



Cohort Profile

Cohort Profile: Longitudinal Study of Adult Health (ELSA-Brasil)

Maria Inês Schmidt,^{1*} Bruce B Duncan,¹ José Geraldo Mill,² Paulo A Lotufo,³ Dóra Chor,⁴ Sandhi Maria Barreto,⁵ Estela ML Aquino,⁶ Valéria Maria Azeredo Passos,⁵ Sheila MA Matos,⁶ Maria del Carmen B Molina,² Marília S Carvalho⁷ and Isabela M Bensenor³

¹Faculdade de Medicina and Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil, ²Centro de Ciências da Saúde, Universidade Federal do Espírito Santo, Vitória, Brazil, ³Faculdade de Medicina and Hospital Universitário, Universidade de São Paulo, São Paulo, Brazil, ⁴Escola Nacional de Saúde Pública, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil, ⁵Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil, ⁶Instituto de Saúde Coletiva, Universidade Federal da Bahia, Salvador, Brazil and ⁷Programa de Computação Científica-FIOCRUZ, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil

*Corresponding author. Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Av. Ramiro Barcelos, 2600 Sala 414, 90035-003 Porto Alegre, RS Brazil. E-mail: maria.schmidt@ufrgs.br

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Abstract

Chronic diseases are a global problem, yet information on their determinants is generally scant in low- and middle-income countries. The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) aims to contribute relevant information regarding the development and progression of clinical and subclinical chronic diseases, particularly cardiovascular diseases and diabetes, in one such setting. At Visit 1, we enrolled 15 105 civil servants from predefined universities or research institutes. Baseline assessment (2008–10) included detailed interviews and measurements to assess social and biological determinants of health, as well as various clinical and subclinical conditions related to diabetes, cardiovascular diseases and mental health. A second visit of interviews and examinations is under way (2012–14) to enrich the assessment of cohort exposures and to detect initial incident events. Annual surveillance has been conducted since 2009 for the ascertainment of incident events. Biological samples (sera, plasma, urine and DNA) obtained at both visits have been placed in long-term storage. Baseline data are available for analyses, and collaboration via specific research proposals directed to study investigators is welcome.

Key words: Cardiovascular diseases, chronic diseases, cohort studies, developing countries, diabetes mellitus, occupational health, social determinants of health, obesity.

Key Messages

- Baseline findings from ELSA-Brasil show a high frequency of behavioural risk factors and clinical milestones for non-communicable diseases: 63.1% excess weight, 61.5% high cholesterol, 35.8% high blood pressure and 20.3% impaired glucose tolerance. The main diseases of interest are also frequently observed, diabetes is present in 19.7%, common mental disorders in 26.7% and a history of coronary heart disease in 4.7%.
- Subjective social status, assessed by three 10-rung ladders, was independently associated with poor self-rated health and weakly associated with former smoking.
- The use of antidepressant and benzodiazepine medication was less frequent than in high-income countries. Increasing age and educational achievement were associated with greater use of these medications. The presence of major depression and generalized anxiety disorder were poor predictors of such use, suggesting misuse/overuse among those without and underuse among those with psychiatric conditions.
- Starting in the midst of the obesity epidemic and having information on a wide range of exposures, including the role of neighbourhood and social life-course adversities, ELSA-Brasil will permit novel investigations which will allow the testing of more comprehensive causal models for diabetes, cardiovascular and other chronic diseases.

Why was the cohort set up?

Chronic non-communicable diseases (NCDs) are a global health problem.^{1,2} In Brazil, 72% of all deaths are attributable to cardiovascular diseases and other NCDs. Given population ageing and the reduction in morbidity and mortality related to infections and to maternal and child problems, the proportional burden of chronic diseases is likely to increase over the next decades. Brazil is also experiencing a rapid nutritional transition, with marked increases in overweight and obesity across all social strata but more so among the poor and those with lesser education. Not surprisingly, diabetes morbidity and mortality are increasing.^{3,4}

Few longitudinal assessments of chronic diseases are available in Brazil, or for that matter, in other low- and middle-income countries. Thus, the Brazilian Longitudinal Study of Adult Health (in Portuguese, 'Estudo Longitudinal de Saúde do Adulto', ELSA-Brasil) aims to investigate the development of chronic diseases, primarily diabetes and cardiovascular diseases, over a long-term follow-up. The ongoing demographic, nutritional and epidemiological changes occurring in a context of high social inequalities and socio-economic progress create a window of opportunity to understand how macro- and micro-level factors influence chronic disease causation and prevention.

