Supplementary Online Content

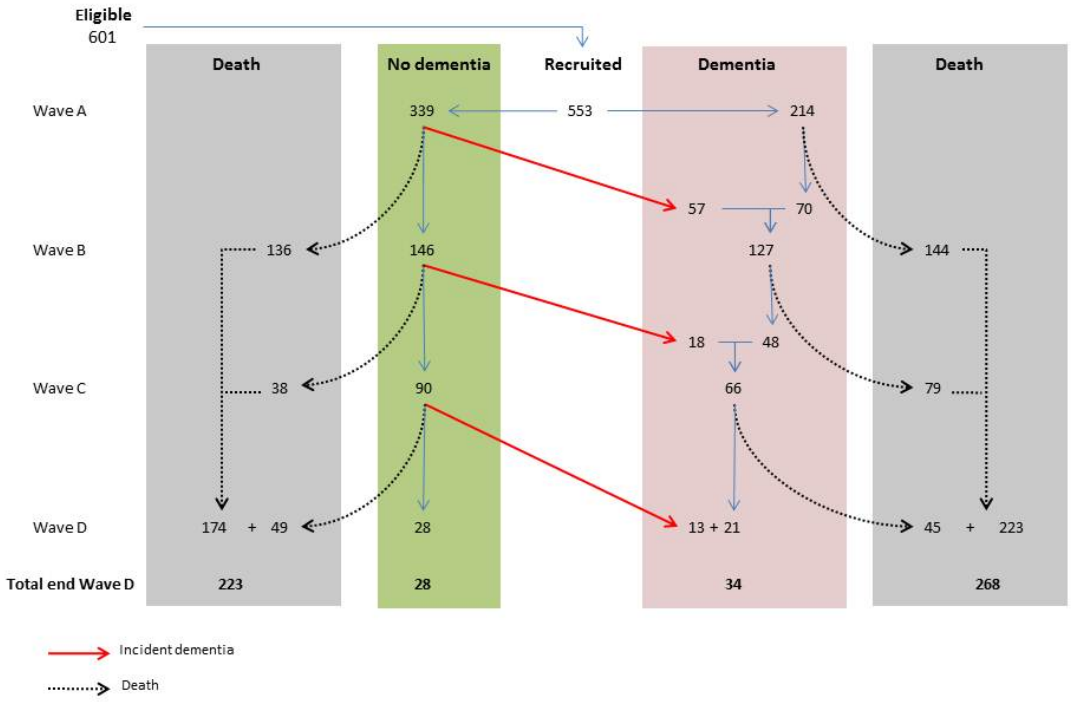
Davis DHJ, Muniz-Terrera G, Keage HAD, et al; Epidemiological Clinicopathological Studies in Europe (EClipSE) Collaborative Members. Association of delirium with cognitive decline in late life: a neuropathologic study of 3 population-based cohort studies. *JAMA Psychiatry.* Published online January 18, 2017. doi:10.1001/jamapsychiatry.2016.3423

eAppendix. Neuropsychological Evaluation of the Cohorts

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Neuropsychological Evaluation of the Cohorts

