

COHORT PROFILE

Cohort profile: The 'Seguimiento Universidad de Navarra' (SUN) study

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How did the study come about?

The SUN study began at the Universidad de Navarra's Department of Preventive Medicine and Public Health and has since integrated other universities (Santiago de Compostela, Cantabria, Las Palmas, Jaen and Saragossa).

The motivation behind its development, dating back to the late 1990s, was the lack of scientific evidence detailing the benefits of the Mediterranean Food Pattern. Starting a Spanish cohort was a unique opportunity to sample participants who are more likely to follow variations of this food pattern.^{1,2}

To explore this idea further, Professor Miguel Ángel Martínez travelled to the Harvard School of Public Health to learn about similar large cohort studies currently being conducted in the US, such as the Nurses' Health Study and the Health Professionals' Follow-up study.³ An outline of the SUN study was designed during his sabbatical at Harvard.

What does the study cover?

In the development stages, the initial focus on diet, and its impact on disease prevention, was broadened to encompass certain lifestyle issues and other diseases beyond just cardiovascular disease and cancer.⁴ Thus, a multipurpose cohort was set up that would allow assessment of other conditions such as obesity, hypertension, diabetes, or injuries, particularly those related to traffic. Accordingly, a group of multidisciplinary researchers with complementary expertises share the management of the cohort.

Who is in the sample?

The SUN Study is an open-enrolment cohort in Spain, consisting of 16 390 university graduates as of summer 2006. The key characteristic of the study is the permanently open recruitment, allowing continuous growth for an ever-increasing sample. Graduate status is necessary as previous studies with university graduate samples have exhibited greater reliability and validity, and higher retention rates, particularly in studies requiring self-completion of extensive questionnaires. Participants

are recruited through collaborations with alumni and professional associations throughout the country (e.g. Universidad de Navarra Alumni Association, regional associations of Physicians, Nurses, Pharmacists, Dentists, and Engineers). A few hundred students were recruited during their last years at university, with follow-up questionnaires confirming their graduate status. Approximately 20% of invitees agreed to participate in the study. Table 1 illustrates the range of professional degrees among cohort participants.

As of May 2006, the sample consisted of 16 390 participants: 9721 females (59.3%) and 6669 males (40.7%). The age range is 18–101 with mean ages of 42.7 (SD: 13.3) for men and 35.1 (SD: 10.7) for women. Table 2 presents the gender and age category distribution of participants in more detail.

Because we do not have any health or lifestyle information on those refusing to participate in the study, we cannot evaluate differences between participants and non-participants. With regard to the similarities between participants and the general adult population in Spain, we have conducted a number of comparisons that illustrate that cohort participants have a lower prevalence of obesity and diabetes, their consumption of fibre is higher, and they smoke less. In contrast, they travel more, drive after drinking more frequently, and have higher hospitalization rates due to motor vehicle crashes, although the statistical significance of these differences is still under evaluation (M. Seguí, A. Mateos, M.A. Martínez, F. Guillén-Grima, J. Llorca, E. Smyth, manuscript in preparation).

How is it funded?

For the past 7 years, the project has been publicly funded by Spanish agencies including the Spanish Ministry of Health and the Government of Navarra (Autonomous Government Department of Health). In addition, a grant from the Banco Santander-Central-Hispano and seed funds from the Universidad de Navarra Alumni Association were an integral part in project funding.

The official website for the project <http://www.unav.es/preventiva/sun> has a complete listing of secured grants.

In addition to the funds necessary for project development, the success of the SUN project is, in large part, due to the help of six PhD candidates who were working on analyses of the cohort as part of their doctoral work at the initial stages of the cohort launching.

