




Cohort Profile

Cohort Profile Update: The PATH Through Life Project

Kaarin J Anstey,^{1,2,3*} Peter Butterworth,^{1,4} Helen Christensen,⁵ Simon Easteal,⁶ Nicolas Cherbuin,¹ Liana Leach,⁷ Richard Burns,¹ Kim M Kiely ,^{2,3} Moyra E Mortby,^{2,3} Ranmalee Eramudugolla^{1,2,3} and Imogen Gad^{1,3}

¹Centre for Research on Ageing, Health and Wellbeing, Research School of Population Health, Australian National University, Canberra, ACT, Australia; ²School of Psychology, University of New South Wales, Randwick, NSW, Australia; ³Neuroscience Research Australia, Randwick, NSW, Australia; ⁴Melbourne Institute of Applied Economic and Social Research, University of Melbourne, Melbourne, Victoria, Australia; ⁵Black Dog Institute, University of South Wales, Sydney, NSW, Australia; ⁶John Curtin School of Medical Research, Australian National University, Canberra, ACT, Australia; ⁷National Centre for Epidemiology and Population Health, Research School of Population Health, Australian National University, Canberra, ACT, Australia

*Corresponding author. Matthews Building, School of Psychology, University of New South Wales, Randwick, 2031, NSW, Australia. E-mail: k.anstey@unsw.edu.au

Editorial decision 10 August 2020; Accepted 9 September 2020

The original cohort

This paper updates the earlier profile of the PATH Through Life Project (PATH), a cohort study which recruited in 1999–2001 from the Australian Capital Territory (ACT) and nearby town of Queanbeyan, NSW, in Australia,¹ with new findings from the 12-year follow-up at Wave 4. The PATH study was designed to investigate the epidemiology of common mental disorders, including depression, anxiety, substance use and cognitive decline, with a focus on risk factors, comorbidities and their life course trajectories. At baseline, the study included 7485 adults in three narrow age cohorts of 20–24, 40–44 and 60–64 years. In the original cohort profile we described how the three age cohorts had been interviewed for three waves of data collection every 4 years, the foci of several sub-studies, and we summarized important findings relating to depression, anxiety and suicidality, and cognitive decline and dementia.

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

Many of the key questions relating to trajectories of mental health and cognitive development across the lifespan can only be answered with longitudinal data. The preceding follow-up of the cohorts took place in 2007–10, 8 years following baseline interview when the cohorts were aged 28–32 years, 48–52 years and 68–72 years. The new data collection at 12 years of follow-up aimed to address relevant life course transitions for each cohort (e.g. fertility in the 20s cohort, menopause and workplace bullying in the mid-life cohort and age expectations and dementia in the 60s cohort). The fourth wave also aimed to continue collecting data on the key domains of the study, so that changes in the outcomes and risks and protective factors could be studied over the adult life course. As a study of life course adult development and cognitive and mental health, it is important to continue to assess the cohorts at regular intervals to capture transitions in risks and

protective factors and outcomes. Table 1 reports the sample characteristics at Wave 4.

What will be the new areas of research?

New and expanded areas of research in the PATH Study at Wave 4 include some domains that were consistently introduced to all three cohorts, and other domains that were unique to individual cohorts (see Table 2). In the area of mental health, additional measures were included, for all cohorts, on mental health service use and perceived need for care. All cohorts were also asked if they had ever played a musical instrument. The Composite International Diagnostic interview (CIDI: a fully structured diagnostic interview used to assess mental disorders according to the Diagnostic and Statistical Manual of Mental Disorders [DSM]/International Classification of Diseases [ICD]

criteria)² was added to the 20 s and 40 s cohorts, providing assessment of lifetime, annual and 30-day prevalence of Major Depressive Episode and Generalized Anxiety Disorder. The Acquired Capability for Suicide Scale (ACSS)³ was added to the suicidality module for the 20 s and 60 s cohorts. New measures of apathy, loneliness, childhood attention-deficit hyperactivity disorder, Burn's hopelessness scale and neuropsychiatric symptoms were added to the assessment for the 60 s cohort.

