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The importance of weight stabilization amongst those with overweight or obesity: Results from a large health care system

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ABSTRACT

Data on patterns of weight change among adults with overweight or obesity are minimal. We aimed to examine patterns of weight change and associated hospitalizations in a large health system, and to develop a model to predict 2-year significant weight gain.

Data from the Duke University Health System was abstracted from 1/1/13 to 12/31/16 on patients with BMI $\geq$ 25 kg/m^2 in 2014. A regression model was developed to predict patients that would increase their weight by 10% within 2 years. We estimated the association between weight change category and all-cause hospitalization using Cox proportional hazards models.

Of the 37,253 patients in our cohort, 59% had stable weight over 2 years, while 24% gained $\geq$ 5% weight and 17% lost $\geq$ 5% weight. Our predictive model had reasonable discriminatory capacity to predict which individuals would gain $\geq$ 10% weight over 2 years (AUC 0.73). Compared with stable weight, the risk of hospitalization was increased by 37% for individuals with $>$ 10% weight loss [adj. HR (95% CI): 1.37 (1.25,1.5)], by 30% for those with $>$ 10% weight gain [adj. HR (95% CI): 1.3 (1.19,1.42)], by 18% for those with 5–10% weight loss [adj. HR (95% CI): 1.18 (1.09,1.28)], and by 10% for those with 5–10% weight gain [adj. HR (95% CI): 1.1 (1.02,1.19)].

In this examination of a large health system, significant weight gain or loss of $>$ 10% was associated with increased all-cause hospitalization over 2 years compared with stable weight. This analysis adds to the increasing observational evidence that weight stability may be a key health driver.

1. Introduction

The prevalence of obesity in the US is rapidly growing; with almost 40% of adults currently classified as having obesity (body-mass index (BMI) $\geq$ 30 kg/m^2) (Ogden et al., 2014). This epidemic poses a massive public health challenge, as obesity has been associated with multiple health concerns including diabetes mellitus, chronic kidney disease, cancer, and cardiovascular disease (Jensen et al., 2014). Weight loss can decrease these risks and lead to improvement in cardiovascular disease (CVD) risk factors such as hypertension, hyperlipidemia, and hyperglycemia (Wing et al., 2011). Though multiple effective strategies for weight loss exist, including lifestyle modification, pharmacotherapies, and bariatric surgery, it remains unclear to what extent individuals with obesity in clinical settings are actually losing weight. Understanding patterns of weight change within health systems can inform strategies to improve the overall trajectory of obesity in the U.S.

It is also unclear whether significant weight change over the intermediate-term, such as gaining $\geq$ 10% of body weight over 2 years, leads to worse health outcomes and increased healthcare resource utilization such as hospitalization. Previous studies on the impact of significant weight gain over this time period have yielded conflicting results (Breeze et al., 2006; Stevens et al., 2013; Berentzen et al., 2010; Newman et al., 2001). If it is indeed the case that significant weight gain over 2 years leads to worse outcomes, then identifying the individuals who are most at risk of gaining weight might allow us to intervene and prevent worsening obesity. This in turn might improve overall health outcomes and decrease burden on the health system.

We aimed to examine patterns of weight change in the Duke Health System and subsequent healthcare utilization associated with different patterns of weight change over 2 years. Specifically, we aimed to

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understand how frequently patients with overweight or obesity lose (or gain) weight, and what the predictors and clinical impact of this weight change are. Specifically, we evaluated whether different levels of weight change lead to different rates of all-cause hospitalization over 2 years. This is an important outcome both from the perspective of the patient, and from the perspective of the health system. Further, we developed a model to predict which individuals are most likely to gain a significant amount of weight over 2 years. Our goal in developing this model was to be able to identify individuals who should be targeted for weight gain prevention interventions.

2. Methods

2.1. Data source

We abstracted data from the Duke University Health System (DUHS) electronic health record (EHR) system. DUHS consists of 3 hospitals and 144 outpatient clinics and has been on an integrated EHR system since 2014. As the primary provider and only hospital system in Durham, North Carolina and provides up to 85 to 90% of the primary care to Durham County residents (Miranda et al., 2013). We abstracted data covering January 1, 2013 – December 31, 2016.

2.2. Study population

In order to define a local patient population, adults ≥ 18 years old were included in this study if they had a Durham County address in 2014 and had at least two primary care encounters within DUHS between 2013 and 2014, with at least one of these encounters in 2014. In addition, eligible individuals had to have at least 2 BMI measurements at least 365 days apart, with the second in 2014 and ≥ 25 kg/m^2. Individuals who were pregnant at any point during 2014 were excluded from this analysis. Patients were censored at death, when they moved out of Durham County based on changed zip code, or at their last indicated encounter.

