BJPsych | The British Journal of Psychiatry (2024)
225, 321–327. doi: 10.1192/bjp.2024.84

Original Article

Mapping 15-year depressive symptom transitions in late life: population-based cohort study

Federico Triolo, Davide Liborio Vetrano, Caterina Trevisan, Linnea Sjöberg, Amaia Calderón-Larrañaga, Martino Belvederi Murri, Laura Fratiglioni and Serhiy Dekhtyar

Background

The longitudinal course of late-life depression remains understudied.

Aims

To describe transitions along the depression continuum in old age and to identify factors associated with specific transition patterns.

Method

We analysed 15-year longitudinal data on 2745 dementia-free persons aged 60+ from the population-based Swedish National Study on Aging and Care in Kungsholmen. Depression (minor and major) was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision; subsyndromal depression (SSD) was operationalised as the presence of ≥2 symptoms without depression. Multistate survival models were used to map depression transitions, including death, and to examine the association of psychosocial (social network, connection and support), lifestyle (smoking, alcohol consumption and physical activity) and clinical (somatic disease count) factors with transition patterns.

Results

Over the follow-up, 19.1% had ≥1 transitions across depressive states, while 6.5% had ≥2. Each additional somatic disease was associated with a higher hazard of progression from no depression (No Dep) to SSD (hazard ratio 1.09; 1.07–1.10) and depression (Dep) (hazard ratio 1.06; 1.04–1.08), but also with a lower recovery ($HR_{SSD–No\ Dep}$ 0.95; 0.93–0.97 [where 'HR' refers to 'hazard ratio']; $HR_{Dep–No\ Dep}$ 0.96; 0.93–0.99). Physical activity was associated with an increased hazard of recovery to no depression from SSD (hazard ratio 1.49; 1.28–1.73) and depression (hazard ratio 1.20; 1.00–1.44), while a richer social network was associated with both higher recovery from ($HR_{SSD–No\ Dep}$ 1.44; 1.26–1.66; $HR_{Dep–No\ Dep}$ 1.51; 1.34–1.71) and lower progression hazards to a worse depressive state ($HR_{No\ Dep–SSD}$ 0.81; 0.70–0.94; $HR_{No\ Dep–Dep}$ 0.58; 0.46–0.73; $HR_{SSD–Dep}$ 0.66; 0.44–0.98).

Conclusions

Older people may present with heterogeneous depressive trajectories. Targeting the accumulation of somatic diseases and enhancing social interactions may be appropriate for both depression prevention and burden reduction, while promoting physical activity may primarily benefit recovery from depressive disorders.

Keywords

Late-life depression; transitions; risk factors; recovery; subthreshold depression.

Depression in older people represents a multifaceted condition associated with high individual burden and societal costs.[1] Besides its impact on quality of life and well-being, depression in old age, including both its milder and more severe clinical presentations, has been linked with accelerated biological ageing, disability and premature mortality.[1,2] Similar to other geriatric syndromes, such as sarcopenia and frailty, depression can be viewed as a multifactorial and potentially reversible condition with heterogeneous clinical trajectories.[3–5] While identifying individuals at risk of developing more severe depression is key for prevention, characterising those more likely to revert from depression to milder states or non-depression may also be important for planning and implementing effective interventions in those already affected by the disorder.

The natural course of late-life depression has been described as highly heterogeneous, with recurrence rates ranging from 25 to 44% and remission rates from 13 to 23%.[6–9] Such evidence stems from studies based on observations of initially depressed people from primary or psychiatric care services[7,8] or population-based cohorts.[6,9] Fewer studies have investigated the transitions along different depressive states within population-based cohorts, capturing both the development of symptoms in non-depressed individuals and their potential remission in those with depression.[10] As depression can be conceptualised as a continuum of severity that spans from absence of clinical symptoms to milder and more severe forms, describing how older people transition across different severity states may improve our understanding of this syndrome throughout the ageing process.

In addition to describing diverse trajectories of depression in older adults, it is crucial to identify potentially modifiable factors that are differentially associated with specific patterns of transition, such as progressing to more severe states or recovering from severe states to milder ones. This is particularly critical given the concern for potentially lower efficacy and higher risk of pharmacological treatment side-effects in frail older adults. The modifiable risk and protective factors implicated in depression in late life are diverse, span multiple life stages and overlap with factors linked to the ageing process.[11–14] For instance, factors such as the burden of somatic diseases, the extent and quality of social relationships and physical activity engagement have been associated with the ageing process, as well as depression in old age.[15–17] However, the contribution of these factors to the likelihood of transitioning across the spectrum of depressive states remains unclear. Importantly, these factors can themselves change considerably with ageing. Accounting for such longitudinal variation both in outcome transitions and in their associated factors is essential for providing a comprehensive description of depression occurrence in old age, which could reinforce clinical guidelines already

https://doi.org/10.1192/bjp.2024.84 Published online by Cambridge University Press

recommending psychosocial intervention for individuals with depression and complex health needs.[18]

Within a population-based cohort of older adults, we aimed to map 15-year transitions across depressive states (i.e. no depression, subsyndromal depression and depression) and to examine the association of time-varying psychosocial, behavioural and clinical factors with different transition patterns. We hypothesised that the course of old-age depression would be characterised by considerable heterogeneity, and that the aforementioned factors would be differentially associated with specific transition patterns.