New stressor items assessed workplace bullying in the young and mid-life cohorts. The 40 s cohort was also asked if they were a member of the Australian Defence Force and if they had served overseas. Handling pesticide at work was also added to the 20 s and 40 s cohorts. In the area of physical health, new items were added to complement measures of sleep including the Pittsburgh Sleep Quality Index⁴ and Insomnia Severity Index,⁵ and the Fagerstrom

Table 1 Follow-up and mortality-adjusted attrition rates at Wave 4 relative to baseline characteristics

Baseline characteristic	Original <i>n</i>			% followed up at Wave 4			% attrition ^b		
	20+	40+	60+	20+	40+	60+	20+	40+	60+
Total sample	2404	2530	2551	1286	1806	1645	1116	692	573
% of original <i>n</i>				53%	71%	64%	47%	29%	24%
Sex									
Male	1162	1193	1234	47	70	69	53	29	21**
Female	1242	1337	2551	59	73	59	40**	26	24
BMI									
Underweight (<18.5 kg/m ²)	129	25	20	59	68	63	42	52	25
Healthy weight (ref.)(18.5 to 24.9 kg/m ²)	1519	1041	890	54	73	64	47	28	25
Overweight (25.0 to 29.9 kg/m ²)	490	825	954	53	73	68	48	28	23
Obese (30 to 34.9 kg/m ²)	123	298	327	54	72	64	50	30	24
Severely obese (35 kg/m ² or more)	45	151	128	51	66	62	60	34	23
Smoker									
Yes	750	481	276	47	63	49	53**	35**	27**
No (ref.)	1634	2047	2271	57	73	66	43	26	22
Employment status									
Employed (ref.)	2044	2276	1040	55	73	68	45	26	22
Unemployed	137	59	24	45	51	88	55*	46**	4*
Not in labour force	222	194	1485	47	64	61	53*	34*	23
Education									
<12 years	107	317	602	31	62	52	69**	36**	32**
12+ years (ref.)	2296	2211	1944	55	73	69	45	26	20
Marital status									
Married (ref.)	212	1800	1911	53	73	65	47	26	22
De facto	346	206	77	56	70	71	44	28	19
Separated	19	119	68	63	68	54	37	31	22
Divorced	<5 ^a	184	244	— ^a	64	59	— ^a	33*	28*
Widowed	<5 ^a	18	180	— ^a	67	66	— ^a	33	18
Never married	1807	201	68	53	73	57	47	27	26

BMI, body mass index; ref., reference value.

^aCells with count less than 5.

^bLoss to follow-up, excluding mortality.

p* < 0.05; *p* < 0.01; mortality-adjusted binary logistic regression with Wave 4 follow-up as outcome and baseline characteristics as predictors.

Table 2 Main categories of measures included in the PATH study by age cohort

Category	Measurements	20s	40s	60s
Demographics	Age, gender, marital status, education, employment, housing, income	✓	✓	✓
	Region of birth, language, race	✓ ^b	✓ ^b	✓ ^b
Health and health behaviour	BMI, medical conditions, head injury, medication, menopause, cigarette smoking, alcohol consumption, illicit drug use	✓	✓	✓
	Women's health	✓	✓	✓ ^b
	Pregnancy and fertility	✓		
	Gambling	✓	✓	✓ ^b
	Physical activity, mental activity, sleep	✓	✓	✓
	Food frequency questionnaire	✓ ^a	✓ ^a	✓ ^a
	Fish and seafood consumption		✓ ^a	✓ ^a
	Pesticide exposure	✓ ^a	✓ ^a	
	Bayer IADLs, Neuropsychiatric Inventory, family history of dementia and diabetes, hearing rating scale			✓ ^a
Stressors	Lifetime trauma, life events, stress, financial stress	✓	✓	✓
	Work stress, life transition, role strain	✓	✓	
Social	Social support, social network, dyadic adjustment, child care	✓	✓	✓
	Pet ownership	✓ ^b	✓	✓
	Caregiving, volunteering			✓
	Work	✓	✓	
	Play musical instrument	✓ ^b	✓ ^b	✓ ^b
	Interpersonal needs questionnaire	✓ ^b		✓ ^b
Physical measures	Blood pressure, visual acuity, hand grip, lung function, handedness, reaction time	✓	✓	✓
	Physical tests (walk, stand, balance)			✓ ^b
Cognitive measures	CVLT immediate and delayed recall, symbol digit modalities test, digit span backwards, Purdue pegboard, simple and choice reaction time, Spot the Word, Trails A and B, Faces	✓	✓	✓
	Mini Mental State Examination, Boston naming test			✓
	Game of dice, Stroop colour word test, Benton visual retention test, BADS Zoo map, reading the mind in the eye			✓ ^a
	Rush cognitive activities	✓ ^a	✓ ^a	✓ ^a
	Memory and cognitive decline questionnaire, Dysexecutive symptoms questionnaire			✓ ^a
Mental health self-report	Patient health questionnaire, positive-negative affect scale, Goldberg anxiety and depression, suicide, seasonal pattern assessment, past depression	✓	✓	✓
	Self-harm	✓	✓ ^b	✓ ^b
	CIDI depression and anxiety	✓	✓	
	3-item loneliness, apathy, Burns hopelessness			✓ ^a
Psychological scales	Mastery, ruminative style, Eysenck personality, life satisfaction, Connor-Davidson Resilience	✓	✓	✓
	Religiosity, bushfire experience, Brief COPE inventory	✓ ^b	✓ ^b	✓ ^b
	Reciprocity, future time perspective, dialectical thinking, Brief Big Five personality measure			✓ ^b
	Childhood ADHD Wender Utah Rating Scale			✓ ^a
	Perceived need for care	✓ ^a	✓ ^a	✓ ^a
	Expectations of ageing			✓ ^a
General health self-report	SF-12	✓	✓	✓
	Memory items, Instrumental activities of daily living, driving			✓
	Self-report IQCODE			✓ ^b

