

# Predicting unintentional weight loss in patients with gastrointestinal cancer

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## Abstract

**Background** Unintentional weight loss is a major problem for patients with gastrointestinal (GI) cancers because it affects treatment, survival outcomes, and quality of life. To date, little is known about the trajectory of weight loss and the relationship between baseline body mass index (BMI), location of the cancer, and outcomes. The aims of this study were to investigate patterns of weight loss over time in patients with GI cancer according to BMI groups (low, normal, and high) and location of cancer.

**Methods** We examined de-identified electronic medical record data of 801 adults (>21 years) with GI cancer using ICD-9 codes (150–159). Descriptive statistics and linear mixed models were used to examine unintentional weight loss over time by BMI group (low, normal, and high) and to determine the effect of primary cancer site and patient characteristics on weight loss.

**Results** The mean age of patients was  $66.5 \pm 11.9$  years (21–95 years), with 58% male and 86% White. Mean weight loss over 3 years was 21.39 kg. At the first observation point, 7.8% were in the low BMI group, 30.1% were in the normal, and 62% were in the high group. At the end of observation, a majority of deaths (35.5%) occurred in the low BMI group (BMI < 20 kg/m<sup>2</sup>). Significant weight loss was observed in patients with gastric ( $t = -5.11$ ,  $P < 0.001$ ), oesophageal ( $t = -4.18$ ,  $P < 0.001$ ), and pancreatic (35.8%,  $t = -3.58$ ,  $P < 0.001$ ) cancers. Predictors of weight change were gender ( $F = 64.93$ ,  $P < 0.001$ ), cancer stage ( $F = 7.28$ ,  $P < 0.001$ ), and site by days ( $F = 8.24$ ,  $P < 0.001$ ). Weight loss rates were similar among the three BMI groups, but patterns were different based on primary cancer type as a function of days within each group.

**Conclusions** Weight loss in patients with GI cancers has implications for survival. Patients with upper GI cancers experienced more weight loss and decreased survival rates compared with patients with lower GI cancers. Patients with a combination of upper GI cancer (oesophagogastric or pancreatic) and low baseline BMI had the fewest survival days and worst patient outcomes. Early intervention for weight management plays a critical role for improving the health outcomes and fatality rates of these patients.

**Keywords** Unintentional weight loss; Weight loss trajectory; Cachexia; Gastrointestinal cancer; Body mass index; Survival

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## Introduction

Unintentional weight loss impairs physical functioning,<sup>1</sup> quality of life (QoL), treatment outcomes, and survival in patients diagnosed with gastrointestinal (GI) cancer.<sup>2</sup> Up to 20% of deaths among cancer patients are caused by *cachexia*,<sup>3</sup>

unintentional weight loss of 5% or more body weight in a 6 month period or greater than 2% if patients' body mass index (BMI) is less than 20 kg/m<sup>2</sup>.<sup>4,5,1</sup> Greater than 15% weight loss leads to impaired physiological function, and 30% can lead to imminent death in cancer patients.<sup>2</sup> Half of all cancer deaths worldwide<sup>6</sup> are associated with cachexia: pancreatic (0.33

million deaths), oesophageal (0.40 million), gastric (0.72 million), pulmonary (1.59 million), hepatic (0.75 million), and colorectal (0.69 million) cancers.<sup>7</sup> GI cancers are estimated to have the highest incidence of cachexia among all cancer types and the second highest death rate due to the condition.<sup>8</sup> Although cachexia may occur across all cancer populations including patients with obesity,<sup>9</sup> patients suffering from GI cancer are at particular risk for severe cachexia<sup>3</sup> because of reduced nutritional intake, impaired GI function, and metabolic and hormonal alteration.<sup>10</sup>

Cachexia is difficult to control because its causes are multifactorial. Cancer treatments such as chemotherapy can substantially alter GI motility,<sup>11,12</sup> causing nausea and vomiting as well as modifying digestion and worsening malabsorption of nutrients.<sup>13</sup> Tumour-host factors such as tumour necrosis factor- $\alpha$ , interleukin-1, interleukin-6, and leptin dysregulation may significantly influence appetite, muscle mass, and adipose tissues, leading to weight loss.<sup>14</sup> Dysphagia resulting from obstruction related to location of tumour mass (e.g. oesophageal cancer) can contribute to weight loss,<sup>15</sup> and treatment or location can also affect consumption of pharmacological drugs that quell the inflammatory response, leading to weight loss and the progression of cachexia.

A recent review of the literature<sup>16</sup> revealed that the relationship between the natural progression of weight changes over time and BMI in patients with cancer is not well studied. More research on this important topic is warranted to understand the weight loss trajectory, particularly among patients with GI cancers, throughout cancer treatment to determine optimal timing for intervention.

### Specific aims

The aims of this study were to (i) investigate weight changes over time in patients with GI cancer diagnoses, (ii) identify factors that may be associated with weight changes over time, and (iii) examine characteristics of weight changes by baseline BMI (low, BMI < 20 kg/m<sup>2</sup>; normal, 20 ≤ BMI < 25 kg/m<sup>2</sup>; and high, BMI ≥ 25 kg/m<sup>2</sup>) among patients with GI cancers.

