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PRE FRAIL 80: MULTIFACTORIAL INTERVENTION TO PREVENT PROGRESSION OF PRE-FRAILTY TO FRAILTY IN THE ELDERLY

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Abstract: *Objectives:* Preventing or delaying frailty has important benefits in the elderly, and in health and social services. Studies have demonstrated the effectiveness of multifactorial interventions in the frail elderly, but there are fewer studies on community-dwelling pre-frail individuals. Identifying pre-frail individuals susceptible to intervention could prevent or delay frailty and its consequences and associated disability and might reverse the state from pre-frail to robust. To evaluate a multifactorial, interdisciplinary primary care intervention in community-dwelling pre-frail elderly patients aged ≥ 80 years. *Design:* Randomized clinical trial in a Barcelona primary healthcare centre. *Setting:* We included 200 community-dwelling subjects aged ≥ 80 years meeting the Fried pre-frailty criteria. Participants were randomized to intervention and control groups. *Intervention:* The intervention group received a 6-month interdisciplinary intervention based on physical exercise, Mediterranean diet advice, assessment of inadequate prescribing in polypharmacy patients and social assessment, while the control group received standard primary healthcare treatment. *Results:* 173 pre-frail participants (86.5%) completed the study; mean age 84.5 years, 64.5% female. At twelve months, frailty was lower in the intervention group (RR 2.90; 95%CI 1.45 to 8.69). Reversion to robustness was greater in the intervention group (14.1% vs.1.1%, p <0.001). Functional and nutritional status, adherence to Mediterranean diet, quality of life, and functional mobility were improved in the intervention group (p ≤0.001). *Conclusion:* A multifactorial, interdisciplinary primary healthcare intervention focused on physical exercise, nutrition, review of polypharmacy and social assessment prevented frailty in pre-frail elderly patients, and improved functional capacity, quality of life and adherence to the Mediterranean diet.

Key words: Frailty, multifactorial intervention, exercise, Mediterranean diet, primary health care.

How this fits in

The elderly population will increase in forthcoming decades, making frailty an increasing public health problem. The effectiveness of multifactorial interventions in the frail elderly is known. However, the Pre frail 80 study provides evidence on preventing progression from pre-frailty to frailty by means of an interdisciplinary intervention using primary health resources, which reduced the progression of disability while lowering the use of allocated resources.

Introduction

Frailty, a pathophysiological state of high vulnerability to diseases and external aggressions, conditions a decrease in functional reserve, and a greater probability of adverse health episodes such as complications of chronic pathologies, new diseases, falls, disability, institutionalization, and death (1, 2) and is accompanied by weight loss, reduced strength and muscle mass, fatigue and poor physical activity (1).

The prevalence of frailty varies between studies, mainly because there is no common operational definition (3). The prevalence in people aged ≥ 65 years, measured using Fried's (4) criteria, is 17%, and pre-frailty 42.3% in Europe and 27.3% and 50.9%, respectively in Spain. Frailty and pre-frailty increase with age (6, 7) and are more prevalent in women (5, 8).

There are two visions of frailty: one centred on the phenotype as a biological process reflecting the progressive deterioration of the underlying physical substrate and the functional capacity prior to disability, known as frailty syndrome, and measurable by Fried's criteria (1), is useful in population screening of pre-frailty. Secondly, frailty understood as accumulated deficits (9-11) resulting from a disease-driven process and conditions leading to frailty. Other instruments for assessing frailty incorporate elements of the Comprehensive Geriatric Assessment (VGI), such as VGI-Frail (12), inter-RAI

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frailty scale (13), and the Clinical Frailty Scale (14), which are used to detect advanced frailty in order to measure the health reserve to aid decision-making.

Identifying and treating pre-frailty may prevent or delay frailty. Evidence suggests that the pre-frail elderly may respond better to interventions than already-frail people (15-17). There is evidence of the nutritional impact and physical activity on muscle mass and strength, and physical and functional levels (1, 18, 19). Counter-resistance, cardiovascular and aerobic training (20) reduce mortality and disability in the elderly, with the maintenance of muscle mass, increasing strength, functionality and cognitive status, stabilizing bone mineral density, favouring hydrocarbon metabolism and cardiovascular dynamics, which improve after 30-60 minute exercise programs, three days weekly for 3-6 months (21).

