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Cohort Profile Update: The Irish Longitudinal Study on Ageing (TILDA)

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The original cohort

As outlined in the original cohort profile,[1] The Irish Longitudinal Study on Ageing (TILDA) is a prospective cohort study designed to provide an evidence base for addressing the challenges and opportunities associated with population ageing in Ireland. The sampling and study design are described in Whelan *et al.*[2] Briefly, the sampling frame is based on the Irish Geodirectory, a comprehensive and up-to-date listing and mapping of all residential addresses in the Republic of Ireland, compiled by An Post (the Irish Postal Service) and Ordnance Survey Ireland.[3] Participants were randomly selected using the RANSAM sampling procedure, so that each residential address in Ireland had an equal probability of selection. Community-dwelling adults aged 50 years and over and their spouses (of any age) who were non-demented and able to provide informed consent were eligible to participate.

There are three components to data collection: (i) a computer-assisted personal interview (CAPI) administered by trained social interviewers in the participants' own homes; (ii) a self-completion questionnaire (SCQ) completed in the participants' own time; and (iii) a comprehensive health assessment delivered by trained research nurses in a dedicated health centre, or a modified version delivered in the participant's home. Baseline interviews on 8504 participants took place between October 2009 and February 2011; 85% and 72% of these participants completed the SCQ and health assessment, respectively. The first four waves of the study, scheduled to take place every 2 years, was funded by the Irish Government, The Atlantic Philanthropies and Irish Life plc. Ethical approval for each wave of data collection was obtained from the Trinity College Dublin Faculty of Health Sciences Research Ethics Committee.

What is the reason for the new focus and new data collection?

There are two main reasons for the cohort profile update. First, three additional waves of data collection have been completed since the profile was originally published.[1] As data are analysed and collaborative opportunities became available, the research focus has been refined and consequently new questions and tests have been included. A notable change to the health assessment was the addition of the magnetic resonance imaging (MRI) brain sub-study in Wave 3, funded through the Irish Health Research Board. Ethical approval for the MRI sub-study was obtained from St James' Hospital Research Ethics Committee. Second, a number of new features have been introduced to cater for

changes in participant circumstances. From Wave 2 onwards, proxy interviews were obtained to provide a greater insight into the lives and experiences of individuals who experience severe cognitive or physical decline, and end-of-life (EOL) interviews provide insight into the final year of life, particularly around health care use. This paper provides an update on data collected in Waves 2, 3 and 4 and describes the refined research focus.

What will be the new areas of research?

TILDA has rich data on neurocognitive function,[4] mental health,[5] cardiovascular function,[6] kidney function,[7] locomotion,[8] falls,[9] fear of falling,[10] vision,[11] socioeconomic status[12] and social circumstances,[13] obtained during multiple waves of data collection.

Hypertension affects over 60% of people aged 50 years and over in Ireland,[14] and 18.9% of TILDA participants failed to stabilize blood pressure (BP) 30 s after standing.[15] This impairment in blood pressure behaviour is associated with poor cognitive function,[16] depression[17] and unexplained falls,[18] and is thought to be linked to impaired cerebral blood perfusion.[19] However, it is important to understand which type of blood pressure behaviour (e.g. hypertension, hypotension, increased BP variability) causes the most serious damage to the brain. Building on this existing work, a key future research focus in TILDA is to address the major challenges of advancing age, including cardiovascular disease, the maintenance of optimal brain health and prevention of falls.

At Wave 3, MRI scans and near-infrared spectroscopy (NIRS) were included to provide insights into ageing-related changes in brain structure and function and brain tissue perfusion. These data afford an opportunity to better understand the key challenges of ageing, by coupling neuro-imaging data with the comprehensive physical, functional and biological data available.

Blood samples and hair samples have been obtained, providing analytes relating to general health, cardiovascular health, kidney function, vision and hormone function. Future plans aim to identify novel biomarkers and modifiable risk factors of age-related conditions, with research themes focusing on epigenetics, genome-wide association studies, inflammation, allostatic load, immunity, neurocardiovascular instability, frailty and dementia across the life course.

Who is in the cohort?

Wave 4 took place between January and December 2016. At Wave 1 there were 8504 participants, and at Wave 4 there were 6149 participants (completing self, proxy or EOL interviews). Descriptive characteristics of the Wave 1 and Wave 4 participants who completed self-interviews are provided in Table 1. As expected, the Wave 4 sample were older and had higher educational attainment than those participating at baseline.

How often have they been followed up?

Participants complete the CAPI and SCQ at each wave (every 2 years) and the health assessment at alternate waves (Waves 1 and 3). In non-health assessment waves, interviewers are trained to deliver two physical measures (grip strength and timed up-and-go, TUG) during the CAPI. Proxy and EOL interviews have been included since Wave 2, and participants who required a proxy interview at Wave 3 were eligible for a health assessment if they had completed this at Wave 1.

