

SUPPLEMENTARY MATERIALS

Supplementary Methods

Missing Longitudinal Data

The Thinking and Living with Cancer Study is a longitudinal cohort study of older breast cancer survivors and frequency matched controls funded under two rounds of an National Cancer Institute grant (R01CA129769). Among the 708 participants included in the analytic sample, there were two real-world ways that data could be missing over the study period: 1) administrative losses, and 2) death or drop-out. We examined each of these causes of missing data to evaluate whether they could potentially be associated with changes in deficits accumulation scores or trajectories, cognition, or physical activity. We describe those analyses in the following sections.

First, the study began in 2010 under the original grant and included a protocol with 24-months of follow-up. New funding obtained in 2016 was discontinuous with the initial grant but allowed for extension of follow-up from 24 to 60 months for those still active in the study under a revised protocol. Thus, participants enrolled in the early study years completed assessments through 24-months under the original protocol and those that were not active at the time of the revised protocol were considered “administrative losses” at 36-months (n=219). These administrative losses were non-informative with respect to deficit accumulation or study outcomes (Supplementary Table 2). There was a difference in baseline sleep disturbances among the survivors that were administrative losses at 36 months vs. not, so we considered sleep as a covariate in analyses since sleep could potentially affect outcomes.

The second way that data could be missing was due to dropping out of the study or death. Study drop-out occurred among 8.6% of participants (11.6% [n=41] and 5.6% [n=20] in survivors and controls, respectively). Death rates were very low (0.7% of participants (0.8% [n=3] and 0.6% [n=2] in survivors and controls, respectively). Characteristics of those that dropped out or died compared to the remainder of the analytic sample are summarized on Supplementary Table 3.

Overall, missing data were primarily due to administrative losses unrelated to the study hypotheses. Missing data did not vary by trajectory group or study outcomes and analyses employed in the manuscript allow for random missingness and do not require participants to contribute complete data to be included.

Supplementary Tables

Supplement Table 1. Deficits Accumulation Frailty Index with Baseline Distributions for Older Breast Cancer Survivors and Controls by Trajectory Group from Separate Latent Class Models

Item	Scoring	Remain Robust		Prefrail		Become Frailer	
		Survivors (n=269)	Controls (n=297)	Survivors (n=53)	Controls (n=24)	Survivors (n=31)	Controls (n=34)
Percent							
IADL Subdomain (14 items)							
1. Can take bath/shower							
Without help	0	98.9	99.7	92.5	95.8	100.0	100.0
With some help	0.5	1.1	0.3	7.5	4.2	0.0	0.0
Completely unable	1	0.0	0.0	0.0	0.0	0.0	0.0
2. Can dress/undress self							
Without help	0	98.9	100.0	92.5	100.0	100.0	100.0
With some help	0.5	1.1	0.0	7.5	0.0	0.0	0.0
Completely unable	1	0.0	0.0	0.0	0.0	0.0	0.0
3. Can get in/out of bed							
Without help	0	100.0	100.0	94.3	100.0	100.0	100.0
With some help	0.5	0.0	0.0	5.7	0.0	0.0	0.0
Completely unable	1	0.0	0.0	0.0	0.0	0.0	0.0
4. Can walk							
Without help	0	100.0	100.0	90.6	95.8	100.0	100.0
With some help	0.5	0.0	0.0	9.4	0.0	0.0	0.0
Completely unable	1	0.0	0.0	0.0	4.2	0.0	0.0
5. Can eat							
Without help	0	100.0	100.0	100.0	100.0	100.0	100.0
With some help	0.5	0.0	0.0	0.0	0.0	0.0	0.0
Completely unable	1	0.0	0.0	0.0	0.0	0.0	0.0
6. Take care of own appearance							
Without help	0	99.6	100.0	96.2	100.0	100.0	100.0
With some help	0.5	0.4	0.0	3.8	0.0	0.0	0.0
Completely unable	1	0.0	0.0	0.0	0.0	0.0	0.0
7. Trouble getting to bathroom on time							
No	0	96.3	92.6	69.2	45.8	87.1	79.4
Yes or catheter	1	3.7	7.4	30.8	54.2	12.9	20.6
8. Can go shopping for groceries or clothes							
Without help	0	97.4	100.0	83.0	87.5	100.0	100.0
With some help	0.5	2.6	0.0	17.0	12.5	0.0	0.0
Completely unable	1	0.0	0.0	0.0	0.0	0.0	0.0
9. Can do your housework							
Without help	0	85.5	91.2	43.4	60.9	80.6	87.9
With some help	0.5	14.1	8.4	50.9	34.8	16.1	12.1
Completely unable	1	0.4	0.3	5.7	4.3	3.2	0.0
10. Can prepare own meals							
Without help	0	98.5	100.0	84.9	91.7	100.0	100.0
With some help	0.5	1.5	0.0	15.1	8.3	0.0	0.0
Completely unable	1	0.0	0.0	0.0	0.0	0.0	0.0

