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HDL-cholesterol and physical performance: results from the ageing and longevity study in the sirente geographic area (*ilSIRENTE* Study)

Francesco Landi[1], Andrea Russo[1], Matteo Cesari[2], Marco Pahor[2,3], Roberto Bernabei[1], Graziano Onder[1]

[1]Department of Gerontology, Geriatrics and Physiatry, Catholic University of Sacred Heart, Roma, Italy
[2]Department of Aging and Geriatric Research, University of Florida—College of Medicine, Gainesville, FL, USA
[3]Geriatric Research, Education and Clinical Center (GRECC), Malcom Randall Veteran's Affairs Medical Center, North Florida/South Georgia Veterans Health System, Gainesville, FL, USA

Address correspondence to: Francesco Landi. Email: francesco_landi@rm.unicatt.it

Abstract

Background high-density lipoprotein (HDL) cholesterol has been hypothesised to be a reliable marker of frailty and poor prognosis among the oldest elderly. We evaluate the relationship of HDL-cholesterol with measures of physical performance, muscle strength, and functional status in older persons aged 80 years or older.

Methods data are from baseline evaluation of the ageing and longevity study in the Sirente geographic area (ilSIRENTE study) ($n = 364$). Physical performance was assessed using the physical performance battery score [short physical performance battery (SPPB)], which is based on three-timed tests: 4-m walking-speed, balance, and chair-stand tests. Muscle strength was measured by hand-grip strength. Analyses of covariance were performed to evaluate the relationship of different HDL-cholesterol levels with physical function.

Results in the unadjusted analyses, physical function (as measured by the 4-m walking-speed, theSPPB score, the basic and instrumental activities of daily living scales scores), but not hand-grip strength, improved significantly as HDL-cholesterol tertiles increased. After adjustment for potential confounders, which included age, gender, living alone, alcohol abuse, physical activity, congestive heart failure, diabetes, cerebrovascular diseases, osteoarthritis, albumin, urea, C-reactive protein and LDL cholesterol, the association of HDL-cholesterol tertiles with the 4-m walking-speed and the SPPB score was still consistent.

Conclusion the present study suggests that among very old subjects living in the community the higher levels of HDL-cholesterol are associated with better functional performance.

Keywords: *HDL-cholesterol, physical performance, frail, elderly*

Introduction

Functional disability has been demonstrated to be more prevalent among older subjects with multiple chronic diseases [1–3]. High-density lipoprotein (HDL) cholesterol has been hypothesised to be a reliable marker of frailty and poor prognosis among the oldest elderly [4]. Numerous studies have demonstrated the importance of obesity and dyslipidaemia as risk factors for vascular events, especially in the oldest population. Serum cholesterol concentration is associated with mobility-reducing diseases such as stroke, heart disease, osteoarthritis and lower-extremity arterial diseases [5–8]. However, most of these studies have considered only body mass index (BMI) or total serum cholesterol concentration. More recently, some authors have shown that other lipid variables, such as serum triglycerides and HDL-cholesterol, may play a role in predicting the risks of vascular disease and mortality [9, 10].

Despite the growing importance of physical performance and cholesterol metabolism in older persons, there is still a lack of information explaining whether and how they are related to each other. In the present study, we evaluate the relationship of HDL-cholesterol with measures of physical performance [4-m walking test, short physical performance battery (SPPB)], muscle strength (hand-grip strength), and functional status [basic and instrumental activities of daily living (IADL)] in older persons aged 80 years or older enrolled in the 'invecchiamento e longevità nel Sirente' (ageing and longevity in the Sirente geographic area, *ilSIRENTE* study) study.

Methods

The *ilSIRENTE* study is a prospective cohort study performed in the mountain community living in the Sirente geographic area (L'Aquila, Abruzzo) in the Central Italy. This study was designed by the Department of Gerontology of the Catholic University of Sacred Heart (Rome, Italy) and developed by the teaching nursing home Opera Santa Maria della Pace (Fontecchio, L'Aquila, Italy) in a partnership with local administrators and primary care physicians of Sirente mountain community municipalities. The Catholic University of Sacred Heart ethical committee ratified the entire study protocol. All the participants signed an informed consent at the baseline visit. Details of the *ilSIRENTE* study protocol are described in detail elsewhere [11].

