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Lifestyle and nutrition related to male longevity in Sardinia: An ecological study

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Abstract *Background and aims:* A demographic analysis in the Mediterranean island of Sardinia revealed marked differences in extreme longevity across the 377 municipalities and particularly identified a mountain inner area where the proportion of oldest subjects among male population has one of the highest validated value worldwide. The cause(s) of this unequal distribution of male longevity may be attributed to a concurrence of environmental, lifestyle and genetic factors.
Methods and results: In this study we focussed on some lifestyle and nutrition variables recorded in the island's population in early decades of 20th century, when agricultural and pastoral economy was still prevalent, and try to verify through ecological spatial models if they may account for the variability in male longevity. By computing the Extreme Longevity Index (the proportion of newborns in a given municipality who reach age 100) the island's territory was divided in two areas with relatively higher and lower level of population longevity. Most nutritional variables do not show any significant difference between these two areas whereas a significant difference was found with respect to pastoralism ($P = 0.0001$), physical activity estimated by the average slope of the territory in each municipality ($P = 0.0001$), and average daily distance required by the active population to reach the usual workplace ($P = 0.0001$).
Conclusion: Overall, these findings suggest that factors affecting the average energy expenditure of male population such as occupational activity and geographic characteristics of the area where the population mainly resides, are important in explaining the spatial variation of Sardinian extreme longevity.

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Introduction

The geographic distribution of human longevity displays a wide variability among different nations [1] and even within single regions of the world [2]. The analysis of the spatial distribution of long-living people in the Mediterranean island of Sardinia allowed identifying a mountain inner area, dubbed as "*Blue Zone*" (BZ), where the proportion of male centenarians born in the last two decades of 19th century reaches one of the highest value in Europe (more than 15 per ten thousand newborns) and the femininity ratio (F/M) among centenarians is 1.34, i.e. remarkably lower than in most western countries, including Italy [3]. Outside this BZ the corresponding figures are quite similar to that of other regions of Italy [4]. The exceptional survival in this sub-region of Sardinia seems to be a phenomenon restricted to males, as the distribution of extreme longevity among females is relatively uniform across all the island's areas.

To identify the potential determinants of this exceptional male longevity, some factors investigated in other populations, such as genetic [5], environmental [6], socio-cultural [7], economic factors [8] and lifestyle appear to be the most suitable candidates. As for genetic factors, several association studies carried out using a limited number of genetic markers did not reveal up to now any positive association with Sardinian longevity [9,10], and genetic research ruled out the existence of major genetic differences between subregions within the island [11]. Moreover, socio-cultural factors were very similar in most municipalities of Sardinia before the lifestyle transition, which occurred at the end of 1950s [12].

It may be postulated that extreme longevity, as it was observed in persons who reached their 100th birthday between 1980 and 2000, was very likely influenced by past lifestyle habits. Particularly, nutrition and physical activity recorded in the first half of 20th century, when the subjects who eventually have become centenarians were young, appear of major importance than lifestyle recorded in more recent years. In this regard, historical data such as those published by Fermi [13] in the 1930s and Peretti [14] in the 1940s, allow reconstructing a reliable picture of past lifestyle of Sardinians — including nutrition habits.

Evidences from animal models as well as from humans suggest that a diet low in calories [15] and a regular physical activity [16] may significantly prolong maximum life span. However, no information about the relationship between nutrition, lifestyle and longevity is available up to now in the Sardinian population. In particular, the possible role played by traditional dietary regimen and differences in the occupational activity of the male population in relation to extreme longevity has not yet been investigated.

The objectives of the current ecological study were to compare two areas within Sardinia characterised by relatively high and low levels of male longevity in regard of the distribution of historical lifestyle data, such as occupation, nutrition, and physical activity, and to test, through a spatial model, their possible association with exceptional male longevity in Sardinia at municipality level.

Methods

Study areas and demographic data sources

The whole Sardinian territory, encompassing 377 administrative municipalities, was partitioned into two areas where population is characterized by distinct levels of extreme longevity, using an appropriate demographic index, i.e. the probability for a newborn in a given municipality to reach age 100 (Extreme Longevity Index, ELI), as defined in a previous study [3]. It compares the number of centenarians born in a given place with the number of persons born in that place a century ago, wherever these centenarians are living. The main advantage of ELI, compared to the centenarians' prevalence, is that it limits biases due to migration. For Sardinia as a whole, 516,276 births (B) (265,454 boys and 250,822 girls) were registered between 1880 and 1900, and 1132 subjects (415 men and 717 women) who reached age 100 (C) were identified. The Extreme Longevity Index was then computed as: $ELI = 10{,}000^{*}C/B$. Accordingly, the value of the male ELI (mELI) is 15.6 per ten thousand newborns ($10^4 \times 415/265{,}454$). After a Gaussian smoothing procedure [3], the level of mELI computed for each municipality was used to assign each of them to the two spatially non-overlapping areas. One hundred ninety two municipalities were included in an area labelled 'Blue Zone' (BZ) with an average mELI of 21.8 per ten thousand, whereas the remaining 185 municipalities were included in an area labelled 'Non-BZ' (NBZ) with an average mELI of 10.3 per ten thousand (Fig 1).