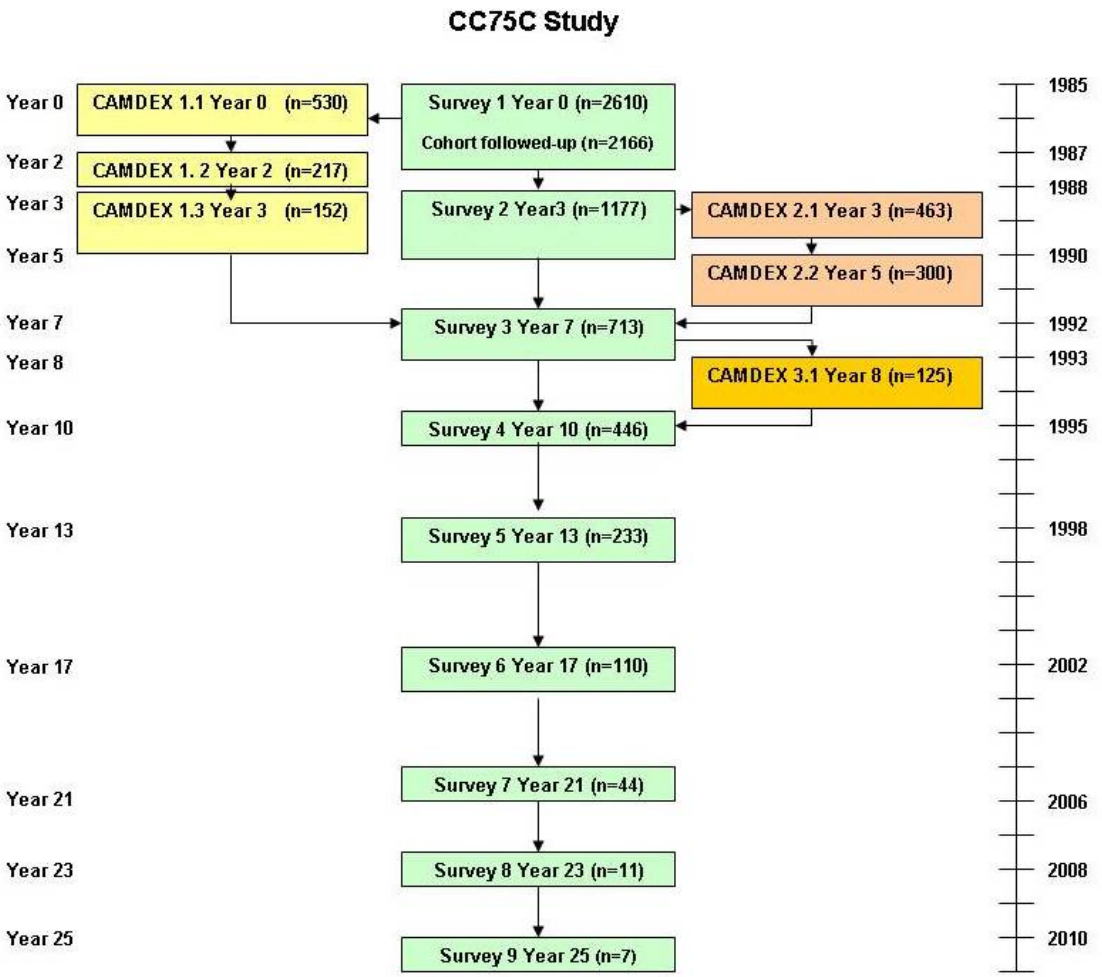
Vantaa 85+ study



Measures

- Mini-Mental State Examination
- Short Portable Mental Status Questionnaire
- Clinical Dementia Rating Scale

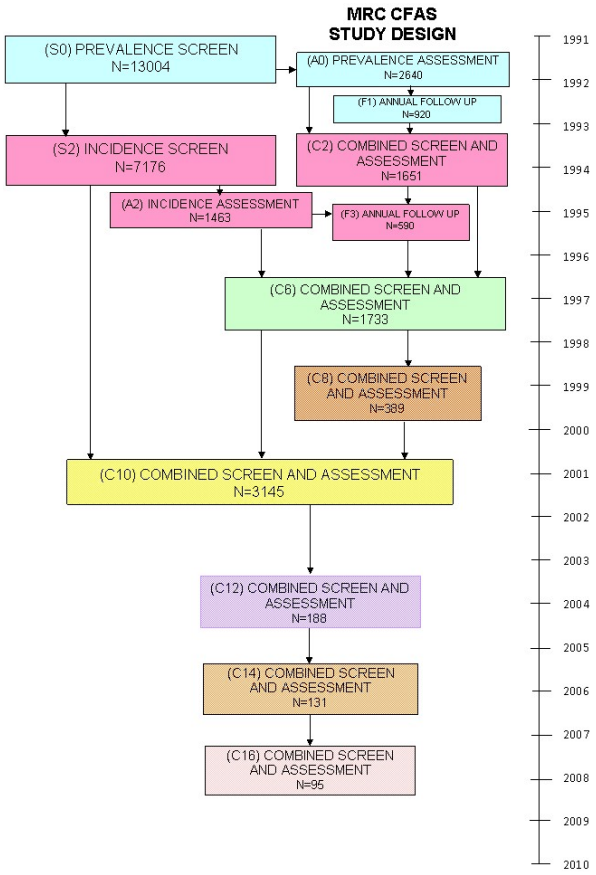
Cambridge City over-75s Cohort



Measures

- Mini-Mental State Examination
- Cambridge Mental Disorders of the Elderly Examination
- Retrospective Informant Interview (brain donors)

MRC Cognitive Function and Ageing Study



Measures

- Mini-Mental State Examination
- Geriatric Mental State Examination, including History and Aetiology Schedule interview of informants (Assessment subsamples)
- Retrospective Informant Interview (brain donors)
- Full details: http://www.cfas.ac.uk/pages/bcfasidi/index.html

