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Original article

Effectiveness of an oral diabetes-specific supplement on nutritional status, metabolic control, quality or life, and functional status in elderly patients. A multicentre study

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SUMMARY

Background & aims: The purpose of this study was to assess nutritional status, quality of life (QoL) and function in malnourished or at risk for malnutrition community-dwelling (CD) and nursing home-dwelling (NHD) elderly patients with type 2 diabetes mellitus (DM2), receiving treatment with a diabetes-specific oral nutritional supplement (DSONS).

Methods: A prospective, multicentre, observational study was conducted. A DSONS (high-calorie, high-protein, with slow-digestible carbohydrate and high monounsaturated fatty acid – MUFA-content – Glucerna® 1.5 Cal) had been prescribed the week before inclusion. The following assessments were undertaken at baseline (BL), at week 6 (V1) and at month 3 (FV): body mass index (BMI), glycosylated haemoglobin (HbA_{1c}), nutritional status (Mini Nutritional Assessment – MNA), QoL (EQ-5D questionnaire), and functional status (Katz Index – KI of Independence in Activities of Daily Living). The data were reported in the overall population (OP) and in the CD and NHD groups.

Results: A total of 402 patients aged 80.8 ± 8.5 years were evaluable (44.5% men), including 61.7% CD and 38.3% NHD. BMI (kg/m^2) increased in the OP from 22.0 ± 3.5 at BL to 22.5 ± 3.6 at V1 ($p < 0.001$) and 23.0 ± 3.7 at the FV ($p < 0.001$). BMI also increased in the CD group ($p < 0.001$) and in the NHD group ($p < 0.001$). HbA_{1c} decreased in the OP from 7.3 ± 1.1% at BL to 7.2 ± 1.0% at V1 and 7.0 ± 0.9% at the FV ($p < 0.001$), in both the CD ($p < 0.001$) and the NHD groups ($p = 0.020$). The mean overall MNA score increased in the OP from 13.1 ± 4.8 at BL to 17.0 ± 4.7 at V1 and 18.6 ± 5.1 at the FV ($p < 0.001$). The mean overall MNA score also increased in the CD ($p < 0.001$) and the NHD groups ($p < 0.001$). The mean overall EQ-5D score improved in the OP from 46.0 ± 18.0 at BL to 54.8 ± 17.5 at V1 and 59.7 ± 18.8 at the FV ($p < 0.001$). The mean overall EQ-5D score also improved in the CD ($p < 0.001$) and the NHD groups ($p < 0.001$). Gastrointestinal adverse events were seen in only 2% of patients. Treatment compliance was 94.4%.

Conclusions: In this study, conducted in routine, multicentre, clinical settings, the treatment with the high-calorie, high-protein, with slow-digestible carbohydrate, and high MUFA content DSNOS – Glucerna® 1.5 Cal-, was associated with improvements in HbA_{1c}, nutritional status, BMI and QoL following 6 weeks and 3 months of treatment in both institutionalised and non-institutionalised elderly patients

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with diabetes who were malnourished or at risk for malnutrition. A slight improvement in functional status was also observed at 12 weeks. As this is an observational effectiveness study, a randomized controlled trial would be necessary to establish a causal relationship between the DSNOS and the described events.

1. Background

The incidence of type 2 diabetes mellitus (DM2) has been climbing steadily over the last few decades as a result of changes in Western and emerging societies that are closely related to the obesity pandemic [1]. It is estimated that over 365 million people worldwide will suffer from DM2 by 2030 [2]. As a consequence of such high prevalence, most patients with DM2 will develop multiple cardiovascular risk factors, e.g. hypertension, dyslipidemia, chronic kidney disease and microalbuminuria, in addition to the complications inherent to DM2, which are also more frequent than in the general population [3]. Moreover, cardiovascular complications are also more common in patients with diabetes than in the non-diabetic population [3]. For this reason, DM2 is an important public health problem with enormous direct and indirect health costs related to its management.

In addition to these cardiovascular and metabolic comorbidities, elderly patients with diabetes can suffer from malnutrition and malnutrition-associated diseases, which are more prevalent than in the general population [4]. Malnutrition in patients with diabetes worsens if not corrected and leads to treatment intolerance, poorer prognosis and more hospital admissions, which become complicated by acquired infections, poorer wound healing and longer hospital stays [5]. High-protein oral nutritional supplements (ONS) have been shown to improve several nutritional parameters and reduce mortality in malnourished older patients after 90 days of treatment [6]. Hence, malnourished patients with diabetes could be treated with diabetes-specific ONS (DSONS), which have been shown to be efficacious in improving postprandial glycaemic control [7]. DSONS rich in monounsaturated fatty acids (MUFA) and slow-digestible carbohydrates, have been demonstrated to significantly reduce plasma glucose levels in fed conditions [8–10].

