Screening for frailty in primary care

Accuracy of gait speed and hand-grip strength

Linda Lee MD MCISc(FM) CCFP(COE) FCFP **Tejal Patel** PharmD **Andrew Costa** PhD **Erin Bryce** PhD **Loretta M. Hillier** MA
Karen Slonim PhD **Susan W. Hunter** PT PhD **George Heckman** MD MSc FRCPC **Frank Molnar** MSc MD CM FRCPC

Abstract

Objective To examine the accuracy of individual Fried frailty phenotype measures in identifying the Fried frailty phenotype in primary care.

Design Retrospective chart review.

Setting A community-based primary care practice in Kitchener, Ont.

Participants A total of 516 patients 75 years of age and older who underwent frailty screening.

Main outcome measures Using modified Fried frailty phenotype measures, frailty criteria included gait speed, hand-grip strength as measured by a dynamometer, and self-reported exhaustion, low physical activity, and unintended weight loss. Sensitivity, specificity, accuracy, and precision were calculated for single-trait and dual-trait markers.

Results Complete frailty screening data were available for 383 patients. The overall prevalence of frailty based on the presence of 3 or more frailty criteria was 6.5%. The overall prevalence of individual Fried frailty phenotype markers ranged from 2.1% to 19.6%. The individual criteria all showed sensitivity and specificity of more than 80%, with the exception of weight loss (8.3% and 97.4%, respectively). The positive predictive value of the single-item criteria in predicting the Fried frailty phenotype ranged from 12.5% to 52.5%. When gait speed and hand-grip strength were combined as a dual measure, the positive predictive value increased to 87.5%.

Conclusion There is a need for frailty measures that are psychometrically sound and feasible to administer in primary care. While use of gait speed or grip strength alone was found to be sensitive and specific as a proxy for the Fried frailty phenotype, use of both measures together was found to be accurate, precise, specific, and more sensitive than other possible combinations. Assessing both measures is feasible within primary care.

EDITOR'S KEY POINTS

- Little attention has been given to the concept of frailty in primary care medicine relative to its importance. Many existing measures for assessing frailty are not feasible in the busy primary care environment. This study aimed to examine the relative accuracy of individual frailty markers to identify measures that might be useful for screening in the primary care setting.
- The dual-trait measure of gait speed with grip strength is accurate, precise, specific, and more sensitive than individual traits and other possible dual-factor combinations; the measurement of gait speed and grip strength is feasible in primary care settings.
- With the rapidly aging population, primary care physicians will be increasingly required to identify and manage frail seniors and their associated complex chronic conditions with judicious use of the limited available geriatric specialist resources.

This article has been peer reviewed.
Can Fam Physician 2017;63:e51-7

Dépister les patients fragiles dans un contexte de soins primaires

Vitesse de la marche et force de la poigne sont des critères précis

Linda Lee MD MCISc(FM) CCFP(COE) FCFP **Tejal Patel** PharmD **Andrew Costa** PhD **Erin Bryce** PhD **Loretta M. Hillier** MA
Karen Slonim PhD **Susan W. Hunter** PT PhD **George Heckman** MD MSc FRCPC **Frank Molnar** MSc MD CM FRCPC

Résumé

Objectif Déterminer la précision des méthodes de mesure individuelles du phénotype de fragilité de Fried afin de repérer les clients du milieu des soins primaires qui correspondent à ce phénotype.

Type d'étude Revue rétrospective de dossiers.

Contexte Une clinique communautaire dispensant des soins primaires à Kitchener, en Ontario.

Participants Un total de 516 patients âgés d'au moins 75 ans ayant participé au dépistage de la fragilité.

Principaux paramètres à l'étude Pour mesurer le phénotype modifié de Fried, on a utilisé les critères suivants : la vitesse de marche, la force de la poigne telle que mesurée au dynamomètre, de même que la sensation de fatigue, la réduction de l'activité physique et la perte de poids non planifiée telles que rapportées par le patient. La sensibilité, la spécificité et la précision ont été calculées pour chacun des critères et pour des paires de critères.

