

Life course trajectories of affective symptoms and their early life predictors

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Abstract

Background: Life course trajectories of affective symptoms (i.e., depression and anxiety) are heterogeneous. However, few studies have investigated the role of early life risk factors in the development of these trajectories. The present study aimed to: 1) derive latent trajectories of affective symptoms over a period of more than 50 years (from age 13 through age 69), and 2) examine early life risk factors for associations with specific life course trajectories of affective symptoms.

Method: Participants are from the MRC National Survey of Health and Development (NSHD) ($n = 5362$). Affective symptoms were measured prospectively at ages 13, 15, 36, 43, 53, 60-64 and 69. A latent variable modelling framework was implemented to model longitudinal profiles of affective symptoms. Twenty-four prospectively measured early life predictors were tested for associations with different symptom profiles using multinomial logistic regression.

Results: Four life course profiles of affective symptoms were identified: 1) absence of symptoms (66.6% of the sample); 2) adolescent symptoms with good adult outcome (15.2%); 3) adult symptoms only (with no symptoms in adolescence and late life) (12.9%); 4) symptoms in adolescence and mid adulthood (5.2%). Of the twenty-four early life predictors observed, only four were associated with life course trajectories, with small effect sizes observed.

Conclusions: People differ in their life course trajectories of anxiety and depression symptoms and that these differences are not largely influenced by early life factors tested in this study.

There is a wealth of evidence regarding the lifetime prevalence and morbid risk of mental health disorders in the population. Estimates from large scale population-based studies indicate the lifetime prevalence of affective disorders, such as depression and anxiety, are high, showing that 1 in 4 people worldwide live with or experience these types of disorders, as defined by the Diagnostic and statistical manual – 4th edition (DSM-IV) (Kessler *et al.*, 2012). Estimates are also high for those who experience disorders that fall below the diagnostic threshold (i.e., sub-clinical anxiety or depressive symptoms, referred to hereafter as affective symptoms), with around 1 in 6 individuals over 16 years of age in the UK indicating they have experienced high levels of affective symptoms, as measured by the revised Clinical Interview Schedule (CIS-R) (Stansfeld *et al.*, 2014). The majority of affective symptoms have early onset, with 50% of individuals presenting symptoms by the age of 14 years, and 75% by the age of 24 years (Kessler *et al.*, 2007). Early onset affective symptoms are associated with longer time-to-treatment, and, without intervention, are often characterised by greater severity and persistence into adulthood (Raven *et al.*, 2017). However, notably, some individuals with early onset affective symptoms do not develop recurrent symptoms, whereas others have repeated affective episodes across the life course.

Accordingly, evidence from prospective studies of children followed into early adulthood, as well as from adult samples with follow-up of more than ten years, suggests that long-term trajectories of affective symptoms are heterogeneous and can vary in terms of onset, severity (low, medium and high) and stability (stable, increasing, decreasing) (Musliner *et al.*, 2016; Paksarian *et al.*, 2016; Colman *et al.*, 2007). In one study, latent variable mixture modelling was used to identify longitudinal profiles of affective symptoms from childhood (age 13) through to mid-adulthood (age 53) using

data from the MRC National Survey of Health and Development (NSHD) (Colman *et al.*, 2007). They found six distinct profiles of affective symptoms including an absence of symptoms; repeated moderate symptoms; adult-onset moderate symptoms adolescent symptoms with good adult outcomes; adult-onset severe symptoms; and repeated severe symptoms.

This evidence highlights the importance of assessing affective symptoms longitudinally as opposed to using measures at a single time point. Investigating life course differences in recurrent affective symptoms allows us to identify the proportion of the population with persistent trajectories as well as those who have an increased risk of severe symptoms at specific points across the life course (Burton-Jeangros *et al.*, 2015; Power, Kuh and Morton, 2013).

Moreover, identifying groups of people who differ in the age of onset and recurrence of affective symptoms across the life course provides an indicator of public health burden and aids identification of subgroups in which targeted prevention and treatment strategies may have greater impact.