Method

Study population

This study used longitudinal data from the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K, http://www.snac-k.se/). SNAC-K is an ongoing population-based study initiated in 2001 examining people aged 60+ residing in the urban district of Kungsholmen in Stockholm, Sweden. Out of the 5111 randomly sampled individuals within specific age cohorts (i.e. 60, 66, 72, 78, 81, 84, 87, 90, 93, 96 and 99+ years) from the Kungsholmen population, 3363 (73% participation rate) agreed to participate in the baseline examination (2001–2004). It comprised a comprehensive and standardised health assessment, which was carried out by healthcare professionals, and was repeated every 3 (for age cohorts 78+ years) or 6 years (age cohorts 60–72 years). The present work considers data from baseline (2001–2004) to wave 6 (2016–2019), for a 15-year follow-up. Participants were linked through their personal identification numbers to the Swedish National Patient and Cause of Death registers to trace their health histories and survival status over the follow-up. In this study, from the total sample initially enrolled, participants with a baseline diagnosis of dementia ($n = 240$) or intellectual disability ($n = 1$) were excluded, along with those who refused to undergo the medical examination ($n = 10$). Participants who dropped out of the study before their first follow-up were excluded ($n = 367$), resulting in the analytical sample of 2745 individuals (see Supplementary Table 1 available at https://doi.org/10.1192/bjp.2024.84 for comparison of descriptive characteristics).

SNAC-K has been authorised by the Karolinska Institutet Ethics Committee and the Regional Ethical Review Board in Stockholm in accordance with the Helsinki Declaration of 1975 and its subsequent modifications. The approval numbers for the study are: 01–114, 04–929/3, Ö26–2007, 2009/595–32, 2010/447–31/2, 2013/828–31/3 and 2016/730–31/1. All participants gave written informed consent at each examination, either personally or through their next of kin for those with cognitive impairment.

Depressive status

Trained physicians assessed depressive symptoms using the Comprehensive Psychopathological Rating Scale (CPRS) at baseline and follow-up examinations. CPRS is an interview-based tool to rate the presence and severity of psychiatric symptoms and behaviours. Following a previously described algorithm, specific CPRS items were employed to ascertain the nine diagnostic criteria for depression according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR).[19] The depressive status of each participant was classified based on the number and combination of diagnostic criteria: (a) depression, defined as major or minor depression (presence of at least two diagnostic criteria, with one being either low mood or loss of interest); (b) subsyndromal symptomatic depression (SSD), defined by the presence of at least two diagnostic criteria in the absence of major or minor depression;[20] and (c) no depression in case of absence of the aforementioned conditions.

Predictors of depressive transitions

Psychosocial factors: index of social network

At each examination, a composite index was computed to evaluate the size and quality of social networks by combining the domains of social connection and social support. Social connection was assessed through the number of relationships, marital status, living situation, social network size and frequency of direct or remote contact. Social support incorporated information on the perceived level of support, satisfaction with relationships, and the sense of affinity and belonging to a social circle (please see Triolo et al[21] for a comprehensive description of all items included in the social connections and support measures). For each study wave, we first standardised individual indicators based on the baseline mean and standard deviation values, averaged the resulting z-scores separately within the connection and support domains, and subsequently combined the two domain scores into a composite index of social network (mean correlation between social connections and support across all waves: 0.60). In the analysis, social network was used as a continuous variable (z-score range across all waves: −2.17 to 1.27). In secondary analysis, the continuous indices of social connections and social support were used separately to disentangle the effect of social network's subcomponents.

Behavioural factors: lifestyle behaviours

Lifestyle behaviours were captured at each examination through questionnaires administered by trained nurses. Smoking was classified as current versus non-current smoker. Alcohol consumption was defined as none or occasional (none up to three drinks/month) versus moderate-to-heavy use (at least one drink/week). Physical activity was defined in accordance with the World Health Organization recommendations and was dichotomised as active (engagement in light and/or moderate-to-intense exercise several times a week) versus inactive (engagement in such activities ≤3 times per month).[22]

Clinical factors: somatic disease burden

Somatic disease burden was operationalised as the count of somatic diseases, which were ascertained and updated at each examination through a combination of different sources, including the SNAC-K clinical assessment performed by physicians, medications, laboratory testing, and out-patient and in-patient diagnoses retrieved from the Swedish National Patient Register.[23] Following previous studies from our group,[2] we used a list of 54 somatic diseases with clinical relevance for older people, excluding psychiatric conditions and dementia (Supplementary Table 2 for disease list with prevalence; we refer to Calderón-Larrañaga et al[23] for the complete description of information sources and list of codes from the International Classification of Diseases – 10th Revision (ICD-10). In the analyses, somatic disease count was used as a continuous variable (baseline range 0–16).

Covariates

Sociodemographic information on age, gender and formal educational attainment (operationalised as high school and below versus university) was collected at baseline during the nurse interview. Antidepressant use (yes versus no) was assessed at each examination through the medication list provided by the participant, which was reviewed by the physician and coded according to the Anatomical Therapeutic Chemical (ATC drug classes N06A) system. History of depression before baseline was examined during the medical interview through self-report and was

https://doi.org/10.1192/bjp.2024.84 Published online by Cambridge University Press

operationalised as presence or absence. Gait speed was used as a proxy of frailty and was measured at each study wave over 6 m, or 2.4 m if the person reported walking slowly or the assessment was carried out in limited space. A cut-off of 0.8 m/s was adopted based on its association with mortality in community-dwelling older adults.[24] For descriptive reasons, the Mini Mental State Examination (MMSE) was used as a global measure of cognition at baseline.