Study population

A preliminary list of all persons living in this well-defined area was obtained at the end of October 2003, from the registry offices of the 13 municipalities involved in the study. From this preliminary list, potential study participants were identified by selecting all persons born in the Sirente area before 1 January 1924, and actually living in such area. As a result, the overall sample population enrolled in the *ilSIRENTE* study consisted of 364 subjects. Five subjects were excluded because during the baseline visit it was not possible to obtain the blood sample for the haematological assessment (for 2 subjects the blood sample was insufficient, while 3 subjects refused to participate). Finally, the sample included in the present study was of 359 subjects.

Data collection

Baseline participants' assessments began in December 2003 and were completed in September 2004. Assessors were trained on how to perform each component of the *ilSIRENTE* study protocol [11]. The minimum data set for home care(MDS-HC) form was administered to all study participants following the guidelines published in the MDS-HC manual [12, 13]. The MDS-HC contains over 350 data elements including socio-demographics, physical and cognitive status-variables, as well as major clinical diagnoses [14]. Moreover, the MDS-HC also includes information about an extensive array of signs, symptoms, syndromes and treatments [12, 13]. All these domains are not self- or proxy-report but are derived from direct assessor's observations. The MDS items have shown an excellent interrater and test-retest reliability when completed by nurses performing usual assessment duties (average weighted kappa = 0.8) [12, 15]. Additional information about family history, lifestyle, physical activity and behavioural factors were collected using specific questionnaires shared with the 'Invecchiare in Chianti Study' [16]. Finally, it is important to underline that the method of assessment was identical among all subjects enrolled in the study.

Physical performance, muscle strength and functional status measures

Physical performance measures

The physical performance was assessed by the SPPB score. This battery is composed by three timed tests: 4-m walking speed, balance and chair-stand tests [17, 18]. Timed results from each test were rescored from zero (worst performers) to four (best performers). The sum of the results from the three categorised tests (ranging from 0 to 12) was used for the present analyses [17, 18].

The walking speed was evaluated by measuring the participant's usual gait-speed (in m/s) over a 4-m course. The following cut-points (based on sample population quartiles) for gait speed were used to categorise the variable: ≤0.38 m/s, a score of 1; 0.39–0.57 m/s, a score of 2; 0.58–0.76 m/s, a score of 3; ≥0.77 m/s, a score of 4. Participants unable to complete the task were scored 0.

To assess the chair-stand test, the participants were asked to stand up from a chair with their arms folded across the chest five times in a row as quickly as possible. The time needed to complete the task was recorded. The quartiles for the length of the time required for this measure were used for scoring as follows: ≥17.0 s, a score of 1; 14.1–16.9 s, a score of 2; 11.9–14.0 s, a score of 3; and ≤11.8 s, a score of 4. Subjects unable to complete the test received a score of 0.

To assess the balance test, the participants were asked to perform three increasingly-challenging standing- positions: side-by-side position, semi-tandem position, and tandem position. Participants were asked to hold each position for 10 s. Participants were scored as 1 if they were able to hold a side-by-side standing position for 10 s, but were unable to hold a semi-tandem position for 10 s; a score of 2 if they were able to hold a semi-tandem position for 10 s, but were unable to hold a tandem position for more than 2 s; a score of 3 if they were able to stand in tandem position for 3–9 s; and a score of 4 if they were able to hold the tandem position for 10 s.The participants unable to complete the test were scored 0 [17, 18].

Muscle strength measure

The muscle strength was assessed by hand-grip strength measured by a dynamometer. Hand-grip strength has shown to be predictive of major health-related events in older persons [19, 20].

Functional status measures

The basic and IADL were assessed by the assessor using the MDS-HC instrument [12, 13]. Theactivities of daily living(ADL) scale is based on seven levels of self-performance including dressing, eating, toilet use, bathing, mobility in bed, locomotion and transfer. Similarly, the IADL scale is based on seven levels of self-performance including meal preparation, house work, managing finance, phone use, shopping, transportation and managing medications.

Blood measurements

Venus blood samples were drawn in the morning after an overnight fast. The samples were immediately centrifuged and stored at −80°C until final analysis. Standard determinations of serum albumin, cholesterol (HDL and LDL), C-reactive protein and urea were performed by commercially available kits (Olympus, Italy) suitable on Olympus 2700 instrumentation.