## Methods

### Study design

This was a retrospective analysis study, which used de-identified data from the Integrated Data Repository (IDR) at the institution's Health Science Center after receiving Institutional Review Board approval.

### Sample

Inclusion criteria for patient data were (i) 21 years or older at time of visit, (ii) diagnosed with any GI cancer (e.g. gastric, biliary, oesophageal, colorectal, pancreatic, and small intestinal cancers) (ICD-9 codes: 150–159), and (iii) at least two weight measurement points in the chart. Exclusion criteria were (i) only one documented weight measurement during the visits, (ii) GI cancer not a primary cancer, and (iii) without BMI data.

### Data acquisition and ethical considerations

The institution's IDR, 'a secure clinical data warehouse', is an actively managed database system integrating multiple electronic medical record systems to provide patient-oriented, clinical data for clinical and translational research using the Informatics for Integrating Biology and the Bedside (i2b2) Platform. The study team collaborated with members of the institution's IDR to obtain de-identified data aggregated between June 2011 and March 2014 that met the inclusion/exclusion criteria of the protocol approved by the institution's Institutional Review Board (#201400215). No study staff interacted directly with patients or followed up with patients for research purposes. Data were kept on secure encrypted computer servers within the institution's academic Health Science Center network.

### Variables of interest

To collect de-identified patients information, the following variables were requested from the IDR.

- 1 Demographic information including age, gender, ethnicity, marital status, and height.
- 2 Types of GI cancer based on ICD-9 codes from 150 to 159 with confirmed cancer stages.
- 3 All measured weight values from the first entry point until the last weight value from June 2011 to March 2014. The first data entry point on 1 June 2011 was counted as Day 0 and the next encounter for the measurement point as the number of days (e.g. if the next visit was 1 July 2011, it was marked as 31, accordingly).
- 4 Body mass index at the first observation point.

### Statistical analysis

Data were analysed using SPSS 24.0 software (IBM Corporation, Armonk, NY, USA, 2016). Linear mixed models (LMMs) were constructed to examine unintentional weight loss over time and to investigate the effect of the primary cancer site and patient characteristics. The primary cancer site, four

explanatory variables (gender, ethnicity, age, and cancer stages), and observation days (from now on, 'days' will be used) were included from the start of the analysis. Before constructing the final model, including the primary cancer site and patient characteristics, a separate LMM model was constructed for each variable, and the variable's interaction with days was examined. Only statistically significant variables and interactions of variables with days were included in the final LMM. Finally, for all patients, the interaction of primary cancer site with days, gender, and cancer stages was included in the final LMM as between-subjects fixed effects (Table A1). In the model, 'days' was regarded as a continuous covariate. Apart from the fixed effects, the model included a random intercept and a random effect for days. In addition, an LMM for each of the three BMI groups was constructed according to their baseline BMI. The steps and approach methods for constructing the final LMMs for the three BMI groups were the same as those used to construct the LMM for all patients.

The variables included in the final LMM for all patients and for each of the three BMI groups can be found in Table A1. Based on Akaike's information criterion and  $-2$  restricted log likelihood, an unstructured covariance matrix, which showed superior model fit compared with other covariance matrixes, was applied for model convergence in this study. We used one-tailed statistical tests in the analysis and considered a  $P$ -value of 0.05 or less significant.

## Results

### Patient characteristics

This sample group consists of 801 GI patients with 10 802 observation points included in the final model (Figure 1). The baseline characteristics of patients are summarized in Table 1. About 58% of patients were male, and 86.0% were White Americans. The mean age of patients was  $66.5 \pm 11.9$  years (21–95 years). The total number of patients with upper GI cancers (67.7%) was more than double compared with the number of patients with lower GI cancers (32.3%). The average body weight of patients was  $81.18 \pm 19.96$  kg, with a mean BMI of  $27.40 \pm 6.17$  kg/m<sup>2</sup> at the beginning of the observation. At the first observation point, 62.0% of patients were in the high BMI group ( $\text{BMI} \geq 25$  kg/m<sup>2</sup>), 30.1% of patients were in the normal BMI group ( $20 \text{ kg/m}^2 \leq \text{BMI} < 25 \text{ kg/m}^2$ ), and 7.8% of patients were in the low BMI group ( $\text{BMI} < 20 \text{ kg/m}^2$ ). The average follow-up times were  $230.6 \pm 244.4$  days (0.1–929.6 days) in the low BMI group,  $235.1 \pm 267.0$  days (0.0–991.03 days) in the normal, and  $247.6 \pm 258.4$  days (0.0–1001.8 days) in the high group. There was no significant

difference among average follow-up times for the three BMI groups ( $F = 0.24$ ,  $P = 0.781$ ).