Item	Scoring	Remain Robust		Prefrail		Become Frailer	
		Survivors (n=269)	Controls (n=297)	Survivors (n=53)	Controls (n=24)	Survivors (n=31)	Controls (n=34)
11. Can take own medicine							
Without help	0	99.6	100.0	96.2	100.0	100.0	100.0
With some help	0.5	0.4	0.0	3.8	0.0	0.0	0.0
Completely unable	1	0.0	0.0	0.0	0.0	0.0	0.0
12. Can handle own money							
Without help	0	100.0	100.0	100.0	100.0	100.0	100.0
With some help	0.5	0.0	0.0	0.0	0.0	0.0	0.0
Completely unable	1	0.0	0.0	0.0	0.0	0.0	0.0
13. Can use telephone							
Without help	0	100.0	100.0	100.0	100.0	100.0	100.0
With some help	0.5	0.0	0.0	0.0	0.0	0.0	0.0
Completely unable	1	0.0	0.0	0.0	0.0	0.0	0.0
14. Get to places out of walking distance							
Without help	0	98.9	99.7	88.7	83.3	100.0	94.1
With some help	0.5	1.1	0.3	11.3	16.7	0.0	5.9
Completely unable	1	0.0	0.0	0.0	0.0	0.0	0.0
Physical Health Subdomain (5 items)							
15. Health limited moderate activities (SF-12)							
No, not limited at all	0	88.1	89.2	45.3	37.5	80.6	55.9
Yes, limited a little	0.5	10.0	9.1	32.1	45.8	19.4	29.4
Yes, limited a lot	1	1.9	1.7	22.6	16.7	0.0	14.7
16. Health limited climbing stairs (SF-12)							
No, not limited at all	0	84.0	82.7	30.8	20.8	58.1	38.2
Yes, limited a little	0.5	13.0	14.6	36.5	41.7	41.9	38.2
Yes, limited a lot	1	3.0	2.7	32.7	37.5	0.0	23.5
17. Physical health limited work or activities (SF-12)							
No, not limited at all	0	84.3	86.4	26.9	33.3	74.2	44.1
Yes, limited a little	0.5	13.5	12.5	51.9	54.2	25.8	47.1
Yes, limited a lot	1	2.2	1.0	21.2	12.5	0.0	8.8
18. Physical health resulted in accomplishing less (SF-12)							
No, not limited at all	0	83.3	83.4	11.3	20.8	51.6	47.1
Yes, limited a little	0.5	16.0	15.2	62.3	62.5	48.4	44.1
Yes, limited a lot	1	0.7	1.4	26.4	16.7	0.0	8.8
19. Timed Up and Go in seconds							
Age 60-69: ≤8.1 sec							
70-<80: ≤9.2 sec,	0	6.3	10.8	3.8	0.0	0.0	5.9
80+: ≤11.3 sec							
Age 60-69: >8.1 sec							
70 to <80: >9.2 sec	1	91.4	88.6	75.5	91.7	93.5	85.3
80+: >11.3 sec							
Unable to get up	1	2.2	0.7	20.8	8.3	6.5	8.8

Item	Scoring	Remain Robust		Prefrail		Become Frailer	
		Survivors (n=269)	Controls (n=297)	Survivors (n=53)	Controls (n=24)	Survivors (n=31)	Controls (n=34)
Emotional Health Subdomain (4 Items)							
20. Emotional problems limited work or activities (SF-12)							
No, not limited at all	0	97.0	94.9	74.0	70.8	87.1	82.4
Yes, limited a little	0.5	3.0	4.7	22.0	16.7	9.7	17.6
Yes, limited a lot	1	0.0	0.3	4.0	12.5	3.2	0.0
21. Emotional problems resulted in accomplishing less (SF-12)							
No, not limited at all	0	94.8	92.3	64.2	66.7	87.1	76.5
Yes, limited a little	0.5	4.5	6.7	30.2	20.8	12.9	23.5
Yes, limited a lot	1	0.7	1.0	5.7	12.5	0.0	0.0
22. Felt downhearted or blue (SF-12)							
None of the time	0	70.3	61.4	55.8	33.3	51.6	38.2
A little of the time	0.25	25.2	27.8	21.2	25.0	35.5	50.0
Some of the time	0.5	3.0	9.2	15.4	29.2	12.9	8.8
Good bit of the time	0.75	0.0	0.7	3.8	8.3	0.0	2.9
Most of the time	1	1.5	1.0	3.8	4.2	0.0	0.0
All of the time	1	0.0	0.0	0.0	0.0	0.0	0.0
23. Felt calm or peaceful (SF-12)							
All of the time	0	19.9	19.3	11.5	4.2	6.5	2.9
Most of the time	0	62.9	56.9	40.4	25.0	54.8	44.1
Good bit of the time	0.25	9.4	12.5	15.4	37.5	16.1	20.6
Some of the time	0.5	5.2	6.8	19.2	20.8	19.4	29.4
A little of the time	0.75	1.1	3.4	11.5	8.3	3.2	2.9
None of the time	1	1.5	1.0	1.9	4.2	0.0	0.0
General Health Subdomain (1 item)							
24. General Health (SF-12)							
Excellent	0	43.1	40.5	1.9	8.3	6.5	0.0
Very Good	0.25	42.8	38.9	35.8	37.5	38.7	41.2
Good	0.5	12.6	19.3	45.3	33.3	45.2	47.1
Fair	0.75	1.5	1.4	17.0	16.7	9.7	11.8
Poor	1	0.0	0.0	0.0	4.2	0.0	0.0
Social Function Subdomain (2 items)							
25. Physical or emotional health interfered with social activities (SF-12)							
None of the time	0	91.8	84.7	47.1	54.2	87.1	61.8
A little of the time	0.25	6.3	8.8	33.3	20.8	9.7	29.4
Some of the time	0.5	1.5	4.4	11.8	12.5	3.2	5.9
Good bit of the time	0.5	0.0	0.7	3.9	4.2	0.0	2.9
Most of the time	1	0.4	1.0	3.9	4.2	0.0	0.0
All of the time	1	0.0	0.3	0.0	4.2	0.0	0.0
26. Marital status							
Married	0	64.7	52.9	39.6	16.7	64.5	38.2
Non-married	1	35.3	47.1	60.4	83.3	35.5	61.8