Glucerna® 1.5 Cal (Abbott Laboratories) is a high-calorie, high-protein DSONS with low glycaemic index containing, a complex carbohydrate that eludes absorption in the upper gastrointestinal tract and that is partially fermented by bacteria when it reaches the large bowel, producing short-chain fatty acids. This DSONS has been shown to improve glycaemic control in fed conditions [8–10] and several parameters of nutritional status, thereby reducing healthcare costs in elderly patients with diabetes [5]. The main objective of this study was to describe the 3-month effectiveness of a DSONS (Glucerna® 1.5 Cal) on nutritional status in non-institutionalised and institutionalised diabetic elderly patients with malnutrition or at risk for malnutrition. In addition, glycaemic control, serum lipids, quality of life (QoL) and functional status were evaluated.

2. Materials and methods

2.1. Study design

This was an uncontrolled, multicentre, prospective, observational study. The protocol was conducted by geriatricians, nutritionists, endocrinologists and primary care physicians. The study visits took place in outpatient clinics of hospitals, primary care facilities and nursing homes representative of all Spanish regions (Annexed 1).

2.2. Study population

The study population included patients aged 65 years and older with malnutrition or at risk for malnutrition (Mini Nutritional Assessment [MNA] score $\leq$ 23.5) receiving hypoglycaemic treatment for DM2 and who were prescribed the DSONS by their physicians a few days before inclusion in the study, in accordance with best medical practice. Patients who did not sign the informed consent form, those who were prescribed a different ONS and patients who had an estimated glomerular filtration rate $\leq$60 ml/min/1.73 m^2 were excluded from the study.

2.3. Study protocol

Three study visits were conducted by the investigators, including a baseline (BV) visit, a visit at week 6 $\pm$ 7 days (V1) and a final visit (FV) at week 12 $\pm$ 7 days. At baseline, subjects had been taking the studied DSNOS for a few days (each portion containing 220 ml, 329 kcal, 16.5 g protein, 28.05 g carbohydrate, 16.5 g fat of which 1.28 g saturated fatty acids and 10.78 g MUFA, 3.3 g dietary fibre, 2.2 g prebiotics, minerals and vitamins). Participants were instructed to drink 2 servings of the DSONS daily between regular meals throughout the duration of the study. They also were instructed to continue their usual diet, physical activity, and lifestyle habits. Demographic data, anthropometric measurements and metabolic control parameters were collected at regular visits. Supplements treatments were recorded at each visit. Nutritional status, QoL, and dependency in activities of daily living were also assessed.

2.4. Outcomes

Nutritional status was assessed using the full version of the MNA [11], which comprises a screening component (up to 14 points) and an assessment section with up to 16 points. A score between 24 and 30 indicates normal nutritional status; a score between 17 and 23.5 indicates risk of malnutrition; and a score below 17 indicates malnutrition. The threshold to consider that subjects were malnourished or at risk for malnutrition was set at $\leq$23.5. Body mass index (BMI) was expressed in units of kg/m^2 (patients were weighed and measured without shoes and wearing light clothes) and metabolic control was assessed by measuring plasma glycosylated haemoglobin (HbA_{1c}) levels (%). Also, serum lipids were quantified at BV and at FV. QoL was assessed using the validated Spanish version of the EuroQol-5D (EQ-5D) scale, including the 5 dimensions of mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels: no problems (1), some problems (2), and extreme problems (3). The respondent's health is rated on a vertical scale from 0 (worst imaginable health state) to 100 (best imaginable health state) and an index score is derived accordingly, by applying a formula that essentially attaches values to each of the levels in each dimension

[12]. Functional status was assessed using the Katz Index (KI of Independence in Activities of Daily Living) [13], which rates the level of dependence or independence for the activities of "bathing", "dressing", "toileting", "transferring", "continence" and "feeding", giving a point when the patient is independent for that activity. The Katz Index is expressed as the Katz Score, which classified the patients in 3 categories based on the level of dependence for activities of daily living, from little dependence to total dependence. A score of 6–5 indicates full function; 4–3 moderate impairment; and 2 or less severe functional impairment. Participants were considered as compliant if they drank 2 servings of the DSONS daily between regular meals throughout the duration of the study, as they were instructed. Also adverse events were recorded.

2.5. Statistical analysis

The statistical analyses were performed using IBM's SPSS Statistics package version 21.0. Quantitative variables were assessed for normality using the Kolmogorov–Smirnov test and numerical variables were represented as the mean ± standard deviation (SD) or the median (25th percentile – 75th percentile) based on whether distribution was normal or not. Qualitative variables were expressed as the absolute and relative frequencies. For intergroup comparisons, the Student *t*-test was used for independent samples if distribution was adjusted to normality; otherwise, the non-parametric Mann–Whitney *U*-test was used. Qualitative values were compared using Pearson's chi-squared test or Fisher's exact test for small samples, with 2 × 2 tables, or maximum plausibility correction for tables of over 2 × 2. The differences between quantitative values of the MNA and EQ-5D questionnaires and other variables measured at different time points (BV, V1, FV) were assessed using general repeated-measure linear models. For measurements taken at two time points (BV and FV), the paired Student *t*-test was used if normality was present; otherwise, the Wilcoxon test was used. Qualitative variables were assessed using McNemar's chi-squared test. Changes in MNA and EQ-5D scores from FV to BV were expressed as the arithmetic mean with the relevant 95% confidence intervals (95% ICs). The index score of EQ-5D was calculated by deducting the appropriate weights from 1, the value for full health. The analyses were conducted in the overall population (OP) and in the community-dwelling (CD) and nursing home-dwelling (NHD) groups. The study was reviewed and approved by the Clinical Research Ethics Committee at Hospital Clínico San Carlos, Madrid (Exp.n. 14/518-O), and patients signed an informed consent form before being included.

