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Does the Severity of Autism Symptoms Change Over Time? A Review of the Evidence, Impacts, and Gaps in Current Knowledge

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Abstract

Studies evaluating change in autism symptom severity across the lifespan have yielded inconsistent results, making it difficult to assess the prevalence of meaningful change in autism symptom severity, and what characterizes it. Better understanding the ways in which autism symptoms change over time is crucial, with important implications for intervention. Synthesizing information across past studies, autism symptom severity change (especially decreases) appears common, though stability of symptoms is also frequent. Symptom severity change is characterized by variability in patterns of change *between* different individuals (between-person), variability in change *within* a person's trajectory across time (within-person), and variability in change *patterns* across symptom domains (i.e., social-communication, restricted/repetitive behaviors). Variability in severity change is likely impacted by differences in person-level characteristics (e.g., sex, IQ, sociodemographic factors) as well as developmental processes across time. Numerous methodological issues may impact our ability to understand how common change in symptom severity is, including varying measurement tools, analytic approaches, and change patterns between symptom domains across time. Potential implications of better understanding and characterizing symptom severity change include incorporation of severity change patterns and predictors of change into research on biomarkers, and consideration of such predictors as moderators or mediators of change in clinical practice.

Keywords

Autism Spectrum Disorder; Autism symptom severity; Symptom severity change; Symptom trajectories

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Introduction

In 1943, Leo Kanner first identified a unique behavioral phenotype (Kanner, 1943), now known as autism spectrum disorder (ASD). In this initial work, Kanner described eleven children (eight boys, three girls) between the ages of 2 to 8, all of whom exhibited a common set of symptoms. From early childhood, these children did not relate to others as expected, failed to use language to communicate, showed an obsessive tendency to maintain sameness, a restricted repertoire of behaviors, and limited spontaneity. In 1971, Kanner outlined the long-term outcomes of 9 of these 11 children: Two gained independence skills and were fully employed adults, one lived on a farm with his adoptive parents, five experienced worsening symptoms and lived in state hospitals or institutions, and one had died (Kanner, 1971).

Kanner's depictions of longer-term outcomes and change in behavioral phenotype were an important first step for evaluating developmental trajectories. They lacked in methodology, however, as they were mainly based on letters from family members and reports of treating physicians or educational staff at institutions. Since then, the rigor of longitudinal studies to evaluate outcomes has considerably increased. This is due to several advancements made in the field including early identification of large samples of autistic children followed prospectively across development (Georgiades, et al., 2021; Waizbard-Bartov, et al., 2022), individuals of diverse backgrounds being included in research samples (Giserman-Kiss & Carter, 2019), use of innovative analytic techniques for analysis of longitudinal data (Gotham, Pickles, & Lord, 2012; Kim, Macari, Koller, & Chawarska, 2016), and most importantly the development of standardized tools for assessment of autism symptoms (Lord, et al., 2000; Lord, et al., 2012; Lord, Rutter, & Le Couteur, 1994).

Although the diagnostic definitions of ASD have changed over time, the *DSM-5* currently separates the core symptoms into two domains: deficits in social communication and social interaction (SC symptoms), and restricted, repetitive patterns of behavior, interests, and activities (RRB) (American Psychiatric Association, 2013). In the 1980s, initial standardized assessment measures were developed to evaluate autism symptoms, informing clinical judgment and assisting clinicians in determining whether an individual met criteria for an autism diagnosis. The development of such tools changed the state of both autism research and clinical practice, providing a common framework and a valid, reliable way to measure autism symptomatology across researchers and clinicians (Lord, et al., 2022).

