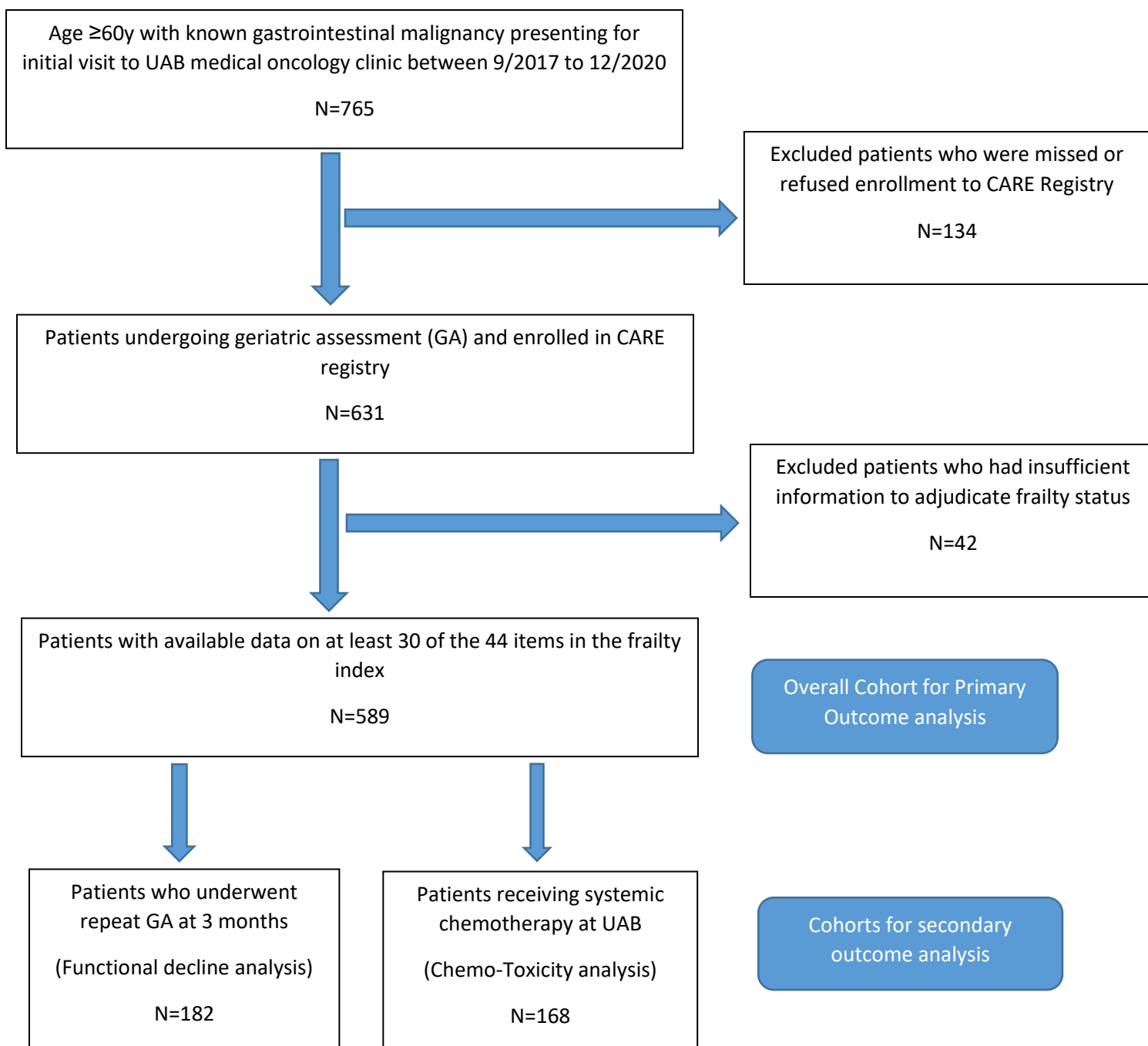


**A Novel Patient-Reported Geriatric Assessment-based Frailty Index among Older Adults with  
Gastrointestinal Malignancies**

**SUPPLEMENTARY FILES**

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**Figure S1:** Flow Chart showing the process of study cohort selection. Of 765 patients presenting to UAB GI Oncology clinic for initial visit, 631 (83%) underwent geriatric assessment and were enrolled in CARE registry. After excluding 42 patients with insufficient information for frailty index computation, 589 patients were included in the final analysis. Among these patients, 182 underwent a second geriatric assessment at 3-month time point whereas 168 received systemic chemotherapy at UAB.