3. Results

3.1. Baseline characteristics

A total of 76 physicians took part from 47 hospitals, 12 nursing homes and 5 primary care centres between February 2015 and November 2015. A total of 417 patients were screened, of whom 15 were excluded (Fig. 1). At the baseline visit, 402 patients were eligible for the study, with mean age 80.8 years (SD = 8.5 years) and 44.5% men. Community dwellers (CDs) made up 61.7% of the study population, whereas the remaining 38.3% were nursing home dwellers (NHDs). Table 1 shows the baseline characteristics of the OP and the CD and NHD groups. Body Mass Index, prevalence of cancer, frequency of current smokers, plasma glucose and total protein levels were higher in the CD group. Conversely, patients were older and there were more women in the NHD group.

3.2. Body mass index

At baseline, 333 patients (82.8%) had normal weight or were underweight (BMI < 25 kg/m^2), 57 patients (14.2%) were overweight (BMI 25–29.99 kg/m^2) and 12 patients (3%) were obese (BMI ≥ 30 kg/m^2). In the OP, BMI increased from BV to V1 and the FV by 0.51 kg/m^2 (95% CI: 0.37–0.64, $p < 0.001$) and 0.97 kg/m^2 (95% CI: 0.80–1.14, $p < 0.001$), respectively. This increase was also seen in both the CD and NHD groups (Table 2). A change in BMI categories throughout the study was seen in the OP and in the CD group ($p < 0.001$), but not in the NHD group ($p = 0.102$) (Table 2).

3.3. Nutritional status: MNA score

Based on the global MNA score, 312 (77.6%) patients had malnutrition and 90 (22.4%) patients were at risk for malnutrition at BV, with differences between the CD and the NHD groups (Fig. 2).

A significant improvement was seen in global MNA scores at V1 and at the FV from BV, both in the OP and in the CD and NHD groups (Table 2). At V1, the mean global MNA score in the OP increased by 3.9 points from baseline (CI 95%: 3.5–4.3, p < 0.001). A higher score was observed in the CD group versus the NHD group (17.6 ± 4.9 vs. 15.8 ± 4.5; n = 373; p < 0.001). At the FV, the mean global MNA score in the OP increased by 5.5 points from baseline (CI 95%: 5.0–5.9, p < 0.001). A higher score was observed in the CD group versus the NHD group (19.3 ± 5.2 vs. 17.4 ± 4.8; n = 356; p < 0.001).

At V1, there were 161 (45.6%) patients with malnutrition, 168 (47.6%) patients at risk for malnutrition, and 24 (6.8%) patients with normal nutritional status. In the CD and NHD groups, respectively, there were 81 (38.9%) patients and 80 (55.2%) patients with malnutrition, 107 (51.4%) patients and 61 (42.1%) patients at risk for malnutrition, and 20 (9.6%) patients and 4 (2.8%) patients with normal nutritional status (p = 0.001) (Fig. 2).

At the FV, further improvements in nutritional status were noted (Fig. 2), with 121 (34.0%) patients with malnutrition, 170 (47.8%) patients at risk for malnutrition, and 65 (18.3%) patients with normal nutritional status. In the CD and NHD groups, respectively, there were 60 (28.4%) patients and 61 (42.1%) patients with malnutrition, 99 (46.9%) patients and 71 (49.0%) patients at risk for malnutrition, and 52 (24.6%) patients and 13 (9.0%) patients with normal nutritional status (p < 0.001).

3.4. Metabolic control (HbA_{1c}) and plasma lipids

Table 2 shows changes in HbA_{1c} levels at 6 and 12 weeks of taking the DSONS. A significant decrease in HbA_{1c} from BV was seen at the FV: 0.3% in the OP and the CD group (p < 0.001) and 0.2% in the NHD group (p = 0.020). The percentage of patients with HbA_{1c} levels <7% from BV at the FV increased by 10.4% in the OP (p = 0.004), 8.3% in the CD group (p < 0.001) and 11.9% in the NHD group (p < 0.001). The percentage of patients with HbA_{1c} levels <8% from BV increased by 10% in the OP (p = 0.004), 12% in the CD group (p < 0.001) and 5.9% in the NHD group (p = 0.259).

Mean total cholesterol increased from the BV in the OP −15.10 mg/dl (CI 95% 10.84/19.39); p < 0.001− (CD 15.2 mg/dl; p < 0.001; NHD 15.1 mg/dl; p < 0.001), as did the mean LDL-cholesterol −5.67 mg/dl (CI 95% 1.52/9.81); p = 0.008− (CD 2.2 mg/dl; p < 0.001; NHD 9.9 mg/dl; p < 0.001), and the mean HDL-cholesterol −3.35 mg/dl (CI 95% 1.82/4.87); p < 0.001− (CD 3.9 mg/dl; p < 0.001; NHD 2.7 mg/dl; p < 0.001). The increase in median tryglicerides did not reach statistical significance – OP 11.0 mg/dl (CI 95% (−0.27/27.13); p = 0.062 (CD 9.0 mg/dl; p = 0.107; NHD 10.0 mg/dl; p = 0.071) (Table 2).