Résultats On a obtenu des données pour tous les critères de fragilité chez 383 patients. Avec au moins 3 critères, la prévalence de la fragilité était de 6,5%. La prévalence globale des marqueurs du phénotype de fragilité de Fried variait entre 2,1% et 19,6%. Les différents critères avaient chacun une sensibilité et une spécificité de plus de 80%, à l'exception de la perte de poids (8,3% et 97,4% respectivement). La valeur prédictive positive des critères individuels pour établir la présence du phénotype de fragilité de Fried variait entre 12,5% et 52,5%. En utilisant la combinaison vitesse de marche et force de la poigne, la valeur prédictive augmentait à 87,5%.

Conclusion Dans un milieu de soins primaires, il est essentiel d'effectuer des mesures de fragilité qui soient valables sur le plan psychométrique et applicables. Même si les mesures séparées de la vitesse de marche et de la force de la poigne étaient assez sensibles et spécifiques pour établir la présence du phénotype de fragilité de Fried, la combinaison de ces deux mesures s'est avérée précise, spécifique et plus sensible que toute autre combinaison. L'évaluation de ces deux critères est faisable dans un milieu de soins primaires.

POINTS DE REPÈRE DU RÉDACTEUR

- Malgré son importance, le concept de fragilité n'a pas suscité beaucoup d'intérêt dans les milieux de soins primaires. Bon nombre des méthodes actuellement utilisées pour en évaluer l'incidence ne sont pas applicables dans le milieu trop exigeant des soins primaires. Cette étude visait à vérifier la précision relative de certains marqueurs de fragilité afin d'identifier ceux qui pourraient être utilisés dans un milieu de soins primaires.

- La mesure combinée de la vitesse de marche et de la force de la poigne est précise, spécifique et plus sensible que tout critère isolé ou que toute autre combinaison de deux critères; elle peut être effectuée dans un contexte de soins primaires.

- Étant donné le vieillissement rapide de la population, les médecins de première ligne devront de plus en plus identifier et soigner les problèmes de santé chroniques complexes de personnes âgées fragiles, et ce, en utilisant de façon judicieuse des ressources gériatriques limitées.

Cet article a fait l'objet d'une révision par des pairs.
Can Fam Physician 2017;63:e51-7

Frailty has been defined as a state of increased vulnerability due to age-associated decline in reserve and function resulting in reduced ability to cope with stressors.[1,2] Currently, frailty is recognized as a multidimensional concept with dynamic interrelated factors in the physical, psychological, social, and environmental domains that affect the physiologic equilibrium of the person.[3] Frailty has been associated with higher risk of adverse health outcomes,[4] functional impairment and mortality,[5,6] emergency department visits and hospitalizations,[7] and postoperative complications and reduced survival.[8,9] Early frailty is easily overlooked because its manifestations can be subtle or dismissed as normal aging, and physicians' training has been focused on identifying specific medical diseases rather than overall vulnerability and the overall effect of diseases on homeostasis.

Although a number of conceptualizations of frailty have been proposed,[10,11] frailty has been frequently described as a clinical phenotype of slowed walking speed, low physical activity, unintentional weight loss, low energy, and low grip strength (weakness), where the presence of 3 of 5 criteria indicates frailty.[5] Multiple frailty scales have been developed to date.[12] Although several systematic reviews have not conclusively identified a preferred instrument for measuring frailty in the elderly, the Fried frailty phenotype measure has been extensively tested for its validity and is a widely used instrument in frailty research.[12-17]