Further to modelling life course trajectories of health, the past two decades have seen an increased interest in investigating environmental exposures associated with life course mental health.

Previous studies have provided strong evidence for the important role of early life factors including both socio-economic and psychosocial adversities, as well as their accumulation, in life-long mental health and well-being (Secinti *et al.*, 2017; Evans, Wells and Moch, 2003; Stafford *et al.*, 2015; Selous *et al.*, 2019; Chapman *et al.*, 2004; Danese *et al.*, 2009). For example, using data from the Dunedin longitudinal study (Poulton, Moffitt and Silva, 2015), prior evidence has shown that children

exposed to both single and cumulative adverse psychosocial experiences are at elevated risk of adolescent and adulthood depression (Danese *et al.*, 2009).

However, most of the existing evidence tends to focus on mental health outcomes at a single time point (often in young adulthood), without considering association between early life risk and life course trajectories of affective symptoms. Investigating the role of early life in the development of health trajectories extends the evidence for associations between early life risk factors and later life affective symptoms. Furthermore, these life course models are extremely useful in identifying individuals who may have an increased vulnerability to developing maladaptive outcomes and generating preventative methods (Ben-Shlomo and Kuh, 2002).

Twenty-four early life risk factors were chosen to capture the array of differing socio-economic and family rated circumstances, previously found to be associated with poor health outcomes at different time points across the life course (Felitti *et al.*, 1998; Campbell, Walker and Egede, 2016; Hughes *et al.*, 2017; Green *et al.*, 2010).

The present study aims to extend the previous research in NSHD by 1) deriving trajectories of affective symptoms over a longer period of six decades, from childhood (age 13) through late life (age 69); and 2) testing whether a wide range of early life factors (from birth through age 15) are independently associated with these life course trajectories of affective symptoms

Method

Sample

The MRC National Survey of Health and Development (NSHD) is an ongoing longitudinal study with the original sample of 5362 (47.5% female) individuals born in England, Scotland, and Wales during one week in March 1946 (<http://www.nshd.mrc.ac.uk/nshd>). The NSHD cohort members have been prospectively studied 2 times, from birth up to 69 years of age. (Wadsworth *et al.*, 2006; Kuh *et al.*, 2016). The MRC NSHD is the longest running British birth cohort, with cohort members reaching age 70 in 2016, one of the aims of the NSHD is to maintain a representative population of individuals born in post-war Britain, specific attention is paid to the predictors of drop out. At age 69, 2546 (47%) were contacted for follow up (Kuh *et al.*, 2016). Attrition by age 69 was due to death ($n = 957$), emigration ($n = 574$), prior refusal ($n = 620$), and those untraceable for more than 5 years ($n = 395$). Of note, complete representativeness of an aged matched national population cannot be established because the selection of the survey member predated major immigration flows and as noted, births outside of marriage and multiple births (Wadsworth *et al.*, 2003).

Ethical approval was granted by the National Research Ethics Service Committee London Queen Square (14/LO/1073) and by the Scotland A Research Ethics Committee (14/SS/1009). All study members gave signed informed consent. (Kuh *et al.*, 2011, 2016).

Measures

Affective symptoms

Affective symptoms were assessed at ages 13, 15, 36, 43, 53, 60-64 and 69 years. At age 13 and 15 affective symptoms were assessed using a forerunner of the Rutter

Behaviour Questionnaire for teachers (Rutter, 1967). For Rutter's Behaviour Questionnaire teachers were asked to describe aspects of the children's personality, behaviour and attitudes on a three-point scale (i.e., more, the same, or less than classmates). Questionnaires have previously been analysed using factor analysis, in which affective symptoms were identified as one factor (Rutter, 1967; Rodgers, 1990).

