Heterogeneity in long-term trajectories of depressive symptoms: Patterns, predictors and outcomes

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Abstract

Background—Evidence suggests that long-term trajectories of depressive symptoms vary greatly throughout the population, with some individuals experiencing few or no symptoms, some experiencing transient symptoms and others experiencing chronic depression. The goal of this paper was to review studies that examined heterogeneity in long-term trajectories of depressive symptoms and summarize the current knowledge regarding a) the number and patterns of trajectories and b) antecedents and outcomes associated with different trajectory patterns.

Methods—We conducted a systematic review of literature in the Medline and PsychINFO databases. Articles were included if they a) modeled trajectories of depressive symptoms, b) used a group-based trajectory modeling approach, c) followed participants for 5+ years and d) had a sample size of at least 200.

Results—We identified 25 studies from 24 separate cohorts. Most of the studies identified either 3 or 4 distinct trajectory classes. Trajectories varied in terms of severity (low, medium, high) and stability (stable, increasing, decreasing). In most studies, the majority of participants had consistently few or no depressive symptoms, but a notable minority (usually < 10%) reported persistent symptoms. Predictors of trajectories with greater symptom burden included female gender, lower income/education and non-white race. Other predictors were specific to different populations (i.e. mothers, older adults). High symptom burden trajectories were associated with poor psychiatric and psychosocial outcomes.

Limitations—Comparisons between studies were qualitative.

Conclusions—Trajectories of depression symptoms in the general population are heterogeneous, with most individuals showing minimal symptoms but a notable minority experiencing chronic high symptom burden.

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Introduction

Evidence suggests that long-term symptom trajectories of depression are heterogeneous; for some, depressive symptoms are transient; for others, stable; and for still others, symptoms come and go with varying degrees of frequency (Angst, 1988; Eaton et al., 2008; Keller et al., 1992; Merikangas, Wicki, & Angst, 1994; Mueller et al., 1996; Solomon et al., 1997). These group differences have important implications for our understanding both of the underlying cause (or causes) of depression and the distribution of the burden of depression. Different trajectory patterns may be indicative of underlying differences in etiology. In addition, individuals with particular long-term trajectory patterns may contribute disproportionately to the public health burden of depression, and suffer a disproportionate amount of the negative consequences.

Statistical methodologies for analyzing trajectories have advanced significantly over the past 15 years with the development of group-based trajectory modeling. These methods allow for the identification and characterization of distinct trajectories patterns within a population, and can also be used to identify predictor and outcome variables associated with different trajectory patterns (Muthen, 2004; Nagin, 1999). To date, numerous studies have been published using these methods to examine heterogeneity in trajectories of depressive symptoms. The time is right, therefore, for a review to synthesize the findings of these studies and provide an overview of the current state of knowledge on this topic.

The goal of this paper is to critically review the existing literature on heterogeneity in long-term trajectories of depressive symptoms. For our purposes, 'long-term' is defined as 5 or more years of follow-up. Of particular interest for this review were 1) the numbers of distinct trajectory patterns, 2) the prevalence of different trajectory patterns, 3) predictors/antecedents of different trajectory patterns and 4) outcomes associated with different trajectories.

Method

Selection criteria

Articles were included in the review if they met the following criteria: a) The response variable in the trajectory analysis was depressive symptoms (as opposed to internalizing problems, for example), b) the length of follow-up was at least 5 years, c) the sample included at least 200 individuals and d) the study employed a group-based trajectory modeling approach.

Group-based trajectory models are a collection of statistical methods designed specifically to identify patterns of trajectories separately for different sub-groups within a population. Group-based trajectory models are latent variable models, meaning they use correlations

between observed (i.e. indicator) variables to make inferences about unobserved (i.e. latent) variables, such as membership in an unobserved class (Bartholomew & Knott, 1999). Unlike other methods for analyzing trajectories, such as hierarchical linear models (Bryk & Raudenbush, 1987) and latent growth curve models (Willett & Sayer, 1994), group-based trajectory models do not assume that the trajectory of growth within a population varies around a single mean. Rather, they assume that the population in question is in fact composed of homogenous (or at least more homogenous) sub-populations with different trajectory parameters (Wang & Bodner, 2007). Rather than modeling the trajectory of the population as a whole, these models identify groups following distinct trajectories over time and estimate trajectory parameters separately for each group. Types of group-based mixture models include Latent Class Growth Analysis (LCGA; also known as semi-parametric group-based modeling (Jung & Wickrama, 2008; Nagin & Land, 1993; Nagin, 1999; Roeder, Lynch, & Nagin, 1999), in which within-group variation is assumed to be zero, and Growth Mixture Models (GMM; (Muthen, 2004), in which within-group variation can be incorporated as a random effect. Growth Mixture Models in which course trajectories are related to a distal outcome are referred to as General Growth Mixture Models (GGMM). Parameters of group-based trajectory models include the probability of membership in a particular latent trajectory class for each individual, as well as the intercept and slope of the trajectory for each class. Models that include covariates have additional coefficients for the associations between each covariate and membership in a given trajectory class, relative to a reference class.

Identification of relevant literature

The initial search was conducted using the MEDLINE and PsychINFO databases via the Ebscohost search engine. The following search terms were used: (depression OR depressive symptoms) AND (trajectories OR latent class growth analysis OR growth mixture model OR semi-parametric group-based modeling). We restricted the search to articles published in English in peer-reviewed journals between 1999 and June 2015. This search yielded 1,231 results. The titles, abstracts and, where appropriate, manuscripts of the resulting records were then reviewed by the first author to determine whether each study met criteria for inclusion in the review. Finally, the reference lists of relevant articles were reviewed to identify any papers that might have been missed in the initial search.