BMI, Body Mass Index; IADLs, Instrumental Activities of Daily Living; CVLT, California Verbal Learning Test; BADS, Behavioural Assessment of Dysexecutive Symptoms; CIDI, Composite International Diagnostic Interview; COPE, Coping Orientations to Problems Experienced; ADHD, Attention-Deficit Hyperactivity Disorder; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly. ^aAdded at Wave 4. ^bMeasure collected once during Waves 1-3. ✓ Longitudinal data.

test for nicotine dependence⁶ was added to the cigarette smoking module. Family history of diabetes and dementia and hearing difficulties were added for the 60 s.

In the oldest cohort, new items were included to measure expectations of ageing, mental activity, additional aspects of diet and activities of daily living. A new cognitive assessment battery was included to enable Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) diagnosis of neurocognitive disorders.

Who is in the cohort?

After the 8-year follow-up, the 20 s cohort was surveyed again in 2011–12 (aged 32–36 years). The 40 s cohort was followed up in 2012–13 (aged 52–56 years) and the 60 s cohort was followed up in 2013–15 (aged 72–76 years) (Figure 1). For the 20 s cohort, retention at Wave 4 was 53% (<1% mortality and 47% attrition), for the 40 s cohort 71% (1% mortality, 29% attrition) and for the 60 s cohort 64% (10% mortality, 25% attrition).

Follow-up rates relative to baseline demographics are presented in Table 1. The sex distribution has changed in the 20 s cohort (more females than males retained) and 60 s cohort (more males than females retained) but is unchanged for the 40 s cohort. Retention was lower for participants with less than 12 years of education in all three cohorts (65% vs 78%). This was true for all three cohorts. Fewer participants who were smokers (59% vs 77%) or were unemployed (72% vs 79%) at baseline were retained. In the 20 s cohort, attrition rates between baseline marital status were comparable, but in the 40 s and 60 s cohorts, attrition was higher for divorcees at baseline.

Participants in the magnetic resonance imaging (MRI) sub-study, who were randomly selected at Wave 1 for the 60 s cohort ($n=479$), and Wave 2 for the 40 s cohort ($n=431$), were followed up at Wave 4 with 49.7% retention for the 60 s and 68% retention for the 40 s. At each wave, participants in the 60 s cohort were screened into the Health and Memory sub-study, based on performance on selected cognitive tests—comprising 5% to 8% of the cohort. At Wave 4, the screening criteria used a broader cognitive test battery as well as measures of informant-rated and subjective decline, and therefore screened in 22% of the Wave 4 cohort.

What has been measured?

Assessments at Wave 4 for the 40 s and 60 s continued to comprise a questionnaire and face-to-face assessment involving cognitive and functional tests. Additional biomarkers were collected from participants in the sub-studies. Assessment administration for the 20 s cohort in Wave 4 was conducted online, with a subset of participants completing a face-to-face assessment. In Wave 4, the 60 s assessment included a new battery of tests to inform dementia diagnosis.