2.3. BMI and other clinical characteristics

Body-mass index (BMI) classes were defined according to the World Health Organization BMI categories as follows: overweight (BMI 25–29.9 kg/m^2), obese class I (30–34.9 kg/m^2), obese class II (35–39.9 kg/m^2), and obese class III (≥40 kg/m^2) (Carnethon et al., 2012). The index BMI was defined as the last recorded BMI in 2014. Change in BMI was defined as the difference between the first BMI in 2013 and the index BMI (Fig. 1).

Weight changes were categorized as 5–10% weight change and > 10% weight change. These thresholds were chosen because weight loss of 5–10% has been shown to be associated with significant improvements in cardiovascular disease (CVD) risk factors, and weight loss of > 10% is associated with even greater improvements in risk factors (Wing et al., 2011).

Additional clinical characteristics were abstracted at the time of the index BMI. Comorbid diagnoses defined by ICD-9 and ICD-10 codes listed prior to index BMI date were recorded. Vital signs and laboratory data were recorded if measured within 24 months of the index BMI. Medications were included if they were listed prior to index date.

2.4. Endpoints

The primary clinical endpoint was time to all-cause hospitalization occurring after the landmark date of January 1, 2015. As a secondary outcome we looked at number of hospitalizations in the next year.

2.5. Statistical analyses

We summarized characteristics of the cohort at the time of index BMI using descriptive statistics (median and interquartile range (IQR) for continuous variables, frequencies and percentages for binary and class variables). We compared baseline characteristics between groups using Pearson chi-square or Fisher's exact tests.

In order to assess impact of weight and weight change on time to hospitalization we performed a time-to-event analysis. We estimated Kaplan-Meier rates of all-cause hospitalization according to weight change category. We estimated the association between weight change category and all-cause hospitalization using Cox proportional hazards models, with the < 5% weight change group as the reference. We fit a minimally adjusted model, adjusted only for age, sex, and race and a fully adjusted model further adjusted for hypertension, hyperlipidemia, chronic kidney disease, myocardial infarction (MI), peripheral arterial disease, congestive heart failure, stroke, cancer, smoking status, number of previous inpatient encounters, and number of previous outpatient encounters.

To determine whether the association between weight change category and clinical outcome was affected by the sub-group of patients with congestive heart failure, we performed a sensitivity analysis in which individuals with an ICD-9 or ICD-10 code consistent with heart failure

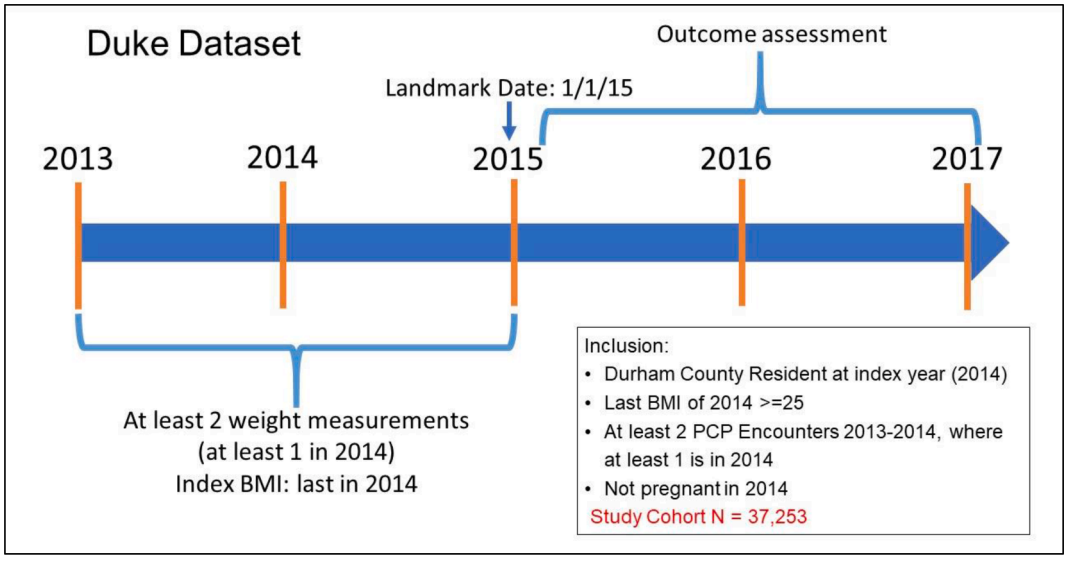

Fig. 1. Study cohort description.

were excluded from the analysis. This was performed because weight changes in patients with heart failure could be due to shifts in volume rather than to true changes in weight. Cox proportional hazards models using the same adjustment criteria as above were developed.

