Supporting information

Appendix A. Sample code to fit the four parameters sigmoidal model

```
*************************************************************************************************
Macro to fit empty model and estimate initial values for theta 1 to theta 4
dt= dataset, t=time from death,  id= participant id, y=outcome, ref_time= for example 3 years before death
*************************************************************************************************;
%macro plcvdtinit (dt,t, id,y,ref_time);
proc univariate data=&dt. (where =( &t.<0.5)); var &y. ; output out=m mean= mean_death; run;
data _null_;    set m ;
     call symput (compress("initial_theta1") ,mean_death);
     call symput (compress("initial_ theta4") ,-(mean_death/2));
run;
proc mixed data=&dt. (where=( &t.< ref_time))
  method=reml covtest noclprint ratio maxfunc=250 maxiter=100 namelen=50;
     class &id. ;       model &y.= &t./s outp=pred covb ddfm=bw cl;
     random intercept &t./type=un subject=&id.  g gcorr;
     ods output  SolutionF=fl;
run; quit;
proc mixed data=&dt. (where=(&t.> ref_time))
  method=reml covtest noclprint ratio maxfunc=250 maxiter=100 namelen=50;
     class &id. ;      model &y.= &t./s outp=pred covb ddfm=bw cl;
     random intercept &t./type=un subject=&id.  g gcorr;
     ods output  SolutionF=fh;
run; quit;
data _null_;
  merge fl(where=(effect ="&t.") rename=(estimate=low)) fh (where=(effect ="&t.") rename=(estimate=high)) ;
  by effect;
     if 0.5<abs(low/high)<1.5 then theta3_val=1.05; else theta3_val =0.5;
     if 0.5<abs(low/high)<1.5 then theta2_val=30; else theta2_val=2;
```

Capuano AW, Wilson RS, Leurgans SE, Dawson JD, Bennett DA, Hedeker D.
Sigmoidal mixed models for longitudinal data. Stat Methods Med Res. 2016 Apr 28.
pii: 0962280216645632. PubMed PMID: 27130491.

```
    call symput (compress("initial_theta3") , theta3_val);
    call symput (compress("initial_theta2") , theta2_val);
run;
proc nlmixed data=&dt. cov;
  parms theta1   &initial_ theta1 theta2   &initial_ theta2 theta3   &initial_ theta3 theta4   &initial_ theta4
          var_e     0.25        var1    1.5        var2      0.5        cv  -0.5;
   bounds  var_e >0, var1>0, var2>0;
   if &t.= 0 then mu = theta1 +u1;
    else mu = (theta4+u2) + ((theta1+u1)-(theta4+u2))/((1 + exp((theta3)*(log(&t.)-log(theta2)))));
    model &y. ~ normal( mu , var_e);  random u1 u2 ~ normal([0,0], [var1, cv, var2])  subject = &id. ;
run;
%mend plcvdtinit;
**************************************************************************
Sample code to add risk factors into the model (replace bold by your information)
**************************************************************************;
proc nlmixed data=dataset_name   cov;
  parms  theta1   initial theta2   initial theta3   initial theta4   initial
          theta1_risk   initial theta2_risk   initial theta3_risk   initial theta4_risk   initial
          var_e  initial  var1 initial  var2 initial  cv  initial;
   bounds  var_e >0, var1>0, var2>0;
   if outcome= 0 then mu = theta1 +u1; else mu = (theta4+ theta4_risk*risk+u2) + ((theta1+ theta1_risk*risk+u1)-(theta4+
theta4_risk*risk+u2))/((1 + exp((theta3+ theta3_risk*risk)*(log(time)-log(theta2+ theta2_risk*risk+)))));
    model outcome ~ normal( mu ,var_e);
    random u1 u2 ~ normal([0,0], [var1, cv, var2])  subject = id ;   run;
```

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Appendix B. Simulation results of sigmoid mixed modeling of 1000 randomly generated					
	Number of observations per participant				
Variable	5	7	10	20	30
Mean					
θ_1	-0.61	-0.60	-0.61	-0.61	-0.61
$-\theta_2$	1.83	1.83	1.83	1.83	1.83
θ_3	0.74	0.74	0.74	0.74	0.74
θ_4	0.53	0.53	0.53	0.53	0.53
Bias					
θ_1	0.00	0.01	0.00	0.00	0.00
$-\theta_2$	0.00	0.01	0.01	0.00	0.01
θ_3	0.00	0.00	0.00	0.00	0.00
θ_4	0.00	0.00	0.00	0.00	0.00
MSE					
θ_1	0.03	0.03	0.03	0.03	0.03
θ_2	0.01	0.01	0.01	0.01	0.01
θ_3	0.00	0.00	0.00	0.00	0.00
θ_4	0.00	0.00	0.00	0.00	0.00
Cover					
θ_1	0.95	0.94	0.95	0.95	0.94
θ_2	0.95	0.96	0.95	0.96	0.96
θ_3	0.95	0.95	0.95	0.94	0.94
θ_4	0.93	0.95	0.94	0.95	0.94
n=100, θ_1= -0.6111, θ_4= 0.5293, θ_3= 0.7418, - θ_2=1.8259, σ_u =1.7374, σ_v =0.1870					