Nutritional data

Nutrition habits before the nutritional transition, which in Sardinia occurred at the end of 1950s [12], have been taken into account. To this aim the analysis included several nutritional data published in the first half of 1930s by the Italian hygienist C. Fermi in a classical study about Sardinia [13] where he reported data about demography, socioeconomic status, occupation, dietary habits, and lifestyle of the population living in all municipalities of the island. These historical data are quite accurate and reflect the lifestyle of Sardinian population long before the epidemiological transition. According to the original description of this author all variables were collected through a structured questionnaire filled up by sanitary personnel in each village. Table 1 shows a list of the variables selected for this analysis. The quality of the diet of the population in each village, originally expressed through adjectives (from "very poor" to "good"), was re-coded into an ordinal variable ranging from 1 to 5. However, as it was usual in the 1930s, the criteria to calculate the diet score were not as accurate as we would expect today. The exact calorie intake or the percentage of macro- and micronutrients were not used to calculate the score. Instead, as in other contemporary surveys, the score resulted from a mixture of both qualitative and quantitative information on the diet, mostly based on the relative proportion of animal protein intake. The other nutritional variables were scalar. In addition, data reported in Fermi's study regarding the average body

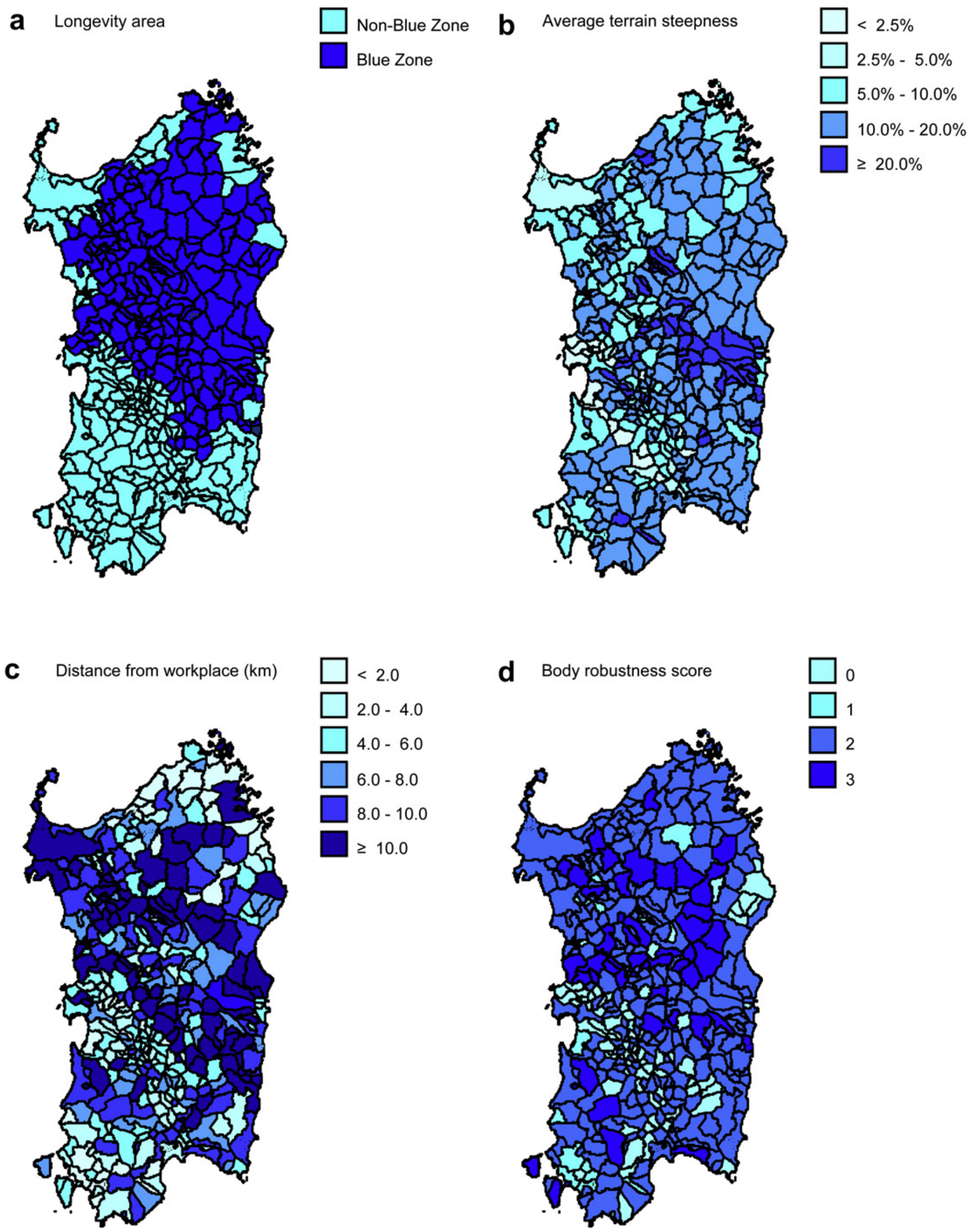

Figure 1 a) Longevity area; b) Average terrain's steepness (GIS); c) Average daily distance from usual workplace (km); d) Body robustness score e) Diet score; f) Meat consumption; g) Wine consumption; h) Pastoralism score. Maps were produced using GeoBUGS, the add-on module included in WinBUGS 1.4 package.

height and robustness of the male population, derived from existing military lists, were included in the analysis, as they may partly reflect the nutritional status of the population. The original categorical variables were re-coded into a scoring system by giving 0 to 3 points for having low, subnormal, medium and strong robustness, respectively, and from 1 to 3 points for having low, medium or high body height, respectively. Robustness, according to the military records as reported by Fermi himself, derived mostly from chest circumference as it was usual in Italian army until recent times.

An additional source of nutrition data used in this analysis was the "*Agricultural Cadastre*" a nation-based census of agricultural activities published up to 1929 [17]. The selected variables, related to the annual production of certain foods in each municipality of the island, are reported in Table 1. Although these variables reflect essentially food production, they may be considered an acceptable proxy for consumption by the population in each municipality, as it is usual in traditional agripastoral societies. However, although up to the end of WWII market exchanges among Sardinian communes were limited [18],

