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PERMANYER

Rev Inves Clin. 2016;68:92-8

ORIGINAL ARTICLE

Predictive Value of Frailty Indices for Adverse Outcomes in Older Adults

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ABSTRACT

Background: There are two widely used tools to classify frailty in older adults: the frailty phenotype and the frailty index. Both have been validated for prediction of adverse outcomes. **Objective:** To assess the ability of different frailty indices to predict a number of adverse outcomes (falls, disability, and mortality) by adding deficits in a fixed sequence (with the first five deficits as in the frailty phenotype: weakness, weight loss, slowness, exhaustion and low physical activity) or randomly. **Methods:** This is an analysis of the Costa-Rican Longevity and Healthy Aging Study in which ≥ 60-year-old adults were included and followed up for four years. Frailty indices were constructed, including the frailty phenotype components in the first five indices followed by the random addition of other deficits and estimating for each one the odds ratios for falls and disability and hazard ratios for mortality, adjusted for age and sex. **Results:** We included 2,708 adults; mean age was 76.31 years, 54.28% were women. Indices with the highest number of deficits had the highest estimates for each adverse outcome, independent of the deficit. **Conclusion:** The higher the number of deficits in an index, the higher the estimates for adverse outcomes, independent of the type of deficit added. (REV INVES CLIN. 2016;68:92-8)

Key words: Frail elder adult. Aged. Accidental falls. Disability. Aging epidemiology.

INTRODUCTION

The way individuals age has been the main concern of geriatric medicine in recent years, focusing in particular on the identification of those in whom aging could be considered "pathologic" and are at a higher risk of adverse outcomes (e.g., falls, disability, institutionalization, mortality)[1,2]. Frailty is defined as a loss of the ability to face stressors (internal and external) leading to a longer recovery or transition to a worse health status (e.g., from independence to dependence)[3,4]. Currently, there are a number of scales for the classification of frailty in older adults, with different sets of items and scoring systems and mainly validated by their ability to predict adverse outcomes[5,6]. In fact, there is a substantial heterogeneity within and between tools[7,8], not only in the items they include but also in the scoring system (e.g., some items have higher weights than others)[9-12]. A recent systematic review showed how this heterogeneity results in a wide range of prevalence between studies[13].

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Received for publication: 21-10-2015
Accepted for publication: 18-12-2015

In this context, there is still no agreement on which is the best tool to measure frailty[1,4].

Two main tools to consider an older adult as frail are currently in use in clinical and research settings: the frailty index and the frailty phenotype. The frailty index quantifies a predetermined set of deficits for a given population, with the particular feature of having an arithmetic model base (e.g., arithmetical accumulation of deficits)[14-16]. It has been widely validated in different settings for predicting adverse outcomes[3,7,8]. On the other hand, the frailty phenotype relies on the measurement of five items: gait speed, handgrip strength, physical activity, exhaustion, and weight loss. An older adult that has at least three of the five items is considered to be frail[4]. Different studies also validated this index to predict adverse outcomes.

Our hypothesis is that the items on the frailty phenotype could be taken as deficits in a frailty index; however, when doing this, the higher the number of deficits included in the frailty index will have the highest risk estimates of adverse outcomes, independent of which deficit is added. Therefore, the aim of this study is to assess the ability of different frailty indices to predict a number of adverse outcomes (falls, disability, and mortality) by adding deficits in a fixed sequence (with the first five deficits as in the frailty phenotype: weakness, weight loss, slowness, exhaustion, and low physical activity) or randomly.

MATERIAL AND METHODS

Design and setting

This is a secondary longitudinal analysis of the Costa-Rican Longevity and Healthy Aging Study (CRELES). It is a publicly available dataset of Costa Rican older adults born in or before 1946; it included a representative sample (stratified two-stage probabilistic) of ≥ 60-year-old adults from Costa Rica. A full description of sampling methods and objectives may be found elsewhere[17]. Briefly, this study has three waves in which face-to-face interviews are conducted by trained and standardized staff at the homes of older adults, including in-depth data on demographics, current activities, health-related issues, social support, healthcare use, financial status, functionality, cognitive status, anthropometry, and blood sampling. For the purpose of this report, data from the first (2005) and third (2009) waves were used. Both interviews assessed the same information, with the exception of mortality data in 2009, including a next-of-kin interview for the deceased participants.

