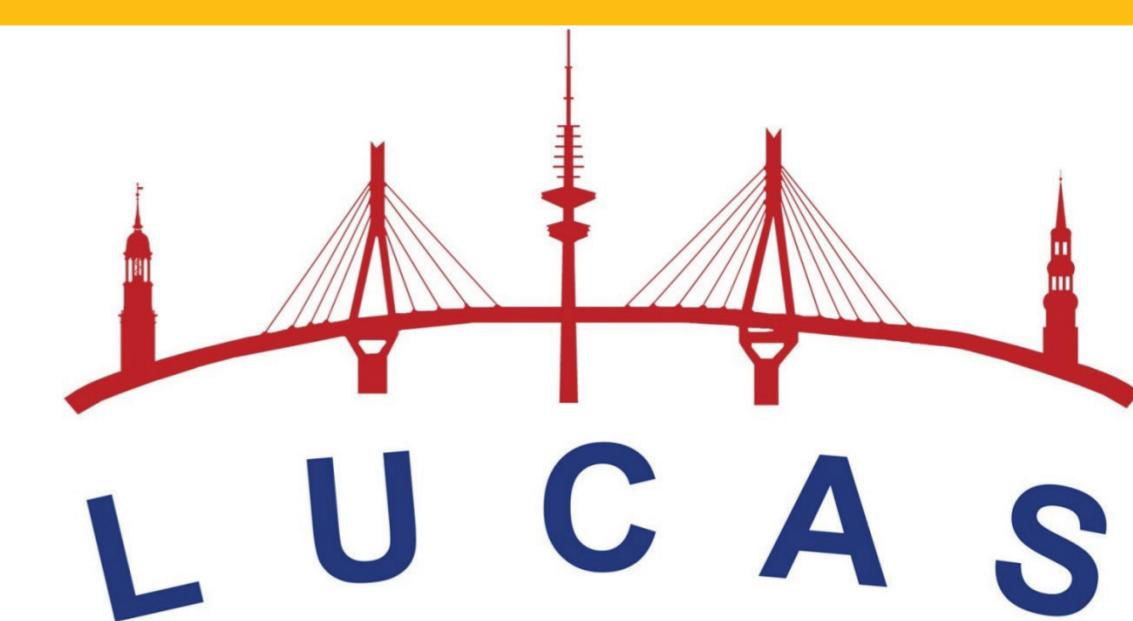




Longitudinal Urban Cohort Ageing Study



The interrelationship between depressed mood, functional decline and disability over a ten year observational period within the Longitudinal Urban Cohort Ageing Study (LUCAS)

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Introduction: The WHO defines 'healthy ageing' as 'the process of developing and maintaining the functional ability' (*Word Report on Ageing and Health, WHO 2015*). Late-life depression and frailty compromise wellbeing and independence of older people. To date, there exists little research on the interaction of the dynamic processes of frailty and depression and only a few studies were longitudinal. Conclusions about the direction of effects remained uncertain. Our study is the first longitudinal study working with frailty phenotype criteria and distinct disability. This allows distinguishing between the conflicting concepts described in the literature.

Aim: To investigate the mutual relationships between frailty, disability and depression/depressed mood. Therefore, our research questions were

1. Do persons reporting depressed mood have an increased risk of subsequent functional decline/frailty in contrast to persons who do not report depressed mood?
2. Do persons reporting functional decline/frailty have an increased risk of subsequent depressed mood over those not reporting functional decline?
3. Do persons reporting depressed mood have an increased risk of subsequent disability (BADL-dependency) over those not reporting depressed mood?
4. Do persons reporting disability (BADL-dependency) have an increased risk of subsequent depressed mood over those not reporting disability?

Methods: Data were obtained from each of the last six biyearly waves (2007–2017) of the Longitudinal Urban Cohort Ageing Study (LUCAS) in Hamburg, Germany, a prospective observational cohort study of manifold aspects of ageing to evaluate transitions within the geriatric functional continuum from independence to frailty and disability. Factors influencing functional status transitions are of particular interest for prevention and health-care planning.