Because the vast majority of the studies that met criteria for inclusion used self-reported measures of depressive symptoms, we chose not to include the two studies which used measures based on parental report rather than self-report (Dekker et al., 2007; Prinzie, van Harten, Dekovic, van den Akker, & Shiner, 2014). We also chose not to include studies of joint trajectories (i.e. depression and anxiety (e.g. Coté, Boivin, Liu, Nagin, Zoccolillo & Tremplay, 2009; Olino, Klein, Lewinsohn, Rohde, & Seeley, 2010)), depression and substance abuse (e.g. D. W. Brook, Brook, & Zhang, 2014; Pahl, Brook, & Lee, 2014) or depression and delinquent or disruptive behavior (e.g. J. S. Brook, Lee, Finch, & Brook, 2014; Reinke, Eddy, Dishion, & Reid, 2012). Two additional studies were excluded because they focused on depressive symptoms within the context of a stressful event, either a cancer diagnosis (Burton, Galatzer-Levy, & Bonanno, 2014) or bereavement in caregivers (Aneshensel, Botticello, & Yamamoto-Mitani, 2004).

Results

Study characteristics

We identified 25 studies from 24 separate samples that met the above criteria for inclusion in the review. Characteristics of these studies, including the country, sample size, average age (or grade) at baseline, percent female, length of follow-up, measure of depression, analytic method (GMM, GGMM, LCGA) and a description of the final trajectory model are shown in Table 1. The table is organized by age group, with studies of children/adolescents listed first, followed by studies of adults and finally older adults.

With one exception (Cronkite et al., 2013), all of the studies used general population samples (as opposed to samples of people with a clinical depression diagnosis). This is important to keep in mind when interpreting the findings, as the trajectories described in this review should not necessarily be viewed as trajectories of illness course. Length of follow-up ranged from 5 to 23 years and sample size ranged from 206 to 17,196 participants. The majority of the studies were conducted in the US, although several other countries including Canada, Australia and Taiwan, were represented. Of the 25 studies included in the review, 7 studies identified 3 distinct classes of depressive symptom trajectories, 11 studies identified 4 trajectory classes, 4 studies identified 5 classes and 3 studies identified 6 trajectory classes. Seven of the 25 studies focused exclusively on depression trajectories in children/adolescents, 4 in adults, 6 in mothers and 8 in older adults.

The majority of the studies included information on both males and females, however 7 studies included only female participants (Byers et al., 2012; Campbell, Matestic, von Stauffenberg, Mohan, & Kirchner, 2007; Gross, Shaw, Burwell, & Nagin, 2009; Luoma, Korhonen, Salmelin, Helminen, & Tamminen, 2015; Matijasevich et al., 2015; van der Waerden et al., 2015; Wickham, Senthilselvan, Wild, Hoglund, & Colman, 2015) and one study only included male participants (Stoolmiller, Kim, & Capaldi, 2005). The most common measure of depressive symptoms was the Centers for Epidemiologic Studies Depression Scale (CES-D).

Patterns of long-term depression trajectories

Results of the studies illustrated in Table 1 suggest that long-term trajectories of depressive symptoms vary in terms of two characteristics: severity (low, medium, high) and stability (stable, increasing, decreasing). All of the studies reviewed here identified one or more classes characterized by stable low, minimal or mild symptoms. This group (or groups) was typically the largest trajectory class, containing over 45% of the sample in all but five (Cronkite et al., 2013; Duchesne & Ratelle, 2014; Salmela-Aro, Aunola, & Nurmi, 2008; Stoolmiller et al., 2005; Yaroslavsky, Pettit, Lewinsohn, Seeley, & Roberts, 2013) of the studies. Another trajectory pattern observed frequently was a trajectory characterized by persistently high depressive symptoms. This was almost always the smallest class, containing roughly 2.5–7% of the samples, although several studies (Chaiton et al., 2013; Cronkite et al., 2013; Luoma et al., 2015; Stoolmiller et al., 2005; Yaroslavsky et al., 2013) reported proportions as high as 24–32% in this group. Many of the studies also identified a group with moderate, stable symptoms ranging in size from 16–61% of the sample. Some of

the studies identified groups of individuals with depressive symptoms that were unstable, either increasing or decreasing over time. The proportion of individuals falling in unstable trajectory classes was highly variable, ranging from 2.4–37% for increasing symptoms and from 2.7–71% for decreasing symptoms. Other trajectory patterns, such as U shaped (Campbell et al., 2007) or reverse U shaped (Wickham et al., 2015) were rare.

Gender differences

Five of the studies examined trajectories of depressive symptoms separately for males and females. Mazza et al. (2010) examined 6-year depression trajectories in 1st and 2nd graders and found similar trajectory patterns for boys and girls, but the proportion of participants in classes with higher symptom burden was larger for girls than for boys. Chaiton et al. (2013) examined 5-year trajectories in adolescents and found similar results: the same overall trajectory patterns in males and females, but more females in the high symptoms group. Melchior et al. (2013) examined 13-year trajectories in adults and again found similar patterns in men and women. They found equal numbers (6%) of men and women in the "persistent depression" class, but fewer women (58% vs. 72%) in the "no depression" class. Hsu et al. (2012) examined 18-year trajectories of depressive symptoms in older adults and again found similar patterns among males and females, but more females than males in the trajectory classes characterized by higher symptoms, particularly the increasing and declining classes. Finally, Montagnier et al. (2014) examined 20-year trajectories in older adults and found that while both groups contained a "no depression" class and an "increasing depression" class, the most symptomatic class in women displayed stable high symptoms over time, while the most symptomatic class in men exhibited a fluctuating pattern in which symptoms decreased slightly and then began to rise in a linear fashion with age. As with the other three studies, a higher proportion of women than of men fell within classes with higher depressive symptom burdens.