Two measures, in particular, are now viewed as the "gold standard" assessment tools for autism symptoms: The Autism Diagnostic Interview-Revised (ADI-R) (Lord, et al., 1994) and the Autism Diagnostic Observation Schedule (ADOS) (Lord, et al., 2000; Lord, et al., 2012). The ADI-R is a semi-structured caregiver interview conducted by a clinician trained to a reliability standard on this tool. It assesses both current and early childhood (ages 4-5 years) autism symptoms, and yields three subdomain scores, with the "Reciprocal Social Interaction" and "Communication" (verbal and nonverbal) subdomains assessing SC symptoms and a "Restricted, Repetitive, and Stereotyped Patterns of Behavior" subdomain for assessing RRB symptoms (Lord, et al., 1994). In contrast, the ADOS is a semi-structured assessment based on direct observation of autism symptoms in a standardized setting by a

trained clinician. The current version (2nd edition; ADOS-2) includes five modules, each adapted for use with individuals of a specific age and/or language development level, from pre-verbal to fluent speech. The ADOS-2 yields algorithm scores for two subscales: the Social Affect subscale (SC symptoms) and the RRB subscale, as well as an overall total algorithm score. In addition, the ADOS-2 allows for ascertainment of a Calibrated Severity Score (CSS), which is a standardized, 10-point severity metric that transforms algorithm scores into standardized scores relatively independent of individual characteristics such as age and language ability (Gotham, Pickles, & Lord, 2009). The CSS are available for the overall total algorithm score (ADOS CSS) as well as for the Social Affect (SA CSS) and RRB (RRB CSS) algorithms, separately (Hus, Gotham, & Lord, 2014). The CSS allows researchers and clinicians to use the ADOS-2 to measure autism symptom severity in a standardized way across modules, time, and developmental abilities. Most studies evaluating core autism symptom trajectories across time have incorporated the ADI-R, the ADOS, or both (Gotham, et al., 2012; Pellicano, Cribb, & Kenny, 2019; Shattuck, et al., 2007).

Several other standardized tools have been developed for the purpose of measuring autism symptoms. These include questionnaires based on parental report such as the Autism Behavior Checklist (ABC) (Krug, Arick, & Almond, 1980), the Social Responsiveness Scale (SRS) (Constantino & Gruber, 2005), and the Social Communication Questionnaire (SCQ) (Rutter, Bailey, & Lord, 2003); the Childhood Autism Rating Scale (CARS), a combination of clinician-rated observation informed by parent report (Schopler, Reichler, & Renner, 1986); and clinical interviews with parents such as the Diagnostic Interview for Social and Communication Disorders (DISCO) (Wing, Leekam, Libby, Gould, & Larcombe, 2002).

The ADI-R, ADOS, and these other standardized measures were not developed with the purpose of evaluating change in autism symptom severity over time. But, as they have been used repeatedly for diagnostic purposes with the same individuals, longitudinal studies have utilized them to examine individuals' symptom trajectories across the lifespan and to evaluate the possibility of change in symptom levels.

Several large studies have indicated that, for most individuals, autism symptom severity tends to remain stable across the lifespan (Gotham, et al., 2012; Szatmari, et al., 2015; Venker, Ray-Subramanian, Bolt, & Ellis Weismer, 2014). In contrast, a recent study examined patterns of autism symptom trajectories in a large sample of children (N=6975) from California (USA), finding evidence of six distinct trajectories, with symptom severity change being common across childhood (Fountain, Winter, & Bearman, 2012). However, this study did not use a standardized assessment tool for autism symptoms; rather, symptoms were evaluated based on a parent/caregiver interview conducted by trained California Department of Developmental Services staff. Such differences in findings across studies imply that the extent to which autism symptoms are prone to change across time is not yet clear. In addition, once change does occur, little is understood about what accounts for, or predicts, such change. Better understanding the ways in which autism symptoms change in severity over time could have important implications for intervention.

Aims and methods of the current review

The current paper reviews and synthesizes the literature focused on autism symptom severity trajectories over the lifespan. We evaluate 2 key questions: (1) How common is autism symptom severity change, and what characterizes it? and (2) What factors (individual/developmental characteristics as well methodological factors) influence findings concerning symptom severity change?

As the goal of this review is to both characterize symptom severity change as well as to identify factors that impact the inconsistent findings in the area, we describe a range of different aspects for each of the studies surveyed including main results, measure(s) used, analytic approach, sample characteristics and developmental period evaluated. We do this in order to identify factors that can help unpack different underlying causes that might contribute to the variability in findings in the area of symptom severity change.