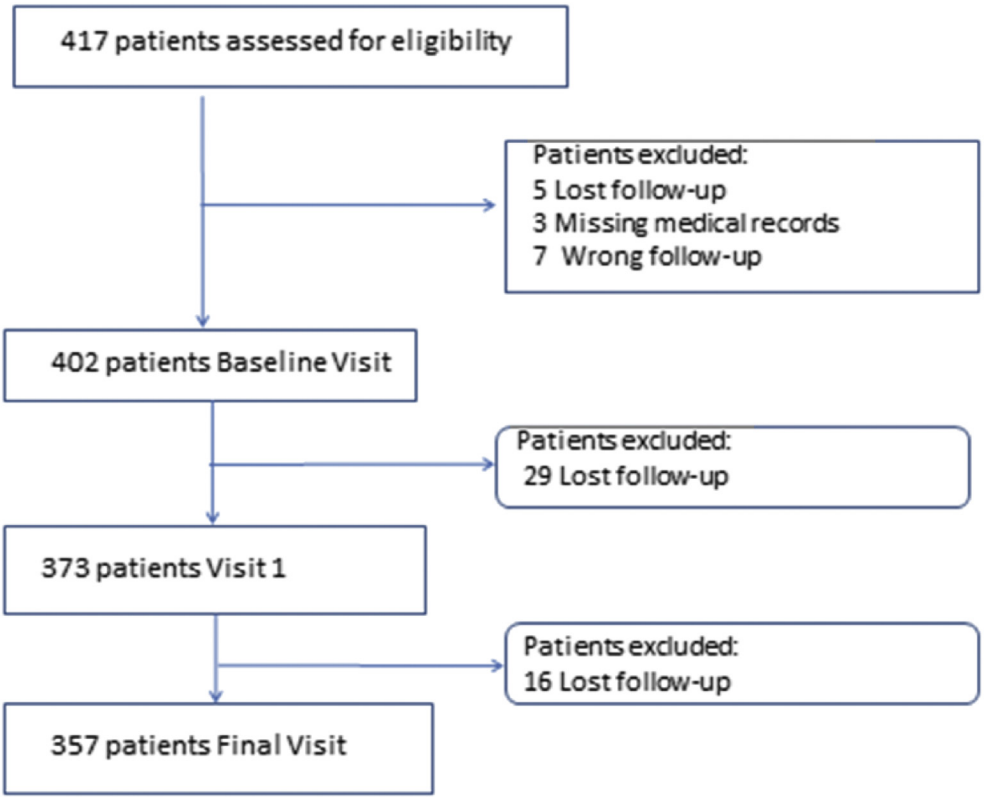

Fig. 1. Patients recruitment flow-chart.

Table 1
Baseline demographic clinical characteristics and laboratory characteristics of the sample.

	Overall	Community dwellers	Nursing home dwellers	p-value[a]
Gender (male)	179 (44.5)	130 (52.4)	49 (31.8)	<0.001
Age	80.8 ± 8.5	78.6 ± 8.4	84.2 ± 7.5	<0.001
Body mass index (kg/m^2)	22.0 ± 3.6	22.6 ± 3.7	21.1 ± 3.2	<0.001
Body mass index in ranges				0.004
< 25 kg/m^2	333 (82.8)	197 (79.4)	136 (88.3)	
25–29.99 kg/m^2	57 (14.2)	39 (15.7)	18 (11.7)	
≥ 30 kg/m^2	12 (3.0)	12 (4.8)	0	
Insulin therapy	271 (67.6)	163 (66.0)	108 (70.1)	0.389
High blood pressure	287 (71.4)	184 (74.2)	103 (66.9)	0.115
Dyslipidemia	173 (43.0)	116 (46.8)	57 (37.0)	0.055
Smoker (current)	49 (12.2)	38 (15.3)	11 (7.1)	0.015
Cardiovascular disease	207 (51.5)	128 (51.6)	79 (51.3)	0.951
Kidney Disease	57 (14.2)	33 (13.3)	24 (15.6)	0.524
Hepatobiliary disease	41 (10.2)	29 (11.7)	12 (7.8)	0.209
Cancer	113 (28.1)	96 (38.7)	17 (11.0)	<0.001
Other disease	253 (62.9)	139 (56.0)	114 (74.0)	<0.001
Multiple pathologies				<0.001
1	31 (7.7)	15 (6.0)	16 (10.4)	
2	90 (22.4)	44 (17.7)	46 (29.9)	
3	128 (31.8)	83 (33.5)	45 (29.2)	
4	92 (22.9)	57 (23.0)	35 (22.7)	
5 or more	61 (15.1)	49 (19.7)	12 (7.7)	
Haemoglobin (g/dl)	11.4 ± 1.6	11.3 ± 1.6	11.7 ± 1.7	0.065
Glucose (mg/dl)	141.7 ± 65.0	145.8 ± 63.1	131.8 ± 68.1	0.106
Creatinine (mg/dl)	0.88 ± 0.31	0.91 ± 0.34	0.82 ± 0.26	0.012

Data are expressed as mean ± standard deviation (SD) or the median (25th percentile – 75th percentile) based on whether distribution was normal or not for continuous variables, and categorical variables as number (percentage) for each group.
[a] Between community dwellers and nursing home dwellers groups.