Frail elderly people not receiving help for disabilities or basic activities of daily living have greater decompensation (22), but the difference disappears when their needs are addressed, due to reductions in emergency visits and hospital admissions (23). There is evidence of the benefit of isolated or multifactorial interventions on frail individuals, but there is little evidence of comprehensive interventions performed in pre-frail community-dwelling patients.

The aim of this study was to evaluate a multifactorial intervention, centred on four axes: nutrition, physical activity, assessment of inadequate prescription in polypharmacy patients, and social, using Primary Healthcare Centre (PHC) resources to prevent frailty in community-dwelling elderly patients with incipient frailty and determine the prevalence of pre-frailty.

Methodology

Study design and population

We conducted a randomized clinical study in pre-frail patients. A randomized list was reviewed to detect patients fulfilling the inclusion criteria: non-institutionalized males or females aged ≥ 80 years attended by the Borrell PHC, Barcelona (assigned population 32,621) who fulfilled one or two Fried criteria (see box 1). Exclusion criteria were: diagnosis of advanced dementia, patients on palliative care/ life expectancy < 6 months, clinically-unstable patients (e.g. uncontrolled angina), patients already considered frail with home-only care, patients with chronic complex diseases, in wheelchairs or totally-blind or included in other programs for the elderly, other studies or clinical trials.

Participants fulfilling the criteria were invited consecutively from a practice register by telephone to participate until the number of participants established was reached.

The assessment was made from June to September 2016. The intervention lasted from October 2016 to March 2017. Follow-up lasted from March to July 2017 and all participants were evaluated in a final visit.

The study followed the standards of good clinical practice, the principles of the Helsinki Declaration and all applicable legal regulations. The study protocol, information sheet and informed consent form were approved by the Clinical Research Ethics Committee, Hospital Clínic of Barcelona (7/2016). All patients recruited signed the informed consent form.

Box 1
Fried Criteria

1. Unintentional weight loss, positive if > 4.5Kg or > 5% during the last year.
2. Tiredness, positive if answer is 3 or 4 in any of the two questions:
- How many times during the last week have you felt that anything takes an effort?
- How many times during the last week have you felt you «couldn't get going» or that you were completely shattered?
Rarely/never (<1 day); Sometime (1-2 days); Often (3-4 days); Most of the time (> 4 days).
3. Poor physical activity, positive if you do not leave home or usually walk <30 minutes/day.
4. Slowness of walking, positive if walking 4.6 meters (without help of other people) takes:
- > 7 seconds (males <173cm tall and females <159cm).
- > 6 seconds (males > 174 cm tall and females > 160 cm).
5. Weakness. Pressing muscle force according to dynamometer (in Kg), positive if: Males strength <30 Kg and females <17 Kg.

* 0 criteria: robust; 1-2 criteria: pre-frail; ≥ 3 criteria: frail

Given that the population aged ≥ 80 years attended by the Borrell PHC is 2,373 and assuming a prevalence of pre-frailty in the population aged ≥ 75 years of 54% (8), and applying 95% confidence intervals and a margin of error of 7%, the sample size required was 181 participants. Assuming losses of 9%, the target sample size was 200 patients.

Group study

Pre-frail participants who agreed to participate were randomized to a control (CG) or intervention group (IG) by a randomized computer list. Patients randomized to the IG received a 6-month multifactorial intervention based on four axes:

(1) Assessment of inadequate prescription in polypharmacy patients (≥ 5 drugs using the STOPP-START (2014) (24) criteria). Treatment changes were recommended to individual family physicians.

(2) Group session, led by a PHC nurse expert on the Mediterranean diet who advised on individual nutritional changes (25).

(3) Physical exercise program led by a PHC physician and expert nurse. Patients were instructed in exercises and recommendations for home-performance using an illustrated pamphlet, agreed with the Hospital Clínic of Barcelona Rehabilitation Service. The approach was: (1) Aerobic exercise (walking 30-60 minutes a day for ≥ 3 days a week), (2) Programme of exercises to gain strength, resistance, balance and coordination (26), with nine fortnightly sessions in the PHC

for six months and at home 3-4 days a week. Ten repetitions were initially recommended, rising to 15 repetitions at two months, with a one-minute rest between repetitions.

(4) Review of personal and environmental conditions and social support. IG participants were assessed by phone by the PHC social worker, who evaluated the need for home telecare. Home telecare consists of a telephone service in contact with a paramedic unit that activates resources when necessary (e.g., a fall) and follows the patient as necessary. In the case of high social risk, assessed by the Gijón test (27), conventional measures were initiated, with a PHC visit.

