index	0.65	0.26–1.62	0.354
ICU admission			
Unadjusted model	1.06	0.86–1.32	0.739
Adjusted model excluding Charlson index	1.08	0.87–1.35	0.493
Adjusted model with Charlson index	1.06	0.85–1.32	0.584
ICU LOS			
Unadjusted model	1.04 *	0.83–1.30	0.058
Adjusted model excluding Charlson index	1.05 *	0.84–1.31	0.675
Adjusted model with Charlson index	1.03 *	0.82–1.30	0.801
Complications			
Unadjusted model	1.00	0.94–1.08	0.793
Adjusted model excluding Charlson index	1.02	0.95–1.09	0.587
Adjusted model with Charlson index	1.00	0.93–1.07	0.996
30 day readmission			
Unadjusted model	1.06	0.87–1.29	0.571
Adjusted model excluding Charlson index	1.04	0.86–1.27	0.674
Adjusted model with Charlson index	1.02	0.83–1.25	0.818

* IRR, incident risk ratio; OR, odds ratio; LOS, length of hospital stay; ICU, intensive care unit.

Table 5. Multilevel mixed effects regression models comparing clinical outcomes in morbidly obese with obese patients.

Outcome	OR/IRR	95% CI	p Value
LOS			
Unadjusted model	1.09 *	1.07–1.12	<0.001
Adjusted model excluding Charlson index	1.14 *	1.11–1.16	<0.001
Adjusted model with Charlson index	1.13 *	1.11–1.16	<0.001
In-hospital mortality			
Unadjusted model	0.55	0.22–1.40	0.208
Adjusted model excluding Charlson index	0.67	0.26–1.70	0.395
Adjusted model with Charlson index	0.66	0.26–1.62	0.354
ICU admission			
Unadjusted model	1.12	0.96–1.22	0.208
Adjusted model excluding Charlson index	1.16	0.91–1.47	0.226
Adjusted model with Charlson index	1.15	0.91–1.46	0.251
ICU LOS			
Unadjusted model	1.12 *	0.89–1.41	0.334
Adjusted model excluding Charlson index	1.16 *	0.91–1.47	0.226
Adjusted model with Charlson index	1.15 *	0.91–1.46	0.251
Complications			
Unadjusted model	1.05	1.01–1.09	0.010
Adjusted model excluding Charlson index	1.10	1.02–1.19	0.012
Adjusted model with Charlson index	1.09	1.02–1.18	0.017
30 day readmission			
Unadjusted model	1.08	0.88–1.34	0.437
Adjusted model excluding Charlson index	1.09	0.88–1.34	0.416
Adjusted model with Charlson index	1.08	0.88–1.33	0.465

* IRR, incident risk ratio; OR, odds ratio; LOS, length of hospital stay; ICU, intensive care unit.

3.4.2. Comparison of Outcomes between Morbidly Obese and Obese Patients

When compared to obese patients, the overall hospital LOS was significantly longer in morbidly obese patients (IRR 1.13; 95% CI 1.11–1.16; p value < 0.001) (Table 5). Morbidly obese patients also had a significantly higher number of complications during admission when compared to obese patients (IRR 1.09; 95% CI 1.02–1.18, p value 0.017) (Table 5). However, there was no significant difference in in-hospital mortality in morbidly obese patients when compared to the obese group (aOR 0.66; 95% CI 0.26–1.62; $p = 0.354$) (Table 5). Other clinical outcomes such as ICU admission, length of ICU stay and 30-day readmissions were also not significantly different between the two groups (Table 5).

4. Discussion

The results of this study indicate that overall 6.1% of patients hospitalised during the study period were morbidly obese and these morbidly obese patients were more likely to be younger and female, with a higher comorbidity burden, and belonged to a lower socio-economic category than the non-morbidly obese group. When compared to normal/overweight patients and obese patients, morbidly obese patients had a significantly longer LOS. The number of complications were significantly higher in morbidly obese patients when compared to obese patients but not when compared to normal/overweight patients and other clinical outcomes were similar between the different groups.

The prevalence of morbid obesity according to this study was 6.1%, which is much lower than a United States (US) study [20] which included 800,417 hospitalised patients and found that 23.4% were morbidly obese. This discrepancy in the prevalence rates of morbid obesity in hospitalised patients between the two studies could partly be a reflection of in general a higher prevalence of obesity in US compared to Australia [28]. In addition, the discrepancy could be related to the differences in selection criteria between the two studies because the American study included only patients who were over the age of 40 years who were admitted with a diagnosis of cancer, chronic obstructive pulmonary disease (COPD), asthma and cardiovascular disease (CVD) compared to our inclusion of relatively younger patients presenting with a broader range of clinical diagnoses in our study. The prevalence rate of morbid obesity in our study, however, matches another study which included >18,000 patients discharged with a diagnosis of pneumonia and found that 4% of these patients were morbidly obese [29].

Our study found that morbidly obese patients have a longer LOS than the non-morbidly obese group. These results are similar to a study by Harris et al. [30], which explored 31730 diabetic foot infection/ulcer related hospitalisations and found that morbidly obese patients (BMI $\geq$ 40 kg/m^2) were more likely to be younger females, mean age (56.9 years) with a higher Charlson comorbidity score than non-obese patients and stayed for a longer time in hospital (mean LOS 5.5 days vs. 5.0 days, $p < 0.01$) (adjusted mean difference 0.47; 95% CI 0.13–0.81) than the non-morbidly obese group. Their study also found that morbidly obese patients had greater hospital resource utilisation and incurred higher hospitalisation charges than non-morbidly obese patients. Similarly, a Canadian study [31] which included 7560 patients, who underwent coronary artery bypass grafting, found that morbid obesity was significantly associated with a prolonged LOS when compared to those who had normal BMI (median (IQR) LOS 7 (5, 10) days vs. 6 (5, 9) days) and speculated that this could due to an increased risk of post-operative infection in morbid obese subjects. This study, however, did not find any significant differences between pulmonary or renal complications which could have accounted for an increased LOS between morbidly obese patients and those with a normal BMI.

We found no association between morbid obesity and in-hospital mortality in our study population and the probability of making a Type 2 error (false rejection of null hypothesis when it is true) is unlikely because of the presence of reasonable sample size in our data set. In addition, we tested this association by splitting the data over individual years and found no significant association between morbid obesity and in-hospital mortality. The results of our study in terms of mortality are similar to a study by Harris et al. [30], who included 4334 morbidly obese diabetic patients admitted with foot ulcers/infections and found no significant differences in in-hospital mortality (aOR 3.89, 95% CI 0.79–19.30, $p = 0.09$) when compared to the non-morbidly obese group. Akinyemiju et al. [20] in their study involving 800,417 US patients, hospitalised with a primary diagnosis of cancer, COPD, asthma and cardiovascular disease, found that there was a bell shaped relationship between in-hospital mortality and BMI with a trend towards reduction at higher ranges of BMI. This study, however, did not specifically compare clinical outcomes between morbidly obese patients and those with normal BMI or between those in the other obese categories.

Our study results also correspond to another study by King et al. [29], who included 18,746 hospitalised patients with a discharge diagnosis of pneumonia and found that 4%

of patients were morbidly obese (BMI $\geq$ 40 kg/m^2) and, when compared to patients with normal weight, morbid obesity was not associated with an increased 90-day mortality (aOR 0.96, 95% CI 0.72–1.28). Similar to our study, this study also did not find any association between morbid obesity and the risk of ICU admission.

Obese individuals are at an increased risk of obstructive sleep apnoea and obesity hypoventilation syndrome and have altered lung mechanics including reduced lung volumes, decreased respiratory compliance and impaired respiratory muscle function with a reduction in gas exchange [32–34]. In addition, obesity has been associated with increased susceptibility to various infections including bacteraemia, surgical site infections and poor wound healing, and obese subjects demonstrate a more severe illness with certain viral infections such as influenza and COVID-19 [35–39]. Given this demonstrated increased risk of infection and alteration in lung function, it is logical to believe that obesity will be associated with an increased risk of pneumonia and other nosocomial infections with a resultant increased risk of ICU care and higher mortality. However, current evidence does not support this hypothesis. On the contrary, more recent data support an association between obesity and improved hospital outcomes measured in terms of mortality and complications [29,40,41]. Studies in hospitalised patients have suggested mortality benefits of obesity in pneumonia; benefits which were maintained after adjustment for age and the presence of diabetes [29,41]. The protective effects of obesity could be related to an attenuated inflammatory response to an acute infection or stress because of the fact that obesity is already associated with a low-level inflammation at baseline [42] and studies suggest that the relative increase in inflammation in response to an acute stressor in subjects with obesity may be relatively less than that seen in subjects with a normal BMI [29,43]. This could potentially lead to less tissue injury in obese subjects and thus a lesser severity of nosocomial infections with a reduction in adverse clinical outcomes.

Another possible explanation for the protective effects of obesity could be related to differences in immunological function. Obese individuals demonstrate increased leptin levels, a hormone produced by adipocytes that participates in both adaptive and innate immune responses [44,45]. Leptin promotes macrophage activation, neutrophil chemotaxis, natural killer cells cytotoxicity and lymphopoiesis, and thus, leptin helps to increase bacterial clearance [46,47]. Immunological and inflammatory effects of obesity are fascinating areas that may be playing a protective role in these patients and both deserve further research to further clarify their clinical impact.

Limitations

The dataset contains only about 10% of patients admitted to the two institutions over the period of study which could have introduced a selection bias in this study. This poor capture of patient anthropometry is disappointing but not unusual. However, the BMI distribution in our study matches another recent Australian study [48], which captured data of all hospitalised patients. The retrospective design of this study is another limitation because of possibility of unknown confounders which could have influenced our results.

5. Conclusions

About 6% of patients presenting to hospitals were morbidly obese (BMI $\geq$ 40 kg/m^2). Although morbid obesity was associated with a slightly longer LOS (less than half a day on average), other clinical outcomes were similar among hospitalised adult patients < 80 years of age.

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Data Availability Statement: The data presented in this study are available on request from the corresponding author only after permission is granted by the ethics committee.