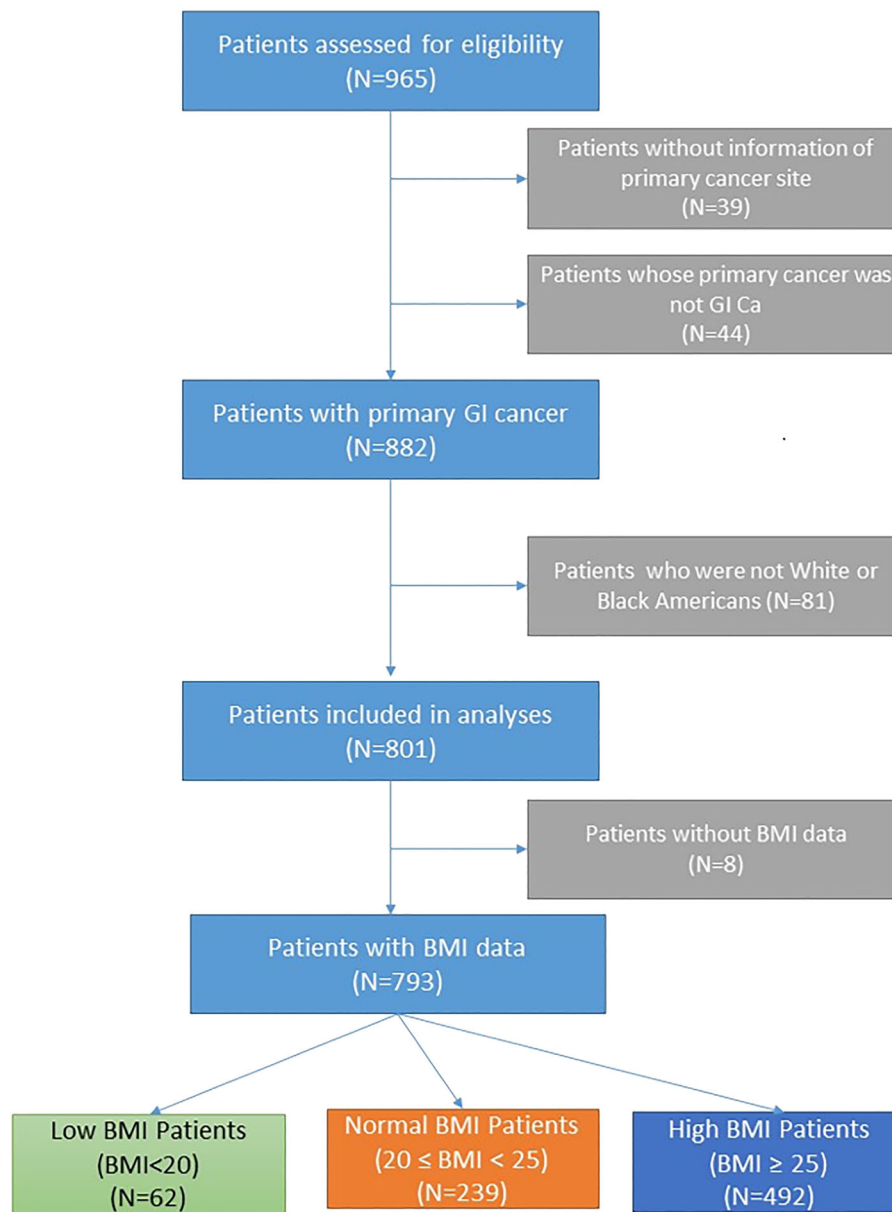
In the low BMI group, the majority of patients (62.9%) were female; 53.2% were younger adults, and 46.8% were older. In the high BMI group, the majority of patients (60.2%) were male, with 62.0% older adults. Overall, the survival rate throughout the observational period was 72.5%, and the low BMI group had the highest number of patient deaths (35.5%) among all three BMI groups.

### Weight loss over time

There were statistical significances in both intercept ( $F = 11971.81$ ,  $P < 0.001$ ) and days ( $F = 126.17$ ,  $P < 0.001$ ). Patients' body weight was negatively associated ( $t = -11.23$ ,  $P < 0.001$ ) with the days since the first observation. In this LMM, mean weight loss per patient was 0.0212 kg/day (Figure 2A). Figure 2A and 2B displays the trends in weight loss according to (A) all study patients and (B) the three BMI groups. While the low BMI group had the most weight loss per day among all three groups, all groups demonstrated similar weight loss patterns (Figure 2B). We examined whether the patterns of weight loss differ between the overweight ( $n_1 = 271$ ) and the obese ( $n_2 = 221$ ) groups within the high BMI group ( $N = 492$ ) because the sample size for two subgroups was large enough for analysis. The subgroup analysis showed similar weight loss patterns over time between overweight and obese groups. There was no significant difference in weight loss patterns when all four groups (low, normal, overweight, and obese) were compared ( $F = 2.334$ ,  $P = 0.072$ ). We concluded that keeping the high BMI group together provided sufficient information for the purpose of the study.