Studies included in the current review were selected based on the following inclusion criteria: A) Study evaluated samples incorporating only individuals diagnosed with autism, B) Study participants were assessed repeatedly at multiple time points across development, C) Study used standardized assessment tools at each of the assessment time point (with the same tool used repeatedly at 2 or more time points), D) Study analyses assessed change in the severity of autism symptoms for the sample (either for total symptoms or both symptom domains separately). Since the ADI-R and ADOS-2 are considered to be the gold-standard, most widely used assessment tools for autism symptoms, we focus mainly on studies employing these measures across time. A detailed account of studies reviewed can be found in Table 1. The current review incorporates studies published by April 2022.

The term “autism symptom severity” includes a broad range of possible definitions. In the current review, we define autism symptom severity level based on scores on a standardized assessment tool for autism symptoms. We use the term “change in autism symptom severity” to mean statistically significant change in such severity levels across time. The authors recognize that traditional medical model terms related to autistic traits/characteristics, such as “symptom” and “severity”, have the potential of contributing to stigmatization and marginalization of autistic individuals. These terms are used in the current review in order to maintain consistency with the studies surveyed (and the measures they rely on) and so the use of these terms was unavoidable.

Does autism symptom severity change across time? Assessing change using standardized measures

Parent/caregiver report

ADI-R—In this section, we describe studies employing the ADI-R across childhood, from childhood into adulthood and prospectively from childhood, through adolescence and into adulthood, to identify autism symptom trajectories across time. All studies are detailed in Table 1.

Two studies have employed the ADI-R to identify short-term change in autism symptom severity across childhood, between 2-7 years of age. During this period, some children were found to remain stable while others decreased in severity, and to different degrees (Charman, et al., 2005). Severity change has also been shown to differ between toddlerhood (from 2 to 3 years of age) and early childhood (from 3 to 7 years) (Charman, et al., 2005), as well as between symptom domains based on childrens' symptom levels and other characteristics (Starr, Szatmari, Bryson, & Zwaigenbaum, 2003).

Studies using the ADI-R to evaluate change across a longer time period, from childhood to adolescence or adulthood, have also demonstrated a tendency for symptom severity decrease, with some stability. A number of studies have evaluated symptom severity change from early childhood through adolescence or adulthood by comparing the two types of scores ascertained from the ADI-R: "past/lifetime" scores (symptom presentation at age 4-5) and "current" scores. Most of these studies have identified a decrease in symptom severity from childhood to later ages. Decreases in total symptom severity were identified at a group level (i.e., for entire samples of individuals with ASD combined) (Boelte & Poustka, 2000; Fecteau, Mottron, Berthiaume, & Burack, 2003), as well as when evaluating the different ADI-R subdomains separately. Decreases in social and communication symptoms were found at a group level from early childhood through late adolescence (McGovern & Sigman, 2005), and individually, most participants (82%) tended to decrease in these subdomains (Piven, Harper, Palmer, & Arndt, 1996). RRBs have been found to either decrease in severity or remain stable at the group level, while at the individual level, about half (55%) of individuals show decreases in RRB severity (McGovern & Sigman, 2005; Piven, et al., 1996). In addition to this general trend of severity decrease, these studies have also found variability in severity change patterns between individuals; most participants either decreased or retained stable severity levels from early childhood up to adulthood, with a much lower incidence of severity increase (Fecteau, et al., 2003). Rates of change also differed between individuals.

The longer-term period evaluated, from childhood to adulthood, also allowed these studies to compare differences in severity change across development. While change is evident during both adolescence and adulthood, it can differ in specific pattern (decrease or increase) based on the period evaluated (Gillespie-Lynch, et al., 2012), and between symptom domains in both in terms of pattern and amount of change (Gillespie-Lynch, et al., 2012; Seltzer, et al., 2003).