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References

1. Ng, M.; Fleming, T.; Robinson, M.; Thomson, B.; Graetz, N.; Margono, C.; Mullany, E.C.; Biryukov, S.; Abbafati, C.; Abera, S.F.; et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet* **2014**, *384*, 766–781. [CrossRef]
2. Australian Institute of Health and Welfare (AIHW): A Picture of Overweight and Obesity in Australia in 2017. Available online: https://www.aihw.gov.au/reports/overweight-obesity/a-picture-of-overweight-and-obesity-in-australia/summary (accessed on 27 July 2021).
3. Atlantis, E.; Kormas, N.; Samaras, K.; Fahey, P.; Sumithran, P.; Glastras, S.; Wittert, G.; Fusco, K.; Bishay, R.; Markovic, T.; et al. Clinical Obesity Services in Public Hospitals in Australia: A position statement based on expert consensus. *Clin. Obes.* **2018**, *8*, 203–210. [CrossRef] [PubMed]
4. Must, A.; Spadano, J.; Coakley, E.H.; Field, A.E.; Colditz, G.; Dietz, W.H. The disease burden associated with overweight and obesity. *JAMA* **1999**, *282*, 1523–1529. [CrossRef] [PubMed]
5. Bogers, R.P.; Bemelmans, W.J.; Hoogenveen, R.T.; Boshuizen, H.C.; Woodward, M.; Knekt, P.; van Dam, R.M.; Hu, F.B.; Visscher, T.L.; Menotti, A.; et al. Association of overweight with increased risk of coronary heart disease partly independent of blood pressure and cholesterol levels: A meta-analysis of 21 cohort studies including more than 300 000 persons. *Arch. Intern. Med.* **2007**, *167*, 1720–1728. [CrossRef] [PubMed]
6. Renehan, A.G.; Roberts, D.L.; Dive, C. Obesity and cancer: Pathophysiological and biological mechanisms. *Arch. Physiol. Biochem.* **2008**, *114*, 71–83. [CrossRef]
7. Dee, A.; Kearns, K.; O'Neill, C.; Sharp, L.; Staines, A.; O'Dwyer, V.; Fitzgerald, S.; Perry, I.J. The direct and indirect costs of both overweight and obesity: A systematic review. *BMC Res. Notes* **2014**, *7*, 242. [CrossRef]
8. Bertakis, K.D.; Azari, R. Obesity and the use of health care services. *Obes. Res.* **2005**, *13*, 372–379. [CrossRef]
9. Hauck, K.; Hollingsworth, B. The impact of severe obesity on hospital length of stay. *Med. Care* **2010**, *48*, 335–340. [CrossRef]
10. Doehner, W.; Erdmann, E.; Cairns, R.; Clark, A.L.; Dormandy, J.A.; Ferrannini, E.; Anker, S.D. Inverse relation of body weight and weight change with mortality and morbidity in patients with type 2 diabetes and cardiovascular co-morbidity: An analysis of the PROactive study population. *Int. J. Cardiol.* **2012**, *162*, 20–26. [CrossRef]
11. Carnethon, M.R.; De Chavez, P.J.; Biggs, M.L.; Lewis, C.E.; Pankow, J.S.; Bertoni, A.G.; Golden, S.H.; Liu, K.; Mukamal, K.J.; Campbell-Jenkins, B.; et al. Association of weight status with mortality in adults with incident diabetes. *JAMA* **2012**, *308*, 581–590. [CrossRef]
12. Tobias, D.K.; Pan, A.; Jackson, C.L.; O'Reilly, E.J.; Ding, E.L.; Willett, W.C.; Manson, J.E.; Hu, F.B. Body-mass index and mortality among adults with incident type 2 diabetes. *N. Engl. J. Med.* **2014**, *370*, 233–244. [CrossRef]
13. Elagizi, A.; Kachur, S.; Lavie, C.J.; Carbone, S.; Pandey, A.; Ortega, F.B.; Milani, R.V. An Overview and Update on Obesity and the Obesity Paradox in Cardiovascular Diseases. *Prog. Cardiovasc. Dis.* **2018**, *61*, 142–150. [CrossRef] [PubMed]
14. Landbo, C.; Prescott, E.; Lange, P.; Vestbo, J.; Almdal, T.P. Prognostic value of nutritional status in chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* **1999**, *160*, 1856–1861. [CrossRef] [PubMed]
15. Yoon, H.H.; Lewis, M.A.; Shi, Q.; Khan, M.; Cassivi, S.D.; Diasio, R.B.; Sinicrope, F.A. Prognostic impact of body mass index stratified by smoking status in patients with esophageal adenocarcinoma. *J. Clin. Oncol.* **2011**, *29*, 4561–4567. [CrossRef]
16. McEwen, L.N.; Karter, A.J.; Waitzfelder, B.E.; Crosson, J.C.; Marrero, D.G.; Mangione, C.M.; Herman, W.H. Predictors of mortality over 8 years in type 2 diabetic patients: Translating Research Into Action for Diabetes (TRIAD). *Diabetes Care* **2012**, *35*, 1301–1309. [CrossRef] [PubMed]
17. Chaturvedi, N.; Fuller, J.H. Mortality risk by body weight and weight change in people with NIDDM. The WHO Multinational Study of Vascular Disease in Diabetes. *Diabetes Care* **1995**, *18*, 766–774. [CrossRef]
18. Després, J.P. Excess visceral adipose tissue/ectopic fat the missing link in the obesity paradox? *J. Am. Coll. Cardiol.* **2011**, *57*, 1887–1889. [CrossRef]
19. Nazare, J.A.; Smith, J.; Borel, A.L.; Aschner, P.; Barter, P.; Van Gaal, L.; Tan, C.E.; Wittchen, H.U.; Matsuzawa, Y.; Kadowaki, T.; et al. Usefulness of measuring both body mass index and waist circumference for the estimation of visceral adiposity and related cardiometabolic risk profile (from the INSPIRE ME IAA study). *Am. J. Cardiol.* **2015**, *115*, 307–315. [CrossRef]

20. Akinyemiju, T.; Meng, Q.; Vin-Raviv, N. Association between body mass index and in-hospital outcomes: Analysis of the nationwide inpatient database. *Medicine* **2016**, *95*, e4189. [CrossRef] [PubMed]
21. Forbang, N.I.; Hughes-Austin, J.M.; Allison, M.A.; Criqui, M.H. Peripheral artery disease and non-coronary atherosclerosis in Hispanics: Another paradox? *Prog. Cardiovasc. Dis.* **2014**, *57*, 237–243. [CrossRef]
22. Dinsa, G.D.; Goryakin, Y.; Fumagalli, E.; Suhrcke, M. Obesity and socioeconomic status in developing countries: A systematic review. *Obes. Rev.* **2012**, *13*, 1067–1079. [CrossRef] [PubMed]
23. Islam, S.; Fitzgerald, L. Indigenous obesity in the news: A media analysis of news representation of obesity in Australia's Indigenous population. *BMC Obes.* **2016**, *3*, 30. [CrossRef] [PubMed]
24. Sharma, Y.; Thompson, C.; Kaambwa, B.; Shahi, R.; Miller, M. Validity of the Malnutrition Universal Screening Tool (MUST) in Australian hospitalized acutely unwell elderly patients. *Asia Pac. J. Clin. Nutr.* **2017**, *26*, 994–1000. [CrossRef]
25. McNeish, D. Estimation Methods for Mixed Logistic Models with Few Clusters. *Multivar. Behav. Res.* **2016**, *51*, 790–804. [CrossRef]
26. Apovian, C.M. Obesity: Definition, comorbidities, causes, and burden. *Am. J. Manag. Care* **2016**, *22*, s176–s185.
27. Austin, P.C. A Tutorial on Multilevel Survival Analysis: Methods, Models and Applications. *Int. Stat. Rev.* **2017**, *85*, 185–203. [CrossRef]
28. Adair, T.; Lopez, A.D. The role of overweight and obesity in adverse cardiovascular disease mortality trends: An analysis of multiple cause of death data from Australia and the USA. *BMC Med.* **2020**, *18*, 199. [CrossRef]
29. King, P.; Mortensen, E.M.; Bollinger, M.; Restrepo, M.I.; Copeland, L.A.; Pugh, M.J.; Nakashima, B.; Anzueto, A.; Hitchcock Noël, P. Impact of obesity on outcomes for patients hospitalised with pneumonia. *Eur. Respir. J.* **2013**, *41*, 929–934. [CrossRef]
30. Harris, C.M.; Abougergi, M.S.; Wright, S. Clinical outcomes among morbidly obese patients hospitalized with diabetic foot complications. *Clin. Obes.* **2019**, *9*, e12285. [CrossRef]
31. Terada, T.; Johnson, J.A.; Norris, C.; Padwal, R.; Qiu, W.; Sharma, A.M.; Janzen, W.; Forhan, M. Severe Obesity Is Associated with Increased Risk of Early Complications and Extended Length of Stay Following Coronary Artery Bypass Grafting Surgery. *J. Am. Heart Assoc.* **2016**, *5*, e003282. [CrossRef] [PubMed]
32. Parsons, P.E.; Eisner, M.D.; Thompson, B.T.; Matthay, M.A.; Ancukiewicz, M.; Bernard, G.R.; Wheeler, A.P. Lower tidal volume ventilation and plasma cytokine markers of inflammation in patients with acute lung injury. *Crit. Care Med.* **2005**, *33*, 1–6. [CrossRef]
33. Ware, L.B.; Matthay, M.A.; Parsons, P.E.; Thompson, B.T.; Januzzi, J.L.; Eisner, M.D. Pathogenetic and prognostic significance of altered coagulation and fibrinolysis in acute lung injury/acute respiratory distress syndrome. *Crit. Care Med.* **2007**, *35*, 1821–1828. [CrossRef] [PubMed]
34. McClintock, D.; Zhuo, H.; Wickersham, N.; Matthay, M.A.; Ware, L.B. Biomarkers of inflammation, coagulation and fibrinolysis predict mortality in acute lung injury. *Crit. Care* **2008**, *12*, R41. [CrossRef] [PubMed]
35. Dossett, L.A.; Dageforde, L.A.; Swenson, B.R.; Metzger, R.; Bonatti, H.; Sawyer, R.G.; May, A.K. Obesity and site-specific nosocomial infection risk in the intensive care unit. *Surg. Infect.* **2009**, *10*, 137–142. [CrossRef]
36. Anaya, D.A.; Dellinger, E.P. The obese surgical patient: A susceptible host for infection. *Surg. Infect.* **2006**, *7*, 473–480. [CrossRef]
37. Doyle, S.L.; Lysaght, J.; Reynolds, J.V. Obesity and post-operative complications in patients undergoing non-bariatric surgery. *Obes. Rev.* **2010**, *11*, 875–886. [CrossRef]
38. Viasus, D.; Paño-Pardo, J.R.; Pachón, J.; Campins, A.; López-Medrano, F.; Villoslada, A.; Fariñas, M.C.; Moreno, A.; Rodríguez-Baño, J.; Oteo, J.A.; et al. Factors associated with severe disease in hospitalized adults with pandemic (H1N1) 2009 in Spain. *Clin. Microbiol. Infect.* **2011**, *17*, 738–746. [CrossRef]
39. Stefan, N.; Birkenfeld, A.L.; Schulze, M.B.; Ludwig, D.S. Obesity and impaired metabolic health in patients with COVID-19. *Nat. Rev. Endocrinol.* **2020**, *16*, 341–342. [CrossRef] [PubMed]
40. Corrales-Medina, V.F.; Valayam, J.; Serpa, J.A.; Rueda, A.M.; Musher, D.M. The obesity paradox in community-acquired bacterial pneumonia. *Int. J. Infect. Dis.* **2011**, *15*, e54–e57. [CrossRef]
41. Inoue, Y.; Koizumi, A.; Wada, Y.; Iso, H.; Watanabe, Y.; Date, C.; Yamamoto, A.; Kikuchi, S.; Inaba, Y.; Toyoshima, H.; et al. Risk and protective factors related to mortality from pneumonia among middleaged and elderly community residents: The JACC Study. *J. Epidemiol.* **2007**, *17*, 194–202. [CrossRef]
42. Kim, C.S.; Park, H.S.; Kawada, T.; Kim, J.H.; Lim, D.; Hubbard, N.E.; Kwon, B.S.; Erickson, K.L.; Yu, R. Circulating levels of MCP-1 and IL-8 are elevated in human obese subjects and associated with obesity-related parameters. *Int. J. Obes.* **2006**, *30*, 1347–1355. [CrossRef]
43. Stapleton, R.D.; Dixon, A.E.; Parsons, P.E.; Ware, L.B.; Suratt, B.T. The association between BMI and plasma cytokine levels in patients with acute lung injury. *Chest* **2010**, *138*, 568–577. [CrossRef] [PubMed]
44. Iikuni, N.; Lam, Q.L.; Lu, L.; Matarese, G.; La Cava, A. Leptin and Inflammation. *Curr. Immunol. Rev.* **2008**, *4*, 70–79. [CrossRef] [PubMed]
45. Pérez-Pérez, A.; Vilariño-García, T.; Fernández-Riejos, P.; Martín-González, J.; Segura-Egea, J.J.; Sánchez-Margalet, V. Role of leptin as a link between metabolism and the immune system. *Cytokine Growth Factor Rev.* **2017**, *35*, 71–84. [CrossRef] [PubMed]
46. Maurya, R.; Bhattacharya, P.; Dey, R.; Nakhasi, H.L. Leptin Functions in Infectious Diseases. *Front. Immunol.* **2018**, *9*, 2741. [CrossRef] [PubMed]