The timeline and response rates for the CAPI, SCQ and health assessments at each wave are provided in Table 2. CAPI self-interview response rates were 84–90% at Waves 2, 3 and 4, and 85–86% of these participants completed the SCQ at each wave. Compared with Wave 1, a higher proportion of Wave 3 participants completed any health assessment (81% versus 72%) and a home-based assessment (20% versus 14%), reflecting the importance of including this option for older and frailer participants.[20,21]

Follow-up was attempted for all participants who moved house or to a nursing home located in the Republic of Ireland or Northern Ireland. During Waves 2, 3 and 4, 48 self-interviews took place with participants resident in nursing homes. 'Soft refusals' i.e. participants who did not participate in a particular wave were contacted again at subsequent waves, but confirmed withdrawals were not. Details of sample attrition are illustrated in Figure 1, and characteristics of participants no longer in the study are provided in Table 1. The most noticeable difference was the lower level of education in this group.

TILDA was designed to be nationally representative; however, sampling weights are required due to under- and over-representation in some age groups. Observable sources of sampling bias (through non-response and by chance) in the initial recruitment period (CAPI Wave 1) were examined by comparing age group, sex, educational attainment level, marital status and urban/rural household location of the sample with those of the national population of older people, obtained from Census 2011 data. A post-stratification, inverse-probability weight variable was then derived based on the discrepancies between the proportions in the sample and the proportions in the population. This base weight reduces the effects of non-response bias and produces more accurate estimates and inferences of the population parameters, derived from the sample data.

Table 1. Participant characteristics of the Wave 1 and Wave 4 samples, the MRI subsample and those who dropped out or were lost to follow-up after Wave 1

	Completed self-interview at Wave 1 ($n = 8504$)	Completed self-interview at Wave 4[a] ($n = 5856$)	MRI sub-study at Wave 3 ($n = 558$)	Drop-outs[b] ($n = 1211$)
Age group, *n* (%)				
<50	330 (3.9)	35 (0.6)	1 (0.2)	50 (4.1)
50–64	4668 (54.9)	2319 (39.6)	127 (22.8)	689 (56.9)
65–74	2164 (25.4)	2097 (35.8)	315 (56.4)	307 (25.4)
75+	1342 (15.8)	1405 (24.0)	115 (20.6)	165 (13.6)
Age, mean ± SD	63.1 ± 10.2	68.1 ± 9.1	68.6 ± 7.6	62.3 ± 9.9
Sex, *n* (%)				
Male	3780 (44.5)	2587 (44.2)	269 (48.2)	525 (43.4)
Female	4724 (55.5)	3269 (55.8)	289 (51.8)	686 (56.6)
Education, *n* (%)				
Primary	2521 (29.7)	1380 (23.6)	121 (21.7)	431 (35.7)
Secondary	3431 (40.4)	2331 (39.8)	197 (35.3)	491 (40.6)
Tertiary	2548 (30.0)	2145 (36.6)	240 (43.0)	287 (23.7)
Marital status				
Married	5966 (70.2)	4046 (69.1)	414 (74.2)	883 (72.9)
Never married	791 (9.3)	492 (8.4)	38 (6.8)	111 (9.2)
Separated/divorced	552 (6.5	420 (7.2)	31 (5.6)	69 (5.7)
Widowed	1195 (14.0)	898 (15.3)	75 (13.4)	148 (12.2)
Location				
Dublin city or county	2012 (23.7)	1428 (24.4)	126 (22.6)	283 (23.4)
Other town/city	2390 (28.1)	1701 (29.0)	151 (27.1)	348 (28.7)
Rural	4102 (48.2)	2727 (46.6)	281 (50.4)	580 (47.9)

Ages provided reflect the age at the time of completing the interview at the specified wave. Primary, secondary and tertiary education correspond to ≤8, 9–13 and >13 years of education, respectively.

[a]Includes 141 participants who joined the study at Waves 2, 3 or 4.

[b]These participants took part in Wave 1 only and subsequently refused to participate at all subsequent waves, withdrew from the study, moved outside of Ireland (and so were ineligible) or were lost to follow-up.

What has been measured?

The broad topics included in the CAPI, SCQ and EOL interviews at each wave are provided in Tables 3 and 4. These topics have remained largely the same, with some additions, removals and modifications to specific questions or measurement scales. For example, the NEO Five-Factor Inventory-3 (NEO-FFI-3), which provides scores for the Big 5 personality dimensions,[22] was included in Wave 2 only; whereas health literacy, which has been linked to poorer health, riskier behaviours, less self-management, greater hospitalization and increased mortality,[23,24] was introduced in Wave 4. Where possible, questions and scales are chosen to be comparable to other studies of ageing such as the Health and Retirement Survey (HRS), the English Longitudinal Study of Ageing (ELSA) and the Survey for Health, Ageing and Retirement in Europe (SHARE). This developmental process is informed by initial analysis, future research directions and through engagement with stakeholders, government and non-governmental organizations, health care professionals, researchers and funders.