Recognition of frailty is important because there is evidence that the degree of frailty can be improved with interventions such as high-intensity exercise training and nutritional supplementation.[18,19] The presence of frailty can affect the potential risks and benefits of medical interventions, as well as alter appropriate treatment targets when managing comorbid conditions such as hypertension and diabetes.[18,20,21] When frailty is identified, management can be directed at identifying and addressing conditions that might underlie frailty and mitigating stressors that might precipitate adverse outcomes. Yet in the busy clinical setting of primary care practice, there is currently a lack of consensus as to how best to screen for, assess, and diagnose frailty.[22] Care processes in typical primary care practice are not conducive to the administration of many existing measures of frailty that are time intensive. There is a need to identify measures that are both psychometrically sound and feasible to administer in the primary care setting. The feasibility of assessing frailty in primary care might be facilitated by the use of single-trait markers, rather than composite measures such as the Fried criteria. Commonly used single traits include gait speed and grip strength.[23,24] Single-trait studies[23-25] have measured outcomes associated with frailty such as morbidity, mortality, hospitalizations, and falls. To our knowledge, no studies have assessed the test accuracy of Fried frailty phenotype measures in identifying the Fried frailty phenotype itself.

The purpose of this study was to examine the relative accuracy of individual Fried frailty phenotype measures in identifying the Fried frailty phenotype in a primary care setting.

METHODS

This was a retrospective chart review of consecutive patients aged 75 years and older who were assessed through a comprehensive screening program to identify at-risk seniors at the Centre for Family Medicine Family Health Team (CFFM FHT) in Kitchener, Ont, from April 1, 2013, to April 31, 2014. The CFFM FHT is a primary care setting comprising 18 family physician practices with a combined population of 27 997 patients, 1291 of whom are 75 years of age or older. The Case-finding for Complex Chronic Conditions in Seniors 75+ (C5-75) program at the CFFM FHT is designed to identify seniors who are frail and might have unrecognized comorbid conditions underlying their frailty.

Before regularly scheduled medical appointments, all patients 75 years of age or older were assessed through the C5-75 screening program by specially trained nurses. There are 2 levels to the C5-75 screening, the first of which screens for frailty. Patients identified as frail proceed to the second level, which is a more comprehensive screening for common geriatric issues associated with frailty such as polypharmacy, fall risk, cognitive impairment, mood disorders, and social isolation. When concerns are identified, the patient is referred to the appropriate care professional for assessment and intervention. Any patients for whom 1 or more frailty criteria were not measured during the period of April 1, 2013, to April 31, 2014, were excluded from this analysis.

This study was approved by the McMaster University Research Ethics Board in Hamilton, Ont.

Measures

The Fried frailty phenotype was selected to identify frailty because it has been validated in a number of studies[12,26,27] and is widely used in studies examining frailty associated with various health conditions and outcomes.[16,17,28] The 5 Fried frailty phenotype elements were assessed.[5] Gait speed was calculated as the time (in seconds) to walk 4 m at a usual pace. The fastest time of 2 trials was recorded.[29] Grip strength (in kilograms) was measured as the higher score of 2, 3-second trials (with each hand) using a hand-held dynamometer (Jamar Hydraulic Hand Dynamometer, model 281-12-0600, J.A. Preston Corporation, Clifton, NJ). Self-reported exhaustion was measured using the Center for Epidemiologic Studies Depression Scale item "I could not get going,"

with response choices for frequency in the past week: rarely or none of the time (<1 day), some or a little of the time (1 to 2 days), a moderate amount of the time (3 to 4 days), or most of the time (5 to 7 days).[5,30] Weight loss was measured as self-reported unintentional weight loss in the previous year. Physical activity was measured by self-reported descriptions (I am physically active; I do 30 minutes or more of moderate intensity physical activities on 5 or more days per week; I am physically active occasionally or during some seasons much more than others; I am not physically active beyond moving around or walking during activities of daily living).[31] Patients were classified as frail if they met at least 3 of the following 5 criteria.[5]

- Gait speed measured as 6 seconds or more to walk 4 m, independent of sex.
- Grip strength measured as a score within the lowest 20%, stratified by sex.[32]
- Exhaustion measured as not being able to get going a moderate amount of the time or all of the time.
- Weight loss measured as unintentional loss of 4.5 kg or more in the past year.
- Activity level measured as not being physically active beyond walking around during activities of daily living.