Adverse outcomes (dependent variables)

We selected three adverse outcomes to test the predictive ability of the frailty indices: mortality, disability, and falls. As previously mentioned, survival status was obtained from next of kin, and the date of death was recorded to estimate the time (days) to death in the survival analysis (see below). Falls were assessed with the question: "Have you fallen down in the last two years?" If the answer was "yes", the outcome was present. According to the World Report on Disability by the WHO, disability was defined as the "umbrella term for impairments, activity limitations, and participation restrictions". It was operationalized as having incident difficulty in any activity of daily living (from a list of six activities: walking in a room, bathing, eating, moving in and out from bed, toileting, dressing) present in the third wave and absent in the first wave.

Frailty index

As stated previously, 38 deficits were included in the frailty indices: exhaustion, weight loss, low physical activity, slowness, weakness, cognitive decline, spirometry, calf circumference, endurance, reaching test, number of persons living in the same household, self-rated health, hypertension, hypercholesterolemia, diabetes mellitus, cancer, lung disease, heart attack, heart failure, stroke, articular disease, osteoporosis, bone fracture, self-rated vision, self-rated hearing, edentulous, life satisfaction, swelling feet, dizziness, urinary and fecal incontinence, locus of control, self-rated financial status, exercise, recent accident, childhood poverty, self-rated health in childhood, number of hospital days in the last year, and number of currently used drugs. Complete description and scoring of the variables is shown in table 1. Scoring of individual items was rescaled to 0 (absent deficit) or 1 (present deficit), with some items having intermediate scores (e.g., 0.25-0.5-0.75-1). Each item score was added and then divided by 38 to have an overall index score also from 0 (no deficit present) to 1 (all deficits present).

To test our hypothesis, a total of 190 (5 × 38) frailty indices were integrated to be used as independent variables in the regression models and estimate increasing

Table 1. Description of the deficits included in the Frailty Index

Deficit	Definition	Descriptive statistics, n (%)
Exhaustion, n (%)	In the last 12 months, have you had severe fatigue or exhaustion?	1,106 (40.92)
Weight loss, n (%)	In the last 6 months, have you lost 5 or more kilograms unintentionally?	273 (10.98)
Low physical activity, n (%)	Lowest quintile of hours of physical activity of its group by sex	714 (26.37)
Slowness, n (%)	Lowest quintile of gait speed of its group by sex and height	566 (20.9)
Weakness, n (%)	Lowest quintile of handgrip strength of its group by sex and body mass index quartile	561 (20.72)
Cognitive decline, n (%)	Answering less than 75% of the items correctly from a modified version of the MMSE	557 (20.17)
Spirometry in l/min, mean (SD)		202.84 (133.4)
Calf circumference in centimeters, mean (SD)		32.54 (4.23)
Endurance in seconds, mean (SD)	Time to stand up five times from a chair	13.59 (4.72)
Reaching in centimeters, mean (SD)	From a standing position, reach for a pencil on the floor	1.9 (2.53)
Number of persons living with the older adult, median (IQR)	How many persons live in this household?	2 (0-20)
Fair or poor self-rated health, n (%)	How would you rate your health today?	1,366 (50.44)
Hypertension, n (%)	Has a physician ever told you that you have high blood pressure?	1,329 (49.3)
Hypercholesterolemia, n (%)	Has a physician ever told you that you have high cholesterol levels?	937 (35.12)
Diabetes mellitus, n (%)	Has a physician ever told you that you have diabetes (high blood sugar levels)?	523 (19.4)
Cancer, n (%)	Has a physician ever told you that you had cancer or a tumor, excluding small skin tumors?	183 (6.8)
Lung diseases, n (%)	Has a physician ever told you that you have any lung disease such as emphysema, chronic bronchitis, tuberculosis, or asthma?	486 (18.09)
Heart attack, n (%)	Has a physician ever told you that you had a heart attack or infarction?	146 (5.41)
Heart failure, n (%)	Has a physician ever told you that you have heart failure?	371 (13.81)
Stroke, n (%)	Has a physician ever told you that you had a stroke?	146 (5.41)
Articular diseases, n (%)	Has a physician ever told you that you had any articular disease?	446 (16.68)
Osteoporosis, n (%)	Has a physician ever told you that you have osteoporosis?	256 (9.63)
Bone fracture, n (%)	Have you had a bone fracture after your 60th birthday?	462 (17.1)
Self-rated vision, median (IQR)	Rate how good is your vision from one to seven (seven is better)	5.5 (1-7)
Self-rated hearing, median (IQR)	Rate how good is your hearing ability from one to seven (seven is better)	6 (1-7)
Edentulous, n (%)	More than half of the teeth missing	2,349 (86.74)
Not satisfied with life, n (%)	In general, how do you feel with your life?	206 (10.11)
Swelling feet, n (%)	In the last 12 months, have you had swelling feet?	851 (31.45)
Dizziness, n (%)	In the last 12 months, have you had dizziness?	1,034 (38.32)
Urinary incontinence, n (%)	In the last 12 months, have you had involuntary urinary loss?	544 (20.13)
Fecal incontinence, n (%)	In the last 12 months, have you had involuntary fecal loss?	123 (4.55)
Locus of control score, median (IQR)	Set of seven questions exploring health-related locus of control	22 (0-32)
Low self-rated financial status, n (%)	How would you rate your current financial status?	1,643 (60.9)
Not exercised, n (%)	In the last 12 months, have you regularly exercised or done moderate physical activity such as running, biking, or hard work at least 3 days a week?	2,054 (75.91)
Recent accident, n (%)	In the last 10 years, have you suffered from any car accident?	133 (4.82)
Childhood poverty, n (%)	During the first 15 years of your childhood, did your family have economic trouble that prevented you from eating, dressing, or receiving healthcare appropriately?	1,160 (42)
Fair or poor childhood self-rated health, n (%)	How was your health most of the time during your childhood?	173 (6.26)
Hospital days, median (IQR)	How many days were you hospitalized in the last 12 months?	0 (0-200
Drugs, median (IQR)	Number of medications being taken	3 (0-17)