47. Mancuso, P.; Curtis, J.L.; Freeman, C.M.; Peters-Golden, M.; Weinberg, J.B.; Myers, M.G., Jr. Ablation of the leptin receptor in myeloid cells impairs pulmonary clearance of Streptococcus pneumoniae and alveolar macrophage bactericidal function. *Am. J. Physiol. Lung Cell Mol. Physiol.* **2018**, *315*, L78–L86. [CrossRef]
48. Dennis, D.M.; Carter, V.; Trevenen, M.; Tyler, J.; Perrella, L.; Lori, E.; Cooper, I. Do acute hospitalised patients in Australia have a different body mass index to the general Australian population: A point prevalence study? *Aust. Health Rev.* **2018**, *42*, 121–129. [CrossRef]

CHAPTER THREE

Chapter three consists of the published paper **'The Impact of Weight Loss Prior to Hospital Readmission'**

Chapter 3: Statement of Authorship

Statement of Authorship

Title of Paper	The Impact of Morbid Obesity on the Health Outcomes of Hospital Inpatients: An Observational Study
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Name of Principal Author (Candidate)	Kellie Fusco		
Contribution to the Paper	Conceptualisation, statistical analysis, original draft preparation, critical review and editing		
Overall percentage (%)	75%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research Candidature and is not subject to any obligations or contractual agreement with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	25/01/24

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. The candidate's stated contribution to the publication is accurate (as detailed above)
ii. Permission is granted for the candidate in include the publication in the thesis; and
iii. The sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Contribution to the Paper	Conceptualisation, critical review and editing, supervision		
Signature		Date	4/2/2024

Journal of Clinical Medicine

Article

The Impact of Weight Loss Prior to Hospital Readmission

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Abstract: Hospital readmissions place a burden on hospitals. Reducing the readmission number and duration will help reduce the burden. Weight loss might affect readmission risk, especially the risk of an early (<30 days) readmission. This study sought to identify the predictors and the impact of weight loss prior to a delayed readmission (>30 days). Body mass index (BMI) was measured during the index admission and first readmission. Patients, after their readmission, were assessed retrospectively to identify the characteristics of those who had lost >5% weight prior to that readmission. Length of stay (LOS), time spent in the intensive care unit (ICU) and the one-year mortality of those patients who lost weight were compared to the outcomes of those who remained weight-stable using multilevel mixed-effects regression adjusting for BMI, Charlson comorbidity index (CCI), ICU hours and relative stay index (RSI). Those who were at risk of weight loss prior to readmission were identifiable based upon their age, BMI, CCI and LOS. Of 1297 patients, 671 (51.7%) remained weight-stable and 386 (29.7%) lost weight between admissions. During their readmission, those who had lost weight had a significantly higher LOS (IRR 1.17; 95% CI 1.12, 1.22: $p < 0.001$), RSI (IRR 2.37; 95% CI 2.27, 2.47: $p < 0.001$) and an increased ICU LOS (IRR 2.80; 95% CI 2.65, 2.96: $p < 0.001$). This study indicates that weight loss prior to a delayed readmission is predictable and leads to worse outcomes during that readmission.

Keywords: unplanned hospital readmissions; clinical outcomes; length of stay; weight loss

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1. Introduction

The avoidance or shortening of the duration of any readmission is a target for health care improvement because these actions will improve hospital congestion if not patient outcomes. Flares in chronic conditions are frequently the cause of an unplanned hospital admission [1–6], and patients with chronic conditions are often subsequently readmitted [1]. These chronic conditions include, but are not limited to, chronic heart failure, chronic kidney disease, depression, metastatic cancer, bacterial pneumonia, chronic obstructive pulmonary disease (COPD), hypertension and stroke. In fact, these chronic illnesses not only increase the risk of readmission, but they can also be associated with weight loss. Weight loss and malnutrition have been identified as risk factors for an early readmission (within 30 days of discharge) [4,7–9], but there are no studies that have looked at how weight change prior to a delayed readmission (>30 days following discharge) impacts upon the outcomes of the patient during and after the readmission episode.

Unplanned hospital readmission is mostly studied for readmissions up to 30 days following discharge. There are several studies that have looked at unplanned but delayed readmissions occurring after more than 30 days following discharge [1,5,7,9–12], although none of these studies have also studied the impact of weight loss prior to readmission and how this affects patient outcomes.

Since readmission and the length of stay after readmission place a considerable burden upon already congested hospitals [13,14], we sought to determine the characteristics of those at risk of experiencing weight loss prior to any delayed readmission and to determine whether weight loss after an index admission had any influence upon the outcomes of a delayed readmission to hospital. Such information, if obtained at a time for the patient when an intervention can be initiated, might help guide and improve patient care as well as improve hospital efficiency.

Therefore, the first aim of this paper is to identify, from the characteristics and outcomes of the index admission, those patients who are most likely to lose weight prior to any delayed readmission. The second aim is to determine whether pre-readmission weight loss produces any differences in health outcomes during and following the delayed readmission. For context, the characteristics and outcomes are reported of those who gained weight prior to their delayed readmission.

2. Materials and Methods

Routinely collected data were accessed for patients who were admitted to three South Australian teaching hospitals (the Royal Adelaide Hospital, Flinders Medical Centre and Repatriation General Hospital) between 1 January 2015 and 31 December 2018 and who were given a score using the Malnutrition Universal Screening Tool (eMUST) screening tool [15]. The eMUST database contains information such as patient identification number, date of birth, date of hospital admission, height, weight and BMI. The eMUST data were linked to the hospital inpatient database. The following variables were added through the hospital database linkage: age, sex, Charlson comorbidity index (CCI), socioeconomic category as determined by the Index of Relative Social Disadvantage (IRSD), LOS, relative stay index (RSI) defined as LOS divided by expected LOS, admission to the intensive care unit (ICU), LOS in ICU, patients' indigenous status and hospital readmissions within 7 days and 30 days of discharge.

Our study was focused on those who experienced a delayed readmission (i.e., readmission commencing at least 30 days following discharge from the index admission). Therefore, patients who experienced in-hospital mortality during their index admission, mortality within 30 days of index discharge or readmission within 30 days of index discharge were all excluded from the analysis.

The dataset contained 28,907 admissions of patients who had an eMUST performed during their hospital admission (Figure 1). Patients with a BMI < 18.5 kg/m^2 (n = 2113) were removed, leaving 26,974 in the dataset. All patients who were admitted only once were removed (n = 21,286), leaving 5508 index admissions and readmissions (comprising 2754 patients) in the dataset. Those with heart failure (HF) as a primary diagnosis (n = 520; 260 patients) were removed from the analysis, those with a LOS greater than 15 days for their index admission were removed (n = 410:205 patients) and subsequent admissions (third, fourth, fifth, etc.) for any patient were removed (1216 readmissions). Patients who either died within 30 days of index discharge (n = 34 patients) or were readmitted within 30 days of index discharge (n = 350 patients) were also removed from the dataset. The remaining 1297 patients (representing 2594 admissions and readmissions) were analyzed for the study.

Patients who had a BMI < 18.5 kg/m^2 were excluded because previous evidence suggests an association of this group of patients with known health issues [16–19]. All patients with a primary diagnosis of HF were also excluded because these patients may develop significant fluid shifts manifesting as weight loss during and between hospital admissions [20,21]. Patients whose index admission LOS was greater than 15 days were excluded from the analysis due to the possibility of their weight loss occurring during a prolonged hospital stay [22–24].

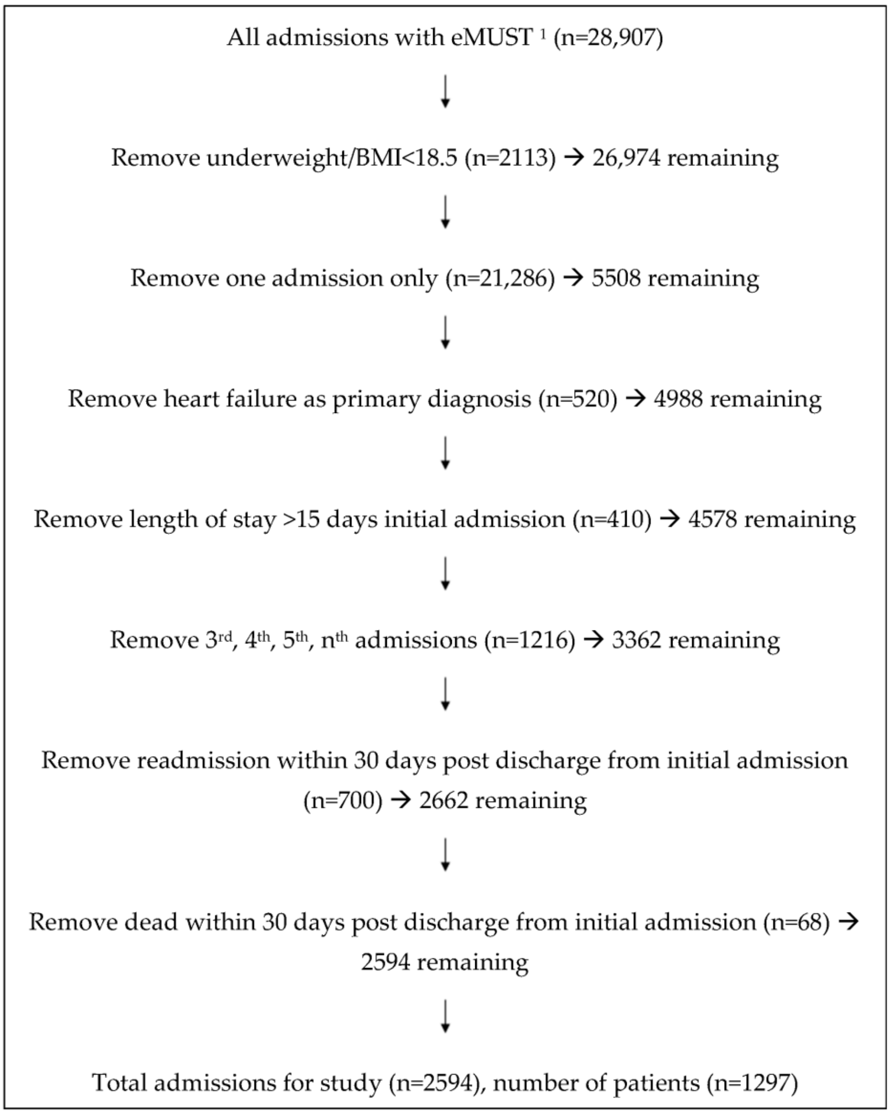

Figure 1. Study Flow Diagram. [1] eMUST is an electronic malnutrition universal screening tool which includes body mass index.