Questionnaire

The study questionnaire contains a set of core measures. At each wave it has been complemented with additional items relating to the priorities of the funding source or to measures of current policy, social or medical relevance. Questionnaire items draw from multiple domains. Demographics variables include marital and partner status, education, employment, housing and income. Health and lifestyle behaviour data collected include weight and height, medical conditions,

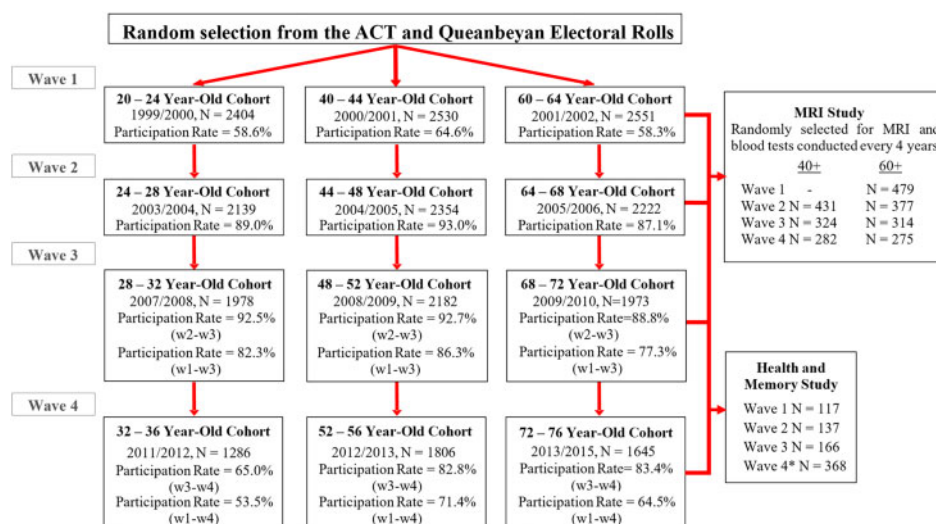


Figure 1 Flow chart of participants in the PATH Through Life Study. *Screening criteria for Health and Memory Study at Wave 4 varied from that used in previous waves. ACT, Australian Capital Territory; MRI, magnetic resonance imaging

medication use, reproductive health, smoking and alcohol consumption, drug use, physical activity and mental activities. Psychosocial function measures include questions on lifetime trauma, work stress, role strain, social networks, social interactions and financial hardship. Mental health questions include the Patient Health Questionnaire,⁷ positive and negative affect, Goldberg anxiety and depression scales, suicide, self-harm and past depression, and psychological scales on life satisfaction, behavioural inhibition/activation, rumination and mastery. Health-related quality of life is assessed using the Short Form 12 (SF12).

Face-to-face assessment

The face-to-face assessment objectively measures blood pressure, lung capacity, grip strength, fine motor speed, visual acuity, reaction time, verbal ability and memory at each wave. The CIDI depression and anxiety diagnostic assessments were added at Wave 4 for the 20 s and 40 s. Additional tests of executive function and social cognition were included for the 60 s, to aid classification of participants according to DSM-5 criteria for major and mild neurocognitive disorder.

Informant interview

At Wave 4 a new informant interview for the 60 s cohort was introduced. The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) provided additional data on the participant's instrumental activities of daily living, symptoms of dysexecutive function, and participant's medical conditions and health history. The Neuropsychiatric Inventory assessed the presence and severity of neuropsychiatric symptoms.⁸

Data linkage

PATH data have been linked to the National Deaths Index, the Pharmaceutical Benefits Scheme and Medicare Benefits Schedule, providing administrative data on mortality, medications and health service use, respectively.

What has it found? Key findings and publications

Descriptive statistics for key variables are shown in [Table 1](#). A selection of key findings is reported here by theme.