2.6. Development of predictive model

A least absolute shrinkage and selection operator (LASSO) regression was performed to predict patients who would increase their weight by at least 10% within 2 years (Tibshirani, 1996). LASSO is a type of regression model that performs an implicit variable selection. As our goal for this model was to allow clinicians to be able to predict who is most likely to gain 10% weight over ensuing two years, we framed this as a landmark analysis using only baseline factors for prediction. Since not all patients had weights measured exactly 2 years after the landmark date, we allowed a 3 month window and used the latest weight in that period. Percent weight change was defined by: (24 mo weight – baseline weight)/baseline weight. Model covariates included the following characteristics: index BMI, time of index BMI, sex, race, age, insurance status, baseline medications (ACEi/ARB, beta blocker, statin, metformin, aspirin, orlistat, lorcaserin, bupropion, topiramate, pramlintide, exenatid, liraglutide, phentermine, naltrexone), counts of types of prior encounters, diagnosis codes, number of prior lab/vital measurements and indicator for abnormal values (systolic and diastolic blood pressure, HbA1c, creatinine, lipids, AST, ALT), smoking, and socioeconomic status index. Data was split into 80/20 training/testing sets. Model performance was expressed by area under the curve (AUC) of the receiving operating characteristic. Prediction error was optimized using square error loss and internal cross validation.

Statistical analyses were performed using SAS 9.4 and R 3.5. This study received approval from the Duke Institutional Review Board.

3. Results

3.1. Characteristics of study population by weight change category:

Overall, 71,174 Durham County residents had at least 2 primary care physician visits in the Duke Health System between 2013 and 2014. Of these, 37,253 (52.3%) individuals met inclusion criteria of BMI $\geq$ 25 kg/m^2 in 2014 without a history of pregnancy in that year. Within this group, 14,922 (40.1%) of individuals were in the overweight category, 11,076 (29.7%) were in obese class I, 5,824 (15.6%) were in obese class II, and 5,431 (14.6%) were in obese class III (Fig. 2). Baseline characteristics by BMI category are presented in Supplemental Table 1.

Between 2013 and 2014, the majority of patients (n = 22,047; 59.2%) had stable weight with < 5% change (Table 1). The remainder of individuals had significant weight change: 11.4% lost 5–10% of their weight and 5.7% lost > 10% of their weight, while 14.7% gained 5–10% of their weight and 9.0% gained > 10% of their weight (Fig. 2).

Compared with individuals with stable weight, those who lost > 10% of their weight more frequently had hypertension (67.6% vs 59.5%, p $\leq$ 0.001), diabetes (40.1% vs 26.2%, p $\leq$ 0.001), prior MI (4.8% vs 2.3%, <0.001), stroke/transient ischemic attack (7.4% vs 3.6%, p $\leq$ 0.001), and cancer (14.5% vs 11.8%, p $\leq$ 0.001). In contrast, those who gained > 10% of their weight less frequently had hypertension (50.6% vs 59.5%, p $\leq$ 0.001), hyperlipidemia (30.1% vs 39.9%, p $\leq$ 0.001), diabetes (23.0% vs 26.2%, p $\leq$ 0.001), and cancer (9.8% vs 11.8%, p = 0.001). Overall use of anti-obesity medications, including orlistat, lorcaserin, buproprion, topiramate, and liraglutide, was very low at 9.6%, with 12.5% of patients with > 10% weight loss on anti-obesity medications, and 12.5% of patients with > 10% weight gain on these therapies.

3.2. Predictive model characteristics

The LASSO model for at least 10% weight gain over 2 years had an AUC of 0.73, indicating reasonable discrimination, or ability of the model to separate individuals who gain $\geq$ 10% body weight from those who do not. The model also had a calibration slope of 1.698, indicating that the model's predictions matched overall observed rates of $\geq$ 10% weight gain quite well. The most important predictors in the model were: index BMI, BMI value present in January 2013-April 2013 (i.e. longer follow-up time period), and age at baseline. Other predictors emerging from the model were: comorbidities, counts for labs/vitals (blood pressure, creatinine, alanine aminotransferase, high-density lipoprotein cholesterol (HDL)), out of range lab (A1C, low-density lipoprotein cholesterol (LDL), triglycerides, HDL), sex, race, and smoking status (Fig. 3).