### Weight loss according to primary cancer site

The most weight loss (48.8%) was observed in patients with gastric cancer. This was followed by weight loss in patients with pancreatic cancer (35.8%), with the least amount of weight loss reported by patients with colorectal cancer (12.0%) (Figure 3). An LMM was used to evaluate weight changes among patients with various types of GI cancer. The primary cancer site itself was not statistically significant for weight change ( $F = 1.01$ ,  $P = 0.207$ ), but the primary cancer site by days interaction was ( $F = 6.71$ ,  $P < 0.001$ ). Compared with patients with colorectal cancer, patients with gastric cancer had the most weight loss per day [0.033 kg more per day ( $t = -4.74$ ,  $P < 0.001$ )], followed by patients with oesophageal cancer [0.026 kg more per day ( $t = -3.68$ ,  $P < 0.001$ )], patients with pancreatic cancer [0.017 kg more per day ( $t = -3.22$ ,  $P < 0.001$ )], and patients with hepatobiliary cancer [0.010 kg more per day ( $t = -2.24$ ,

**Figure 1** Sample selection flowchart. BMI, body mass index; GI, gastrointestinal.

$P = 0.013$ ) (Figure 4A). There was also statistical significance in both intercept ( $F = 3881.95$ ,  $P < 0.001$ ) and days ( $F = 65.36$ ,  $P < 0.001$ ) in this LMM.

The patterns of weight loss over time differed among three BMI groups (Figure 4B–D). The normal (Figure 4C) and high (Figure 4D) BMI groups indicated significant differences in weight loss patterns over time according to primary cancer site ( $F = 5.20$ ,  $P < 0.001$ ;  $F = 3.39$ ,  $P = 0.006$ , respectively), but no significant differences in weight loss patterns over time were noted in the low BMI group according to this variable ( $F = 0.49$ ,  $P = 0.781$ ) (Figure 4B). In the normal BMI group, the most weight loss per day was observed among patients

with oesophageal cancer [0.020 kg more per day ( $t = -3.47$ ,  $P = 0.001$ )], followed by patients with gastric cancer [0.017 kg more per day ( $t = -2.92$ ,  $P = 0.002$ )] and patients with pancreatic cancer [0.013 kg more per day ( $t = -2.90$ ,  $P = 0.002$ )] (Figure 4C) compared with weight loss in patients with colorectal cancer. Conversely, in the high BMI group, the most weight loss per day was observed in patients with gastric cancer [0.035 kg more per day ( $t = -3.73$ ,  $P < 0.001$ )], followed by patients with oesophageal cancer [0.018 kg more per day ( $t = -2.10$ ,  $P = 0.019$ )] and patients with hepatobiliary cancer [0.010 kg more per day ( $t = -1.75$ ,  $P = 0.041$ )] (Figure 4D).

**Table 1** Baseline demographic characteristics

Variables	Total # of patients (N = 801) Number (%)	Patients with BMI data (N <sub>1</sub> = 793) <sup>a</sup>		
		BMI groups		
		Low BMI (BMI < 20) Number (%)	Normal BMI (20 ≤ BMI < 25) Number (%)	High BMI (BMI ≥ 25) Number (%)
BMI	801 (100)	62 (7.8)	239 (30.1)	492 (62.0)
Gender				
Female	335 (41.8)	39 (62.9)	96 (40.2)	196 (39.8)
Male	466 (58.2)	23 (37.1)	143 (59.8)	296 (60.2)
Ethnicity				
Blacks	112 (14.0)	10 (16.1)	26 (10.9)	76 (15.4)
Whites	689 (86.0)	52 (83.9)	213 (89.1)	416 (84.6)
Age (years)				
<65	318 (39.7)	33 (53.2)	96 (40.2)	187 (38.0)
≥65	483 (60.3)	29 (46.8)	143 (59.8)	305 (62.0)
Cancer stages				
Stage 0	7 (0.9)	1 (1.6)	2 (0.8)	4 (0.8)
Stage I	153 (19.1)	3 (4.8)	36 (15.1)	114 (23.2)
Stage II	151 (18.9)	9 (14.5)	41 (17.2)	99 (20.1)
Stage III	101 (12.6)	11 (17.7)	42 (17.6)	47 (9.6)
Stage IV	145 (18.1)	21 (33.9)	44 (18.4)	79 (16.1)
Unknown	236 (29.5)	16 (25.8)	71 (29.7)	145 (29.5)
Missing stages	8 (1.0)	1 (1.6)	3 (1.3)	4 (0.8)
Primary cancer site				
Upper GI cancer	<b>542 (67.7)</b>	<b>41 (66.1)</b>	<b>165 (69.0)</b>	<b>330 (67.1)</b>
Oesophageal Ca	72 (9.0)	4 (6.5)	24 (10.0)	43 (8.7)
Gastric Ca	73 (9.1)	10 (16.1)	23 (9.6)	40 (8.1)
Pancreatic Ca	173 (21.6)	19 (30.6)	56 (23.4)	95 (19.3)
Hepatobiliary Ca	224 (28.0)	8 (12.9)	62 (25.9)	152 (30.9)
Lower GI cancer	<b>259 (32.3)</b>	<b>21 (33.9)</b>	<b>74 (31.0)</b>	<b>162 (32.9)</b>
Colorectal Ca	249 (31.1)	20 (32.3)	71 (29.7)	156 (31.7)
Small intestinal Ca	10 (1.2)	1 (1.6)	3 (1.3)	6 (1.2)
Expired at last time point				
Yes	220 (27.5)	22 (35.5)	71 (29.7)	123 (25.0)
No	581 (72.5)	40 (64.5)	168 (70.3)	369 (75.0)

BMI, body mass index; GI, gastrointestinal.