Participants randomized to the CG received standard PHC treatment from family physicians, nurses and social workers.

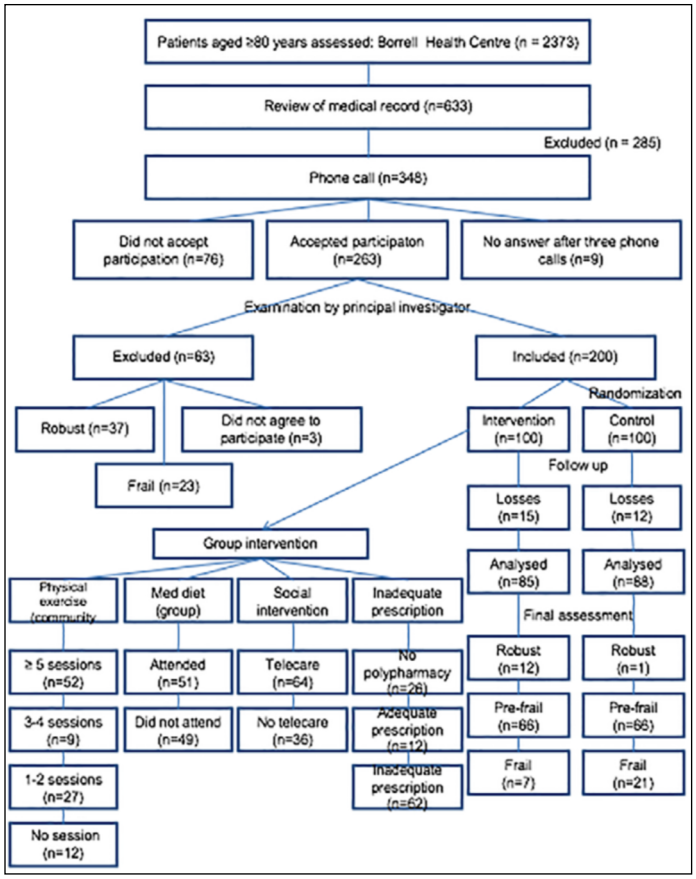
Data collection

The variables collected were: sociodemographic (age, sex, educational level, marital status, need for caregiver), tobacco and alcohol intake, current treatment, comorbidities (diabetes mellitus type 2, hypertension, dyslipidaemia, chronic obstructive pulmonary disease, asthma, osteoporosis, osteoarthritis, heart failure, ischemic heart disease, arrhythmia, liver disease), falls in the last year and geriatric syndromes (reduced visual acuity, hearing loss, polypharmacy, immobility, decubitus ulcers, malnutrition, urinary incontinence and constipation, depression and/or insomnia and cognitive deterioration). The test administered were: 1.- Barthel index (28) of activities of daily living (100 independence, ≥ 60 mild dependence, 40-55 moderate, 20-35 severe and <20 total dependence); 2.- Lawton and Brody (29) test of instrumental activities of daily life (males; 5 autonomous, 4 mild dependence, 2-3 moderate dependence, 1 serious dependence and 0 total dependence: females; 8 autonomous, 6-7 mild dependency, 4-5 moderate, 2-3 serious and, 0-1 total dependence; 3.- Pfeiffer (30) cognitive status test (0-2 errors normal, 3-7 errors mild-to-moderate impairment, and 8-10 errors severe impairment); 4.- Mini Nutritional Assessment (MNA) (31) (<17 malnutrition, 17-23.5 risk of malnutrition and 27-30 normal nutrition); 5.- Adherence to Mediterranean diet (32) (0-6 points low adherence, 7-10 moderate and 11-14 high adherence); 6.- Charlson comorbidity (33): the higher the score the greater the burden of comorbidity, 7.- EuroQol-5 (34) quality of life questionnaire: the higher the score, the better the health status; and 8.- Gijón (27) social assessment (<10, normal/low social risk, 10-16 intermediate social risk and ≥ 17 high social risk). Physical assessment included 1.- the Timed Up and Go test (TUG) (21) (≤ 10 seconds normal, 10.1 to 19.9 good mobility and ≥ 20, altered; 2.- walking speed (35) (≤ 0.8 m/s pathological); and 3.- Five Times Sit to Stand Test (FTSST) (36) (≤ 11 optimal, 11.2-13.6, normal, 13.7-16.6 risk of falls, and ≥ 16.7 marker of frailty).

