

Supplementary Table 1 - Odds Ratio for pre-specified outcomes according to trajectory of depressive symptoms in subgroups divided by gender:

Outcome	Male (N = 8,331): OR (95% CI)	Female (N = 10,779): OR (95% CI)
Any outcome		
Non-depressed	REF	REF
Subthreshold depression	1.05 (0.89, 1.23)	1.35 (1.06, 1.34)
Persistent depression	1.83 (1.46, 2.29)	1.99 (1.61, 2.48)
Emerging depression	1.49 (1.15, 1.93)	1.32 (0.99, 1.76)
Disability		
Non-depressed	REF	REF
Subthreshold depression	1.49 (0.98, 2.26)	2.43 (1.72, 3.42)
Persistent depression	5.73 (3.70, 8.89)	4.17 (2.75, 6.31)
Emerging depression	2.58 (1.45, 5.59)	2.50 (1.45, 4.31)
Death		
Non-depressed	REF	REF
Subthreshold depression	0.96 (0.79, 1.18)	1.14 (0.91, 1.43)
Persistent depression	1.24(0.91, 1.70)	1.58 (1.51, 2.17)
Emerging depression	1.35 (0.99, 1.87)	1.09 (0.71, 1.66)
Cardiovascular disease (CVD)		
Non-depressed	REF	REF
Subthreshold depression	1.14 (0.91, 1.41)	1.09 (0.85, 1.41)
Persistent depression	1.19 (0.83, 1.69)	1.27 (0.86, 1.87)
Emerging depression	1.21 (0.82, 1.78)	1.40 (0.91, 2.16)
Dementia		
Non-depressed	REF	REF
Subthreshold depression	1.06 (0.80, 1.42)	1.15 (0.88, 1.51)
Persistent depression	1.09 (0.67, 1.78)	1.53 (1.03, 2.26.)

Emerging depression	1.48 (0.94, 2.35)	1.29 (0.78, 2.10)
Cancer		
Non-depressed	REF	REF
Subthreshold depression	1.19 (1.03, 1.37)	1.04 (0.88, 1.21)
Persistent depression	1.20 (0.95, 1.51)	1.21 (0.95, 1.54)
Emerging depression	1.53 (1.21, 1.94)	1.04 (0.77, 1.39)
Depression		
Non-depressed	REF	REF
Subthreshold depression	15.58 (12.65, 19.20)	13.72 (11.99, 15.70)
Persistent depression	127.26 (102.10, 158.61)	76.67 (65.85, 89.27)
Emerging depression	23.10 (18.38, 29.03)	16.31 (14.01, 19.00)
Major hemorrhage		
Non-depressed	REF	REF
Subthreshold depression	1.20 (0.92, 1.57)	1.28 (0.99, 1.66)
Persistent depression	1.65 (1.11, 2.46)	1.27 (0.84, 1.93)
Emerging depression	2.30 (1.57, 3.37)	1.40 (0.89, 2.22)

Footnote: Results from logistic regressions using generalized estimating equations (GEEs) with robust variance estimator and within-group exchangeable correlation matrix to account for clustered nature of data. Model was adjusted for age, gender, race, smoking, alcohol consumption, education, and living arrangement.

Supplementary Table 2 - Odds Ratio for pre-specified outcomes according to trajectory of depressive symptoms in subgroups divided by treatment group (placebo vs aspirin) and antidepressant use.