Age differences

There did not appear to be any consistent differences in terms of the number or patterns of depression trajectories by age group, however the proportion of the samples in chronic high depression symptom trajectory classes decreased with age, from 14–32% in adolescents to 1.7–28% in adults (including mothers) and finally 2.1–7.2% in older adults. Trajectory patterns characterized by instability (increasing or decreasing symptoms) were more common among children/adolescents.

Racial/ethnic differences

Costello et al. (2008) examined race/ethnicity as a predictor of depression trajectory among students in the National Longitudinal Study of Adolescent Health (Add Health). They found that black and Asian students were both more likely to be in the 'low depression' and 'early high depression' classes relative to the 'no depression' class, and Latino students were more likely to be in the 'early high depression' class relative to the 'no depression' class. Liang et al. (2011) examined race/ethnicity as a predictor of depression trajectory in older adults from the Health and Retirement Study (HRS). They found that black and Hispanic participants were more likely to be in the low, moderate, decreasing and increasing trajectory classes relative to the minimal depressive symptoms class. In contrast, Lincoln et

al. (2010) examined heterogeneity in depressive symptom trajectories in black and white adults in the Americans' Changing Lives Study and did not find a statistically significant association between race and depression trajectory class membership, and Kuchibhatla et al. (2012) found a larger proportion of whites in the stable-high depression trajectory.

Predictors of trajectory group membership

Female gender was almost universally associated with membership in trajectory classes characterized by higher depressive symptoms. This is consistent with the studies that examined trajectories separately in males and females discussed above, in which trajectory patterns were similar across genders but the proportion of women in trajectories with higher symptom burdens was larger. Lower education (or in the case of children/adolescents, lower academic achievement) and lower income (or in the case of children/adolescents, lower family income) were also consistently associated with higher symptom burden trajectories. Stressful life events were associated with membership in depression trajectories with higher symptom burdens in adolescents (Stoolmiller et al., 2005) and adults (Melchior et al., 2013), mothers (van der Waerden et al., 2015) and older adults (Kuchibhatla, Fillenbaum, Hybels, & Blazer, 2012) but not in children (Mazza, Fleming, Abbott, Haggerty, & Catalano, 2010). Alcohol use was associated with higher symptom trajectories in adolescents (Costello, Swendsen, Rose, & Dierker, 2008; Yaroslavsky et al., 2013) but lower symptom trajectories in adults (Melchior et al., 2013). In older adults, ever consuming alcohol was found to be protective against a high-chronic symptom trajectory (Kuo, Lin, Chen, Chuang, & Chen, 2011) while daily alcohol consumption was not associated with trajectory class membership (Byers et al., 2012; Montagnier et al., 2014). Tobacco smoking was associated with poor depressive symptom trajectories in adolescents (Costello et al., 2008), older women (Byers et al., 2012) and adult men (Melchior et al., 2013). Previous history of psychopathology, particularly previous history of depression and anxiety (measured directly, or indirectly via antidepressant medication use), was associated with poor trajectories in all age groups (Andreescu, Chang, Mulsant, & Ganguli, 2008; Duchesne & Ratelle, 2014; Hsu, 2012; Liang et al., 2011; Luoma et al., 2015; Mazza et al., 2010; Melchior et al., 2013; Montagnier et al., 2014; Stoolmiller et al., 2005; van der Waerden et al., 2015; Yaroslavsky et al., 2013).

Additional predictors of trajectories characterized by higher symptom burdens in adolescents (Table 2) included problems with peer relationships such as peer rejection, lack of social competency or lack of connection with friends (Costello et al., 2008; Mazza et al., 2010; Yaroslavsky et al., 2013) as well as problems with family relationships including family conflict or lack of connection/attachment to parents (Costello et al., 2008; Duchesne & Ratelle, 2014). Parental depressive symptoms (Stoolmiller et al., 2005) and parental history of major depressive disorder (Yaroslavsky et al., 2013) were also predictive of higher symptom burden trajectories in adolescents. Other predictors of trajectories with high symptom burden in adolescents included lack of self-esteem (Costello et al., 2008), rumination (Mezulis, Salk, Hyde, Priess-Groben, & Simonson, 2014), loneliness, poor coping skills (Yaroslavsky et al., 2013) and early puberty (Mezulis et al., 2014). Means and odds ratios for most predictor variables followed a dose-response-like pattern, such that as the severity of the trajectory increased, so did the mean or odds ratio for that predictor variable. For example, Stoolmiller et al. (2005) found that average family income was

$28,921 among children in the very-low symptom group, $21,316 in the moderate-decreasing group, $17,634 in the high decreasing group and $15,679 in the high-persistent group.

Studies of depression trajectories in mothers (Table 3) examined risk factors related to characteristics of both the mother and the child. Characteristics related to the mother associated with maternal trajectories with higher symptom burdens included younger maternal age and marital instability/poor marital relationship quality (Campbell et al., 2007), past history of mental health problems, anxiety during pregnancy (Luoma et al., 2015; van der Waerden et al., 2015), overinvestment in work and a past history of childhood adversity (van der Waerden et al., 2015), poor life satisfaction, loneliness and a poor relationship with the child's grandmother (Luoma et al., 2015). Noncompliance in the child was associated with higher symptom trajectories in the mother (Gross et al., 2009). As with adolescents, there was an overall dose-response-like relationship between most predictor variables and depressive symptom trajectory. For example, Campbell et al. (2007) found that the proportion of women with stable marriages across the entire follow-up period was 82.3% in the low-stable group, 60% in the moderate-stable and intermittent groups, 43% in the moderate increasing and high-decreasing groups, and 38.7% in the high-chronic group.