Statistical analysis

Categorical variables were expressed as absolute frequency and percentage (%) and continuous variables as mean (standard deviation). Between-group baseline characteristics were compared using the chi- square test for categorical variables and the t-test for independent samples for continuous variables. The pre vs. post-intervention comparison used the t-test for repeated samples. Changes in the assessment scales during follow-up as predictors of frailty were measured by logistic regression. The net effect of changes in the scales on frailty was measured using logistic regression models adjusted for age, gender, marital status, incontinence, constipation and intervention group. Values of $p < 0.05$ were considered statistically significant. The 95% confidence intervals (95%CI) were calculated. The statistical analysis was performed using R version 3.2.3 for Windows.

Figure 1
Participant flow



Results

Participant characteristics

A total of 633 (26.7%) of the 2373 eligible patients were assessed: 348 patients not meeting criteria were excluded. We contacted 263 patients who agreed to participate, of whom 60 were excluded as not pre-frail (37 robust and 23 frail); 3 patients finally decided not to participate (Figure 1). Of the 200 participants finally included, 100 each were assigned to the IG and CG. Table 1 shows baseline sociodemographic

Table 1
Baseline characteristics of intervention and control groups

Variable	Total (n = 200)	Control (n = 100)	Intervention (n = 100)	P-value
Sociodemographic				
Age, years	84.5 ± 3.5	84.5 ± 3.7	84.5 ± 3.4	0,984
Sex, female	129 (64.5)	61 (61)	68 (68)	0,375
Educational level				0,266
Primary	78 (39)	44 (44)	34 (34)	
High school	83 (41.5)	40 (40)	43 (43)	
University	39 (19.5)	16 (16)	23 (23)	
Civil status				0,621
Married	88 (44)	47 (47)	41 (41)	
Widower	91 (45.5)	41 (41)	50 (50)	
Single	19 (9.5)	11 (11)	8 (8)	
Divorced	2 (1)	1 (1)	1 (1)	
Carer	16 (8)	11 (11)	5 (5)	0,193
Risk factors and comorbidities				
Smoking				0,345
Not smoker	137 (68.5)	65 (65)	72 (72)	
Active smoker	10 (5)	7 (7)	3 (3)	
Ex-smoker	53 (26.5)	28 (28)	25 (25)	
Diabetes mellitus	51 (25.5)	22 (22)	29 (29)	0,33
Hypertension	146 (73)	67 (67)	79 (79)	0,08
Dyslipidaemia	102 (51)	45 (45)	57 (57)	0,12
COPD	24 (12)	13 (13)	11 (11)	0,828
Asthma	8 (4)	7 (7)	11)	0,071
Osteoporosis	70 (35)	37 (37)	33 (33)	0,657
Osteoarthritis	86 (43)	48 (48)	38 (38)	0,199
Heart failure	4 (2)	1 (1)	3 (3)	0,614
Ischemic heart disease	19 (9.5)	8 (8)	11 (11)	0,63
Arrhythmia	33 (16.5)	15 (15)	18 (18)	0,703
Liver disease	6 (3)	3 (3)	3 (3)	1
Fractures	38 (19)	21 (21)	17 (17)	0,589
Geriatric syndromes				
Sight	79 (39.5)	39 (39)	40 (40)	1
Hearing	102 (51)	55 (55)	47 (47)	0,322
Polypharmacy	143 (71.5)	68 (68)	75 (75)	0,347
Immobility	2 (1)	2 (2)	0 (0)	0,477
Malnutrition	3 (1.5)	2 (2)	1 (1)	1
Incontinence	83 (41.5)	40 (40)	43 (43)	0,774
Constipation	56 (28)	28 (28)	28 (28)	1
Depression	36 (18)	18 (18)	18 (18)	1
Insomnia	77 (38.5)	40 (40)	37 (37)	0,771
Cognitive impairment	11 (5.5)	8 (8)	3 (3)	0,215

Values expressed as mean ± standard deviation or as n (%); COPD, chronic obstructive pulmonary disease.