Item	Scoring	Remain Robust		Prefrail		Become Frailer	
		Survivors (n=269)	Controls (n=297)	Survivors (n=53)	Controls (n=24)	Survivors (n=31)	Controls (n=34)
Fatigue Subdomain (2 items)							
27. Had a lot of energy (SF-12)							
All of the time	0	26.9	22.0	2.0	8.3	9.7	2.9
Most of the time	0	53.7	53.7	35.3	12.5	35.5	47.1
Good bit of the time	0.25	10.8	11.8	17.6	8.3	19.4	11.8
Some of the time	0.5	6.3	10.1	29.4	58.3	25.8	23.5
A little of the time	0.75	1.5	1.4	9.8	4.2	9.7	14.7
None of the time	1	0.7	1.0	5.9	8.3	0.0	0.0
28. FACIT-F Fatigue Subscale ^a							
None	0	11.2	18.5	0.0	12.5	3.2	2.9
39-<52: Little	0.25	75.0	77.8	52.8	54.2	64.5	67.6
26-<39: Somewhat	0.5	10.8	3.4	34.0	29.2	22.6	20.6
13-<26: Quite a bit	0.75	2.2	0.3	9.4	4.2	6.5	8.8
0 to <13: Severe	1	0.7	0.0	3.8	0.0	3.2	0.0
Disease Subdomain (10 items)							
29. Heart Disease (angina, arrhythmia, congestive heart failure, heart attack)							
None	0	87.7	86.9	64.2	62.5	80.6	97.0
Any	1	12.3	13.1	35.8	37.5	19.4	3.0
30. Diabetes							
None	0	94.8	94.9	62.3	91.7	86.7	78.1
Any	1	5.2	5.1	37.7	8.3	13.3	21.9
31. Arthritis, Rheumatism, or other connective tissue disorder							
None	0	61.6	58.6	18.9	16.7	38.7	21.9
Any	1	38.4	41.4	81.1	83.3	61.3	78.1
32. Emphysema, chronic bronchitis, asthma, chronic Obstructive Pulmonary Disease							
None	0	88.5	88.6	64.2	79.2	71.0	84.4
Any	1	11.5	11.4	35.8	20.8	29.0	15.6
33. Chronic Liver or Kidney Disease							
None	0	97.8	98.3	96.2	91.7	90.3	90.6
Any	1	2.2	1.7	3.8	8.3	9.7	9.4
34. Other Cancer (non-melanoma skin cancer, other cancer)							
None	0	97.8	99.3	100.0	100.0	93.5	100.0
Any	1	2.2	0.7	0.0	0.0	6.5	0.0
35. Glaucoma, Cataracts, or decreased vision							
None	0	84.8	80.1	56.6	66.7	74.2	81.3
Any	1	15.2	19.9	43.4	33.3	25.8	18.8
36. Hypertension							
None	0	59.1	67.9	35.8	29.2	35.5	45.5
Any	1	40.9	32.1	64.2	70.8	64.5	54.5
37. Osteoporosis							
None	0	83.5	79.7	71.2	56.5	90.3	80.6
Any	1	16.5	20.3	28.8	43.5	9.7	19.4
38. Thyroid disease (hyperthyroidism, hypothyroidism)							
None	0	80.3	82.8	66.0	66.7	74.2	78.1
Any	1	19.7	17.2	34.0	33.3	25.8	21.9

Item	Scoring	Remain Robust		Prefrail		Become Frailer	
		Survivors (n=269)	Controls (n=297)	Survivors (n=53)	Controls (n=24)	Survivors (n=31)	Controls (n=34)
Weight Subdomain (1 item)							
39. BMI							
18.5 to <30: Normal/overweight	0	74.3	77.8	35.3	47.8	44.4	50.0
>=30: Obese	1	24.9	21.1	62.7	52.2	55.6	47.1
<18.5: Under-weight	1	0.8	1.1	2.0	0.0	0.0	2.9
Poly-pharm Subdomain (1 item)							
40. Polypharmacy							
<5 prescriptions	0	78.8	80.5	9.4	33.3	51.6	61.8
>=5 prescriptions	1	21.2	19.5	90.6	66.7	48.4	38.2
Depression Subdomain (1 item)							
41. Depression -CES-D ^b							
0 to <16: No to mild depression	0	90.6	97.3	71.4	75.0	85.7	85.3
16 to <24: Moderate depression	0.5	6.0	2.4	10.2	16.7	7.1	8.8
24 to <60: Severe depression	1	3.4	0.3	18.4	8.3	7.1	5.9
Anxiety Subdomain (1 item)							
42. STAI A-State scale ^c							
20 to <38: No or low anxiety	0	89.6	94.6	77.4	82.6	83.3	93.8
38 to <45: Moderate anxiety	0.5	6.3	5.1	11.3	4.3	6.7	0.0
45 to 80: Severe anxiety	1	4.1	0.3	11.3	13.0	10.0	6.3

a. Fatigue includes 13 items scored from 0-4 each for a total of 0-52 (higher=less fatigue). Non-missing items are averaged and then multiplied by 13 to calculate the total score. Must have 50%+ or 7+ items to score. Total score is used to assign frailty item score.

b. Depression is based on 20 items scaled from 0-3 each for a total of 0-60 (higher=more depression, 16+ is clinically significant). Non-missing items are averaged and then multiplied by 20 to calculate the total score. Must have 95%+ or 19+ items to score. Total score is used to assign frailty item score.

c. Anxiety is based on 20 items scaled from 1-4 each for a total of 20-80 (higher=more anxiety, 38+ is recommended cutoff). Non-missing items are averaged and then multiplied by 20 to calculate the total score. Must have 90%+ or 18+ items to score. Total score is used to assign frailty item score.

Supplementary Table 2. Characteristics of Participants by Administrative Loss at 36-months						
	Controls			Survivors		
	Administrative loss			Administrative loss		
	Yes (n=112)	No (n=243)	P value	Yes (n=107)	No (n=246)	P value
	Mean (SD) or % (n)			Mean (SD) or % (n)		
Age	68.7 (7.6)	67.6 (6.8)	0.18	68.0 (5.6)	68.2 (6.1)	0.79
Race			0.72			0.36
White	81.1 (90)	79.4 (193)		76.6 (82)	80.9 (199)	
Non-white	18.9 (21)	20.6 (50)		23.4 (25)	19.1 (47)	
Education			0.70			0.17
<=12	12.5 (14)	14.0 (34)		20.6 (22)	14.6 (36)	
>12 years	87.5 (98)	86.0 (209)		79.4 (85)	85.4 (210)	
Education, years	15.3 (2.1)	15.5 (2.4)	0.47	15.0 (2.2)	15.4 (2.1)	0.08
WRAT4 score	109.6 (14.5)	113.0 (16.5)	0.06	110.0 (13.7)	112.7 (15.9)	0.14
Baseline deficit accumulation score	0.13 (0.07)	0.13 (0.07)	0.99	0.15 (0.10)	0.14 (0.08)	0.27
Frailty trajectory group			0.19			0.38
Robust	87.5 (98)	81.9 (199)		78.5 (84)	75.2 (185)	
Robust, becomes frail	5.4 (6)	11.5 (28)		5.6 (6)	10.2 (25)	
Pre-frail	7.1 (8)	6.6 (16)		15.9 (17)	14.6 (36)	
Baseline self-reported cognition	128.8 (13.7)	130.1 (17.0)	0.48	127.2 (18.4)	130.6 (17.3)	0.10
Objective cognition						
Global score	-0.10 (0.61)	-0.03 (0.62)	0.27	-0.08 (0.63)	-0.06 (0.64)	0.77
APE domain	-0.13 (0.65)	-0.04 (0.65)	0.22	-0.18 (0.75)	-0.08 (0.63)	0.17
LM domain	-0.08 (0.83)	-0.01 (0.82)	0.49	0.01 (0.84)	-0.05 (0.82)	0.51
Baseline physical activity, met minutes/week	1958 (1673)	2073 (2127)	0.61	1360 (1351)	1258 (1341)	0.52
Baseline sleep disturbance	28.6 (32)	24.0 (58)	0.35	45.8 (49)	31.3 (77)	<.01
Stage	---	---	---			0.74
DCIS				8.4 (9)	11.8 (29)	
Stage 1				56.1 (60)	56.1 (138)	
Stage 2a				26.2 (28)	22.4 (55)	
Stage 2b+				9.3 (10)	9.8 (24)	
Treatment	---	---	---			0.18
Chemotherapy				23.3 (24)	30.4 (72)	
Hormonal only				76.7 (79)	69.6 (165)	