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Table 1 Type of university degree held by participants

Graduates	Medical doctors	Pharmacists	Biologists	Nurses	Dieticians	Other health professionals	Non-health professionals	Still university students	Other
<i>N</i>	2803	1198	554	2564	330	515	6636	1724	66
Percentage	17.0	7.0	3.4	15.6	2.0	3.1	40.5	10.5	0.9

Table 2 Age strata of participants by gender

Age Group	<25 years	25–44 years	45–64 years	>65 years
Men	6.1% (<i>n</i> = 404)	50.4% (<i>n</i> = 3355)	37.5% (<i>n</i> = 2499)	6.1% (<i>n</i> = 405)
Women	15.3% (<i>n</i> = 1486)	63.9% (<i>n</i> = 6220)	19.9% (<i>n</i> = 1933)	0.9% (<i>n</i> = 89)
Total	11.5% (<i>n</i> = 1890)	58.4% (<i>n</i> = 9875)	27.0% (<i>n</i> = 4432)	3.0% (<i>n</i> = 494)

Table 3 Items in questionnaires

Questions	% of total items			
	Baseline 554 items	Second year follow-up 160 items	Fourth year follow-up 196 items	Sixth year follow-up 184 items
Anthropometry	1.4	1.5	0.9	4.5
Check-up	10.8	11.1	6.7	6.8
Traffic injuries	0.7	6.3	3.8	4.5
SF36	–	–	34.3	2.3
Tobacco	2.0	–	3.8	4.5
Diet assessment	27.2	14.3	8.6	20.5
Diagnosis of diseases/injuries	33.7	54.0	34.3	42.1
Current medication	4.1	9.5	5.7	6.8
Blood measures (cholesterol, glycaemia, etc.)	0.9	–	–	8.0
Physical activity	13.3	3.2	1.9	–
Socio-demographic	3.8	–	–	–

How often are participants followed-up and what is measured?

Upon completion of the first questionnaire, the participant becomes a member of the cohort. The first questionnaire is the most detailed one and contains 554 items; these answers are then used as baseline information for that participant. The questions are intended to gather participants' socio-demographic variables, lifestyle factors,^{5,6} as well as information related to health and diet.^{7,8} The tedious nature of this initial questionnaire is meant to guarantee participation in future questionnaires (i.e. increasing the retention rate), although as a drawback it is also likely to reduce the participation rate. In addition, this initial response includes the following: three addresses (home, work, relative, or friend), telephone number, and e-mail address (if possible). This information is essential to avoid future attrition.

After the initial questionnaire, additional questionnaires are mailed every 2 years in order to follow-up the participant. The follow-up questionnaires are shorter and less detailed. The 2 year follow-up questionnaire contains 160 items, the 4 year contains 196 items, and the 6 year contains 184 items.

The distribution of these items by topic (anthropometry, lifestyle, diseases/injuries, medication intake, etc.) is shown in Table 3. Starting in 2008, participants will be eligible for the 8 year follow-up questionnaire, which is currently being constructed.

These follow-up questionnaires are sent every 2 years with the objective of tracking any changes in food habits, diagnosis of new diseases, and overall well-being. Diet is assessed using a semi-quantitative food frequency questionnaire that has been previously validated in Spain.^{9,10} Anthropometric measurements are self-reported and when measurements are requested, a tape is mailed together with the questionnaire. As for all other items, many of them (e.g. weight, hypertension, physical activity, kilometres travelled, and traffic hospitalizations) have been subject to reliability/validity investigations specifically conducted to prove their validity.^{11–14}

At baseline and at the 6 year follow-up, we asked participants to self-report on blood test results for total cholesterol, blood glucose, cholesterol subfractions (LDLc, HDLc), and tryglicerides. The specific questions used for blood pressure and blood tests are shown in Box 1. In our

Box 1 Actual wording of the items requesting information about blood tests and blood pressure**Baseline assessment (Q_0)**

Cholesterol level (mg/dl) (only tests taken <5 years ago)	And HDLc (mg/dl)?	Actual blood pressure (mm Hg) (Only measured <2 years ago)	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)
I have no tests	I have had no test	Not measured	<100	<60
I don't remember it	I don't remember it	It was measured, but I don't remember it	101–110	61–70
<180 (low)	<35 (low)		111–120	71–80
180–200 (normal)	36–60 (normal)		121–130	81–90
201–240 (slightly high)	>60 (high)		131–140	91–100
241–300 (high)			141–150	101–110
>300 (very high)			151–160	111–120
			161–172	121–130
			>175	>130