Table 2
Fried criteria and assessment scales (functional, nutritional, socio-family status, quality of life and mobility) between the control and intervention group

Variable	Control (n = 88)			Intervention (n = 85)			Difference (Intervention - Control)	
	Baseline	12 months	P-value †	Baseline	12 months	P-value †	Mean [95%CI]	P-value ‡
Fried criteria								
Unintentional weight loss	9 (10.2)	9 (10.2)	1	5 (5.9)	6 (7.1)	1		
Feeling of exhaustion	25 (28.4)	52 (59.1)	<0.001	37 (43.5)	28 (32.9)	0,11		
Low physical activity	9 (10.2)	19 (21.6)	0,024	13 (15.3)	11 (12.9)	0,773		
Slowness in mobility	9 (10.2)	20 (22.7)	0,01	10 (11.8)	11 (12.9)	1		
Muscular weakness	70 (79.5)	70 (79.5)	1	65 (76.5)	59 (69.4)	0,264		
Rating scales								
Functional state (Barthel)	95.2 ± 6.4	94.1 ± 7.9	0,032	94.9 ± 5.4	96.2 ± 5.1	0,001	2.37 [1.14 - 3.61]	<0.001
Mild dependence (60-95)	45 (51.1)	47 (53.4)		48 (56.5)	38 (44.7)			
Independence (100)	43 (48.9)	41 (46.6)		37 (43.5)	47 (55.3)			
Degree of autonomy for ADL (Lawton)	6.4 ± 1.6	6.0 ± 2.0	0,007	6.5 ± 1.6	6.4 ± 1.7	0,567	0.26 [-0.01 - 0.53]	0,062
Total dependence (0-1)	0 (0)	3 (3.4)		0 (0)	0 (0)			
Severe dependence (2-3)	1 (1.1)	0 (0)		1 (1.2)	3 (3.5)			
Moderate dependence (4-5)	4 (4.5)	9 (10.2)		5 (5.9)	3 (3.5)			
Mild dependence (6-7)	25 (28.4)	20 (22.7)		16 (18.8)	18 (21.2)			
Independence (8)	58 (65.9)	56 (63.6)		63 (74.1)	61 (71.8)			
Nutritional status (MNA)	24.4 ± 2.5	24.7 ± 2.5	0,189	24.6 ± 2.1	25.2 ± 2.1	0,021	0.23 [-0.44 - 0.90]	0,5
Malnutrition (<17)	2 (2.3)	0 (0)		0 (0)	0 (0)			
Risk of malnutrition (17-23.5)	25 (28.4)	26 (29.5)		27 (31.8)	21 (24.7)			
Normal (24-30)	61 (69.3)	62 (70.5)		58 (68.2)	64 (75.3)			
Adherence - the Mediterranean diet	7.9 ± 2.0	7.4 ± 1.7	0,003	7.8 ± 2.3	8.2 ± 2.0	0,011	0.91 [0.47 - 1.36]	<0.001
Low (≤3)	26 (29.5)	26 (29.5)		25 (29.4)	16 (18.8)			
Medium (4-7)	53 (60.2)	55 (62.5)		51 (60)	57 (67.1)			
High (≥8)	9 (10.2)	7 (8)		9 (10.6)	12 (14.1)			
Quality of life (EQ-5D)	6.7 ± 1.3	6.9 ± 1.5	0,075	7.1 ± 1.5	6.2 ± 1.1	<0.001	-1.11 [-1.48 to -0.74]	<0.001
Socio-family risk (Gijón)	8.4 ± 2.0	8.3 ± 2.2	0,753	8.1 ± 2.0	7.9 ± 2.0	0,156	-0.14 [-0.59 - 0.31]	0,531
Normal or low social risk (<10)	69 (78.4)	66 (75)		63 (74.1)	65 (76.5)			
Intermediate social risk (10-16)	19 (21.6)	22 (25)		22 (25.9)	20 (23.5)			
Functional mobility (TUG), seconds	13.4 ± 5.1	14.0 ± 5.9	0,013	13.4 ± 4.3	12.4 ± 4.2	0,004	-1.57 [-2.36 to -0.78]	<0.001
Normal (<10)	22 (25)	22 (25)		15 (17.6)	25 (29.4)			
Frailty (10-20)	60 (68.2)	56 (63.6)		63 (74.1)	52 (61.2)			
Risk of falls (> 20)	6 (6.8)	10 (11.4)		7 (8.2)	8 (9.4)			
Functional mobility (FTSST), seconds	18.3 ± 5.2	17.7 ± 4.8	0,661	19.6 ± 6.8	17.0 ± 6.0	<0.001	-2.46 [-3.87 to -1.06]	0,001
4 (<11.2)	5 (5.7)	4 (4.5)		2 (2.4)	13 (15.3)			
3 (11.2-13.6)	7 (8)	12 (13.6)		9 (10.6)	13 (15.3)			
2 (13.7-16.6)	22 (25)	19 (21.6)		18 (21.2)	16 (18.8)			
1 (> 16.6)	46 (52.3)	43 (48.9)		47 (55.3)	36 (42.4)			
0 (unable to complete)	8 (9.1)	10 (11.4)		9 (10.6)	7 (8.2)			