1. Delirium Questions in CAMDEX (CC75C) and GMS (CFAS)

Delirium symptom	CC75C	CFAS	Source	Item
Attention / Arousal		X	Judgment	Errors made in clouded consciousness, i.e. subject was falling asleep, under the influence of alcohol, drugs or delirium due to acute physical illness. The individual will be very distractible, unfocussed and may drift in and out of consciousness. Often worse in the evening and afternoon
		X	Judgment	Errors made in clouded consciousness
	X	X	Judgment	Impaired ability to focus sustain and shift attention
		X	Judgment	Attention impairment
		X	Judgment	Repeatedly falls asleep
		X	Judgment	Sleepy, but not asleep
	X	X	Examination	Count backwards from 20 to 1
	X	X	Examination	Serial 7s
		X	Informant	Disturbance of consciousness, that is either being sleepy, or awake but unaware of their surroundings
		X	Informant	Or drowsy now?
		X	Informant	Were there marked fluctuations in his/her level of attention or alertness?
Acute	X		Informant	Has there been sudden worsening in mental confusion in recent weeks or months, which has continued to the present time?
		X	Informant	Had there been an abrupt change towards mental confusion in the period before the final illness?
Abnormal perception		X	Informant	Has s/he been troubled by voices or visions not experienced by others?
Fluctuation	X	X	Informant	Are there episodes lasting days or weeks when his/her thinking seems quite clear and then becomes muddled?
		X	Informant	Are there long periods during the day when s/he is lucid and not confused (that is, knows where s/he is and knows what s/he is doing and saying)?
		X	Informant	Does s/he get confused at night, wander about or talk nonsense?
		X	Informant	Or at any other time? What about during the day time?

	X	X	Informant	Were there periods lasting days or weeks when his/her thinking still seemed quite clear?
	X	X		Were there brief episodes during the 24 hours when s/he seemed much worse and then times when quite clear?
		X	Informant	Did s/he become completely normal when the confusion cleared?
	X	X	Informant	Was the confusion worse towards dusk or evening?
Duration	X	X	Informant	How long has this difficulty been present (months)?
	X	X	Informant	How long had the confusion been present (months)?
Physical illness	X		Judgment	Is s/he physically ill at present?
		X	Judgment	Rate if actively physically ill (mild/moderate/severe)
		X	Judgment	Do you think there was anything specific that caused these changes?
Overall		X	Judgment	Could a physical illness (not drugs or alcohol intoxication) be sufficient explanation for the subject's mental or psychiatric symptoms (e.g. delirious due to acute infection)?
	X		Informant	Did he/she suffer… confusion or delirium… during his/her final illness?

Judgment = rated by interviewer

Informant = assessment by informant interview

Examination = direct examination of participant

2. Neuropathology methods

Vantaa 85+

Paraffin-embedded tissue samples were assessed for neuropathology. All specimens were performed by one pathologist using exactly the same dissection and examination protocol, blinded to all clinical data. The protocols for assessing Alzheimer-type,[1,2] vascular,[3,4] and Lewy body[5] pathologies have been described previously. After fixation (phosphate-buffered 4% formaldehyde for at least two weeks), samples were obtained from the middle frontal, superior temporal and middle temporal gyri, and inferior parietal lobule, according to the standard Consortium to Establish a Registry for Alzheimer's Disease (CERAD) protocol.[6]

Alzheimer pathology

10µm sections were stained with a modified Bielschowsky method for neuritic pathology.[6] For scoring, the maximum density of the neuritic plaques was evaluated in the cortical sections. Tissue blocks were embedded in polyethylene glycol 1,000 and then cut (80µm) for free-floating staining with the Gallyas silver method for neurofibrillary pathology.[7] Apolipoprotein E (ApoE) genotyping was performed using a combination of polymerase chain reaction and solid-phase minisequencing technique.[8] Braak stage is a semi-quantitative measure of neurofibrillary tangle load,[9] and was performed without knowledge of clinical diagnosis, neuritic plaque score or ApoE genotype.

Vascular pathology

Cavitary lesions or solid cerebral infarcts visible to the naked eye were identified by examination of the intact brain and from 1-cm-thick coronal slices of the cerebral hemispheres, from 5-mm-thick transverse slices of the brain stem and sagittal slices of the cerebellum. These lesions were histologically ascertained to be infarcts (≥10mm diameter), lacunes (<10mm) or hemorrhages.