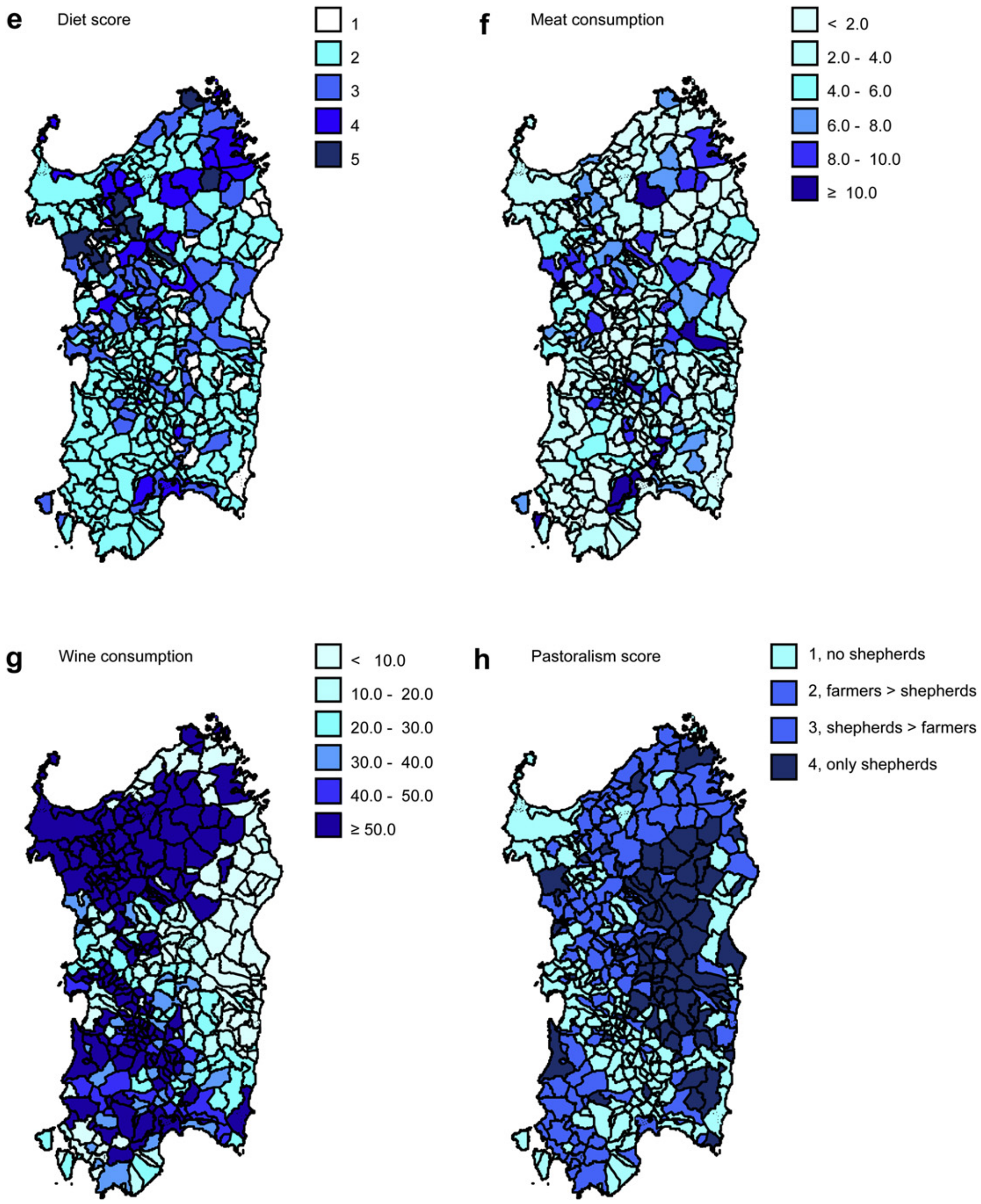

Figure 1 *(continued)*

certain goods such as wheat and olive oil were largely exchanged between villages [19].

Occupational and environmental data

In this study we addressed only factors which were available at the municipality level and that may have influenced the average energy expenditure (AEE) of male population in the past. In particular we have considered:

- the degree of pastoralism in each municipality according to Fermi's database [13]. Shepherds did less intense but more continuous physical activity than farmers. A score number was obtained by coding each municipality as 1 (no shepherds), 2 (farmers outnumbered shepherds), 3 (shepherds outnumbered farmers), 4 (only shepherds);
- the mean daily distance (in km) for the active population to reach the workplace when located outside the village. We presumed that the longer was this distance the higher was the active energy expenditure during most of the working life [18].
- finally, based on the assumption that living in a village lying on a slope entails a lifelong energy expenditure higher than living in a lowland village [20], we collected

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Table 1 Lifestyle and nutrition variables used in the current analysis.

Variable	Description	Source
Diet score	Originally expressed through adjectives (very poor-poor-sufficient-more than sufficient-good) and re-coded into an ordinal variable from 1 to 5	Fermi *et al.*, 1934 [13]
Meat consumption	Reflects how many times in a month a meat servings appeared in the population diet	Fermi *et al.*, 1934 [13]
Wine consumption	Expressed as lt/person/year	Fermi *et al.*, 1934 [13]