Values expressed as mean ± standard deviation or as n (%); 95% CI, 95% confidence interval. ADL, Activities of Daily Living. MNA, Mini Nutritional Assessment.EQ-5D, EuroQol- 5 Dimension; TUG, Timed Up and Go. FTSST, Five Times Sit to Stand Test; † Paired t-test.

characteristics, risk factors, comorbidities and geriatric syndromes. The mean age was 84.5 (SD 3.5) years and 64.5% were female.

Table 3
Association between frailty and sociodemographic variables, comorbidities and geriatric syndromes

Variable	Non-frail (n = 145)	Frail (n = 28)	P-value
Fried Criteria			
Unintentional weight loss	7 (4.8)	8 (28.6)	
Feeling of exhaustion	53 (36.6)	27 (96.4)	
Low physical activity	11 (7.6)	19 (67.9)	
Slowness in mobility	11 (7.6)	17 (60.7)	
Muscular weakness	103 (71)	26 (92.9)	
Sociodemographic			
Age, years	84.9 (3.4)	86.0 (4.0)	0,184
Gender, woman	87 (64.4)	23 (82.1)	0,043
Civil status			0,022
Married	75 (51.7)	7 (25.0)	
Widower	61 (42.1)	17 (60.7)	
Single	8 (5.5)	3 (10.7)	
Divorced	1 (0.7)	1 (3.6)	
Comorbidities			
Diabetes mellitus	36 (24.8)	3 (10.7)	0,138
Hypertension	110 (75.9)	17 (60.7)	0,106
Dyslipidaemia	69 (47.6)	12 (42.9)	0,684
COPD	18 (12.4)	2 (7.1)	0,537
Asthma	4 (2.8)	3 (10.7)	0,085
Osteoporosis	47 (32.4)	12 (42.9)	0,286
Osteoarthritis	57 (39.3)	8 (28.6)	0,394
Heart failure	3 (2.1)	0 (0)	1
Ischemic heart disease	12 (8.3)	3 (10.7)	0,713
Arrhythmia	21 (14.5)	8 (28.6)	0,094
Liver disease	4 (2.8)	1 (3.6)	0,591
Fractures	6 (4.1)	3 (10.7)	0,162
Geriatric syndromes			
Sight	48 (33.1)	11 (39.3)	0,522
Hearing	69 (47.6)	14 (50)	0,839
Polypharmacy	95 (65.5)	21 (75)	0,386
Incontinence	50 (34.5)	16 (57.1)	0,033
Constipation	43 (29.7)	15 (53.6)	0,017
Depression	27 (18.6)	9 (32.1)	0,128
Insomnia	60 (41.4)	16 (57.1)	0,147
Cognitive impairment	4 (2.8)	3 (10.7)	0,085

COPD, chronic obstructive pulmonary disease.

Impact of the intervention

Figure 1 shows participation in the intervention activities: 52 participants attended > 50% of physical exercise sessions; 51 participated in the dietary group session; 64 accepted the social intervention and had a home telecare service installed, and 62 participants had inadequate prescription, of which 30 were resolved (48,4%).

Finally, 173 (86.5%) participants completed the follow-up (88 CG and 85 IG). Table 2 shows the results at baseline and 12 months of follow-up. There were few changes in the Fried criteria in the IG but there was significant worsening in the CG in which exhaustion (28.4% baseline vs. 59.1% follow-up, p <0.001), low physical activity (10.2% vs. 21.6%, p = 0.024) and slow mobility (10.2% vs. 22.7%, p = 0.010) doubled.

Functional status (baseline 94.9 vs. 96.2 follow-up, p = 0.001), adherence to the Mediterranean diet (7.8 vs. 8.2, p = 0.011), quality of life (7.1 vs. 6.2, p <0.001), and the TUG (13.4 vs.12.4, p = 0.004) and FTSST (19.6 vs. 17.0, p <0.001) significantly improved in the IG compared with the CG (mean 0.23, 95%CI -0.44 to 0.90).