Some studies have used the ADI-R prospectively at multiple time points to evaluate symptom severity change. From childhood to late adolescence, a decrease in the severity of social-communication symptoms was identified, yet the rate of decrease (linear or quadratic) varied based on participants' symptom severity levels and cognitive ability at their final assessment (Lord, Bishop, & Anderson, 2015). Severity change also differed between and within symptom domains, with RRB tending to decrease in one subtype (repetitive sensorimotor), and exhibit variable change patterns (including increases) in another subtype (Insistence on Sameness) for some participants Studies evaluating change prospectively across adolescence and adulthood have shown that autism symptoms, including the majority of ADI-R subdomains, tend to decrease in severity across this period (Taylor & Seltzer,

2010). At the individual level, however, change appears highly variable between participants in this developmental period, with a substantial proportion decreasing (26-61% across the different studies and symptom domains evaluated), many remaining stable (20-55%), and a minority of participants increasing in symptom severity (12-26%) (Shattuck, et al., 2007; Woodman, Smith, Greenberg, & Mailick, 2015). In addition, rate of change, specifically of decreasing severity (slower vs faster), has been found to vary during adolescence and adulthood, both between individuals with different characteristics (Woodman, Smith, Greenberg, & Mailick, 2016) as well as across age within this period (Taylor & Seltzer, 2010)

Summary: Evaluating autism symptom severity change using the ADI-R, studies focusing on short-term change across childhood (ages 2 to 7), have shown change to be common across childhood, and also varied between children with different developmental profiles, symptom domains, and across childhood periods. Studies using the ADI-R to evaluate longer-term change, from early childhood to adulthood, have identified a tendency for severity decrease, but severity change was also highly variable between individuals, between symptom domains, and across development. Finally, using the ADI-R to evaluate change prospectively from childhood and across adolescence into adulthood, autism symptoms tended to decrease in severity, with some stability identified as well. Severity change also varied between individuals, in the rate at which individuals decreased over time and change differed between adolescence and adulthood.

Other standardized measures (CARS, SRS, SCQ, ABC)—Some studies have employed other parent/caregiver report measures beyond the ADI-R to identify autism symptom trajectories across childhood through adolescence and up to adulthood (detailed in Table 1).

Similar to those utilizing the ADI-R to evaluate change across childhood through adolescence, studies using other standardized measures across this period have also identified substantial decrease in symptom severity (Lin, Chiu, Wu, Tsai, & Gau, 2022; Mesibov, Schopler, Schaffer, & Michal, 1989; Pellicano, 2012; Szatmari, et al., 2009), as well as some evidence of stability (Eaves & Ho, 2004; Lin, et al., 2022), over time. These studies have also identified high variability in severity change within samples. Subgroups of individuals (33%) within larger “stable” samples have been shown to either decrease or increase in severity (Eaves & Ho, 2004). Patterns of change seem to also differ based on the developmental period evaluated (e.g., childhood vs adolescence; Lin, et al. (2022)). Moreover, rate of change (especially of decreasing severity) differs between symptom domains, with social symptoms decreasing more rapidly than RRB symptoms (Pellicano, 2012). Rate of change also varies across time, with the rate of decrease in symptom severity slowing with age (Szatmari, et al., 2009). Finally, in a very large sample (N=6975), Fountain, et al. (2012) demonstrated all three types of variability in symptom trajectories. First, they identified six distinct group pattens for symptoms (in each of the domains: social, communication, RRB) that differed according to symptom development from age 2 to 14. Second, most group trajectories for social and for communication symptoms decreased in severity over time, while RRB trajectories tended to remain stable. Last,

symptom trajectories were variable in rate of severity change; some children showed rapid improvements while others demonstrated slower and less marked improvements over time.

Simonoff and colleagues (2019) evaluated autism symptom severity change prospectively across adolescence and adulthood, finding stability across time (Simonoff, et al., 2019). However, the pattern of change differed based on educational placement, with individuals attending specialist schools increasing in severity over time compared to those attending mainstreamed schools.

Summary: Evaluation of symptom severity change across childhood to adolescence using a variety of standardized measures shows a tendency for decreases in symptom severity, alongside three types of variability in change: between children, between symptom domains, and in pattern and rate of change within a person across time and developmental period. Evaluation of severity change from adolescence through adulthood indicated symptom stability, but individual change patterns also varied, with some individuals showing a stronger tendency to increase in severity across time.