Covariates

Medical diagnoses and drugs were directly collected by general practitioners. Medical diagnoses were defined as conditions that have a relationship to the patient's functional, cognitive and behavioural status, medical treatment and risk of death. The diagnoses were listed on the MDS-HC form in a check-box section containing 27 specific diagnostic categories. BMI is defined as the weight (kilograms) divided by the square of height (metres). The alcohol consumption was assessed by asking the participants about the number of glasses of wine drunk during a standard day. Alcohol abuse was defined as consumption of more than half a litre of wine per day. Physical activity was assessed by asking the participant to provide data on past and current activities involving energy expenditure, including recreational and work-related ones. For the present analyses, we considered as physically active those participants reporting light intensity activities (e.g. walking, dancing, gardening) performed for at least 2–4 h per week during the last year.

Statistical analysis

For the present study, from the initial sample of 364 participants, we excluded five participants because HDL cholesterol was not determined. This selection resulted in a final sample size of 359 participants. For analytical purpose three groups of HDL-cholesterol were created based on the tertiles of this variable: first teritile (HDL-cholesterol <40 mg/dl; $n = 115$), second tertile (HDL-cholesterol >40 mg/dl and <49 mg/dl; $n = 125$), and third tertile (HDL-cholesterol >49 mg/dl; $n = 119$).

The characteristics of the study sample were presented separately for the tertiles of HDL-cholesterol. The differences in proportions and the means of covariates between the different HDL-cholesterol tertiles were assessed using Fisher's Exact Test and *t* test statistics, respectively.

The analysis of covariance (ANCOVA) was used to examine the effect of different level of HDL-cholesterol tertiles on physical performance (SPPB, walking speed, hand-grip, and ADL and IADL scores). The variables considered for adjustment were those thought to be clinically significant or showing a significant difference between the different HDL-cholesterol tertiles at the univariate analysis. The final analyses were adjusted for age, gender, living alone, alcohol abuse, physical activity, congestive heart failure, diabetes, cerebrovascular diseases, osteoarthritis, albumin, urea, C-reactive protein and LDL cholesterol. Because the use of statins or any other lipid-lowering agent was very low within the study sample (20 subjects), it was not included in our analyses.

All analyses were performed using SPSS software (version 9.0, SPSS Inc., Chicago, IL).

Results

Mean age of 359 subjects participating in the study was 85.9 (standard deviation 4.9) years, and 240 (67.0%) were women. Characteristics of the study population according to the different levels of HDL-cholesterol tertiles are summarised in Table 1. Compared with the participants with the first tertile of HDL-cholesterol, those in the third tertile were younger, more likely to be women and had a higher prevalence of osteoarthritis. On the contrary, subjects in the third tertile of HDL-cholesterol had a lower prevalence of congestive heart failure, diabetes and cerebrovascular diseases, and tended to be more physically active, compared with other participants. Albumin, urea and LDL-cholesterol increased as HDL-cholesterol increased, while C-reactive protein declined with increasing HDL-cholesterol tertiles.

Unadjusted and adjusted results from ANCOVA models are reported in Table 2. In the unadjusted analyses physical function (as measured by the 4-m walking speed, the SPPB score, the Basic and IADL scales scores, but not hand-grip strength, improved significantly as HDL-cholesterol tertiles increased. After adjustment for potential confounders, which included age, gender, living alone, alcohol abuse, physical activity, congestive heart failure, diabetes, cerebrovascular diseases, osteoarthritis, albumin, urea, C-reactive protein, and LDL cholesterol, the association of HDL-cholesterol tertiles with the 4-m walking speed and the SPPB score was still consistent. Furthermore, if the 4-m walking speed score was excluded from SPPB score, the association was still significant (data not shown). By contrast, the association of HDL cholesterol tertiles with the Basic and IADL scales scores was weaker and no longer significant.