3.5. Quality of life: EQ-5D questionnaire

The mean health state score in the OP improved throughout the study in all 354 patients assessed (BV, V1, FV: 46.4 ± 18.0, 54.8 ± 17.5 and 59.7 ± 18.8 points, respectively, $p < 0.001$). The improvement was seen in both the CD group (49.4 ± 17.6, 57.9 ± 16.6 and 62.4 ± 18.8 points, $p < 0.001$) and the NHD group (42.2 ± 17.9, 50.4 ± 17.7 and 55.8 ± 18.2 points, $p < 0.001$). The index

Table 2
Change in body mass index, MNA, glycosylated haemoglobin (HbA_{1c}) and serum lipids 6 weeks and 3 months after supplementation with the DSONS.

	Overall study population				Community dwellers				Nursing home dwellers			
	Baseline	6 Weeks	3 Months	p[a]	Baseline	6 Weeks	3 Months	p[a]	Baseline	6 Weeks	3 Months	p[a]
Body mass index (mean ± SD)	22.0 ± 3.5	22.5 ± 3.6	23.0 ± 3.7	<0.001	22.6 ± 3.6	23.1 ± 3.2	23.6 ± 3.5	<0.001	21.2 ± 3.2	21.7 ± 3.4	22.1 ± 3.4	<0.001
Body mass index in ranges (%)				<0.001				<0.001				0.102
< 25 kg/m^2	82.9	80.5	76.5		79.7	77.5	71.2		87.6	84.8	84.1	
25–29.99 kg/m^2	14.0	15.8	18.5		15.1	17.2	21.2		12.4	13.8	14.5	
≥ 30 kg/m^2	3.1	3.7	5.0		5.2	5.3	7.5		0.0	1.4	1.4	
MNA (mean ± SD)	13.1 ± 4.8	17.0 ± 4.7	18.6 ± 5.1	<0.001	13.7 ± 4.7	17.8 ± 4.6	19.4 ± 5.3	<0.001	12.1 ± 4.8	15.8 ± 4.5	17.4 ± 4.8	<0.001
Hb1Ac (%) (mean ± SD)	7.3 ± 1.1	7.2 ± 1.0	7.0 ± 0.9	<0.001	7.3 ± 1.0	7.2 ± 0.9	7.0 ± 0.9	<0.001	7.2 ± 0.9	7.1 ± 1.1	7.0 ± 1.0	0.020
HbA_{1c} (%) in ranges (%)												
<6.5	22.0	20.7	23.9	0.125	18.1	18.1	21.5	0.089	26.5	24.2	26.5	0.869
<7.0	39.1	42.7	49.5	<0.001	37.2	39.0	45.5	<0.001	41.9	47.7	52.9	<0.001
<8.0	75.8	79.0	85.8	0.004	72.8	79.1	84.8	<0.001	80.1	78.8	86.0	0.259
Cholesterol (mg/dL) (mean ± SD)	151.6 ± 41.0	–	166.7 ± 38.6	<0.001	152.4 ± 43.0	–	167.6 ± 40.4	<0.001	150.5 ± 38.2	–	165.6 ± 36.0	<0.001
HDL-c (mg/dL) (mean ± SD)	41.7 ± 15.5	–	45.0 ± 13.1	<0.001	42.2 ± 1.3	–	46.1 ± 14.5	<0.001	40.9 ± 12.8	–	43.6 ± 11.0	<0.001
LDL-c (mg/dL) (mean ± SD)	91.8 ± 33.7	–	97.5 ± 27.8	0.008	93.7 ± 36.7	–	95.9 ± 29.3	<0.001	89.5 ± 29.8	–	99.4 ± 25.9	<0.001
TG (mg/dL) (median (p_{25}–P_{75}))	119 (89–154)	–	130 (97–160)	0.062	126 (95–159)	–	135 (100–164)	0.107	110 (82–145)	–	120 (85–151)	0.071

MNA: Mini Nutritional Assessment. The sample reflects patients who completed the study: body mass index, 354 patients; MNA, 356 patients; HbA_{1c}, 350 patients; and Serum Lipids, 350 patients. HDL-c: High density lipoprotein-cholesterol, LDL-c: Low density lipoprotein-cholesterol, TG: tryglicerides.
[a] Between visits.

