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COHORT PROFILE

Cohort Profile: The Longitudinal Aging Study Amsterdam

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How did the study come about?

The Longitudinal Aging Study Amsterdam (LASA) was initiated by the Dutch Ministry of Welfare, Health and Culture (currently Ministry of Health, Welfare and Sports). By the end of the 1980s, ministry officials recognized that ageing would be a major demographic driving force, shaping the need for health care in the Dutch population in the near future. Therefore, they became increasingly interested in the process of ageing and ageing-related determinants of health-care use, and wanted to develop policies for older people in The Netherlands who were in need of extra care and support. Maintaining independent functioning, quality of life and participation of older people were recognized to be major challenges for Dutch society. Multi-disciplinary and longitudinal scientific research was considered to be needed to inform the ministry's policy and monitor functioning and well-being of older Dutch people, leading to the start of the LASA study in 1991.

The study was designed by researchers from the VU University and VU University Medical Center in Amsterdam, in a close collaboration between social and biomedical scientists. This collaboration ensured a thoroughly multi-disciplinary approach fitting the scope of the intended focus of LASA.

What does the study cover?

The primary aim of LASA has been to study the determinants, trajectories and consequences of physical, cognitive, emotional and social functioning in relation to ageing. The following research questions were central to the general LASA framework at the outset.[1]

- Which changes over time take place in the physical, cognitive, emotional and social components of functioning in older persons?
- Which predictors of change can be recognized in these components of functioning?
- How are changes in the four components of functioning interrelated?
- What are the consequences of changes in functioning in terms of contributions to society, the necessity of adjustment, and the need for care?

Who is in the sample, how long have they been followed and what is attrition like?

The LASA cohort is based on a nationally representative sample of older adults aged 55–85 years (years of birth 1908–37), based in three geographic regions in The Netherlands. These three regions were selected so that an optimal representation of the older Dutch population would be achieved, with respondents from the protestant north, the catholic south and secular parts of The Netherlands and from both urbanized and rural areas within each of these regions. The sample is used in two studies: first the NESTOR study on Living Arrangements and Social Networks (LSN) of older adults,[2] and second LASA. The sample was recruited from municipal registries in 1992, with an oversampling of older people and older men in particular. The initial response rate

[calculated following guidelines from the American Association for Public Opinion Research (AAPOR[3])] is 60% ($n=3805$), and the cooperation rate is 62%. The response rate is defined here as the number of complete and partial interviews with persons divided by the total number of eligible persons in the sample plus a fraction of those persons who were in the sample but of whom eligibility could not be determined. The cooperation rate is defined as the proportion of completed interviews in the number of contacted eligible persons.

On average, 11 months after the LSN interview (Wave A), the participants were approached to participate in the first LASA cycle (Wave B), with a response rate of 85% and a cooperation rate of 89%. Since the 1992 LSN interview, there have been six LASA cycles to date (Table 1). At the sixth cycle (LASA Wave G), a total of 985 respondents of the original sample had been retained.

An additional cohort was recruited from the same sampling frame in 2002/2003, exactly 10 years after the first LASA cycle of the original cohort, so that differences between cohorts in physical, cognitive, emotional and social components of functioning could be studied. This new cohort consisted of 1002 men and women who were born between 1938 and 1947 (initial response rate was 55%; cooperation rate was 62%). In the subsequent observation cycles, respondents from this new cohort were combined with those from the original one. At Wave G, data on a total of 833 respondents from the new cohort had been obtained.

A specific concern for studies on ageing is that attrition is considerable. Therefore, men and the oldest participants were oversampled in LASA to ensure that there would be reasonable numbers of very old men, even after long periods of follow-up. Attrition in LASA can be attributed for the largest part to mortality, and to lesser extent to refusal, or other reasons. In LASA, the share of other causes than mortality [frailty (=ineligible), refusal, no contact] to total attrition is limited (Table 2 and Figure 1). Even though attrition due to mortality does not necessarily influence the representativeness of the sample because high mortality is characteristic of older populations, attrition due to mortality is related to specific sample characteristics and may bias estimates of longitudinal relationships between variables. As shown in Table 2, attrition in LASA is associated with predictors and outcomes of interest to our research. Therefore, an important challenge will be to employ either multiple imputation or perform advanced statistical analyses capable of handling missing data without introducing bias in longitudinal analysis.