The three predictor and response variables depressed mood, functional decline/frailty and disability were identically in all six LUCAS waves.

Depressed mood: One question from the 5-item Mental Health Inventory Screening Test (Stewart AL et al. *Med Care* 1988;26:724-32);

Frailty: LUCAS Functional Ability Index, status 'frail' (Dapp U et al. *BMC Geriatr* 2014;14:141);

Disability: One question on need for help with basic activities of daily living (Katz S et al. *JAMA* 1963;185:914-9).

Kaplan-Meier curves and Cox's proportional hazards regression were used for **time-to-event analyses with shifting baseline**.

Ordinary time-to-event analysis is illustrated in **Fig. 1a**. Our predictors (**P**) depressed mood, functional decline (frailty) and disability (BADL-dependency) were all binary; we gave them the generic term **P signalling their presence**. Similarly, **endpoints were termed E, dropouts D**. Thus, time intervals either began in 2007 or at the **first presentation of P**, and **ended either at E or at D**. Three aspects were different in our data from ordinary time-to-event data (**Fig. 1b**). First, our data were granular: time values were accurate only up to one year. Second, when a person e.g. was responding at wave 2011, but no more at wave 2013 (i.e., dropped out between 2011 and 2013), we assumed the associated time interval ended at the midpoint of these times, i.e. at year 2012 (marked as **D** for dropout).

Third, we used a **shifting baseline**. For those presenting **P** at least once, we started the time interval of observation at the **first occurrence of P**. For some, this was in 2007, but for many others, it was later. For those never presenting **P**, we started in 2007.

Baseline data, i.e. the values of the predictors (**P**), age, sex and education, were always collected at the beginning of the time interval, i.e. at varying time points (**shifting baseline; Fig. 1b**).