score (median [p25–p75]) in the OP also improved throughout the study (BV, V1, FV: 0.61 [0.57–0.72], 0.64 [0.59–0.76] and 0.65 [0.59–0.80] points, respectively, $p < 0.001$). The improvement was seen in both the CD group (0.65 [0.59–0.80], 0.67 [0.60–0.83] and 0.68 [0.60–0.85] points, respectively, $p < 0.001$) and the NHD group (0.60 [0.56–0.65], 0.61 [0.56–0.67] and 0.62 [0.56–0.68] points, respectively, $p < 0.001$). Table 3 shows the changes in the EQ-5D dimensions in the OP and in the CD and NHD groups. In all EQ-5D dimensions, less dysfunction was seen in the CD group versus the NHD group, except for the pain/discomfort dimension. Throughout the study, improvements were seen in the OP and in both the CD and NHD groups in the usual activities dimension ($p = 0.002$, $p = 0.004$ and $p = 0.015$, respectively), in pain/discomfort ($p < 0.001$, $p < 0.001$ and $p = 0.006$, respectively), and in anxiety/depression ($p < 0.001$, $p < 0.001$ and $p = 0.001$, respectively). Fewer people had mild or severe problems with mobility in the CD group at the FV ($p = 0.042$), and in the NHD group an improve in the self-care dimension was seen ($p = 0.046$) (Table 3).

3.6. Katz index

Table 4 shows the KI dimensions assessed at BV at V1 and at the FV, in the OP and in both the CD and NHD groups. The dimension with the least dependence was feeding, in 38% of patients, whereas bathing was the dimension requiring most help, in 70.4% of patients. All dimensions assessed showed poorer independence in the NHD group versus the CD group, both at BV and at the V1 and FV visits ($p < 0.05$). Severe functional impairment was seen in 52% of patients and moderate impairment or no impairment was seen in 49% of patients. An improvement in the dressing dimension was seen in the OP ($p = 0.042$), in the CD ($p = 0.038$), and in the NHD ($p = 0.046$). Feeding improved in the NHD group ($p = 0.035$). Fewer people showed severe functional impairment at FV in the OP, CD, and NHD groups, but this difference did not reach statistical significance ($p = 0.729$, $p = 0.901$, and $p = 0.806$, respectively) (Table 4).

3.7. Treatment adherence and safety

At V1, 94.1% of patients were compliant with 2 servings daily of the DSONS, with a lower proportion in the CD group versus the NHD group (90.7% and 99.3%; $p = 0.001$). At the FV, compliance to the DSONS remained at 94.4% of patients, again with a lower proportion in the CD versus the NHD groups (91.5% and 98.6%; $p < 0.001$). A total of 51 adverse events including 30 deaths for different reasons were recorded; however, no relationship to the study DSONS was suspected by the investigators. Adverse events were considered serious in 33 of the 51 patients (64.7%); causality was assessed as unrelated in 31 patients (60.8%) and unlikely in 13 patients (25.5%). Only in 7 patients (13.7%) was causality considered likely or possible. The study product was withdrawn in only 8 patients. The most commonly reported adverse events were diarrhoea in 8 patients (2.0%) and urinary tract infection in 6 patients (1.5%).

4. Discussion

In this study the DSONS Glucerna® 1.5 taken twice daily for 3 months was associated with improvements in nutritional status, HbA1c levels, and QoL in both institutionalised and CD elderly diabetic patients with malnutrition or at risk for malnutrition.

DSONS are intended to improve nutritional status of patients with diabetes without altering their metabolic control. DSONS have demonstrated improvements in the glycaemic profiles of patients with DM [7]. This is the first time that a DSONS was found to be