Assessments based on direct clinician observation

ADOS CSS—Since the development of the ADOS CSS (Gotham, et al., 2009), many studies have used it to evaluate symptom severity change across time. Here, we describe studies employing the ADOS CSS to identify symptom severity trajectories across early childhood, from early childhood through adolescence, and from middle childhood up to adulthood (detailed in Table 1).

Evaluating symptom severity change across early childhood, several studies have identified large groups of children (ranging from 78% to 89% of samples) characterized by stable symptom trajectories (Kim, et al., 2016; Szatmari, et al., 2015; Venker, et al., 2014). They also showed some variability in change between children, with smaller subgroups either decreasing (11%-14%) or increasing (8%-16%) in severity. Another study, however, identified higher prevalence of change during this period, with 29% of the children decreasing and 17% increasing in severity (54% retained stable levels) (Waizbard-Bartov, et al., 2020). Reduction in symptom severity has also been found for children who had received intervention during early childhood (Giserman-Kiss & Carter, 2019), with higher rates of decreasing severity identified among children diagnosed early (65%) compared to those diagnosed at a later age (23%) (Gabbay-Dizdar, et al., 2021).

The ADOS CSS has also been used to evaluate symptom trajectories beginning in early childhood and across a longer duration, up to middle childhood and adolescence. Most studies have identified high prevalence of severity change, again characterized by substantial variability. Grouping participants according to their individual severity change patterns, 7-27% of individuals have been shown to decrease in symptom severity with 9-24% showing increases in severity across this period (Georgiades, et al., 2021; Gotham, et al., 2012; Waizbard-Bartov, et al., 2022). Other studies that have grouped participants based on their individual outcomes in adolescence or adulthood (e.g., retaining/not retaining ASD diagnosis, having typical-range IQ or intellectual disability) have found that most individuals

(79-100%) show change in symptom severity levels over time, whether decreasing or increasing in severity (Clark, Barbaro, & Dissanayake, 2017; Zachor & Ben-Itzchak, 2020).

These studies also suggest that symptom severity change is characterized by variability across development. Severity change patterns appear to differ between early childhood/preschool years and middle childhood/school-age, with earlier ages having a stronger tendency toward severity decrease, and later ages being characterized by a slower rate of severity decrease, a plateauing symptom trajectory, or increasing severity (Clark, et al., 2017; Georgiades, et al., 2021; Waizbard-Bartov, et al., 2022). One recent study found that, at the individual level, most children tend to experience severity change during either early *or* middle childhood, remaining stable during the other period (Waizbard-Bartov, et al., 2022).

One recent study used the ADOS CSS to evaluate symptom severity change from middle childhood into adulthood. While symptom severity appeared stable across this period at a group level, at the individual level, severity change was quite common. More than half of individuals were shown to experience significant change, either decreasing (29%) or increasing (29%) in severity (Pellicano, et al., 2019).

Summary: While all studies reviewed using the ADOS CSS have identified some change in symptom severity during early childhood, some have identified a strong tendency for symptom stability while others have emphasized a tendency for severity decrease during this period. Thus, the extent to which autism symptoms either change or remain stable across this period is unclear (and might also be related to other characteristics). Studies using the ADOS CSS to evaluate change from early childhood through adolescence have shown change to be common across this time, with substantial proportions of children either decreasing or increasing in severity. Severity change also differed across time and between developmental periods, with decreases being more prominent during early childhood, and middle childhood being characterized less often by symptom decreases and more often by stable trajectories or increasing symptom severity. Only one study has focused on change from middle childhood into adulthood using the ADOS CSS, showing that the majority of individuals experienced change in severity (either increasing or decreasing) rather than stability through this developmental period.

Summary: Does autism symptom severity change over time, and how is change characterized?