Figure reports the associations of the 4-m walking speed and the SPPB score with the HDL-cholesterol tertiles according to different gender (Figure 1). As HDL-cholesterol tertile increased, both 4-m walking test and SPPB score progressively improved significantly, in both man and female

Table 1. Characteristics of study population according to the HDL-cholesterol tertiles

	Total sample (n = 359) HDL-cholesterol tertiles			
Characteristic	**I** (n = 115)	**II** (n = 125)	**III** (n = 119)	***P***
Age, years	86.3 ± 4.7	86.7 ± 5.4	84.3 ± 3.9	<0.001
Female	66 (57)	81 (65)	93 (78)	0.003
Marital status				0.2
Married	36 (31)	30 (24)	34 (29)	
Widowed	72 (63)	77 (62)	72 (60)	
Never married	7 (6)	18 (14)	13 (11)	
Living alone	28 (25)	33 (27)	42 (38)	0.05
Number of diseases	2.2 ± 1.3	2.0 ± 1.2	2.2 ± 1.3	0.4
Specific Diseases				
Hypertension	79 (68)	89 (71)	91 (76)	0.3
Ischemic heart disease	12 (10)	16 (13)	15 (13)	0.8
Congestive heart failure	13 (11)	6 (5)	3 (3)	0.01
Cancer	4 (4)	7 (6)	6 (5)	0.7
Chronic obstructive pulmonary disease	18 (16)	16 (13)	15 (13)	0.7
Renal failure	1 (1)	1 (1)	1 (1)	0.9
Thyroid diseases	3 (3)	2 (2)	4 (3)	0.6
Diabetes	48 (41)	36 (28)	25 (21)	0.002
Cerebrovascular diseases	12 (10)	2 (2)	3 (2)	0.002
Osteoarthritis	15 (13)	24 (19)	32 (27)	0.02
Parkinson's disease	1 (1)	3 (2)	2 (2)	0.6
Number of medications	3.6 ± 2.0	3.2 ± 2.3	2.9 ± 2.0	0.07
Physical activity	56 (50)	68 (54)	82 (70)	0.006
BMI, kg/m^2	25.1 ± 4.3	26.2 ± 4.8	25.4 ± 4.3	0.1
Alcohol abuse[a]	15 (13)	24 (19)	6 (5)	0.002
Smoking habit	2 (2)	3 (2)	3 (2)	0.9
Hematological parameters				
Albumin, g/dl	4.0 ± 0.3	4.2 ± 0.3	4.2 ± 0.2	0.002
Urea, mg/dl	42.2 ± 28.5	46.7 ± 17.3	44.3 ± 16.7	0.02
LDL-cholesterol, g/dl	114 ± 35	134 ± 38	142 ± 35	<0.001
Reactive C protein, g/dl	5.1 ± 4.0	4.1 ± 3.2	3.2 ± 2.9	<0.001

Data are given as number (percent) for the following variables: gender, marital status, living alone, specific diseases, alcohol abuse, physical activity; for all the other variables means ± SD are reported. BMI.Body mass index

[a] More than 1/2 litre of wine per day.

groups. It is important to highlight that similar data were obtained by exploring this association in different age groups [see the Figure Appendix 1 in the supplementary data on the journal website (www.ageing.oupjournals.org/)].

Discussion

In the present study, we explored the association of serum HDL-cholesterol concentration with physical performance, muscle strength and functional status measures in a sample of community-dwelling older persons aged 80 years and older. Our findings show that, in older persons, physical function declines as serum HDL-cholesterol level declines. However, after adjustment for potential confounders, only physical performance measures (the 4-m walking test and the SPPB score were directly associated with serum HDL-cholesterol. This association was consistent also in very old participants and in both gender groups.

Why are elderly subjects with higher HDL-cholesterol levels healthier and have better physical performance?

Cholesterol levels may be associated inversely with the onset and outcomes of specific diseases [21]. For example, previous studies have shown a graded negative relation between serum cholesterol levels and the risk of nosocomial infections, and in-hospital mortality related to infectious diseases has been associated with low cholesterol levels [22]. Higher cholesterol levels have been associated with better short-term health outcomes after acute strokes [23]. Another study found that cholesterol levels were related inversely to morbidity and mortality after surgery [24]. Furthermore, although elevated serum cholesterol levels increase coronary heart disease incidence, morbidity and mortality, they do not affect in-hospital outcomes among patients with acute myocardial infarction [25]. Finally low cholesterol concentration is often associated with poor health status and impaired disability recovery [5, 26]. Even though genetic predisposition and specific metabolic conditions are the most important determinants of serum cholesterol concentration, reduced HDL-cholesterol levels have been hypothesised to be a general marker of poor wellbeing and reduced physical condition [5, 26]. Previous studies have demonstrated that lower HDL-cholesterol levels characterise institutionalised or community-dwelling elderly subjects with functional impairments and chronic diseases [27, 28].