At age 36 symptoms were assessed using a short version of the Present State Examination (PSE) was used. The PSE is a clinical interview aims to assess the frequency and severity of affective symptoms over the previous month and was administered by trained nurses. At age 43 symptoms were further assessed using the Psychiatric Symptom Frequency (PSF) scale. The PSF is an 18-item scale used to measure symptoms of anxiety and depression which have occurred over the previous 12 months. Questions on this scale are phrased as 'have you...?' (E.g., 'have you felt on edge or keyed up or mentally tense?'), and responses to each question were coded as 0 = 'not in the last year', 1 = 'occasionally', 2 = 'sometimes', 3 = 'quite often', 4 = 'very often', and 5 = 'everyday'. From these codes a total score ranging from 0 to 90 could be calculated. A previous investigation of the PSF found that a cut off score of 22 adequately identified those with evidence of affective symptoms (Lindelow, Hardy and Rodgers, 1997).

Furthermore, affective symptoms were reported at 53, 60-64 and 69 years using the 28-item version of the General Health Questionnaire (GHQ-28) (Goldberg and Hillier, 1979). The GHQ-28) is a scaled questionnaire used to detect common mental health symptoms in the general population. Items on this questionnaire asked participants about specific complains over the past few weeks. Examples included 'have you recently been getting scared or panicky for no good reason?' and, 'have you recently been thinking of yourself as a worthless person?' Each of these questions are

accompanied by four responses, typically being, 'not at all', 'no more than usual', 'rather more than usual' and 'much more than usual', scoring from 0 to 3, respectively. Thus, a total score on the GHQ can range from 0-84, allowing means and distributions to be calculated.

Early life factors

In total, 24 measures of early life factors across six domains: family instability, family socio-economic status, parental age, childrearing environment and parenting, parental health and 'child's health, were selected a priori, based on previous reports using data from the MRC NSHD (Rodgers, 1990; Stafford *et al.*, 2015). All early life factors were measured prospectively through a variety of sources, including reports of health visitors, parents and teachers. Supplementary Information 1 provides further detail on the early life factors measured. Notably, as a large amount of data was missing across different types of early life predictors, multiple imputation using chained equations was implemented to impute missing data with five imputations. Supplementary Table 1 provides counts and percentages of complete case and imputed early life predictors. This missing data approach was used as it allows for the inclusion of a large number of covariates and auxiliary variables in the models, which maximises the plausibility of the missing at random (MAR) assumption, and limits possibility of missing not at random (MNAR) data (Little *et al.*, 2014). Previously identified predictors of drop out including low education attainment, mild cognitive impairment and socioeconomic disadvantage (Kuh *et al.*, 2016; Stafford *et al.*, 2013), were included as auxiliary variables.

Analytical procedure

In order to make comparisons to prior evidence and to improve precision of measurement (Colman *et al.*, 2007), a latent variable modelling framework was

applied to affective symptom measures at ages 13, 15, 36, 43, 53, 60-64 and 69. Confirmatory factor analysis for categorical data was applied to derive latent factor scores, which were treated as continuous measures of anxiety and depression at each time point (Supplementary table 2 provides stability correlations for the derived factor scores). These latent factor scores were then grouped in order to create four-category ordinal variables at each time-point: $\leq 50^{\text{th}}$, 50.1 to 75^{th} , 75.1 to 90^{th} , and ≥ 90.1 percentile. These derived ordinal measures were used in latent profile analyses in a sample with at least one of the seven assessments of affective symptoms ($n = 4974$, 93%).

Latent profile analyses

Latent profile analysis (LPA) is a statistical method designed to identify patterns of trajectories for different sub groups within a population (Jung and Wickrama, 2008). We employed LPA, with ordinal indicators being entered as continuous variables in the model to derive growth trajectories between ages 13 and 69 (see Colman *et al.*, 2007). When applying this method, as the number of suitable latent profiles is initially unknown, model fit indices were compared and the substantive coherence of the class solution selected is considered (Bauer and Curran, 2004). For this analysis, a series of models were fitted estimating three to seven class solutions. In order to identify the most parsimonious description of early to later life trajectories of affective symptoms, model fit indices were compared using Likelihood ratio bootstrap p value, Bayesian Information Criteria (BIC), Akaike's Information Criteria (AIC). Lo-Mendell-Rubin bootstrap p value of likelihood ratio test, and entropy. All models were run with random starting values, using maximum likelihood estimation with robust standard errors. As LPA draws on all of the data points available in the data set (i.e. it included all individuals who has at least one of the seven assessments of affective symptoms – n

= 4974) missing data points are included in the analysis using full information maximum likelihood (FIML) when estimating the posterior probabilities of class membership. All latent variable modelling was run using Mplus version 7.1. (Muthén and Muthén, 2013).