Most of the studies reviewed above suggest that, rather than remaining stable over time, autism symptoms change in severity in a substantial proportion of individuals. Moreover, the evidence indicates that the most common pattern of change over time is decreasing symptom severity. More specifically, most studies reviewed describe decreases in the mean severity level of entire groups, or among substantial proportions of individuals within a sample, as the dominant pattern of change across time. However, findings are not consistent across all studies, and some have identified very large groups of individuals that retain stable symptom levels.

Findings also suggest symptom severity change is characterized by extensive variability. Specifically, three types of variability were identified. The first is *between*-person variability, that is, variability in patterns of change, indicating that autism symptoms change differently for different individuals or groups of individuals. Many individuals show decreases in symptoms over time, while a substantial proportion retain stable symptom levels, and a relatively smaller subgroup appears to increase in symptom severity. Even among individuals who demonstrate the same general pattern of change, rates of change across time can differ with symptoms changing at either a slower or more rapid pace. For instance, Fountain, et al. (2012) identified 6 distinct trajectories of communication and of social symptoms across childhood, each of them showing different rates of symptom severity decrease.

The second type of variability identified is *within*-person variability, that is, variability in change across time/development within a specific individual. These are differences in pattern and rate of change across time and development, within a person's own trajectory. For example, Waizbard-Bartov, et al. (2022) found that most children experience severity change (increase or decrease) rather than stability during either early *or* middle childhood, but not both (i.e., most retain stable severity levels during the other period). Many studies indicate that decreases tend to occur at faster rates during earlier ages, either slowing or plateauing with time (Fountain, et al., 2012; Georgiades, et al., 2021; Lord, et al., 2015; Szatmari, et al., 2009; Taylor & Seltzer, 2010; Waizbard-Bartov, et al., 2022). It is important to note that these different types of variability (between and within person) are not mutually exclusive. For instance, rates of change can differ both between different individuals or groups as well as within a specific individual across various developmental periods and across symptom domains (see below).

The third type of variability identified is *between symptom domains.* Social-communication and RRB symptoms (and subcategories of RRB) appear to show different change patterns within entire samples (Pellicano, 2012), within subgroups of individuals in a given sample (Lord, et al., 2015), and within specific individuals across time (Fountain, et al., 2012). For example, subgroups of individuals have been found to decrease in one symptom domain (SC symptoms) and increase in the other (RRB subcategory Insistence on Sameness) (Lord, et al. (2015).

Research gaps: Contributors and implications

The significant variability characterizing symptom trajectories in autism presents a challenge to the analysis of change and the ability to draw consistent conclusions regarding its prevalence. Findings are mixed and substantial gaps in the literature are apparent. In addition, studies in this area have utilized many different methodological approaches to identify and analyze changes in symptom severity over time. These different research approaches may have contributed to the mixed pattern of results reported in the literature. Indeed, a number of factors may contribute to such differences, including the use of diverse standardized tools for assessing autism symptoms, the variety of analytic methods employed for evaluating change, and the fact that the two symptom domains show different severity change patterns across time, yet are often lumped together.

Measurement Issues

The use of different standardized assessment tools may have contributed to somewhat different results. Studies utilizing the ADI-R, a clinician-administered parent interview, have consistently identified decreases in symptom severity across development (Fecteau, et al., 2003; Lord, et al., 2015; McGovern & Sigman, 2005; Woodman, et al., 2015). Studies employing the ADOS CSS, in contrast, have yielded more mixed results, especially concerning the prevalence of severity change during early childhood. As noted previously, several studies using the ADOS CSS have documented substantial decreases in severity across this period (Clark, et al., 2017; Georgiades, et al., 2021; Giserman-Kiss & Carter, 2019; Waizbard-Bartov, et al., 2020), while others have emphasized symptom stability (Gotham, et al., 2012; Kim, et al., 2016; Szatmari, et al., 2015; Venker, et al., 2014).