Data analysis

Descriptive statistics were used to summarize the data. Sex differences in frailty indicators were determined using Fisher exact tests (2-tailed). Sensitivity, specificity, accuracy, and positive predictive value were calculated for single-trait and dual-trait markers by constructing 2×2 contingency tables. Standard epidemiologic definitions were used for the calculations. The 95% CIs were calculated using the Wilson procedure with continuity correction.[33] Analyses were performed using R, version 3.0.1.

RESULTS

A total of 516 patients were screened in the C5-75 program. Complete data on the frailty criteria measured in this study were available for 383 patients (**Table 1**). Patients ranged in age from 75 to 94 years of age; 53.5% were female.

The prevalence of frailty based on the Fried criteria (ie, positive on 3 or more indicators) was 6.5% (n=25). As shown in **Table 2**, the overall incidence of each frailty marker ranged from 2.1% (weight loss) to 19.6% (lack of exercise). Frailty in grip strength was defined as those in the lowest quintile and by definition should be 20%. Deviations from 20% are a result of multiple patients near the lowest quintile having the same measured grip strength. Female patients were significantly more likely than male patients were to meet the Fried frailty criteria for slow gait (P=.026) and low activity level (P=.030). There were no significant sex differences for the other frailty components.

Table 1. Characteristics of patients excluded from and included in the study

CHARACTERISTICS	EXCLUDED PATIENTS (N=133)	INCLUDED PATIENTS (N=383)	*P* VALUE
Female, n (%)	86 (64.7)	205 (53.5)	.02
Female-to-male ratio	1.9	1.2	.02
Mean (SD) age for females, y	82.3 (5.4)	80.6 (4.4)	.003
Mean (SD) age for males, y	81.5 (4.2)	80.1 (4.2)	.04

Table 2. Incidence of single-trait frailty indicators

FRAILTY INDICATOR	MALE PATIENTS (N=178, 46.5%) N (%)	FEMALE PATIENTS (N=205, 53.5%) N (%)	TOTAL (N=383) N (%)
Gait speed	16 (9.0)	24 (11.7)	40 (10.4)
Grip strength	26 (14.6)	33 (16.1)	59 (15.4)
Exhaustion	11 (6.2)	17 (8.3)	28 (7.3)
Weight loss	4 (2.2)	4 (2.0)	8 (2.1)
Low exercise	28 (15.7)	47 (22.9)	75 (19.6)

Diagnostic accuracy

The individual traits comprising the Fried frailty phenotype all showed sensitivity and specificity of more than 80%, with the exception of weight loss, which appears to be a poor indicator of frailty in this sample (**Table 3**). The predictive value of the single traits in predicting the Fried frailty phenotype ranged from 12.5% to 52.5%, suggesting a large number of false positives. All possible dual-trait combinations were tested in this population (data not shown); of these, gait speed and hand-grip strength yielded the most precise results. When gait speed and hand-grip strength were combined as a dual measure, the positive predictive value increased to 87.5%.

DISCUSSION

This study found that while use of either gait speed or grip strength alone was sensitive and specific as a proxy for the Fried frailty phenotype, the dual-trait measure of gait speed *with* grip strength was accurate, precise, specific, and more sensitive than individual traits and other possible dual-factor combinations. To our knowledge, this is the first study to empirically examine the accuracy and precision of the individual Fried phenotype elements as a proxy for the original Fried frailty phenotype

Table 3. Diagnostic accuracy of frailty markers

FRAILTY-DEFINING CRITERION	SENSITIVITY, % (95% CI)	SPECIFICITY, % (95% CI)	POSITIVE PREDICTIVE VALUE, % (95% CI)	ACCURACY, % (95% CI)	POSITIVE LIKELIHOOD RATIO (95% CI)
Individual markers					
• Gait speed	87.5 (66.5-96.7)	94.6 (91.6-96.7)	52.5 (36.3-68.1)	94.2 (91.2-96.3)	16.2 (10.3-26.0)
• Grip strength	100.0 (83.4-100.0)	90.5 (86.9-93.2)	42.4 (29.8-55.9)	91.1 (87.7-93.6)	10.5 (7.6-14.5)
• Low exercise	100.0 (83.4-100.0)	86.0 (81.9-89.3)	33.3 (23.1-45.2)	86.9 (83.0-90.0)	7.1 (5.5-9.2)
• Weight loss	8.3 (0.4-40.2)	97.4 (94.4-98.8)	12.5 (0.7-53.3)	93.5 (90.0-96.0)	3.2 (0.4-23.6)
• Exhaustion	81.8 (47.8-96.8)	90.4 (85.2-94.0)	32.1 (16.6-52.4)	90.0 (84.9-93.5)	8.5 (5.1-14.2)
Combined markers					
• Gait speed and grip strength	87.5 (66.5-96.7)	99.2 (97.3-99.8)	87.5 (66.5-96.7)	98.4 (96.4-99.4)	103.5 (33.2-322.7)