Where is it located, who set it up, and how has it been funded?

With funding from the Brazilian government, as detailed in Acknowledgements, a group of Brazilian epidemiologists and clinicians from six institutions (Federal Universities of Bahia, Espírito Santo, Minas Gerais and Rio Grande

do Sul; University of São Paulo; and Oswaldo Cruz Foundation), led by the authors of this article, organized the Study in centres located in state capitals of the north-eastern, south-eastern and southern regions of Brazil.

Who is in the cohort?

All active or retired employees of the six institutions (and, in a few instances, also of related educational or health institutions), of both sexes, and with ages between 35 and 74 years, were eligible for the study, totalling, in 2008, 52 137 potential participants. We chose civil servants as the source of the study population in order to minimize losses to follow-up related to geographical mobility. Exclusion criteria were severe cognitive or communication impairment, intention to quit work at the institution in the near future for reasons not related to retirement, and, if retired, residence outside the corresponding metropolitan area. Women with current or recent pregnancy were rescheduled so that the first interview could take place ≥ 4 months after delivery.

Volunteers were recruited through on-site and radio announcements, mailings, outdoor billboards and telephone calls, the latter more commonly used to attract retirees. A randomly ordered list of employees, stratified by sex, age and occupational category, was also used to actively recruit eligible participants. Efforts were made to recruit similar proportions of men and women as well as predefined proportions of age groups and occupational categories.⁵ From a total of 16 435 who expressed interest in participation, 15 821 were pre-enrolled, gave written consent, responded to an initial interview and were scheduled for the baseline examination. Only 716 (4.5%) of those pre-enrolled did not complete the baseline examination.

A total of 15 105 participants were enrolled, 6887 men and 8218 women, thus giving reasonably large numbers for sex-specific analyses. Table 1 shows that, as assessed through self-identification, 52.2% considered themselves to be White, 16.1% Black and 28.2% Brown ('pardo'). Given the nature of the sample, about half had a university degree and a smaller proportion (12.7%) did not have a complete secondary level of education. Worth noting, however, as indicated by the frequency of maternal schooling, the background of the cohort participants was very different: only a small proportion (6.5%) of participants' mothers had a university degree and about half had never attended or did not complete elementary school.

In collaboration with economists from the Centre of Regional Development and Planning (CEDEPLAR) of the University of Minas Gerais, information concerning present (or last, if retired) and first employment together with educational achievement and income were used to classify participants according to social class, nature of occupation and social mobility (based on nature of occupation). One-fourth of participants were classified as being of low social class and over half as having non-manual, non-routine jobs and an ascending job trajectory. These results will allow us to investigate new aspects of the social determinants of health in a changing social environment of an emerging economy.

How often have they been followed up? What has been measured?

After about 4 years (August 2009 to December 2013) of follow-up, 178 (1.2%) participants have died. All participants who are alive are being invited for the second visit of interviews and examinations according to the date of enrolment. As of December 2013, 9916 (66.2%) have completed this examination.

Table 2 summarizes the broad categories of measurements taken at baseline (detailed description can be found in a previous report⁶) and at the second visit to the ELSA centres. Annual telephone interviews include questions on self-rated health, new diagnosis of conditions of interest, hospitalizations and specific medical procedures such as dialysis, revascularization and cancer biopsy.⁷ Potential events are then investigated and classified according to study protocol by a panel of physicians trained according to international classification criteria. Surveillance of clinical events is also conducted through employer reports and linkage to national databases such as the National Mortality System. Main clinical endpoints are acute myocardial infarction, unstable angina pectoris, cardiac revascularization, sudden cardiac death, heart failure, peripheral arterial disease, stroke, hypertension, chronic

Table 1. Socio-demographic characteristics and socio-economic categories of study participants in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil), *N* = 15 105, 2008–10