MMSE: Mini-Mental State Examination; SD: standard deviation; IQR: interquartile range.

hazard ratios (HR) for mortality or odds ratio (OR) for falls and disability. The first five indices corresponded to the items of the frailty phenotype, added one by one as follows: weakness, slowness, weight loss, exhaustion, and low physical activity. In the rest of the indices, the variables were added randomly using four different lists of random numbers. For example, for the re-scaled frailty phenotype, the frailty index (FI) was determined as follows: FI = weakness + slowness + weight loss + exhaustion + low physical activity/5; then, the rest of the deficits was randomly added. This procedure was repeated four times; however, as stated previously, only the first five deficits were constant, and from there on, deficits were randomly added.

Statistical analysis

We used descriptive statistics to analyze the variables included in the frailty index, as well as age, sex, and adverse outcomes (falls, disability, and mortality). Each adverse outcome was sequentially used as the dependent variable in logistic multiple regression models for falls and disability, and Cox regression models for mortality. Effects estimates and their 95% confidence intervals (CI) were determined for each adverse outcome and for each of the 190 indices; all models were adjusted for sex and age. Estimates were plotted against the number of deficits for each of the 190 indices and for each adverse outcome. Pearson correlation between the estimates and the frailty indices was also calculated. A statistical significance < 0.05 was considered significant. All analyses were made using STATA 14, and plots were done in Excel 2016.

Ethical considerations

The CRELES was approved by the Ethical Science Committee of the University of Costa Rica (VI-763-CEC-23-04), research project number 828-A2-825. All subjects signed informed consent, and all procedures of the study are according to the last version of Helsinki declaration. In addition, the secondary analysis of this report was registered in the National Institute of Geriatrics of Mexico.

RESULTS

There were 2,708 older adults included; mean age was 76.31 years (± standard deviation [SD] 10.19) and 54.28% were women (n = 1,470). Participants lost to follow-up (n = 419, 15.17%) were significantly younger (73.88 vs. 76.69 years; p < 0.001), were not different in distribution by sex, and had a significantly lower frailty index score (0.243 vs. 0.26; p = 0.004). During follow-up, 531 (19.6%) participants died, 816 (44.32%) had at least one fall, and incident disability was present in 997 (54.1%).