Suicidality

Analyses of the 20 s cohort investigated how resilience related to suicidality over 4 years of follow-up. Low resilience was only associated with future suicidality if suicidal

thoughts and behaviours were also present, and was largely explained by suicidality risk factors.⁹ An expanded assessment of active and passive suicidal ideation at Wave 4 (using the Psychiatric Symptoms Frequency scale) evaluated the interpersonal theory of suicide (IPITS) which emphasizes belonging and burdensomeness.¹⁰

Depression and anxiety and neuropsychiatric symptoms

The mental health scales Medical Outcomes Study Short Form 12 (SF12 MCS),¹¹ Goldberg depression scale (GDS), Goldberg anxiety scale (GAS)¹² and Brief Patient Health Questionnaire (PHQ-9)¹³ have been collected longitudinally since baseline and were validated against the CIDI in Wave 4 in the 20 s and 40 s cohorts.¹⁴ Various life course/ stage-specific factors associated with depression and anxiety have been examined using the PATH cohorts, as the cohorts have aged. For example, in analyses of the youngest cohort using data from Waves 1–4 (as men entered fatherhood), we have shown that expectant and new fathers do not report an increase in depressive symptoms.¹⁵ In a study examining cross-sectional and longitudinal well-being outcomes associated with job strain, those moving into high job strain were at greater risk of reporting any depression, whereas those moving away from high strain were more likely to change from any depression to no depression.¹⁶

In the 60 s cohort, 39% reported neuropsychiatric symptoms (NPS) across the cognitive spectrum from cognitively healthy to dementia.¹⁷ Those reporting NPS reported a 3- and 2-fold increased risk of dementia and mild cognitive impairment (MCI), respectively. Latent class analysis revealed four distinctive sub-populations for those reporting two or more NPS: (i) frontal/low comorbidity; (ii) high prevalence/high comorbidity; (iii) affective/low comorbidity; and (iv) sleep/low comorbidity.¹⁷ Prevalence of mild behavioural impairment (MBI), which is present in late-life NPS in normal to MCI individuals, was similarly examined in the Wave 4 60 s cohort. Results indicate relatively high prevalence of MBI in preclinical dementia, particularly in men.¹⁸ These findings are important for differential diagnosis of early clinical symptoms and prodromal dementia.

Predictors of cognitive decline and impairment

In all PATH cohorts, the shock of sudden financial hardship was strongly associated with time-dependent declines in fluid cognitive abilities, independent of mental health.¹⁹ Dietary predictors of transition to MCI and dementia were evaluated in the 60 s cohort. Participants who adhered to the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet had reduced risk of cognitive impairment

and dementia. The MIND diet combines aspects of the Mediterranean diet and the Dietary Approaches to Stop Hypertension (DASH) diet. A reduction in risk was not observed for participants adhering to the Mediterranean diet.²⁰ To our knowledge, this was the first examination of the MIND diet outside the USA.

We also evaluated our algorithmic approach to estimating DSM-5 diagnoses of minor and major neurocognitive impairment and compared these with DSM-4 classifications.²¹ Analyses confirmed earlier reports of the DSM-5 criteria being more inclusive than DSM-4, and demonstrated the effectiveness of an algorithmic approach to dementia classification in epidemiology studies. Inflammatory markers introduced at Wave 4 allowed for examination of inflammation and MCI. We adopted a novel approach by identifying pro-inflammatory states rather than testing individual markers, and concurrently investigated inflammatory biomarkers with neurodegeneration (via change in hippocampal volume) and cognitive decline [(via Mini-Mental State Examination (MMSE) score change)].²²

Gene-environment interactions and cognitive impairment

We examined the contribution of a polygenic risk (GRS) score for Alzheimer's disease and a lifestyle risk index as predictors of MCI at Wave 4.²³ Higher scores on the lifestyle risk index predicted transition from normal cognitive decline to MCI, whereas the GRS predicted transitioning from normal cognitive ageing to dementia, but not to MCI.²⁴ We also examined associations between genetic loci that have been shown to predict late onset Alzheimer's disease, and evaluated whether they predicted MBI in the oldest PATH cohort.²⁵ Using Wave 4 data from the 60s cohort, risk of MBI was linked to Alzheimer's genetic risk score (*APOE*, *MS4A*, *BIN1*, *EPHA1*, *NME8* and *ZCWPW1*), suggesting a common aetiology for MBI and AD.²⁵

Brain imaging

More than 2000 magnetic resonance imaging (MRI) scans were used to estimate brain shrinkage in the 40s and 60s between baseline and Wave 4, for an age range spanning 44–76 years.²⁶ More limited thinning of the cerebral cortex was observed in the 40s (0.21%/year) than in the 60s (0.3%/year). On average, brain shrinkage was somewhat greater in males than in females but only in the 60s.²⁷