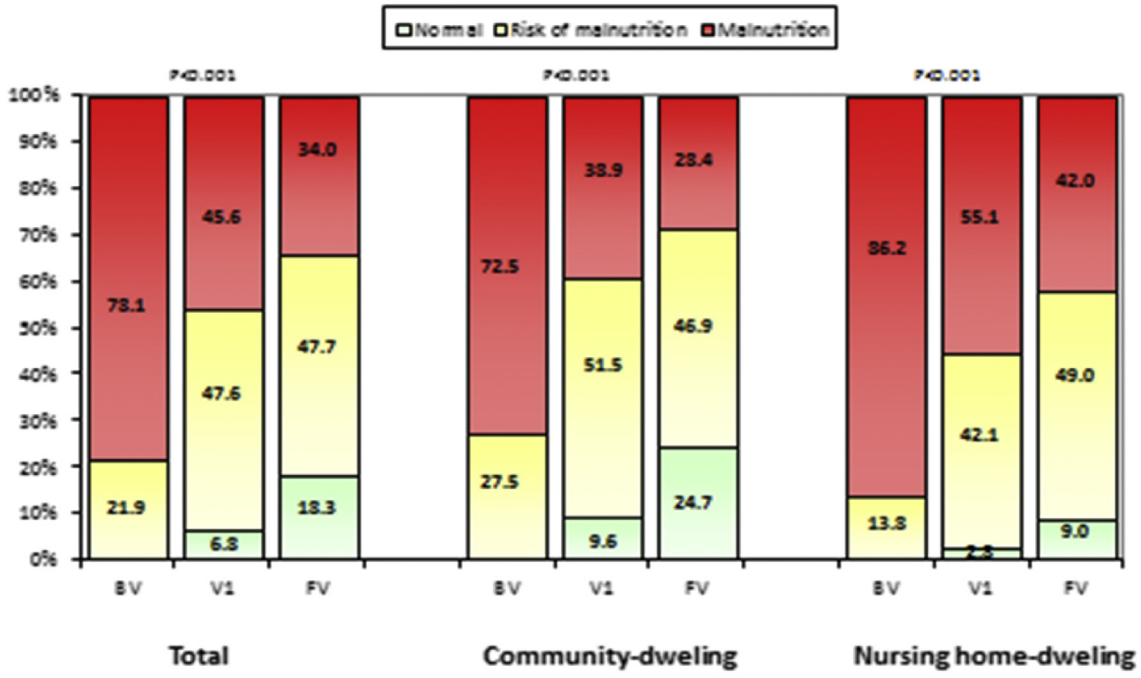

Fig. 2. Distribution of nutritional status according to patients' visit and residence.

associated both with nutritional status and QoL in elderly patients with diabetes [14,15]. In both groups, improvements were seen in the global MNA score at 6 weeks and at 3 months of taking 2 daily servings of the DSONS. IMC improved by 0.5 kg/m^2 in both groups at 6 weeks and by 1.0 kg/m^2 at 3 months after the DSONS was prescribed. This increase in weight is in keeping with data from a systematic review on oral nutritional supplements in the elderly in which an increase in body weight is reported [16], specifically with high-protein oral nutritional supplements [17]. As body composition was not measured in this study, we are unable to claim that the improvement in BMI is due to an increase in lean body mass; however, it has been established that high-protein diets improve

Table 3
Change in Quality of Life (EQ-5D) 6 weeks and 3 months after supplementation with the DSONS.

Domains EQ-5D[a]	Overall study population				Community dwellers				Nursing home dwellers			
	Baseline	6 Weeks	3 Months	p[a]	Baseline	6 Weeks	3 Months	p[a]	Baseline	6 Weeks	3 Months	p[a]
Mobility (%)	80.6	76.9	75.6	0.056	73.4	70.4	66.8	0.042	92.2	89.1	88.3	0.165
Self-care (%)	75.8	74.3	72.4	0.159	64.1	64.1	63.5	0.582	94.8	89.8	85.6	0.046
Usual activities (%)	85.8	84.1	81.2	0.002	79.4	76.7	73.5	0.004	96.1	95.2	92.4	0.015
Pain/Discomfort (%)	75.9	66.7	60.6	<0.001	80.3	69.1	63.5	<0.001	68.8	63.3	56.6	0.006
Anxiety/depression (%)	68.2	60.0	53.6	<0.001	66.2	56.1	49.7	<0.001	71.4	66.0	59.3	0.001

Results in patients with mild or severe problems. The sample reflected for the EQ-5D is the sample completing the study: n = 354 patients.
[a] Between visits.

Table 4
Change in independence in activities of daily living 6 weeks and 3 months after supplementation with the DSONS.

	Overall study population				Community dwellers				Nursing home dwellers			
	Baseline	6 Weeks	3 Months	p[a]	Baseline	6 Weeks	3 Months	p[a]	Baseline	6 Weeks	3 Months	p[a]
Bathing (%)	70.4	69.7	70.9	0.865	57.7	57.0	58.9	0.821	90.9	89.1	88.3	0.869
Dressing (%)	60.0	58.4	56.5	0.042	45.6	44.4	41.6	0.038	83.1	79.6	77.9	0.046
Toileting (%)	54.5	54.6	53.1	0.384	37.5	39.0	36.8	0.526	81.8	78.2	76.6	0.098
Transferring (%)	45.5	44.9	44.9	0.825	32.7	31.4	30.1	0.116	66.2	65.3	66.2	0.981
Continence (%)	51.7	51.1	53.7	0.236	36.3	34.5	38.3	0.321	76.6	76.2	75.9	0.215
Feeding (%)	38.1	37.8	37.0	0.157	25.8	26.9	26.3	0.856	57.8	54.4	52.4	0.035
Katz (%)				0.729				0.901				0.806
0	52.0	49.9	49.6		34.9	33.5	33.0		76.6	73.1	73.1	
1	24.6	25.1	25.4		30.1	30.6	31.1		16.6	17.9	17.2	
2	23.4	25.1	25.1		34.9	35.9	35.9		6.9	9.0	9.7	

KI: Katz Index of Independence in Activities of Daily Living. Results in patients with problems in each domain evaluated. The sample reflected for the KI is the sample completing the study: n = 354. Three categories according to the level of dependence for activities of daily living: a score of 6 indicates full functionality (2), 3–5 indicates moderate impairment (1), and 2 or less indicates severe functional impairment (0).
[a] Between visits.

body weight by improving lean mass [18]. Administration of macronutrients and micronutrients with high energy and protein contents reduces the risk of malnutrition in patients with diabetes [19]. These data in elderly patients with diabetes are confirmed in this study, too. After 3 months of supplementation with the DSONS, normal nutritional status was restored in 9.0% of patients in the NHD group and 24.6% of patients in the CD group. The greater nutritional recovery seen in the less dependent patients suggests that greater benefits could be achieved by starting treatment with DSONS earlier, i.e. before patients deteriorate further, as is the case of NHD patients.