The mean score of the complete frailty index (38 items) was 0.257 (± SD 0.08), with the lowest score being 0.054 and the highest, 0.579. The median was 0.254, the 25th percentile was 0.2, and the 75th percentile, 0.31. The deficit with the highest proportion was having more than half of the teeth missing (edentulous) (n = 2,349, 86.74%), and the lowest for fecal incontinence 4.55% (n = 123). The rest of the deficits are described in table 1.

Regarding mortality, the lowest adjusted HR was found with the lowest number of deficits, independent of the initial deficit; the same occurred with the highest HR, which ranged from 1.01 with one deficit, to 49.17 with all deficits present. The correlation for all the scores was positive and significant, ranging from 0.89 to 0.977 (Fig. 1).

For falls, the lowest OR (1.11) resulted when only one deficit was added to the score, while the OR was 74.12 when all the deficits were present. The correlation for all the scores was positive and significant, ranging from 0.935 to 0.978 (Fig. 2).

Finally, incident or worsening disability also had the lowest estimates when only one deficit was present (OR 1.28) and the highest when all the deficits were present (11.78). The correlation for all the scores was positive and significant, ranging from 0.878 to 0.967 (Fig. 3).

DISCUSSION

According to our results, the deficit-accumulation frailty index seems to be valid in Costa Rican older adults, and when the elements of the frailty phenotype were taken as deficits, there was no difference in risk estimate of adverse outcomes when compared to randomly assembled frailty indices: the higher the number of deficits, the higher the estimates of risk[19]. It has been

Figure 1. Increasing hazard ratios for mortality adjusted for age and sex by adding deficits to the frailty index, either with the first five deficits fixed, as in the frailty phenotype, or in a random sequence.

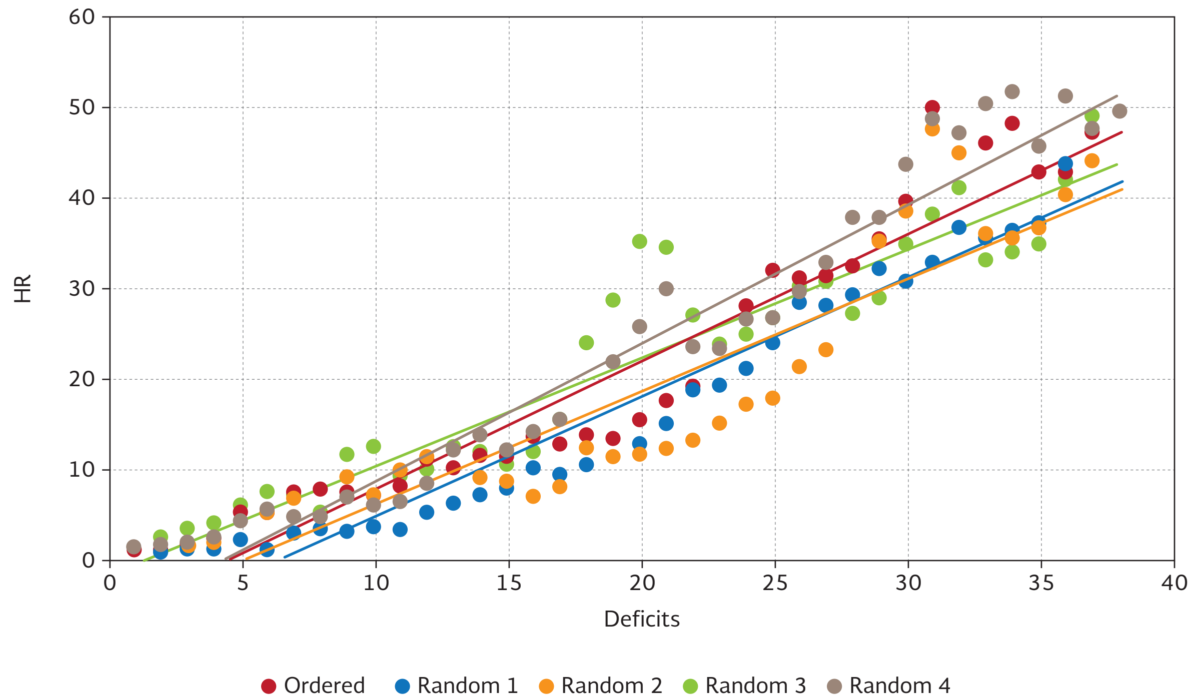


Figure 2. Increasing odds ratio for falls adjusted for age and sex by adding deficits to the frailty index, either arranged as in the frailty phenotype or randomly.