3.3. Association between weight change and all-cause hospitalization:

Over a 2-year follow-up period, the Kaplan-Meier event rate for all-cause hospitalization was 0.18 in the overall study cohort. The event rate was greatest for those individuals with > 10% weight loss, intermediate for those with either 5–10% weight loss or > 10% weight gain, and least for those with either 5–10% weight gain or stable weight (<5% weight change) (Fig. 4). After full adjustment, compared with the stable weight group, individuals with > 10% weight loss had a 37% increased risk of hospitalization [HR (95% CI): 1.37 (1.25, 1.5)], while those with > 10% weight gain had a 30% increased risk [HR (95% CI): 1.3 (1.19,

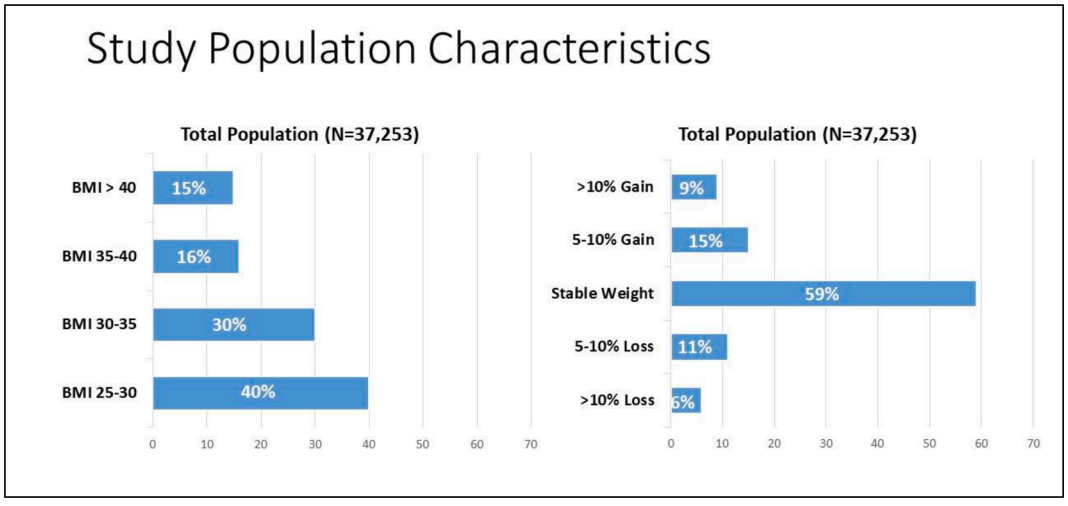

Fig. 2. Study cohort characteristics by BMI and percent weight change.

Table 1
Baseline characteristics by weight change category.