Statistical analysis

The characteristics of the analytical sample were tabulated and compared across baseline depressive states with Student's *t*-test and $\chi 2$ test as appropriate. The flow of individuals through depressive states over the 15-year follow-up, along with study exits due to drop-out or mortality, were graphically represented with an alluvial plot. Markov multistate survival modelling was used (see Supplementary Figure 1 for the specified model), incorporating three depressive states (no depression, subsyndromal symptomatic depression (SSD) and depression) and death as an absorbing state, resulting in three progression transitions, three recovery transitions and three transitions to death.[25] Given the episodic nature of depression, individuals were allowed to move to and revert from non-adjacent states (e.g. from no depression to depression). In Supplementary Table 4 we present baseline characteristics of individuals exhibiting different transition patterns, tabulated according to transition type (i.e. no transition, progression or recovery) and frequency.

For each transition, we explored the association of psychosocial (social network), behavioural (physical activity, alcohol consumption and smoking) and clinical (somatic disease burden) factors in models further adjusted for age, gender and education. All main exposures were entered as time-varying variables, updated at the wave preceding the transition. Age was adopted as the timescale, with participants contributing from study entry until loss-to-follow-up, death or study end. To limit missing data on depression and explanatory factors in participants who otherwise attended the study visits, multiple imputation by chained equations was performed. At each examination, variables with missing values (proportion missing over the total population ranged from 0.004 to 19%) were imputed into 20 datasets employing all predictors and outcomes used in the model. We also added the full range of 60 chronic conditions, which had no missing information, as auxiliary information in the imputation model to improve prediction.[23] A multistate survival model was computed in each imputed data-set, and hazard ratios with 95% confidence intervals were pooled to estimate the association between each factor and different transitions using Rubin's rule. All analyses were performed with STATA 17 for Windows (StataCorp, College Station, TX) and R for Windows (R Foundation for Statistical Computing, version 4.3.0).

Sensitivity analysis

To account for the influence of depression vulnerability and treatment in the association between depressive transitions and their correlates, the analyses were repeated with additional adjustment for the history of depression and the use of antidepressant medication (the latter was entered as time-varying). Further time-varying adjustment for gait speed was also performed as a measure of frailty.

Results

The analytical sample included 2745 individuals, whose baseline characteristics according to depressive status at study entry are reported in Table 1.

Up to 10% of the analytical sample presented with any depressive state at baseline, of which 4% with SSD and 6% with depression (major or minor). Compared with those with no depression, individuals with any depressive state were more likely to be older, female, less educated, current smokers and with higher somatic burden. Further, they were less physically active, had poorer social networks and were less likely to be heavy drinkers. Last, they were more likely to report a history of depression and current antidepressant use. Compared with individuals with SSD, those with depression tended to be current smokers, physically inactive and with a poorer social network, while presenting with higher education and slightly fewer somatic diseases.

The flow of individuals across depressive states over a 15-year follow-up is visually presented in Fig. 1, while the total number of underlying transitions is reported in Supplementary Table 3. Among participants with at least one repeated measurement over the follow-up, the majority (75.6%) did not experience any depressive state (at either baseline or over the follow-up), while 4.5% with any depressive state at baseline either maintained their depressive status (28.1%) or died before the first follow-up (71.9%) (Supplementary Table 4). Conversely, 19.9% of study participants experienced at least one transition across depressive states during the follow-up, while 6.5% had two or more transitions.

Participants' baseline characteristics based on the type of transitions experienced over the follow-up (i.e. no transition, progression to a worse depressive state or recovery to a better state) are presented in Supplementary Table 4. Of those individuals who experienced at least one progression to a worse state, those reaching depression as their worst outcome were more likely to have higher smoking levels, poorer social networks, a prior history of depression and antidepressant use, compared with those who reached SSD as their worst state (Supplementary Table 4). Of those who had at least one recovery, there were no differences in

Table 1 Baseline characteristics of the study sample according to baseline depression status

	Total	No depression	Subsyndromal depression	Depression[a]	Missing	
	N = 2745	*n* = 2454, 89%	*n* = 112, 4%	*n* = 154, 6%	*n* = 25, 1%	*P*-value
Age, mean (s.d.)	73.8 (10.7)	73.1 (10.5)	79.9 (10.2)	78.3 (11.8)	84.6 (10.4)	<0.001
Gender (women), *n* (%)	1737 (63.3%)	1537 (62.6%)	80 (71.4%)	103 (66.9%)	17 (68.0%)	0.19
Education (university), *n* (%)	942 (34.4%)	881 (36.0%)	19 (17.0%)	38 (24.7%)	4 (18.2%)	<0.001
Alcohol (moderate-to-heavy use), *n* (%)	1805 (66.2%)	1671 (68.4%)	54 (48.6%)	73 (48.3%)	7 (36.8%)	<0.001
Smoking (current), *n* (%)	388 (14.3%)	330 (13.5%)	21 (19.1%)	35 (23.0%)	2 (10.5%)	0.005
Physical activity (active), *n* (%)	1817 (76.9%)	1697 (78.3%)	49 (66.2%)	61 (56.0%)	10 (76.9%)	<0.001
Social network index,[b] mean (s.d.)	0.0 (0.5)	0.1 (0.5)	−0.2 (0.6)	−0.4 (0.6)	−0.3 (0.7)	<0.001
History of depression, *n* (%)	356 (13.2%)	287 (11.8%)	21 (18.9%)	46 (31.9%)	2 (10.0%)	<0.001
Somatic disease count, mean (s.d.)	3.8 (2.4)	3.7 (2.3)	5.3 (2.8)	4.8 (2.6)	4.8 (3.2)	<0.001
MMSE, mean (s.d.)	28.5 (2.2)	28.7 (1.8)	27.4 (3.4)	26.9 (3.6)	23.3 (8.2)	<0.001
Antidepressant use, *n* (%)	230 (8.4%)	164 (6.7%)	20 (17.9%)	43 (27.9%)	3 (12.0%)	<0.001