Supplementary Table 3. Characteristics of Participants by Death or Drop Out						
	Controls			Survivors		
	Dropped out/died			Dropped out/died		
	Yes (n=22)	No (n=333)	P value	Yes (n=44)	No (n=309)	P value
	Mean (SD) or % (n)			Mean (SD) or % (n)		
Age	68.8 (10.5)	67.9 (6.8)	0.54	68.3 (6.2)	68.1 (6.0)	0.86
Race			0.18			0.43
White	90.9 (20)	79.2 (263)		84.1 (37)	79.0 (244)	
Non-white	9.1 (2)	20.8 (69)		15.9 (7)	21.0 (65)	
Education, years	15.1 (2.2)	15.4 (2.3)	0.50	14.8 (2.4)	15.4 (2.1)	0.12
WRAT score	112.7 (16.1)	111.9 (16.0)	0.83	110.4 (17.5)	112.1 (14.9)	0.48
Baseline deficit score	0.11 (0.09)	0.14 (0.07)	0.11	0.14 (0.07)	0.15 (0.08)	0.41
Frailty trajectory group			0.66			0.39
Robust	86.4 (19)	83.5 (278)		84.1 (37)	75.1 (232)	
Robust, becomes frail	4.5 (1)	9.9 (33)		4.5 (2)	9.4 (29)	
Pre-frail	9.1 (2)	6.6 (22)		11.4 (5)	15.5 (48)	
Baseline self-reported cognition	131.2 (13.8)	129.6 (16.2)	0.65	129.7 (17.3)	129.6 (17.8)	0.95
Objective cognition						
Global score	0.01 (0.54)	-0.05 (0.62)	0.64	-0.15 (0.72)	-0.06 (0.62)	0.36
APE domain	0.06 (0.44)	-0.08 (0.66)	0.33	-0.14 (0.71)	-0.10 (0.67)	0.74
LM domain	-0.04 (0.77)	-0.03 (0.83)	0.94	-0.16 (0.91)	-0.01 (0.82)	0.26
Baseline physical activity, met minutes/week	2426 (2902)	2011 (1920)	0.35	1295 (1504)	1288 (1320)	0.97
Baseline sleep disturbance	22.7 (5)	25.6 (85)	0.76	25.0 (11)	37.2 (115)	0.11
Stage	---	---	---			0.95
DCIS				9.1 (4)	11.0 (34)	
Stage 1				54.5 (24)	56.3 (174)	
Stage 2a				25.0 (11)	23.3 (72)	
Stage 2b+				11.4 (5)	9.4 (29)	
Treatment	---	---	---			0.91
Chemotherapy				27.5 (11)	28.3 (85)	
Hormonal only				72.5 (29)	71.7 (215)	

Supplementary Table 4. Model of Adjusted Deficits Accumulation Scores over Time used for Figure 2.

Mixed Model of Adjusted Deficits Accumulation Scores over Time (n=687)

	Beta (SE)	P value
Age per one-year increase	0.0020 (0.0004)	<.001
Race (non-white vs white)	0.0160 (0.0076)	0.0350
WRAT score per one-point increase	-0.0001 (0.0002)	0.5566
Chemotherapy +/- hormonal vs. hormonal vs. control	---	0.0045
Chemotherapy +/- hormonal vs. control	0.0237 (0.0086)	0.0063
Hormonal only vs. control	0.0160 (0.0062)	0.0107
Time (vs. baseline)		<.001
12 months	0.0121 (0.0024)	<.001
24	0.0192 (0.0025)	<.001
36	0.0211 (0.0034)	<.001
Baseline sleep disturbance (vs. no)	0.0207 (0.0061)	0.0063
Model fit - BIC	-5262.8	

Controlling for recruitment site; p-values from tests of fixed effects

Supplementary Table 5. Model results used with mean centered scores to calculate adjusted mean scores plotted on Figure 2, Panel A and B.

	Adjusted mean score (95% CI) by time point, [sample size]			
	Baseline	12	24	36
Panel A				
Survivors	0.157 (0.142, 0.171), [338]	0.169 (0.154, 0.184), [243]	0.176 (0.161, 0.191), [210]	0.178 (0.162, 0.193), [98]
Controls	0.137 (0.121, 0.152), [349]	0.149 (0.133, 0.164), [301]	0.156 (0.140, 0.172), [246]	0.158 (0.142, 0.174), [118]
Panel B				
Survivors				
Chemo +/-HT	0.160 (0.142, 0.179), [94]	0.173 (0.154, 0.191), [67]	0.180 (0.161, 0.198), [60]	0.182 (0.162, 0.201), [32]
HT alone	0.153 (0.137, 0.169), [244]	0.165 (0.149, 0.181), [176]	0.172 (0.156, 0.188), [150]	0.174 (0.157, 0.190), [66]
Controls	0.137 (0.121, 0.152), [349]	0.149 (0.133, 0.164), [301]	0.156 (0.140, 0.172), [246]	0.158 (0.142, 0.174), [118]