Outcome	Placebo group (N = 8,429)	Aspirin group (N=8,359)	Antidepressant use (N = 1,059)	Combination of aspirin and antidepressant (N = 1,065)
Any outcome	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Non-depressed	REF	REF	REF	REF
Subthreshold depression	1.03 (0.87, 1.22)	1.25 (1.06, 1.49)	1.51 (0.93, 2.45)	1.66 (0.97, 2.84)
Persistent depression	1.41 (1.07, 1.84)	2.21 (1.74, 2.81)	2.13 (1.26, 3.60)	2.32 (1.30, 4.15)
Emerging depression	1.37 (1.02, 1.84)	1.44 (1.07, 1.93)	1.26 (0.58, 2.72)	1.75 (0.78, 3.96)
Disability				
Non-depressed	REF	REF	REF	REF
Subthreshold depression	1.82 (1.25, 2.66)	1.98 (1.29, 3.03)	1.45 (0.56, 3.73)	3.16 (1.07, 9.37)
Persistent depression	4.55 (2.89, 7.15)	5.14 (3.09, 8.55)	3.38 (1.29, 8.87)	3.58 (1.14, 11.27)
Emerging depression	2.59 (1.46, 4.60)	2.08 (1.04, 4.14)	1.82 (0.44, 7.47)	5.39 (1.42, 20.49)
Death				
Non-depressed	REF	REF	REF	REF
Subthreshold depression	0.86 (0.68, 1.08)	1.15 (0.92, 1.44)	1.36 (0.69, 2.67)	1.15 (0.59, 2.22)
Persistent depression	0.91 (0.60, 1.39)	1.85 (1.34, 2.56)	1.52 (0.69, 3.34)	1.09 (0.49, 2.42)
Emerging depression	1.22 (0.82, 1.81)	1.51 (1.05, 2.16)	0.44 (0.11, 1.73)	0.49 (0.10, 2.31)
Cardiovascular disease (CVD)				
Non-depressed	REF	REF	REF	REF
Subthreshold depression	1.13 (0.89, 1.44)	1.13 (0.87, 1.46)	0.71 (0.34, 1.51)	1.08 (0.53, 2.22)
Persistent depression	1.09 (0.71, 1.67)	1.30 (0.85, 2.00)	0.89 (0.39, 2.01)	1.16 (0.52, 2.59)
Emerging depression	1.27 (0.82, 1.98)	1.49 (0.99, 2.26)	0.98 (0.33, 2.86)	0.28 (0.03, 2.24)
Dementia				

Non-depressed	REF	REF	REF	REF
Subthreshold depression	1.05 (0.78, 1.40)	1.15 (0.85, 1.55)	1.91 (0.73, 4.99)	0.83 (0.28, 2.43)
Persistent depression	0.81 (0.45, 1.46)	1.40 (0.86, 2.28)	2.05 (0.73, 5.69)	2.57 (0.94, 7.04)
Emerging depression	1.18 (0.69, 2.01)	1.38 (0.83, 2.30)	2.26 (0.62, 8.19)	2.39 (0.64, 8.89)
Cancer				
Non-depressed	REF	REF	REF	REF
Subthreshold depression	0.94 (0.80, 1.10)	1.26 (1.08, 1.47)	0.91 (0.55, 1.49)	2.07 (1.19, 3.62)
Persistent depression	1.18 (0.90, 1.54)	1.38 (1.06, 1.79)	0.77 (0.42, 1.43)	1.38 (0.70, 2.70)
Emerging depression	1.50 (1.15, 1.94)	1.33 (1.01, 1.75)	0.78 (0.31, 1.92)	0.40 (0.08, 1.85)
Depression				
Non-depressed	REF	REF	REF	REF
Subthreshold depression	15.47 (12.94, 18.49)	13.49 (11.42, 15.94)	12.69 (8.07, 19.95)	9.15 (6.08, 13.77)
Persistent depression	102.58 (84.29, 124.84)	90.20 (74.55, 109.14)	58.78 (36.54, 94.55)	50.76 (33.19, 77.62)
Emerging depression	20.09 (16.45, 24.55)	17.63 (14.59, 21.30)	15.03 (9.19, 24.57)	11.72 (7.61, 18.06)
Major hemorrhage				
Non-depressed	REF	REF	REF	REF
Subthreshold depression	1.29 (0.95, 1.76)	1.07 (0.82, 1.40)	5.16 (1.13, 23.40)	1.28 (0.65, 2.52)
Persistent depression	1.43 (0.85, 2.41)	1.09 (0.68, 1.73)	7.26 (1.57, 33.49)	1.19 (0.53, 2.65)
Emerging depression	2.17 (1.36, 3.46)	1.34 (0.86, 2.09)	8.92 (1.71, 46.48)	1.92 (0.75, 4.93)

Footnote: Results from logistic regressions using generalized estimating equations (GEEs) with robust variance estimator and within-group exchangeable correlation matrix to account for clustered nature of data. Model was adjusted for age, gender, race, smoking, alcohol consumption, education, and living arrangement.