Lewy body pathology

For the assessment of Lewy body pathology, brain samples were obtained following recommendations of the First DLB Consortium International Workshop [10] and assessed for changes in α-synuclein pathology.[11] Sections of the substantia nigra were stained with the hematoxylin and eosin (H&E) method and with antibodies against α-synuclein. If any Lewy bodies were detected in the screened areas, the immunohistochemistry for α-synuclein was performed on cortical samples. The type of α-synuclein pathology (none, brainstem-predominant, limbic, diffuse neocortical) was determined for every participant.[5] A semiquantitative grading of the cell loss/atrophy in the

ventrolateral tier of SN pars compacta was determined from none (0) to severe (3), as reported earlier.[5]

City of Cambridge over-75s Cohort

After death, the brains were removed as soon as feasible in the local mortuary. The brains were cut in the sagittal plane. One hemisphere was dissected coronally into approximately one cm slices, macroscopically examined, and snap frozen at −80◦C. All assessments were performed blind to clinical status by neuropathologists at Addenbrooke's Hospital, Cambridge, UK.

Alzheimer pathology

The CERAD protocol was followed. Typical Alzheimer's lesions were considered by taking the CERAD ratings for neuritic plaques, diffuse plaques, and neurofibrillary tangles in the following areas: entorhinal, hippocampal, frontal, temporal, parietal, and occipital. Ratings for tau reactive tangles were estimated according to Braak stage and ratings for neuritic amyloid-β-reactive plaques were estimated according to the age dependent CERAD protocol for all areas.

Tau and amyloid-β protein were assessed on immunohistochemical preparations using antibodies obtained from the Cambridge Brain Bank Laboratory. Anti-tau antibody (mAb 11.57) was used to immunostain neurofibrillary tangles, neuritic plaques, and dystrophic neurites. Plaques were assessed using anti-amyloid-β antibody (DAKO (M872) Clone 6F/3D). Diffuse amyloid-β-reactive plaques were distinguished from neuritic plaques by the presence or absence of dystrophic neurites. All sections were counterstained with Ehrlich's haematoxylin with 3,3'-diaminobenzidine as the chromagen.

Vascular pathology

Microinfarcts, irrespective of age of infarct, were assessed by their presence or absence in the following areas: entorhinal, hippocampal, frontal, temporal, parietal, occipital, deep grey, and other neocortical and subcortical areas. White matter pallor was assessed as present or absent in the occipital, parietal, frontal, temporal cortices, and as pallor in the deep white matter or internal capsule in slides containing the basal ganglia.

Macroscopic vascular burden was assessed by the number, size, and location of visible macrovascular lesions in any area. The age of the infarct or whether they were present in grey or white matter was not noted. The arterial distribution for the largest infarct involved was recorded.

Number of lacunes was recorded in categories of 0, 1–4, 5–9, or 10 or more in each of the following locations: basal ganglia, thalamus, cerebral white matter, brainstem, and other. For diagnostic purposes, blocks for paraffin embedding were taken from: the hippocampus (at the level of the lateral geniculate body), entorhinal cortex (at the level of the mammillary body), frontal, temporal, parietal, and occipital lobes, the basal ganglia, thalamus, pons, medulla, cerebellum, and from two levels of the midbrain. The tissue blocks included subcortical white matter, deep cerebral white matter, and the internal capsule.

Ten micrometer thick sections were stained with hematoxylin and eosin to qualitatively assess white matter pallor, perivascular gliosis, presence of microinfarcts, and microvascular changes in each area sampled. Separate scores were recorded in white and grey matter for V-R space expansion, perivascular gliosis, and microinfarcts. Small-vessel disease was defined as presence of white matter pallor, perivascular gliosis or 'other' microscopic vascular disease.

Lewy body pathology

Lewy bodies were assessed by their presence or absence in entorhinal, hippocampal, frontal, or temporal areas and, in addition, in the substantia nigra, nucleus basalis, dorsal raphe nucleus, locus coeruleus, and dorsal vagal nucleus. Sections were either immunolabelled with anti-ubiquitin antibody (pAb BR 251 DAKO Z0458, early cases) or anti-α-synuclein antibody (Biomol International SA3400, later cases), or stained with haematoxylin and eosin to visualize Lewy bodies..