Most health assessment tests were included at Waves 1 and 3 but some changes were introduced to reflect the refined research focus (see Table 5). As Cronin *et al.*[21] describes the Wave 1 health assessment tests in detail, only additional Wave 3 tests are described in Table 6. Due to resource constraints, only a subsample completed accelerometry, oral health assessments and MRI scans (see Table 2 for response rates). Wrist-based accelerometers, which recorded 7 days of data for 1683 participants,[25] will be used to determine the duration of sleep and wake periods, sleep quality and activity intensity; 59% ($n = 2525$) of participants attending the health centre had an optional oral health assessment, conducted by a dentist. As the MRI sub-study required detailed planning and management, it is described in detail below.

MRI sub-study

To be eligible, participants must have completed the cardiovascular tests during the health assessment. Participants aged ≥65 years were prioritized, to enable identification of

Table 2. Response rates for each Wave of TILDA

	Achieved response rates			
	Wave 1 (October 2009-February 2011)	Wave 2 (February 2012-March 2013)	Wave 3 (March 2014-October 2015)	Wave 4 (January-December 2016)
CAPI				
Self[a]	$n = 8504$	$n = 7375$ (88%)	$n = 6566$ (85%)	$n = 5856$ (84%)
Proxy[b]	n/a	$n = 80$ (79%)	$n = 121$ (62%)	$n = 121$ (64%)
EOL[c]	n/a	$n = 160$ (84%)	$n = 215$ (83%)	$n = 172$ (73%)
Within-CAPI physical measures				
Timed up-and-go	n/a	$n = 7165$ (97%) ($+ n = 15$ proxy)	n/a	$n = 5342$ (91%) ($+n = 16$ proxy)
Grip strength	n/a	$n = 7173$ (97%) ($+ n = 18$ proxy)	n/a	$n = 5568$ (95%) ($+ n = 21$ proxy)
SCQ[d]	$n = 7196$ (85%)	$n = 6274$ (85%)	$n = 5565$ (85%)	$n = 5064$ (86%)
Health assessment[e]	$n = 6150$ (72%)	n/a	$n = 5391$ (81%)	n/a
Centre	$n = 5275$ (86%)	n/a	$n = 4307$ (80%) ($+n = 2$ proxy)[f]	n/a
Home	$n = 875$ (14%)	n/a	$n = 1057$ (20%) ($+n = 25$ proxy)[f]	n/a
Sub-studies				
MRI	n/a	n/a	$n = 558$ (13%)[g]	n/a
Accelerometry	n/a	n/a	$n = 1683$ (31%)[g]	n/a
Oral health	n/a	n/a	$n = 2523$ (59%) ($+n = 2$ proxy)[g]	n/a

n/a, not available.

[a]Self-interview response rates based on eligible number of participants at each wave, i.e. those still participating and cognitively capable of carrying out a self-interview.

[b]Proxy interviews required if participant unable to complete interview themselves due to physical or cognitive impairment. Proxy response rates based on the number of participants requiring proxy interview (note: due to change in category labelling at Wave 2, the Waves 2 and 3 response rates are not directly comparable).

[c]End-of-life (EOL) interviews sought if participant passed away (minimum 6 months after death). Depending on timing of death, EOL interview can be completed in the current wave or, if necessary, carried over to the subsequent wave if this is preferable to the EOL respondent. Wave 2 EOL response rate = (number EOL interviews completed during Wave 2) / (Deaths at Wave 2 - deaths to be followed up at Wave 3). Wave 3 End-of-life (EOL) response rate = (number of EOL interviews completed during Wave 3) / (Deaths carried over from Wave 2 + deaths during Wave 3 – deaths to be followed up at Wave 4). Wave 4 End-of-life (EOL) response rate = (number of EOL interviews completed during Wave 4) / (deaths carried over from Wave 3) + (deaths during Wave 4 – deaths to be followed up at Wave 5).

[d]Denominator for self-completion questionnaire (SCQ) response rate is number of participants who completed a self-interview.

[e]Wave 1 health assessment (completed July 2011) included measures of cognitive function, cardiovascular function, mobility, bone health, vision, anthropometry and blood samples. Wave 3 health assessment (completed December 2015) also included hair samples, accelerometry, oral health and magnetic resonance imaging (MRI). Denominator for health assessment response rate is number of participants who completed a self-interview.

[f]Participants who required proxy interview at Wave 3 were eligible for health assessment if completed at Wave 1, i.e. centre-based assessment if completed a centre-based assessment at Wave 1 or home-based assessment if completed a home-based assessment at Wave 1.

[g]*n* for sub-studies reflects the available data. Denominator for sub-studies is number of participants (self) who completed a centre- or home-based health assessment (accelerometer); participants (self) who completed centre-based assessment (MRI); participants (self) who completed centre-based assessment (dental).