in a primary care setting. A recent systematic review concluded that in predicting risk of adverse outcomes, use of gait-speed measurements alone was as good as use of other composite tools and that there was sufficient evidence to support the use of gait speed as a single-item assessment tool for screening for frailty in community-dwelling older adults.[23] The intent of finding a single-trait marker for frailty is predicated on the desire for a rapid assessment tool without a substantial loss of diagnostic accuracy. However, if intended as a proxy for the Fried frailty phenotype, then one must consider the positive predictive value of the tests. Other researchers[15] have corroborated our finding that single-trait markers of frailty have moderate to low predictive value; that is, they produce too many false positives. In our study, gait speed alone identified greater than 60% more patients as frail compared with using both gait speed and hand-grip strength. In clinical practice, this is an important consideration because identifying a patient as frail can initiate a cascade of investigations and follow-up testing that can be both time-consuming and intensive.[34]

Screening for all 5 frailty markers within primary care practice might be impractical and a barrier to widespread frailty screening. As a proxy measure of the Fried frailty phenotype, we suggest that adding grip strength to gait speed would substantially increase the precision of screening without a large additional investment of time, training, or cost.[29] This is feasible, as the required time for a nurse to measure gait speed is estimated to be less than 5 minutes, and measuring grip strength using a dynamometer takes approximately 2 minutes. Dynamometer use requires minimal staff training, and the cost is relatively affordable for most medical practices. With substantially reduced false positives, the potential benefits for patients associated with identifying and managing frailty and reducing adverse outcomes through proactive interventions might be important enough to justify the time and resource investments required for assessing gait speed and grip strength in seniors.

In primary care practice, recognition of frailty offers the opportunity to identify and optimize the management of coexisting conditions that might contribute to, or be affected by, frailty and to mitigate stressors that might precipitate adverse outcomes. Management of frail seniors might include medication review[35]; more frequent outpatient visits with the primary care physician[36,37]; exercise interventions for strength, endurance, and balance training[18,38]; and informed discussion about risks associated with surgical procedures.[39] Because frailty is a predictor of survival,[10] identification of frailty might help to determine the appropriateness of preventive interventions that require years for benefit, helping physicians to individualize goals of care for their geriatric patients or refer them for specialized assessment.[40] Future studies will be aimed at examining clinical outcomes associated with identifying frailty using this dual-trait measure of gait speed with grip strength.

Limitations

Our study population was older than that studied by Fried and colleagues[5] (100% vs 33% 75 years of age or older) and had a lower prevalence of frailty (6.5% vs 13%), which might indicate population differences beyond that of age; this is likely affected by slightly different cutoffs for the lowest quintiles for measuring some criteria. Compared with Fried and colleagues' study[5] there were some differences in the measurement of the frailty criteria; however, we do not expect these differences to affect the results greatly. Slight differences in the measurement of these frailty criteria are prevalent in the published literature.

Data from 133 out of 516 patients (25.8%) were removed from further analysis because they were missing 1 or more Fried criteria measures, usually exhaustion, as this was added during the course of the study to allow us to make comparisons with the Fried frailty criteria. Patients whose data were removed were significantly more likely to be female ($P = .02$) and older ($P = .003$ for women, $P = .04$ for men) than the patients

who were left in the study. However, we believe the significance of our findings is unaffected because cutoffs for gait speed and grip strength were calculated based on the entire sample of 516 patients, so the determination of frailty markers is unaffected by removing part of the sample, particularly as the patients who were removed from the study tended to be missing exhaustion or weight-loss assessments; more than 84% of the 133 people who were removed had both gait-speed and grip-strength measurements.