Chemo=chemotherapy; HT= hormonal therapy

Supplementary Table 6. Mixed Model Results for Self-Reported Cognition (Figure 4, Panel A)

Mixed model results	Self-reported Cognitive Function (FACT-Cog Total)			
	Model with Survivors (n=335)		Model with Controls (n=346)	
	Beta (SE)	P value	Beta (SE)	P value
Age per one-year increase	-0.06 (0.15)	.6919	0.02 (0.10)	.8462
Race (non-white vs white)	-0.35 (2.26)	.8770	1.75 (1.98)	.3766
WRAT score per 1-point increase	0.05 (0.06)	.3956	0.10 (0.05)	.0320
Deficits accumulation trajectory group (vs. remains robust)	---	.002	---	<.001
Prefrail	-8.19 (2.71)	.0028	-15.9 (3.27)	<.001
Starts robust, becomes frailer	-1.51 (3.33)	.6507	-13.1 (2.76)	<.001
Chemotherapy +/- hormonal vs. hormonal	-0.62 (1.93)	.7483	---	---
Time (vs. baseline)		.0025		.5447
12 months	-1.61 (1.12)	.1527	0.31 (0.82)	.7090
24	-1.19 (1.16)	.3068	-0.03 (0.87)	.9734
36	-3.24 (1.61)	.0454	1.57 (1.18)	.1823
Deficits accumulation trajectory group by time	---	.0950	---	.0011
12m prefrail vs. baseline robust	1.75 (2.92)	.5484	3.01 (2.84)	.2890
24m prefrail vs. baseline robust	-1.98 (3.14)	.5283	6.49 (3.22)	.044
36m prefrail vs. baseline robust	2.01 (3.91)	.6071	7.18 (4.01)	.0737
12m frail vs. baseline robust	-3.34 (3.15)	.2889	-5.33 (2.42)	.0281
24m frail vs. baseline robust	-10.28 (3.43)	.0028	-9.63 (2.61)	.0002
36m frail vs. baseline robust	-6.38 (4.46)	.1532	-7.53 (3.30)	.0229
Model fit - BIC	7174.1		7839.4	

Controlling for recruitment site; p-values from tests of fixed effects

Supplementary Table 7. Model results used with mean centered scores to calculate adjusted scores plotted on Figure 4, Panel A.

	Adjusted mean FACT-Cog Total score (95% CI) by time point, [sample size]			
	Baseline	12	24	36
Survivors				
Robust	133.0 (129.6, 136.5), [253]	131.4 (127.8, 135.0), [181]	131.9 (128.2, 135.5), [163]	129.8 (125.6, 134.0), [72]
Prefrail	124.9 (119.4, 130.3), [51]	125.0 (118.8, 131.2), [31]	121.7 (115.1, 128.3), [25]	123.6 (115.9, 131.3), [15]
Frail	131.5 (124.8, 138.3), [31]	126.6 (119.6, 133.6), [27]	120.1 (112.6, 128.0), [21]	121.9 (112.9, 131.0), [11]
Controls				
Robust	133.2 (130.8, 135.6), [289]	133.5 (131.1, 136.0), [241]	133.2 (130.7, 135.7), [205]	134.8 (131.8, 137.8), [93]
Prefrail	117.4 (111.0, 123.8), [23]	120.7 (114.3, 127.1), [23]	123.8 (116.8, 130.8), [16]	126.1 (117.8, 134.4), [9]
Frail	120.1 (114.7, 125.5), [34]	115.1 (109.6, 120.6), [31]	110.4 (104.6, 116.2), [25]	114.1 (107.3, 121.0), [14]

Supplementary Table 8. Mixed Model Results for Attention, Processing Speed, and Executive Function (APE) Domain Score (Figure 4, Panel B)

Mixed model results	APE z-score			
	Model for Survivors (n=340)		Model for Controls (n=354)	
	Beta (SE)	P value	Beta (SE)	P value
Age per one-year increase	-0.03 (0.01)	<.001	-0.02 (0.00)	<.001
Race (non-white vs white)	-0.28 (0.08)	.0005	-0.39 (0.08)	<.001
WRAT score per 1-point increase	0.02 (0.00)	<.001	0.01 (0.00)	<.001
Deficits accumulation trajectory group (vs. remains robust)		.0004		.0521
prefrail	-0.34 (0.09)	<.001	-0.24 (0.11)	.0300
Starts robust, becomes frailer	-0.02 (0.10)	.8364	-0.12 (0.09)	.1935
Chemotherapy +/- hormonal vs. hormonal vs. control	-0.03 (0.07)	.6101	---	---
Time (vs. baseline)		<.001		<.0001
12 months	0.09 (0.03)	.0016	0.08 (0.02)	.0011
24	0.11 (0.03)	.0001	0.12 (0.02)	<.0001
36	0.15 (0.04)	.0004	0.09 (0.03)	.0070
Deficits accumulation trajectory group by time	---*	---	---*	---
Model fit - BIC	1287.0		1231.9	

Controlling for recruitment site; p-values from tests of fixed effects

* interaction not significant and not retained in either final case or final control model

Supplementary Table 9. Model results used with mean centered scores to calculate adjusted scores plotted on Figure 4, Panel B

	Adjusted mean APE z-score (95% CI) by time point, [sample size]			
	Baseline	12	24	36
Survivors				
Robust	-0.07 (-0.20, 0.05), [256]	0.02 (-0.11, 0.14), [193]	0.04 (-0.08, 0.16), [172]	0.07 (-0.06, 0.21), [76]
Prefrail	-0.42 (-0.60, -0.24), [53]	-0.33 (-0.51, -.15), [34]	-0.30 (-0.49, -0.12), [27]	-0.27 (-0.46, -0.08), [17]
Frail	-0.10 (-0.31, 0.12), [31]	-0.01 (-0.22, 0.21), [29]	0.02 (-0.20, 0.24), [25]	0.05 (-0.17, 0.27), [11]
Controls				
Robust	-0.14 (-0.23, -0.05), [296]	-0.06 (-0.16, 0.03), [258]	-0.02 (-0.11, 0.07), [217]	-0.05 (-0.15, 0.05), [99]
Prefrail	-0.38 (-0.60, -0.16), [24]	-0.30 (-0.52, -0.09), [23]	-0.26 (-0.48, -0.04), [17]	-0.29 (-0.52, -0.07), [11]
Frail	-0.26 (-0.45, -0.07), [34]	-0.19 (-0.37, 0.00), [33]	-0.14 (-0.33, 0.05), [26]	-0.17 (-0.37, 0.02), [16]