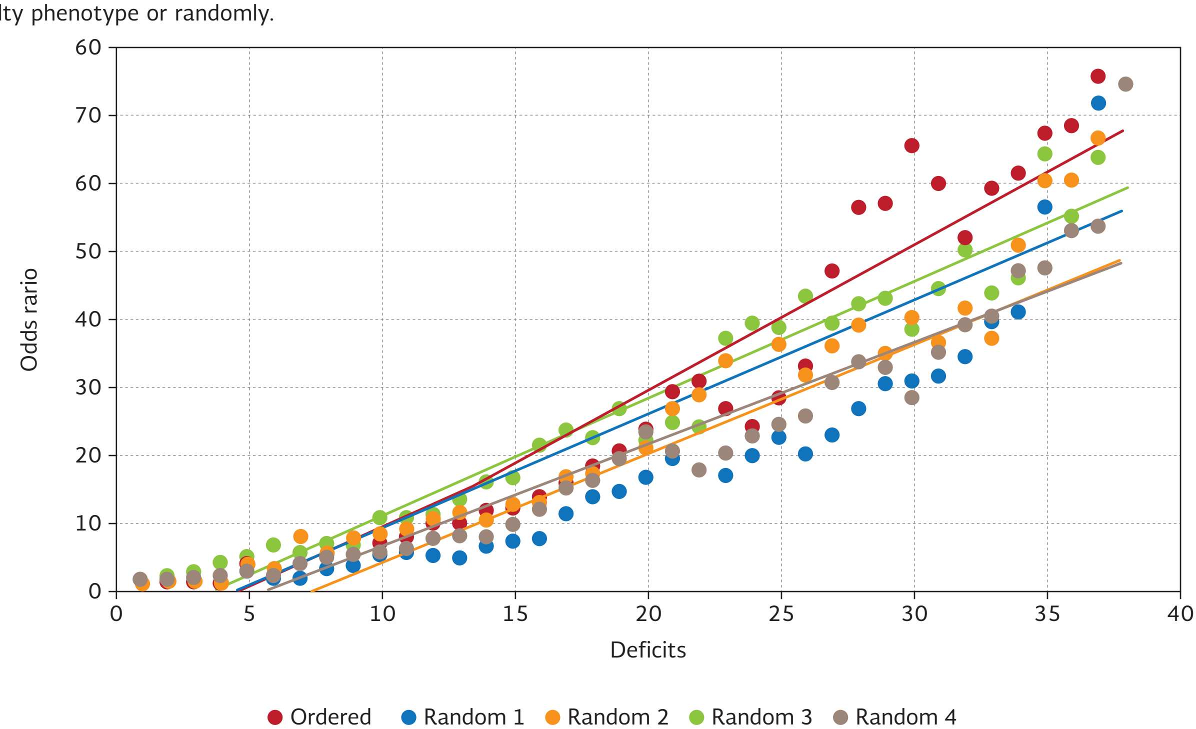
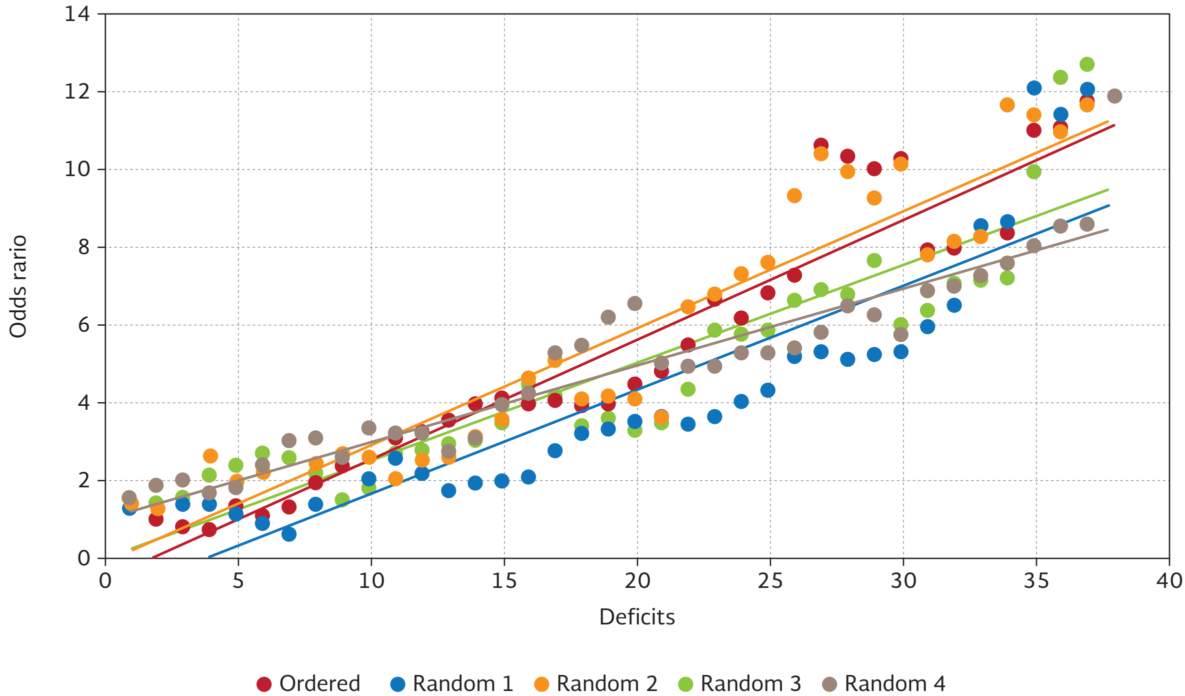