Three categories of patients were developed based upon whether they gained weight (≥5%), lost weight (≥5%) or remained weight-stable (<5% weight change) between their first admission and their readmission. A 5% weight change was selected because it has been shown to have clinical meaning in obese patients [25]. Data were assessed for normality by a visual assessment of histograms (see supplementary files). The differences between the three weight change groups were assessed using the one-way analysis of variance (ANOVA) or the Kruskal–Wallis H test, as appropriate, for continuous variables, and the chi square test was used for the categorical variables. We used multilevel regression models to determine associations between patient characteristics/outcomes and weight change after adjustment for hospital-level variation. Similarly, the relationships between weight change and the continuous outcome variables (such as LOS and ICU hours) were examined using the mixed-effects Poisson regression model after adjustment for age, CCI, LOS during index admission, ICU time spent during index admission and the RSI during index admission, and incidence risk ratios (IRR) were determined. For categorical outcome variables (such as admission to ICU and mortality), we used the mixed-effects logistic regression model and odds ratios (OR) were determined after adjustment for the above-mentioned variables. Model specification was tested by use of the link test [26] in Stata and the linearity assumption was tested by plotting the model residuals vs. predictors using scatter graphs. To achieve proper model specification, we transformed CCI (0 = low CCI, 1 = high CCI) and BMI (18.5–24.9 kg/m^2 = normal BMI $\geq$ 25 kg/m^2 = high BMI) into categorical variables. All statistical analyses were performed by use of Stata software version 21.0 (StataCorp LP, College Station, TX, USA). All outcomes were assessed using a 2-sided type 1 error rate of alpha = 0.05.

3. Results

The data analyzed included 1297 patients who had an eMUST measured at both their index admission and readmission to hospital (Figure 1). The number of elapsed days from discharge to readmission for the stable weight group was 190 ((85,445) median, IQR) and for the weight loss group the median (IQR) elapsed days was 256 (103,207) and these differed significantly ($p < 0.001$).

As shown in Table 1, patients who lost weight prior to their readmission had a higher BMI ($p = 0.036$) and a higher CCI ($p < 0.001$), whilst patients who gained weight prior to their readmission were younger in age than those who were weight-stable ($p < 0.001$). There were significant differences in the outcomes of the index admission for the patients who went on to lose or gain weight prior to their readmission. Patients who lost weight prior to readmission had a longer LOS during their index admission ($p < 0.001$), higher CCI ($p < 0.001$) and spent more time in the ICU (if they were admitted to the ICU) ($p < 0.001$) when compared to weight-stable patients. The outcomes of the index admission for patients who gained weight prior to readmission indicate that these patients spent less time in the ICU ($p = 0.001$) and had a higher RSI than those who remained weight-stable.

Table 1. Characteristics and outcomes of index admission after categorization according to weight change at subsequent admission.

Characteristics of Index Admission	Stable Weight	Weight Gain > 5%	*p* Value [2]	Weight Loss > 5%	*p* Value [2]	*p* Value [3]
Total n = 1297 (%)	n = 671 (52)	n = 240 (18)		n = 386 (30)		
Age (median, IQR)	74 (58, 84)	68 (55, 81)	<0.001	74 (60, 84)	0.004	<0.001
Gender (male, n (%))	356 (53)	122 (50)	1.000	194 (50)	1.000	0.445
BMI (median, IQR)	26.5 (22.9, 30.4)	25.2 (21.5, 30.9)	0.383	26.7 (23.7, 31.4)	0.036	0.030
ATSI, n (%)	11 (2)	6 (2)	1.000	6 (2)	1.000	0.877
CCI (median, IQR)	1 (0, 2)	1 (0, 2)	0.686	1 (0, 2)	<0.001	<0.001
Outcomes of index admission						
LOS [1] (median, IQR)	4 (3, 8)	5 (3, 8)	0.426	5 (3, 8)	<0.001	0.002
ICU admission, n (%)	20 (3)	13 (5)	0.235	10 (3)	1.000	0.135
ICU hours (median, IQR)	45 (28.5, 74.5)	41 (17, 68)	0.001	70 (43, 87)	<0.001	<0.001
RSI median (IQR)	0.96 (0.56, 1.56)	1 (0.58, 1.67)	<0.001	0.98 (0.58, 1.60)	<0.001	<0.001

ATSI = Aboriginal/Torres Strait Islander, BMI = Body Mass Index, CCI = Charlson Comorbidity Index, LOS = length of stay, ICU = Intensive Care Unit, RSI = relative stay index, IQR = Inter-Quartile Range; [1] LOS adjusted for inpatient mortality, [2] when compared to the weight-stable group, [3] chi square test and ANOVA or Kruskal–Wallis H test.

As shown in Table 2, patients who lost weight prior to readmission had, for that readmission, a significantly increased LOS ($p < 0.001$), inpatient mortality ($p = 0.012$), one year mortality ($p < 0.001$), RSI ($p < 0.001$), number of hours in the ICU once admitted ($p = 0.001$) and were more likely to be discharged somewhere other than home ($p < 0.001$) when compared to weight-stable patients. Patients who gained weight prior to readmission had, for that readmission, a significantly increased LOS, RSI and number of hours in the ICU once admitted (all $p < 0.001$) when compared to weight-stable patients.

Table 2. Outcomes of readmission after categorization according to weight change at subsequent admission.

Outcomes of Readmission	Stable Weight	Weight Gain > 5%	*p* Value [3]	Weight Loss > 5%	*p* Value [3]	*p* Value [4]
LOS [1] median (IQR)	5 (2, 10)	6 (3, 10)	0.001	7 (3, 12)	<0.001	<0.001
Inpatient mortality, n (%)	3 (0)	5 (2)	0.188	10 (3)	0.012	0.010
One-year mortality [2], n (%)	67 (10)	22 (9)	1.000	69 (18)	<0.001	<0.001
RR30, n (%)	145 (22)	48 (20)	1.000	87 (23)	1.000	0.754
RSI (median, IQR)	0.95 (0.54, 1.89)	1.01 (0.54, 1.79)	<0.001	1.13 (0.60, 2.08)	<0.001	<0.001
ICU admission, n (%)	31 (5)	12 (5)	1.000	23 (6)	0.186	0.633
ICU hours (median, IQR)	59 (40, 93)	80.5 (42, 155)	<0.001	95 (63, 167)	<0.001	<0.001
Discharge elsewhere (not home), n (%)	106 (16)	44 (18)	0.068	85 (22)	0.001	0.004

RR30 = readmission within 30 days; [1] LOS adjusted for inpatient mortality, [2] excluding inpatient mortality and 30-day mortality, [3] when compared to the weight-stable group, [4] chi square test and ANOVA or Kruskal–Wallis H test.

These outcomes of patients and their hospital admission can interact with and influence observed weight changes. Therefore, we applied a multilevel logistic regression analysis to determine the characteristics and outcomes from the index admission that were likely to result in the patient losing weight prior to their readmission. As shown in Table 3, after adjustment for age, BMI, CCI and LOS, index admission LOS remained a significant predictor for a patient to lose weight prior to readmission, as did BMI, age and higher CCI.

Table 3. Multilevel logistic regression model comparing patient characteristics and outcomes during the index admission to predict whether weight loss will occur prior to readmission compared with weight-stable patients.

Outcome/Characteristic	Unadjusted Model			Adjusted Model		
	IRR	95% CI	*p* Value	IRR	95% CI	*p* Value
BMI	1.02	1.00, 1.04	0.043	1.02	1.00, 1.04	0.031
Age	1.01	1.00, 1.01	0.029	1.01	1.00, 1.02	0.012
CCI	1.11	1.04, 1.17	0.001	1.09	1.03, 1.16	0.004
LOS	1.04	1.01, 1.08	0.009	1.04	1.00, 1.07	0.030
ICU hours	1.51	1.37, 1.67	<0.001	1.00	0.99, 1.01	0.973

IRR = Incidence Rate Ratio.

Table 4 shows the multilevel regression model for the outcomes of patients during their readmission to hospital. This multilevel regression model adjusts for age, BMI, CCI, LOS, ICU hours and RSI. This showed an increased LOS for patients who had lost weight since their index admission when compared to patients who remained weight-stable. These weight loss patients also had an increased RSI and increased ICU hours if admitted to the ICU. The one-year mortality was significantly increased among patients who lost weight when compared to mortality in weight-stable patients; however, there was no significant difference in the 30-day readmission rate between these two groups (Table 4).

Table 4. Multilevel regression model comparing clinical outcomes of patients with >5% weight loss with weight-stable patients in their readmission.

Outcome	Unadjusted Model			Adjusted Model		
	OR/IRR	95% CI	*p* Value	OR/IRR	95% CI	*p* Value
LOS	1.25	1.20, 1.30	<0.001	1.17	1.12, 1.22	<0.001
RSI	2.39	2.29, 2.49	<0.001	2.37	2.27, 2.47	<0.001
One-year mortality	2.02	1.40, 2.90	<0.001	1.50	0.99, 2.26	0.055
ICU hours	3.20	3.03, 3.37	<0.001	2.80	2.65, 2.96	<0.001
ICU admission	1.31	0.75, 2.28	0.343	1.11	0.62, 2.01	0.725
RR30	0.95	0.70, 1.28	0.725	0.96	0.70, 1.31	0.801

OR/IRR = Odds Ratio/Incidence Rate Ratio, (OR used for ICU admission, one-year mortality, RR30; IRR for LOS, RSI and ICU hours).

4. Discussion

Of the 1297 patients who were weighed when first admitted and weighed again when readmitted to hospital during the data period, 51.7% maintained a stable weight whilst 18.5% gained weight and 29.8% lost at least 5% of their initial weight. On average, the patients recruited for this analysis were readmitted more than six months after their initial discharge and no patient readmitted within 30 days of index discharge was included.

Patients at risk of losing at least 5% of their weight prior to readmission were identifiable beforehand by their age, BMI, CCI and LOS and had worse outcomes during their readmission than those who remained weight-stable. During readmission, the patients who had lost weight had a longer LOS, RSI and LOS in the ICU than those whose weight remained stable. Patients who gained at least 5% of their weight prior to readmission were identifiable beforehand by being younger and spending less time in the ICU but they had a significantly longer RSI than those who were weight-stable. The exclusion of readmissions within 30 days of discharge ensured that any patients experiencing only immediate, short-term weight loss had been excluded from the analysis.

The predictors and outcomes of unplanned hospital readmissions have been extensively studied, but most of these readmission studies have looked at readmission within 30 days. While weight loss immediately following discharge might predict early readmission [4], studies looking at hospital readmission after 30 days have not looked at weight change between admissions [10,27–29]. The most relevant studies are one study which found that the significant factors for being readmitted within 60 days were (i) a cumulative inpatient LOS of more than 7 days, (ii) having a cancer diagnosis and (iii) being older than 85 years of age [27], while another relevant study found malnourished patients were at higher risk of readmission between 8 and 180 days after discharge [10].