Table 2. Unadjusted and adjusted[a] means of physical function measures (dependent variable) according to HDL-cholesterol tertiles

	Unadjusted				Adjusted[a]			
	I tertile ($n = 115$)	II tertile ($n = 125$)	III tertile ($n = 119$)	P	I tertile ($n = 115$)	II tertile $n = 125$)	III tertile ($n = 119$)	P
Physical performance measures								
4-m walking speed (m/s)	0.40 (0.03)	0.44 (0.02)	0.59 (0.02)	<0.001	0.44 (0.02)	0.46 (0.02)	0.54 (0.02)	0.004
SPPB	5.47 (0.39)	6.50 (0.33)	7.82 (0.30)	<0.001	5.90 (0.32)	6.54 (0.30)	7.31 (0.30)	0.003
Muscle strength measure								
Hand-Grip Strength (kg)	28.81 (1.64)	29.59 (1.29)	32.21 (1.16)	0.189	29.31 (1.20)	29.66 (1.06)	31.34 (1.16)	0.44
Functional status measures								
ADL scale score	2.24 (0.27)	1.36 (0.20)	0.75 (0.16)	<0.001	1.77 (1.17)	1.32 (0.16)	1.35 (0.17)	0.14
IADL scale score	3.71 (0.26)	3.25 (0.22)	2.19 (0.20)	<0.001	3.16 (0.18)	3.13 (0.16)	2.88 (0.17)	0.47

The SPPB score (composed by usual gait speed, balance, and chair stand tests) ranges from 0 (worse performance) to 12 (best performance). ADL (range 0–7, a higher number indicates higher impairment). IADL (range 0–7, a higher number indicates higher impairment).
[a] Adjusted for age, gender, living alone, alcohol abuse, physical activity, congestive heart failure, diabetes, cerebrovascular diseases, osteoarthritis, albumin, urea, C-reactive protein and LDL cholesterol.

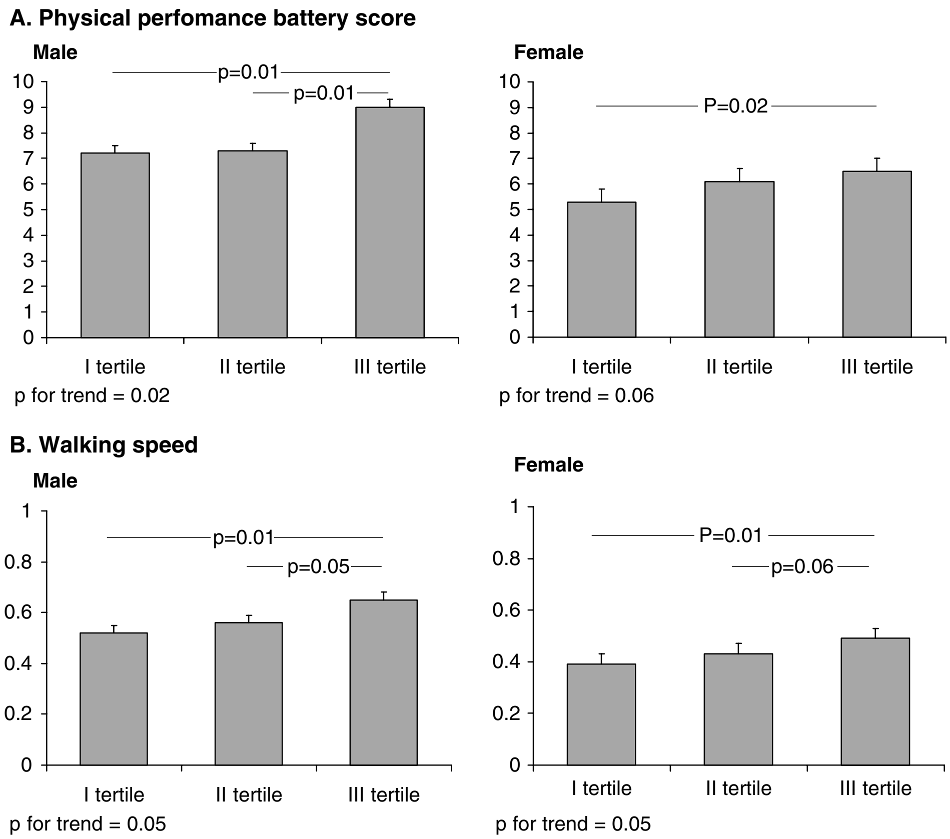

Figure 1. Adjusted means (standard errors) of physical performance battery score (panel A) and walking speed (panel B) according to gender. Analyses are adjusted for age, living alone, alcohol abuse, physical activity, congestive heart failure, diabetes, cerebrovascular diseases, osteoarthritis, albumin, urea, C-reactive protein and LDL cholesterol.

