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Cohort Profile

Cohort Profile: The Lausanne cohort 65+ (Lc65+)

Yves Henchoz , 1* Juan Manuel Blanco, 1 Sarah Fustinoni, 1 David Nanchen, 1 Christophe Büla, 2 Laurence Seematter-Bagnoud, 1,2 Armin von Gunten 3 and Brigitte Santos-Eggimann 1

¹Centre for Primary Care and Public Health (Unisanté), Department of Epidemiology and Health Systems, University of Lausanne, Lausanne, Switzerland, ²Service of Geriatric Medicine and Geriatric Rehabilitation, Department of Medicine, University of Lausanne Hospital Centre, Lausanne, Switzerland and ³Service of Old-age Psychiatry, Department of Psychiatry, University of Lausanne Hospital Centre, Lausanne, Switzerland

*Corresponding author. Centre for Primary Care and Public Health (Unisanté), University of Lausanne, Route de la Corniche 10, CH-1010 Lausanne, Switzerland. E-mail: yves.henchoz@unisante.ch

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Key Features

- The Lc65+ study is a population-based longitudinal study with a cohort-sequential design. It aims to gain new knowledge of the determinants, the development and the consequences of age-related frailty from its initial manifestations in the youngest old.
- Three representative samples of the non-institutionalized population of Lausanne (Switzerland) aged 65 to 70 years were recruited at 5-year intervals in 2004 (birth year 1934–1938, N = 1564), 2009 (birth year 1939–1943, N = 1489) and 2014 (birth year 1944–1948, N = 1678). Follow-up combined annual postal questionnaires as well as in-person interviews and examinations planned every third year at the study centre. The response rate has remained above 90% over the years, with 779 (50%) of the initial respondents in 2004 still participating 16 years later.
- Postal questionnaires address a large set of both objective and subjective measures, including life history, physical and mental health, socioeconomic status, health services use and health behaviours. *Ad hoc* surveys have been conducted on topics such as falls, quality of life and COVID-19. In-person interviews and examinations include a set of anthropometric and cardiovascular indices, as well as physical and cognitive performance tests.
- Collaboration proposals are welcome via a request including a description of the planned project (email: dess.lc65@ unisante.ch).

Why was the cohort set up?

The proportion of the population over the age of 65 years has doubled from 1950 to nowadays in Switzerland¹ as everywhere else in the world,² and will continue to increase

until 2030 when the youngest Baby Boomers turn 65. This demographic shift represents a major challenge to society in general and to the health care system in particular, but it also brings potential opportunities, thanks to

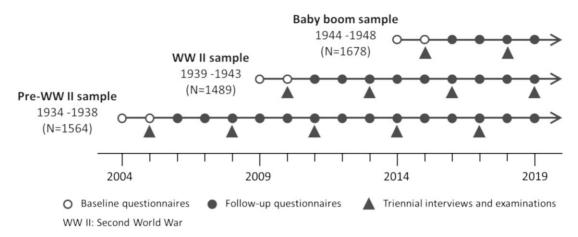


Figure 1 Cohort-sequential design of the Lc65+ study

the growing contribution of older adults in terms of volunteering, working and consuming. The magnitude of these difficulties and opportunities mainly hinges on the extent to which individuals reach old age in a fragile or robust state of health.

The Lausanne cohort 65+ (Lc65+) was set up to contribute to the epidemiological and public health research on ageing with a particular focus on the determinants, manifestations and outcomes of frailty. Specifically, the study compares cohorts of community-dwelling older adults born before, during and at the end of the Second World War (WW II), to assess the impact of life history and childhood environment on health outcomes (Figure 1). The study also provides continuous health indicators to offer guidance on public health actions to the Public Health Department of the canton Vaud. The Lc65+ study was initiated in 2004 by the Institute of Social and Preventive Medicine of the University of Lausanne Hospital Centre (CHUV, canton Vaud, Switzerland) in collaboration with clinical partners from the CHUV and from the Department of Ambulatory Care and Community Medicine of the University of Lausanne (UNIL).³ When the Centre for Primary Care and Public Health (Unisanté) was created in 2019, the Lc65+ study joined the latter's Department of Epidemiology and Health Systems.

The protocol was approved by the Ethics Committee of the Faculty of Biology and Medicine of the University of Lausanne (19/04). Written informed consent was obtained from the participants.