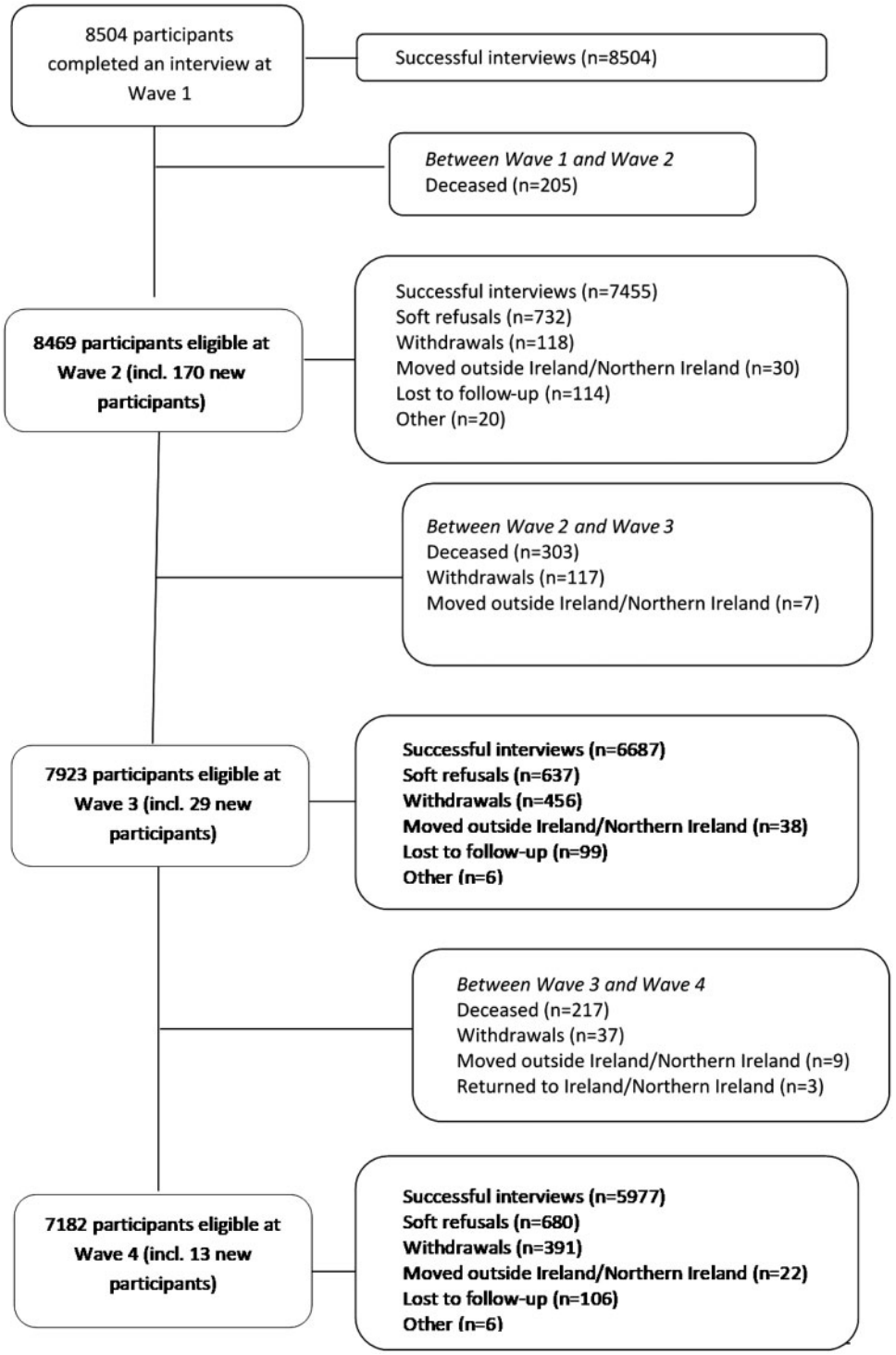

Figure 1. Attrition across each wave.

structural brain changes with age. Research nurses informed participants about the sub-study and provided an information booklet, and interested participants were screened for basic MRI exclusion criteria (see Table 6). They were subsequently contacted by phone to schedule an appointment and make travel arrangements. Participants were sent an appointment confirmation letter and a consent form allowing TILDA to contact their general practitioner (GP). Following receipt of a signed consent form, TILDA informed the participant's GP of the impending scan in writing. The scans were scheduled within 180 days (for participants aged 50–64 years) and 90 days (for