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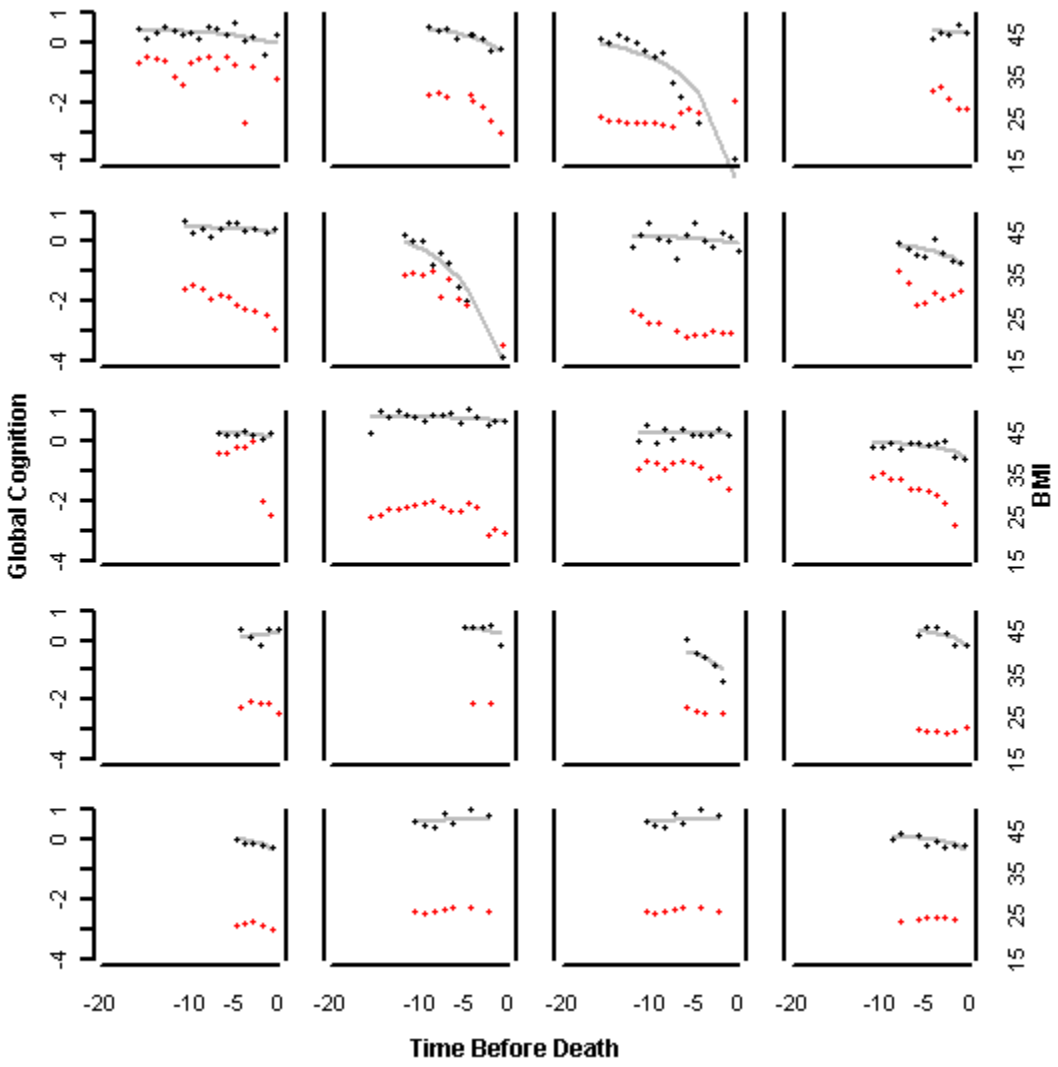
Appendix C. A random sample of person-specific observed global cognition (outcome variable, in black) and observed BMI (in red), and predicted global cognition (in grey) from the sigmoidal model of the main analyses



Capuano AW, Wilson RS, Leurgans SE, Dawson JD, Bennett DA, Hedeker D. Sigmoidal mixed models for longitudinal data. Stat Methods Med Res. 2016 Apr 28. pii: 0962280216645632. PubMed PMID: 27130491.