Standard nutritional formulae for malnutrition may cause hyperglycaemia, which can be an independent prognostic factor of mortality in patients with enteral nutrition [20]; for this reason, DSONS are usually recommended. In all our study subjects improvements were seen in plasma HbA_{1c} levels, consistent with previous studies conducted with this DSONS. This oral nutritional supplement has demonstrated a reduction in postprandial glucose levels, partly because it contains slow digested carbohydrates, which are not absorbed in the upper gastrointestinal tract but are partially fermented by bacteria in the large intestine [8–10]. However, self-monitored capillary blood glucose records were not considered in this study, and therefore it is not possible to estimate the proportion of the observed HbA_{1c} benefit linked to a reduction in glycaemic abnormalities.

The observed increase in plasma cholesterol could be analysed under two perspectives. Although the general agreement is to keep LDL-cholesterol under 100 or even 70 mg/dl in very high-risk patients with diabetes, some concerns arise in aged population. Guidelines suggest the use of moderate/high-intensity statin therapy in the elderly patients with diabetes, but the individualization must guide each decision [21,22]. In this regard, the percentage of patients fulfilling the LDL-cholesterol levels recommendations was higher than 50% at FV in both groups, in spite of the increment observed. In addition, HDL-cholesterol improved from the BV, and at the end of the study 42.6% of the sample fulfils the objectives (only 33.3% at BV), reducing in that way the cardiovascular risk lipid profile. From another point of view, in high-risk elderly subjects, two of the strongest predictors of mortality are low BMI and low HDL-cholesterol. This two are related either to malnutrition and to chronic disease, and in same way these associations indicate the presence of a reverse epidemiological effect of classic cardiovascular risk factors on mortality [23]. Therefore, in our study, the rise in LDL-cholesterol could have been counterbalanced by the improvements in HDL-cholesterol and in the BMI of the sample at FV.

Assessment of QoL is important to identify health-related needs in patients with chronic diseases [24]. In elderly subjects, malnutrition has an impact on QoL [25]. In patients with DM2, metabolic complications, lifestyle changes and fear of long-term complications all add up to the reduction in QoL [26]. At V1 and at FV global health state score improvements were seen in both groups. These improvements were progressive, which suggests that as nutritional status improves, QoL also improves in elderly patients with diabetes. This improvement should be stressed, as QoL usually worsens as DM progresses and its associated complications arise [26,27]. Depression is one of the most common health problems in the elderly and it affects QoL [28]. One of the areas that improved with the DSONS was depression, which affected 68.2% of patients at baseline and decreased to 53.6% at 3 months of treatment. Depression is known to lead to weight loss and malnutrition in the elderly [29]; therefore, it could be assumed that the improvement in this QoL dimension could also contribute to the improvement of body weight seen at 3 months of DSONS use or vice versa; however, the relationship between depression and nutritional status remains poorly understood [30]. Other dimensions relating to malnutrition are pain and usual activities [31], both of which also improved after 3 months of treatment with the DSONS. However, improvements in the mobility dimension were only seen in the CD group, which could indicate that a poorer nutritional status in the NHD group could preclude improvements; alternatively, the assessment period may not have been long enough to detect differences.

It is vitally important to improve the patients' degree of independence, as the risk of malnutrition associated to dependence for usual activities leads to poorer survival rates in patients aged 60 and older [32]. Progressive improvements in the KI were not seen in this study with DSONS, but better percentages were seen in the OP at the FV versus baseline. The relationship between malnutrition and functional status is well-established and there is feedback between one another [33].

This study does have, however, several limitations. There was no control group with a standard ONS or an organoleptically similar placebo. Information regarding previous use of non-specific ONS, their effectiveness, adverse events, and the reasons for a prescription change were not recorded in the studied sample, so we cannot assess the efficacy of nutrition therapy before study entry. The positive influence of physicians or caregivers on the answers to subjective specific items could have gone undetected. Because the study DSONS contains multiple ingredients, the observed benefits may not be accurately attributed to any one specific ingredient or to the synergy between some ingredients. Furthermore, as this was a non-randomized study, decisions were based on the physicians' clinical criteria and the nutritional education could differ based on the guidelines and dedication of the different sites. Self-monitored capillary glucose measurements were not recorded, as were not the changes in drug therapy. However, the fact that the study was conducted in routine, multicentre, clinical settings are positive aspects that should be considered.

In conclusion, in this observational effectiveness study, improvements in the nutritional status of elderly patients with diabetes and malnutrition, or at risk for malnutrition, and in their glycaemic control were observed in this study at 6 weeks and 3 months of taking 2 daily servings of the DSONS Glucerna® 1.5 Cal. Improvements were also seen in health state as assessed by the EQ 5D questionnaire. A tendency to improve the usual daily activities was also observed. Adherence was high and almost no adverse events were reported. However, blind randomized controlled clinical trials would be necessary to establish a causal relationship between this DSONS and the observed events in these elders.

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Conflict of interest

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Annexed 1

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	Hospital Ernest Lluch	Berta Mª Jiménez Rubiano
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