**Table S1: Comparison of baseline demographic and clinical characteristics between participants who underwent GA assessment versus those who did not.**

<b>Variable</b>	<b>Non-Participants</b>	<b>Participants</b>	<b>P value</b>
<b>N</b>	134	631	
<b>Age, median (IQR) y</b>	67 (64-75)	69 (64-74)	.37
<b>Age category</b> - 60-65y - 66-70y - >70y	43 (32.8%) 40 (30.5%) 48 (36.6%)	193 (30.8%) 151 (24.1%) 283 (45.1%)	.16
<b>Sex</b> - Female - Male	64 (47.8%) 70 (52.2%)	284 (45.0%) 347 (55.0%)	.56
<b>Race</b> - Non Hispanic White - Others <sup>a</sup>	86 (70.5%) 36 (29.5%)	450 (72.5%) 171 (27.5%)	.66
<b>Cancer Type</b> - Colorectal - Pancreatic - Other GI Cancers <sup>b</sup>	33 (24.6%) 43 (32.1%) 58 (43.3%)	189 (30.0%) 166 (26.3%) 276 (43.7%)	.30
<b>Cancer Stage</b> - Stage I-II - Stage III-IV	25 (19.4%) 105 (80.6%)	166 (26.4%) 462 (73.6%)	.09
<b>Line of Therapy</b> - 1 <sup>st</sup> line - 2 <sup>nd</sup> line and beyond	95 (81.9%) 21 (18.1%)	518 (86.8%) 79 (13.2%)	.17

GI, gastrointestinal; CI, confidence interval

<sup>a</sup> Other race includes Black (146) and Hispanics (12).

<sup>b</sup> Other GI includes Hepatobiliary (104), Gastroesophageal (60), Anal cancer (13), Appendiceal Cancer (7), Gastrointestinal stromal tumor (17), Neuroendocrine carcinoma (51), and GI not otherwise specified (5)

**Table S2: Cox Proportional Hazards Regression Model showing the impact of Frailty Score as a continuous variable on overall survival.**

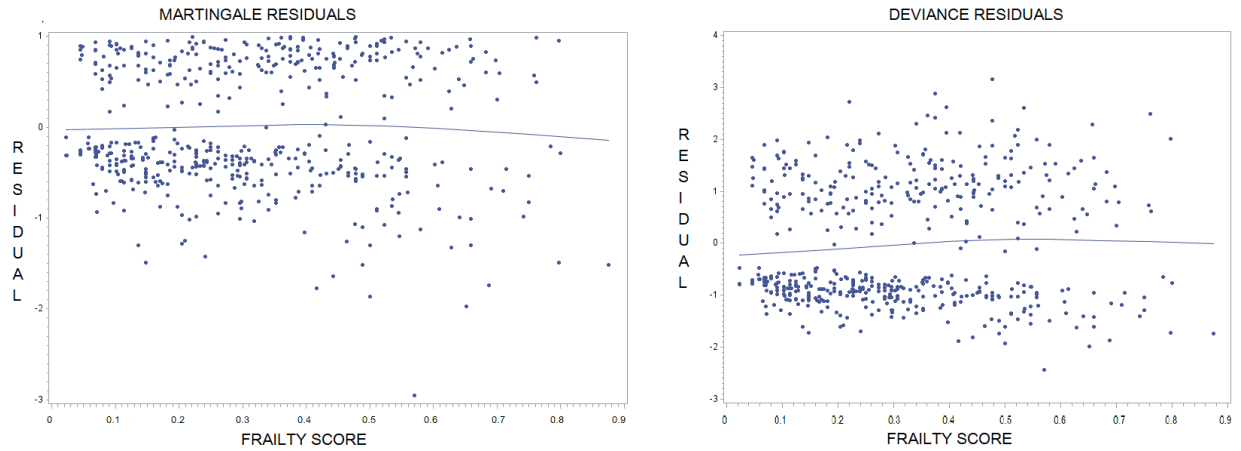
Variable	Hazards Ratio	95% CI	P value
<b>Frailty Score</b> (per 0.1 unit increase)	1.12	1.05-1.20	.001
<b>Age category</b>			
- 60-65	Ref	-	
- 66-70	0.84	0.58-1.21	.35
- >70y	1.05	0.78-1.41	.75
<b>Sex</b>			
- Female	Ref		
- Male	1.16	0.90-1.51	.26
<b>Race</b>			
- White/Caucasian	Ref	-	
- Others <sup>a</sup>	0.75	0.55-1.02	.07
<b>Cancer Stage</b>			
- Stage I/II	Ref	-	
- Stage III/IV	1.36	0.99-1.87	.06
<b>Cancer Type</b>			
- Colorectal	Ref	-	
- Pancreatic	2.05	1.45-2.88	<.001
- Other GI cancers <sup>b</sup>	1.10	0.79-1.53	.58
<b>Line of Therapy</b>			
- 1 <sup>st</sup> line	Ref		
- 2 <sup>nd</sup> line and beyond	1.37	0.96-1.96	.08