MRC Cognitive Function and Ageing Study

At necropsy, frozen samples of brain tissue were removed for storage. The remainder of the brain was fixed for standardized assessment on paraffin-embedded tissues, following the CERAD protocol with minor modifications (see the MRC CFAS website: www.cfas.ac.uk). Neuropathological examination was carried out without knowledge of clinical or interview data, with semiquantitative rating of specific lesions and a prediction of clinicopathological preliminary diagnosis, according to likely importance. To ensure consistency between the centers, inter-rater reliability was addressed at the start of the study, including circulation of macroscopic brain photographs and microscopic slides.

Alzheimer pathology

Amyloid protein pathology and neurofibrillary tangles (NFTs) were assessed in the hippocampus (CA1), entorhinal cortex and in the frontal (Brodman Area 8/9), temporal (BA21), occipital (BA17/18)

and parietal (BA7) lobes. Severity of pathology was scored as none, mild, moderate, or severe. Plaque pathology was assessed with Congo red, silver stains (including Bielschowsky, Palmgren and Gallyas), or immunohistochemistry. NFTs were assessed with immunohistochemistry (mAb AT8 or mAb 11/57). All slides were counterstained with Ehrlich's hematoxylin and visualized with 3,3'-diaminobenzidine. For this analysis, burden of classical AD features was taken from the CERAD ratings in the entorhinal and hippocampal regions combined and in the neocortex. Each variable was defined as the maximum score in each region.

Vascular pathology

Vascular pathologies were assessed for each area examined using hematoxylin-eosin slides. Cerebrovascular pathology measures included the presence or absence of hemorrhages, infarcts (parenchymal ischemic lesions >10 mm), lacunes (parenchymal ischemic lesions <10 mm) and small vessel disease (diffuse pallor of myelin staining in white matter associated with hyaline degeneration of subcortical arteries and arterioles, micro-infarcts or a combination of these features).

Lewy body pathology

Lewy bodies (LB) were identified using haematoxylin-eosin and ubiquitin immunohistochemistry in the cortices, locus coeruleus, substantia nigra, nucleus basalis of Meynert, raphe nuclei, and dorsal efferent nucleus of vagus nerve.

3. Statistical analyses

All analyses were conducted in Stata 12.1 (StataCorp, Texas). Consistent with previous approaches, delirium exposure was operationalized as 'never' or 'ever'.[12] Change in MMSE before death was modeled using a time-to-death random-effects model.[13] We were interested in estimating the final trajectory towards death as this makes relationships with pathological data easier to define. The mean time to death was 5.2 years, and so the intercept for this final trajectory was set (centered) at 6 years. This intercept is not so near point of death such that rates of change (slopes) cannot be estimated, yet not so far from death that the pathology findings at autopsy might not plausibly be related to the estimated parameters. Six years before death is also comparable to intercepts from change-point models of the final trajectory of cognitive decline,[14-16] and in the range observed in other analyses (3 – 8 years).[17]

Terms for time-to-death and delirium were used to model the intercept (-6 years) and slopes. All models were adjusted by age at death (centered at mean age = 90 years), sex (0=men, 1=women), years of education (0-3; 4-7; 8-11; 12 or more) and study (0=Vantaa 85+, 1=CC75C, 2=CFAS). Covariance matrices were unstructured. Model fit was assessed using the Bayesian Information Criterion (BIC), which is based on maximum likelihood with a penalization for number of parameters. Missing data were assumed to be missing-at-random. After fitting models, assumptions were checked visually by constructing Q–Q plots of the standardized residuals.

Four pathological parameters were examined: Braak stage, neocortical amyloid plaques, vascular pathology (large artery infarcts, lacunes or hemorrhage) and Lewy bodies in substantia nigra. In keeping with previous methods, neuropathological variables were dichotomized ('none-mild' = 0; 'moderate-severe' = 1).[12,18,19] This approach allows for simpler interpretation and is more likely to be robust. Individuals were assigned a 'pathology burden score' based on the number of times they scored in the higher category for each of the four markers. Therefore, the overall pathological

burden score ranged between 0 and 4, i.e. being in the lower category for all markers (pathology burden score=0), in the upper category of all four markers (pathology burden score=4) or some combination. Finally, interactions between delirium and pathology burden ([delirium history]*[pathology score]) in terms of their effect on the intercept (-6 years before death) and slope (rate of change of MMSE).