One of the most important mechanism by which HDL-cholesterol plays its atheroprotective function is the reverse cholesterol transport, a process by which cholesterol is extracted from macrophages, foam cells, and atherosclerotic plaque, and delivered back to the liver for elimination as bile salts or biliary cholesterol [10]. Other anti-atherothrombotic mechanisms have been hypothesised for HDL-cholesterol. Some authors have documented that HDL-cholesterol may be able to reduce the acute vascular inflammation that is associated with conditions such as acute coronary syndrome and stroke [29]. Furthermore, HDL-cholesterol exerts direct nitric oxide-mediated vasodilatory effects. The capacity of HDL-cholesterol to enhance the activity of nitric oxide in the small arteries may have a role in the reduction of arterial inflammation at the place of atheroma formation [29, 30].

Some methodological issues may have influenced our results. As in all cohort studies, selective survival before entry into the cohort has to be taken into account. Furthermore, in this observational study, results may be confounded by unmeasured factors. However, our homogeneous population of old people born and living in a well-defined geographical area, minimises the possibility that subjects with higher HDL-cholesterol levels had substantially better health care or health knowledge than those with lower HDL-cholesterol levels. Second, the cross-sectional design of the study does not allow us to clarify any cause–effect mechanism. The *ilSIRENTE* study gives us the opportunity to adjust our analyses for many health and disease-related characteristics that are potentially correlated to the functional performance and/or to the level of serum HDL-cholesterol. In this respect, it is important to highlight that the results were robust to adjustments for these numerous potential confounders. Finally, the *ilSIRENTE* sample population was composed by persons aged 80 years or older, so our results may not be applicable to other age groups.

In conclusion, the present study suggests that among very old subjects living in the community the higher levels of HDL-cholesterol are associated with better functional performance. It is of particular importance whether improved HDL-cholesterol levels by pharmacological intervention could get better physical performance in the oldest elderly. To achieve further information about the possible roles of HDL-cholesterol in the physiology of 'geriatric syndrome', a much greater effort should be provided in this research field.

Key points

- The growing interest in the heterogeneity of functional ability in the elderly has resulted in the need of expanding the measurement of physical function beyond the standard self-reported measures of disability.
- High-density lipoprotein (HDL) cholesterol has been hypothesised to be a reliable marker of frailty and poor prognosis among the oldest elderly.
- The present data suggests that among elderly subjects living in the community higher levels of HDL-cholesterol are associated with better functional performance.

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The *ilSIRENTE* Study Group is composed as follows:

Steering Committee: R. Bernabei, F. Landi

Coordination: A. Russo, M. Valeri, G. Venta

Writing Panel: C. Barillaro, M. Cesari, L. Ferrucci, G. Onder, M. Pahor, V. Zamboni, E. Capoluongo

Participants: Comune di Fontecchio: P. Melonio, G. Bernabei, A. Benedetti; Comune di Fagnano: N. Scarsella, A. Fattore, M. Fattore; Comune di Tione: M. Gizzi; Comune di Ovindoli: S. oltellate, E. Chiuchiarelli; Comune di Rocca di Mezzo: S. Pescatore; Comune di Rocca di Cambio: G. Scoccia; Comune di Secinaro: G. Pizzocchia; Comune di Molina Aterno: P. Di Fiore; Comune di Castelvecchio: A. Leone; Comune di Gagliano Aterno: A. Petriglia; Comune di Acciano: A. Di Benedetto; Comune di Goriano Sicoli: N. Coltella; Comune di Castel di Ieri: S. Battista; RSA Opera Santa Maria della Pace: A. De Santis, G. Filieri, C. Gobbi, G. Gorga, F. Cocco, P. Graziani.

Conflicts of interest

None declared.

Supplementary data

Supplementary data for this article are available online at http://ageing.oxfordjournals.org.

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