MMSE, Mini Mental State Examination.
a. Depression refers to the presence of either major or minor depression according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision.
b. Z-score of multiple quantitative and qualitative measures of social relationships; see methods for details.

https://doi.org/10.1192/bjp.2024.84 Published online by Cambridge University Press

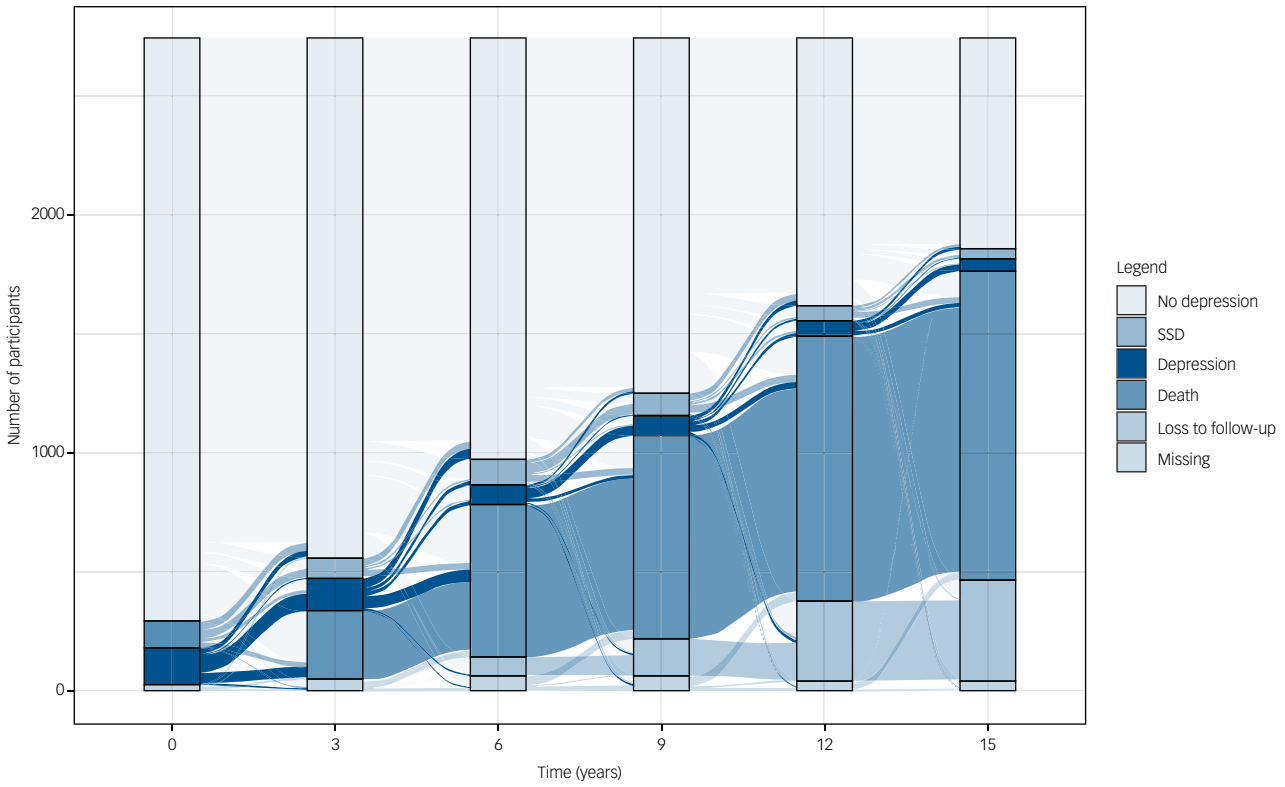

Fig. 1 Alluvial plot depicting transitions between no depression, subsyndromal symptomatic depression (SSD), depression, death and loss to follow-up.

baseline characteristics between those who reached SSD, compared with those who fully recovered to no depression. Of note, more of those who reached SSD as their best recovery state had at least two transitions (across both progression and recovery directions) than those who had reached no depression.

The association between individual factors and transitions across depressive states are reported in Fig. 2 (Supplementary Table 5 for all estimates).

In multi-adjusted models, for each additional somatic disease, there was an increased hazard of progression from no depression