Wheat production	Expressed as hl/person/years[a]	*Catasto Agrario*, 1929 [17]
Barley production	Expressed as hl/person/year	*Catasto Agrario*, 1929 [17]
Nuts production	Expressed as kg/person/year	*Catasto Agrario*, 1929 [17]
Cheese production	Cheese production, in kg/person/year	*Catasto Agrario*, 1929 [17]
Pastoralism score	Pastoralism score. Numbers from 1 to 4 reflect increasing prevalence of shepherds as main occupation in the municipality.	Fermi *et al.*, 1934 [13]
Average terrain's slope (%)	Average slope of the municipality's terrain	GIS database
Distance to workplace (km)	Average distance of the active population to reach the working place daily (km)	Fermi *et al.*, 1934 [13]
Body robustness	Body robustness score (0—4) of the male population in the municipality based on military lists.	Fermi *et al.*, 1934 [13]
Body height	Body height score of the male population in the municipality based on military lists.	Fermi *et al.*, 1934 [13]

[a] the original data in hl or kg was divided by the total population of each municipality.

terrain data from available Geographical Information System (GIS) database (www.gis.com) to calculate the average slope of municipality territory. We assumed that in the population of each municipality the AEE for walking in plane is increased by an additional component varying in function of the average terrain's steepness [21].

Moreover, we are aware that other variables, such as social network, cultural traditions, isolation, endogamy and so on, that are prevalent in mountains, may be additional explanatory variables as well, but unfortunately they were not available from the historical sources used in the current study.