Baseline characteristics by weight change | N = 37,253					
Characteristic	>10% Loss (N = 2128)	5–10% Loss (N = 4248)	<5% Change (N = 22047)	5–10% Gain (N = 5485)	>10% Gain (N = 3345)
Demographics					
Age (yrs) (Median, Percentiles)	54.4 (43.0–66.4)	56.3 (44.0–67.0)	55.5 (44.0–65.7)	51.5 (40.0–62.7)	48.5 (35.3–60.7)
Female sex	1502 (70.6%)	2713 (63.9%)	13,429 (60.9%)	3680 (67.1%)	2447 (73.2%)
RACE					
White	779 (36.6%)	1594 (37.5%)	9015 (40.9%)	2169 (39.5%)	1246 (37.2%)
Black	1149 (54.0%)	2224 (52.4%)	10,638 (48.3%)	2655 (48.4%)	1708 (51.1%)
Other	200 (9.4%)	430 (10.1%)	2394 (10.9%)	661 (12.1%)	391 (11.7%)
Insurance					
Private	890 (43.5%)	1999 (49.4%)	12,250 (58.3%)	3098 (59.6%)	1586 (49.9%)
Public	997 (48.7%)	1739 (43.0%)	7325 (34.9%)	1690 (32.5%)	1257 (39.6%)
Self-Pay	161 (7.9%)	309 (7.6%)	1420 (6.8%)	407 (7.8%)	333 (10.5%)
Index BMI Class					
Overweight	969 (45.5%)	1891 (44.5%)	9115 (41.3%)	1967 (35.9%)	980 (29.3%)
Obese I	630 (29.6%)	1239 (29.2%)	6552 (29.7%)	1663 (30.3%)	992 (29.7%)
Obese II	298 (14.0%)	594 (14.0%)	3395 (15.4%)	918 (16.7%)	619 (18.5%)
Obese III	231 (10.9%)	524 (12.3%)	2985 (13.5%)	937 (17.1%)	754 (22.5%)
Comorbidities					
Hypertension	1438 (67.6%)	2728 (64.2%)	13,120 (59.5%)	2874 (52.4%)	1694 (50.6%)
Hyperlipidemia	923 (43.4%)	1842 (43.4%)	8804 (39.9%)	1917 (34.9%)	1006 (30.1%)
Diabetes	853 (40.1%)	1480 (34.8%)	5782 (26.2%)	1185 (21.6%)	770 (23.0%)
MI	102 (4.8%)	144 (3.4%)	516 (2.3%)	121 (2.2%)	104 (3.1%)
Coronary Revascularization	73 (3.4%)	118 (2.8%)	370 (1.7%)	83 (1.5%)	68 (2.0%)
CAD	252 (11.8%)	436 (10.3%)	1763 (8.0%)	392 (7.1%)	253 (7.6%)
Stroke/TIA	157 (7.4%)	202 (4.8%)	802 (3.6%)	203 (3.7%)	158 (4.7%)
PAD	150 (7.0%)	247 (5.8%)	915 (4.2%)	190 (3.5%)	168 (5.0%)
Current Smoker	210 (9.9%)	381 (9.0%)	1387 (6.3%)	369 (6.7%)	363 (10.9%)
Cancer	309 (14.5%)	539 (12.7%)	2593 (11.8%)	623 (11.4%)	329 (9.8%)
Labs and Vitals					
SBP (Median, Percentiles)	127 (119–136)	128 (120–136)	127 (119–136)	125 (118–134)	125 (116–134)
DBP (Median, Percentiles)	77 (71–82)	78 (72–82)	78 (72–82)	78 (72–82)	77 (71–82)
A1C (Median, Percentiles)	6 (6–8)	7 (6–8)	6 (6–7)	6 (6–7)	6 (6–7)
eGFR (Median, Percentiles)	87 (67–105)	86 (70–103)	87 (71–102)	91 (74–106)	94 (75–111)
Total Cholesterol (Median, Percentiles)	177 (151–203)	180 (154–207)	184 (159–210)	184 (160–210)	182 (158–208)
HDL-C (Median, Percentiles)	45 (37–55)	46 (39–55)	47 (39–56)	48 (40–58)	49 (40–59)
LDL-C (Median, Percentiles)	104 (80–125)	105 (82–129)	108 (86–131)	108 (87–131)	105 (85–128)
Triglycerides (Median, Percentiles)	112 (81–160)	118 (84–168)	117 (83–169)	110 (79–158)	113 (79–165)
Medication History					
Statin	945 (44.4%)	1933 (45.5%)	8746 (39.7%)	1937 (35.3%)	1099 (32.9%)
ACEi/ARB	1037 (48.7%)	2027 (47.7%)	9530 (43.2%)	2004 (36.5%)	1136 (34.0%)
BB	844 (39.7%)	1444 (34.0%)	6607 (30.0%)	1518 (27.7%)	1024 (30.6%)
Aspirin	977 (45.9%)	1945 (45.8%)	8976 (40.7%)	1891 (34.5%)	1092 (32.6%)
Orlistat	12 (0.6%)	33 (0.8%)	174 (0.8%)	48 (0.9%)	24 (0.7%)
Lorcaserin	3 (0.1%)	1 (0.0%)	25 (0.1%)	11 (0.2%)	6 (0.2%)
Bupropion	165 (7.8%)	285 (6.7%)	1297 (5.9%)	394 (7.2%)	270 (8.1%)
Topiramate	86 (4.0%)	102 (2.4%)	442 (2.0%)	135 (2.5%)	145 (4.3%)
Metformin	514 (24.2%)	1027 (24.2%)	4055 (18.4%)	780 (14.2%)	454 (13.6%)
Liraglutide	0 (0.0%)	1 (0.0%)	6 (0.0%)	1 (0.0%)	1 (0.0%)
Service Utilization 2013–2014					
Outpatient Encounters (Median, Percentiles)	13.0 (6.0–24.0)	11.0 (5.0–21.0)	9.0 (5.0–18.0)	10.0 (5.0–18.0)	11.0 (5.0–21.0)
Inpatient Encounters (Median, Percentiles)	0.0 (0.0–1.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)
Emergency department Encounters (Median, Percentiles)	1.0 (0.0–2.0)	0.0 (0.0–1.0)	0.0 (0.0–1.0)	0.0 (0.0–1.0)	0.0 (0.0–2.0)
Any Inpatient Encounter	699 (32.8%)	800 (18.8%)	2500 (11.3%)	693 (12.6%)	666 (19.9%)
Any Emergency department Encounter	1072 (50.4%)	1720 (40.5%)	6719 (30.5%)	1836 (33.5%)	1469 (43.9%)