Six year follow-up assessment (Q_6)

Please, indicate the results of the last tests you took within the last 2 years

Measurements (Numeric data)

Waist perimeter^a (cm) —
 Hip perimeter^a (cm) —
 Systolic blood pressure (mm Hg) —
 Diastolic blood pressure (mm Hg) —
 Glycaemia (mg/dl) —
 Total cholesterol (mg/dl) —
 Triglycerides (mg/dl) —
 HDL cholesterol (mg/dl) —
 LDL cholesterol (mg/dl) —

^aA paper measuring tape was provided by mail together with the questionnaire.

experience to date, these values have a higher missing rate compared with other values in the questionnaire. The proportions with missing data on these questions vary from 33% for cholesterol levels to 58% for HDLc in the baseline assessment and from 40% for glycaemia to 65% for LDLc in the 6 year follow-up assessment. Regarding blood pressure levels, the proportions with missing data were 30% at baseline and 21% at the 6 year follow-up assessment. Table 4 presents response rates for the self-reported measurements in more detail.

Participants have the option to fill out the questionnaire using a hard copy they received by mail or an online copy through the SUN website. They can return the hard copy using the pre-addressed self-stamped envelope provided with the mailing. With the online option, they can use the temporary identification information and password, also included in the mailing, to access the SUN website, where the participant is then directed to the appropriate questionnaire (second, fourth, or sixth year follow-up).

In the time between follow-up questionnaires, participants are sent a card to remind and thank them for their involvement in the project. This card is also meant to verify any changes in mailing addresses.

Project personnel evaluate all completed questionnaires for consistency and quality. After data have been cleared for quality, the information is uploaded on a secured web-based database, where all participating researchers can download applicable information in order to conduct proper analyses.

What is the attrition like?

Despite intensive tracking and follow-up methods (including five mailings of each follow-up questionnaire, the last one with certified mail), loss of participants is inevitable and has occurred.

As of today, of the existing participants, 41 have died, as reported by relatives. Another 82 decided to stop their participation in the project for a variety of reasons. We lost contact with 103 owing to a lack of notification in change of address. We are currently in the process of using National Death files to see if any of these losses are because of the death of a participant.

Because of the open enrolment strategy, loss to follow-up is an ever-changing figure that is closely monitored with the

Table 4 Response rates for the self-reported measurements

Measurements	Response rate in Q ₀ (%)	Response rate in Q ₆ (%)
Waist	–	97
Hip	–	97
Systolic blood pressure (mm Hg)	68.5	80
Diastolic blood pressure (mm Hg)	71.5	78
Glycaemia	–	60
Total cholesterol	67	57
Triglycerides	–	47
HDL cholesterol	42	39
LDL cholesterol	–	35

above-mentioned web-tracking system. The current overall retention rate of completed questionnaires is 89%.

What has SUN found?

The most comprehensive findings to date from the SUN project relate to the health effects of the Mediterranean Food Pattern, as this topic has been under investigation since the project inception. However, research has been expanded to include: accidents and injuries, nutrition and fertility, depression, tobacco, and alcohol consumption. A complete list of presentations and published papers is available on SUN's website at <http://www.unav.es/preventiva/sun>.

Some of the major findings on diet and health are highlighted below:

A. Diet and reduced risk of hypertension

In early epidemiological studies conducted primarily in the United States of America, monounsaturated fatty acids were shown to have either a harmful association with blood pressure or no relationship at all. However, more recent studies carried out in Mediterranean countries have shed new light on this issue.¹⁵ It is conceivable that, despite high rates of alcohol intake, the high consumption of olive oil may explain the lower blood pressure levels and relatively low prevalence of hypertension found in Spain. This effect is due to a high supply of energy coming from the monounsaturated fatty acids found in olive oil.