Predictors of trajectories with higher symptom burden in older adults (Table 4) included poor self-rated health (Kuchibhatla et al., 2012; Kuo et al., 2011; Liang, Xu, Quiñones, Bennett, & Ye, 2011) number of chronic somatic diseases at baseline (Hsu, 2012; Kuo et al., 2011; Liang et al., 2011) past history of ischemic heart disease or stroke (Byers et al., 2012; Montagnier et al., 2014), diabetes, hypertension, obesity and breast cancer (Byers et al., 2012). Functional impairment was a robust predictor of higher symptom trajectory across a number of studies (Andreescu et al., 2008; Byers et al., 2012; Hsu, 2012; Kuchibhatla et al., 2012), but the evidence for cognitive impairment was mixed, with two studies reporting no effect of cognitive impairment on depression trajectory class membership (Byers et al., 2012; Kuo et al., 2011) and three studies reporting that it increased risk for membership in a trajectory class with a higher symptom burden (Andreescu et al., 2008; Kuchibhatla et al., 2012; Montagnier et al., 2014). Lack of social support was also a risk factor in older adults for membership in a trajectory class characterized by higher symptoms (Byers et al., 2012; Hsu, 2012; Kuchibhatla et al., 2012), although somewhat surprisingly, marital status was not (Byers et al., 2012; Hsu, 2012; Montagnier et al., 2014). Once again there was a dose-response-like relationship between the majority of predictor variables and odds of membership in trajectory classes of escalating severity. For example, Byers et al. (2012) found that odds ratios for being in the persistently low, increasing, and persistently high trajectory classes relative to the minimal symptom class were 1.60, 2.09 and 2.41, respectively, for past history of myocardial infarction. Among individuals with a clinical depression diagnosis, higher age, lower education, male gender, past year mental health treatment, medical conditions, avoidance coping, low self-esteem lack of psychological flexibility, number of close relationships, quality of significant relationships and social activities predicted membership in trajectory classes characterized by higher symptom burdens, although only lower education, medical conditions, psychological inflexibility and avoidance coping were significant in adjusted models (Cronkite et al., 2013).

Outcomes associated with trajectory group membership

Trajectories with higher depressive symptom burdens were frequently associated with subsequent psychiatric diagnoses: Stoolmiller et al. (2005) and Mezulis et al. (2014) found that adolescents in high depressive symptom trajectory classes were more likely to receive a diagnosis of major depressive disorder. Chaiton et al. (2013) looked at the effect of depressive symptom trajectories in adolescents on mental health in young adulthood and found that the rate of diagnosed mood or anxiety disorders was 3 times as high among girls and twice as high among boys who experienced a depression trajectory in adolescence characterized by high symptom burden. Individuals in the high trajectory group were also more likely to have taken antidepressant medications in the past month and to report higher stress levels, and boys in the high depression trajectory group were more likely than boys in the moderate or low trajectory groups to have sought psychiatric care.

Yaroslasky et al. (2013) looked at the impact of depression trajectories in adolescence on outcomes at age 30, including marital status, educational attainment, income, coping, dysfunctional attitudes, life events and daily hassles, self-esteem and social adjustment. They found that individuals who were in the high or moderate depressive symptoms trajectory classes during adolescence were less well-adjusted at age 30 than individuals in the low trajectory group. Specifically, they were less likely to be married (both more likely to be never married and more likely to be divorced), less likely to have a high school or a college degree, more likely to be lower or working class in terms of income, more likely to have dysfunctional attitudes, low self-esteem and poor coping skills and more likely to have experienced stressful life events and daily hassles. They also reported more episodes of major depression, anxiety and substance abuse relative to individuals in the low depression trajectory class. Salmela-Aro et al. (2008) looked at outcomes associated with depression trajectories in young adults. They found that individuals in the moderate and high depression trajectory classes in their 20s were less likely to have graduated from college, had lower salaries, more symptoms of burnout, poorer quality of interaction with partners, lower achievement and self-efficacy and greater social avoidance in their early 30s relative to individuals in the low trajectory class.

Studies of depression trajectories in mothers found that maternal depression trajectories were associated with poor outcomes in their children, including higher rates of both internalizing and externalizing behavior (Campbell et al., 2007; Gross et al., 2009; Matijasevich et al., 2015). Campbell et al. (2007) found that moderate increasing and high decreasing maternal symptom trajectories were associated with poorer social skills and, along with high-chronic symptom trajectories, with poorer cognitive skills in the child relative to low and moderate stable depression trajectories. They also found that a high-chronic trajectory in mothers was associated with lower behavioral competence in children relative to the low stable class. Wickham et al. (2015) found that maternal depressive symptom trajectories, particularly trajectories with high symptoms during middle childhood, were associated with risky health behaviors in adolescent offspring including common and illicit drug use, nonviolent delinquent behavior and violent delinquency.

Kuo et al. (2011) examined differences in BMI, metabolic functions and cortisol by depression trajectory class at the end of a 10-year follow-up period and found that older

adults who experienced persistent higher depressive symptoms had on average lower BMIs and higher levels of cortisol than older adults with low depressive symptom trajectories. The authors found no differences in blood pressure, blood glucose or cholesterol between the different depression trajectory classes. Hybels et al. (2015) found that older adults with depression trajectories characterized by higher symptom burdens were more likely to experience oral health problems. Several studies (Andreescu et al., 2008; Liang et al., 2011; Kuchibhatla et al., 2012) found that trajectories with higher depressive symptom burden were associated with higher mortality among older adults.