Placebo and Aspirin sub-groups exclude users of antidepressant medication, individually investigated as shown in Supplement Table 4.

Supplementary Table 3: Model diagnosis and posterior classification data:

Number of trajectories	Number of parameters	Log-likelihood	AIC	BIC	Entropy	% in class1	% in class2	% in class3	% in class4	% in class5
<i>Best performing models with non-linear spline link function for each number for trajectories</i>										
1	14	-21313	442654	4427638	1.00	100.0	NA	NA	NA	NA
2	19	-215959	431955	432105	0.44	33.8	66.2	NA	NA	NA
3	22	-215879	431801	431974	0.57	65.8	2.0	32.2	NA	NA
4	25	-215827	431704	431900	0.49	39.0	9.3	6.6	45.5	NA
5	28	-215828	431712	431932	0.42	10.1	9.5	10.4	52.5	17.6
<i>Best performing models with linear link function for each number for trajectories</i>										
1	11	-247212	494446	494532	1.00	100.0	NA	NA	NA	NA
2	14	-245495	491018	491128	0.86	9.0	91.0	NA	NA	NA
3	17	-245525	491084	491218	0.42	9.3	90.7	0.0	NA	NA
4	20	-243903	487847	488004	0.86	80.8	6.9	1.9	10.3	NA
5	23	-245495	491035	491216	0.25	0.0	0.6	12.4	87.0	0.0

AIC, Akaike information criterion; BIC, Bayesian information criterion.

Entropy is used to measure accuracy of classification ranging from 0 to 1, with higher values of entropy indicating better classification. The AIC and BIC provide information on how well each model fit the data, with lower values indicating better model fit (reference). Log-likelihood represents the combination of model parameter values that maximize the probability of drawing the sample obtained (reference) with larger Log-likelihood indicating better consistency between model and obtained data.

Supplementary Table 4. Posterior classification probabilities and posterior probabilities above 60%, 80%, and 90% thresholds for the selected model.

	Class 1	Class 2	Class 3	Class 4
<i>Posterior classification probabilities</i>				
Class 1 membership probability	61	21	28	13
Class 2 membership probability	9	72	5	0
Class 3 membership probability	17	7	55	62
Class 4 membership probability	13	0	12	81
<i>Posterior probabilities above a threshold</i>				
Class membership probability >70%	23	58	12	72
Class membership probability >80%	4	39	4	59
Class membership probability >90%	0	24	1	42

Class 1= Subthreshold depression class; Class 2= Persistent depression class; Class 3=Emerging depression class, Class 4= non-depressed

Posterior classification probabilities show the average estimated probability of being in a class in participants who were classified in a class. For example, the average probability of being classified to class 1, class 2, class 3, and class 4 in those who were classified to class 1 were 61%, 9%, 17%, and 13%, respectively.

Posterior probabilities above a threshold shows the proportion of participants in each class whose probability of being classified to their class was above a threshold. For example, among 42% of those who classified in class 4, the estimated probability of being classified to class 4 was greater than 90%.

Supplementary Table 5 - Evaluating Criterion validity: Evaluating the role of socio-demographics in predicting group classification membership