Table 3. Data collected in the CAPI and SCQ at each wave

Demographic data	Physical health
Education[1–4]	Self-rated health[1–4]
Languages (SCQ)[2]	Limiting long-standing illness/disability[1–4]
Childhood and siblings[1–4]	Sensory function[1–4]
Migration history[1–4]	Cardiovascular disease[1–4]
Marital status and marriage history[1–4]	Non-cardiovascular chronic illness[1–4]
	Falls/fear of falling/steadiness[1–4]
Social circumstances	Fractures[1–4]
Transfers to (and from) children[1–4]	Chronic pain[1–4]
Transfers to (and from) parents[1–4]	Incontinence[1–4]
Transfers to (and from) others[1–4]	Medical screening[1–4]
(Instrumental) activities of daily living[1–4]	Oral health[1–4]
Helpers[1–4]	Medications[1–4]
Social networks[1–4]	Health care use[1–4]
Volunteering and caring[1–4]	
Participation in social activities (SCQ)[1–4]	Mental and psychological health
Religion[1–4]	Self-reported mental health[1–4]
Relationship quality (SCQ)[1–4]	Depression[1–4]
Sexual activity (SCQ)[2,4]	Life satisfaction[1–4]
	Anxiety[1 (SCQ)2–4]
Employment and lifelong learning	Worry (SCQ)[1–4]
Employment situation[1–4]	Loneliness (SCQ)[1–4]
Job history[1–4]	Perceived stress (SCQ)[1,3,4]
Lifelong learning[1]	Stressful life events (SCQ)[1,2]
	Coping Inventory for stressful situations (SCQ)[3]
Retirement and expectations	Quality of life (SCQ)[1–4]
Planning for retirement[1–4]	Resilience[3,4]
Expectations[1–4]	Ageing perceptions (SCQ)[1,3]
Fear of crime[3,4]	Personality (SCQ)[2]
Advanced Care Planning[4]	Falls efficacy (SCQ)[2,3]
	Post-traumatic stress disorder (SCQ)[4]
Income and assets	Purpose in life (SCQ)[4]
Sources of income[1–4]	
House ownership[1–4]	Cognitive health
Other assets[1–4]	Self-rated memory[1–4]
	Mini-Mental State Examination (MMSE)[2–4]
Literacy	Word-list learning (recall)[1–4]
Financial literacy[3]	Verbal fluency[1–4]
Health literacy[4]	Prospective memory[1–4]
Behavioural health	Other
Smoking[1–4]	Heating and accommodation (SCQ)[2–4]
Physical activity[1–4]	Neighbourhood[2,4]
Sleep[1–4]	Address history[3]
Alcohol (SCQ)[1–4, a]	Transport and driving[1]
Dietary intake (SCQ)[3,4]	

[1–4]Indicate the wave in which data were collected (i.e. Wave 1, Wave 2, Wave 3, Wave 4). Data collected in CAPI unless otherwise stated.
[a]Alcohol questions are included in the CAPI for proxy interviews but in the SCQ for self-interviews.

participants aged ≥65 years) of completing the health assessment, to ensure that the health assessment measures could be interpreted with the MRI data.

MRI scans were obtained using a 32-channel head detector coil on a 3 T MRI scanner (Achieva TX, Philips, The Netherlands) located at the National Centre for Advanced Medical Imaging (CAMI), St James's Hospital, Dublin. On the day of the scan, participants were accompanied by a TILDA staff member who obtained written informed consent and reimbursed participants' travel, accommodation

Table 4. Data collected in the End-of-life CAPI at each wave

Demographic data	Physical, mental and cognitive health
Circumstances of death[2–4]	Cardiovascular disease[2–4]
Residence before death[2–4]	Non-cardiovascular chronic illness[2–4]
Funeral/wake events[2–4]	Falls/fracture[2–4]
	Chronic pain[2–4]
Social and health care circumstances	Cognitive function[2–4]
(Instrumental) activities of daily living[2–4]	Mood[2–4]
Helpers[2–4]	
Health care use[2–4]	Behavioural health
Home modifications[2–4]	Smoking[2–4]
	Weight and weight loss[2–4]
Assets and planning	
Assets and life insurance policies[2–4]	
Advanced Care Planning[4]	

[2–4]Indicate the wave in which data were collected (i.e. Wave 2, Wave 3, Wave 4).

Table 5. Tests included in the TILDA health assessment at each health wave

Neuropsychological function	Gait and mobility
Mini-Mental State Examination (MMSE)[1,a]	Timed up-and-go (TUG)[1,3,d]
Montreal Cognitive Assessment (MOCA)[1,3]	Repeated chair stands[3]
Sustained Attention to Response Task (SART)[1,3]	GAITRite assessment
Picture memory test[1]	– normal pace[1,3,c]
National Adult Reading Test (NART)[3]	– dual task (manual)[1,c]
Visual reasoning[1]	– dual task (cognitive)[1,3,c]
Choice reaction time[1,3]	– maximum pace[3,c]
Colour trails test[1,3]	
Centre for Epidemiological Studies Depression (CES-D) 8-item scale[1,3,b]	Bone health
State trait anxiety inventory[3]	Heel bone ultrasound[1,3,c]
	Anthropometric/other
Cardiovascular function	Grip strength[1,3,d]
Blood pressure (Omron)[1,3]	Height[1,3]
Pulse wave velocity[1,3,c]	Weight[1,3]
Heart rate variability[1,3,c]	Waist and hip circumference[1,3]
Phasic blood pressure[1,3,c]	Blood samples[1,3,e]
Near-infrared spectroscopy (NIRS)[3,c]	Hair sample[3,f]
	Physical activity question[3,c]
Sensory function	Oral health[3,c,g]
Visual acuity[1,3,c]	Accelerometry[3,g]
Contrast sensitivity[1,3,c]	MRI[3,c,g]
Macular pigment optical density[1,c]	
Retinal photograph[1,3,c]	
Sound-induced flash illusion (SHAMS)[3,c]	

[1,3]Indicate the wave in which data were collected (i.e. Wave 1, Wave 3).