Supplementary Table 10. Mixed Model Results for Learning and Memory (LM) Domain Score (not shown in text)

Mixed model results	LM z-score			
	Model for Survivors (n=340)		Model for Controls (n=354)	
	Beta (SE)	P value	Beta (SE)	P value
Age per one-year increase	-0.39 (0.50)	0.0144	-0.02 (0.01)	<.001
Race (non-white vs white)	-0.02 (0.01)	<0.001	-0.22 (0.10)	0.0321
WRAT score per 1-point increase	-0.38 (0.10)	<.001	0.02 (0.00)	<.001
Deficits accumulation trajectory group (vs. remains robust)		0.0880		0.008
prefrail	-0.22 (0.11)	0.0345	-0.37 (0.15)	0.0133
Starts robust, becomes frailer	0.04 (0.13)	0.7436	0.21 (0.13)	0.1000
Chemotherapy +/- hormonal vs. hormonal	0.02 (0.08)	0.7829	---	---
Time (vs. baseline)		<.001		<.001
12 months	0.18 (0.04)	<.001	0.19 (0.03)	<.001
24	0.23 (0.04)	<.001	0.16 (0.04)	<.001
36	0.30 (0.06)	<.001	0.37 (0.05)	<.001
Deficits accumulation trajectory group by time	---*	---	---*	---
Model fit - BIC	1800.0		2000.9	

Controlling for recruitment site; p-values from tests of fixed effects

* interaction not significant and not retained in either final case or final control model

Supplementary Table 11. Model results used with mean centered scores to calculate adjusted scores (not shown in paper)

	Adjusted mean LM z-score (95% CI) by time point, [sample size]			
	Baseline	12	24	36
Survivors				
Robust	-0.12 (-0.27, 0.03), [256]	0.05 (-0.10, 0.21), [193]	0.11 (-0.05, 0.26), [172]	0.17 (0.00, 0.34), [76]
Prefrail	-0.35 (-0.57, -0.13), [53]	-0.17 (-0.40, 0.05), [34]	-0.12 (-0.35, 0.11), [27]	-0.05 (-0.29, 0.18), [17]
Frail	-0.08 (-0.35, 0.18), [31]	0.09 (-0.17, 0.36), [29]	0.15 (-0.12, 0.42), [25]	0.21 (-0.06, 0.49), [11]
Controls				
Robust	-0.13 (-0.25, -0.00), [296]	0.06 (-0.06, 0.19), [258]	0.04 (-0.09, 0.16), [217]	0.24 (0.10, 0.38), [99]
Prefrail	-0.50 (-0.80, -0.20), [24]	-0.31 (-0.61, - 0.01), [23]	-0.34 (-0.64, - 0.04), [17]	-0.13 (-0.44, 0.17), [11]
Frail	0.08 (-0.17, 0.34), [34]	0.27 (0.02, 0.53), [33]	0.25 (-0.01, 0.50), [26]	0.45 (0.19, 0.72), [16]

Supplementary Table 12. Mixed Model Results for Self-reported Physical Activity

	Model for Survivors (n=332)		Model for Controls (n=352)	
	Beta (SE)	P value	Beta (SE)	P value
Age per one-year increase	-0.1277 (0.1270)	.3157	-0.1727 (0.1166)	.1395
Race (non-white vs white)	0.6045 (1.9485)	.7566	2.9736 (2.1969)	.1768
WRAT score per 1-point increase	-0.06019 (0.0505)	.2339	0.08755 (0.05415)	.1068
Deficits accumulation trajectory group (vs. remains robust)	---	<.001	---	.0004
Prefrail	-7.632 (2.5456)	.0029	-5.2448 (3.1604)	.0979
Starts robust, becomes frailer	-1.6688 (3.1287)	.5941	-10.0348 (2.6761)	.0002
Chemotherapy +/- hormonal vs. hormonal	-1.4832 (1.6706)	.3753	---	---
Time (vs. baseline)	---	---	---	.7222
12 months	3.8837(1.2792)	.0025	-0.7865 (1.0995)	.4747
24	4.9274 (1.3364)	.0003	-1.3086 (1.1763)	.2664
36	8.2056 (1.8280)	<.0001	-0.8508 (1.5776)	.5899
Deficits accumulation trajectory group by time	---	0.0479	---	---
12m prefrail vs. baseline robust	0.7687 (3.3864)	.8205	---	---
24m prefrail vs. baseline robust	3.2463 (3.5620)	.3625	---	---
36m prefrail vs. baseline robust	-3.5697 (4.6490)	.4429	---	---
12m frail vs. baseline robust	-6.0263 (3.6197)	.0965	---	---
24m frail vs. baseline robust	-8.5829 (3.8715)	.0271	---	---
36m frail vs. baseline robust	-15.9020 (5.4611)	.0037	---	---
Model fit - BIC	7163.2		8563.1	

