JNCCN

JOURNAL OF THE NATIONAL COMPREHENSIVE CANCER NETWORK

Supplemental online content for:

Association of Polypharmacy and Potentially Inappropriate Medications With Frailty Among Older Adults With Blood Cancers

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J Natl Compr Canc Netw 2022;20(8):915–923.e5

eTable 1. Frailty Scoring Values

eTable 1.1: Cumulative Deficit Model Variable Index and Scoring

Obtainment		Measured Variable	CDM Scoring (Scaled 0–1)
Patient questionnaire	1	Bathing	With some help or completely unable = 1; Without help = 0
	2	Dressing	
	3	Getting in/out of chair	
	4	Walking around house[a]	
	5	Eating	
	6	Grooming	
	7	Using toilet	
	8	Getting up/down stairs	
	9	Lifting 10 lb	
	10	Shopping	
	11	Doing housework	
	12	Meal preparations	
	13	Taking medication	
	14	Handling finances	
	15	Walk outside	<3 days = 1; ≥3 days = 0
	16	Self-report ECOG PS	3–4 = 1; 1–2 = 0.5; 0 = 0
	17	Self-rating of health	Poor = 1; Fair = 0.75; Good = 0.5; Very good = 0.25; Excellent = 0
	18	How health has changed in last year	Worse = 1; Better/Same = 0
	19	Stayed in bed at least half the day due to health (in last month)	Yes = 1; No = 0
	20	Cut down on usual activity (in last month)	
	21	Lost >10 lb in last year[a]	
	22	Feel everything is an effort[a]	Most of time = 1; Some of the time = 0.5; Rarely = 0
	23	Have trouble getting going[a]	
	24	Feel depressed	
	25	Feel lonely	
	26	Feel happy	Most of time = 0; Some of the time = 0.5; Rarely = 1
Patient medical record	27	High blood pressure	Yes = 1; Suspect = 0.5; No = 0
	28	Heart attack	
	29	Congestive heart failure	
	30	Stroke	
	31	Cancer	
	32	Diabetes	
	33	Arthritis	
	34	Chronic lung disease	
	35	Body mass index	

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eTable 1. Frailty Scoring Values (cont.)

eTable 1.1: Cumulative Deficit Model Variable Index and Scoring (cont.)

Obtainment		Measured Variable	CDM Scoring (Scaled 0–1)
Assessed by research staff	36	Grip strength[a]	See eTables 1.1A–C for cutpoints
	37	Usual pace walk speed	
	38	Rapid pace walk speed[a]	
	39	MoCA 5-word delayed recall	
	40	Clock-in-the-Box test	
	41	Ability to explain presentation to DFCI	With help or unable = 1; Without help = 0
	42	Ability to fill out the questionnaire	

Abbreviations: CDM, cumulative deficit model; DFCI, Dana-Farber Cancer Institute; MoCA, Montreal Cognitive Assessment; PS, performance status.
[a]Also used in calculation of Phenotype Frailty Score.

eTable 1.1A: Physical Variable Cutpoints[1]

Variable	Deficit for Men	Deficit for Women	Source of Cutpoint
Body mass index (kg/m^2)	<18.5, ≥30 as a deficit, 25 to <30 as a 'half deficit'	<18.5, ≥30 as a deficit 25 to <30 as a 'half deficit'	Published[2]
Grip strength (kg)	For BMI ≤24: GS ≤29 For BMI 24.1–28: GS ≤30 For BMI >28: GS ≤32	For BMI ≤23: GS ≤17 For BMI 23.1–26: GS ≤17.3 For BMI 26.1–29: GS ≤18 For BMI >29: GS ≤21	Published[3,4]
Rapid pace walk	<0.61 m/s (6.56 s)	<0.61 m/s (6.56 s)	Published[4]
Usual pace walk	<0.38 m/s (10.50 s)	<0.38 m/s (10.50 s)	Published[5]

Abbreviations: BMI, body mass index; GS, grip strength.

eTable 1.1B: MoCA 5-Word Delayed Recall Normative Data and Cutpoints[6]

	Normal Control		Mild Cognitive Impairment		Alzheimer's Disease	
	Average	SD	Average	SD	Average	SD
Memory	3.73	1.27	1.17	1.47	0.52	1.03
Words recalled successfully	5	4	3	2	1	0

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eTable 1. Frailty Scoring Values (cont.)

eTable 1.1B: (cont.)

	Normal Control		Mild Cognitive Impairment		Alzheimer's Disease	
	Average	SD	Average	SD	Average	SD
Corresponding CDM score	0	0.25	0.5	0.75	1	1

eTable 1.1C: CIB Normative Data for Age and Education and Cutpoints[7]

	Education			
Age	Less Than High School [SD]	High School [SD]	College [SD]	Graduate School [SD]
75–79 y	5.1 [1.9]	6.3 [1.6]	6.4 [1.3]	6.6 [1.4]
80–84 y	4.6 [1.9]	5.8 [1.5]	5.9 [1.6]	6.7 [1.2]
≥85 y	4.9 [1.3]	5.4 [1.3]	5.8 [1.7]	6.5 [1.5]

CIB score	8	7	6	5	0–4
Corresponding CDM score	0	0.25	0.5	0.75	1

Abbreviations: CDM, cumulative deficit model; CIB, Clock-in-the-Box.