GI, gastrointestinal; CI, confidence interval

<sup>a</sup> Other race includes Black (146) and Hispanics (12).

<sup>b</sup> Other GI includes Hepatobiliary (104), Gastroesophageal (60), Anal cancer (13), Appendiceal Cancer (7), Gastrointestinal stromal tumor (17), Neuroendocrine carcinoma (51), and GI not otherwise specified (5)

**Figure S2:** Relationship between CARE-Frailty Index as a continuous variable and Martingale (left panel) and Deviance (right panel) Residuals from the multivariate Cox model in Table S5 (excluding Frailty Score). An approximately straight fitted smooth line indicates a somewhat linear relationship between CARE Frailty scores and survival, with increasing CARE-Frailty Index associated with increasing risk of all-cause mortality. Based on Cox model as shown in Table S5, each 0.1 increase in CARE-Frailty Index was associated with 12% increased risk of all-cause mortality.



**Table S3: Logistic Regression Model showing the association of baseline frailty status on grade  $\geq 3$  chemotherapy related toxicity.**

Variable	Odds Ratio	95% CI	P value
<b>Frailty Category</b> - Robust - Pre-frail - Frail	Ref 1.15 2.21	- 0.52-2.55 1.00-4.88	.73 .05
<b>Age category</b> - 60-65y - 66-70y - >70y	Ref 1.17 1.04	- 0.51-2.71 0.49-2.21	.71 .93
<b>Sex</b> - Female - Male	Ref 1.00	- 0.51-1.95	.99
<b>Race</b> - White/Caucasian - Others <sup>a</sup>	Ref 1.00	- 0.47-2.10	.99
<b>Cancer Type</b> - Colorectal - Pancreatic - Other GI Cancers <sup>b</sup>	Ref 1.93 1.25	- 0.87-4.26 0.57-2.76	.10 .58
<b>Cancer Stage</b> - Stage I-II - Stage III-IV	Ref 1.25	- 0.59-2.66	.55
<b>Line of Therapy</b> - 1 <sup>st</sup> line - 2 <sup>nd</sup> line and beyond	Ref 1.10	- 0.22-5.50	.91

GI, gastrointestinal; CI, confidence interval

<sup>a</sup> Other race includes Black (146) and Hispanics (12).

<sup>b</sup> Other GI includes Hepatobiliary (104), Gastroesophageal (60), Anal cancer (13), Appendiceal Cancer (7), Gastrointestinal stromal tumor (17), Neuroendocrine carcinoma (51), and GI not otherwise specified (5)

**Table S4: Logistic Regression Model showing the association of baseline frailty status on grade  $\geq 3$  Non-hematologic toxicity**

Variable	Odds Ratio	95% CI	P value
<b>Frailty Category</b> - Robust - Pre-frail - Frail	Ref 1.05 3.65	- 0.38-2.83 1.54-8.69	.92 .003
<b>Age category</b> - 60-65y - 66-70y - >70y	Ref 0.88 1.14	- 0.33-2.37 0.49-2.69	.81 .76
<b>Sex</b> - Female - Male	Ref 1.45	- 0.66-3.17	.36
<b>Race</b> - White/Caucasian - Others <sup>a</sup>	Ref 0.93	- 0.39-2.20	.87
<b>Cancer Type</b> - Colorectal - Pancreatic - Other GI cancers <sup>b</sup>	Ref 1.24 0.59	- 0.52-2.96 0.23-1.53	.63 .28
<b>Cancer Stage</b> - Stage I-II - Stage III-IV	Ref 2.01	- 0.81-5.00	.13
<b>Line of Therapy</b> - 1 <sup>st</sup> line - 2 <sup>nd</sup> line and beyond	Ref 2.12	- 0.41-11.06	.37

GI, gastrointestinal; CI, confidence interval

<sup>a</sup> Other race includes Black (146) and Hispanics (12).