Model construction

1. Intercept only model

mmse	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
death_age_c	-.1628004	.0320588	-5.08	0.000	-.2256344	-.0999663
sex	-2.263875	.3983975	-5.68	0.000	-3.044719	-1.48303
cat_educ						
1	1.397545	1.000307	1.40	0.162	-.563021	3.358111
2	1.744542	1.53071	1.14	0.254	-1.255594	4.744679
3	5.476379	1.547757	3.54	0.000	2.442832	8.509927
study						
2	-1.005207	1.336974	-0.75	0.452	-3.625628	1.615215
3	.1506752	1.25684	0.12	0.905	-2.312685	2.614036
_cons	21.78409	.9334968	23.34	0.000	19.95447	23.61371

Model	Obs	ll(null)	ll(model)	df	AIC	BIC
.	2570	.	-7704.098	12	15432.2	15502.42

2. Add delirium and pathology variables

```
------------------------------------------------------------------------------
        mmse |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
 death_age_c |  -.1504382   .0307454    -4.89   0.000    -.2106981   -.0901783
         sex |  -2.030025   .3843093    -5.28   0.000    -2.783258   -1.276793
             |
    cat_educ |
           1 |   1.491175   .9153817     1.63   0.103    -.3029406     3.28529
           2 |    .618857   1.423069     0.43   0.664    -2.170308    3.408022
           3 |   3.992727   1.439935     2.77   0.006     1.170505    6.814948
             |
    del_flag |  -2.866873   .3873046    -7.40   0.000    -3.625976    -2.10777
             |
  path_level |
           1 |  -.0614932   .5066416    -0.12   0.903    -1.054493    .9315061
           2 |  -1.644467   .5098953    -3.23   0.001    -2.643843   -.6450903
           3 |  -3.945659   .6210421    -6.35   0.000     -5.16288   -2.728439
             |
       study |
           2 |  -.0610921   1.279335    -0.05   0.962    -2.568543    2.446358
           3 |   .8247395   1.185773     0.70   0.487    -1.499332    3.148811
             |
       _cons |   23.34317   .9616507    24.27   0.000     21.45837    25.22797
------------------------------------------------------------------------------

------------------------------------------------------------------------------
       Model |    Obs    ll(null)   ll(model)     df          AIC         BIC
-------------+----------------------------------------------------------------
           . |   2570           .    -7653.62     16     15339.24    15432.87
------------------------------------------------------------------------------
```

3. Remove study, add slope:

- Model + study BIC=15433 (model above)
- Model + slope + study = BIC 14988
- Model + slope BIC = 14981 (model below)

```
------------------------------------------------------------------------------
        mmse |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
 death_age_c |  -.1998794   .0293812    -6.80   0.000    -.2574656   -.1422932
         sex |  -1.926914     .36447    -5.29   0.000    -2.641262   -1.212566
             |
    cat_educ |
           1 |   1.113882    .880197     1.27   0.206    -.6112723    2.839036
           2 |   .3064669    .828071     0.37   0.711    -1.316523    1.929456
           3 |   2.007399   .8433255     2.38   0.017     .3545116    3.660287
             |
    del_flag |  -2.736559    .360538    -7.59   0.000    -3.443201   -2.029918
             |
  path_level |
           1 |   .0769343   .4788823     0.16   0.872    -.8616579    1.015526
           2 |  -1.377791   .4794888    -2.87   0.004    -2.317572   -.4380102
           3 |  -3.390308   .5838123    -5.81   0.000    -4.534559   -2.246057
             |
         ttd |  -.8690382   .0369577   -23.51   0.000     -.941474   -.7966024
       _cons |   23.60515   .9203264    25.65   0.000     21.80134    25.40896
------------------------------------------------------------------------------

------------------------------------------------------------------------------
       Model |    Obs    ll(null)   ll(model)     df          AIC         BIC
-------------+----------------------------------------------------------------
           . |   2570           .   -7431.422     15     14892.84    14980.62
------------------------------------------------------------------------------
```

4. Add slope terms

mmse	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
death_age_c	-.2122174	.0299058	-7.10	0.000	-.2708317	-.1536032
sex	-1.986311	.3637041	-5.46	0.000	-2.699157	-1.273464
cat_educ						
1	1.099545	.8725966	1.26	0.208	-.610713	2.809803
2	.4186961	.8215354	0.51	0.610	-1.191484	2.028876
3	2.175091	.8373293	2.60	0.009	.533956	3.816227
del_flag	-3.711029	.377406	-9.83	0.000	-4.450731	-2.971327
path_level						
1	.1229048	.4783989	0.26	0.797	-.8147397	1.060549
2	-1.311049	.4787992	-2.74	0.006	-2.249478	-.3726195
3	-3.398172	.5820621	-5.84	0.000	-4.538993	-2.257351
dageBYttd	-.0157115	.00614	-2.56	0.011	-.0277457	-.0036773
delBYttd	-.6439718	.0739116	-8.71	0.000	-.7888359	-.4991076
ttd	-.6493764	.0415634	-15.62	0.000	-.7308392	-.5679137
_cons	23.66975	.9146661	25.88	0.000	21.87704	25.46246