<sup>a</sup>N<sub>1</sub>—patients with BMI data.

### Model of weight loss according to primary cancer site and patient characteristics

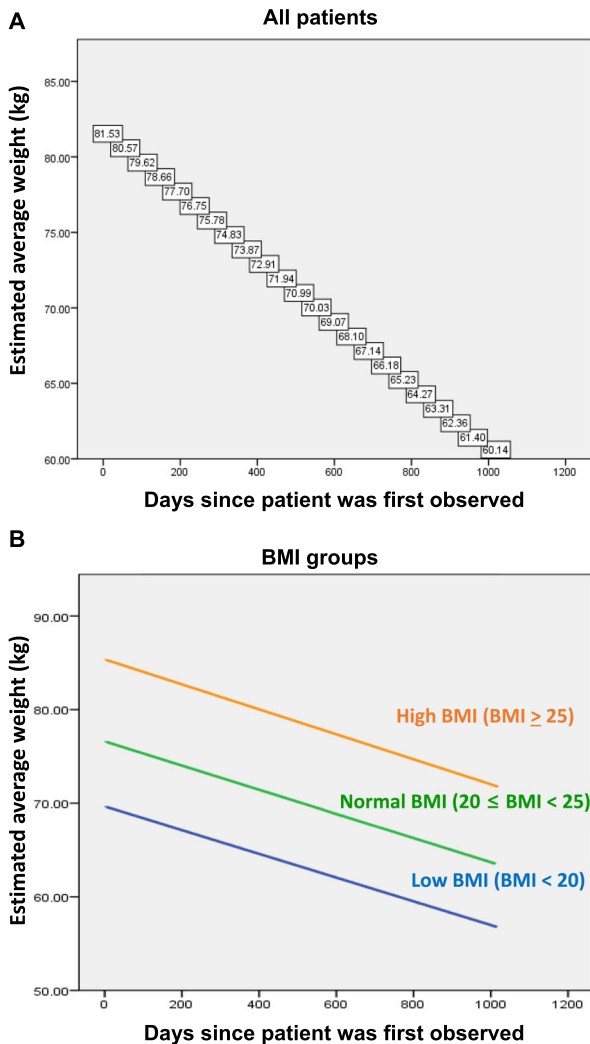
There were significant differences in weight based on gender ( $F = 64.93$ ,  $P < 0.001$ ) and cancer stage at baseline ( $F = 7.28$ ,  $P < 0.001$ ) as we expected with this population. The gender difference remained consistent throughout the observation period ( $t = -8.06$ ,  $P < 0.001$ ). Interaction between primary cancer sites and days ( $F = 8.24$ ,  $P < 0.001$ ) was statistically significant in the final mixed model to predict body weight change. In this final model, patients with gastric cancer [0.033 kg more per day ( $t = -5.11$ ,  $P < 0.001$ )] showed the largest additional weight loss per day, followed by patients with oesophageal cancer [0.027 kg more per day ( $t = -4.18$ ,  $P < 0.001$ )], patients with pancreatic cancer [0.018 kg more per day ( $t = -3.58$ ,  $P < 0.001$ )], and patients with hepatobiliary cancer [0.008 kg more per day ( $t = -1.90$ ,  $P = 0.029$ )] compared with patients with colorectal cancer. The body weight of patients in cancer stage II ( $t = -3.21$ ,  $P = 0.001$ ), cancer stage III ( $t = -5.23$ ,  $P < 0.001$ ), cancer stage IV ( $t = -4.81$ ,  $P < 0.001$ ), and cancer stage unknown

( $t = -2.90$ ,  $P = 0.002$ ) was lower than the body weight of patients in cancer stage I.

Significant predictors of weight loss were different in each of the three BMI groups (Table 2). Among the baseline characteristics, gender was a significant predictor of weight loss in all three BMI groups, but the remaining variables differed in statistical significance according to each BMI group. For the low BMI group, only age by days interaction was a significant predictor of weight loss ( $F = 3.45$ ,  $P = 0.034$ ).

Patients aged 65 years or older lost 0.007 kg/day more than those younger than 65 years ( $t = -1.857$ ,  $P = 0.034$ ). In the normal BMI ( $F = 5.541$ ,  $P < 0.001$ ) and high BMI ( $F = 3.208$ ,  $P = 0.004$ ) groups, the primary cancer site by days interaction was a significant predictor of weight loss, but this variable was not a significant predictor of weight loss in the low BMI group. For the normal BMI group, the most weight loss per day was observed in patients with oesophageal cancer [0.017 kg more per day ( $t = -3.54$ ,  $P = 0.001$ )], followed by patients with gastric cancer [0.016 kg more per day ( $t = -3.25$ ,  $P = 0.001$ )] and patients with pancreatic cancer [0.010 kg more per

**Figure 2** (A) Model-based estimated marginal mean of weight over time for all patients. (B) Model-based estimated marginal mean of weight over time for the three body mass index (BMI) groups.



day ( $t = -2.53$ ,  $P = 0.007$ ) compared with weight loss in patients with colorectal cancer.