A two-step estimation approach was used for this analysis. Recently one-step approaches have been criticised on the basis that including predictors into the measurement model may lead to an unintended and problematic circular relationship in which the classes from the trajectory modelling are determined in part by the distal outcome which they are meant to be predicting (Bakk and Vermunt, 2016; Vermunt, 2010). This analysis was therefore conducted in a stepwise fashion to avoid drawbacks associated with one-step estimation methods.

Sensitivity analyses

A series of sensitivity analyses were also run for the LPA. First, as prior evidence has consistently demonstrated sex differences in affective symptoms (Van de Velde, Bracke and Levecque, 2010; Piccinelli and Wilkinson, 2000), sex-specific differences of the profiles were investigated through running the LPA separately for males and females. Secondly, as a wealth of evidence has shown that affective symptoms are associated with an increase in risk of mortality across the life course (Cuijpers *et al.*, 2014; Cuijpers and Smit, 2002; Henderson *et al.*, 2011; Archer *et al.*, 2018), the LCA models were re-run excluding those who died by age 69 ($n = 300$).

Multinomial logistic regression analyses

A series of multinomial logistic regression analyses were conducted to investigate whether each early life predictor was associated with our four identified life course profiles of affective symptoms. In order to run the multinomial logistic regression, cohort members were assigned their most likely class membership. As no

significant sex*early life predictor interactions on life course profiles of affective symptoms was found (all p-values > .05), sex was adjusted for in each model. Furthermore, for each analysis, the no affective symptoms profile was used as the comparison group.

Results

Life course profiles of affective symptoms

The four-class solution was selected to be the best fitting model as this was the most parsimonious model with the highest entropy value (Table 1). As LPA draws on all of the data points available in the data set (i.e. it included all individuals who has at least one of the seven assessments of affective symptoms – $n = 4974$) missing data points are included in the analysis using full information maximum likelihood (FIML) when estimating the posterior probabilities of class membership. The four longitudinal profiles of affective symptoms are shown in Figure 1) no affective symptoms ($n = 3315$; 66.6%); 2) affective symptoms in adolescence only ($n = 757$; 15.2%); 3) affective symptoms in adulthood only ($n = 643$; 12.9%); and 4) affective symptoms in adolescence and mid adulthood ($n = 259$; 5.2%).

Insert table 1

Insert figure 1

Trajectories by Sex

When LPA models were investigated separately for males and females, although the three-class model had a slightly higher entropy value for females, the four-class solution was shown to be the best fitting model for both males and females (i.e., based on the BIC and AIC fit criteria; Supplementary Table 3; see supplementary Figure 1 and 2).

When running the LCA on those who survived by age 69 and had at least one of the seven assessments of affective symptoms ($n = 4,031$), again the four-class solution was deemed to be the best fitting model based on the observed fit statistics (see Supplementary Table 3). Moreover, observed trajectories did not appear to differ after excluding those died (see Supplementary Figure 1).