Because LASA has had several side studies among a selection of its participants in-between the regular measurement waves, we had some concern about the potential effects of these studies on participation in future cycles. However, even though participation in one or more of these side studies must have been burdensome to participants, we did not find indications that this has led to increased drop-out later on during follow-up by those who were included in them.[4] Participants in side studies were less likely to refuse participation later on when approached for participation in the main study.

What has been measured?

Measurements are performed by trained interviewers who visit respondents at home. On average, this interview takes 1 h 45 min to complete. To obtain additional data, respondents are asked to fill out a written questionnaire separately, which is left at the respondent's home after the visit. During the main interview respondents are asked to participate in a subsequent medical interview. After consent, a separate visit is made to administer clinical measurements and ask additional questions.

Table 3 gives an overview of measures that are included in the study. It includes the measures that we consider to be our core indicators of functioning and which are part of each or most measurement cycle(s). We have taken care to include informative measures of functioning for each of the four functioning domains that are central in the study and to pair objective with subjective measures of functioning as much as possible. More detailed information about many of our measurements can be obtained from our web site: www.lasa-vu.nl.

Several side studies have been performed among a selection of LASA participants when data from the regular measurement cycles were insufficient or lacked detail to answer specific research questions. For example, a selection of respondents ($n=277$) have been followed more regularly across a span of 6 years because 3-yearly intervals were deemed too long to capture the natural course of depression.[5] In addition to 5-monthly measurements of depressive symptoms with the Center for Epidemiologic Studies Depression Scale,[6] these respondents were also subjected to a diagnostic interview once every 3 years. Some other side studies among selections of participants focused on a diversity of issues, i.e. the structure and function of the social network and their network members; adaptation to widowhood in widowed participants; precursors and consequences of (recurrent) falling; God image; lifestyle factors such as physical activity, sports and diet; and end of life.

What has the study found?

Over 300 international scientific publications have appeared based on LASA data, encompassing a broad

Table 1 Composition of the realized sample with respect to year of birth

Birth year	1992	1992–93	1995–96	1998–99	2001–02	2002–03	2005–06	2008–09
	Wave A (LSN)[a]	Wave B (LASA), main interview	Wave C (LASA), main interview	Wave D (LASA), main interview	Wave E (LASA), main interview	Wave A/B (LASA second cohort), main interview	Wave F (LASA plus LASA second cohort), main interview	Wave G (LASA plus LASA second cohort), main interview
1908–12	774	580	384	233	133		42	16
1913–17	712	575	431	318	215		109	63
1918–22	589	472	384	313	242		160	105
1923–27	593	492	441	386	335		278	216
1928–32	580	512	463	416	385		330	284
1933–37	557	476	442	410	381		338	301
1938–42	–	–	–	–	–	508	459	411
1943–47	–	–	–	–	–	494	449	422
Total	3805	3107	2545	2076	1691	1002	2165	1818
		Medical interview[b]	Medical interview[c]	Medical interview[d]	Medical interview	Medical interview	Medical interview	Medical interview
1908–12		460	272	154	61		20	6
1913–17		476	316	237	145		65	37
1918–22		412	311	262	178		111	72
1923–27		432	361	326	275		211	161
1928–32		468	249	277	319		282	229
1933–37		423	–	126	329		292	256
1938–42		–	–	–	–	464	412	357
1943–47		–	–	–	–	455	412	376
Total		2671	1509	1382	1307	919	1805	1494

[a]The complete LSN sample also included 689 respondents born between 1903 and 1907, making the complete LSN sample 4494 respondents. However, these were not part of the LASA sample, which only included respondents who were born in 1908–1937.
[b]All those who participate in the medical interview participated in the main interview.
[c]Only participants born before 1931 were included in the sample of the medical interview at Wave C.
[d]Only participants born before 1931 plus a control group of participants were included in the sample of the medical interview at Wave D.