Weight changes in the months leading up to hospital admission or leading up to unplanned hospital readmission are usually unknown. Once admitted, inpatients categorized as underweight and patients with obesity have different outcomes to those categorized as normal and overweight [9,30]. Patients with an increased BMI have been shown to have a shorter LOS, lower in-hospital mortality and improved outcomes after discharge when compared to non-obese patients [1,31], whereas underweight patients have higher LOS and mortality when compared to patients in the normal BMI range [17,18].

The present study reports markedly different outcomes for those who lost weight when compared to those who remained weight-stable. A sub-analysis looking at patients with a BMI< or >30 kg/m^2 during their index admission did not significantly alter the present study's findings. The current study provides no supportive evidence for counselling the obese inpatient to lose weight after discharge.

The relative risk to health of increased weight varies with age [31], and a higher percentage of readmissions occur as age increases [2,27,32]. The studies investigating age and readmission risk unfortunately varied significantly in their categorization of age groups, one looked at age over 50 years, another over 85 years. Both showed that age increased readmission risk. A third study found that age (a watershed at 85 years) did not have a significant impact on readmission [32]. A sub-analysis of our data looking at patients aged over or under 75 years at their index admission did not significantly alter the present study's findings.

The present study did not look at the cause of the unplanned readmission but retrospectively determined the characteristics of patients that were predictive of experiencing significant weight loss before a readmission. Those readmissions occurred, on average, six months or more after discharge; all readmissions within 30 days were excluded. Patients at risk of weight loss prior to any readmission had identifiable characteristics during their index admission. Specifically, those at risk were older, had a higher BMI, a higher CCI and a longer LOS than those who were weight-stable between admissions. If patients who are not only at risk of readmission but are also at risk of weight loss prior to that readmission can be identified during their index admission, they could possibly be targeted with an intervention during or at the end of that index admission.

Over and above identifying the at-risk population during their index admission, information concerning patients' inter-admission weight loss, available at the time of being weighed during the readmission, offers a second opportunity to highlight to clinicians a group of patients at risk of adverse health outcomes at a time when a targeted intervention is possible.

One limitation of this work is that the determination of patients' BMIs was infrequent and only performed in approximately 10% of all admissions [30]. Admittedly, the BMI distribution of the present study matches another study of a whole hospital within Australia [33]. The present study uses retrospective data and may include unknown confounders and hence lead to incorrect inference of the results obtained. Because the present work is observational, it calls for a prospective study looking at an intervention where weight loss is prevented or avoided after discharge and prior to any readmission.

5. Conclusions

Those who are older, have a higher BMI, a higher CCI and a longer LOS are at greater risk of weight loss prior to a readmission. Patients who lose weight prior to a delayed (>30 days) readmission are at risk of having a worse outcome (i.e., a longer inpatient LOS and, if relevant, a longer ICU stay) during and after that readmission than if no weight loss had occurred. This prolonged LOS can adversely affect patient health as well as provoke hospital congestion issues.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcm12093074/s1, Figure S1: Histograms–test for normal distribution.

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Informed Consent Statement: Informed consent was not obtained due to the retrospective collection of data in this study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author only after permission is granted by the ethics committee.

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References

1. Ram, P.; Shah, M.; Lo, K.B.U.; Agarwal, M.; Patel, B.; Tripathi, B.; Arora, S.; Patel, N.; Jorde, U.P.; Banerji, S. Etiologies and predictors of readmission among obese and morbidly obese patients admitted with heart failure. *Heart Fail. Rev.* **2021**, *26*, 829–838. [CrossRef]
2. Braet, A.; Weltens, C.; Sermeus, W.; Vleugels, A. Risk factors for unplanned hospital re-admissions: A secondary data analysis of hospital discharge summaries. *J. Eval. Clin. Pract.* **2015**, *21*, 560–566. [CrossRef] [PubMed]
3. Brunner-La Rocca, H.P.; Peden, C.J.; Soong, J.; Holman, P.A.; Bogdanovskaya, M.; Barclay, L. Reasons for readmission after hospital discharge in patients with chronic diseases-Information from an international dataset. *PLoS ONE* **2020**, *15*, e0233457. [CrossRef]
4. Allaudeen, N.; Vidyarthi, A.; Maselli, J.; Auerbach, A. Redefining readmission risk factors for general medicine patients. *J. Hosp. Med.* **2011**, *6*, 54–60. [CrossRef] [PubMed]
5. Mudge, A.M.; Kasper, K.; Clair, A.; Redfern, H.; Bell, J.J.; Barras, M.A.; Dip, G.; Pachana, N.A. Recurrent readmissions in medical patients: A prospective study. *J. Hosp. Med.* **2011**, *6*, 61–67. [CrossRef] [PubMed]

6. Graham, K.L.; Wilker, E.H.; Howell, M.D.; Davis, R.B.; Marcantonio, E.R. Differences between early and late readmissions among patients: A cohort study. *Ann. Intern. Med.* **2015**, *162*, 741–749. [CrossRef] [PubMed]
7. Friedmann, J.M.; Jensen, G.L.; Smiciklas-Wright, H.; McCamish, M.A. Predicting early nonelective hospital readmission in nutritionally compromised older adults. *Am. J. Clin. Nutr.* **1997**, *65*, 1714–1720. [CrossRef]
8. Cruz, P.L.M.; Soares, B.L.M.; da Silva, J.E.; Lima, E.S.R.R. Clinical and nutritional predictors of hospital readmission within 30 days. *Eur. J. Clin. Nutr.* **2022**, *76*, 244–250. [CrossRef] [PubMed]
9. Sharma, Y.; Miller, M.; Kaambwa, B.; Shahi, R.; Hakendorf, P.; Horwood, C.; Thompson, C. Malnutrition and its association with readmission and death within 7 days and 8-180 days postdischarge in older patients: A prospective observational study. *BMJ Open* **2017**, *7*, e018443.
10. Sharma, Y.; Miller, M.; Kaambwa, B.; Shahi, R.; Hakendorf, P.; Horwood, C.; Thompson, C. Factors influencing early and late readmissions in Australian hospitalised patients and investigating role of admission nutrition status as a predictor of hospital readmissions: A cohort study. *BMJ Open* **2018**, *8*, e022246. [CrossRef]
11. Jepma, P.; Ter Riet, G.; van Rijn, M.; Latour, C.H.M.; Peters, R.J.G.; Scholte Op Reimer, W.J.M.; Buurman, B.M. Readmission and mortality in patients >/=70 years with acute myocardial infarction or heart failure in the Netherlands: A retrospective cohort study of incidences and changes in risk factors over time. *Neth. Heart J.* **2019**, *27*, 134–141. [CrossRef] [PubMed]
12. Hua, M.; Gong, M.N.; Brady, J.; Wunsch, H. Early and late unplanned rehospitalizations for survivors of critical illness. *Crit. Care Med.* **2015**, *43*, 430–438. [CrossRef]
13. Berenson, R.A.; Paulus, R.A.; Kalman, N.S. Medicare's readmissions-reduction program—A positive alternative. *N. Engl. J. Med.* **2012**, *366*, 1364–1366. [CrossRef] [PubMed]
14. Hansen, L.O.; Young, R.S.; Hinami, K.; Leung, A.; Williams, M.V. Interventions to reduce 30-day rehospitalization: A systematic review. *Ann. Intern. Med.* **2011**, *155*, 520–528. [CrossRef]
15. Sharma, Y.; Thompson, C.; Kaambwa, B.; Shahi, R.; Miller, M. Validity of the Malnutrition Universal Screening Tool (MUST) in Australian hospitalized acutely unwell elderly patients. *Asia Pac. J. Clin. Nutr.* **2017**, *26*, 994–1000. [PubMed]
16. Zhao, Y.; Li, Z.; Yang, T.; Wang, M.; Xi, X. Is body mass index associated with outcomes of mechanically ventilated adult patients in intensive critical units? A systematic review and meta-analysis. *PLoS ONE* **2018**, *13*, e0198669. [CrossRef] [PubMed]
17. Laukkanen, J.A.; Kunutsor, S.K.; Hernesniemi, J.; Immonen, J.; Eskola, M.; Zaccardi, F.; Niemela, M.; Makikallio, T.; Hagnas, M.; Piuhola, J.; et al. Underweight and obesity are related to higher mortality in patients undergoing coronary angiography: The KARDIO invasive cardiology register study. *Catheter. Cardiovasc. Interv.* **2022**, *100*, 1242–1251. [CrossRef]
18. Finkielman, J.D.; Gajic, O.; Afessa, B. Underweight is independently associated with mortality in post-operative and non-operative patients admitted to the intensive care unit: A retrospective study. *BMC Emerg. Med.* **2004**, *4*, 3. [CrossRef]
19. Sayeed, Z.; Anoushiravani, A.A.; Chambers, M.C.; Gilbert, T.J.; Scaife, S.L.; El-Othmani, M.M.; Saleh, K.J. Comparing In-Hospital Total Joint Arthroplasty Outcomes and Resource Consumption Among Underweight and Morbidly Obese Patients. *J. Arthroplasty* **2016**, *31*, 2085–2090. [CrossRef]
20. Zacharias, H.; Raw, J.; Nunn, A.; Parsons, S.; Johnson, M. Is there a role for subcutaneous furosemide in the community and hospice management of end-stage heart failure? *Palliat. Med.* **2011**, *25*, 658–663. [CrossRef]
21. Gill, G.S.; Lam, P.H.; Brar, V.; Patel, S.; Arundel, C.; Deedwania, P.; Faselis, C.; Allman, R.M.; Zhang, S.; Morgan, C.J.; et al. In-Hospital Weight Loss and Outcomes in Patients With Heart Failure. *J. Card. Fail.* **2022**, *28*, 1116–1124. [CrossRef]
22. Zannidi, D.; Patel, P.S.; Leventea, E.; Paciepnik, J.; Dobson, F.; Heyes, C.; Goudie, R.J.B.; Griep, L.M.O.; Preller, J.; Spillman, L.N. Factors Associated with Significant Weight Loss in Hospitalised Patients with COVID-19: A Retrospective Cohort Study in a Large Teaching Hospital. *Nutrients* **2022**, *14*, 4195. [CrossRef] [PubMed]
23. Tadokoro, R.; Iida, T.; Mikura, K.; Imai, H.; Murai, N.; Kaji, M.; Hashizume, M.; Kigawa, Y.; Endo, K.; Iizaka, T.; et al. Factors involved in body weight loss and its maintenance in morbidly obese inpatients. *Diabetol. Int.* **2020**, *11*, 41–48. [CrossRef]
24. Cereda, E.; Klersy, C.; Pedrolli, C.; Cameletti, B.; Bonardi, C.; Quarleri, L.; Cappello, S.; Bonoldi, A.; Bonadeo, E.; Caccialanza, R. The Geriatric Nutritional Risk Index predicts hospital length of stay and in-hospital weight loss in elderly patients. *Clin. Nutr.* **2015**, *34*, 74–78. [CrossRef] [PubMed]
25. Williamson, D.A.; Bray, G.A.; Ryan, D.H. Is 5% weight loss a satisfactory criterion to define clinically significant weight loss? *Obesity* **2015**, *23*, 2319–2320. [CrossRef] [PubMed]
26. Zhang, Z. Residuals and regression diagnostics: Focusing on logistic regression. *Ann. Transl. Med.* **2016**, *4*, 195. [CrossRef]
27. Maali, Y.; Perez-Concha, O.; Coiera, E.; Roffe, D.; Day, R.O.; Gallego, B. Predicting 7-day, 30-day and 60-day all-cause unplanned readmission: A case study of a Sydney hospital. *BMC Med. Inform. Decis. Mak.* **2018**, *18*, 1. [CrossRef]
28. Averin, A.; Shaff, M.; Weycker, D.; Lonshteyn, A.; Sato, R.; Pelton, S.I. Mortality and readmission in the year following hospitalization for pneumonia among US adults. *Respir Med.* **2021**, *185*, 106476. [CrossRef]
29. Leitao, A.; Brito, A.; Pinho, J.; Alves, J.N.; Costa, R.; Amorim, J.M.; Ribeiro, M.; Pinho, I.; Ferreira, C. Predictors of hospital readmission 1 year after ischemic stroke. *Intern. Emerg. Med.* **2017**, *12*, 63–68. [CrossRef]
30. Fusco, K.; Thompson, C.; Woodman, R.; Horwood, C.; Hakendorf, P.; Sharma, Y. The Impact of Morbid Obesity on the Health Outcomes of Hospital Inpatients: An Observational Study. *J. Clin. Med.* **2021**, *10*, 4382. [CrossRef]
31. Woolley, C.; Thompson, C.; Hakendorf, P.; Horwood, C. The Effect of Age upon the Interrelationship of BMI and Inpatient Health Outcomes. *J. Nutr. Health Aging* **2019**, *23*, 558–563. [CrossRef] [PubMed]