1.42)]. Individuals with 5–10% weight loss had an 18% increased risk [HR (95% CI): 1.18 (1.09, 1.28)], and those with 5–10% weight gain had a 10% increased risk [HR (95% CI): 1.1 (1.02, 1.19)] (Table 2).

In a sensitivity analysis excluding 1,903 individuals with a heart failure diagnosis code prior to the index date, the above relationships held. Specifically, individuals with > 10% weight loss had the greatest adjusted risk of hospitalization [HR (95% CI): 1.46 (1.32, 1.62)], followed by those with > 10% weight gain [HR (95% CI): 1.3 (1.18, 1.43)] and those with 5–10% weight loss [HR (95% CI): 1.17 (1.07, 1.28)]. Those with 5–10% weight gain had similar risk of hospitalization to those with stable weight [HR (95% CI):1.09 (1.0, 1.18)].

4. Discussion

In this study of 2-year weight change among individuals with overweight and obesity in a large academic health system, we found that the majority of individuals had stable weight. Our predictive model to predict ≥ 10% weight gain over 2 years had reasonable discriminative capacity to predict which individuals are at greatest risk of short-term weight gain. Individuals who gained or lost > 10% of body weight had the highest risk of all-cause hospitalization over the 2 years after their documented weight change.

The majority of individuals in our cohort had stable weight over 2 years, while approximately one-quarter gained > 5% body weight and

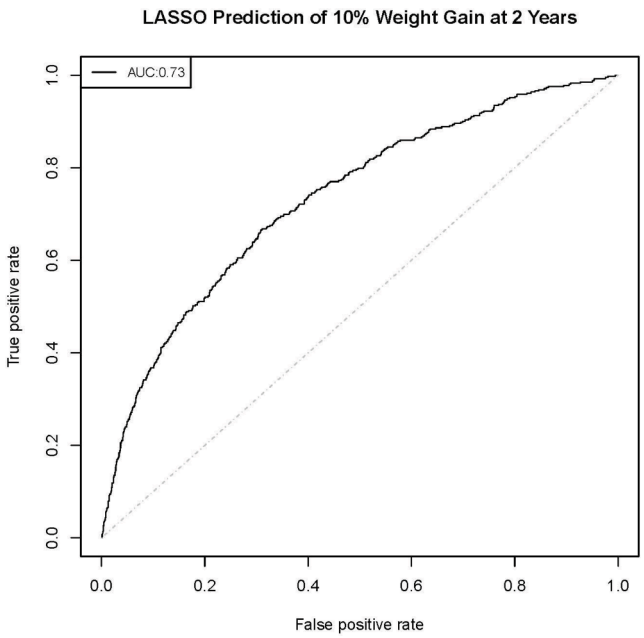

Fig. 3. Prediction model for ≥ 10% weight gain (vs. all other weight change groups) over 2 years.

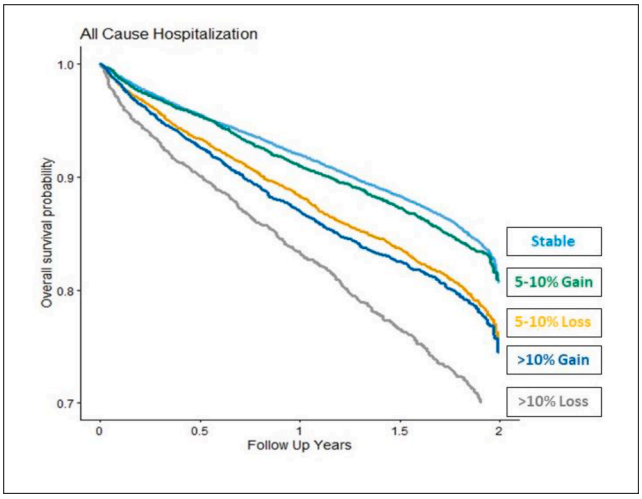

Fig. 4. Kaplan-Meier curves for association between weight change and all-cause hospitalization.