<sup>b</sup> Other GI includes Hepatobiliary (104), Gastroesophageal (60), Anal cancer (13), Appendiceal Cancer (7), Gastrointestinal stromal tumor (17), Neuroendocrine carcinoma (51), and GI not otherwise specified (5)

**Table S5: Logistic Regression Model showing the association of baseline frailty status on grade  $\geq 3$  hematologic toxicity**

Variable	Odds Ratio	95% CI	P value
<b>Frailty Category</b>			
- Robust	Ref	-	
- Pre-frail	1.35	0.60-3.06	.47
- Frail	1.01	0.46-2.22	.97
<b>Age category</b>			
- 60-65y	Ref	-	
-66-70y	0.94	0.40-2.20	.88
- >70y	1.04	0.48-2.24	.92
<b>Sex</b>			
- Female	Ref		
- Male	0.81	0.42-1.59	.55
<b>Race</b>			
- White/Caucasian	Ref	-	
- Others <sup>a</sup>	1.10	0.52-2.32	.81
<b>Cancer Type</b>			
- Colorectal	Ref	-	
- Pancreatic	2.69	1.19-6.07	.02
- Other GI cancers <sup>b</sup>	2.81	1.22-6.48	.02
<b>Cancer Stage</b>			
- Stage I-II	Ref	-	
- Stage III-IV	0.99	0.47-2.09	.98
<b>Line of Therapy</b>			
- 1 <sup>st</sup> line	Ref		
- 2 <sup>nd</sup> line and beyond	0.47	0.08-2.73	.40

GI, gastrointestinal; CI, confidence interval

<sup>a</sup> Other race includes Black (146) and Hispanics (12).

<sup>b</sup> Other GI includes Hepatobiliary (104), Gastroesophageal (60), Anal cancer (13), Appendiceal Cancer (7), Gastrointestinal stromal tumor (17), Neuroendocrine carcinoma (51), and GI not otherwise specified (5)



## Appendix 1: Construction of CARE Frailty Index:

We constructed a frailty index (hereafter known as the CARE Frailty Index) using the deficit accumulation approach originally described by Rockwood et al<sup>12</sup>, and following the standard procedures outlined by Searle et al<sup>13</sup>. Similar methods have been used by Guerard et al<sup>14</sup> and Cohen et al<sup>15</sup> to construct frailty indices that have been shown to be predictive of chemotherapy toxicity and drug discontinuation<sup>15</sup> as well as all-cause mortality<sup>14</sup> among older adults with cancer. We selected 44 GA variables from the CARE survey, each of which captured a health deficit, and recoded responses as '0' for absence of the deficit and '1' for presence of the deficit. For variables that included a single intermediate response (e.g. 'sometimes' or 'maybe'), we used an additional value of '0.5'. We combined the 44 individual scores into an aggregate frailty score reflecting the overall proportion of deficits (range 0-1), and then categorized patients as robust (0-0.2), pre-frail (0.2-0.35) or frail (>0.35), as previously described.<sup>13</sup> In case of missing data, we required responses to at least 30 items to construct a valid frailty index. An index constructed with at least 30 variables has been previously shown to be sufficiently accurate for predicting adverse outcomes among older adults.<sup>16</sup> The 44 variables used for construction of CARE-frailty index are as below.

1. Falls  $\geq 1$ , 1 point
  2. Walk one block = limited a lot , 1 point
  3. IADL mobility (unable to/ with some help) , 1 point
  4. IADL shopping (unable to/ with some help) , 1 point
  5. IADL meal prepare ( unable to/ with some help) , 1 point
  6. IADL housework ( unable to/ with some help) , 1 point
  7. IADL medication ( unable to/ with some help) , 1 point
  8. IADL money ( unable to/ with some help) , 1 point
  9. ADL get in and out of bed ( unable to/ with some help) , 1 point
  10. ADL dress ( unable to/ with some help) , 1 point
  11. ADL bath ( unable to/ with some help) , 1 point
  12. Global health, good =0.5 point, fair/poor = 1 point
  13. Global quality of life, good =0.5 point, fair/poor = 1 point
  14. Global physical health, good =0.5 point, fair/poor = 1 point
  15. Global mental health, good =0.5 point, fair/poor = 1 point
  16. Global satisfaction with social activities and relationship, good =0.5 point, fair/poor = 1 point
  17. Global everyday activities, moderately=0.5 point, a little/not at all = 1 point
  18. Global anxious/depression, sometimes =0.5 point, often/always = 1 point
  19. Global fatigue, moderate =0.5 point, severe/very severe = 1 point
  20. Global pain, pain level 4-6 =0.5 point, pain level 7-10 = 1 point
  21. Global social activities and roles, good =0.5 point, fair/poor = 1 point
  22. Weight loss 3 months or 6 months' weight loss  $\geq 5\%$ , 1 point
  23. Food intake less than usual, 1 point
  24. Activities and function (self-rated activity)  $\geq 2$  (in bed or chair less than half the day/ able to do little activity / Pretty much bedridden) , 1 point
  25. Anxiety PROMIS T score  $>60$ , 1 point
  26. Depression PROMIS T score  $>60$ , 1 point
  27. Impaired Cognition, PROMIS T score  $<40$ , 1 point
  28. Number of daily medication  $\geq 9$ , 1 point
  29. Social activity interference, Some of the time=0.5 point, Most/ All of the time=1 point
- Comorbidities:**
30. Eyesight Fair/Poor/totally blind, 1 point
  31. Hearing fair/Poor/Totally Deaf, 1 point
  32. Other Cancers or leukemia, 1 point
  33. Arthritis or rheumatism, 1 point