32. Caughey, G.E.; Pratt, N.L.; Barratt, J.D.; Shakib, S.; Kemp-Casey, A.R.; Roughead, E.E. Understanding 30-day re-admission after hospitalisation of older patients for diabetes: Identifying those at greatest risk. *Med. J. Aust.* **2017**, *206*, 170–175. [CrossRef] [PubMed]
33. Dennis, D.M.; Carter, V.; Trevenen, M.; Tyler, J.; Perrella, L.; Lori, E.; Cooper, I. Do acute hospitalised patients in Australia have a different body mass index to the general Australian population: A point prevalence study? *Aust. Health Rev.* **2018**, *42*, 121–129. [CrossRef] [PubMed]

CHAPTER 4: CONCLUSIONS, LIMITATIONS AND FUTURE DIRECTIONS

Results summary

This thesis addressed two issues: firstly, it determined whether morbid obesity (BMI ≥ 40kg/m^2) was associated with a longer inpatient LOS. Secondly, it addressed whether weight loss before a readmission produces any differences in health outcomes during and following an unplanned hospital readmission.

In a cohort of 16,579 inpatients aged less than 80 years, those with a BMI over 40kg/m^2 experienced a slightly (but significantly (p=0.012)) longer inpatient LOS when compared with those of a lower BMI (those with a BMI below 18.5kg/m^2 having been excluded). Other measured outcomes (in-hospital mortality, number of hospital-acquired complications during admission, LOS in ICU (if admitted to that unit) and 30 day readmission rates) showed no difference between populations. Whilst this finding of an adverse effect of obesity has been previously reported (Hauck and Hollingsworth, 2010, Akinyemiju et al., 2016) the present analysis was performed on the heaviest 6% of inpatients. The present analysis included important, previously unreported confounders such as the comorbidity burden, socioeconomic status and the ethnicity of the participants. The hypothesis for this study was proven; that after adjustment for these confounders, hospitalised patients with morbid obesity have worse clinical outcomes than patients without morbid obesity.

The third chapter considered whether weight loss after a hospital admission would result in a more favourable outcome for the patient should they be readmitted. The first aim of Chapter 3 was to identify patients who were more likely to change weight prior to a readmission. The second aim was to determine whether this weight change produced any differences in health outcomes during or following that readmission. Here, we found that those who were going to lose weight prior to a readmission were identifiable on the basis of their age, their co-morbidity burden, the LOS of their index admission and their BMI at the time of their index admission. Unexpectedly however, after adjustment for age, BMI, CCI, LOS and LOS in ICU (if admitted to that unit) if the patient was readmitted, those who had lost weight prior to that readmission were worse off (longer inpatient LOS, LOS in ICU (if admitted to that unit) and higher mortality) when compared to those who remained weight stable. Data for weight changes over time after discharge for those patients who were not readmitted was not captured in this study.

Sub-analysis (BMI <40kg/m^2 or ≥40kg/m^2)

A sub-analysis of the data from the third chapter was performed looking at the clinical outcomes for patients categorised according to their BMI (<40 or ≥40kg/m^2) at their first admission. This analysis compared those who had lost >5% of their weight between hospital admissions to patients who remained weight stable between hospital admissions. The outcomes were assessed using a 2-sided type 1 error rate of alpha = 0.05. This sub-analysis indicated patients with a BMI ≥40kg/m^2 at their first hospital admission who lost >5% of their original weight did not have a significantly different LOS or a significant change in one year mortality when compared to those in an equivalent BMI category who were weight stable (Table 4.1). Those with a BMI <40kg/m^2 who lost >5% of their original weight had a significantly increased LOS, LOS in ICU (if admitted to that unit) and one year mortality rate when compared to those in an equivalent BMI category who remained weight stable.

Table 4.1. Outcomes and characteristics of readmission when patients had lost >5% of their body weight from their initial admission categorised into those with BMI <40kg/m^2 and BMI ≥40kg/m^2 at their initial admission

Outcome/Characteristic	**Stable weight**		**Weight loss>5%**		**P value**[b]	
	BMI <40kg/m^2	BMI ≥40kg/m^2	BMI <40kg/m^2	BMI ≥40kg/m^2	BMI <40kg/m^2	BMI >40kg/m^2
Total n=1310, n (%) [c]	759 (49.09)	37 (40.66)	484 (31.31)	30 (32.97)		
Age (years), median (IQR)	74 (58,84)	64 (54,71)	75 (61,84)	56.5 (52,70)	<0.001	0.031
Gender: Male, n (%)	436 (57.44)	8 (21.62)	246 (50.83)	6 (20.00)	0.044	0.272
Charlson index, median (IQR)	1 (0,2)	2 (0,3)	1 (0,3)	1 (0,2)	<0.001	0.147
LOS days, median (IQR)	5 (3,11)	7 (3,12)	7 (3.5,14)	7 (4,12)	<0.001	0.146
In-patient mortality, n (%)	10 (1.32)	0 (0.00)	14 (2.89)	0 (0.00)	0.145	0.244
One year mortality [a], n (%)	77 (10.28)	1 (2.70)	84 (17.87)	1 (3.323)	<0.001	0.693
ICU admission, n (%)	38 (5.01)	7 (18.92)	29 (5.99)	3 (10.00)	0.449	0.205
ICU hours, median (IQR)	69 (40,101)	71 (47,88)	86 (62,175)	145 (68,167)	<0.001	0.017
NOS, n (%)						
Home	619 (81.55)	30 (85.08)	652 (72.73)	22 (73.33)	0.167	0.476
Other	140 (18.45)	7 (18.92)	132 (27.27)	8 (26.67)		
RR30 [a], n (%)	162 (21.34)	7 (18.92)	111 (22.93)	9 (30.00)	0.683	0.571

BMI=body mass index (kg/m^2), LOS= length of stay, ICU = intensive care unit, NOS = nature of separation, RR30 = readmission within 30 days, IQR = inter-quartile ratio, [a] excluding inpatient mortality and 30 day mortality, [b] when compared to weight stable group, [c] n (%) do not add up to 100% as weight gain group was not included in table

Therefore, weight loss for patients with morbid obesity who lost >5% of their original weight did not produce detectably worse outcomes for the patient when compared to the outcomes for those who remained weight stable. Admittedly, numbers of patients with morbid obesity were small in this sub-analysis (n=30 and 37) limiting the power of the analysis.

A multilevel regression model adjusted for age, sex, elapsed days (from day of discharge of first admission to the day of readmission), CCI, IRSD and Aboriginal/Torres Strait Islander (ATSI) found an increase in LOS, one year mortality and hours spent in ICU (if admitted to that unit) for those patients who lost weight between admissions when their initial BMI was <40kg/m^2. Additionally, for patients admitted to ICU who had lost weight prior to their readmission, there was a significant decrease in ICU hours (if readmitted to that unit) when their BMI was ≥40kg/m^2. For the BMI sub-analysis, even though (or because) numbers are very small, there is a suggestion that >5% weight loss in the morbidly obese is not as harmful for the patient as >5% weight loss in those with obesity but a BMI below 40kg/m^2.

Table 4.2. Multilevel regression model for patients had lost >5% of their body weight from their initial admission categorised into those with BMI <40kg/m^2 and BMI ≥40kg/m^2

	BMI<40kg/m2			**BMI≥40 kg/m2**		**P value**
Outcome	OR/IRR	95% CI	P value	OR/IRR	95% CI	
LOS	1.30	1.26, 1.35	<0.001	1.03	0.87, 1.22	0.721
One year mortality [a]	1.58	1.09, 2.30	<0.001	N/A	N/A	N/A
ICU hours	2.16	2.06, 2.70	<0.001	0.80	0.69, 0.92	0.002
ICU admission	1.06	0.63, 1.79	0.454	0.36	0.05, 2.40	0. 289
RR30	0.88	0.67, 1.17	0.509	0.46	0.12, 1.69	0.378

OR/IRR = Odds Ratio or Incident Rate Ratio, CI = Confidence Interval, multivariate analysis: adjusted for age, sex, elapsed days from discharge of first admission to readmission, Charlson index, socioeconomic status and Aboriginal/Torres Strait Islander status. BMI=body mass index, LOS= length of stay, ICU = intensive care unit, RR30 = readmission within 30 days. [a] excluding inpatient and 30 day mortality

Sub-analysis (<80 years or ≥80 years)

A sub-analysis of the data from the third chapter looked at patients categorised as to whether they were aged <80 years or ≥80 years at their first admission. This analysis indicated an increased LOS and one year mortality in patients who lost weight when compared to those outcomes in the stable weight group. This finding was the same in both age categories (Table 4.3).

Table 4.3. Outcomes and characteristics of readmission when patients had lost >5% of their body weight from their initial admission categorised into those aged <80 years and ≥80 years

Outcome/Characteristic	Stable weight		Weight loss>5%		P value[b]	
Age, years	<80yrs	≥80yrs	<80yrs	≥80yrs	<80yrs	≥80yrs
Total[c] n=1060 (<80 yrs); n=577 (≥80 yrs)	503 (47.45)	288 (49.91)	329 (31.04)	182 (31.54)		
Gender (male (n, %))	285 (56.66)	160 (55.6)	174 (52.89)	81 (44.51)	0.548	0.065
Charlson index, median (IQR)	1 (0,2)	1 (0,2)	1 (0,4)	1 (0,2)	<0.001	0.117
LOS, median (IQR)	6 (3,12)	5 (2,11)	8 (4,15)	7 (3,12)	<0.001	<0.001
In-patient mortality, n (%)	5 (0.99)	5 (1. 74)	8 (2.43)	7 (3.85)	0.242	0.371
One year mortality [a], n (%)	47 (9.44)	32 (11.31)	49 (15.22)	39 (22.29)	0.025	0.004
ICU admission, n (%)	38 (7.55)	8 (2.78)	32 (9.73)	2 (1.10)	0.481	0.456
ICU hours, median (IQR)	69 (41,101)	80.5 (43.5,112.5)	93.5 (66,171)	35 (15,55)	<0.001	<0.001
NOS, n (%) Home Other	 418 (83.10) 85 (16.90)	 229 (79.51) 59 (20.49)	 249 (75.68) 80 (24.32)	 124 (68.13) 58 (31.87)	 0.136	 0.050
RR30[a], n (%)	114 (22.66)	56 (19.44)	85 (25.84)	35 (19. 23)	0.281	0.996

LOS= length of stay, ICU = intensive care unit, NOS = nature of separation, RR30 = readmission within 30 days, IQR = inter-quartile ratio, [a] excluding inpatient mortality and 30 day mortality, [b] when compared to age compatible and weight stable group, [c] total (%) do not add up to 100% as weight gain group was not included in table

Patients aged <80 years who lost weight between hospital admissions had a higher comorbidity index than those who didn't have any weight change and an increased number of hours spent in ICU (if they were admitted to that unit). Patients ≥80 years at their index admission who lost weight had a significantly lower number of hours spent in the ICU (if admitted to that unit) compared to the stable weight group. For this age-related sub-analysis, there is little difference between these results and those seen in the third chapter.