Table 2 Seventeen-year attrition in LASA, birth cohorts 1908–1937

	Still participating (%)	Deceased (%)	Refused (%)	Too frail plus could not be contacted (%)	Multivariate associations with vital status (deceased = 1) (odds ratios)	Multivariate associations with total attrition (due to mortality, refusal, frailty or not contacted = 1) (odds ratios)
Total ($N = 3107$)	985 (31.7)	1615 (52.0)	302 (9.7)	205 (6.6)	1615 (vs 985)	2122 (vs 985)
Men ($N = 1506$)	395 (26.2)	894 (59.4)	129 (8.6)	88 (5.8)	2.49 (2.06–3.01)	2.08 (1.71–2.52)
Women ($N = 1601$)	590 (36.9)	721 (45.0)	173 (10.8)	117 (7.3)	1.00	1.00
1908–1912 ($N = 580$)	16 (2.8)	507 (87.4)	21 (3.6)	36 (6.2)	24.51 (16.91–35.52)	41.38 (23.91–71.65)
1913–1917 ($N = 575$)	63 (11.0)	438 (76.2)	32 (5.6)	42 (7.3)	12.56 (9.04–17.43)	10.83 (7.68–15.26)
1918–1922 ($N = 472$)	105 (22.2)	275 (58.3)	51 (10.8)	41 (8.7)	6.08 (4.42–8.35)	5.03 (3.73–6.78)
1923–1927 ($N = 492$)	216 (43.9)	184 (37.4)	64 (13.0)	28 (5.7)	2.82 (2.05–3.87)	2.02 (1.54–2.64)
1928–1932 ($N = 512$)	284 (55.5)	133 (26.0)	62 (12.1)	33 (6.4)	1.68 (1.22–2.32)	1.32 (1.01–1.71)
1933–1937 ($N = 476$)	301 (63.2)	78 (16.4)	72 (15.1)	25 (5.3)	1.00	1.00
Primary education or less ($N = 1376$)	347 (25.2)	789 (57.3)	133 (9.7)	107 (7.8)	0.92 (0.69–1.24)	1.45 (1.07–1.97)
Secondary education ($N = 1370$)	507 (37.0)	639 (46.6)	138 (10.1)	86 (6.3)	0.90 (0.67–1.19)	1.22 (0.91–1.63)
Tertiary education ($N = 353$)	131 (37.1)	181 (51.3)	29 (8.2)	12 (3.4)	1.00	1.00
Never married ($N = 190$)	50 (26.3)	112 (58.9)	19 (10.0)	9 (4.7)	1.45 (1.00–2.12)	1.28 (0.85–1.90)
Divorced ($N = 162$)	50 (30.9)	73 (45.1)	15 (9.3)	24 (14.8)	0.97 (0.66–1.43)	1.34 (0.90–2.01)
Widowed ($N = 813$)	158 (19.4)	548 (67.4)	52 (6.4)	55 (6.8)	1.57 (1.25–1.97)	1.25 (0.97–1.60)
Married ($N = 1942$)	727 (37.4)	882 (45.4)	216 (11.1)	117 (6.0)	1.00	1.00
Chronic diseases						
More than or equal to four ($N = 76$)	6 (7.9)	65 (85.5)	3 (3.9)	2 (2.6)	4.87 (2.37–9.99)	3.42 (1.38–8.49)
Three ($N = 186$)	30 (16.1)	133 (71.5)	8 (4.3)	15 (8.1)	2.22 (1.49–3.31)	2.10 (1.30–3.40)
Two ($N = 535$)	120 (22.4)	347 (64.9)	36 (6.7)	32 (6.0)	1.80 (1.39–2.32)	1.42 (1.08–1.87)
One ($N = 1093$)	365 (33.4)	554 (50.7)	96 (8.8)	78 (7.1)	1.32 (1.08–1.61)	1.19 (0.97–1.46)
No chronic disease ($N = 1197$)	486 (40.6)	503 (42.0)	152 (12.7)	56 (4.7)	1.00	1.00
Cognitive impairment (MMSE < 24) ($N = 342$)	24 (7.0)	268 (78.4)	24 (7.0)	26 (7.6)	2.06 (1.48–2.88)	2.99 (1.87–4.78)
No cognitive impairment (MMSE $\geqslant 24$) ($N = 2749$)	957 (34.8)	1337 (48.6)	276 (10.0)	179 (6.5)	1.00	1.00
Depressed (CES-D $\geqslant 16$) ($N = 448$)	100 (22.3)	273 (60.9)	36 (8.0)	39 (8.7)	1.12 (0.87–1.45)	1.30 (0.98–1.73)
Not depressed (CES-D < 16) ($N = 2608$)	883 (33.9)	1305 (50.0)	261 (10.0)	159 (6.1)	1.00	1.00

Marital status, *N* chronic diseases, cognitive impairment and depression measured at Wave B (1992–1993).