Who is in the cohort?

The Lc65+ study is a population-based longitudinal study with cohort-sequential design, as illustrated in Figure 1. It consists of three samples selected at 5-year intervals in 2004, 2009 and 2014 by simple random sampling in the

Residents' Register of the canton Vaud, Switzerland. The inclusion criteria were: (i) to be a resident in the city of Lausanne; and (ii) to be aged 65 to 69 years on the 1 January of the enrolment year. The exclusion criteria were: (i) to be institutionalized; or (ii) to be unable to respond due to cognitive impairment.

Lausanne is the main city and the administrative capital of the canton Vaud. In 2004, the city had 117 000 inhabitants, of whom 17% were aged 65 years or over. Only 1% of those aged 65 to 70 years lived in an institution. The number of residents aged 65 to 69 years on the 1 January was 4879 in 2004, 4921 in 2009, and 5375 in 2014. Among them, 3236 (66.3%) individuals were randomly sampled into the Lc65+ study in 2004 (Pre-WW II sample), 3293 (66.9%) in 2009 (WW II sample) and 3796 (70.6%) in 2014 (Baby Boom sample), respectively. Participation rates were expected to be lower among Baby Boomers. All sampled individuals received an invitation by mail to participate. The mail included an initial questionnaire, a contact form and study information announcing the in-person interview and examination to be carried out at the study centre over the following year, to complete the baseline assessment as well as the long-term yearly followups. Two reminders were sent including the material. After the a posteriori exclusion of 183 ineligible individuals in 2004, 114 in 2009 and 141 in 2014, the number of participants was 1564 in 2004 (51.2% of 3053), 1489 in 2009 (46.8% of 3179) and 1678 in 2014 (45.9% of 3655). These participation rates are likely underestimated, as eligibility could not be verified in persons who did not respond to the invitation to participate.

To assess representativeness at baseline, we compared demographic characteristics in participants and non-participants. No significant difference was observed in the proportion of females (Pre-WW II sample: 58.7% versus 58.6%, WW II sample: 58.7% versus 58.3%, Baby Boom

sample: 56.2% versus 57.3%, respectively) or in the distribution of birth years in females or in males. A more indepth analysis of the representativeness of the Pre-WW II sample, using data from the 2000 federal census for the Lausanne resident population, indicated that participants' socioeconomic characteristics (nationality, place of birth, marital status, living arrangement and engagement in professional activity) closely reflected the target population. Detailed results of these comparisons have been previously published,³ and are available on the Lc65+ study's website [https://www.lc65plus.ch/en/content/representativeness].

How often have they been followed up?

Baseline assessment was performed in 2004–05, 2009–10 and 2014–15 for the Pre-WW II, WW II and Baby Boom samples, respectively (see Figure 1). A two-step procedure included: (i) a self-administered mailed questionnaire at recruitment; (ii) followed a year later by another mailed questionnaire and an in-person interview and examination at the study centre. Participants were thereafter contacted annually to complete a follow-up mailed questionnaire. In addition, they were invited every third year at the study centre to repeat the in-person interview and examination carried out at baseline. As illustrated in Figure 2, around

nine in 10 persons recruited in 2004 (Pre-WW II sample), 2009 (WW II sample) and 2014 (Baby Boom sample) also participated over the subsequent year (i.e. in 2005, 2010 and 2015, respectively). As expected following other studies, this proportion was slightly lower in the Baby Boom sample (88.2%) than in the WW II (92.0%) and Pre-WW II (90.0%) samples.

Each year after the baseline assessment, all participants who were still alive and who did not express any wish to leave the study were eligible for assessment. The conditional response rate (i.e. the proportion of participants among eligible persons) has remained above 90% each year in the Pre-WW II (range 92.3% to 96.2%), WW II (91.7% to 96.4%) and Baby Boom (91.0% to 94.5%) samples. From the beginning of the study, several retention strategies have been used at every step of recruitment and follow-up. Non-responders were contacted in various ways (reminder letters, phone calls repeated at different times of the day). To facilitate follow-up contact with participants, details of two close relatives or friends were collected at baseline, and written consent was obtained to contact their general practitioner if needed. Invalid addresses are regularly checked with the Residents' Registration Office. To maintain contact and foster a trustworthy relationship with the participants, greeting cards (Christmas, birthday)