During the study time frame of 13 months, 516 of the 1291 patients identified in this medical practice as being 75 years of age or older underwent screening. It is possible that this might have affected the frailty prevalence rate, as those who did not visit their family physicians during the study time period might have been either too frail to visit the clinic or too well to schedule a visit with their family physicians. Further, some of the screening items rely on self-reporting, and it is possible responses to these questions might have been affected by unrecognized cognitive impairment in this population.

Conclusion

Despite its limitations, this study contributes to knowledge about frailty measures that might be feasibly administered in primary care settings. Although single-trait measures of gait speed or grip strength alone were found to be sensitive and specific as proxies for the Fried frailty phenotype, use of gait speed with grip strength was found to be accurate, precise, specific, and more sensitive than other possible combinations. Future studies aimed at identifying frailty in seniors based on Fried frailty phenotype criteria might consider using gait speed with grip strength as a feasible means of identifying this condition within primary care settings.

Dr Lee is a family physician with the Centre for Family Medicine Family Health Team (CFFM FHT) in Kitchener, Ont, Schlegel Research Chair in Primary Care for Elders at the Schlegel-UW Research Institute for Aging, and Associate Clinical Professor in the Department of Family Medicine at McMaster University in Hamilton, Ont. **Dr Patel** is a pharmacist with the CFFM FHT and Assistant Clinical Professor at the University of Waterloo School of Pharmacy. **Dr Costa** is Schlegel Research Chair in Clinical Epidemiology and Aging and Assistant Professor in the Department of Clinical Epidemiology and Biostatistics and the Department of Medicine at McMaster University. **Dr Bryce** is a research manager with the Department of Health, Aging, and Society at McMaster University. **Ms Hillier** is a research associate with Specialized Geriatric Services at St Joseph's Health Care London and the Aging, Rehabilitation and Geriatric Care Research Centre of the Lawson Health Research Institute in London, Ont. **Dr Slonim** is a research associate with the CFFM FHT. **Dr Hunter** is Assistant Professor in the School of Physical Therapy at Western University in London. **Dr Heckman** is Schlegel Research Chair in Geriatric Medicine, Associate Professor in the Faculty of Applied Health Sciences in the School of Public Health and Health Systems at the University of Waterloo, and Assistant Clinical Professor of Medicine at McMaster University. **Dr Molnar** is a geriatrician in Ottawa, Ont, Medical Director of the Regional Geriatric Program of Eastern Ontario, and Associate Professor in the Department of Medicine at the University of Ottawa.

Acknowledgment

This work was supported by the Centre for Family Medicine Family Health Team, the Ontario Ministry of Health and Long-Term Care and Ontario Medical Association Medically Complex Patient Demonstration Project, and the Canadian Mental Health Association Waterloo Wellington Dufferin. We thank **Veronique Boscart** and **Niraj Maulkhan** for their contributions to this study.

Contributors

Drs Lee and **Patel** contributed to the study concept and design; data analysis, review, and interpretation; and final manuscript preparation and approval. **Dr Costa** contributed to the study concept and design, data analysis and interpretation, and final manuscript preparation and approval. **Dr Bryce** and **Ms Hillier** contributed to data analysis and interpretation, and final manuscript preparation and approval. **Drs Slonim, Hunter, Heckman,** and **Molnar** contributed to the study concept and design, data analysis and interpretation, and final manuscript preparation and approval.