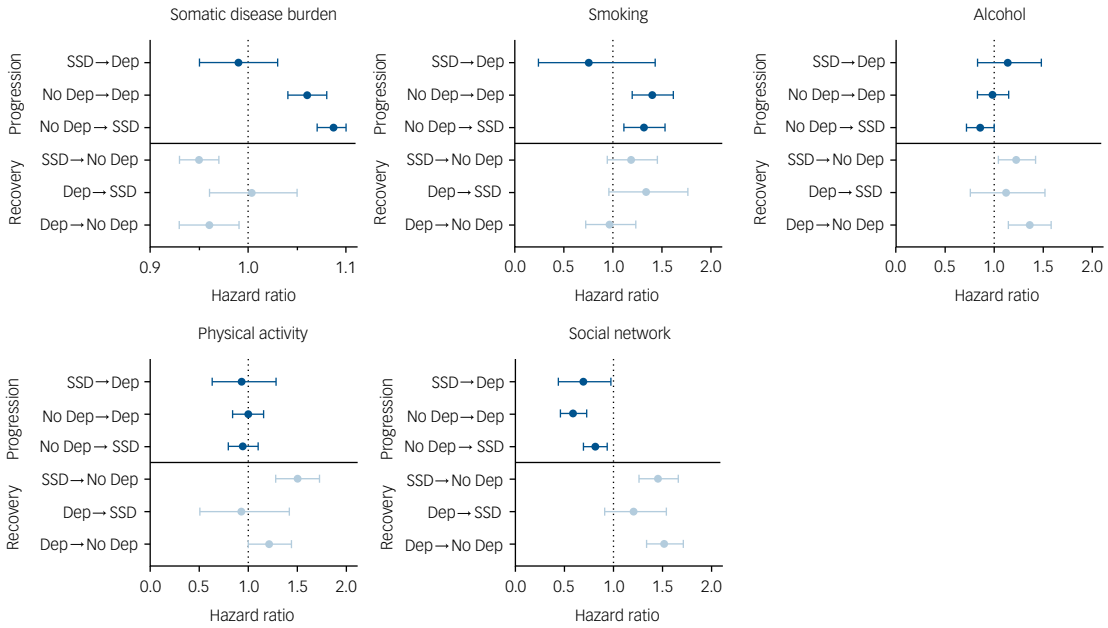

Fig. 2 Adjusted hazard ratios with 95% CI for the association between specific transitions across depressive states and their predictors. Adjusted hazard ratios were estimated from the same model, additionally adjusted for age, gender and education. Underlying point estimates are presented in Supplementary Table 5. Somatic disease burden (continuous), smoking (current versus non-current), alcohol (moderate-to-heavy versus no-to-occasional), physical activity (active versus inactive), social network (continuous). SSD, subsyndromal symptomatic depression; Dep, depression; No Dep, no depression.

https://doi.org/10.1192/bjp.2024.84 Published online by Cambridge University Press

to both SSD and depression (hazard ratio 1.09; 95% CI 1.07–1.10; and hazard ratio 1.06; 95% CI 1.04–1.08, respectively). Further, smoking was associated with a higher transition hazard from no depression to SSD (hazard ratio 1.31; 95% CI 1.11–1.54) and depression (hazard ratio 1.39; 95% CI 1.20–1.62), while moderate-to-heavy alcohol use was predictive of reduced transition hazard from no depression to SSD (hazard ratio 0.85; 95% CI 0.72–1.00). Conversely, a richer social network was associated with a decreased hazard of transitioning from no depression to both SSD (hazard ratio 0.81; 95% CI 0.70–0.94) and depression (hazard ratio 0.58; 95% CI 0.46–0.73), as well as from SSD to depression (hazard ratio 0.66; 95% CI 0.44–0.98). Of note, higher levels of social support were associated with a decreased likelihood of progression from no depression to SSD (hazard ratio 0.81; 95% CI 0.70–0.95) and depression (hazard ratio 0.67; 95% CI 0.55–0.82), while this pattern was not observed for social connections (Supplementary Table 6).

A higher number of somatic diseases was associated with a lower transition hazard from both SSD (hazard ratio 0.95; 95% CI 0.93–0.97) and depression (hazard ratio 0.96; 95% CI 0.93–0.99) to no depression. Further, engagement in physical activity was associated with an increased hazard of moving from SSD (hazard ratio 1.49; 95% CI 1.28–1.73) and depression (hazard ratio 1.20; 95% CI 1.00–1.44) to no depression, as was alcohol consumption (hazard ratio 1.22; 95% CI 1.05–1.42; and hazard ratio 1.35; 95% CI 1.15–1.58, respectively). Last, a higher transition hazard from both SSD (hazard ratio 1.44; 95% CI 1.26–1.66) and depression (hazard ratio 1.51; 95% CI 1.34–1.71) to no depression was observed for participants with richer social network. This association was present for both social support (hazard ratio 1.18; 95% CI 0.99–1.39 (SSD–no depression); hazard ratio 1.40; 95% CI 1.22–1.60 (depression–no depression)) and social connections (hazard ratio 1.32; 95% CI 1.15–1.52) (SSD–no depression)), although for the latter, the association with the depression–no depression transition was attenuated (hazard ratio 1.14; 95% CI 0.96–1.35) (Supplementary Table 6).

Sensitivity analysis

Additional adjustment for history of depression, antidepressant use and gait speed (as a measure of frailty) did not alter the trend of the results beyond a loss of statistical significance for the estimates on physical activity (see Supplementary Table 7 for detailed information).

Discussion

In this longitudinal study, we described how older community-dwellers transitioned across depressive spectrum states over 15 years, and identified factors associated with changes in depressive status. Our findings suggested that a considerable proportion of participants exhibited diverse patterns of transitions, involving both progression and recovery transitions. Further, clinical, lifestyle and psychosocial predictors were associated with different transitions, reinforcing the notion that the longitudinal course of depressive states in old age is a product of factors across multiple domains.

Depression transitions during ageing

We found that the majority of the participants (75.6%) did not experience any depression at either baseline or during the 15-year follow-up. A previous multi-cohort study exploring the stability of depressive symptoms found 85% of older participants to be free of depression during the study period.[10] The slight discrepancy with our findings may be due to multiple reasons, including the different lengths of follow-ups (4–11 years) and the study designs of the cohorts included. Further, the methods of depression ascertainment may play a role, as our assessment included an intermediate state of subsyndromal depression, which could also account for the lower share of ever-depression-free persons in our data.[10] Importantly, our findings suggest that up to 24.4% of older adults may experience any depression state during ageing, with 19.1% experiencing at least one change in depressive state over time. This underlines how depression occurrence in old age is characterised by a degree of variability, similar to that observed in other geriatric syndromes such as sarcopenia and frailty.[4,5] These findings emphasise the importance of regular and comprehensive monitoring in old age to ensure appropriate interventions are implemented.