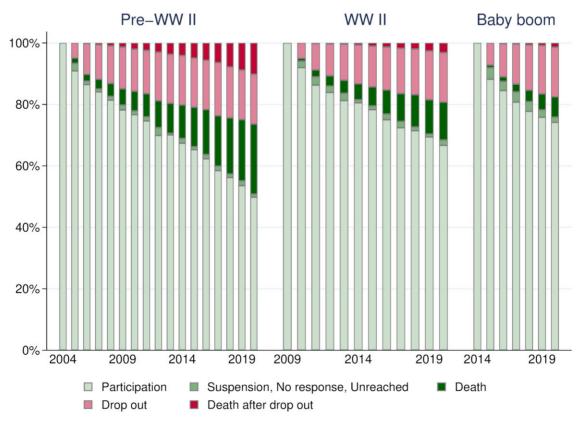


Figure 2 Participation over time in the three Lc65+ samples

and thank-you cards are regularly sent. Finally, participants receive a newsletter each year presenting the main results and analyses in progress, new sources of funding, external collaborations and information about the nature and modalities of data collection planned for the following year [https://www.lc65plus.ch/en/content/results].

After 16 years of follow-up, 779 (50%) of the respondents enrolled in 2004 were still alive and participated in 2020 (see Figure 2). This is higher than the retention rates reported in other cohorts of community-dwelling older adults after 15 years (21.5%)⁵ or after 17 years (31.7%).⁶ Nevertheless, as in all cohort studies, attrition was higher among individuals with unfavourable socioeconomic and health characteristics at recruitment. Table 1 presents these characteristics separately in retained participants who were either still alive or dead in Year 5 (85%, in green in Figure 2) and in those who had dropped out (15%, in red in Figure 2). In both crude and mutually adjusted logistic regression models, dropping out was independent of sex, but positively associated with a foreign country of birth, a lower level of education, the presence of financial difficulties and a health status self-rated as average, poor or very poor. Similar associations were found at 10-year follow-up in the Pre-WW II and WW II samples, and at 15-year follow-up in the Pre-WW II sample only (data not shown).

What has been measured?

Measures taken at each wave of data collection in the three Lc65+ samples are detailed in Table 2 and have been previously described.³ In brief, the content of the questionnaires, interviews and performance tests was inspired by other Swiss and international population-based health surveys: the Swiss Health Survey (Federal Statistical Office), Swiss Household Panel,⁷ MONICA study⁸ or SHARE European survey.⁹ Furthermore, participants gave their written consent for linking their data with hospital discharge records and death certificates, which allows a passive follow-up at the end of each year to ascertain vital status by consultation with the Residents' Registration Office of canton Vaud.

Self-completed questionnaires

The initial questionnaire covered specific life course characteristics such as life history from childhood, through adulthood and until the time of completing the questionnaire (i.e. 65 to 70 years). Sections were structured in chronological order to enhance recall, and included indications of socioeconomic status and health and functional status, as well as of the use of health services. Subsequent yearly questionnaires repeated a large set of these questions to assess longitudinal changes (e.g. self-rated health status), but

also introduced additional measures over time as they became more relevant (e.g. memory difficulties). The frequency at which questions were repeated ranged from every year to every 5 years (e.g. sleep). In parallel, *ad-hoc* surveys were regularly conducted on topics such as sexuality (2007), falls (falls diary, 2011), quality of life (2011), care and medication (2012), the new national adult protection law (2014) and COVID-19 (2020).

In-person interviews and examinations

In-person visits are performed at the study centre, and include physical and cognitive performance tests as well as a set of anthropometric and cardiovascular indices. Assessments are conducted by medical research assistants according to a standardized protocol and an instruction manual, under the supervision of a senior research coordinator. To enhance the reliability and homogeneity of the assessments, all medical research assistants complete a 2-week specific training at the study centre prior to their first assessment. An additional training is conducted at the beginning of every year of a sample of volunteers enrolled for the piloting of questionnaires and tests. Monitoring and quality control of medical research assistants' records are performed by their supervisor at 3month intervals. Any heterogeneity in assessments identified among research assistants is discussed in monthly meetings, leading to corrective measures and clarifications of the instruction manual. Furthermore, at 2-month intervals, the supervisor attends an in-person visit conducted by each of the medical research assistants, and each assistant attends a tandem with a colleague. Finally, after completion of the in-person visit, each record is carefully checked for quality by the supervisor to identify any errors that are then discussed with the medical research assistants.