Competing interests

None declared

Correspondence

Dr Linda Lee; e-mail **lee.linda.lw@gmail.com**

References

1. Xue QL. The frailty syndrome: definition and natural history. *Clin Geriatr Med* 2011;27(1):1-15.
2. Bergman H, Ferrucci L, Guralnik J, Hogan DB, Hummel S, Karunananthan S, et al. Frailty: an emerging research and clinical paradigm—issues and controversies. *J Gerontol A Biol Sci Med Sci* 2007;62(7):731-7.
3. Gill TM, Gahbauer EA, Allore HG, Han L. Transitions between frailty states among community-living older persons. *Arch Intern Med* 2006;166(4):418-23.
4. Martin FC, Brighton P. Frailty: different tools for different purposes? *Age Ageing* 2008;37(2):129-31.
5. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M146-56.
6. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 2004;59(3):255-63.
7. McNallan SM, Singh M, Chamberlain AM, Kane RL, Dunlay SM, Redfield MM, et al. Frailty and healthcare utilization among patients with heart failure in the community. *JACC Heart Fail* 2013;1(2):135-41.
8. Farhat JS, Velanovich V, Falvo AJ, Horst HM, Swartz A, Patton JH Jr, et al. Are the frail destined to fail? Frailty index as a predictor of surgical morbidity and mortality in the elderly. *J Trauma Acute Care Surg* 2012;72(6):1526-30.
9. Afilalo J, Eisenberg MJ, Morin JF, Bergman H, Monette J, Noiseux N, et al. Gait speed as an incremental predictor of mortality and major morbidity in elderly patients undergoing cardiac surgery. *J Am Coll Cardiol* 2010;56(20):1668-76.
10. Mitnitski AB, Mogilner AJ, MacKnight C, Rockwood K. The mortality rate as a function of accumulated deficits in a frailty index. *Mech Ageing Dev* 2002;123(11):1457-60.
11. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005;173(5):489-95.
12. Bouillon K, Kivimaki M, Hamer M, Sabia S, Fransson EI, Singh-Manoux A, et al. Measures of frailty in population-based studies: an overview. *BMC Geriatr* 2013;13:64.
13. De Vries NM, Staal JB, van Ravensberg CD, Hobbelen JS, Rikkert MG, Nijhuis-van der Sanden MW. Outcome instruments to measure frailty: a systematic review. *Ageing Res Rev* 2011;10(1):104-14. Epub 2010 Sep 17.
14. Pialoux T, Goyard J, Lesourd B. Screening tools for frailty in primary health care: a systematic review. *Geriatr Gerontol Int* 2012;12(2):189-97. Epub 2012 Jan 10.
15. Clegg A, Rogers L, Young J. Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: a systematic review. *Age Ageing* 2015;44(1):148-52. Epub 2014 Oct 29.
16. Singer JP, Diamond JM, Gries CJ, McDonnough J, Blanc PD, Shah R, et al. Frailty phenotypes, disability, and outcomes in adult candidates for lung transplantation. *Am J Respir Crit Care Med* 2015;192(11):1325-34.
17. McAdams-DeMarco MA, Tan J, Salter ML, Gross A, Meoni LA, Jaar BG, et al. Frailty and cognitive function in incident hemodialysis patients. *Clin J Am Soc Nephrol* 2015;10(12):2181-9. Epub 2015 Nov 16.
18. Theou O, Stathokostas L, Roland KP, Jakobi JM, Patterson C, Vandervoort AA, et al. The effectiveness of exercise interventions for the management of frailty: a systematic review. *J Aging Res* 2011;2011:569194.
19. Ng TP, Feng L, Nyunt MS, Feng L, Niti M, Tan BY, et al. Nutritional, physical, cognitive, and combination interventions and frailty reversal among older adults: a randomized controlled trial. *Am J Med* 2015;128(11):1225-36.e1. Epub 2015 Jul 6.
20. Yaffe K, Falvey CM, Hamilton N, Harris TB, Simonsick EM, Strotmeyer ES, et al. Association between hypoglycemia and dementia in a biracial cohort of older adults with diabetes mellitus. *JAMA Intern Med* 2013;173(14):1300-6.
21. Liu H, Gao S, Hall KS, Unverzagt FW, Lane KA, Callahan CM, et al. Optimal blood pressure for cognitive function: findings from an elderly African-American cohort study. *J Am Geriatr Soc* 2013;61(6):875-81. Epub 2013 May 6.
22. Abellan van Kan G, Rolland Y, Houles M, Gillette-Guyonnet S, Soto M, Vellas B. The assessment of frailty in older adults. *Clin Geriatr Med* 2010;26(2):275-86.
23. Abellan van Kan G, Rolland Y, Andrieu S, Bauer J, Beauchet O, Bonnefoy M, et al. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force. *J Nutr Health Aging* 2009;13(10):881-9.