Discussion

The goal of this paper was to review studies examining heterogeneity in long-term (5+ years) trajectories of depressive symptoms. We identified 25 studies from 24 separate cohorts that met our search criteria. All but one of these studies examined depressive symptom trajectories in general population samples (as opposed to samples of clinically depressed patients), without regard to depression diagnosis. Collectively, the results of these studies support the idea that trajectories of depressive symptoms in the general population are heterogeneous: the number of latent trajectory classes ranged from 3 to 6, with most of the studies identifying either 3 or 4 classes. Patterns of trajectories varied in terms of severity (low, medium, high) and stability (stable, increasing, decreasing). Predictors of poor depressive symptom trajectory were similar to predictors of depression onset, and included female gender, low income (or in the case of children/adolescents, low parental income), low education (or in the case of children/adolescents, low academic achievement), past history of depression or other psychopathology, and stressful life events. Additional predictors of poor depression trajectories in adolescents included problems with peers and parents, alcohol/tobacco/drug use, parental history of depression and negative cognitive styles. Additional predictors of poor depression trajectories in mothers included younger maternal age, marital instability, past history of depression or anxiety and behavioral problems in the child. Additional predictors of poor depression trajectory in older adults included poor self-rated health, past history of somatic illness, functional and cognitive impairment and low social support. Outcomes associated with poor depression trajectories included increased risk for psychiatric diagnoses and use of antidepressant medications, lower adult income and educational attainment, lower probability of being married and lower self-esteem/self-efficacy. In mothers, poor depression trajectories were associated with poor social and behavioral outcomes in offspring. In older adults, poor depression trajectory predicted higher cortisol levels, poor oral health and higher mortality.

A comparison of depression trajectory patterns from the 25 studies included in this review yields several observations. First, stability of depressive symptoms over time appears to be more common than instability. Second, the majority of individuals either have no depressive symptoms or minimal depressive symptoms over time. Third, experiencing a trajectory that includes moderate depressive symptoms, even chronic moderate symptoms, appears to be common, particularly among adolescents, but a trajectory characterized by high depressive symptoms is rare. Nevertheless, a small proportion (< 10%) of individuals across different populations and age groups persistently report chronic, high levels of depressive symptoms for extended periods of time. Individuals following this type of trajectory pattern were more

likely to be diagnosed with depression or anxiety disorders, which suggests that individuals with this type of trajectory either suffer from clinical depression already, or will do so in the future. Either way, from a clinical perspective, this group is highly important and warrants further attention and study.

The studies in this review revealed consistent differences in long-term depression trajectories based on gender, age and race. Although not associated with differences in trajectory patterns, female gender was a robust predictor of membership in a trajectory class characterized by higher depressive symptoms. This is consistent with the finding that depression is more common in females than in males (Weissman & Klerman, 1985), as well as the finding that female gender is a risk factor for recurrence among individuals diagnosed with clinical depression (Kessing, Andersen, & Mortensen, 1998; Mueller et al., 1999). High symptom trajectories and unstable trajectories (i.e. increasing, decreasing) contained larger proportions of the sample in studies conducted in adolescents compared to studies conducted in adults and older adults, which is consistent with previous evidence that depression symptoms are highest and most variable among adolescents (Garber, Keiley, & Martin, 2002; Sutin et al., 2013). Finally, several studies found that non-white race was associated with membership in a trajectory class with higher symptoms. This may be driven at least in part by correlations between race and other demographic variables associated with depression trajectory, including education and income. It may also reflect higher levels of stress due to discrimination faced by many individuals in non-white racial groups.

Methodological considerations

Group-based trajectory models require large sample sizes in order to accurately and precisely estimate trajectories for multiple classes, particularly when the proportion of individuals falling within a given class is small. This review was limited to studies with at least 200 people in the sample, but many of the studies far exceeded this requirement: 72% (18 out of 25) of the studies had samples sizes greater than 500 individuals, and 60% (15 out of 25) had samples greater than 1,000 individuals. Similarly, although the inclusion criteria specified that the time-frame of follow-up be at least 5 years, many of the studies far exceeded this as well: 68% (17 out of 25) followed participants for 10 or more years.

Despite the large sample sizes and lengthy durations of follow-up, many of the studies assessed depression in participants at only a few time points. Three time points is the bare minimum required to estimate a quadratic trajectory, however additional time points are often needed in order to estimate trajectories with cubic or quartic shapes (Andruff, Carraro, Thompson, Gaudreau, & Louvet, 2009). The observation that stability in depressive symptoms over time was more common than instability must be interpreted with caution in light of this fact, as these studies may have had insufficient data to estimate more complex trajectory patterns. An additional limitation of many of these studies is the fact that they used shortened forms of established depressive symptom measures. Depression was measured with as few as 3–6 items at each time point in some studies, which brings the validity of their assessments of depression into question.

Directions for future research

As mentioned previously, only one of the 25 studies identified for this review (Cronkite et al., 2013) examined heterogeneity in long-term depressive symptom trajectories among individuals with a diagnosis of major depressive disorder (MDD). Examining trajectories of depressive symptoms in general population samples, as opposed to patient samples, has several distinct advantages: First, there is reason to believe that depression exists along a spectrum within the population (Kendler & Gardner, 1998). Individuals with MDD represent the severe end of that spectrum, but examining trajectories of depression in the entire population will likely result in a more accurate representation of the true underlying continuum of the disorder. From a public health standpoint, subclinical depressive symptoms are relevant both because they predict future clinical illness (Horwath, Johnson, Klerman, & Weissman, 1994; Laborde-Lahoz et al., 2015; Pietrzak et al., 2013) and because they themselves are associated with significant morbidity (Chachamovich, Fleck, Laidlaw, & Power, 2008; Kang, Eno Louden, Ricks, & Jones, 2015) and negative outcomes (Allen, Chango, Szwedo, & Schad, 2014; Grabovich, Lu, Tang, Tu, & Lyness, 2010). In addition, studies of depressive symptom trajectories in general population samples of children and adolescents can speak to the role of depressive symptoms in normal child/adolescent development, something that studies restricted to patient samples would be unable to do.