Characteristics	<i>N</i>	%
Sex		
Men	6887	45.6
Women	8218	54.4
Age (years)		
35–44	3340	22.1
45–54	5939	39.3
55–64	4234	28.0
65–74	1592	10.6
Self-identified skin colour / race category		
White	7791	52.2
Black	2397	16.1
Brown ('pardo')	4202	28.2
Asian	374	2.5
Indigenous	157	1.0
Region		
North-east	2029	13.4
South-east	11015	72.9
South	2061	13.7
Educational level		
Never attended school or incomplete elementary school	894	5.9
Complete elementary school or incomplete secondary school	1028	6.8
Complete secondary school	5233	34.6
University degree	7950	52.7
Maternal educational level		
Never attended school or incomplete elementary school	8357	56.7
Complete elementary school or incomplete secondary school	2869	19.5
Complete secondary school	2558	17.3
University degree	955	6.5
Social class		
Low	4317	25.1
Middle	5974	43.5
High	3455	31.4
Occupation		
Manual	3019	18.4
Routine, non-manual	2360	29.0
Non-routine, non-manual	7355	53.0
Intragenerational social mobility		
Descending	3019	23.7
Stable	2360	18.5
Ascending	7355	57.8

Small differences in total *N* for each variable are due to missing values. Social class coded for the 13 746 with available information, and occupation and intragenerational social mobility for the 12 734 with this information.

kidney diseases and diabetes. The study also ascertains diabetes-related events (blindness, amputation) and acute complications resulting in hospitalizations (ketoacidosis, hyperosmolar state and severe hypoglycaemia), chronic kidney disease, venous thrombosis, pulmonary embolism

Table 2. Measurements obtained at different phases of the study

Phase	Measurements
Baseline 2008–10 ⁶	Questionnaires with contextual and individual information on social determinants, health-related behaviours, self-reported chronic conditions, diagnosis of common mental disorders, reproductive health, cognitive function Anthropometry Blood pressure (resting and after postural change) Ankle-brachial index, pulse wave velocity Electrocardiogram (ECG), heart rate variability Retinal photographs Ultrasound (carotid; liver; abdominal fat; echocardiography) Oral glucose tolerance test (meal challenge test in diabetes) Biochemical and haematological determinations in blood, overnight urine collection Stored DNA, plasma, serum and urine in liquid nitrogen Geo-coding
Visit 2 2012–14	Questionnaires Socio-economic position and social class Self-rated health Changes in occupational status and assessment of job stress ^a Health-related behaviours (smoking, alcohol consumption, physical activity, changes in diet since baseline) Neighbourhood characteristics (leisure, sports, built environment, access to foodstuffs) Cognitive function (among ≥55 years old) Mental health Marital status and family context Reproductive health Medication use Body weight trajectory (Stunkard scale) ^b Social network ^b Life satisfaction (The Satisfaction with Life Scale) ^b Sleep (pattern, insomnia, apnoea) ^b Anthropometric measures: weight, height, waist and hip circumference; Bioimpedance spectroscopy Blood pressure Hand grip strength ^b Monofilament sensitivity testing in diabetes ^b ECG Oral glucose tolerance test Biochemical and haematological determinations (in fasting or post-load blood, and overnight urine) Stored blood plasma, serum and urine in liquid nitrogen
Yearly follow-up (2009 to present)	Phone interview with reported events investigated through chart review.

^aThrough effort-reward imbalance model (at baseline, job stress was initially assessed through a questionnaire based on the demand-control model).

^bNot addressed at baseline.

and common sites of cancer. Additionally, we will investigate changes in weight, lipids and other metabolic markers, urinary albumin-to-creatinine ratio, cognitive function and the diagnosis of specific common mental disorders.

What has it found? Key findings and publications

As seen in Table 3, behavioural risk factors at baseline were highly prevalent, especially among men, illustrating the study's potential for risk factor analyses with relevant outcomes; of note, the prevalence of ex-smokers is high, reflecting the decline in smoking observed in Brazil over the

past two decades.³ Table 3 also presents the frequency of self-reported chronic clinical or subclinical conditions relevant to the investigation of diabetes and cardiovascular diseases at baseline. As the study was initiated within the global obesity epidemic, overweight and obesity are highly prevalent (63.1% presenting excess weight). Other chronic conditions such as mild chronic inflammation, hypertension/pre-hypertension, hypercholesterolaemia, high triglycerides and low high-density lipoprotein-C (HDL-C), diabetes/pre-diabetes, elevated urinary albumin-to-creatinine ratio and low estimated glomerular filtration rate are also prevalent. Seropositivity for Chagas disease, seen in 115 participants (0.8%), will permit better