Statistical analysis

Multiple logistic regression analysis, using the SPSS Enter procedure (SPSS statistical software, v. 16.0, Chicago, USA) was used to test the association between nutrition/lifestyle variables and extreme male longevity using the data in each municipality as observation units and their odds to be included or not (0/1) in the BZ as dependent variable. Odds ratios (ORs) were then calculated as the relative amount of increase of odds for municipalities to be classified within the BZ from one-unit change in the independent variables, after controlling for the confounding effect of all covariates. *P*-values lower than 0.05 were considered statistically significant. In addition, the spatial correlations between the longevity index and covariates in the 377 Sardinian municipalities, regardless of the subdivision into previously-defined longevity areas, was analysed by using a Bayesian conditional autoregressive (CAR) model which allows both to control the problem of low mELI in smaller municipalities and the influence of municipality's "neighbouring" [22]. The spatial modelling was carried out by using WinBUGS (Version 1.4) which implements Markov Chain Monte Carlo (MCMC) algorithms [23]. Posterior coefficient estimates and their 95% credible intervals (95% CI) were calculated.

Results

Multiple logistic regression analysis (Table 2) showed that a higher prevalence of shepherds (OR 1.69; 95% CI 1.30—2.20), a higher terrain slope (OR 1.17; 95% CI 1.10—1.26), a longer daily distance (in km) required to reach the usual workplace (OR 1.14; 95% CI 1.07—1.19), and a higher average body robustness in the population (OR 1.53; 95% CI 1.15—2.04) were all strongly and positively associated with the likelihood that a village population would be included in the BZ, whereas among the nutrition variables only the diet score was positively associated to extreme longevity (OR 1.94; 95% CI 1.29—2.90). Interestingly, the diet score was positively related with the body robustness score ($r = 0.187$; $P = 0.0001$). It is of note that the average per capita meat consumption was very low (4—5 servings/months) all over Sardinia even though the pastoral population in highlands used to eat meat with relatively higher frequency [14]. As far as food production is concerned a significantly higher value for barley was found in the BZ, as previously reported [19].

To complement this first analysis, and regardless of the inclusion of the villages in specific longevity areas, the

Table 2 Differences between the high male longevity area ("BZ") and the rest of Sardinia for nutrition/lifestyle variables.

Covariates	BZ (mean ± SD)	Rest of Sardinia (mean ± SD)	OR (95% CI)	*P* value
Diet score (1–5)	2.6 ± 1.1	2.4 ± 0.8	1.94 (1.29–2.90)	0.004
Meat consumption (servings/person/month)	5.09 ± 3.1	5.10 ± 3.7	0.88 (0.79–1.10)	0.538
Wine consumption (lt/person/yr)	79.3 ± 75.7	89.6 ± 62.4	0.98 (0.97–1.02)	0.337
Food production				
Wheat (hl/person/yr)	1.06 ± 1.61	1.54 ± 1.79	0.85 (0.67–1.04)	0.215
Barley (hl/person/yr)	0.92 ± 0.75	0.52 ± 0.44	2.16 (1.11–5.08)	0.031
Nuts (kg/person/yr)	0.27 ± 0.62	0.07 ± 0.11	1.06 (0.18–5.91)	0.408
Cheese (kg/person/yr)	7.4 ± 4.6	5.2 ± 6.0	1.03 (0.80–1.33)	0.780
Occupation/lifestyle				
Pastoralism score	2.8 ± 1.4	1.6 ± 1.0	1.69 (1.30–2.20)	0.0001
Average terrain's slope (%)	15.2 ± 6.6	11.5 ± 6.2	1.17 (1.10–1.26)	0.0001
Daily distance to workplace (km)	12.4 ± 7.8	8.2 ± 6.0	1.14 (1.07–1.19)	0.0001
Robustness score (0–3)	1.9 ± 0.8	1.4 ± 0.9	1.53 (1.15–2.04)	0.004
Body height score (1–3)	2.0 ± 0.5	1.7 ± 0.6	1.36 (0.77–2.40)	0.289

Cox and Snell "pseudo" R-squared = 0.307.

Bayesian CAR model showed a strong association between extreme male longevity and the covariates related to occupation and physical activity (Table 3). As for nutrition variables, the diet score and barley production displayed a positive association with posterior estimates significantly different from zero, whereas wine consumption per capita showed a weak negative association (−0.007; 95% CI −0.011 to −0.004). Figure 1a–h show the crude geographic distribution of some variables extracted from the Fermi's database over the 377 Sardinian municipalities.