A multilevel regression model adjusted for age, sex, elapsed days, CI, IRSD, BMI and ATSI for those who lost weight between admissions demonstrated a significantly increased LOS and A multilevel regression model adjusted for age, sex, elapsed days, CI, IRSD, BMI and ATSI for those who lost weight between admissions demonstrated a significantly increased LOS and one year mortality regardless of patients' age category at the time of their first admission (Table 4.4). Of those patients admitted to an ICU, those aged <80 years at first admission had an increased LOS in ICU (if admitted to that unit) whereas those aged ≥80 years spent a significantly shorter period of time in ICU (if admitted to that unit).

These were observational rather than interventional studies. They address specific populations namely the younger patient and the patient with morbid obesity. They lay the groundwork for the design and timing of appropriate interventional studies described and discussed later.

Table 4.4. Multilevel regression model for patients had lost >5% of their body weight from their initial admission categorised into those aged <80 years or ≥80 years of age at the time of their initial admission

	Age <80 years			**Age ≥80 years**		
Outcome	OR/IRR	95% CI	P value	OR/IRR	95% CI	P value
LOS	1.46	1.40, 1.52	<0.001	1.14	1.07, 1.21	<0.001
One year mortality [a]	1.72	1.12, 2.64	0.013	2.33	1.33, 4.09	0.003
ICU hours	2.04	1.95, 2.13	<0.001	0.18	0.14, 0.23	<0.001
ICU admission	1.32	0.81, 2.16	0.271	0.40	0.08, 1.99	0.265
RR30[a]	0.84	0.61, 1.16	0.295	0.94	0.58, 1.53	0.805

OR/IRR = Odds Ratio or Incident Rate Ratio, CI = Confidence Interval, multivariate analysis: adjusted for age, sex, BMI, elapsed days from discharge of first admission to readmission, Charlson index, socioeconomic status and Aboriginal/Torres Strait Islander status. BMI=body mass index, LOS= length of stay, ICU = intensive care unit, RR30 = readmission within 30 days. [a] excluding inpatient mortality and 30 day mortality

New knowledge in context of old knowledge

The effect of obesity upon health outcomes is difficult to interpret due to the variety of definitions and classifications used for obesity, the variety of co-morbidities accompanying obesity and a likely presence of age-dependence of the effects of obesity on health outcomes. The effect of weight loss upon health outcomes is equally complex due to the apparent relevance of the intentionality of the weight loss, the duration and amount of weight lost and the body compositional change producing the weight loss.

The second chapter was designed to partially address the former confounding issues and contributed detailed data on associated co-morbidities, socio-economic status of the patients and ethnicity; all of which have been identified as factors which can contribute to both obesity and patients' clinical outcomes (Islam and Fitzgerald, 2016, Dinsa et al., 2012, Bureau of Statistics, 2008, Forbang et al., 2014, Tillin et al., 2015).

While the second chapter describes a deleterious effect on LOS of morbid obesity, the literature is unclear on this topic and perhaps any health advantage from a higher BMI than normal weight is best seen in those with a BMI under 40kg/m^2 (Fusco et al., 2017, Akinyemiju et al., 2016) and in those who are aged over 60 years (Woolley et al., 2019). Here, the impact of very high BMI (>40kg/m^2) on outcomes other than LOS, such as its effect upon mortality or ICU admission risk, was negligible. Protective effects of obesity such as the benefits of excess leptin levels (Perez-Perez et al., 2020, Iikuni et al., 2008) or raised lean body mass in the subject with obesity (Rehunen et al., 2020, Fenger-Gron et al., 2020) add to the complexity of the relation of BMI to health outcomes.

If the effect of obesity on health outcomes is difficult to interpret, the effect of weight loss on health outcomes is even more so. There is a great deal of attention paid to weight loss as a therapeutic strategy, especially for those with a higher-than-normal BMI (Jensen et al., 2021, Jensen et al., 2014). It is established that short term weight loss increases the risk of readmission (Allaudeen et al., 2011) but the data is limited regarding longer term weight loss and hospital admissions. Therefore, Chapter 3 explored the impact of a longer duration over which the weight loss occurred in relation to readmission third chapter. This chapter drew attention to the lack of information on the effects of weight loss (as distinct from no weight loss) on health outcomes for the inpatient with obesity. This lack of data makes it difficult to know whether weight loss is to be recommended for every inpatient with any degree of obesity. It follows, therefore, that weight loss not only increases the risk of readmission for a patient when that weight loss (and readmission) occurs within one month (Allaudeen et al., 2011) but also if it occurs within an average of six months. Other studies that have looked at hospital readmissions after 30 days following discharge did not look at weight change between readmissions (Leitao et al., 2017, Sharma et al., 2018, Maali et al., 2018, Averin et al., 2021).

The unanswered questions raised by these data include the importance of any weight loss observed being intentional weight loss (IWL) or unintentional weight loss (UWL); both, but especially the latter, being an associate of ill-health (Meltzer and Everhart, 1995, Bosch et al., 2017, Perera et al., 2021) and the importance of the nature of the weight being lost whether it be the result of fluid losses, loss of lean body mass or fat mass.

Limitations of performed work

The work presented here is retrospective and observational and unknown confounders may be present. Only approximately 10% of eligible patients were recruited for analysis in each study due to low rates of measurement of inpatients' weights and heights and hence their BMIs. We believe our data is representative of the current population because the BMI distribution is similar to another Australian study which captured the data of all adult inpatients in one hospital on one day (Dennis et al., 2018). Our sample sizes suffered as a result of this data deficiency especially the attempted sub-analysis of those with a BMI over 40 kg/m2 and the effect of weight loss on health outcomes for those with that higher BMI (Table 4.1 and Table 4.2) and the inability to collect weight loss information on patients who did not have a readmission to hospital.

Although this work looked at ethnicity, it only assessed ATSI against non-ATSI. We acknowledge that ethnicity is more than indigenous vs non-indigenous but this was not included in this study.

While the classification of weight loss as IWL or UWL is challenging, the inability to distinguish IWL from UWL in the present work impairs the design of future work in this area. Interventions could be designed to prevent weight loss or to promote healthy weight loss. Considering the average age of the population studied (74 years), much of the weight loss might be UWL (Meltzer and Everhart, 1995, Bouras et al., 2001, Bosch et al., 2017) but this is speculation and requires testing. Had the third chapter demonstrated a poor prognosis following UWL, this would support design of a new study promoting prevention of weight loss for recently discharged older inpatients. Should most of the weight loss observed in the third chapter be IWL, then the nature of the weight loss strategies used should be documented and similar weight loss strategies for recent hospital admissions (up to 6 to 12 months in the past) should be discouraged. On the positive side, two different opportunities for potential interventions have been identified (i.e. the ability to identify patients at risk of poor health outcomes at both their initial admission and at their unplanned hospital readmission).

New questions and residual questions unanswered

Is the acutely unwell patient with obesity a potential target for a weight loss intervention?

The data to date do not support prioritisation of a weight loss strategy especially in the older inpatient with a BMI under 40 kg/m^2. Avoidance of weight loss seems more of a priority, pending further research.

How is the LOS of an admitted or readmitted patient with obesity to be shortened safely and efficiently?

This is not obvious yet from these studies. The effects of increased BMI on LOS were small. Weight loss (IWL) may be the answer but UWL accompanying ill health is unlikely to improve hospital bed flow efficiencies significantly.

Is the hospital inpatient with obesity better or worse off than the inpatient who is not obese?

Especially for the ageing inpatient, obesity does not seem to be the burdensome co-morbidity with which it has been labelled in the past. Perhaps bariatric care within the hospital system has improved over time especially if the BMI lies between 30 and 40kg/m^2 and if the patient is aged over 60 years. (Woolley et al., 2019). Once the BMI exceeds 40kg/m^2, most, but possibly not all, inpatients may be worse off than those with a lower (but not sub-normal) BMI. (Fusco et al., 2017). (Hauck and Hollingsworth, 2010).

Is an inpatient who has lost weight to achieve a BMI of 30kg/m^2 likely to have the same health outcomes as an inpatient with a BMI of 30kg/m^2 who has not lost weight?

This may be an area for future research. A repeat analysis of our data could determine if those who lost >5% of their weight to achieve a particular BMI and were matched to those who were a similar BMI but had remained weight stable between hospital admissions might inform on this matter.

Should weight loss advice be offered to all inpatients?

No; if they are morbidly obese and relatively young, IWL might be an advantage but further research is necessary. Extending this advice indiscriminately to those less overweight and older is not recommended at this stage. At this stage we are not in a good position to even speculate on how the weight should be lost.

Clinical impact and suggested future studies

While there remains a small effect of morbid obesity on hospital outcomes, future work must attend to the concepts and consequences of healthy and unhealthy weight loss and whether that weight loss, in the context of acute illness, conveys an advantage to the patient and/or to the hospital. Regarding the clinical impact of the work in this thesis, at two separate time points, the identification is now possible of those likely to lose weight after discharge and be at increased risk of readmission (and at risk of poorer outcomes of that readmission). First, that identification of those at risk is possible at the time of discharge from that index admission. Later, the identification of those at risk of adverse health outcomes following readmission (longer LOS, longer LOS in ICU (if admitted to that unit), possibly a higher inpatient mortality) can be simply achieved by weighing patients at the time of their readmission. If over 5% weight loss has occurred since a previous admission of that patient within the last year or so, an alert can be posted.

Interventional studies can be performed but would be best informed by further research that uses tighter definitions of “significant” weight loss, that distinguishes IWL from UWL and that applies differing strategies that might have a goal of weight loss or weight maintenance or body composition alteration.

Overarching all this future research is a need to explore the economic impact of weight management for an acutely unwell inpatient and for an outpatient because the literature in this area is not consistent and difficult to interpret. As stated in Chapter 1, health care costs increased as BMI increased with the most significant increase in costs being most likely in women with a BMI ≥40kg/m2. These costs were more than double those women with a BMI between 20 and 22.49kg/m2 (Kent et al., 2017). A community-based weight loss study determined no significant decreases in total health care costs occurred with a weight loss of ≥5% weight loss (Schousboe et al., 2018) and another study (by an employer) invested in well-being initiatives for 3,199 employees found those who attended a wellness centre frequently over a period of 4 years achieved lower health care costs and improvement of their BMI than those who attended less frequently (Borah et al., 2015).