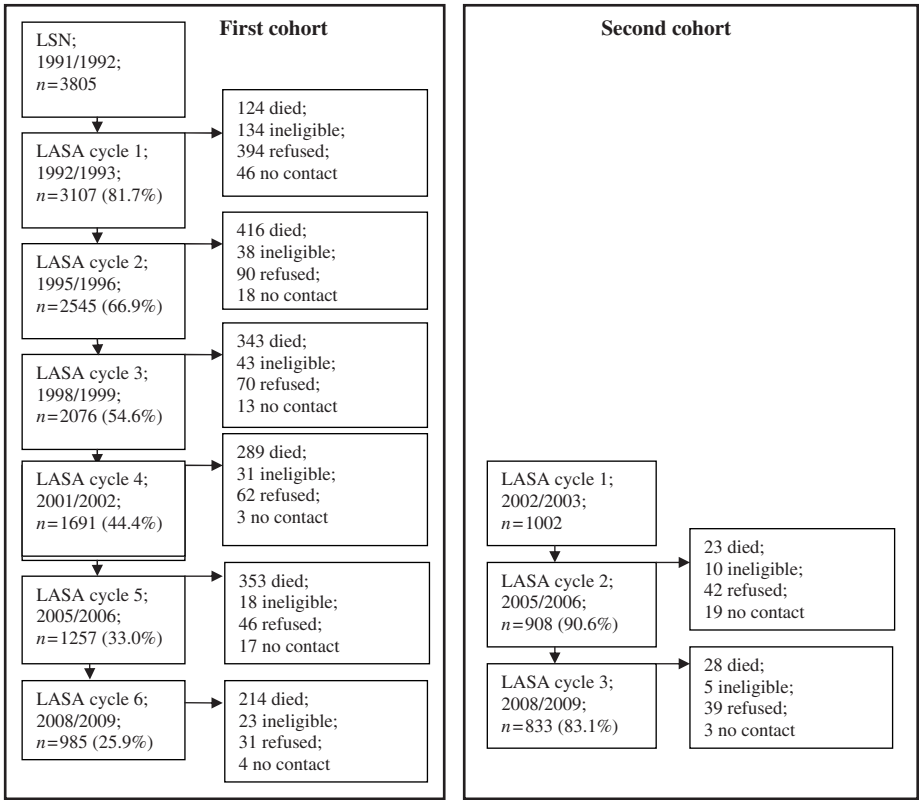

Figure 1 Survival and participation in the LASA study

range of subtopics. A full list of publications can be found on our web site (www.lasa-vu.nl). Here, we discuss a selection of the findings from the four focus domains that LASA was set out to cover: (i) physical functioning; (ii) cognitive functioning; (iii) emotional functioning; and (iv) social functioning.

Physical functioning

Our research on physical functioning is broad and covers a range of health outcomes, as well as earlier stage risk markers, including but not limited to nutritional status, body composition and lifestyle factors. While it is impossible to give a detailed overview of the results from this programme, some key areas can be highlighted.

Researchers in our group have investigated risk factors for osteoporotic fractures, a common source of increased morbidity and mortality in old age.[7,8] They identified that, among others, homocysteine levels[9] and vitamin D-deficiency[10] were independent risk factors for osteoporotic fractures. Moreover, the role of vitamin D has been assessed in relation to other indicators of physical functioning, including factors underlying fractures such as bone mineral density,[11] as well as sarcopenia[12] and overall physical performance,[13] confirming that vitamin D status is implicated in much musculoskeletal morbidity in old age, and identifying threshold levels of vitamin D at which intervention is warranted.

Frailty is a concept stemming from geriatrics that represents a lack of reserve functional capacity which makes people vulnerable to all manner of environmental insults.[14] Frailty usually encompasses low physical activity, weight loss or underweight, weakness (e.g. in arms or legs) and often also either slowness, or problems with memory and attention, or reduced vision or hearing. Studies on frailty in LASA demonstrated that frailty predicted declines in physical functioning, adjusted for the effect of chronic diseases, and predicted mortality,[15] adjusted for the effect of chronic diseases and disability.[16] These results indicate that frailty is a relevant geriatric syndrome that captures elements of functioning that other well-known measures of morbidity, including measures of functional limitations or Activities of Daily Living, do not.