Analyses from the SUN data¹⁶ are consistent with those from a cross-sectional analysis conducted in Greece,¹⁷ a small trial conducted in Italy,¹⁸ and the Omni Heart Randomized Trial¹⁹ and the PREDIMED trial.²⁰ These studies also emphasize the importance of olive oil in decreasing the risk of developing hypertension.

While past observational studies have shown the beneficial effect of dairy product consumption on blood pressure, none have shown this association in free-living middle-aged adults. We assessed whether overall dairy consumption (including both low-fat and whole-fat products) was associated with a lowered risk of hypertension. An inverse association between low-fat dairy and hypertension was found. The hazard ratio of hypertension between extreme quintiles of low-fat dairy product consumption was 0.46 (95% CI: 0.26–0.84; *P* for

trend = 0.02) after adjustment for potential confounding. No association was found between whole-fat dairy product or a combination of low-fat and whole-fat dairy products and incident hypertension.²¹

B. Mediterranean Food Pattern and predictors of weight change

The SUN study has assessed the association between adherence to the Mediterranean Food Pattern and weight change. Although average body weight and body mass index of participants increased during follow-up regardless of their food pattern, overall weight gain was lower among those with a higher adherence to an a priori defined Mediterranean Food Pattern, as well as among those who increased their adherence to the Mediterranean Food Pattern after follow-up.²²

The association between olive oil consumption and the likelihood of weight gain or of being overweight or obese was also assessed. The cohort participants were followed-up for a median period of 28.5 months. A previously validated food frequency questionnaire^{9,10} included in the baseline questionnaire was used to compare results of future questionnaires. A high baseline consumption of olive oil that did not increase during follow-up was found to be associated with a lower likelihood of weight gain (RR –0.16, 95% CI –0.42 to +0.11) for participants in the upper quintile of olive oil consumption (median: 46 g/d) compared with those in the lowest quintile (median: 6 g/d). However, participants with a high baseline of olive oil consumption that did increase during follow-up were found to have a slightly increased risk of overweight or of obesity (RR 1.19, 95% CI 0.73–1.95). Our study, carried out in a sample of free-living people, shows that a high amount of olive oil consumption is not associated with higher/considerable weight gain nor with a higher risk of becoming overweight or obese in the context of the Mediterranean Food Pattern.²³

It is interesting to note that the same data set that did not demonstrate an association between olive oil consumption and weight gain did demonstrate a higher risk of weight gain associated with the consumption of soda and fast food.²⁴ This trend may particularly be affecting populations that are increasingly adopting typical North American dietary patterns, (which are very different from their usual food patterns). This information led to an assessment of whether the consumption of soda and other fast food items increased the likelihood of weight gain in a Mediterranean population. The analysis of SUN data on this matter revealed that 49.5% of the participants increased their weight (average weight gain: 0.64 kg). In the participants who had gained > or =3 kg in the 5 years before baseline, the adjusted odds ratio of subsequent weight gain for the fifth quintile compared with that of the first quintile of soda consumption was 1.6. This association was absent in the participants who had not gained weight in the 5 year period before baseline. The consumption of hamburgers, pizza, and sausage (representative of fast-food products) was also independently associated with weight gain. We also found an association, albeit weaker, between weight gain and the consumption of red meat and sweetened fruit juices.²⁴

Other findings

The SUN study also has important conclusions regarding research on other health issues. For example, when examining tobacco use in the cohort, the prevalence of smoking was higher in women who had obtained less time-consuming university degrees. In particular, the above average prevalence of smoking among female nurses is cause for concern.²⁵

What are the strengths and weaknesses?

The SUN's most important strength is its dynamic participation. Since it is an open cohort, the number of participants is constantly increasing, leading to more powerful results. As the cohort increases, it becomes easier to engage other institutions to collaborate and invite their graduate members to participate in the study. The SUN's high retention rate is another of its strengths; 89% of participants have been followed-up through the use of mailed questionnaires. A further strength is the geographic diversity of participants living throughout Spain. This enables an evaluation of the cohort with the assurance that a wide variation in lifestyle and dietary patterns is represented.