Depressive transitions and associated factors

As for the predictors of progression, we found somatic disease burden and smoking to be associated with a higher hazard of transitioning from no depression to more severe states, while higher levels of social support (but not connections) and higher alcohol consumption were predictive of reduced progression hazards. Conversely, for recovery, richer social network, higher physical activity levels and alcohol use were associated with increased probabilities of transitioning from more to less severe depression states, while higher somatic burden was associated with reduced recovery probabilities.

Somatic disease burden

Multiple studies have observed a link between a higher burden of chronic diseases and the development and recurrence of depression in late life, although fewer studies have examined depression remission.[16] In the study by de la Torre-Luque et al (2019), greater multimorbidity was associated with development and persistence of depression, but also with remission.[10] We observed that a higher count of somatic diseases was associated with a higher hazard of transitioning from no depression to both SSD and depression, but not with progression from SSD to depression. Further, a higher number of diseases was associated with a lower hazard of recovery, that is, transitioning from any depression state to no depression. Overall, these results are in line with previous evidence suggesting that the number of chronic diseases is associated with increased progression across the entire depressive continuum, including subsyndromal states.[9] It can be hypothesised that the accumulation of multiple chronic diseases, captured here through its variation over time, may diminish the resilience levels of older people with depression, thereby reducing recovery and increasing progression rates.[26] Several pathways may explain why individuals with high disease burden are more likely to progress along the depressive spectrum, including an increased biological, psychological and care-related burden.[27] The number of diseases is a useful yet crude measure to detect vulnerability to depression, and further research to identify specific disease patterns implicated in the progression of depression may help uncover underlying mechanisms and provide a more precise characterisation of individuals at risk.

Social network

We found that a richer social network was associated with a decreased likelihood of depression progression and an increased likelihood of recovery. Interestingly, the negative progression hazards appeared to be mainly driven by the social support component, which was a novel finding. Emotional and instrumental support have been suggested as the axes through which social relationships affect psychological health,[28] and future studies may

https://doi.org/10.1192/bjp.2024.84 Published online by Cambridge University Press

examine these aspects in greater detail. By considering time-varying measures of social network, we were able to capture the potential changes in social relationships that oftentimes occur alongside other age-related events. While the influence of social relationships on the development of late-life depression has been extensively studied,[15] we simultaneously highlighted how a richer social network was associated with a reduced hazard of transitioning from no depression to SSD, as well as with a subsequent progression from SSD to depression.[9] Given the increased risk of unfavourable depressive outcomes for older individuals with subsyndromal depression,[6,9] preventing its occurrence and progression to more severe depression states through social integration could be critical. Further, our results showed how higher social network levels in individuals with any depressive states were predictive of recovering to more favourable ones. These findings are in line with previous studies suggesting how different structural and functional components of social interactions are associated with both remission and symptom decrease in middle- to old-aged people with depression.[29,30] This reinforces the view that social relationships play an important role in the course of depression in older people, potentially constituting a target for interventions in the stepped care for depression in individuals with physical health issues as reported in the clinical recommendations from the National Institute for Health and Care Excellence (NICE).[18,31]

Lifestyle behaviours

Last, we observed that lifestyle behaviours were differentially associated with depression transitions in old age. Although we did not find evidence of a reduced likelihood of transitioning from no depression to any depressive state, physical activity was associated with recovery from any depressive state to no depression. This finding aligns with the growing evidence supporting physical activity as an effective intervention for people with depression.[32] As for smoking, we observed that individuals who were current smokers had an increased likelihood of progressing from no depression to both SSD and depression. This finding is consistent with previous literature reporting detrimental effects of smoking on depression risk, as well as progression from subsyndromal to major depression in old age.[9,11] Last, moderate-to-heavy alcohol consumption was linked to a higher likelihood of transitioning to no depression from any depressive states, and lower likelihood to transition from no depression to SSD. While this may be counterintuitive given the overall negative influence of alcohol drinking on health, mixed results have been reported in relation to late-life depression,[8,9,11] which may be due to the healthy survivor effects in longitudinal cohort studies. Overall, these results show that a complex pattern of lifestyle behaviours influences depression transitions, which may provide insights for the design and implementation of interventions to effectively prevent and/or reduce the burden of depression in old age.

Strengths and limitations

This study contains several strengths and points of originality: (a) the population-based setting with 15-year follow-up with a relatively high participation rate, (b) the wide spectrum of depressive states ranging from no depression to different severity levels of depression, derived through clinical examinations, and (c) the detailed information on somatic health, lifestyle behaviours and social interactions assessed at each wave by trained physicians and nurses, which was modelled as time-varying to account for their potential changes throughout ageing.

This study presents several limitations that require acknowledgement. First, we aggregated the diagnoses of major and minor depression into a combined outcome due to a low occurrence of major depression. Further, we did not consider bipolar disorder, given the low number of cases. While this may be linked to the relatively better overall health of this population-based cohort, we recognise that including minor depression as a separate state, as well as considering depressive episodes in the context of bipolar disorder, could have improved the understanding of the depressive continuum in old age. Second, the relatively long time interval between assessments may conceal some of the depressive transitions, and studies with more frequent follow-ups should replicate our findings. Third, participant drop-out may have affected the associations towards an underestimation, although accounting for mortality by including death as an additional state should have minimised this effect. Fourth, the somatic disease burden measure did not account for severity of single diseases, which can influence depression transitions. The crude count of diseases can, however, capture the cumulative burden of diseases and be easily obtained in research and clinical settings. Fifth, missing data reached up to 19% on some predictors, which we dealt with using multiple imputation. Sixth, intervention studies are warranted to provide specific recommendations for physical and social interventions in people with different levels of depression severity. Last, the external validity of the findings should be carefully appraised, given the relatively high socioeconomic status and the homogeneous ethnic composition (predominantly Nordic) of the SNAC-K study sample.