Table 2
Hazard ratios for time to all-cause hospitalization after index date.

Weight change	HR minimally adjusted	HR fully adjusted
>10% Gain	1.65 (1.52, 1.8)	1.3 (1.19, 1.42)
5–10% Gain	1.13 (1.05, 1.23)	1.1 (1.02, 1.19)
5–10% Loss	1.36 (1.26, 1.47)	1.18 (1.09, 1.28)
>10% Loss	2.06 (1.89, 2.26)	1.37 (1.25, 1.5)

Reference: Stable weight group (<5% weight change).
Unadjusted models are adjusted for age, sex, race.
Adjusted Models are adjusted for: age, sex, and race plus hypertension, hyperlipidemia, CKD, MI, PAD, CHF, Stroke, Cancer, Smoking Status, number of previous IP encounters, number of previous OP encounters.

approximately one-fifth lost > 5% body weight. This is consistent with prior literature on patients with overweight and obesity. An analysis of National Health and Nutrition Examination Survey (NHANES) data from 1999 to 2014 revealed that 49% of individuals had < 2.5% weight change over 1 year, while approximately 25% gained weight and 25% lost weight. (Vierboom et al., 2018) Our data confirm that among patients with overweight or obesity, the majority do not significantly change their weight over the short term.

However, our predictive model has reasonable capacity to predict individuals within the Duke Health System who are most likely to gain significant weight over 2 years. Index BMI emerged as a strong predictor in our model, which makes sense since prior BMI tends to predict future BMI. Similarly, a BMI value early in the study period was predictive, indicating that following people for a long enough time period is important in predicting whether or not they will gain a significant amount of weight. This methodology can be used to target interventions to individuals who are most likely to gain weight in the short-term, and who therefore might benefit the most from weight management interventions. While our model has only been developed and validated within the Duke Health System, and therefore may not be generalizable to other health systems, the methodology will likely translate across patient populations.

Our finding that > 10% weight loss is associated with increased hospitalizations is consistent with much, but not all, of the prior literature in this space. Several observational studies have shown worse outcomes with weight loss in broad populations (Karahalios et al., 2014; Pack et al., 2014; Myers et al., 2011; Østergaard et al., 2010) and also in specific sub-groups, including individuals with diabetes, (Lee et al., 2020) patients with ischemic stroke (Wohlfahrt et al., 2015) or coronary heart disease, (Moholdt et al., 2018) and those who have undergone coronary artery bypass graft surgery. (Kocz et al., 2012) However, most of these studies could not distinguish between unintentional and intentional weight loss. While unintentional weight loss may be due to underlying cachexic conditions that lead to increased risk of poor outcomes (De Stefani et al., 2018), intentional weight loss would be expected to improve outcomes given associated improvements in glucose, blood pressure, and lipids. (Wing et al., 2011; Ryan and Yockey, 2017) Indeed, in a *meta*-analysis of 26 studies, weight loss was associated with worse outcomes (all-cause mortality, CV mortality, and major adverse CV events) overall, but when restricted to the 4 cohorts with presumed intentional weight loss, weight loss was associated with improved outcomes (RR 0.67 [95% CI 0.56–0.80], p < 0.001) (Pack et al., 2014). Similarly, the Look AHEAD Study found no significant improvement in CVD among patients with diabetes who were enrolled in a weight loss intervention vs standard education (Look et al., 2013). However, in a post-hoc analysis, it was observed that individuals who lost > 10% body weight (presumably intentionally) had a 20% lower risk of major adverse CV events (Look et al., 2016). Our study was unable to distinguish between unintentional and intentional weight loss, as such information is not generally captured in EHR data. However, it is informative that the groups of individuals with substantial weight loss had higher rates of comorbidities such as diabetes, prior MI, prior stroke, and cancer than individuals with stable weight.

We also found that > 10% weight gain is associated with increased hospitalizations compared with those with stable weight. Prior literature on health outcomes with weight gain is similarly conflicting. Several studies have reported an increased risk of mortality with weight gain (Breeze et al., 2006; Stevens et al., 2013; Zheng et al., 2013; Bamia et al., 2010). In contrast, many observational studies have not found a relationship between weight gain and clinical outcomes (Berentzen et al., 2010; Newman et al., 2001; Karahalios et al., 2014). The reasons for these conflicting data are unclear, and may be related to the fact that sample sizes in these studies were widely variable, and the definitions of weight change across studies also varied. It may also reflect the phenomenon known as the "obesity paradox." This paradox refers to the finding from many observational studies that overweight of mild/moderate obesity can be associated with improved health status compared with normal weight (Horwich et al., 2018). Reasons for this paradox are unclear, but some have hypothesized epidemiologic

artifact, such as lead-time bias, survival or selection bias, and collider stratification bias (Elagizi et al., 2018; Banack and Kaufman, 2015; O'Brien and Thomas, 2016).