Model	Obs	ll(null)	ll(model)	df	AIC	BIC
.	2570	.	-7390.871	17	14815.74	14915.22

Sensitivity analysis for pathology burden score

This was specified by constructing a pathology burden score where the numerator was any instance where pathology was in the higher category and the denominator was total number of pathologies assessed, i.e. a *proportion* of higher category pathologies of pathologies for which the pathology was assessed. This is an alternative formulation to the one used in the main analysis where the denominator was 4, regardless of whether a pathological measure was missing.

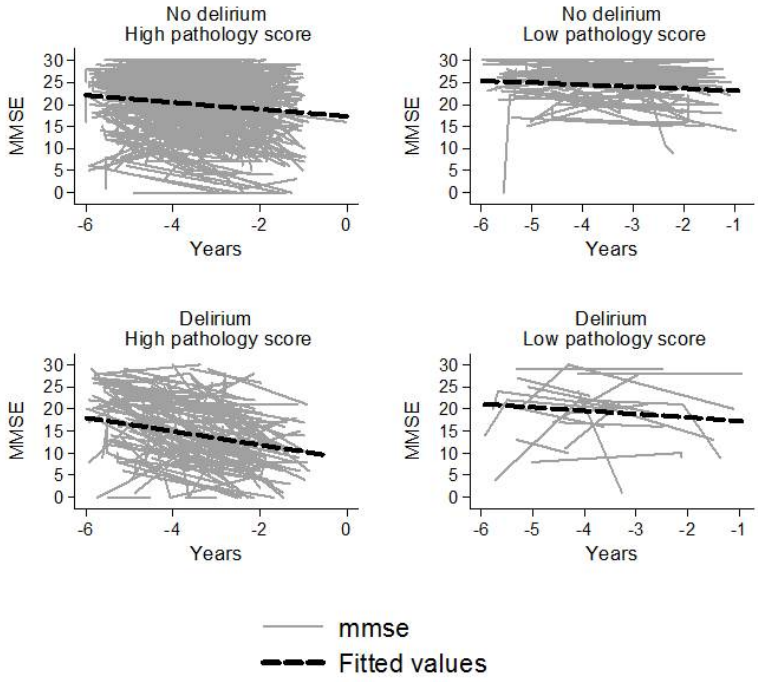
The magnitude and direction of coefficients estimated are comparable using either approach.

```
Mixed-effects ML regression                     Number of obs      =      2558
Group variable: pid                             Number of groups   =       872

                                                Obs per group: min =         1
                                                               avg =       2.9
                                                               max =         7


                                                Wald chi2(15)      =   1092.16
Log likelihood = -7336.7598                     Prob > chi2        =    0.0000

------------------------------------------------------------------------------
        mmse |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
 death_age_c |  -.2057342   .0299757    -6.86   0.000    -.2644855   -.1469829
         sex |  -2.014613   .3658166    -5.51   0.000      -2.7316   -1.297626
             |
   cat_educ  |
           1 |   1.052917    .870749     1.21   0.227    -.6537199    2.759553
           2 |   .1762173   .8214934     0.21   0.830     -1.43388    1.786315
           3 |   1.948117    .837429     2.33   0.020      .306786    3.589447
             |
    del_flag |  -3.128511   .8932198    -3.50   0.000     -4.87919   -1.377832
             |
  path_level |
           1 |  -.6234385   .5687676    -1.10   0.273    -1.738202    .4913255
           2 |  -2.109604   .5718232    -3.69   0.000    -3.230357    -.988851
           3 |  -4.188868   .6606035    -6.34   0.000    -5.483627   -2.894109
             |
    delBYttd |  -.4713217   .1268428    -3.72   0.000     -.719929   -.2227144
   dageBYttd |  -.0119185   .0060676    -1.96   0.049    -.0238107   -.0000263
   panyBYttd |  -.4221593   .0898178    -4.70   0.000     -.598199   -.2461196
     p*d_int |  -.6414385    .972274    -0.66   0.509    -2.547061    1.264184
    p*d_slpe |  -.3581438   .2519654    -1.42   0.155    -.8519869    .1356992
         ttd |  -.3219956   .0802394    -4.01   0.000    -.4792619   -.1647292
       _cons |   24.53638   .9560552    25.66   0.000     22.66255    26.41022
------------------------------------------------------------------------------
```