Figure 1a+1b: Ordinary and shifting baseline time-to-event analysis

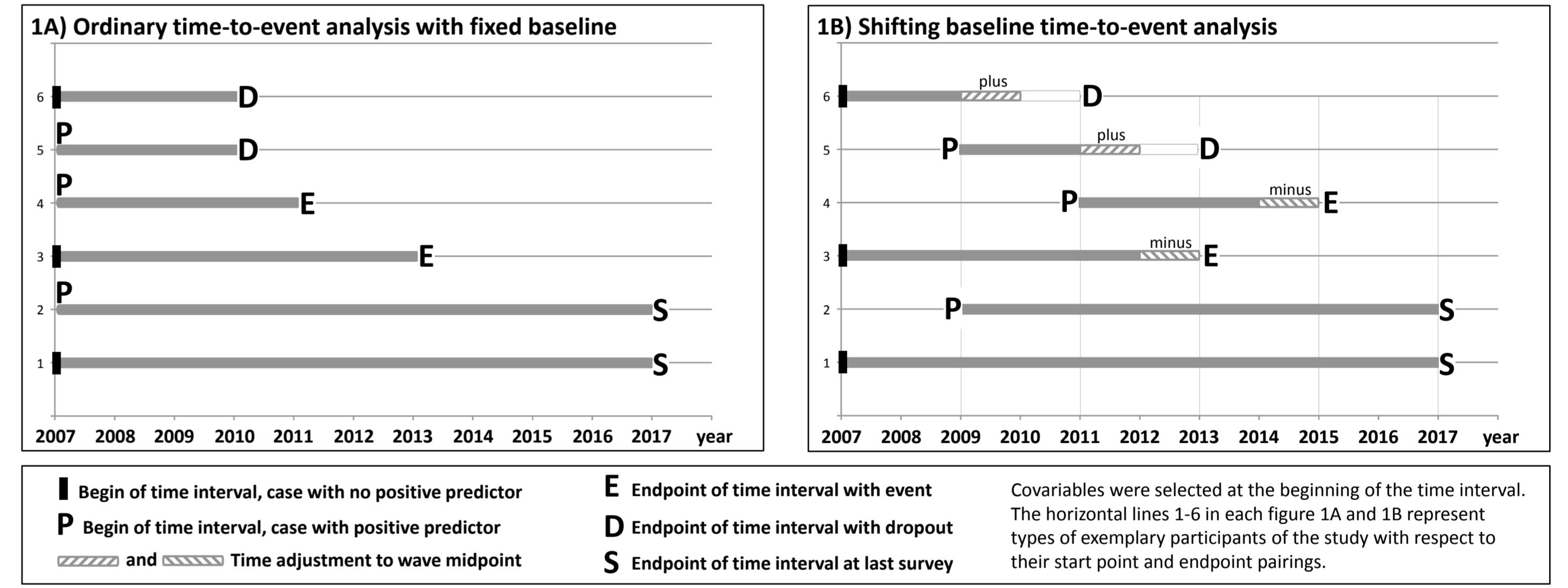


Table 1: Number of cohort members showing predictor and/or event

Cases	Frequency	Percent
(a) Predictor: DeprMood → Event: FunctDecline (n=1444)		
DeprMood and later FunctDecline	90†	6.2
DeprMood but no later FunctDecline	140‡	9.7
No DeprMood but later FunctDecline	431§	29.9
No DeprMood and no later FunctDecline	783	54.2
(b) Predictor: FunctDecline → Event: DeprMood (n=1707)		
FunctDecline and later DeprMood	116	6.8
FunctDecline but no later DeprMood	705	41.3
No FunctDecline but later DeprMood	108	6.3
No FunctDecline and no later DeprMood	778	45.6
(c) Predictor: DeprMood → Event: Disability (n=1834)		
DeprMood and later Disability	60	3.3
DeprMood but no later Disability	344	18.8
No DeprMood but later Disability	112	6.1
No DeprMood and no later Disability	1318	71.9
(d) Predictor: Disability → Event: DeprMood (n=1709)		
Disability and later DeprMood	18	1.1
Disability but no later DeprMood	184	10.8
No Disability but later DeprMood	208	12.2
No Disability and no later DeprMood	1299	76.0

*Interpretation of the frequencies analogous to footnotes of table 2a

†These 90 individuals reported at one wave being in a depressed mood (DeprMood) and at a later wave functional decline (FunctDecline)

‡These 140 individuals reported at one wave being in a depressed mood (DeprMood) and at later waves never showed functional decline (FunctDecline)