For the high BMI group, the most weight loss per day was observed in patients with gastric cancer [0.029 kg more per day ( $t = -3.40$ ,  $P = 0.001$ )], followed by patients with oesophageal cancer [0.020 kg more per day ( $t = -2.56$ ,  $P = 0.006$ )] compared with weight loss in patients with colorectal cancer. Notably, in the high BMI group, the interaction between ethnicity, days, and cancer stage was significant predictors ( $F = 7.38$ ,  $P = 0.004$ ) of weight loss. The body weight of Whites showed more weight loss per day [0.014 kg more per day ( $t = -2.72$ ,  $P = 0.004$ )] compared with that of Blacks. Over the observation period, there was significant loss of body weight among patients with stage II [6.23 kg lower ( $t = -2.93$ ,  $P = 0.002$ )], stage III [6.72 kg lower ( $t = -2.59$ ,  $P = 0.005$ )], and stage IV [6.14 kg lower ( $t = -2.70$ ,

$P = 0.004$ )] cancer compared with that of patients with stage I cancer (Table 2).

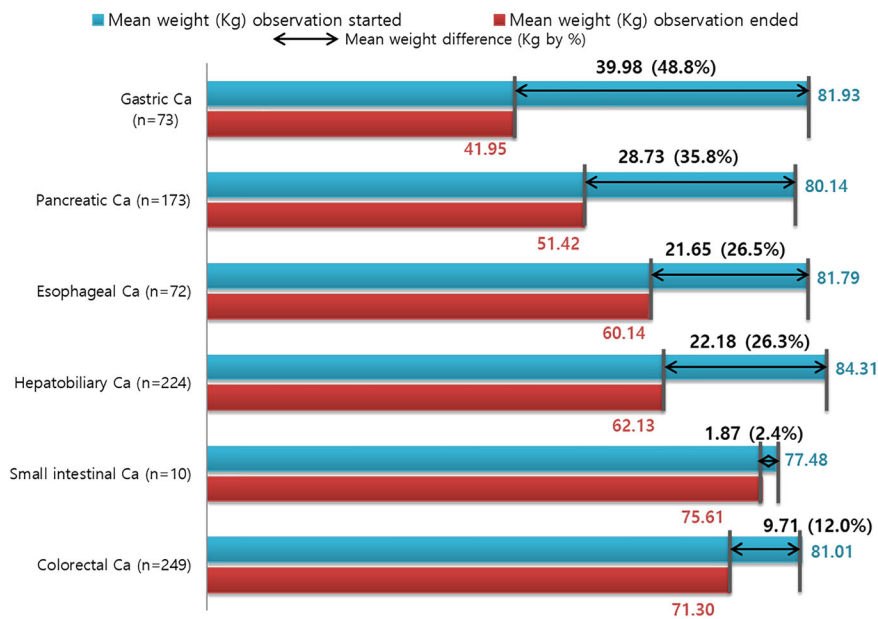
## Discussion

In this study of natural weight loss patterns among patients with GI cancers, unintentional weight loss, or cachexia, was significant. Cancer cachexia varies, based on cancer type,<sup>17,18</sup> site, and stage<sup>17</sup>; however, it is prevalent in patients with either localized or advanced cancers.<sup>18</sup> In our cohort, weight loss was significantly impacted by days of observation (from the first entry), female gender, cancer stage, and primary cancer site. Ethnicity, age, age by days, and primary cancer site, itself, did not significantly predict weight loss. Female patients had consistently significantly lower weight than male patients, and male patients asked more frequently for information about weight loss and nutrition than did their female counterparts.<sup>18</sup> Results also indicated that patients were similar in weights regardless of primary cancer site at the beginning of the observation period; however, the amount of weight loss gradually differed among cancer patients according to interaction between primary cancer sites and days.