The broad disciplinary range of expert knowledge by the research team (e.g. in the fields of epidemiology, medicine, pharmacy, nutrition, biostatistics, informatics engineering) provides a multifaceted perspective in the management and evaluation of the data.

Furthermore, the dynamic relationship between the research team and participants has proven to be valuable. In order to gain and uphold a high level of trust, we maintain close contact with participants through regular newsletters, the project website, telephone calls, and personal replies to all queries. These subtleties in turn lead to high retention rates, as well as high response rates to potentially sensitive questions, such as those related to depression and cancer.

The disadvantage of this study, as it is the case in most cohort studies, is that the sample is not representative of the total population. As the educational level of our participants is above average, this may affect the data on issues such as diet and physical activity. Nevertheless, people who have similar lifestyles should have comparable health effects, regardless of educational level.

Another potential limitation is the manner of data collection employed in this study. Self-report data collection is more prone to result in false reporting of information, as compared with other methods. However, the use of graduate participants was meant to improve this as it has been shown that graduate students are less likely to self report falsely due to their higher education level,²⁶ a finding which we are corroborating in another currently undergoing investigation. Several validation studies have been conducted, to date, that confirm such validity.¹¹⁻¹⁴ Though physical measures and biological samples have yet to be obtained, impending resources will hopefully allow us to do so in the future. However, as with most self-reported measures we anticipate that any existing measurement error will be non-differential.

Can I get hold of the data? Where can I find out more?

Data are held and archived by the SUN research team. In order to obtain additional information beyond what is discussed in this article, interested readers may visit the SUN's website at <http://www.unav.es/preventiva/sun/>. The site includes general information about SUN's initial development, main areas of research, data analysis, as well as information addressing the quality of the data. Researchers interested in utilizing this data in future studies should send a one-page letter stating their project's objectives, funding sources, and contact information to the SUN management team at sun@unav.es. Requests are evaluated by the SUN management team and, if approved, the data are provided free of charge.

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References

- Martínez-González MA. The SUN cohort study (Seguimiento University of Navarra). *Public Health Nutr* 2006;**9**:127-31.
- Martínez-González MA, Sánchez-Villegas A, De Irala J, Martí A, Martínez JA. Mediterranean diet and stroke: objectives and design of the SUN project. *Nutr Neurosci* 2002;**5**:65-73.
- Willet W. *Nutritional Epidemiology*. New York: Oxford University Press, 1998.
- Jacques PF, Tucker KL. Are dietary patterns useful for understanding the role of diet in chronic diseases?. *Am J Clin Nutr* 2001;**73**:1-2.
- Martínez-González MA, Martínez JA, Hu FB, Gibney MJ, Kearney J. Physical inactivity, sedentary lifestyle and obesity in the European Union. *Int J Obes* 1999;**23**:1-10.
- Chasan Taber S, Rimm EB, Stampfer MJ *et al*. Reproducibility and validity of a self-administered physical activity questionnaire for male health professionals. *Epidemiology* 1996;**7**:81-86.
- Mataix J, Mañas M. *Tablas de composición de alimentos españoles*. Granada: Universidad de Granada, 2003.
- Moreiras O, Carbajal A, Cabrera L. *Tablas de composición de alimentos*. Madrid: Pirámide, 2005.