Metabolic health

The investigation of metabolic health, particularly before the emergence of type 2 diabetes, has been a specific focus of Wave 4.²⁸ Substantive and converging evidence have characterized the inter-relationships of major risk factors (obesity, physical activity, diet) and their impact on insulin resistance,

impaired glucose tolerance and cerebral health. For example, higher blood glucose levels in individuals without diabetes were associated with greater weight gain, although physical activity moderated this effect.²⁹ Weight gain was also independently associated with prospective blood glucose increases.³⁰ Together, obesity and higher glucose levels were associated with smaller brain volumes.³¹

Workplace and social determinants of health

In the 40s cohort, 46% of respondents reported they had been bullied at some time in their working life and workplace bullying was an independent predictor of mental health outcomes.³² In the 60s cohort, those who volunteered more at Waves 3 and 4 reported higher life satisfaction.³³ The importance of social engagement, through volunteering, was particularly pertinent for 60s participants who had otherwise seen reductions in their social network size in other areas (e.g. less people with whom they feel close or can call for help).

Driving behaviours in the 60s cohort were compared between Waves 3 and 4.³⁴ In those aged 70 and older, 92% of participants were current drivers, with a decline in driving rates of approximately 1% per annum. Relative to non-drivers, those driving reported fewer health problems (e.g. diabetes, asthma, heart problems), had better vision and grip strength and greater social participation.³⁴

What are the main strengths and weaknesses?

The key strength of PATH is the inclusion of three narrow-aged cohorts assessed on the same group of core measures that collectively provide data covering most of the adult life course by Wave 4. The study has a high retention rate, but consistent with other longitudinal studies, there is attrition which accumulates with each wave. The study includes a wide range of measures, some of which (e.g. illicit drug use, head injury, resilience and social relationships) are rarely incorporated in longitudinal epidemiological studies. We are currently collecting the fifth wave of data, which also includes additional measures relevant to major events, such as the health impacts and behavioural responses to the 2019–20 bushfires in Australia. Ongoing collection will allow for continued response to major events and life transitions in a well-characterized Australian sample. Limitations include the lack of biomarkers in some domains of interest [e.g. positron emission tomography (PET) imaging and cerebrospinal fluid (CSF) biomarkers for Alzheimer's disease], the length of time between follow-ups, a lack of clinical data in some domains and higher than the national average socio-economic status of the sample.

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

Contact [info@pathstudy.org.au] for information and see the project website for more information, questionnaires and a list of current investigators at [www.pathstudy.org.au]. Alternatively, contact Prof. Kaarin Anstey at [k.anstey@unsw.edu.au] or contact Prof. Peter Butterworth at [peter.butterworth@anu.edu.au] for further information.

Update in a nutshell

- The PATH Through Life Study includes a random sample of 7485 adults aged 20–24 years, 40–44 years and 60–64 years, recruited in 1999–2001 from the Australian Capital Territory (ACT) and nearby town of Queanbeyan, NSW, in Australia.
- Wave 4 of the study completed 12 years of follow-up of our cohorts with survey and face-to-face assessments, and a neuroimaging sub-study in the mid-life and older cohorts.
- Core measures of physical and mental health, cognitive function and impairment, and risk and protective factors were repeated.
- Wave 4 was conducted between 2011 and 2013 and included 4737 of the participants in the original sample, aged 32–36 years, 52–56 years and 72–76 years.
- Wave 4 included new measures on work, sleep, social engagement, blood biomarkers, diet, cognitive engagement, expectations about ageing, executive function, mental health service use and neuropsychiatric symptoms.
- For enquiries and new collaborative projects, visit the PATH Through Life Study website at [http://www.pathstudy.org.au].

Funding

This work was supported by National Health and Medical Research Council (NHMRC) grants [1002160, 568969, 1063907], Safe Work Australia, NHMRC Dementia Collaborative Research Centre, Australian Research Council Grants [FT120100227, DP130101705, CE110001029].

Acknowledgements

We are grateful to Tony Jorm, Bryan Rodgers, Keith Dear, Andrew McKinnon, Perminder Sachdev, Patricia Jacomb, Karen Maxwell, Kristine Koh, Chantal Meslin, the PATH Team and the participants for their contributions.

Conflict of interest

None declared.

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