Conclusions

In conclusion, this population-based study contributes to our understanding of depression in old age by examining transitions across depressive states over a 15-year period and identifying factors associated with these transitions. We observed that a higher burden of somatic diseases was linked to progression toward more severe depressive states, while having a rich social life and engaging in physical activity were associated with an increased recovery toward less severe states. These results emphasise depression in late life as a condition with heterogenous trajectories and underscore the importance of interventions aimed at preserving somatic health and fostering social integration and physical activity to enhance the prevention and management of depression in older adults.

Federico Triolo, MD, PhD, Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Sweden; **Davide Liborio Vetrano**, MD, PhD, Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Sweden; and Stockholm Gerontology Research Center, Stockholm, Sweden; **Caterina Trevisan**, MD, PhD, Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Sweden; and Department of Medical Sciences, University of Ferrara, Italy; **Linnea Sjöberg**, PhD, Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Sweden; **Amaia Calderón-Larrañaga**, MPH, PhD, Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Sweden; and Stockholm Gerontology Research Center, Stockholm, Sweden; **Martino Belvederi Murri**, MD, Institute of Psychiatry, Department of Neuroscience and Rehabilitation, University of Ferrara, Italy; **Laura Fratiglioni**, MD, PhD, Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Sweden; and Stockholm Gerontology Research Center, Stockholm, Sweden; **Serhiy Dekhtyar**, PhD, Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Sweden

Correspondence: Federico Triolo. Email: federico.triolo@ki.se

First received 7 Aug 2023, final revision 8 Mar 2024, accepted 2 Apr 2024

Supplementary material

Supplementary material is available online at https://doi.org/10.1192/bjp.2024.84

https://doi.org/10.1192/bjp.2024.84 Published online by Cambridge University Press

Data availability

SNAC-K data (http://www.snac-k.se/) can be accessed by the scientific community upon approval from the SNAC-K management and maintenance committee, and applications can be submitted to Maria Wahlberg (Maria.Wahlberg@ki.se) at the Aging Research Center, Karolinska Institutet.

Acknowledgements

We express gratitude to SNAC-K participants and caregivers for their involvement in the study, and to all those involved in its management and maintenance. Results from this study are partially included in a Doctoral thesis defended by F.T. at Karolinska Institutet on 25 October 2023 (https://openarchive.ki.se/xmlui/handle/10616/48764).

Author contributions

All authors were involved in the study's conception and design. F.T. had complete access to the data and assumes responsibility for its integrity and the accuracy of the analysis. All authors contributed to the interpretation of results. F.T. drafted the first version of the manuscript. D.L.V., C.T., A.C.-L., L.S., M.B.M., L.F. and S.D. critically revised the manuscript. All authors participated in revising and approving the final version of the manuscript, and share responsibilities for all aspects of the work.

Funding

SNAC-K receives financial support from various sources, including the Swedish Research Council (grant no.: 2011-6243; 2017-06088), the Swedish Research Council for Health, Working Life and Welfare (grant no.: 2016-07175), the Swedish Ministry of Health and Social Affairs, and the participating County Councils and Municipalities. Financial support for this specific project was granted by the Swedish Research Council for Health, Working Life and Welfare (grant no.: 2019-01076; 2023-00153) to S.D. and F.T., the Stiftelsen 1759 (project 'Depression och kroniska sjukdomar hos äldre') to S.D. and F.T., and Lindhes Advokatbyrå AB – Stiftelsen Ragnhild och Einar Lundströms Minne (grant no.: LA2022-0080; LA2023-0100) to F.T.

Declaration of interest

The authors have no conflicts of interest to declare.

References

1 Alexopoulos GS. Depression in the elderly. *Lancet* 2005; **365**: 1961–70.

2 Triolo F, Sjöberg L, Calderón-Larrañaga A, Belvederi Murri M, Vetrano DL, Fratiglioni L, et al. Late-life depression and multimorbidity trajectories: the role of symptom complexity and severity. *Age Ageing* 2023; **52**: afac315.

3 de la Torre-Luque A, Ayuso-Mateos JL. The course of depression in late life: a longitudinal perspective. *Epidemiol Psychiatr Sci* 2020; **29**: e147.

4 Trevisan C, Vetrano DL, Calvani R, Picca A, Welmer A-K. Twelve-year sarcopenia trajectories in older adults: results from a population-based study. *J Cachexia Sarcopenia Muscle* 2022; **13**: 254–63.

5 Tazzeo C, Rizzuto D, Calderón-Larrañaga A, Dekhtyar S, Zucchelli A, Xia X, et al. Living longer but frailer? Temporal trends in life expectancy and frailty in older Swedish adults. *J Gerontol* 2024; **79**: glad212.

6 Beekman ATF, Geerlings SW, Deeg DJH, Smit JH, Schoevers RS, de Beurs E, et al. The natural history of late-life depression: a 6-year prospective study in the community. *Arch Gen Psychiatry* 2002; **59**: 605–11.

7 Hybels C, Pieper C, Blazer D, Steffens D. Heterogeneity in the three-year course of major depression among older adults. *Int J Geriatr Psychiatry* 2016; **31**: 775–82.