Progression to frailty

During the follow-up, 21 (23.9%) CG and 7 (8.2%) IG patients progressed to frailty: the RR was 2.90 times higher in the CG (95%CI 1.45-8.69). Twelve (14.1%) patients reverted from pre-frailty to robustness (1.1% CG vs. 14.1% IG, p <0.001). Gender (greater risk in females) and marital status (greater risk for widowers) were associated with progression to frailty (Table 3). There were no significant between-group differences in comorbidities.

Table 4 shows the relationship between progression to frailty and changes in the evaluation scales. Progression to frailty was associated with worse functional status (OR 1.19, 95%CI 1.09-1.33), autonomy (OR 2.98, 95%CI 1.79-5.58), nutritional status (OR 1.25, 95%CI 1.03-1.52), quality of life (OR 1.98, 95%CI 1.39-2.94), social risk (OR 1.35, 95%CI 1.04-1.77) and functional mobility (OR 1.33, 95%CI 1.14-1.58). Non-frail patients had improved functional status (95.9 baseline vs. 96.5 follow-up, p = 0.018), nutritional status (24.8 vs. 25.4, p = 0.001), quality of life (6.8 vs. 6.3, p <0.001), social risk (8.1 vs. 7.8, p = 0.030) and TUG (12.6 vs. 12.1, p = 0.018) at 12 months. Patients progressing to frailty had worse functional status (baseline 90.9 vs. 88.0 follow-up, p = 0.040), autonomy (6.2 vs. 5.2, p = 0.003) and functional mobility (17.5 vs. 19.0, p = 0.009). After adjusting for the IG, age, gender, marital status and geriatric syndromes, all measures, except nutrition, remained significantly associated with frailty. In the multivariate logistic regression analysis, only worsened autonomy remained significantly associated with frailty (OR 2.80, 95%CI 1.36-6.23).

Discussion

Summary

Our results show a multifactorial intervention prevented progression from pre-frailty to frailty in community-dwelling persons aged ≥ 80 years. At 12 months follow-up, 23.9% of CG

Table 4
Changes in rating scales as predictors of frailty

Variable	Non-frail (n = 145)		Frail (n = 28)	
	Baseline	12 months	Baseline	12 months
Functional state (Barthel)[a]	95.9 ± 4.9	96.5 ± 4.4	90.9 ± 8.4	88.0 ± 11.1
Degree of autonomy for ADL (Lawton)[a]	6.4 ± 1.6	6.4 ± 1.7	6.2 ± 1.8	5.2 ± 2.5
Nutritional status (MNA)[a]	24.8 ± 2.2	25.4 ± 2.0	23.1 ± 2.7	22.6 ± 2.6
Adherence - Mediterranean diet[a]	8.0 ± 2.1	8.0 ± 1.9	7.0 ± 2.0	6.9 ± 1.6
Quality of life (EQ-5D)[b]	6.8 ± 1.3	6.3 ± 1.0	7.5 ± 1.9	8.1 ± 1.9
Socio-family risk (Gijón)[b]	8.1 ± 1.9	7.8 ± 1.9	9.2 ± 2.3	9.7 ± 2.3
Functional mobility (TUG)[b], seconds	12.6 ± 3.6	12.1 ± 3.6	17.5 ± 7.0	19.0 ± 7.8
Functional mobility (FTSST)[b], seconds	18.6 ± 6.1	16.8 ± 5.2	21.1 ± 5.3	21.0 ± 5.7
Variable	**P-value †**	**P-value ‡**	**Non-adjusted OR [95%CI]**	**Adjusted OR§ [95%CI]**
Functional state (Barthel)[a]	0,018	0,04	1.19 [1.09 - 1.33]	1.19 [1.07 - 1.37]
Degree of autonomy for ADL (Lawton)[a]	0,676	0,003	2.98 [1.79 - 5.58]	3.00 [1.68 - 6.09]
Nutritional status (MNA)[a]	0,001	0,313	1.25 [1.03 - 1.52]	1.22 [0.98 - 1.54]
Adherence - Mediterranean diet[a]	0,958	0,631	1.06 [0.81 - 1.37]	0.86 [0.60 - 1.20]
Quality of life (EQ-5D)[b]	<0.001	0,061	1.98 [1.39 - 2.94]	1.82 [1.22 - 2.81]
Socio-family risk (Gijón)[b]	0,03	0,26	1.35 [1.04 - 1.77]	1.36 [1.01 - 1.87]
Functional mobility (TUG)[b], seconds	0,018	0,009	1.33 [1.14 - 1.58]	1.31 [1.10 - 1.57]
Functional mobility (FTSST)[b], seconds	<0.001	0,5	1.11 [0.99 - 1.26]	0.96 [0.76 - 1.22]