That being said, results from the 24 trajectory studies conducted using general population samples may not necessarily generalize to course trajectories in clinical MDD patients. Although the samples in these studies certainly contained individuals with clinical depression, these individuals were included in the same trajectory models as individuals without clinical depression. Furthermore, no distinction was made in these 24 studies between first-onset and recurrent depression cases. As the recurrence rate in depression may increase as the illness progresses (Kessing, Andersen, Mortensen, & Bolwig, 1998), it is important to distinguish between incident and prevalent cases when evaluating trajectory patterns. Further research is therefore needed to examine this topic in greater depth. The greatest barrier to such research will be the sample size and data requirements associated with group-based trajectory models, as sufficiently large, longitudinal studies of MDD cases are difficult and costly to assemble.

Another future direction for research in this area is to try to determine the extent to which associations between trajectory patterns and antecedent/outcome variables are causal. The studies in this review identified a wide array of antecedents and outcomes associated with depressive symptom trajectories; however it is unclear whether many of the identified associations are necessarily causal or, if they are causal, what the direction of causality might be. For example, Gross et al. (2009) showed that a high depression trajectory in mothers was associated with later externalizing and antisocial behaviors in children, but it is unclear whether the children were acting out in response to their mother's depression, whether the mothers experienced more depressive symptoms because their children were badly behaved, or whether both maternal depression and child externalizing/antisocial behavior were in fact caused by some third variable. Similarly, Liang et al. (2012) showed that the number of chronic diseases reported by older adults at baseline was associated with higher depressive symptom trajectories during follow-up, but since individuals with

previous depressive symptoms were included in the analysis, it is impossible to determine whether the somatic illness led to higher depressive symptom trajectories or whether previous depressive symptoms led to both increased incidence of somatic illness and higher depressive symptom trajectories during the period of follow-up.

Determining causality requires the establishment of the temporal associations between antecedents, trajectories and outcomes. This endeavor will be more straightforward, particularly for predictor variables, when modeling trajectories of illness course as course trajectories have clear temporal boundaries that are lacking in studies of symptom trajectories in general population samples.

Limitations

The greatest limitation of this review is the fact that it relies solely on qualitative comparisons of studies. To our knowledge, there is no quantitative method currently in existence to combine results from multiple group-based trajectory models, short of combining the individual samples themselves. As a result, it was impossible to account quantitatively for differences in the methodological quality of the studies. A second limitation of this review is that studies were identified, extracted and compared by a single person, the first author.

Conclusions

Long-term trajectories of depressive symptoms are heterogeneous, with most studies identifying either 3 or 4 distinct trajectory patterns. Patterns of depression trajectories vary primarily in terms of severity (low, medium, high) and stability (stable, increasing, decreasing). Overall, stable depressive symptoms over time appear to be more common than unstable depressive symptoms, particular among adults. Most people follow a trajectory characterized by minimal depressive symptoms, but a notable minority (somewhere between 2 and 15%) experience persistent high depressive symptoms over long periods of time. Predictors of membership in a trajectory class characterized by higher depressive symptoms include female gender, younger age, low income/education, non-white race, and stressful life events. Trajectories characterized by high symptoms are associated with poor psychiatric and psychosocial outcomes.

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Highlights

- Long-term trajectories of depressive symptoms are heterogeneous, with most studies identifying either 3 or 4 distinct trajectory patterns.

- Patterns of depression trajectories vary primarily in terms of severity (mild, moderate, severe) and stability (stable, increasing, decreasing).

- Overall, stable depressive symptoms over time appear to be more common than unstable depressive symptoms, regardless of severity.

- Most people follow a trajectory characterized by minimal depressive symptoms, but a notable minority (somewhere between 2 and 15%) experience persistent high depressive symptoms over long periods of time.

- Predictors of membership in a trajectory class characterized by higher depressive symptoms include female gender, younger age, low income/education, non-white race, and stressful life events.

- Trajectories characterized by high symptoms are associated with poor psychiatric and psychosocial outcomes.

Table 1

Studies using group-based trajectory models to examine heterogeneity in long-term trajectories of depression by population

Study	Country	Sample Size	Mean age at Baseline	% Female	Length of Follow-Up/# of time points	Depression Measure/# of items	Analytic Method	Final Model
Children/Adolescents:								
Stoolmiller et al., 2005	USA	206	14–15 years	0%	10 years, (10 time points)	CES-D (20 items)	GGMM	4 Classes: • Very low (5.8%) • Moderate-decreasing (34.0%) • High-decreasing (35.9%) • High-persistent (24.3%)
Costello et al., 2008	USA	11,559	16 years	52%	13 years, (3 time points)	CES-D (3 items)	LCGA	4 Classes: • Early high depressed mood (9.5%) • Late escalating depressed mood (2.4%) • Low depressed mood (59.4%) • No depressed mood (28.7%)
Mazza et al., 2010	USA	951	1st or 2nd grade	46%	6 years, 7 time points	Seattle Personality Questionnaire depression scale (6 items)	LCGA	5 Classes: Girls: • Moderately depressed risers (11.6%) • Moderately depressed changers (11.0%) • Mildly depressed stables (27.7%) • Low depressed risers (22.7%) • Low depressed stables (27.0%) Boys: • Moderately depressed risers (7.0%) • Moderately depressed changers (11.2%) • Mildly depressed stables (20.4%) • Low depressed risers (37.2%)

- Low depressed stables (24.3%)