Table 3 Impact of nutrition and lifestyle covariates on male longevity index in 377 Sardinian municipalities estimated through a spatial CAR model.

	Dependent variable: mELI	
Covariates	Posterior β estimate	Bayesian 95% CI[a]
Diet score (1–5)	0.148	(0.059, 0.263)
Meat consumption (servings/person/yr)	−0.021	(−0.091, 0.019)
Wine consumption (lt/person/yr)	−0.007	(−0.011, −0.004)
Wheat (hl/person/yr)	−0.158	(−0.381, 0.024)
Barley (hl/person/yr)	0.144	(0.054, 0.297)
Nuts (hl/person/yr)	0.217	(−0.271, 0.632)
Cheese (kg/person/yr)	−0.085	(−0.199, 0.028)
Pastoralism score	0.141	(0.017, 0.261)
Average terrain's slope	0.028	(0.011, 0.054)
Distance to workplace	0.020	(0.012, 0.025)
Average robustness	0.119	(0.057, 0.186)
Average body height	0.061	(−0.215, 0.483)

[a] The result is statistically significant if the interval does not include zero.

Discussion

Extreme male longevity in Sardinia shows a peculiar spatial distribution, characterised by a group of villages located in the central inner area with ELI index values twice higher than in the remaining island's territory [3]. Although previous studies [3,24] attempted to identify the determinants of exceptional longevity among Sardinian males, this is the first one that indicates lifestyle in the first half of the 20th century as one of the major factors to explain survival differences. The identification of spatially-distributed variables which correlate with between-village variability of male longevity in Sardinia may be valuable to understand the underlying causes of the BZ phenomenon.

The underlying assumption is that there is likely a wide time delay between the exposure to a certain lifestyle patterns experienced during the first half of the 20th century and the emergence of exceptional longevity in the two last decades of the same century as a phenotype widespread at the population scale. The importance of nutrition as a major determinant of successful ageing is well known [25]. Particularly, it was suggested that calorie restriction could exert a favourable impact on the duration of life span [15]. Although in early decades of 20th century mean calorie intake in Sardinian population as a whole was slightly lower (2600 vs 2800 kCal/d) than in mainland Italy [26] this difference could actually be explained by a lower body height of Sardinians compared to mainland Italians [14,27] thus implying lower basal metabolic requirements. Since our analysis of the diet score reported by Fermi in the 1930s [13] did not reveal a lower dietary intake in areas of Sardinia characterised by superior level of longevity, these findings seem to indicate that caloric restriction had a minor impact on the spatial differences in Sardinia longevity. From Fermi's data it is also evident that male population in the mountains had a stronger robustness, which was highly correlated to the diet score. This population, displaying a better body structure in 1930s, showed a higher proportion of long-living people later in the century.

Additionally, spatial regression analysis in the 377 municipalities provided evidence that dietary variables, such as meat and wine consumption, are not significantly correlated with male ELI. This may be attributed to the very low meat consumption in Sardinia before lifestyle transition and does not necessarily rule out a negative effect of meat consumption on longer survival [28]. As for wine consumption, CAR analysis revealed even a weak inverse correlation with male longevity. Traditionally, wine consumption used to be quite high in the plain villages of Sardinia, where grapevine was intensively cultivated [19], whereas it was less consumed in mountains and especially among shepherds' high-longevity villages. Thus, one may speculate that only villages where wine consumption used to be moderate do experience high longevity at present. This is not in contrast with a previous report of a positive effect of red wine on Sardinia longevity [29] probably owing to its elevated content in polyphenols and other antioxidants.

Finally, the strong association of extreme male longevity with variables related to AEE of the male population, such as the average slope of the territory surrounding each village and the distance from workplace, is intriguing and deserve comments. Evidences are gathering that low-intensity physical exercise throughout life may provide health benefits, increasing the cardiorespiratory fitness and thus enhancing the ability to reach old age [30]. Physical work was traditionally very hard among Sardinian men before 1960s, especially if they were farmer or shepherds, and began very early (8–12 years of age) to end in old age [19]. Farmer's work was concentrated in time and was usually very wearing, whereas that of shepherds was more moderate, constant every day through the year, and implied walking a long distance on steep paths [19]. A very important point is that men living in the BZ were mostly shepherds, whereas in areas outside the BZ agriculture prevailed. The correlation of mELI with terrain slope may be an indication that living in a mountainous area may have increased the average daily energy expenditure of most adult men compared to adult women, whose physical activity was likely uniform all over the island. Although physical activity is not directly related to longevity, extensive literature data suggest that a regular and not too hard physical exercise (such as the one related to traditional pastoral activity) is associated with a reduction of well known cardiovascular risk factors (atherogenic lipid profile, elevated blood pressure, excess fat, insulin resistance) thus acting as a strong protective factor against early mortality [31]. Besides, an increased life expectancy of men living in mountainous village as compared to those living in a plain was reported [20]. Since cardiovascular diseases is the leading cause of premature mortality, physical exercise in these conditions can be expected to facilitate the emergence of the "long-lived phenotype" in the population. Finally, there is evidence that physical activity may change even some genetic characteristics (e.g. telomeres length) that have been associated with a longer survival [32].