Controlling for recruitment site; p-values from tests of fixed effects

* interaction not significant and not retained in final control model

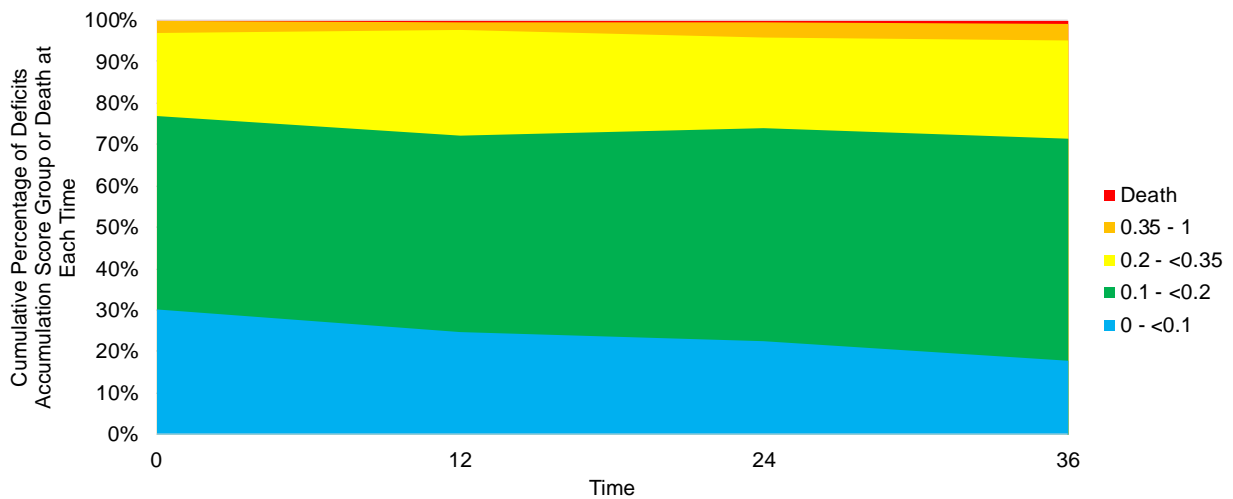
Supplementary Table 13. Adjusted values for self-report physical activity for Figure 4, Panel C

	Adjusted mean IPAQ total score in MET minutes/week (95% CI) by time point, [sample size]			
	Baseline	12	24	36
Survivors				
Robust	1470 (1165, 1776), [250]	1859 (1534, 2183), [182]	1963 (1631, 2295), [161]	2291 (1885, 2697), [72]
Prefrail	707 (206, 1208), [51]	1172 (558, 1786), [29]	1524 (879, 2169), [25]	1171 (335, 2006), [13]
Frail	1303 (681, 1926), [31]	1089 (435, 1743), [27]	938 (236, 1640), [22]	534 (469, 1536), [9]
Controls				
Robust	2138(1864, 2413), [294]	2060 (1774, 2346), [246]	2008 (1711, 2304), [207]	2053 (1692, 2415), [91]
Prefrail	1614 (980, 2248), [24]	1535 (898, 2173), [22]	1483 (838, 2128), [15]	1529 (856, 2201), [10]
Frail	1134.8 (590.2, 1679.5), [34]	1056.2 (508.0, 1604.4), [32]	1004.0 (448.3, 1559.7), [24]	1049.8 (459.8, 1639.8), [14]

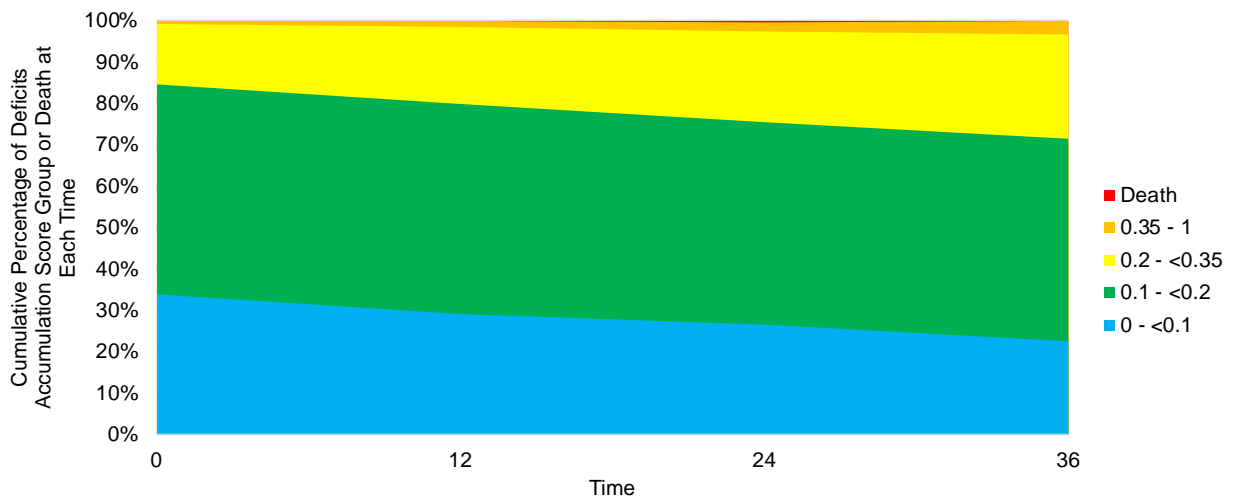
Supplementary Figures

Supplementary Figure 1. Observed Prevalence of Unadjusted Deficits Accumulation Index Scores over 36-months among Older Breast Cancer Survivors and Matched-Non-Cancer Controls