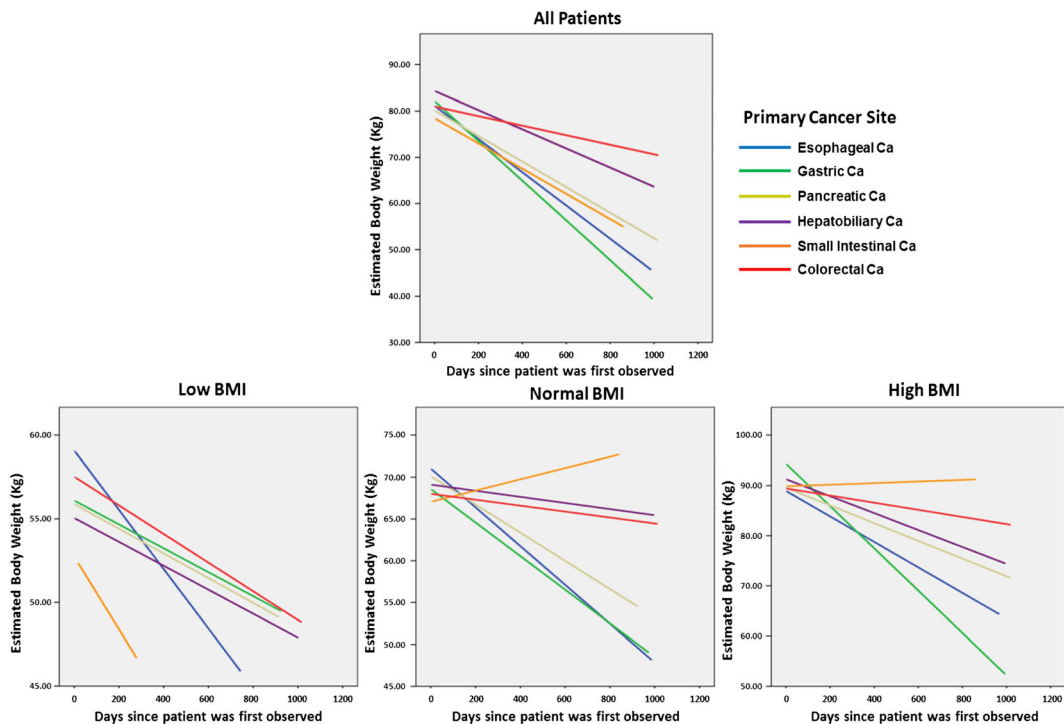
This finding indicates two critical observations. First, over time, cancer sites contribute different metabolic effects to the host,<sup>19</sup> such as hypermetabolism in pancreatic cancer,<sup>20</sup> symptoms (e.g. pain) related neuroendocrine stress response, and various side effects from different treatment protocols, causing a decrease in food intake and fat atrophy.<sup>19</sup> Second, patients lose weight steadily over time, which underscores the importance of weight preservation for overall survival. In patients with colorectal cancer, significantly lower survival was associated with long-term weight loss, weight loss greater than 5%, low BMI, and BMI category change.<sup>21</sup> Studies suggest that more awareness of cachexia,<sup>18</sup> early intervention during pre-cachexia status,<sup>1</sup> and weight stabilization<sup>22</sup> through nutritional intervention<sup>23</sup> are needed to increase survivorship and improve patients' QoL.

About 70% of the population in the USA is estimated to be overweight or obese.<sup>24</sup> Our study population was similar to the US population. At the beginning of the observation, 62% of 801 patients were in the high BMI group with a mean BMI of 27.4 kg/m<sup>2</sup>. The average estimated weight loss was greater than 21 kg (approximately 26%) over a 3 year period. Considering that weight loss over 15% is indicative of high risk of impaired physical function and 30% of weight loss can predict imminent death,<sup>2</sup> all patients with upper GI cancer are expected to experience seriously impaired physical function and poor QoL in the future. Our study also revealed that patients with upper GI cancer experience more severe weight loss compared with those with cancer of the lower GI and patients with gastric and pancreatic cancers had the highest

**Figure 3** Estimated body weight change during observation period.



**Figure 4** Model-based estimated marginal mean of weight according to various gastrointestinal cancers for (A) all patients, (B) low body mass index (BMI) patients, (C) normal BMI patients, and (D) high BMI patients.



percentage of weight loss (48.8% and 35.8%, respectively), which was indicative of shortened survival.<sup>3</sup>

In general, weight loss rates were similar among the three BMI groups, but weight loss patterns were different, based on primary cancer type as a function of days within each

group. Patients in the low BMI group had a steeper weight loss trajectory regardless of the type of the GI cancer. In comparison, patients with upper GI cancers in the normal and high BMI groups showed a similar pattern of weight loss to that of patients in the low BMI group, while patients with

**Table 2** Fixed effects estimated from a mixed model predicting weight loss of gastrointestinal cancer patients with patient baseline characteristics as fixed covariates and days as a fixed and random effect for the three body mass index groups