Most studies that have identified large groups of children with stable symptom trajectories have used the ADOS CSS. This could suggest that the ADOS CSS is better at identifying stable trajectories than other measures, or that it is less sensitive to capture change; that is, it requires relatively higher “amounts” of severity change in an individual’s trajectory over time for such change to manifest in the measurement. Indeed, a meta-analysis of studies that used the ADOS CSS to evaluate symptom severity change from infancy to adolescence concluded that the ADOS CSS tends to remain stable over time across most studies (Bieleninik, et al., 2017). The authors also added that, while the ADOS CSS is the most phenotypically stable measure of autism symptoms, the limited range along with the very fact that symptoms do appear stable over time might indicate they are less sensitive to change in symptom severity and thus may underestimate it. On the other hand, comparing total symptom scores across time, as with the ADI-R, leads to other serious methodological problems because it essentially compares symptom levels in an unstandardized way among individuals spanning different developmental periods, cognitive abilities, and other differentiating characteristics that might affect symptom presentation. It is critical to keep in mind that these assessment tools were not developed to measure change across time; rather, they were devised to inform clinical judgment regarding an individual’s diagnosis at the time of assessment. This emphasizes the crucial need to develop a standardized, sensitive measurement tool with a wide enough range to capture change in symptom severity across time, while considering different individual characteristics. One example of such a tool is the Brief Observation of Social Communication Change (BOSCC) (Grzadzinski, et al., 2016), a relatively new standardized measure aimed to quantify subtle changes in social communication skills over short-term periods (such as related to receiving specific interventions). Future longitudinal studies using this measure could explore if it may also be well-positioned and sufficiently sensitive to measure change in symptoms across time.

The fact that autism symptoms present differently across different ages (e.g., children vs. adults) could also impact the measurement of symptom severity change across time and developmental periods (Bal, Kim, Fok, & Lord, 2019). Standardized assessment tools rely heavily on symptom manifestation in childhood and early adolescence. The ADOS, for instance, was originally developed (and has been revised over time) mostly based on symptom presentation in individuals up to 16 years of age (Gotham, et al., 2008;

Gotham, Risi, Pickles, & Lord, 2007). The ADI-R includes diagnostic cut-off scores for past behaviors only, not accounting for parent-reported current symptom presentation (the Current Behavior Algorithm). To reliably measure and consider symptoms at later ages, however, diagnostic instruments must be sensitive to, and adapted for, symptom presentation across the lifespan (Bal, et al., 2019). Several efforts have been made in this direction. For example, an adult self-report version of the SRS-2 was developed (Constantino & Gruber, 2012), symptom presentations on the DISCO were compared between children and recently-diagnosed adults to understand age impacts (Carrington, et al., 2019), and the ADOS has been adapted for use with both verbally fluent adults (i.e., Module 4) (Hus & Lord, 2014), and minimally verbal adolescents and adults (i.e., Adapted ADOS) (Bal, et al., 2020). As measurement becomes adapted to age-dependent symptom presentations, it is important to determine whether symptom severity change evident across later ages results from true change or, rather, from less reliable assessments of symptoms at these ages.

Differences between rates of change identified using either the ADI-R or the ADOS CSS might also result from the different informants used with each measure. For example, the higher prevalence of symptom severity change, especially severity decrease, identified using the ADI-R might suggest that parents, who are involved in most aspects of their child's life, have more information and are in a better position to *accurately* identify change in symptoms over time compared to clinicians conducting a short assessment in a specific context with a more restricted amount of information. Alternatively, parental-reports of severity change on the ADI-R might be *inflated* compared to those on the ADOS, as parental report is potentially subject to more biases relative to clinical judgment made using direct observation. For instance, scores on the parent-report based ADI-R have been shown to be affected by parental concerns regarding ASD (Havdahl, et al., 2017), and parental report reliant on memory have been previously identified as a serious problem in longitudinal studies (Ozonoff, Li, Deprey, Hanzel, & Iosif, 2018). A third possibility is that a gap between the symptom severity level ascertained based on parent report vs clinician observation might express the fact that symptoms can manifest to different degrees in various contexts for the same individual (i.e., day-to-day experience with familiar others compared to a limited, structured setting with an unfamiliar adult). These are several potential explanations for gaps in severity levels established using different informants, and it remains difficult to sort out the true impact of informant on study findings. This is, of course, exactly the reason why a rigorous clinical assessment of individuals referred for possible ASD, as well as evaluations of severity change over time, should include both parent report as well as direct clinical observation (Havdahl, et al., 2017; Lord, et al., 2022), allowing for comparison and combination of multi-informant data to create a more representative symptomatic presentation across contexts and perspectives.