Panel A. Survivors



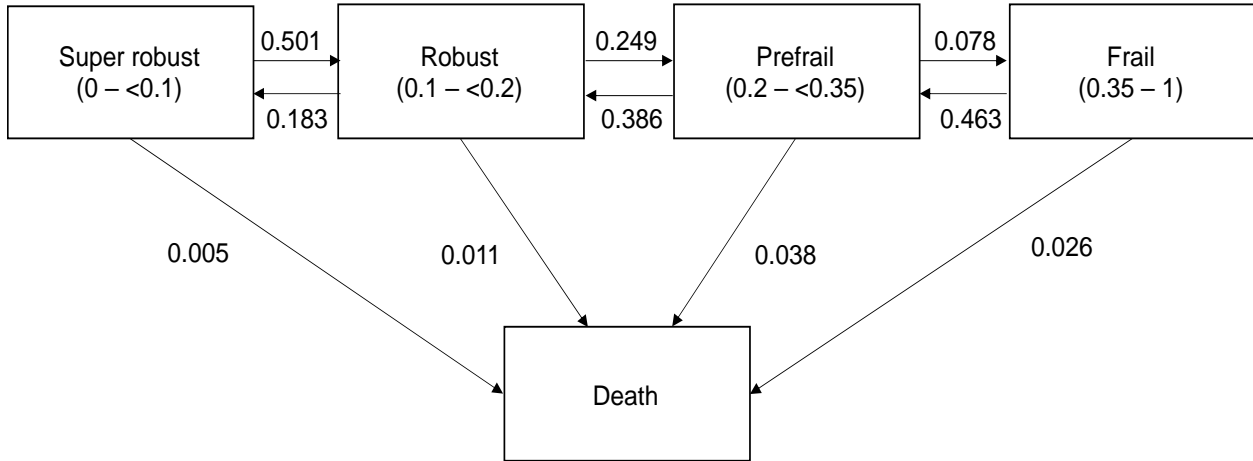
Panel B. Controls



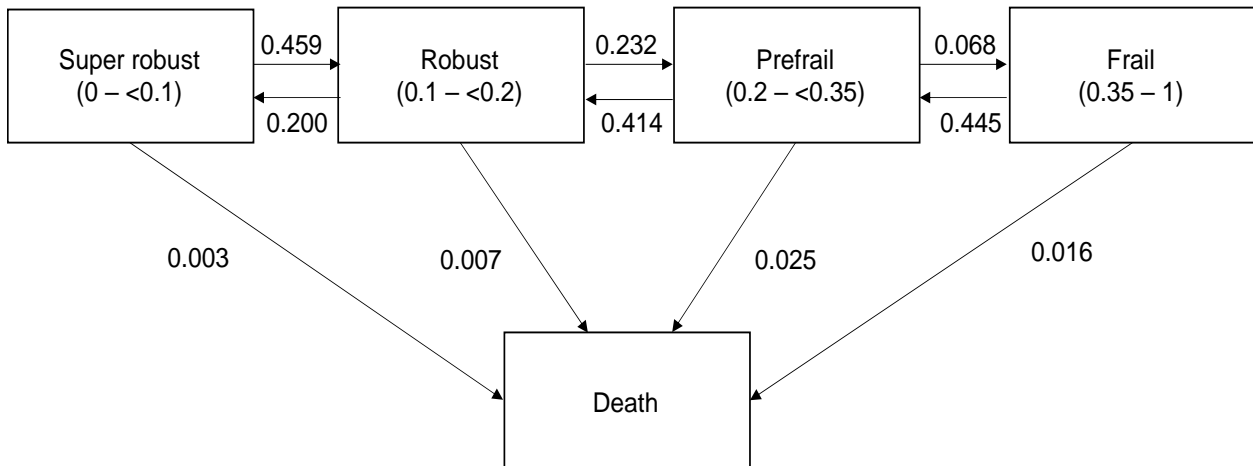
Deficits accumulation index scores range from 0 to 1. The graphs show the percent of women with unadjusted deficits accumulation scores in each of five groups at each time point. We selected five groups to correspond to having 0 to 5 deficits on the Fried phenotypic score range based on the methods described by Stenholm and colleagues.

Supplementary Figure 2. Probability of Transitioning between Deficits Accumulation Categories from Baseline to 36 months

Panel A. Survivors

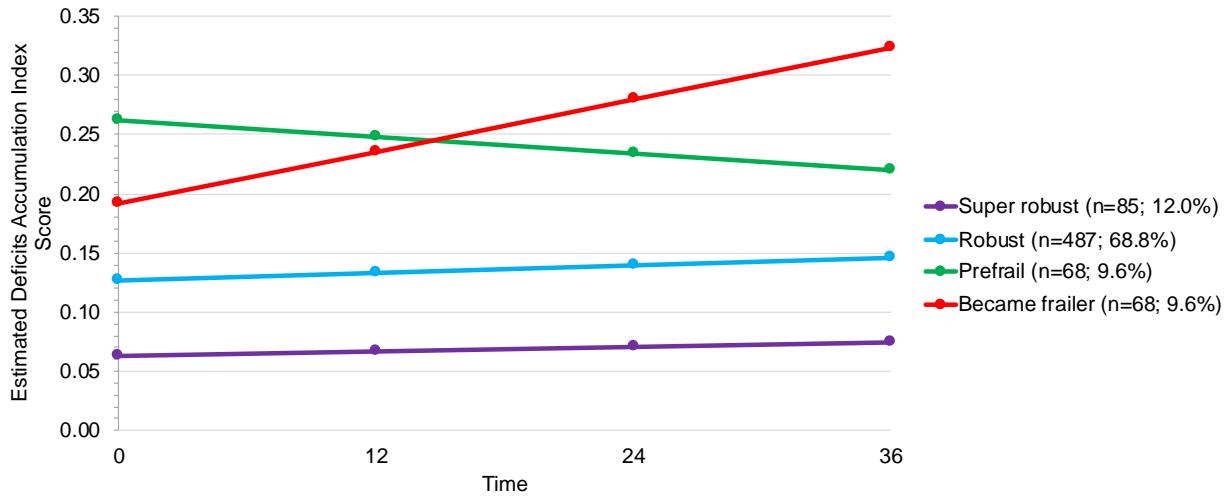


Panel B. Non-Cancer Controls



Multistate models of transitions between deficits accumulation score categories over 36-months from baseline.

Supplementary Figure 3. Deficits Accumulation Frailty Trajectories for Older Survivors and Frequency-Matched Non-Cancer Controls Combined



	Adjusted mean score (95% CI) by time point, [sample size]			
	Baseline	12	24	36
Super robust	0.063 (0.049, 0.077), [84]	0.067 (0.052, 0.081), [76]	0.071 (0.055, 0.086), [66]	0.074 (0.058, 0.091), [26]
Robust	0.127 (0.117, 0.136), [485]	0.133 (0.124, 0.142), [371]	0.139 (0.130, 0.149), [314]	0.146 (0.136, 0.156), [146]
Prefrail	0.262 (0.236, 0.288), [67]	0.248 (0.226, 0.271), [48]	0.234 (0.212, 0.257), [34]	0.220 (0.193, 0.247), [23]
Became frailer	0.191 (0.175, 0.208), [66]	0.235 (0.219, 0.251), [59]	0.280 (0.260, 0.299), [50]	0.324 (0.298, 0.349), [24]

Deficits accumulation index scores at each assessment were used to derive trajectory groups using growth mixture models. All data available are used from all woman. The number of trajectory groups was determined by having at least 2% of participants in a group, likelihood ratio tests, the smallest Bayesian information criterion (BIC), and a priori expectation. Based on these criteria, four groups best fit the data.