The overall implication of our study is that weight stability, i.e. < 5% weight change over 2 years, is associated with improved subsequent clinical outcomes among patients with overweight or obesity. Many studies have shown that obesity itself is associated with poor clinical outcomes, including CVD and overall mortality (Allison et al., 1999; Fontaine et al., 2003; Hu et al., 2004; Calle et al., 1999). However, once adults have become obese, considerable data – including ours – suggest that weight stability may be associated with the best outcomes (Kim et al., 2019; Dong et al., 2018). A *meta*-analysis of observational cohort studies showed that any type of weight change (including weight loss, gain, and fluctuation) was associated with increased mortality among community-dwelling adults at least 60 years old (Cheng et al., 2015). Similarly, an analysis of ischemic stroke patients in Korea revealed that risk of recurrent stroke was increased in individuals who gained or lost > 5% of their weight over 4 years (Cho et al., 2019). A study of the Systolic Hypertension in the Elderly Program revealed that, among older adults, weight stability was associated with a lower mortality risk than weight gain or loss (Somes et al., 2002). In a multi-ethnic cohort, individuals with obesity at baseline had a higher risk of mortality than individuals with normal weight. Further, individuals who gained > 10 kg (HR 1.25 [95% CI 1.11–1.41]) and individuals who lost > 10 kg (HR 2.86 [95% CI 2.62–3.11]) had higher all-cause mortality compared with individuals whose weight remained stable. Thus, improved outcomes were associated with both not having obesity, and maintaining a stable weight regardless of baseline BMI (Park et al., 2018).

While observational research indicates that weight stability, rather than weight loss or gain, may be a key health driver for patients with obesity, this needs to be tested prospectively. Several interventions to promote weight stability, and specifically weight gain prevention, have been reported in the literature. However, it is not clear whether such programs, and consequent weight stability, improve hard clinical outcomes. For example, the Shape Program, which was a primary care-based behavioral weight gain prevention intervention, successfully prevented weight gain among socioeconomically disadvantaged black women (Bennett et al., 2013). This study helped to fuel the "maintain, don't gain" approach to weight management, but longer-term clinical events were not assessed. A series of interventions have been developed that focus on the health gains associated with lifestyle change and psychosocial well-being rather than on weight loss itself; these interventions are termed "health, not weight loss, focused" (HNWL) programs (Khasteganan et al., 2019). While these programs are not specifically targeted to achieve weight stability, many of them do achieve weight stability along with improvements in body satisfaction. However, whether these programs lead to reductions in clinical events or healthcare utilization is as yet unknown.

Our results should be interpreted with several caveats. First, within the confines of EHR data, we were not able to determine reasons for weight change. Therefore, as stated above, we do not know whether weight loss was intentional or unintentional, or whether intentional weight loss is associated with poor clinical outcomes. For weight gain, it is reassuring that the exclusion of patients with heart failure did not change the association between weight gain and hospitalizations. Second, this study reflects the experience of a single health system and results may not be consistent across different health systems. Third, as with all analyses of EHR data, any care that was received outside our institution would not be captured. That being said, DUHS is the primary provider in Durham County, so we expect data capture to be relatively complete. The time horizon of our study was relatively brief, and the association between weight change and longer-term outcomes could not be determined. Finally, our model to predict 2-year weight gain has not yet been externally validated, so its use cannot be generalized to other health systems.

5. Conclusions

In this examination of a large health system, significant weight gain or loss of > 10% was associated with increased all-cause hospitalization over 2 years compared with stable weight. This adds to the increasing observational evidence that weight stability may be a key health driver. Whether weight stability is causally related to improved health outcomes, and whether it should be a health target rather than weight loss, requires prospective study.

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CRediT authorship contribution statement

Neha J. Pagidipati: Conceptualization, Funding acquisition, Methodology, Writing – original draft.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

NJ Pagidipati has received research grants from Amarin, Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, Regeneron, Sanofi, Verily Life Sciences, Novartis; has received consulting fees from Boehringer Ingelheim, Eli Lilly, AstraZeneca, Novo Nordisk, and Esperion; and is on a study board for Novo Nordisk.

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Appendix A. Supplementary data

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