Study	Country	Sample Size	Mean age at Baseline	% Female	Length of Follow-Up/# of time points	Depression Measure/# items	Analytic Method	Final Model
Chaiton et al., 2013	Canada	1,293	12–13 years	52%	5 years, 20 time points	Depressive symptom scale (6 items)	LCGA	3 Classes: Boys: • High (14.0%) • Moderate (36.0%) • Low (50.0%) Girls: • High (28.0%) • Moderate (43.0%) • Low (29.0%)
Yaroslavsky et al., 2013	USA	719	17 years	59%	14 years, 10 time points	CES-D (20 items)	GMM	3 Classes: • High stable (32.0%) • Moderate decreasing (44.0%) • Low decreasing (24.0%)
Duchesne et al., 2014	Canada	416	12 years	55%	6 years, 6 time points	CIDI-S (5 items)	LCGA	4 Classes: • High declining (7.0%) • Moderate increasing (11.3%) • Moderate stable (54.6%) • Low stable (27.2%)
Mezulis et al., 2014	USA	382	11 years	52%	7 years, 4 time points	CIDI (24 items)	GMM	3 Classes: • Early high (12%) • Increasing (37%) • Stable low (51%)
Adults:								
Salmela-Aro et al., 2008	Finland	297	21 years	74%	10 years, 7 time points	BDI-R (13 items)	GMM	3 Classes: • High increasing (16%) • Moderate (61%)

Study	Country	Sample Size	Mean age at Baseline	% Female	Length of Follow-Up/# of time points	Depression Measure/# of items	Analytic Method	Final Model
								• Low (23%)
Lincoln et al., 2010	USA	3,485	54 years (range: 25–75+ years)	63%	16 years, 4 time points	CES-D (11 items)	GMM	4 Classes: • Increasers (11%) • Slow decliners (15%) • High symptoms (5%) • Low symptoms (68%)
Cronkite et al., 2013	USA	382	40 years	55%	23 years 5 time points	Health and Daily Living Form (10 items)	LCGA	3 Classes: • Low severity (22.7%) • Moderate severity (49.5%) • High severity (27.8%)
Melchior et al., 2013	France	12,650	Range = 42–57 years)	26%	13 years, 5 time points	CES-D (20 items)	LCGA	4 Classes: Men: • No depression (72%) • Increasing depression (4.2%) • Decreasing depression (17.8%) • Persistent depression (6%) Women: • No depression (58.1%) • Intermittent depression (21.8%) • Decreasing depression (14%) • Persistent depression (6.1%)
Mothers:								
Campbell et al., 2007	USA	1,261	28 years	100% (mothers)	7 years, 7 time points	CES-D (20 items)	LCGA	6 Classes: • High chronic (2.5%) • Moderate increasing (6.2%) • High decreasing (5.6%) • Intermittent (3.6%) • Moderate-stable (36.4%)

Study	Country	Sample Size	Mean age at Baseline	% Female	Length of Follow-Up/# of time points	Depression Measure/# of items	Analytic Method	Final Model
								• Low-stable (45.6%)
Gross et al., 2009	USA	289	28 years	100% (mothers)	8.5 years, 8 time points	BDI (21 items)	LCGA	4 Classes: • Low symptoms (25.2%) • Moderate low (46.7%) • Moderate high (21.8%) • High chronic (7.3%)
Luoma et al., 2015	Finland	329	27 years	100% (mothers)	16 years, 6 time points	EPDS (10 items)	LCGA	4 classes: • Very low (18%) • Low stable (53%) • High stable (27%) • Intermittent (3%)
Matjasevich et al., 2015	Brazil	3,332	26 years	100% (mothers)	6 years, 5 time points	EPDS (10 items)	LCGA	5 Classes: • Low symptoms (34.8%) • Moderate low (40.9%) • Increasing (9.0%) • Decreasing (9.9%) • High chronic (5.4%)
Van der Waerden, 2015	France	1,807	30 years	100% (mothers)	5.5 years 9 time points	CES-D/EPDS 20/10 items	LCGA	5 Classes: • No symptoms (60.2%) • Persistent intermediate (25.2%) • Persistent high (5.0%) • High, pregnancy only (4.7%) • High, preschool only (4.9%)
Wickham et al., 2015	Canada	2,910	Unspecified	100% (mothers)	10 years, 6 time points	CES-D (12 items)	LCGA	5 Classes: • Low symptoms (47.9%) • Mild symptoms (36.0%) • Increasing symptoms (10.4%)

Study	Country	Sample Size	Mean age at Baseline	% Female	Length of Follow-Up/# of time points	Depression Measure/# items	Analytic Method	Final Model
								• Curvilinear trajectory (4.0%) • Stable high symptoms (1.7%)
Older Adults:								
Andreescu et al., 2008	USA	1,260	75 years	61%	12 years, 6 time points	mCES-D (20 items)	LCGA	6 Classes: • Persisting symptoms (2.1%) • Remitting symptoms (4.8%) • Emerging symptoms (4.2%) • Stable low group (52.6%) • Stable asymptomatic group (28.1%) • Stable asymptomatic group (8.2%)
Liang et al., 2011	USA	17,196	64 years	59%	8–11 years, 5–6 time points	CES-D (9 items)	LCGA	6 Classes: • Minimal (15.9%) • Low (36.3%) • Moderate stable (29.2%) • High decreasing (6.6%) • Moderate increasing (8.3%) • Persistently high (3.6%)
Kuo et al., 2011	Taiwan	3,922	68 years	43%	10 years, 4 time points	CES-D (10 items)	LCGA	4 Classes: • Persistent low (41.8%) • Persistent mild (46.8%) • Late peak (4.2%) • High chronic (7.2%)
Hsu et al., 2012	Taiwan	2,039	72 years	51%	14 years, 5 time points	CES-D (20 items)	LCGA	4 Classes: Males • Low (48.4%) • Medium (41.4%) • Increasing (7.4%) • Declining (2.7%)