- ⁹ Martín-Moreno JM, Boyle P, Gorgojo L *et al.* Development and validation of a food frequency questionnaire in Spain. *Int J Epidemiol* 1993;**22**:512–19.
- ¹⁰ Willett WC, Sampson L, Stampfer MJ, Rosner B, Bain C, Witschi J. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol* 1985;**122**:51–65.
- ¹¹ Bes-Rastrollo M, Pérez Valdivieso JR, Sánchez-Villegas A, Alonso A, Martínez-González MA. Validación del peso e índice de masa corporal auto-declarados de los participantes de una cohorte de graduados universitarios. *Rev Esp Obes* 2005;**3**:183–89.
- ¹² Alonso A, Beunza JJ, Delgado-Rodríguez M, Martínez-González MA. Validation of self reported diagnosis of hypertension in a cohort of university graduates in Spain. *BMC Public Health* 2005;**5**:94.
- ¹³ Martínez-González MA, López-Fontana C, Varo JJ, Sánchez-Villegas A, Martínez JA. Validation of the Spanish version of the physical activity questionnaire used in the Nurses' Health Study and the Health Professionals' Follow-up Study. *Public Health Nutr* 2005;**8**:920–27.
- ¹⁴ Alonso A, Laguna S, Seguí-Gómez M. A comparison of information on motor vehicle crashes as reported by written or telephone interviews. *Inj Prev* 2006;**12**:117–20.
- ¹⁵ Alonso A, Ruiz-Gutiérrez V, Martínez-González MA. Mono-unsaturated fatty acids, olive oil and blood pressure: epidemiological, clinical and experimental evidences. *Public Health Nutr* 2006;**9**:251–57.
- ¹⁶ Alonso A, Martínez-González MA. Olive oil consumption and reduced incidence of hypertension: the SUN study. *Lipids* 2004;**39**:1233–38.
- ¹⁷ Psaltopoulou T, Naska A, Orfanos P, Trichopoulos D, Mountokalakis T, Trichopoulou A. Olive oil the Mediterranean diet, and arterial blood pressure: the Greek European prospective investigation into cancer and nutrition (EPIC) study. *Am J Clin Nutr* 2004;**80**:1012–18.
- ¹⁸ Ferrara LA, Raimondi S, D'episcopo I, Guilda I, Dello Russo A, Marotta T. Olive oil and reduced need for antihypertensive medications. *Arch Intern Med* 2000;**160**:837–42.
- ¹⁹ Appel LJ, Sacks FM, Carey VJ *et al.* Effects of protein mono-unsaturated fat and carbohydrate intake on blood pressure and serum lipids: results of the Omniheart randomized trial. *JAMA* 2005;**294**:2455–64.
- ²⁰ Estruch R, Martínez-González MA, Corella D *et al.* Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. *Ann Intern Med* 2006;**145**:1–11.
- ²¹ Alonso A, Beunza JJ, Delgado-Rodríguez M, Martínez JA, Martínez-González MA. Low-fat dairy consumption and reduced risk of hypertension: the SUN cohort. *Am J Clin Nutr* 2005;**82**:972–79.
- ²² Sánchez-Villegas A, Bes-Rastrollo M, Martínez-González MA, Serra-Majem L. Adherence to a Mediterranean dietary pattern and weight gain in a follow-up study: the SUN cohort. *Int J Obes* 2006;**30**:350–58.
- ²³ Bes-Rastrollo M, Sánchez-Villegas A, de la Fuente C, de Irala J, Martínez JA, Martínez-González MA. Olive oil consumption and weight change: the SUN prospective cohort study. *Lipids* 2006;**41**:249–56.
- ²⁴ Bes-Rastrollo M, Sánchez-Villegas A, Gomez-Gracia E, Martínez JA, Pajares RM, Martínez-González MA. Predictors of weight gain in a Mediterranean cohort: the Seguimiento Universidad de Navarra Study. *Am J Clin Nutr* 2006;**83**:362–70.
- ²⁵ García de Albéniz XA, Guerra-Gutiérrez F, Ortega-Martínez R, Sánchez-Villegas A, Martínez-González MA. Características basales del hábito tabáquico en diplomados y licenciados universitarios españoles: el estudio SUN (Seguimiento Universidad de Navarra). *Gac Sanit* 2004;**18**:108–17.
- ²⁶ Willett WC, Colditz GA. Approaches for conducting large cohort studies. *Epidemiol Rev* 1998;**20**:91–99.