What has it found?

Sixteen years after the inception of the Lc65+ study, this project has produced a large amount of data that are used to answer research questions, provide population-based evidence for decision makers (e.g. during the COVID-19 crisis) and inform the general public. Indicators of older people's health and needs for health services are regularly made available to local public health authorities through extended and brief reports that summarize key findings in a short and attractive format suitable for non-scientific experts and a lay audience. A list of all newsletters, articles and reports is available on the Lc65+ website [https://www.lc65plus.ch/en/content/results]. The paragraphs below present a range of scientific results generated by the Lc65+ data in four

Table 1 Five-year attrition in the three Lc65+ samples by main characteristics at recruitment

	Retained	alive or dead	Drop-out	alive or dead	Association with drop-out											
	(N =	= 4023)	(N	= 708)	(Crude	Mutually adjusted									
	N	%	N	%	OR	95% CI	OR	95% CI								
Sex																
Males	1698	(42.2%)	297	(41.9%)	Ref.		Ref.									
Females	2325	(57.8%)	411	(58.1%)	1.01	[0.86; 1.19]	0.94	[0.80; 1.12]								
Birth country																
Switzerland	2914	(72.5%)	405	(57.4%)	Ref.		Ref.									
Other	1104	(27.5%)	301	(42.6%)	1.96***	[1.66; 2.31]	1.82***	[1.52; 2.17]								
Education																
Post-compulsory	1680	(41.8%)	210	(30.0%)	Ref.		Ref.									
Apprenticeship	1568	(39.1%)	266	(37.9%)	1.36**	[1.12; 1.65]	1.48***	[1.20; 1.81]								
Basic compulsory	767	(19.1%)	225	(32.1%)	2.35***	[1.91; 2.89]	1.97***	[1.58; 2.45]								
Financial difficulties																
No	3299	(82.4%)	487	(70.1%)	Ref.		Ref.									
Yes	707	(17.6%)	208	(29.9%)	1.99***	[1.66; 2.39]	1.48***	[1.22; 1.79]								
Perceived health																
Very good, good	2697	(67.2%)	393	(55.7%)	Ref.		Ref.									
Average, poor, very poor	1315	(32.8%)	312	(44.3%)	1.63***	[1.38; 1.92]	1.28**	[1.08; 1.52]								
Death at 5-year FU																
No	3776	(93.9%)	663	(93.6%)												
Yes	247	(6.1%)	45	(6.4%)												

FU, follow-up;

^{*}P <0 .05;

^{**}P < 0.01;

^{***}P < 0.001.

Table 2 Lc65+ measures taken at each wave of data collection in the samples enrolled in 2004 (Pre-WW II), 2009 (WW II) and 2014 (Baby Boom)

Measures		Study waves (Pre-WW II)														Study waves (WW II)										Study waves (Baby Boom)						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	1	2	3	4	5	6	7	8	9	10	1		2	3	4	5	
Self-completed questionnaires Life history (childhood, adulthood) Self-rated health; difficulties in activities of daily living; difficulties in mobility; chronic conditions and symptoms; depressive symptoms; fatigue; insomnia; medication; falls/ fear of falling; fear of disease; weight loss; stressful events; living arrangement; social engagement; physical activity	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•		•	•	•	•	
Self-perception of ageing Memory difficulties Mood; energy Health services use Financial support Pain Sleep Spirituality Intellectual activities Leisure activities Sense of mastery Quality of life; positive life events; social/emotional	•	•	•	•	•	•	•	•	•	•	• • • • • • • • • • • • • • • • • • • •	•	•	•	•	•	•	•	•	•	• • • • • • • • • • • • • • • • • • • •	•	•	•	•	•			•	•	•	
support Alcohol consumption Smoking Smell and taste; need for cognition; accessibility of amenities; volunteering	•			•			•			•			•		•	•			•			•			•	•				•	•	