Early life predictors of life course profiles of affective symptoms

Association analyses were run to test for associations between early life predictors and derived life course profiles of affective symptoms. Counts and percentages for each early life predictor and life course profile are presented in table 2 and effect sizes and confidence intervals are displayed in table 3. For the profile of symptoms in adolescence only, no early life predictors were found to be significant predictors. For the profile of symptoms in adulthood only, one early life predictor – childhood chronic physical illness – was identified: those who experienced childhood chronic illness were 1.36 times more likely to develop adolescent symptoms only compared to those who did not experience childhood chronic illness ($b = .31$, Wald $\chi^2 = 8.98$, $p = .003$). For the profile of symptoms in adolescence and mid adulthood, three early life predictors were identified: those who lived in a house with 3 or more people per room were 1.9 times more likely to develop these symptoms compared to those who lived in a house with 1-2 persons per room ($b = .64$, Wald $\chi^2 = 1.24$, $p = .031$); those whose fathers had average health were 1.44 times more likely to develop symptoms in adolescence and adulthood than those whose fathers perceived their health as excellent ($b = .37$, Wald $\chi^2 = 6.40$, $p = .01$); those whose mothers reported their health to be poor were 1.44 times more likely to have symptoms in adolescence and mid adulthood than those whose mothers perceived health was excellent ($b = .36$, Wald $\chi^2 = 5.13$, $p = .02$).

Insert table 2

In addition, association analyses were re-run excluding those who died by age 69 (see Supplementary Table 4). Results revealed that for the profile of symptoms in adolescence only, no early life predictors were identified. For the profile of symptoms in adulthood only, two early life predictors –family size and childhood chronic physical illness– were identified. Those who grew up in a family with 4 or more children were 1.33 times more likely to develop adult symptoms only compared to those who grew up in a family with 3 or fewer children ($b = .28$, Wald $\chi^2 = 6.26$, $p = .012$); and those who experienced childhood chronic illness were 1.36 times more likely to develop adolescent symptoms only compared to those who did not experience childhood chronic illness ($b = .31$, Wald $\chi^2 = 6.19$, $p = .013$). For the profile of symptoms in adolescence and adulthood, no early life predictors were identified.

Insert table 3

Discussion

The present study derived four latent profiles of affective symptoms from adolescence (age 13) through to older adulthood (age 69), with the longest period of follow-up (>50 years) to date. Four life course profiles of affective symptoms were identified: no symptoms; symptoms in adolescence only; symptoms in adulthood only; and symptoms in both adolescence and mid adulthood. These results are consistent with findings from a previous systematic review of studies investigating longitudinal trajectories of depressive symptoms that identified three or four trajectories (differing in severity and stability of symptoms) across of maximum period of 23 years (Musliner *et al.*, 2016).

A previous study using NSHD data up to age 53 identified six classes of symptoms when modelling the data using a latent variable framework (Colman *et al.*, 2007). However, when applying the same method, this study found that a four-class solution was the best fit for measures of affective symptoms. Moreover, the previous study using NSHD identified a profile with repeated moderate symptoms (33.6% of participants). However, in the present study, we could not identify a profile with repeated affective symptoms up to age 69. On the contrary, we showed that symptoms decrease for all cohort members after age 64. Similarly to our finding, another study that focused on adult affective symptoms from age 19-20 across three decades of life demonstrated that persistent affective symptoms across the life course are not common (Paksarian *et al.*, 2016).

In consistence with the previous study discussed (Colman *et al.*, 2007), we showed that the profile with 'no affective symptoms' was the largest group (66.6%). Secondly, in both studies the profile with adolescent symptoms only and the profile

with adult symptoms only were identified. Thirdly, although a profile with repeated symptoms was not revealed in the present study, a profile with persistent symptoms from adolescence through to mid-adulthood was found. Therefore, differences between the two studies are largely due to the observed decline of affective symptoms after age 64 and the convergence of most participants to lower levels of affective symptoms. This resulted in less heterogeneity for the surviving sample by age 69. One explanation for this may be due to decrease in mental health symptoms and the increases in overall wellbeing in those over 70 (Gondek *et al.*, 2021). Furthermore, these results imply longitudinal typologies are needed to appropriately capture heterogeneity in affective symptomatology at different stages of lifespan.

The present study explored a wide range of early life factors for associations with four life course profiles of affective symptoms. Only four factors, in line with previous evidence (Secinti *et al.*, 2017; Evans, Wells and Moch, 2003; Stafford *et al.*, 2015), were associated with affective symptom profiles: chronic childhood illness, residential overcrowding, and mothers and father perceived ill health. Notably, effect sizes were relatively small. However longitudinal studies often yield small effect sizes, owing to large intervals between data collections and adjustment for stability effects in autoregressive models (Funder and Ozer, 2019; Adachi and Willoughby, 2015).