Table 3. Prevalence of selected behavioural risk factors, measured diseases or conditions and self-reported chronic diseases in the Brazilian Longitudinal Study of Adult Health, $N = 15\,105$, 2008–10

Factors	Overall		Men		Women	
	N	%	N	%	N	%
Behavioural risk factors						
Excessive drinking ^a	1125	7.5	838	12.2	287	3.5
Binge drinking ^b	1993	13.2	1438	20.9	555	6.8
<recommended daily fruit intake	6413	42.5	3543	51.5	2870	35.0
<recommended daily vegetable intake	7249	48.1	3747	54.5	3502	42.7
Low leisure time physical activity ^c	11456	76.9	4984	73.4	6472	79.9
Current smoking	1977	13.1	984	14.3	993	12.1
Former smoking	4533	30.0	2436	35.4	2097	25.5
Measured diseases/conditions						
Obesity (BMI ≥ 30 kg/m ²)	3463	22.9	1426	20.7	2037	24.8
Overweight ($25 \leq$ BMI < 30 kg/m ²)	6072	40.2	3113	45.2	2959	36.0
Hypertension ^d	5402	35.8	2760	40.1	2642	32.2
Pre-hypertension ^e	3546	23.5	2020	29.4	1526	18.6
Hypercholesterolaemia ^f	9282	61.5	4056	58.9	5226	63.6
Low HDL-C ^g	2712	18.0	1009	14.7	1703	20.7
Hypertriglyceridaemia ^h	4704	31.2	2813	40.9	1891	23.0
Diabetes ⁱ	2969	20.0	1603	23.3	1366	16.6
Impaired fasting glucose, ADA ^j	7947	52.6	4050	58.8	3897	47.4
Impaired fasting glucose, WHO ^k	2887	19.1	1680	24.4	1207	14.7
Impaired glucose tolerance ^l	3066	20.3	1456	21.1	1610	20.0
Elevated hsCRP ^m	4229	28.0	1565	22.8	2664	32.5
Elevated UACR ⁿ	736	5.0	408	6.1	328	4.1
Low eGFR (<60 ml/min) ^o	681	4.6	359	5.3	322	4.0
Hypothyroidism ^p	119	0.8	49	0.7	70	0.8
Chagas disease seropositivity	115	0.8	57	0.8	58	0.7
Common mental disorders ^q	4036	26.7	1265	18.4	2771	33.7
Depression	637	4.2	159	2.3	478	5.8
Anxiety	2436	16.1	762	11.1	1674	20.4
Self reported chronic diseases						
Coronary heart disease ^r	721	4.7	393	5.7	328	4.0
Heart failure	251	1.7	128	1.9	123	1.5
Stroke	197	1.3	90	1.3	107	1.3
Rheumatic fever ^s	433	2.9	155	2.2	278	3.4
Chagas disease	64	0.4	31	0.4	33	0.4
Cancer ^t	695	4.6	284	4.1	411	5.0
Asthma	1758	11.6	691	10.0	1067	13.0
COPD ^u	308	2.0	124	1.8	184	2.2
Cirrhosis or hepatitis	1303	8.6	608	8.8	695	8.5
Polycystic ovary syndrome	–	–	–	–	903	11.1

Small differences in number of participants for each outcome are due to missing values.

^aExcessive drinking defined as >210 g alcohol/week for men and 140 g alcohol/week for women.

^bDefined as the consumption of 5 or more doses of alcohol in a period of 2 h at least 2–3 times per month over the past 12 months.⁶

^cObtained with the International Physical Activity Questionnaire (IPAQ) – Short Form, and defined according to the IPAC Guidelines for Data Processing and Analysis.⁷

^dDefined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg, or verified treatment with anti-hypertensive medication during the past 2 weeks.

^eNon-hypertensive participants with systolic blood pressure 120–139 mmHg or diastolic blood pressure 80–89 mmHg.

^f>5.17 mmol/l (200 mg/dl).

^gMen <1.03 mmol/l (40 mg/dl); women <1.29 mmol/l (50 mg/dl).