95% CI, 95% confidence intervals. ADL, Activities of Daily Living. MNA, Mini Nutritional Assessment.EQ-5D, EuroQol- 5 Dimension; TUG, Timed Up and Go. FTSST, Five Times Sit to Stand Test; † Baseline comparison vs. follow-up in non-frail patients (Paired t-test); ‡ Baseline comparison vs. follow-up in frail patients (Paired t-test); ¶ Association between changes in assessment scales (unit decreasea/ increaseb during follow-up) and frailty through unadjusted logistic regression analysis; § Association between changes in the scales of assessment (unit decreasea/ increaseb during follow-up) and frailty through logistic regression analysis; a. Adjusted by age, gender, marital status, incontinence, constipation and intervention group.

participants progressed to frailty compared with 8.2% in the IG (RR 2.90; 95%CI 1.45 to 8.69): 12 IG patients reverted from pre-frail to robust.

Comparison with existing literature

The positive effects of physical exercise on the health of the elderly are accepted (37). A systematic review of 2003-2015 clinical trials (38) concluded that elderly frail people benefit from physical exercise. Studies show that physical activity programs improve strength, balance, mobility and fitness (18,37,39), but few have studied the effects in preventing pre-frailty using a multifactorial intervention, although the assessment of the elderly is necessarily multidimensional (40).

Significant results were obtained in the main objective, with improvements in functional status, mobility, adherence to the Mediterranean diet, nutritional status and quality of life. Studies have demonstrated the effectiveness of interdisciplinary treatments in reverting frailty (41-43) using secondary healthcare resources. Our intervention provided a PHC physical exercise program.

Our intervention included a group session on the Mediterranean diet, without intervention from a specific nutrition unit. Serra-Prat et al (44) found improvements in adherence to the Mediterranean diet, and in physical function (gait speed, TUG and FTSST) and quality of life, but observed no positive effect on the nutritional status, even though patients were referred to a nutrition unit if necessary. Romera-Liebana et al (43) observed functional and cognitive improvement in frail and pre-frail patients at 12 weeks and 18 months after a four-armed intervention, but focused on protein nutritional supplements rather than the Mediterranean diet, and cognitive intervention instead of social assessment.

Associations are reported between frailty and polypharmacy (45,46), a risk factor for falls and mortality, etc. Our results showed inadequate prescribing which, in 30 out of 62 cases was reverted.

In the present study, 86.5% of patients completed follow-up. Serra-Prat et al (44) reported an adherence of 47.5%, probably because the physical exercise intervention consisted of a single face-to-face encounter in the centre with telephone follow-up of home exercise. Our program required more PHC visits with individualized follow-up.

Progression to frailty was associated with worsened functional status, autonomy, nutritional status, quality of life, social risk and functional mobility. Patients non-frail at 12 months improved in these areas, while patients progressing to

frailty had worsened autonomy, functional status and mobility. The Octabaix study (47) found poor activity, weakness, slowness and exhaustion were frailty criteria associated with unsatisfactory aging. In our study, the only factor associated independently with frailty was worsened autonomy (OR 2.80, 95%CI 1.36-6.23).

Strengths and limitations

The study has some limitations. First, losses were greater (13.5%) than expected (9%), since the sample size was calculated from the prevalence of pre-frailty in elderly people (42). Secondly, difficulties in defining frailty mean the results may not be generalizable to patients diagnosed using other frailty tools or aged < 80 years or in populations with characteristics that differ from those of the Spanish cohort studied. Thirdly, our study lasted for 12 months and did not measure the long-term maintenance of prevention of frailty. The Pre Frail 80 study was carried in real life conditions in order to compare usual health care in these patients with the multifactorial intervention carried out. Therefore, the control group was not a placebo group, as they continued to receive usual health care. In addition, the principal investigator was aware of the group patients were in, meaning there was a possible risk of bias.

Implications for research and/or practice

In summary, our results show a multifactorial intervention using PHC resources prevented progression to frailty in pre-frail elderly patients and suggest that promoting preventive activities focusing on physical exercise, the Mediterranean diet, assessment of inadequate prescription in polypharmacy patients and social assessment, may avoid or delay progression to frailty. Longer-term studies are necessary to determine whether the results of the investigation are maintained in the long-term and to determine the cost-effectiveness of the intervention.

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