A review of the literature indicates that increased BMI is reported to be associated with both good outcomes and poor outcomes (Table 1.3, Chapter 1). Many studies found a lower LOS in patients with mild obesity (Finkielman et al., 2004, Mullen et al., 2009, Akinyemiju et al., 2016) and a higher LOS in patients with morbid obesity (Akinyemiju et al., 2016, Liu et al., 2008, Fusco et al., 2017, Ram et al., 2021) when compared to those of normal weight. However, other outcomes including in-hospital mortality show less consistent findings. Whereas some found increased mortality amongst patients with mild obesity and morbid obesity (Akinyemiju et al., 2016), others found lower mortality amongst patients with mild, moderate and morbid obesity (Ram et al., 2021) when compared to those of normal weight. Other studies, based within the community, observed increasing mortality with increasing BMI (Calle et al., 1999, Global et al., 2016).

Conclusions

As shown in this thesis, morbid obesity (BMI ≥40kg/m^2) was associated with a longer inpatient LOS. Weight loss prior to a readmission was also associated with an increased LOS and increased LOS in ICU when admitted.

The effect of obesity upon health outcomes following an acute admission to hospital is not straightforward and the advisability of weight loss as a health care strategy for those with obesity is even less so. More research and especially more data are required. This could start by mandating more patients being weighed whilst an inpatient.

Bibliography

AKINYEMIJU, T., MENG, Q. & VIN-RAVIV, N. 2016. Association between body mass index and in-hospital outcomes: Analysis of the nationwide inpatient database. *Medicine (Baltimore),* 95**,** e4189.

ALLAUDEEN, N., VIDYARTHI, A., MASELLI, J. & AUERBACH, A. 2011. Redefining readmission risk factors for general medicine patients. *J Hosp Med,* 6**,** 54-60.

AVERIN, A., SHAFF, M., WEYCKER, D., LONSHTEYN, A., SATO, R. & PELTON, S. I. 2021. Mortality and readmission in the year following hospitalization for pneumonia among US adults. *Respir Med,* 185**,** 106476.

BOSCH, X., MONCLUS, E., ESCODA, O., GUERRA-GARCIA, M., MORENO, P., GUASCH, N. & LOPEZ-SOTO, A. 2017. Unintentional weight loss: Clinical characteristics and outcomes in a prospective cohort of 2677 patients. *PLoS One,* 12**,** e0175125.

BOURAS, E. P., LANGE, S. M. & SCOLAPIO, J. S. 2001. Rational approach to patients with unintentional weight loss. *Mayo Clin Proc,* 76**,** 923-9.

BUREAU OF STATISTICS, A. 2008. *Overweight and Obesity - Aboriginal and Torres Strait Islander People: A snapshot, 2004-2005* [Online]. Available: https://www.abs.gov.au/ausstats/abs@.nsf/cat/4722.0.55.006# [Accessed 09/09/2023 2023].

CALLE, E. E., THUN, M. J., PETRELLI, J. M., RODRIGUEZ, C. & HEATH, C. W., JR. 1999. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med,* 341**,** 1097-105.

DENNIS, D. M., CARTER, V., TREVENEN, M., TYLER, J., PERRELLA, L., LORI, E. & COOPER, I. 2018. Do acute hospitalised patients in Australia have a different body mass index to the general Australian population: a point prevalence study? *Aust Health Rev,* 42**,** 121-129.

DINSA, G. D., GORYAKIN, Y., FUMAGALLI, E. & SUHRCKE, M. 2012. Obesity and socioeconomic status in developing countries: a systematic review. *Obes Rev,* 13**,** 1067-79.

FENGER-GRON, M., VINTER, N. & FROST, L. 2020. Body mass and atrial fibrillation risk: Status of the epidemiology concerning the influence of fat versus lean body mass. *Trends Cardiovasc Med,* 30**,** 205-211.

FINKIELMAN, J. D., GAJIC, O. & AFESSA, B. 2004. Underweight is independently associated with mortality in post-operative and non-operative patients admitted to the intensive care unit: a retrospective study. *BMC Emerg Med,* 4**,** 3.

FORBANG, N. I., HUGHES-AUSTIN, J. M., ALLISON, M. A. & CRIQUI, M. H. 2014. Peripheral artery disease and non-coronary atherosclerosis in Hispanics: another paradox? *Prog Cardiovasc Dis,* 57**,** 237-43.

FUSCO, K. L., ROBERTSON, H. C., GALINDO, H., HAKENDORF, P. H. & THOMPSON, C. H. 2017. Clinical outcomes for the obese hospital inpatient: An observational study. *SAGE Open Med,* 5**,** 2050312117700065.

GLOBAL, B. M. I. M. C., DI ANGELANTONIO, E., BHUPATHIRAJU SH, N., WORMSER, D., GAO, P., KAPTOGE, S., BERRINGTON DE GONZALEZ, A., CAIRNS, B. J., HUXLEY, R., JACKSON CH, L., JOSHY, G., LEWINGTON, S., MANSON, J. E., MURPHY, N., PATEL, A. V., SAMET, J. M., WOODWARD, M., ZHENG, W., ZHOU, M., BANSAL, N., BARRICARTE, A., CARTER, B., CERHAN, J. R., SMITH, G. D., FANG, X., FRANCO, O. H., GREEN, J., HALSEY, J., HILDEBRAND, J. S., JUNG, K. J., KORDA, R. J., MCLERRAN, D. F., MOORE, S. C., O'KEEFFE, L. M., PAIGE, E., RAMOND, A., REEVES, G. K., ROLLAND, B., SACERDOTE, C., SATTAR, N., SOFIANOPOULOU, E., STEVENS, J., THUN, M., UESHIMA, H., YANG, L., YUN, Y. D., WILLEIT, P., BANKS, E., BERAL, V., CHEN, Z., GAPSTUR, S. M., GUNTER, M. J.,

HARTGE, P., JEE, S. H., LAM, T. H., PETO, R., POTTER, J. D., WILLETT, W. C., THOMPSON, S. G., DANESH, J. & HU, F. B. 2016. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet,* 388**,** 776-86.

HAUCK, K. & HOLLINGSWORTH, B. 2010. The impact of severe obesity on hospital length of stay. *Med Care,* 48**,** 335-40.

IIKUNI, N., LAM, Q. L., LU, L., MATARESE, G. & LA CAVA, A. 2008. Leptin and Inflammation. *Curr Immunol Rev,* 4**,** 70-79.

ISLAM, S. & FITZGERALD, L. 2016. Indigenous obesity in the news: a media analysis of news representation of obesity in Australia's Indigenous population. *BMC Obes,* 3**,** 30.

JENSEN, C. B., TROELSEN, A., PETERSEN, P. B., CC, J. O., KEHLET, H., GROMOV, K., CENTRE FOR FAST-TRACK, H. & KNEE REPLACEMENT COLLABORATIVE, G. 2021. Influence of body mass index and age on day-of-surgery discharge, prolonged admission, and 90-day readmission after fast-track unicompartmental knee arthroplasty. *Acta Orthop,* 92**,** 722-727.

JENSEN, M. D., RYAN, D. H., APOVIAN, C. M., ARD, J. D., COMUZZIE, A. G., DONATO, K. A., HU, F. B., HUBBARD, V. S., JAKICIC, J. M., KUSHNER, R. F., LORIA, C. M., MILLEN, B. E., NONAS, C. A., PI-SUNYER, F. X., STEVENS, J., STEVENS, V. J., WADDEN, T. A., WOLFE, B. M., YANOVSKI, S. Z., JORDAN, H. S., KENDALL, K. A., LUX, L. J., MENTOR-MARCEL, R., MORGAN, L. C., TRISOLINI, M. G., WNEK, J., ANDERSON, J. L., HALPERIN, J. L., ALBERT, N. M., BOZKURT, B., BRINDIS, R. G., CURTIS, L. H., DEMETS, D., HOCHMAN, J. S., KOVACS, R. J., OHMAN, E. M., PRESSLER, S. J., SELLKE, F. W., SHEN, W. K., SMITH, S. C., JR., TOMASELLI, G. F., AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION TASK FORCE ON PRACTICE, G. & OBESITY, S.

2014. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation,* 129**,** S102-38.

LEITAO, A., BRITO, A., PINHO, J., ALVES, J. N., COSTA, R., AMORIM, J. M., RIBEIRO, M., PINHO, I. & FERREIRA, C. 2017. Predictors of hospital readmission 1 year after ischemic stroke. *Intern Emerg Med,* 12**,** 63-68.

LIU, B., BALKWILL, A., SPENCER, E., BERAL, V. & MILLION WOMEN STUDY, C. 2008. Relationship between body mass index and length of hospital stay for gallbladder disease. *J Public Health (Oxf),* 30**,** 161-6.

MAALI, Y., PEREZ-CONCHA, O., COIERA, E., ROFFE, D., DAY, R. O. & GALLEGO, B. 2018. Predicting 7-day, 30-day and 60-day all-cause unplanned readmission: a case study of a Sydney hospital. *BMC Med Inform Decis Mak,* 18**,** 1.

MELTZER, A. A. & EVERHART, J. E. 1995. Unintentional weight loss in the United States. *Am J Epidemiol,* 142**,** 1039-46.

MULLEN, J. T., MOORMAN, D. W. & DAVENPORT, D. L. 2009. The obesity paradox: body mass index and outcomes in patients undergoing nonbariatric general surgery. *Ann Surg,* 250**,** 166-72.

PERERA, L. A. M., CHOPRA, A. & SHAW, A. L. 2021. Approach to Patients with Unintentional Weight Loss. *Med Clin North Am,* 105**,** 175-186.

PEREZ-PEREZ, A., SANCHEZ-JIMENEZ, F., VILARINO-GARCIA, T. & SANCHEZ-MARGALET, V. 2020. Role of Leptin in Inflammation and Vice Versa. *Int J Mol Sci,* 21.

RAM, P., SHAH, M., LO, K. B. U., AGARWAL, M., PATEL, B., TRIPATHI, B., ARORA, S., PATEL, N., JORDE, U. P. & BANERJI, S. 2021. Etiologies and predictors of readmission among obese and morbidly obese patients admitted with heart failure. *Heart Fail Rev,* 26**,** 829-838.

REHUNEN, S. K., KAUTIAINEN, H., KORHONEN, P. E. & ERIKSSON, J. G. 2020. Lean body mass is not beneficial, but may be detrimental for glucose tolerance - Splitting body mass index according to body composition. *Prim Care Diabetes,* 14**,** 747-752.

SHARMA, Y., MILLER, M., KAAMBWA, B., SHAHI, R., HAKENDORF, P., HORWOOD, C. & THOMPSON, C. 2018. Factors influencing early and late readmissions in Australian hospitalised patients and investigating role of admission nutrition status as a predictor of hospital readmissions: a cohort study. *BMJ Open,* 8**,** e022246.

TILLIN, T., SATTAR, N., GODSLAND, I. F., HUGHES, A. D., CHATURVEDI, N. & FOROUHI, N. G. 2015. Ethnicity-specific obesity cut-points in the development of Type 2 diabetes - a prospective study including three ethnic groups in the United Kingdom. *Diabet Med,* 32**,** 226-34.

WOOLLEY, C., THOMPSON, C., HAKENDORF, P. & HORWOOD, C. 2019. The Effect of Age upon the Interrelationship of BMI and Inpatient Health Outcomes. *J Nutr Health Aging,* 23**,** 558-563.