34. Glaucoma, 1 point
35. Emphysema or chronic bronchitis, 1 point
36. High blood pressure, 1 point
37. Heart disease, 1 point
38. Circulation trouble in arms or legs, 1 point
39. Diabetes, 1 point
40. Stomach or intestinal disorders, 1 point
41. Osteoporosis, 1 point
42. Chronic liver or kidney disease, 1 point
43. Stroke, 1 point
44. Depression, 1 point

**Table S6: Overview of geriatric assessment measures by domain in CARE study**

<b>GA Domain</b>	<b>Patient-Reported Measures</b>
<b>FUNCTION</b>	OARS Instrumental Activities of Daily Living (IADL) OARS Activities of Daily Living (ADL) Patient-reported ECOG Performance Status No. of falls in last 6 months
<b>NUTRITION</b>	Patient-Generated Subjective Global Assessment
<b>COGNITION</b>	PROMIS Cognitive Function
<b>PSYCHOLOGICAL</b>	PROMIS Short Form v1.0 Anxiety 4a PROMIS Short Form v1.0 Depression 4a
<b>SOCIAL SUPPORT</b>	MOS Social Support Survey (Emotional/Informational Support subscales)
<b>COMORBIDITY</b>	No. of medications OARS comorbidity assessment Self-Reported Vision and Hearing Loss
<b>HRQOL</b>	PROMIS 10-item Global Health

**Abbreviations:** GA, Geriatric Assessment; OARS, Older American Resources and Services; ECOG, Eastern Cooperative Oncology Group; PROMIS, patient-reported outcomes measurement information system; MOS, medical outcomes survey; HRQOL, health-related quality of life

**Table S7:** Comparison of baseline demographic/clinical characteristics as well as frailty status between those with and without 3 month functional status assessment

<b>Variable</b>	<b>No follow up functional status assessment *</b>	<b>Underwent follow up functional status assessment</b>	<b>P value</b>
<b>N</b>	407	182	
<b>Age, median (IQR) y</b>	69 (64-74)	68 (63-74)	.26
<b>Age category</b> - 60-65y - 66-70y - >70y	115 (28.5%) 98 (24.3%) 190 (47.1%)	63 (34.6%) 42 (23.1%) 77 (42.3%)	.33
<b>Sex</b> - Female - Male	187 (45.9%) 220 (54.1%)	80 (44%) 102 (56%)	0.65
<b>Race</b> - Non Hispanic White - Others <sup>a</sup>	295 (73.4%) 107 (26.6%)	130 (71.8%) 51 (28.2%)	0.70
<b>Cancer Type</b> - Colorectal - Pancreatic - Other GI Cancers <sup>b</sup>	123 (30.2%) 106 (26.0%) 178 (43.7%)	53 (29.1%) 50 (27.5%) 79 (43.4%)	0.93
<b>Cancer Stage</b> - Stage I-II - Stage III-IV	106 (26.2%) 298 (73.8%)	49 (26.9%) 133 (73.1%)	0.86
<b>Line of Therapy</b> - 1 <sup>st</sup> line - 2 <sup>nd</sup> line and beyond	309 (82.4%) 66 (17.6%)	171 (94%) 11 (6%)	<.001
<b>Frailty Category</b> - Robust - Pre-frail - Frail	124 (30.2%) 113 (27.8%) 171 (42%)	66 (36.3%) 55 (30.2%) 61 (33.5%)	0.14