Figure 3. Increasing odds ratio for disability adjusted for age and sex by adding deficits to the frailty index, either arranged as in the frailty phenotype or randomly.



demonstrated that there is an exponential relationship between the number of deficits and death, independent of how the deficits are added[20], and this was also our finding. This may be the same reason why, when adding other items/dominions to the frailty phenotype or other instruments, the estimates of risk of death (or other adverse outcomes) are higher than when considering the phenotype only[21]. The incremental risk of death as the number of deficits increased was also seen in regards to falls and disability, where the OR increased as more deficits were added to the index, resulting in high correlations (> 0.98). Fang, et al. had a similar finding regarding falls and the frailty index, although in their work they did not report data on the linear association between risk of falling and the number of deficits[22]. On the other hand, the frailty index has shown to be predictive of disability in older adults, although an incremental relationship between the number of deficits and the risk has not been described previously[23].

Even though the frailty index and the phenotype may be used for different purposes, our results show that they may not be so unlike, and the integration of both (and any other) into one single tool may be a robust and definitive way of measuring frailty[24,25]. Another feature of the index is its flexibility so that it may be used in almost any setting, including intensive care units, as recently reported[26]. Bearing in mind that the performance of the index (or any other tool) may improve by increasing the number of deficits tested could aid in generalizing and comparing results of multiple studies, considering the number of items included[18].

Although far from being perfect, this index proved useful in this study to solve at least two problems when measuring frailty. The first one is by reducing the weight of a single parameter in its contribution to the overall score of the frailty index. The second is the possibility of computing the frailty index without a predetermined set of variables, but instead basing it on a sufficient amount of heterogeneous information. This feature is of particular interest in the clinical setting where indices could be easily derived from medical records, as previously shown by Jones, et al.[27].

To our knowledge, this is the second report on validation of the frailty index in Latin American older adults and the first in older adults from Costa Rica. The first report on validation of the index and its ability to predict mortality was on Mexican older adults[28]. In addition, our results provide new evidence on the application of the deficit-accumulation hypothesis in a wide variety of populations and settings.

The number of participants lost to follow-up is one of the main flaws of our study. However, this number was similar to the number of subjects available until the end of the study. The variables we included in the frailty index are not the "classical" ones; we decided to include factors related with social vulnerability and early life experiences to reflect the multidimensional nature of the index.

Further research should aim to implement different indices and to explore how deficits interact and in which way they can provide useful clinical information to help define a problem and intervene in consequence. Meanwhile, the frailty index seems to have advantages over other tools used for frailty detection.

ACKNOWLEDGMENTS

M.U.P.-Z. received support from Instituto Nacional de Geriatría (Mexico), Gérontopôle /Université Toulouse III Paul Sabatier (France), CONACyT (Mexico) (grant number [CB-2011-01-167441]), and Universidad Nacional Autónoma de México (UNAM) to develop this work.

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