	Low BMI		Normal BMI		High BMI	
	Estimate	t (P-value)	Estimate	t (P-value)	Estimate	t (P-value)
Intercept	60.46	81.49 (<0.001)	73.23	149.15 (<0.001)	98.89	63.48 (<0.001)
Days	-1.02E-2	-4.50 (<0.001)	-3.94E-3	-1.75 (0.041)	-1.01E-2	-3.18 (0.001)
Gender						
Female	-8.78	-8.51 (<0.001)	-11.07	-15.17 (<0.001)	-11.42	-7.93 (<0.001)
Male <sup>a</sup>	—	—	—	—	—	—
Age * Days	—	—	—	—	—	—
<65 * Days <sup>a</sup>	—	—	—	—	—	—
≥65 * Days	-6.70E-3	-1.86 (0.034)	-1.71E-2	-3.54 (0.001)	-1.43E-2	-2.72 (0.004)
Upper GI Ca	—	—	-1.57E-2	-3.25 (0.001)	—	—
Oesophageal Ca * Days	—	—	-1.01E-2	-2.53 (0.007)	—	—
Gastric Ca * Days	—	—	0.12E-2	0.36 (0.360)	—	—
Pancreatic Ca * Days	—	—	0.45E-2	0.36 (0.361)	6.04	0.72 (0.235)
Hepatobiliary Ca * Days	—	—	—	—	—	—
Lower GI Ca	—	—	—	—	-6.23	-2.93 (0.002)
Small intestinal Ca * Days	—	—	—	—	-6.72	-2.59 (0.005)
Colorectal Ca * Days	—	—	—	—	-6.14	-2.70 (0.004)
Primary cancer site * Days	—	—	—	—	-2.58	-1.37 (0.085)
Upper GI Ca	—	—	—	—	-1.98E-2	-2.56 (0.006)
Oesophageal Ca * Days	—	—	—	—	-2.90E-2	-3.40 (0.001)
Gastric Ca * Days	—	—	—	—	-0.72E-2	-1.14 (0.127)
Pancreatic Ca * Days	—	—	—	—	-0.79E-2	-1.60 (0.055)
Hepatobiliary Ca * Days	—	—	—	—	-0.74E-2	-0.24 (0.404)
Lower GI Ca	—	—	—	—	—	—
Small intestinal Ca * Days	—	—	—	—	—	—
Colorectal Ca * Days <sup>a</sup>	—	—	—	—	—	—

BMI, body mass index; GI, gastrointestinal.  
<sup>a</sup>Reference.



colorectal cancer had a slower rate of weight loss over time if they were in the normal or high BMI groups than if they were in the low BMI group. Our results indicate that if patients with colorectal cancer have a normal or high BMI at time of diagnosis, their weights may be much more stable compared with weights of patients with gastric, oesophageal, and pancreatic cancers.

This study has some limitations. Missing values of certain variables excluded some patients from analysis. Other potentially relevant variables for weight loss were not considered (e.g. depression, fatigue, or insomnia). Data were from a large single institution in one geographical location, so results may not be generalized to broader settings. Cancer treatment strategies were not included in the analyses. Various cancer treatments impact weight changes over time. Weight fluctuates throughout the course of treatment<sup>25</sup> and type of cancer.<sup>16</sup> Some cancers induce more cachexia than others, and some GI cancers induce more digestive distress than others.<sup>7</sup> This is also true for antineoplastic therapies. Cytotoxic therapies (which the vast majority of patients would have received) have varying levels of anorexia and nausea, whereas targeted therapies have much less. These latter treatments would have only been relevant for a subset of patients with colorectal or gastroesophageal cancers. These potentially confounding variables should be accounted for in prospective studies that result from the hypotheses introduced with this data set. Despite these limitations, this study demonstrates the natural patterns of longitudinal weight changes according to BMI subgroups in patients with a variety of GI cancers, which models the real-world experience. Together, this introduces a novel analysis plan that considers rates of obesity in cancer patients that is worthy of further investigation.

## Conclusions

Unintentional weight loss is a major problem for patients with GI cancers because it affects treatment, survival outcomes,

and QoL. Patients with low BMI and upper GI cancers should receive special attention for weight management interventions, because this population demonstrated the highest death rate among all three BMI groups compared with other cancer types. Future studies should be a priority for examining mechanisms of unintentional weight loss in this population, including all influencing variables, to advance development of interventions that target specific BMI groups and types of cancer.

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The authors certify that they comply with the ethical guidelines for publishing in the Journal of Cachexia, Sarcopenia and Muscle: update 2017.<sup>26</sup>

## Author contributions

S.L.Y. and T.J.G. contributed to the conceptualization and data curation. S.L.Y. and J.A.K. formalized the analysis. S.L.Y., D.L.K., D.E.L., T.J.G., and J.A.K. contributed to the methodology, validation, writing of the original draft, review, and editing.

## Conflict of interest

None declared.

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## APPENDIX

**Table A1** Variables included as between-subjects fixed effects in the final linear mixed model of weight loss according to primary cancer site and patient characteristics

Variables	All patients (N = 801)	BMI groups (N <sub>1</sub> = 793) <sup>a</sup>		
		Low BMI (BMI < 20)	Normal BMI (20 ≤ BMI < 25)	High BMI (BMI ≥ 25)
Days	S	S	S	S
Gender	S	S	S	S
Gender * Days	NS	NS	NS	NS
Ethnicity	NS	NS	NS	NS
Ethnicity * Days	NS	NS	NS	S
Age	NS	NS	NS	NS
Age * Days	NS	S	NS	NS
Cancer stage	S	NS	NS	S
Cancer stage * Days	NS	NS	NS	NS
Primary cancer sites	NS	NS	NS	NS
Primary cancer sites * Days	S	NS	S	S

BMI, body mass index; NS, not statistically significant; S, statistically significant.

<sup>a</sup>N<sub>1</sub>—patients with available BMI data.