[a]MMSE was included in Waves 2, 3 and 4 CAPI.

[b]CESD-20 was included in Waves 1 and 2 CAPI; CESD-8 was included in Waves 3 and 4 CAPI.

[c]Included in the health centre assessment only.

[d]TUG and grip strength were included in Waves 2 and 4 CAPI.

[e]Blood sample analytes: lipid profile, folate, Vitamin B12, Vitamin D, Vitamin E, C-reactive protein, interleukin-18, creatinine, cystatin C, haemoglobin A1c, lutein, zeaxanthin, lycopene, alpha-carotene, beta-carotene, DNA (seven single nucleotide polymorphisms associated with age-related macular degeneration).

[f]Hair sample hormone assays: cortisol, cortisone, testosterone, beta-estradiol, progesterone, melatonin.

[g]Included for a sub-study only, due to resource availability (i.e. limited accelerometers, availability of dentist, limited MRI funding).

Table 6. New health assessment tests introduced in Wave 3

Test or equipment used	Measures
National Adult Reading Test (NART) 50 words	Pre-morbid intelligence
State trait anxiety inventory (STAI) 20-item scale	Transient worry and heightened emotionality
Near-infrared spectroscopy (NIRS) (PortaMon, Artinis Medical Systems, The Netherlands) –non-invasive sensor on prefrontal cortex (approximate EEG site FP1)	Trends in regional tissue oxygen saturations providing an indirect measure of cerebral perfusion
Sound-induced flash illusion (SHAMS test)	Multisensory integration i.e. the ability of the nervous system to integrate sensory information obtained from auditory and visual sources
Repeated chair stands 5 times sit to stand timed with stopwatch	Lower limb strength, coordination and endurance
Gait assessment (maximum pace) GAITRite® walkway, sensored area = 4.88 m	Maximum walking speed
Self-reported physical activity question used in an algorithm along with age, sex, BMI, resting heart rate	Cardiorespiratory fitness
Hair samples minimum length 3 cm, weight 10 mg	Cortisol secretion and other stress hormones
Accelerometers (GENEActiv Original Accelerometers, Activinsights Ltd, UK) worn on non-dominant wrist where possible; 24 , 7 days[a]	Amount, intensity and duration of activity and rest
Oral health assessment conducted by dentist[a]	Oral health indicators e.g. number of teeth, gum and tooth health etc.
Magnetic resonance imaging (MRI)[a,b] 32-channel head detector coil on a 3 T MRI scanner (Achieva TX, Philips, The Netherlands)	Anatomical and functional brain images

[a]MRI, accelerometry and the oral health assessment were provided to a random subsample of participants due to resource availability (i.e. limited funding, limited accelerometers, availability of dentist).

[b]MRI exclusion criteria: cardiac pacemaker or defibrillator, neurostimulator, stent, drug delivery device, metal in the skull or eye (as shown on an X-ray if appropriate), aneurysm clips in the brain, cochlear implant, brain surgery/biopsy, stroke, history of head injury, surgery within 6 weeks of the scan date, claustrophobia. Asthma or chronic obstructive pulmonary disease excluded participants from participating in the hypercapnic component of the scan.

and subsistence costs. The CAMI radiographer completed further safety checks before commencing the MRI scan.

The scan took a maximum of 60 min and ear defenders were worn. A comprehensive neurological scan protocol was followed, incorporating three distinct elements of both anatomical and functional imaging (see Table 7). For the final scan with the hypercapnic challenge, participants wore a face mask attached to a specially designed breathing circuit which allowed for precise control of the CO_2 gas added to the room air, thereby ensuring a 5% CO_2 inspiration level and consequently altered the blood flow and oxygenation of blood to the brain. Participants were monitored throughout scanning and could stop at any stage. CO_2 levels were continuously measured to ensure that the level of inhaled CO_2 did not drop below the desired 5% level throughout the hypercapnic challenge scan. Participants were informed that the altered air composition could have temporary side effects such as increased breathing or mild headache.