Cognitive functioning

Cognitive functioning is known to decline with age, but it is difficult to differentiate between 'normal' cognitive decline and cognitive decline as a consequence of pathological processes such as dementia. Data from LASA respondents demonstrate that 18% of older persons experienced a decline in cognitive functioning (measured by the Mini Mental State Examination) during the first 3 years of follow-up.[17] However, in a large number of persons experiencing decline, the decline was only temporary and

Table 3 Main outcome measures and predictors of functioning in each functioning domain

	Wave B (LASA Cycle 1)	Wave C (LASA Cycle 2)	Wave D (LASA Cycle 3)	Wave E (LASA Cycle 4)	Wave A/B (LASA second cohort Cycle 1)	Wave F (LASA first cohort Cycle 5 plus second cohort Cycle 2)	Wave G (LASA first cohort Cycle 6 plus second cohort Cycle 3)
Physical functioning							
Body composition	Anthropometry	Anthropometry	Anthropometry	Anthropometry	Anthropometry	Anthropometry	Anthropometry
Lifestyle factors (e.g. smoking, alcohol use, physical activity)	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report
Chronic diseases	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report
Functional limitations, physical performance	Functional limitations = self-report, Performance tests	Functional limitations, performance tests	Functional limitations, performance tests	Functional limitations, performance tests	Functional limitations, performance tests	Functional limitations, performance tests	Functional limitations, performance tests
Falls/fractures	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report
Medication use	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report
Self-rated health	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report
Cognitive functioning							
General cognitive functioning	MMSE	MMSE, coding task	MMSE, coding task	MMSE, coding task	MMSE, coding task	MMSE, coding task	MMSE, coding task
Intelligence; crystallized, fluid	RCPM	RCPM, GIT vocabulary test,	RCPM	RCPM	RCPM	RCPM [GIT in second cohort]	RCPM
Memory; memory complaints, everyday memory, metamemory	EMT, 15WT, self-reported complaints	15WT, self-reported complaints	15WT, self-reported complaints	15WT	15WT	15WT	15WT
Emotional functioning							
Anxiety	HADS-A	HADS-A	HADS-A	HADS-A		HADS-A	HADS-A
Depression[a]	CES-D	CES-D	CES-D	CES-D	CES-D	CES-D	CES-D
Life events; e.g. illness, deaths in family, victim of crime, financial problems		List of events	List of events	List of events		List of events	List of events
Personality traits	Self-esteem, mastery, GSS, neuroticism	Self-esteem, mastery, GSS, neuroticism	Self-esteem, mastery, GSS, neuroticism	Self-esteem, mastery, GSS, neuroticism	Self-esteem, mastery, GSS, neuroticism	Self-esteem, mastery, GSS	Self-esteem, mastery, GSS
Quality of life				EuroQol		EuroQol	EuroQol
Social functioning							
Personal network; size, social support, social network	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report
Relationships with all children			Self-report	Self-report			Self-report
Loneliness	LS	LS	LS	LS	LS	LS	LS
Social participation	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report

(continued)

Table 3 Continued

	Wave B (LASA Cycle 1)	Wave C (LASA Cycle 2)	Wave D (LASA Cycle 3)	Wave E (LASA Cycle 4)	Wave A/B (LASA second cohort Cycle 1)	Wave F (LASA first cohort Cycle 5 plus second cohort Cycle 2)	Wave G (LASA first cohort Cycle 6 plus second cohort Cycle 3)
Other							
Demographic and socio-economic factors	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report
Religion, religiosity		Self-report	Self-report	Self-report	Self-report	Self-report	Self-report
Use of care; care needs, medical care, personal/household care	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report	Self-report
Cortisol		Plasma		Salivary			
Blood measurements	Among others: inflammatory markers, cholesterol, glucose	Among others: inflammatory markers, cholesterol, glucose, sex hormones, cortisol, thyroid function, homocysteine cycle			Among others: inflammatory markers, cholesterol, glucose, sex hormones, cortisol, thyroid function, homocysteine cycle		Among others: inflammatory markers, cholesterol, glucose, sex hormones, cortisol, thyroid function, homocysteine cycle

MMSE, mini-mental state examination; RCPM, raven coloured progressive matrices; GIT, Groninger intelligence test; EMT, everyday memory test; 15WT, 15 word test; HADS-A, hospital anxiety depression scale-anxiety subscale; CES-D, center for epidemiologic studies-depression scale; GSS, general self-efficacy scale; LS, loneliness scale.
[a]DSM-IV diagnoses are available for a sub sample.

subsequent improvement or stability in cognitive functioning was observed (49% of those experiencing decline in the first 3 years of follow-up). Older age, memory complaints and incidence of cardiovascular disease during follow-up predicted further deterioration of cognitive functioning. A remarkable finding was that memory decline during the 6 years of follow-up was predicted by loss of a spouse.[18]