Calculation of Cumulative Deficit Frailty Score:
To calculate the cumulative frailty score, sum all points given for each deficit and divide by number of total points possible. Cumulative frailty score cutpoints[5] are as follows: <0.2 is robust, 0.2–0.35 is prefrail, and >0.35 is frail.

eTable 1.2: Phenotype Frailty Score

	Index Item[a]	Measured Variable	Scoring
1	21	Weight loss	Yes = 1; No = 0
2	22, 23	Self-reported exhaustion	Most of the time (for either) = 1; Some or rarely (for both) = 0
3	4	Energy expenditure	Some assistance or completely unable = 1; Without assistance = 0
4	38	Gait speed (rapid pace)	Slower than cutpoint = 1; Faster than cutpoint = 0
5	36	Grip strength	Weaker than cutpoint = 1 (for strongest measurement); Stronger than cutpoint = 0

[a]Numbers correspond to item number in Cumulative Deficit Model Variable Index (see supplemental eTable 1.1).

Calculation of Phenotype Frailty Score:
Sum all points given for each of the 5 deficits. Phenotype frailty cutpoints[3] are as follows: 0 is robust, 1–2 is prefrail, and 3–5 is frail.

References

1. Searle SD, Mitnitski A, Gahbauer EA, et al. A standard procedure for creating a frailty index. BMC Geriatr 2008;8:24.
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3. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146–156.
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eTable 2. Univariable Models of Association Between Polypharmacy and PIMs

Variable	Univariable Analysis (n=468)		
	Frailty[a] OR (95% CI)	MoCA OR (95% CI)	CIB OR (95% CI)
Polypharmacy			
≤5 medications	Ref	Ref	Ref
>5 medications	1.701 (1.104–2.625)[a]	1.421 (0.738–2.971)	1.208 (0.702–2.762)
Polypharmacy			
<8 medications	Ref	Ref	Ref
≥8 medications	3.304 (2.267–4.862)	1.123 (0.662–1.928)	1.716 (1.080–2.769)[a]
Polypharmacy			
Continuous	1.099 (1.062–1.139)	1.014 (0.966–1.061)	1.013 (0.973–1.055)
ARS			
Continuous	1.229 (1.061–1.424)[a]	0.902 (0.691–1.125)	0.882 (0.705–1.070)
GO-PIM scale			
Continuous	1.770 (1.450–2.169)	1.108 (0.834–1.448)	0.943 (0.729–1.203)

Abbreviations: ARS, Anticholinergic Risk Scale; OR, odds ratio, CIB, Check-in-the-Box; MoCA, Montreal Cognitive Assessment; GO-PIM, Geriatric Oncology Potentially Inappropriate Medications; PIMs, potentially inappropriate medications.
[a]Fit with ordinal logistic regression.

eAppendix 1. Supplemental Methods

Anticholinergic Risk Scale

The Anticholinergic Risk Scale (ARS) is a tool developed by Rudolph et al[1] to identify patients who may be at increased risk of anticholinergic adverse effects as a result of the medications they take. To develop this scale, a panel of 2 geropharmacists and 1 geriatrician evaluated a list of the 500 most prescribed medications among a retrospective geriatric evaluation and management cohort and a prospective older primary care population at the Veterans Affairs Boston Healthcare System between 2004 and 2006. The panel members reviewed each medication for (1) the dissociation constant for the cholinergic receptor, (2) evidence reflecting rates of anticholinergic adverse effects compared with placebo, and (3) a review of medical literature related to anticholinergic adverse effects.[1] Panel members then ranked medications on a scale of 0 to 3, where 0 indicated limited to no anticholinergic potential, 1 indicated moderate potential, 2 indicated strong potential, and 3 indicated very strong potential. Topical, ophthalmic, otologic, and inhaled medications were excluded from review and are not included in the scale. An individual's total risk according to the ARS scale is quantified by summing the ranked scores for all medications taken.

Geriatric Oncology Potentially Inappropriate Medications Scale

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) are published annually to provide updated recommendations for health professionals who manage patients with cancer. To provide specific guidelines that address the issues unique to older adults, NCCN releases Guidelines for Older Adult Oncology, produced by a panel of experts in geriatric medicine, oncology, internal medicine, and supportive care.[2] The NCCN Guidelines for Older Adult Oncology provide a list of medications commonly used for supportive care that are of concern for older patients; additionally, the guidelines offer recommendations for dosage, administration, and alternatives for the listed medications. We translated this list, as found in the NCCN Guidelines for Older Adult Oncology, Version 1.2020,[3] into a scale that allowed us to quantify cancer-specific potentially inappropriate medication (PIM) burden for an individual. This scale, called the Geriatric Oncology Potentially Inappropriate Medications (GO-PIM) scale, counts for each patient the number of medications on the NCCN list of Medications Commonly Used for Supportive Care That Are of Concern in Older Patients,[2] with more medications suggesting higher risk.

References

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3. Dotan E, Walter LC, Baumgartner J, et al. NCCN Clinical Practice Guidelines in Oncology: Older Adult Oncology. Version 1.2020. To view the most recent version, visit NCCN.org