The investigation carried out in this study has certain limitations: (i) as in most ecological studies, our analysis relies on aggregate data and its results cannot be extended to individual subjects nor it provides stringent criteria supporting a direct cause-effect relationship; (ii) only a limited number of variables available in historical reports were actually included in the analysis and this may have limited the extent of our findings. Therefore, we cannot rule out that other nutritional variables, not considered in the current analysis, may have had a significant impact on longevity; (iii) we did not take into account the time variation of mELI but merely considered the fixed spatial correlation between lifestyle data in the first quarter of 20th century and the emergence of exceptional longevity nearly 50 years later.

Notwithstanding these limitations, the results of our study suggest that some lifestyle habits, especially physical activity, had a greater importance in the exceptional longevity of Sardinian males born in the last two decades of 19th century who experienced lifestyle transition only later in their life. In contrast, based on available data, nutritional factors and the quality of food seem not to have played a significant role, as it was expected in a population in near-zero energy balance, although a possible influence of other nutritional variables not available from the historical records dating back to 1930s cannot be ruled out. However, the importance of nutritional factors, and especially a positive energy balance, may be increased in younger generations who were already adults in the post-transition era. As a consequence, in these generations a progressive increase in the prevalence of metabolic disease and other cardiovascular risk factors such as obesity, dyslipidemia, diabetes and hypertension is evident even in the BZ population [33], while in pre-transition era obesity and diabetes mellitus in Sardinia were rarer [34]. The lifestyle changes in the Sardinian BZ which occurred fifty years ago – due to increased mechanization in occupational activities and everyday life, as well as the widespread availability of food supply – may influence the level of population longevity in upcoming years. Only further research will elucidate whether the BZ characteristics will be lost or will "become commonplace" [35] in the next few decades.

References

[1] Vaupel JW, Jeune B. The emergence and proliferation of centenarians. In: Jeune B, Vaupel JW, editors. Exceptional longevity: from prehistory to the present, monographs on population aging no. 2. Odense, Denmark: Odense University Press; 1995. p. 109–16.

[2] Kannisto V. Mode and dispersion of the length of life. Population 2001;13:159–71.

[3] Poulain M, Pes GM, Grasland C, Carru C, Ferrucci L, Baggio G, et al. Identification of a geographic area characterized by extreme longevity in the Sardinia island: the AKEA study. Exp Gerontol 2004;39:1423–9.

[4] Passarino G, Calignano C, Vallone A, Franceschi C, Jeune B, Robine JM, et al. Male/female ratio in centenarians: a possible role played by population genetic structure. Exp Gerontol 2002;37:1283–9.

[5] vB Hjelmborg J, Iachine I, Skytthe A, Vaupel JW, McGue M, Koskenvuo M, et al. Genetic influence on human lifespan and longevity. Hum Genet 2006;119:312–21.

[6] Magnolfi SU, Noferi I, Petruzzi E, Pinzani P, Malentacchi F, Pazzagli M, et al. Centenarians in Tuscany: the role of the environmental factors. Arch Gerontol Geriatr 2009;48:263–6.