Table 2 Continued

Measures		Study waves (Pre-WW II)															Study waves (WW II)										Study waves (Baby Boom)					
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	1	2	3	4	5	6	7	8	9	10	1		2	3	4	5	
In-person interviews and																																
examinations																																
Weight and height; arm,	•			•			•			•			•			•			•			•			•	•				•		
waist, hip, and calf																																
circumferences; skinfold																																
thickness; resting blood																																
pressure and heart rate																																
Physical tests: gait speed	•			•			•			•			•			•			•			•			•	•				•		
(single/double/triple task);																																
up-and-go; five chair rises;																																
grip strength; Moberg																																
picking-up; balance; vision																																
and hearing	_			_			_			_			_			_			_			_			_	_				_		
Dominant hand, use of	•			•			•			•			•			•			•			•			•	•				•		
assistive products (glasses,																																
hearing aid, walking aid)																																
Cognitive tests: mini-mental state examination; clock	•			•			•			•			•			•			•			•			•	•				•		
drawing test; verbal fluency;																																
trail making test A and B																																
Health-related quality of life				•			•			•			•						•			•				•				•		
(SF-12)				•						•																						
Health services use;	•			•			•			•			•			•			•			•			•	•				•		
nutrition; income; assets																																
Pain							•			•			•			•			•			•			•	•				•		
Alcohol consumption							•			•			•									•			•					•		
Oral health							•						•			•						•				•				•		
Passive follow-up																																
Vital status, place of																																
residence, home setting																																
(private home, nursing																																
home, sheltered housing,																																
relative's home)																																

selected domains: frailty, health trends, health service research and quality of life.

Frailty

Based on Fried's five criteria: (i) shrinking; (ii) weakness; (iii) poor endurance, exhaustion; (iv) slowness; and (v) low activity, 10 a frailty phenotype is defined according to the number of criteria fulfilled: non-frail (0 criterion), pre-frail (1–2 criteria) or frail (≥3 criteria). Using data from the Lc65+ study, previous analyses indicated a significant association of the frailty phenotype with a variety of health aspects, including specific chronic diseases, 11 blood pressure, 12 fear of falling, 13 alcohol intake 14 and oral health. 15 In a study on handwriting parameters, no specific pattern of handwriting was observed across the frailty spectrum, but pauses between words and contact pressure were related to specific aspects of the frailty phenotype. 16 In a 14-year survival analysis, 17 (pre-)frailty at the age of 66-71 years was significantly associated with mortality in both females and males (see Figure 3), thereby confirming the potential importance of the early identification of prefrailty or frailty.

Health trends

The cohort-sequential design of the Lc65+ study allowed comparison of data collected using identical procedures in

three representative samples of community-dwelling older adults, assessed at the same age but born at 5-year intervals. At the time of enrolment, participants' reports of childhood adversity (i.e. food restrictions, child labour, family economic environment, serious illness or accident and stressful life events) indicated a decreasing trend in younger samples. 18 The three samples did not differ in multiple indicators of perceived health—an observation that challenges the widely held belief that Baby Boomers are ageing in better health. 19 However, diverging trends still arose from objective health assessments.²⁰ Whereas Baby Boomers achieved the highest physical performance levels (e.g. gait speed, timed up and go), they performed worse in cognitive tests (e.g. Mini-Mental State Examination, clock drawing test). Other analyses focusing on health-related behaviours showed positive trends in younger samples regarding the daily consumption of non-alcoholic beverages and the regular practice of sport by females.²¹

Health service research

A postal vignette survey provided insight on older adults' opinions regarding long-term care options for a broad range of disability situations.²² Males were more likely than females to choose a home setting with potential help from a spouse.²³ Among the disability and social characteristics displayed in the vignettes, incontinence was a key factor explaining the perception of a need for institutionalization.²⁴ In a

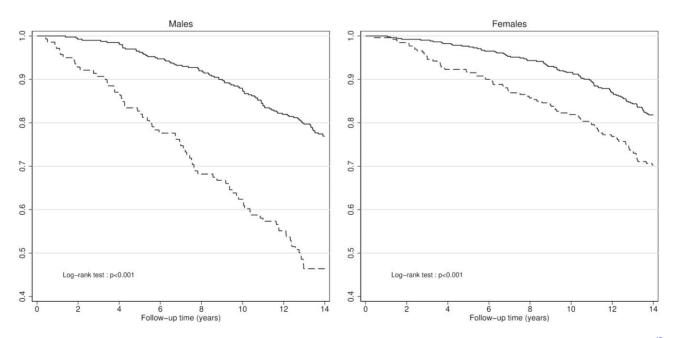


Figure 3 Fourteen-year mortality according to the frailty phenotype at baseline, by sex (continuous line: non-frail, dotted line: pre-frail or frail).¹⁷ Reproduced with the consent of Swiss Medical Weekly