In total, 578 participants attended for an MRI scan and 558 scans were obtained (554 with complete data; four with partial data). Despite the initial screening by the research nurses, brain scans could not be obtained on 20 participants, mainly due to claustrophobia/nervousness (n = 16) or for medical reasons such as metal in brain, previous surgery etc. ($n = 4$). Hypercapnic challenge scans were obtained from 148 participants (an additional 24 were deemed unsuitable or were unwilling, 13 stopped during the scan and there was one technical problem). During follow-up calls, most participants reported that the hypercapnic challenge component was tolerable but not enjoyable. Demographics of those who completed the MRI sub-study are provided in Table 1. The mean delay between the health assessment and the scans was 62 days [standard deviation (SD) 40 days; range 6–202 days]. Each scan was reviewed by a consultant radiologist at St. James's Hospital, and the generated report was then sent to the GP for feedback to the participant. Irregularities were detected in 17 cases, with a recommendation for further imaging and investigation.

Data linkage

Linkage with administrative and health datasets offers huge potential but, unfortunately, Ireland does not have a unique health identifier, making this process difficult. TILDA currently links to the Primary Care Reimbursement Service (PCRS) database, which provides information on pharmaceutical use by medical cardholders,[26,27] and to the death registration records through the General Registry Office (GRO). Ongoing work using geographical information system (GIS) software allows residential addresses to

Table 7. Details of magnetic resonance imaging (MRI) scans obtained in Wave 3

Details of scan component	Purpose	Details of analysis
Anatomical imaging		
Conventional T_2-weighted scan	Used to identify incidental findings	Standard radiological reading of scan performed
Fluid attenuated inversion recovery (FLAIR) scan	Used to identify incidental findings	Standard radiological reading of scan performed
3D T_1-weighted scan, very high spatial resolution (0.9 mm^3)	Allows for accurate brain structure volumetric measurements	Data processed using a standard segmentation-based approach to all major brain structures, to obtain accurate volumetric information
Functional imaging		
Diffusion tensor imaging (DTI), high spatial (1.9 mm^3) and high angular resolution (61-direction) protocol with a high diffusion sensitivity ($b = 1200$ s/mm^2)	Assesses the microstructural organization of white matter in the brain	Uses a standard processing pipeline involving image registration and fitting to the diffusion tensor model. Fractional anisotropy (FA) and mean diffusivity (MD) values determined at each point within the brain
Resting-state fMRI (rs-fMRI) acquired using a gradient echo planar imaging technique with 200 dynamics, each taking 2 s. Participants were requested to look at a simple cross (projected into their field of vision using a projector) and to avoid falling asleep	Assesses age-related changes in connectivity within distinct functional networks in the brain	Data analysed following conventional pre-process of fMRI data (atlas registration, re-sampling, smoothing) followed by network correlation analyses (hub-to-hub, hub-to-voxel, group analyses)
pseudo-Continuous Arterial Spin Labelling (pCASL) scan with hypercapnic challenge involved the inhalation of a gas mixture containing 5% CO_2. Participants wore a face mask attached to a specially designed breathing circuit to allow for precise control of the CO_2 gas added to the room air. First pCASL scan under normacapnic conditions (i.e. 100% room air), second pCASL scan under hypercapnic conditions (i.e. 95% room air plus 5% CO_2)	Provides quantitative cerebral blood flow (CBF) and cerebrovascular reactivity (CVR) information. Regional CVR (difference in CBF between the normacapnic and hypercapnic scans) gives an indication of cerebrovascular health	Registered data to the 3D anatomical images, calculated baseline M_0 values, calculated CBF values at each point in the brain, subtracted normacapnic from hypercapnic values to determine CVR

be linked to social deprivation scores and the distribution of health and social resources, e.g. medical facilities, shops, transport networks, green spaces etc.

What has it found? Key findings and publications

To date, TILDA has published extensively on a broad range of areas including cardiovascular health, mental health, cognitive function, frailty, health care use, medications, retirement and social circumstances. In addition, normative values for cognitive, mobility, anthropometric and heel ultrasound tests have been published.[28] A full list of TILDA publications, including those using baseline data from Wave 1, longitudinal data from subsequent waves and analysis of new measures introduced after Wave 1, are available at [http://tilda.tcd.ie/publications/academic-papers/]. Here the key findings relating to cardiovascular health and cognitive decline and using the biological samples are presented, as these have helped to refine our research focus. We then present findings of longitudinal analyses, and work that has linked TILDA data with other data sources.

Blood pressure behaviour at rest and in response to standing has been well characterized in TILDA participants. High blood pressure (hypertension) affects over 60% of people aged 50 years and over in Ireland, with over half of these unaware that they have the condition.[14] Orthostatic hypotension, or a sustained drop in blood pressure after standing, increases with age, affecting over 40% of Irish adults aged ≥80 years.[15] Adults who have supine hypertension combined with orthostatic hypotension, have poorer global cognition and executive function compared with those without orthostatic hypotension.[29] Orthostatic

hypotension has also been associated with falls[30] and beta blocker therapy,[31] and frailty has been associated with orthostatic intolerance.[30] Work to combine existing data with MRI, biomarker and epigenetic data is under way and will examine the longitudinal associations between these factors.