Furthermore, as affective symptoms have high population prevalence, small effect sizes warrant high public health importance. Our findings also revealed no significant association between a number of previously identified early life risk factors (Clark *et al.*, 2010), including parental divorce (Sands, Thompson and Gaysina, 2017), parental loss (Tyrka *et al.*, 2008; Otowa *et al.*, 2014) and parental psychopathology (Wickramaratne and Weissman, 1998), and affective symptom profiles. One explanation for this inconsistency may be explained by the use of retrospective reports to

measure early life factors, which may be subject to recall bias (Reuben *et al.*, 2016; Newbury *et al.*, 2018). Moreover, the majority of prior studies found on mental health outcomes at a single time point, and therefore the results may not be comparable when considering life course trajectories of affective symptoms.

Strengths and limitations

Birth cohort studies with multiple measures of affective symptoms combined with advances in person-centred approaches to longitudinal data provide a unique opportunity to model individual life-course trajectories of symptoms and illuminate the role of early life influences on life-course mental health (Power, Kuh and Morton, 2013). A notable strength of the study was more than 50 years of follow-up (up to age 69). Another unique feature of the present study was a wide range of prospectively measured early life factors. In order to deal with missing data that are unavoidable in long running birth cohorts such as NSHD, multiple imputation was applied to impute missing data for the early life predictors maximising the sample size available. Furthermore, to identify homogeneous sub-populations with varying trajectory parameters we employed a group-based trajectory modelling approach. As this method of analysis predicts posterior probability of being assigned to a certain 'class', all the data available at each time point was included in the analysis. This approach minimised the amount of missing data when estimating the latent classes. One limitation of latent class analysis is that the outcomes (i.e., the latent classes) are approximations of symptom patterns, and do not represent actual data points. However, the classes derived can be viewed as evidence-based approximations that can be used to infer a valid representation of symptom patterns in the population. Furthermore, due to the different measures of affective symptoms collected at each time

point in the NSHD, the trajectories could not be compared with repeated measures modelling of the data.

This study employed a wide range of prospectively measured childhood and individual contextual risk factors in order to explore associations with latent profiles of affective symptoms. One limitation of the measures utilised for this study is that they do not account for the persistence or continuation of risk. Evidence from longitudinal studies indicate that it is the persistence of early life risk factors that influence the course of affective symptoms rather than their occurrence at a single point in development (Raposa *et al.*, 2014).

Conclusion

Four life course profiles of affective symptoms that differ in onset and persistence of symptoms were identified in the present study. Among a wide range of early life factors tested, only four were significantly associated with different affective symptoms trajectories. These findings demonstrate that people differ in terms of their life course symptoms of anxiety and depression, and that these differences are not largely influenced by early life factors. Understanding the role of factors that influence the development of heterogeneous affective symptom trajectories may help professionals to establish appropriate times for intervention and builds upon our knowledge of why symptoms develop, persist, and diminish over time. Future studies should aim to investigate whether the age of exposure to early life risk influences the onset and development of affective symptom trajectories. Furthermore, future studies should focus on intervening risk factors in order to elucidate the mechanisms of action between early life risk and life course affective symptoms.

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Key Messages:

- This study used data from the MRC National Survey of Health and Development.
- Growth mixture modelling was used to model longitudinal profiles of affective symptoms across 56 years.
- Life course profiles of affective symptoms that differ in onset and persistence of symptoms were identified.
- Few associations were found between early life factors and life course trajectories of affective symptoms.

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Data availability: Data used in this publication are available to bona fide researchers upon request to the NSHD Data Sharing Committee via a standard application procedure. Data requests should be submitted to mrclha.swiftinfo@ucl.ac.uk. Further details can be found at <http://www.nshd.mrc.ac.uk/data>. doi: 10.5522/NSHD/Q101; doi: 10.5522/NSHD/Q102; doi: 10.5522/NSHD/Q103.