Where Braak stage was missing in CFAS cases, a measure for neurofibrillary tangle burden was constructed using the following rules:

- Higher Braak stage = any rating of ‘moderate’ or ‘severe’ score in any neocortical region
- Higher Braak stage = any rating of ‘moderate’ or ‘severe’ score in hippocampal or entorhinal cortex
- Lower Braak stage = any rating of ‘none’ or ‘mild’ score in hippocampal or entorhinal cortex

This algorithm gave 100% sensitivity and 100% specificity for cases with Braak stage, where scores of 0/1/2/3 were defined as ‘Lower Braak Stage’ and scores of 4/5/6 were defined as ‘Higer Braak stage’



References

1. Polvikoski T, Sulkava R, Haltia M, et al. Apolipoprotein E, dementia, and cortical deposition of beta-amyloid protein. The New England journal of medicine 1995;333:1242-7.
2. Polvikoski T, Sulkava R, Rastas S, et al. Incidence of dementia in very elderly individuals: a clinical, neuropathological and molecular genetic study. Neuroepidemiology 2006;26:76-82.
3. Rastas S, Verkkoniemi A, Polvikoski T, et al. Atrial fibrillation, stroke, and cognition: a longitudinal population-based study of people aged 85 and older. Stroke 2007;38:1454-60.
4. Ahtiluoto S, Polvikoski T, Peltonen M, et al. Diabetes, Alzheimer disease, and vascular dementia: a population-based neuropathologic study. Neurology 2010;75:1195-202.
5. Oinas M, Polvikoski T, Sulkava R, et al. Neuropathologic findings of dementia with lewy bodies (DLB) in a population-based Vantaa 85+ study. J Alzheimers Dis 2009;18:677-89.
6. Mirra SS, Heyman A, McKeel D, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part II. Standardization of the neuropathologic assessment of Alzheimer's disease. Neurology 1991;41:479-86.
7. Kondoh H, Matsushita M, Kosaka K, Miyazaki N. Staining senile plaques using Bodian's method modified with methenamine. Biotech Histochem 1993;68:113-6.
8. Syvanen AC, Sajantila A, Lukka M. Identification of individuals by analysis of biallelic DNA markers, using PCR and solid-phase minisequencing. Am J Hum Genet 1993;52:46-59.
9. Braak H, Braak E. Neuropathological stageing of Alzheimer-related changes. Acta Neuropathol 1991;82:239-59.
10. McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology 1996;47:1113-24.
11. McKeith IG, Dickson DW, Lowe J, et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. Neurology 2005;65:1863-72.
12. Davis DH, Muniz Terrera G, Keage H, et al. Delirium is a strong risk factor for dementia in the oldest-old: a population-based cohort study. Brain 2012;135:2809-16.
13. Piccinin AM, Muniz G, Matthews FE, Johansson B. Terminal decline from within- and between-person perspectives, accounting for incident dementia. The journals of gerontology Series B, Psychological sciences and social sciences 2011;66:391-401.
14. Wilson RS, Beck TL, Bienias JL, Bennett DA. Terminal cognitive decline: accelerated loss of cognition in the last years of life. Psychosomatic medicine 2007;69:131-7.
15. Wilson RS, Segawa E, Hizel LP, Boyle PA, Bennett DA. Terminal dedifferentiation of cognitive abilities. Neurology 2012;78:1116-22.
16. MacDonald SW, Hultsch DF, Dixon RA. Aging and the shape of cognitive change before death: terminal decline or terminal drop? The journals of gerontology Series B, Psychological sciences and social sciences 2011;66:292-301.
17. Muniz-Terrera G, Matthews FE, Stephan B, Brayne C. Are terminal decline and its potential indicators detectable in population studies of the oldest old? Int J Geriatr Psychiatry 2011;26:584-92.
18. Savva GM, Wharton SB, Ince PG, Forster G, Matthews FE, Brayne C. Age, neuropathology, and dementia. N Engl J Med 2009;360:2302-9.
19. Brayne C, Ince PG, Keage HA, et al. Education, the brain and dementia: neuroprotection or compensation? Brain 2010;133:2210-6.