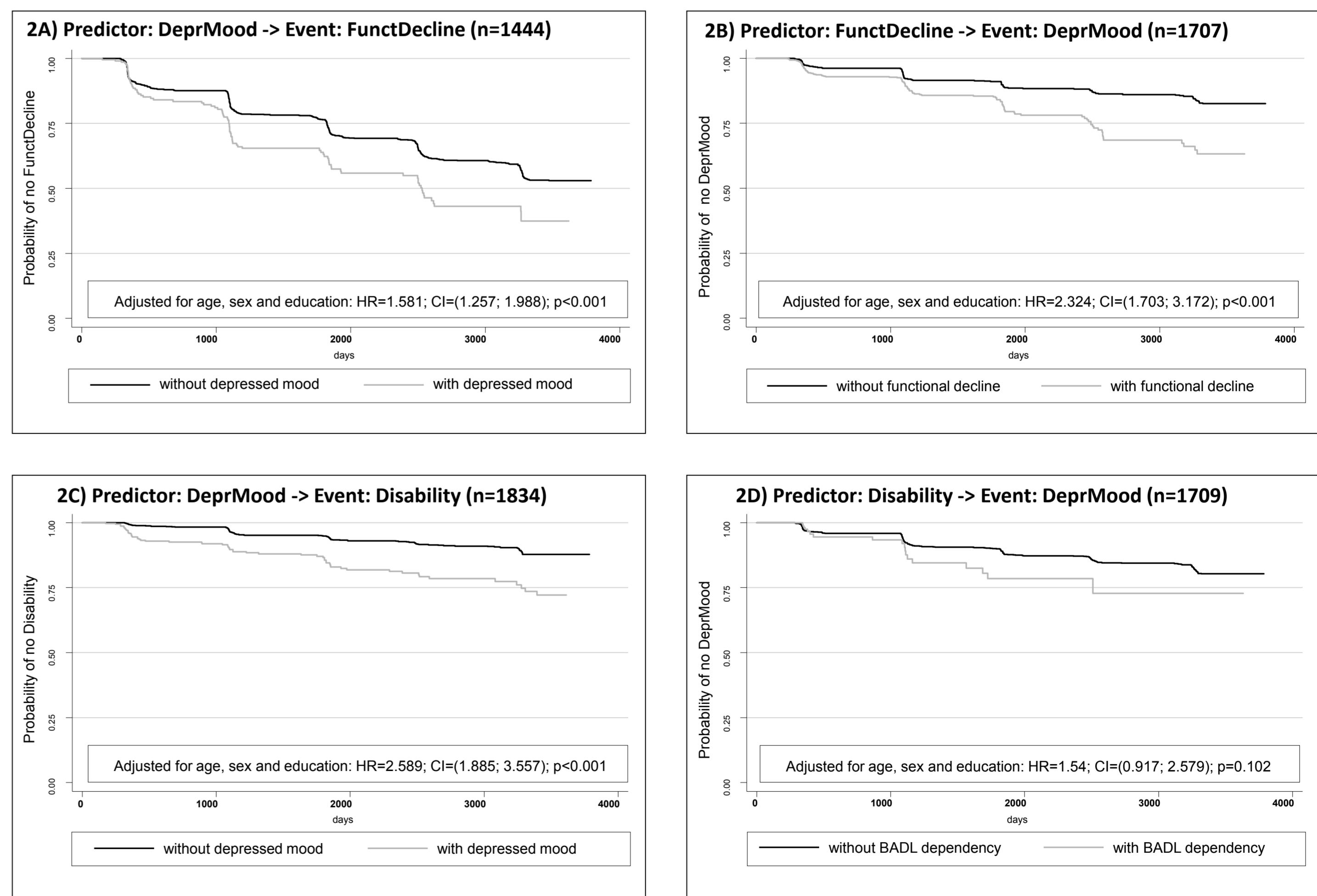
§These 431 individuals reported at no wave being in a depressed mood (DeprMood) before they experienced functional decline (FunctDecline)

||These 783 individuals reported at no wave being in a depressed mood (DeprMood) nor did they experience functional decline (FunctDecline)

Sample size in 2007:

n=2,012; average age 76.2 years (± 6.5); 63.1% women; higher education (A-level / secondary school) 39.9%. Prevalence of individuals with depressed mood 11.7%; frailty 25.6%, and had a disability 6.8%. **Main results (Fig. 2):** (1) depression significantly increased the hazard of subsequent frailty (HR=1.581; 95%CI 1.257-1.988; p<0.001); (2) frailty significantly increased the hazard of subsequent depression (HR=2.324; 95%CI 1.703-3.172; p<0.001); (3) depression significantly increased the hazard of subsequent disability (HR=2.589; 95%CI 1.885-3.557; p<0.001); (4) disability did not significantly increase the hazard of subsequent depression (HR=1.540; 95%CI 0.917-2.579; p=0.102).

Figure 2: Time-to-event analysis; for frequencies of time courses, predictors and event combinations see also Table 1



Tab.1 proved helpful for interpreting these results. First, for each analysis, the smallest and therefore crucial class was the one where both predictor and response were positive. The vast majority of older people in our cohort were not affected neither by frailty nor by disability or depressed mood.

Main conclusions: With six bi-yearly observations over ten years of the Longitudinal Urban Cohort Ageing Study (LUCAS), using time-to-event analyses with shifting baseline, we found solid evidence for an interacting process between depressed mood and functional decline, and depressed mood and disability. Obviously, there is a need for early screening to initiate appropriate community-based interventions on individual & community level.