Study	Country	Sample Size	Mean age at Baseline	% Female	Length of Follow-Up/# of time points	Depression Measure/# items	Analytic Method	Final Model
								Females: • Low (35.6%) • Medium (38.0%) • Increasing (16.3%) • Declining (10.1%)
Byers et al., 2012	USA	7,240	73 years	100%	20 years, 5 time points	GDS-S (15 items)	LCGA	4 Classes: • Minimal (27.8%) • Persistently low (54%) • Increasing (14.8%) • Persistently high (3.4%)
Kuchibhatla et al., 2012	USA	3,973	74 years	65%	10 years, 4 time points	mCES-D (20 items)	GGMM	4 Classes: • Stable low (76.6%) • Initially low, increasing (10.0%) • Stable high (5.4%) • Initially high, improving, reverting (8.0%)
Montagnier et al., 2014	France	2,590	74–75 years	59%	20 years 9 time points*	CES-D (20 items)	LCGA	3 Classes: Males: • Never depressed (65.0%) • Emerging depression (28.0%) • Increasing depression (7.0%) Females: • Never depressed (56.0%) • Rising subclinical (33.0%) • Persistent depression (11.0%)
Hybels et al., 2015	USA	944	75 years	58%	10 years 6 time points	CES-D (8 items)	LCGA	3 Classes: • Minimal depressive symptoms (43.0%) • Low depressive symptoms (41.0%)

Study	Country	Sample Size	Mean age at Baseline	% Female	Length of Follow-Up/# of time points	Depression Measure/# of items	Analytic Method	Final Model
								• Moderate depressive symptoms (16.0%)

Depression measure abbreviations: BDI = Beck Depression Inventory, CES-D = Center for Epidemiologic Studies Depression Scale, CIDI = Children's Depression Inventory, CIDI-S = Children's Depression Inventory – Short Form, EDPS = Edinburgh Postnatal Depression scale, GDS-S = Geriatric Depression Scale – Short Form, HSC = Hopkins Symptoms Checklist, LIFE = Longitudinal Interval Follow-Up Evaluation, mCES-D = modified CES-D (yes/no items). Analytic Method abbreviations: GGMM = Generalized Growth Mixture Model, GMM = Growth Mixture Model, LCGA = Latent Class Growth Analysis

*
Analysis conducted using age as time-metric

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Table 2

Predictors of membership in a trajectory class characterized by higher symptom burden in children/adolescents

Study	Problems with peers[a]	Problems with family[b]	Low family SES	Parent depression	Childhood internalizing/externalizing problems[c]	Poor academic performance	Negative cognitive features[d]	Stressful/negative life events	Alcohol/tobacco/drug use
Stoolmiller et al., 2005	-								
Costello et al., 2008				-				-	
Mazza et al., 2010		ns	*	ns		ns	-	ns	-
Chaiton et al., 2013	-	-	-	-	-	-	-	-	-
Yaroslavsky et al., 2013		ns	-			ns	-	-	
Duchesne et al., 2014	-	-	-	-		-	-	-	-
Mezulis et al., 2014	-	-	-	-		-	-	-	-

' ' = the study examined the variable and found that it was significantly associated with a depression trajectory characterized by high symptom burden

'ns' = the study examined the variable and found that it was not significantly associated with a depression trajectory characterized by high symptom burden

'-' = the variable was not examined in that study

[a] Connection to friends (Costello et al.), peer rejection and social competency (Mazza et al.), interpersonal dependency, loneliness (Yaroslavsky et al.)

[b] Parental transitions (Stoolmiller et al.), single-parent household, connection to parents (Costello et al.), family conflict (Mazza et al.), attachment to parents (Duchesne et al.)

[c] Depressive symptoms (Stoolmiller et al.), delinquent behavior (Costello et al.), anxiety (Duschesne et al.; Mazza et al.), attention problems, antisocial behavior, (Mazza et al.), infant negative affectivity (Mezulis et al.), major depression, substance abuse disorder (Yaroslavsky et al.)

[d] low self-esteem (Costello et al.), rumination, negative cognitive style (Mezulis et al.), personal and cognitive coping (Yaroslavsky et al.)

* Significant in males only

Table 3

Predictors of a membership in a trajectory class characterized by high symptom burden in mothers

Study	Younger Maternal Age	Lower Maternal education	Lower income	Marital instability/quality	Past history of depression/ mental health problems	Behavioral/emotional problems in child
Campbell et al., 2007					-	-
Gross et al., 2009	-	ns		-	-	
Luoma et al., 2015	ns	ns	-	ns		-
Matjasevich et al., 2015				-		-
Van der Waerden et al., 2015	ns			-		-
Wickham et al., 2015	-			-	-	-

' ' = the study examined the variable and found that it was significantly associated with a depression trajectory characterized by high symptom burden

'ns' = the study examined the variable and found that it was not significantly associated with a depression trajectory characterized by high symptom burden

'-' = the variable was not examined in that study

Table 4

Predictors of membership in a trajectory class characterized by higher symptom burden in older adults

Study	Chronic disease	Poor self-reported health	Tobacco/ alcohol	Cognitive impairment	Functional impairment	Past/baseline depression	Low Social Support	Marital Status	Lower education	Lower Income
Andreescu et al., 2008	-	-	-	-	-	-	-	-	-	-
Liang et al., 2011			-	-	-		-			
Kuo et al., 2011			***	ns	-	-	-	-		-
Hsu et al., 2011		-	-	-				ns	*	-
Byer et al., 2012		-		ns		-		ns		-
Kuchibhatla et al., 2012	-		-					-		-
Montagnier et al., 2014		-	ns			**	-	ns	*	-
Hybels et al., 2015	-	-	-	-	-	-	-	-	-	-

' ' = the study examined the variable and found that it was significantly associated with a depression trajectory characterized by higher symptom burden

'ns' = the study examined the variable and found that it was not significantly associated with a depression trajectory characterized by higher symptom burden

'-' = the variable was not examined in that study

*
in women only

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in men only

***
alcohol use was found to be protective a high depressive symptom trajectory