^h ≥ 1.69 mmol/l (150 mg/dl).

ⁱDefined as a report of a previous diagnosis of diabetes or the use of medication for diabetes, or meeting a diagnostic value for diabetes according to one of the following tests: fasting or 2-h plasma glucose obtained during a 75-g oral glucose tolerance test (OGTT); or HbA1C.

^jFasting glucose 5.5–6.9 mmol/l (100–125 mg/dl), American Diabetes Association.

^kFasting glucose 6.1–6.9 mmol/l (110–125 mg/dl), World Health Organization.

^l2-h glucose 7.8–11.0 mmol/l (140–199 mg/dl).

^mHigh sensitivity C-reactive protein ≥ 28.57 nmol/l (3 mg/dl).

ⁿUrine albumin-to-creatinine ratio ≥ 3.4 mg/mmol (30 mg/g), from validated overnight collection.

^oGlomerular filtration rate estimated by Chronic Kidney Disease Epidemiology Collaboration (CKD-Epi), considering Blacks and Browns as Blacks.

^pThyroid-stimulating hormone (TSH) >4.0 mIU/l and thyroxine (T4) <11.6 pmol/l (0.9 ng/dl).

^qDefined as a score ≥ 12 obtained in the Clinical Interview Schedule-Revised (CIS-R).

^rMyocardial infarction, coronary revascularization or a physician diagnosis of angina pectoris.

^sRheumatic fever/ rheumatic heart disease.

^t14.2% (99) of cancers were non-melanoma skin cancer.

^uChronic obstructive pulmonary disease.

characterization of cardiovascular events eventually found in such patients. Additionally, common mental disorders were frequently observed, especially among women; two main disorders stand out: depression and anxiety.

Although the first reports regarding the main baseline findings are in preparation and will be submitted for publication in 2013 and early 2014, three articles have been published focusing on specific topics. First, part of the generally unfavourable risk factor profile here described was reported within highlighting new priorities for research and management of non-communicable disease in Brazil.⁸ Second, subjective social status, assessed by three 10-rung ladders, was independently associated with poor self-rated health and weakly associated with former smoking.⁹ Third, the use of antidepressant and benzodiazepine medication was less frequent than in high-income countries. Increasing age and educational achievement were associated with greater use of these medications, but the presence of major depression and generalized anxiety disorder were poor predictors of such use, suggesting misuse/overuse among those without and underuse among those with psychiatric conditions.¹⁰

Seven additional studies addressing methodological and operational aspects of study design and implementation, including validity and reliability of several key measurements, have been published. Verbal fluency tests, commonly used to assess executive functions and language over time, showed between-supervisor reliability coefficients of 97.9% or higher in all ELSA centres (repeat judging of 120 animals and 120 F letter tests).¹¹ Reliability coefficients for silhouette scales, used to assess body image, varied across centres from 0.92 to 0.97 (repeated over a 7- to 14-day interval).¹² The MacArthur Scale of Subjective Social Status, which measures subjective social status via three numbered stepladder image scales, showed kappa values of 0.62 (0.58 to 0.64) for the overall society ladder, of 0.58 (0.56 to 0.61) for the community-related ladder and of 0.67 (0.66 to 0.72) for the work-related ladder. The reliability coefficients ranged from 0.64 for the community-related ladder to 0.75 for the work-related ladder.¹³ The reliability of the food frequency questionnaire was assessed against 3-day food records collected on two separate occasions during a 12-month period. Coefficients for energy and nutrients ranged from 0.55 for protein to 0.83 for vitamin E.¹⁴ Reproducibility of endothelial dysfunction measured by peripheral arterial tonometry was assessed with examinations performed twice during the same day, yielding a coefficient of variation of 18% and a reliability coefficient of 0.61.¹⁵

Finally, the making of a study of this size and complexity in a middle-income country striving to give the priority needed to research of non-communicable diseases was

addressed in detail (in English and Portuguese) in a recent supplement of the *Revista de Saúde Pública* which can be accessed through the link http://www.scielo.br/scielo.php?script=sci_issuetoc&pid=0034-891020130008&lng=pt&nrm=iso.

What are the main strengths and weaknesses?