longitudinal study applying Andersen's Behavioural Model of Health Services Use, incident utilization of formal home care appeared to be largely determined by need factors such as chronic health conditions and functional limitations, as compared with predisposing factors (e.g. sociodemographic characteristics, beliefs about health services) and enabling factors (e.g. accessibility of health services, social support). A cross-sectional analysis explored the acceptance of health information and communication technologies by community-dwelling older adults and the factors associated with acceptance or rejection. This research complements other publications based on Lc65+ data which addressed older people's perception and knowledge of selected aspects of the health system.

Quality of life

The Older people Quality of Life-7 domains (OQoL-7) is a multidimensional questionnaire developed in the context of the Lc65+ study. 31,32 This scale measures both the perceived importance and the perceived satisfaction regarding 28 aspects of older people's quality of life. A principal component analysis identified a factorial structure comprising seven quality of life domains (Feeling of safety; Health and mobility; Autonomy; Close entourage; Material resources; Esteem and recognition; and Social and cultural life), which was confirmed in a validation sample.³¹ The OQoL-7 showed adequate concurrent and construct validity.³² Building on the development of OQoL-7, cross-sectional analyses were conducted on the relationship between quality of life and frailty, 33 and on the public health impact of chronic symptoms.³⁴ Longitudinal analyses reported temporal changes of the importance of quality of life domains³⁵ and of the satisfaction with quality of life domains.³⁶ To explore temporal trends (i.e. cohort effects), comparisons were made between samples assessed at a 5-year intervals.³⁷ Further work contributed to the assessment and interpretation of quality of life. 38,39

What are the main strengths and weaknesses?

The main strengths of the Lc65+ study include: (i) a cohort-sequential design involving three successive samples, which enables analysis of both longitudinal changes within each sample and societal changes between samples; (ii) an emphasis on the youngest old at baseline, which offers a unique chance to study the incidence and the evolution of frailty from its initial manifestations; (iii) a broad range of measures that cover both self-reported and performance-based assessments obtained using a strictly standardized methodology over time.

One weakness of the Lc65+ study is the lack of biomarkers and genetic data. However, prioritization of non-

biological data was inherent to the conceptualization of the study, which emphasizes medical and psychosocial aspects rather than biological determinants. Furthermore, the choice to include a large range of measures, while avoiding overwhelming participants with burdensome questionnaires and interviews, has limited the level of detail in most measured domains. Finally, the three samples recruited at 5-year intervals in 2004, 2009 and 2014 do not allow for studying societal trends over a period of more than 10 years. This issue may be overcome in the future by recruiting new samples at 10-year intervals, starting in 2024.

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

Lc65+ data are maintained and stored at the study centre in the Department of Epidemiology and Health Systems of the Centre for Primary Care and Public Health (Unisanté). Proposals for collaboration on projects using Lc65+ data are welcome, both nationally and internationally. Enquiries can be submitted to Yves Henchoz [yves.henchoz@unisante.ch] with a description of the planned project, which will be reviewed by the organizing committee of the Lc65+ study.

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From the beginning, the Lc65+ study has been financed exclusively by public funds or non-profit organizations. Currently, funding is provided by the Public Health Department of canton Vaud, the Centre for Primary Care and Public Health (Unisanté) and by a research grant from the Loterie Romande (non-profit organization supporting research and social projects). Other sources of funding for either data collection or exploitation have changed over the years and include the city of Lausanne, the University of Lausanne Hospital Centre (CHUV), the Institute of Social and Preventive Medicine of the CHUV, the Community Health and Medicine Department of the CHUV, the Service of Geriatric Medicine and Geriatric Rehabilitation of the CHUV, the Department of Medicine of the CHUV, the Department of Ambulatory Care and Community Medicine of the UNIL, the Faculty of Biology and Medicine of the UNIL, the Fondation Médecine Sociale et Préventive, the Swiss National Foundation for Scientific Research and the Leenaards Foundation.

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Author Contributions

Y.H. drafted the manuscript. S.F. and J.M.B. conducted the analyses. B.S.E. and Y.H. designed and conducted the data collection as the principal investigators of the Lc65+ study. All authors

contributed to the study concept and design, to the interpretation of data and to the critical review of the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

None declared.

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