Age	OR	95% CI	p-value
Subthreshold depression	0.99	0.98, 1.00	0.005
Persistent depression	0.96	0.94, 0.97	<0.001
Emerging depression	1.01	1.00, 1.03	0.050
Gender			
<i>Male</i>	-	-	
Subthreshold depression	0.85	0.79, 0.92	<0.001
Persistent depression	0.73	0.64, 0.83	<0.001
Emerging depression	0.96	0.96, 1.10	0.6
Living Status			
<i>At home alone in a residential home</i>	-	-	
Subthreshold depression	0.92	0.85, 1.15	0.022
Persistent depression	0.75	0.66, 0.95	<0.001
Emerging depression	1.23	1.07, 1.41	0.003
Race/ Ethnicity			
<i>White/ Caucasian</i>	-	-	
Subthreshold depression	0.99	0.86, 1.15	>0.9
Persistent depression	0.93	0.73, 1.18	0.6
Emerging depression	0.81	0.61, 1.08	0.2
Education			
<i><= 12 yrs education</i>	-	-	
Subthreshold depression	0.91	0.85, 0.97	0.007
Persistent depression	0.79	0.70, 0.90	<0.001
Emerging depression	0.82	0.73, 0.93	0.002
Smoking status			
<i>Never</i>	-	-	
<i>Former:</i> Subthreshold depression	1.08	0.89, 1.30	0.4
Persistent depression	0.85	0.64, 1.13	0.3
Emerging depression	0.89	0.64, 1.23	0.5
<i>Current:</i> Subthreshold depression	0.95	0.78, 1.14	0.6
Persistent depression	0.71	0.54, 0.95	0.020
Emerging depression	0.80	0.58, 1.10	0.2
Alcohol use			
<i>Current</i>	-	-	
<i>Former:</i> Subthreshold depression	0.94	0.81, 1.09	0.4
Persistent depression	1.25	0.99, 1.58	0.062
Emerging depression	1.09	0.84, 1.42	0.5
<i>Never:</i> Subthreshold depression	0.79	0.72, 0.87	<0.001
Persistent depression	0.83	0.70, 0.98	0.031
Emerging depression	0.97	0.82, 1.15	0.7
Body mass index (BMI) categories			
<i><=25 kg/m²</i>	-	-	-

<i>25-30 kg/m²</i>			
Subthreshold depression	0.87	0.80, 0.95	0.002
Persistent depression	0.90	0.77, 1.05	0.2
Emerging depression	0.91	0.78, 1.06	0.2
<i>30-35 kg/m²</i>			
Subthreshold depression	0.87	0.79, 0.97	0.010
Persistent depression	0.87	0.73, 1.04	0.13
Emerging depression	0.92	0.76, 1.10	0.3
<i>35 or more kg/m²</i>			
Subthreshold depression	0.84	0.72, 0.97	0.016
Persistent depression	0.80	0.63, 1.02	0.077
Emerging depression	0.87	0.67, 1.13	0.3
Quality of life scores			
<i>Physical component score</i>			
Subthreshold depression	0.93	0.92, 0.93	<0.001
Persistent depression	0.89	0.88, 0.89	<0.001
Emerging depression	0.96	0.95, 0.96	<0.001
<i>Mental component score</i>			
Subthreshold depression	0.87	0.87, 0.88	<0.001
Persistent depression MCS	0.78	0.78, 0.79	<0.001
Emerging depression MCS	0.93	0.92, 0.94	<0.001
Number of medical comorbidities			
<i>1</i>			
Subthreshold depression	0.96	0.82, 1.14	0.7
Persistent depression	1.16	0.82, 1.65	0.4
Emerging depression	1.07	0.78, 1.46	0.7
<i>2</i>			
Subthreshold depression	0.95	0.81, 1.12	0.6
Persistent depression	1.13	-0.80, 1.58	0.5
Emerging depression	1.03	0.76, 1.40	0.8
<i>3</i>			
Subthreshold depression	1.03	0.87, 1.22	0.7
Persistent depression	1.22	0.87, 1.72	0.3
Emerging depression	1.15	0.84, 1.57	0.4
<i>4 or more</i>			
Subthreshold depression	1.12	0.94, 1.34	0.2
Persistent depression	1.36	0.95, 1.94	0.089
Emerging depression	1.23	0.88, 1.71	0.2
Polypharmacy			
Subthreshold depression	1.13	1.03, 1.24	0.011
Persistent depression	1.27	1.09, 1.47	0.002
Emerging depression	1.29	1.10, 1.51	0.002

Footnote: Results from unadjusted multinomial logistic regressions.