[7] van den Berg GJ, Doblhammer G, Christensen K. Exogenous determinants of early-life conditions, and mortality later in life. Soc Sci Med 2009;68:1591—8.
[8] Randall GK, Martin P, McDonald M, Poon LW, Jazwinski SM, et alGeorgia Centenarian Study. Social resources and longevity: findings from the Georgia centenarian study. Gerontology 2010;56:106—11.
[9] Pes GM, Lio D, Carru C, Deiana L, Baggio G, Franceschi C, et al. Association between longevity and cytokine gene polymorphisms. A study in Sardinian centenarians. Aging Clin Exp Res 2004;16:244—8.
[10] Passarino G, Underhill PA, Cavalli-Sforza LL, Semino O, Pes GM, Carru C, et al. Y chromosome binary markers to study the high prevalence of males in Sardinian centenarians and the genetic structure of the Sardinian population. Hum Hered 2001;52:136—9.
[11] Lampis L, Morelli S, De Virgiliis M, Congia M, Cucca F. The distribution of HLA haplotypes reveals that the Sardinian population is genetically different from the other Caucasian populations. Tissue Antigens 2000;56:515—21.
[12] Tessier S, Gerber M. Factors determining the nutrition transition in two Mediterranean islands: Sardinia and Malta. Public Health Nutr 2005;8:1286—92.
[13] Fermi C. In: Roma SA, Fermi C, editors. Decadenza, risanamento e spesa. Tipografia, vol. 1—3. Sardegna: Regioni malariche; 1934.
[14] Peretti G. Rapporti tra alimentazione e caratteri antropometrici. Studio statistico-biometrico in Sardegna. Quaderni Della Nutrizione 1943;IX:69—130.
[15] Fontana L, Partridge L, Longo VD. Extending healthy life span — from yeast to humans. Science 2010;328:321—6.
[16] Paffenbarger Jr RS, Hyde RT, Wing AL, Lee I-M, Jung DL, Kampert JB. The association of changes in physical-activity level and other life-style characteristics with mortality among men. N Engl J Med 1993;328:538—45.
[17] Catasto Agrario. Compartimento della Sardegna 1929;8(91):120.
[18] Angioni G. Rapporti di produzione e cultura subalterna. Cagliari: Contadini di Sardegna; 1974.
[19] Le Lannou M. Pâtres et paysans de la Sardaigne. Tours; 1941.
[20] Baibas N, Trichopoulou A, Voridis E, Trichopoulos D. Residence in mountainous compared with lowland areas in relation to total and coronary mortality. A study in rural Greece. J Epidemiol Community Health 2005;59:274—8.
[21] Kawata A, Shiozawa N, Makikawa M. Estimation of energy expenditure during walking including Up/Down Hill. In: World congress on medical physics and biomedical engineering. Berlin Heidelberg: Springer; 2006.
[22] Mollié A, Richardson S. Empirical Bayes estimates of cancer mortality rates using spatial models. Stat Med 1991;10: 95—112.
[23] Spiegelhalter DJ, Thomas A, Best NG, Gilks WR. Bugs: Bayesian inference using Gibbs sampling. Version 0.5. Cambridge: Medical Research Council Biostatistics Unit; 1996.
[24] Caselli G. Centenarians in Sardinia: the underlying causes of the low sex ratio. IUSSP; 2006.
[25] Cannella C, Savina C, Donini LM. Nutrition, longevity and behavior. Arch Gerontol Geriatr 2009;49(Suppl. 1):19—27.
[26] Tivaroni J. Nutrition patterns in Sardinia population. Riv Pol Econ 1928;2:1—11.
[27] Livi R. Antropometria militare. Parte II. Roma: Giornale Medico del Regio Esercito; 1905.
[28] Sinha R, Cross AJ, Graubard BI, Leitzmann MF, Schatzkin A. Meat intake and mortality: a prospective study of over half a million people. Arch Intern Med 2009;169:562—71.
[29] Corder R, Mullen W, Khan NQ, Marks SC, Wood EG, Carrier MJ, et al. Oenology: red wine procyanidins and vascular health. Nature 2006;444:566.
[30] Franco OH, de Laet C, Peeters A, Jonker J, Mackenbach J, Nusselder W. Effects of physical activity on life expectancy with cardiovascular disease. Arch Intern Med 2005;165:2355—60.
[31] Kokkinos P, Myers J, Faselis C. Panagiotakos. Exercise capacity and mortality in older men: a 20-year follow-up study. Circulation 2010;122:790—7.
[32] Cassidy A, De Vivo I, Liu Y, Han J, Prescott J, Hunter DJ, et al. Associations between diet, lifestyle factors, and telomere length in women. Am J Clin Nutr 2010;91:1273—80.
[33] Scuteri A, Najjar SS, Orru' M, Albai G, Strait J, Tarasov KV, et al. Age- and gender-specific awareness, treatment, and control of cardiovascular risk factors and subclinical vascular lesions in a founder population: the SardiNIA study. Nutr Metab Cardiovasc Dis 2009;19:532—41.
[34] Palmas S. Clinico-statistical survey on diabetes mellitus in the province of Sassari. Studi Sassaresi 1962;40:388—426.
[35] Appel LJ. Dietary patterns and longevity: expanding the blue zones. Circulation 2008;118:214—5.