24. Rothman MD, Leo-Summers L, Gill TM. Prognostic significance of potential frailty criteria. *J Am Geriatr Soc* 2008;56(12):2211-6.
25. Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum A Jr, Orlandini A, et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet* 2015;386(9990):266-73. Epub 2015 May 13.
26. Di Bari M, Profili F, Bandinelli S, Salvioni A, Mossello E, Corridori C, et al. Screening for frailty in older adults using a postal questionnaire: rationale, methods, and instruments validation of the INTER-FRAIL study. *J Am Geriatr Soc* 2014;62(10):1933-7. Epub 2014 Oct 3.
27. Saum KU, Muller H, Stegmaier C, Hauer K, Raum E, Brenner H. Development and evaluation of a modification of the Fried frailty criteria using population-independent cutpoints. *J Am Geriatr Soc* 2012;60(11):2110-5. Epub 2012 Oct 8.
28. Kooij KW, Wit FW, Schouten J, van de Valk M, Godfried MH, Stolte IG, et al. HIV infection is independently associated with frailty in middle-aged HIV type 1-infected individuals compared with similar but uninfected controls. *AIDS* 2016;30(2):241-50.
29. Karpman C, Benzo R. Gait speed as a measure of functional status in COPD patients. *Int J Chron Obstruct Pulmon Dis* 2014;9:1315-20.
30. Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1977;1(3):385-401.
31. Topolski TD, LoGerfo J, Patrick DL, Williams B, Walwick J, Patrick MB. The Rapid Assessment of Physical Activity (RAPA) among older adults. *Prev Chronic Dis* 2006;3(4):A118. Epub 2006 Sep 15.
32. Auyeung TW, Lee JS, Leung J, Kwok T, Woo J. The selection of a screening test for frailty identification in community dwelling older adults. *J Nutr Health Aging* 2014;18(2):199-203.
33. Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. *Stat Med* 1998;17(8):857-72.
34. Aminzadeh F, Dalziel WB, Molnar FJ. Targeting frail older adults for outpatient comprehensive geriatric assessment and management services: an overview of concepts and criteria. *Rev Clin Gerontol* 2002;12(1):82-92.
35. Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Cumming RG, Handelsman DJ, et al. High-risk prescribing and incidence of frailty among older community-dwelling men. *Clin Pharmacol Ther* 2012;91(3):521-8. Epub 2012 Feb 1.
36. Pugh JA, Wang CP, Espinoza SE, Noel PH, Bollinger M, Amuan M, et al. Influence of frailty-related diagnoses, high-risk prescribing in elderly adults, and primary care use on readmissions in fewer than 30 days for veterans aged 65 and older. *J Am Geriatr Soc* 2014;62(2):291-8. Epub 2014 Jan 21.
37. Bennett A, Gnjidic D, Gillett M, Carroll P, Matthews S, Johnell K, et al. Prevalence and impact of fall-risk-increasing drugs, polypharmacy, and drug-drug interactions in robust versus frail hospitalised falls patients: a prospective cohort study. *Drugs Aging* 2014;31(3):225-32.
38. Cadore EL, Rodríguez-Mañas L, Sinclair A, Izquierdo M. Effects of different exercise interventions on risk of falls, gait ability, and balance in physically frail older adults: a systematic review. *Rejuvenation Res* 2013;16(2):105-14.
39. Hubbard RE, Story DA. Patient frailty: the elephant in the operating room. *Anaesthesia* 2014;69(Suppl 1):26-34.
40. Heckman GA, Molnar FJ, Lee L. Geriatric medicine leadership of health care transformation: to be or not to be? *Can Geriatr J* 2013;16(4):192-5.