8 Jeuring HW, Stek ML, Huisman M, Oude Voshaar RC, Naarding P, Collard RM, et al. A six-year prospective study of the prognosis and predictors in patients with late-life depression. *Am J Geriatr Psychiatry* 2018; **26**: 985–97.

9 Jeuring H, Huisman M, Comijs H, Stek M, Beekman A. The long-term outcome of subthreshold depression in later life. *Psychol Med* 2016; **46**: 2855–65.

10 de la Torre-Luque A, de la Fuente J, Sanchez-Niubo A, Caballero FF, Prina M, Muniz-Terrera G, et al. Stability of clinically relevant depression symptoms in old-age across 11 cohorts: a multi-state study. *Acta Psychiatr Scand* 2019; **140**: 541–51.

11 Vyas CM, Okereke OI. Late-life depression: a narrative review on risk factors and prevention. *Harv Rev Psychiatry* 2020; **28**: 72–99.

12 Colman I, Ataullahjan A. Life course perspectives on the epidemiology of depression. *Can J Psychiatry* 2010; **55**: 622–32.

13 Menassa M, Stronks K, Khatami F, Roa Díaz ZM, Espinola OP, Gamba M, et al. Concepts and definitions of healthy ageing: a systematic review and synthesis of theoretical models. *eClinicalMedicine* 2023; **56**: 101821.

14 Belvederi Murri M, Cattelani L, Chesani F, Palumbo P, Triolo F, Alexopoulos GS. Risk prediction models for depression in community-dwelling older adults. *Am J Geriatr Psychiatry* 2022; **30**: 949–60.

15 Schwarzbach M, Luppa M, Forstmeier S, Konig HH, Riedel-Heller SG. Social relations and depression in late life-a systematic review. *Int J Geriatr Psychiatry* 2014; **29**: 1–21.

16 Triolo F, Harber-Aschan L, Belvederi Murri M, Calderón-Larrañaga A, Vetrano DL, Sjöberg L, et al. The complex interplay between depression and multimorbidity in late life: risks and pathways. *Mech Ageing Dev* 2020; **192**: 111383.

17 Schuch FB, Vancampfort D, Firth J, Rosenbaum S, Ward PB, Silva ES, et al. Physical activity and incident depression: a meta-analysis of prospective cohort studies. *Am J Psychiatry* 2018; **175**: 631–48.

18 National Institute for Health and Care Excellence. *Depression in Adults with a Chronic Physical Health Problem: Recognition and Management*. NICE, 2009 (https://www.nice.org.uk/guidance/cg91).

19 Sjöberg L, Karlsson B, Atti AR, Skoog I, Fratiglioni L, Wang HX. Prevalence of depression: comparisons of different depression definitions in population-based samples of older adults. *J Affect Disord* 2017; **221**: 123–31.

20 Judd LL, Rapaport MH, Paulus MP, Brown JL. Subsyndromal symptomatic depression: a new mood disorder? *J Clin Psychiatry* 1994; **55**: 18–28.

21 Triolo F, Saadeh M, Sjöberg L, Fratiglioni L, Welmer A-K, Calderón-Larrañaga A, et al. Pre-pandemic physical function and social network in relation to COVID-19-associated depressive burden in older adults in Sweden. *Innov Aging* 2022; **6**: igac041.

22 World Health Organization. *Global Recommendations on Physical Activity for Health*. WHO, 2010 (http://www.ncbi.nlm.nih.gov/books/NBK305057/).

23 Calderón-Larrañaga A, Vetrano DL, Onder G, Gimeno-Feliu LA, Coscollar-Santaliestra C, Carfí A, et al. Assessing and measuring chronic multimorbidity in the older population: a proposal for its operationalization. *J Gerontol* 2017; **72**: 1417–23.

24 Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, et al. Gait speed and survival in older adults. *JAMA* 2011; **305**: 50–8.

25 Jackson C. Multi-state models for panel data: the MSM package for R. *J Stat Soft* 2011; **38**: 1–28.

26 Skou ST, Mair FS, Fortin M, Guthrie B, Nunes BP, Miranda JJ, et al. Multimorbidity. *Nat Rev Dis Primers* 2022; **8**: 48.

27 Gold SM, Köhler-Forsberg O, Moss-Morris R, Mehnert A, Miranda JJ, Bullinger M, et al. Comorbid depression in medical diseases. *Nat Rev Dis Primers* 2020; **6**: 69.

28 Kawachi I, Berkman LF. Social ties and mental health. *J Urban Health* 2001; **78**: 458–67.

29 van den Brink RHS, Schutter N, Hanssen DJC, Elzinga BM, Rabeling-Keus IM, Stek ML, et al. Prognostic significance of social network, social support and loneliness for course of major depressive disorder in adulthood and old age. *Epidemiol Psychiatr Sci* 2018; **27**: 266–77.

30 Deng Y, McQuoid D, Potter G, Steffens D, Albert K, Riddle M, et al. Predictors of recurrence in remitted late-life depression. *Depress Anxiety* 2018; **35**: 658–67.

31 National Institute for Health and Care Excellence. *Older People with Social Care Needs and Multiple Long-Term Conditions*. NICE, 2015 (https://www.nice.org.uk/guidance/ng22/chapter/Recommendations#preventing-social-isolation).

32 Belvederi Murri M, Amore M, Menchetti M, Toni G, Neviani F, Cerri M, et al. Physical exercise for late-life major depression. *Br J Psychiatry* 2015; **207**: 235–42.

https://doi.org/10.1192/bjp.2024.84 Published online by Cambridge University Press