Emotional functioning

LASA researchers have had a special interest in the course and outcomes of depressive and anxiety problems over time. They found strong prospective effects of anxiety and depression on wellbeing, functioning, morbidity, mortality and use of care, after adjustment for confounders.[5,19,20] Because effective prevention and treatment interventions are available for both anxiety and depression in old age, these studies provided invaluable information for policy and practice of care. The repeated measurement of personality characteristics is another quite unique feature of LASA. Neuroticism was shown to remain stable up until old age and to have both an important and unique impact on quality of life.[21]

Social functioning

A lot of research using LASA has focussed on the characteristics of social functioning in relation to health or social change. Social integration of older adults in society is seen as an indicator of successful ageing.[22] Core indicators of social functioning in LASA are loneliness and social networks. LASA researchers have investigated potential determinants of loneliness, including but not limited to: self-assessed health, own and spousal disability, residential care, partner status and network size.[23,24] Respondents generally became more lonely during follow-up, where the highest increases were observed in the oldest respondents, in those who were initially healthy but experienced declines in health, and in those who had a partner, suggesting that partner relationships might not offer the same kind of protection against loneliness at advanced ages as it does earlier in the life course.[23]

LASA includes rich information about the family and personal networks of its respondents. Members of respondents' networks are identified in seven domains: household members, children and their partners, other family members, neighbours, members of organizations, contacts through work and others. Several characteristics of each of the contacts are assessed. For example, all children are identified by their name and basic demographic data on the children like partner, parental status, employment and relational data such as travelling time, contact frequency and support exchange are available. It is demonstrated that children's structural circumstances (e.g. being employed, having young children) are less important in supporting their parents than the

process of reciprocal supportive exchanges.[24] Results, furthermore, indicate that many complex step-family structures exist, which might have consequences for care in later life.[25] The widely varying patterns of losses and gains in personal relationships among the respondents squares with a focus on the heterogeneity of developments among ageing people. Furthermore, the instability of the network composition (e.g. one neighbour is replaced by another neighbour) reflects natural circulation in the membership of networks.[26] Higher age of the respondents was associated with an increase in the number of family members in the personal network.[27] It was shown that cognitive and physical decline are important determinants of changes in the personal network, but predicting different types of change. Physical decline was associated with a replacement of friends and neighbours by family members, whereas cognitive decline was associated with losses of friends and neighbours who were not replaced by family members.[28]

Because increased need and use of care correlate with ageing, LASA incorporates broad data on care. Among others, we ask respondents if they receive support with instrumental daily activities such as with shopping and preparing meals, and, if so, from whom. We ask about received support with personal care (e.g. washing and clothing), and we assess received medical and social care, including institution residency. Recently, researchers from our group investigated utilization of acute and long-term care in the last year of life and observed some differences between socioeconomic groups in utilization. People with a higher level of education were more likely to have had contact with medical specialists. Those with a lower income were more likely to live in a care institution than their counterparts with higher incomes.[29]

What are the main strengths and weaknesses of the study?

LASA's main strengths include: (i) its multidisciplinary approach of combining high-quality data on four domains of functioning that we know are interrelated, share part of their aetiology and influence one another; (ii) its follow-up of almost 20 years, which allows investigating long-term trajectories of change in functioning; and (iii) the cohort-sequential design that allows testing trends in functioning between cohorts. During the almost two decades since its conception, LASA has well served the purpose of creating a scientific knowledge base for informing government policy, and becoming a national and international resource for fundamental research on ageing.

There are points for improvement as well. For instance, novel techniques of measuring key variables have been developed and there is some friction between keeping up with these improvements on the one hand and the need to continually measure the same objective and subjective constructs that were used from the beginning on the other. Another limitation is that intervals of 3 years between measurement waves are sometimes too long for trajectories of functional decline to be identified, especially end-of-life trajectories. Finally, there is a trade-off between the breadth of measures included in the study, spanning the four domains of functioning, and the ability to study trajectories in detail.

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

Rich data have been gathered within the LASA framework that may provide answers to hundreds of research questions that cannot all be analysed by the LASA research group alone. This is why we have shared data and are happy to share data with interested researchers who want to study research questions on ageing-related issues. Data sharing for replication analyses is good scientific practice[30] and the LASA team wholeheartedly endorses initiatives like the Integrative Analysis of Longitudinal Studies on Aging (IALSA) and participates in it.[31] We invite colleagues to find out if LASA data can help them answer their research questions. Contact information can be found at the study website: www.lasa-vu.nl.

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