First, the importance of the study outcomes is globally recognized, particularly in a scenario of scarcity of relevant information for low- and middle-income countries with rapid demographic, epidemiological and nutritional transitions. Of note in this regard, the ELSA-Brasil cohort includes participants born before 1950, a period in which Brazil was characterized as having low rates of schooling and low socioeconomic development. As ELSA-Brasil started in the midst of the obesity epidemic, it will allow novel investigations into the aetiology of diabetes and cardiovascular diseases within this current context, taking into account the life course experienced by the cohort, which may be of great relevance to many similar low- and middle-income countries.

Second, the extensive characterization of the cohort in terms of social, psychological and biomedical dimensions will permit the analysis of associations between social and health gradients, as well as mediating mechanisms, within Brazil's unique social and skin colour/race context. Neighbourhood characteristics, life-course adversities, social mobility, gender relations and family context, job stress, social class and nature of occupational, dietary patterns, body weight history and body image, postprandial metabolism, chronic inflammation and clinical and subclinical outcomes will permit ample investigation of aetiological hypotheses and the construction and testing of conceptual frameworks for the determination of chronic diseases. Although recognizing that the choice of the ELSA-Brasil sampling strategy limits investigation in the domains of the extremely poor and the unemployed, as demonstrated by the tables here presented, the racial, social and regional diversity captured in the cohort will permit in-depth investigation of important inequities in health in Brazil.

Additional strengths include: ELSA-Brasil's major governmental financial support; measurements uncommonly done in other large cohort studies, such as the oral glucose tolerance test, 12-h urine, cognitive function and comprehensive mental health assessment; stored serum (including post-load samples), DNA and urine samples; and facility of follow-up within the institutional context.

ELSA-Brasil, being an occupational cohort, was not planned with the aim of producing prevalence data

Table 4. Prevalence of selected self-reported behavioural risk factors and chronic conditions in adults ages 35–74 years in the Brazilian Longitudinal Study of Adult Health, 2008–10 and in the VIGITEL survey, 2010¹⁶

Self-reported characteristic	ELSA-Brasil %	VIGITEL %
Self-reported behavioural risk factors		
Binge drinking ^a	13.2	15.0
Less than 5 day/week fruit intake	34.3	39.3
Less than 5 day/week vegetable intake	37.1	51.0
Low leisure time physical activity ^b	76.9	75.2
Current smoking	13.1	15.7
Former smoking	30.0	30.1
Self-reported diseases or health conditions		
Previous diagnosis of hypertension	34.1	35.3
Previous diagnosis of diabetes	8.8	9.6
Obesity (BMI ≥ 30 kg/m ²)	22.9 ^c	19.1
Overweight (25 \leq BMI < 30 kg/m ²)	40.2 ^c	46.9

^aELSA-Brasil: consumption of 5 or more doses of alcohol in a period of 2 h at least 2–3 times per month over the past 12 months.⁶ VIGITEL: consumption of 5 or more doses of alcohol for men and 4 or more doses of alcohol for women in the past 30 days.

^bELSA-Brasil: defined using the International Physical Activity Questionnaire (IPAQ) – Short Form, according to the IPAC Guidelines for Data Processing and Analysis.⁷ VIGITEL: no leisure time physical activity or <150 min/week total physical activity.

^cELSA-Brasil: based on measured height and weight.

concerning chronic diseases or risk factors for the Brazilian population, particularly since Brazil is well served by a series of periodically repeated health surveys. However, since these surveys are predominantly based on self-report, the measures performed in ELSA-Brasil, in many ways, can provide more accurate assessment and add important supplemental information on relevant outcomes such as diabetes, chronic renal failure and common mental disorders, strongly dependent on laboratory values or on more sophisticated clinical measures or questionnaires. The applicability of these ELSA-Brasil estimates to Brazilian adults is supported by the similarities in prevalences (Table 4) of behavioural risk factors and chronic conditions selected for having been assessed with similar procedures in ELSA-Brasil and in VIGITEL,¹⁶ an annually performed telephone-based behavioural risk factor survey producing representative data for adults living in Brazil's 27 state capitals and Federal District.

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

Collaboration in data analysis and publication will be welcome through specific research proposals sent to individual ELSA investigators. Additional information can be obtained from estatisticaelsa@ufrgs.br.

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