Research using the extensive TILDA Biobank has examined the determinants and prevalence of vitamin D deficiency,[32] and investigated biomarkers for kidney disease,[7] ageing-related disease and stress.[33,34] Canney *et al.*[7] (2017) reported a novel, graded relationship between diminished estimated glomerular filtration rate and impaired orthostatic blood pressure stabilization. Mapping the postural blood pressure response merits further study in kidney disease cohorts, as it may identify those at risk of hypotension-related events such as falls, an important outcome which is not predicted by kidney function alone. The plasma carotenoids, lutein and zeaxanthin, are dietary in origin and accumulate in the retina of the eye, comprising macular pigment. Initial analyses have shown that both higher levels of macular pigment density measured psychophysically and plasma lutein and zeaxanthin are associated with higher educational attainment, good health behaviours, lower cardiovascular risk[35] and better cognitive function,[36] suggesting that increased knowledge and lifestyle modification is likely to improve outcomes in individuals with age-related macular degeneration (AMD). Preliminary genetic work has shown that genetic risk factors are associated with progression of AMD[37] and social adversity and epigenetic ageing.[38]

To date, longitudinal data analyses have investigated determinants for changing health, including cognitive decline,[33,39–42] physical decline and disability[34,43–49] and mood disturbances[12,50–55] Cognitive decline was associated with several risk factors, including age-related cardiovascular changes,[40] perceptions of stress,[33] negative perceptions of ageing[42] and retirement.[41]

Data linkage using geocoded data has enabled us to examine the environmental influences of air pollution, seasonal and meteorological conditions, fluoridation and urban/rural location on health and cognitive decline in ageing. Findings include increased lung cancer in areas with high levels of radon exposure,[56] higher depressive symptoms in winter and in areas with higher rainfall,[57] and improved oral health, but not bone density, associated with water fluoridation.[58] Living in an urban area was associated with better cognitive performance,[59] although this was moderated by disability;[60] however, there was a U-shaped relationship between green spaces and obesity.[61] Linkage of TILDA to the national Primary Care Reimbursement Service prescribing database has shown that both inappropriate prescribing and prescribing omissions are common in older adults[26,62] and are associated with adverse outcomes.[9,63]

What are the main strengths and weaknesses?

The main strengths of this study are the robust sampling procedures and study design, detailed interviews and questionnaires and the comprehensive health assessment which includes cardiovascular, cognitive and visual function, mobility, bone health, anthropometrics, biomarkers, physical activity, oral health and brain imaging. Repeated waves of data collection facilitate longitudinal analysis and, consequently, causal pathways can be investigated. Research findings are therefore becoming increasingly translatable into policy and practice.

The main weaknesses include the limited number of proxy, EOL and nursing home interviews currently available. However, the cumulative number is increasing with each wave, which will soon provide an opportunity to conduct analysis specific to cognitive impairment, institutionalization and EOL issues within these sub-groups. Inevitably, some age-related topics are not included in TILDA, making it impossible to control for all possible covariates. In addition, accelerometry, oral health assessments and MRI scans are only available for a subsample of participants, mainly due to resource and funding constraints. Depending on future resources, it may be possible to supplement existing data in future waves. Finally, despite best efforts to retain the sample, it is inevitable that there will be sample attrition, making replenishment a necessary requirement in future waves.

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

Researchers can apply to access TILDA data through the Irish Social Science Data Archive (ISSDA) at University College Dublin [https://www.ucd.ie/issda/data/tilda/] and the Inter-university Consortium for Political and Social Research (ICPSR) at the University of Michigan [http://www.icpsr.umich.edu/icpsrweb/ICPSR/studies/34315].
Some variables have been removed or top-coded to maintain the anonymity of TILDA participants. The Gateway to Global Aging offers a digital library of survey questions and identically defined variables, allowing comparison of TILDA data with population survey data on ageing obtained from several other countries [https://g2aging.org/?section=homepage]. Any other queries about data access should be forwarded to [tilda@tcd.ie].

Profile in a nutshell

- TILDA is a prospective cohort study of the health, economic and social circumstances of 8504 community-dwelling adults aged ≥50 years resident in Ireland. Wave 1 took place in 2009–11.
- Three subsequent waves of data collection have been completed. A key future research focus is to address major challenges of advancing age including the maintenance of optimal brain health and prevention of falls. Analysis of biological samples, inclusion of new measures and linkage with pharmaceutical and mortality databases and geographical information systems will contribute to the research themes.
- The most recent wave of data collection in 2016 included 6149 participants (5856 self, 121 proxy and 172 end-of-life interviews).
- New health assessment measures at Wave 3 include near-infrared spectroscopy, brain magnetic resonance imagingscans, multisensory integration, accelerometry, hair samples and oral health assessments. These data will couple neuro-imaging data with comprehensive physical, functional and biological data.
- TILDA have several existing collaborations and anonymized datasets are available in public data archives. All queries about data access should be addressed to [tilda@tcd.ie].

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