Analytic Approaches

A variety of analytic approaches have been used to define, analyze, and interpret symptom severity change. Such differences in methodological approaches may also impact results and contribute to the inconsistent findings in the area. For example, as a result of the large variability in change patterns between individuals, evaluating means (aggregated scores) across entire samples could potentially mask changes occurring across individual

participants comprising the samples. For instance, mean scores showing symptom severity decreases for an entire sample might indeed reflect the fact that most individuals decrease in severity to some degree, or rather, that a specific *group* of individuals within the sample substantially decreases in severity, thereby lowering the mean for the entire sample. On the other hand, mean scores showing symptom stability (i.e., no change) over time might be masking the fact that some individuals decrease in severity while others increase. Several studies reviewed herein identified no change in symptom severity levels across time when averaging across entire samples, but once change was analyzed within individuals, between 33-58% demonstrated significant symptom severity change across time (Eaves & Ho, 2004; Pellicano, et al., 2019; Waizbard-Bartov, et al., 2022). It would thus be highly informative, when evaluating means of entire samples, to also consider and interpret the variability around mean levels and mean changes in symptom severity in order to understand the extent of individual differences within the overall trend.

In an attempt to deal with the widely prevalent between-person variability in severity change, many studies have separated participants into subgroups that show different patterns of change. The different analytic methods used for this purpose, however, might have also contributed to inconsistencies in results across studies. One such approach is mixture modeling (Muthén & Muthén, 2000), wherein probability-based latent groups are derived based on the symptom trajectories of all individuals in the sample across time. These groups are characterized by a "shared" pattern of severity change across time points. Many studies utilizing this approach have identified large subgroups that show stable trajectories (Gotham et al., 2012; Venker et al., 2014). Other studies have taken a different approach, evaluating significant change in an individual's severity by comparing levels across time points and often assigning participants into subgroups based on these patterns of individual change (Pellicano, et al., 2019; Shattuck, et al., 2007; Waizbard-Bartov, et al., 2020). Studies employing this latter approach tend to identify larger subgroups of individuals who experience significant symptom severity change across time. In addition, many subgroups in studies of autism severity change are characterized by high within-group variability, as manifested in variability in the direction of change, rate of change, and individual-level deviance from the group trajectory (Georgiades, Bishop, & Frazier, 2017; Georgiades, et al., 2021). That is, groups that are described using a cohesive label such as "improving" (Venker, et al., 2014), "worsening" (Gotham, et al., 2012), or "improving then plateauing" (Georgiades, et al., 2021) actually include different patterns of individual change, which "average out" within the group. This within-group variability is especially evident in groups identified using mixture modeling. For instance, Gotham et al. (2012) described a "worsening" (increased severity) group, but about a third of these individuals showed wide variability in change across time, some having lower severity levels in their final measurement compared to previous ones. Similarly, one-fifth of the individuals in Venker et al.'s (2014) "worsening" group showed the same levels of symptom severity from initial to final measurement. A third of the participants in the "Improving" class (decreased severity) remained stable over time (and one participant worsened). This phenomenon also characterizes very large subgroups labeled as "stable severity". Within the two large stable classes identified by Venker, et al. (2014), comprising 78% of the sample, roughly 40% of participants evidenced decreases in symptoms, along with 23-33% of participants

who increased in symptoms across childhood. The mixture modeling approach requires sufficiently large samples to reliably detect latent subgroups with a shared symptom trajectory (Ram & Grimm, 2009). It may be that the high variability characterizing autism symptom trajectories, in combination with the relatively smaller samples used in longitudinal studies of ASD, impact the ability of statistical models to identify symptom severity change, especially at the individual level. This might contribute to the identification of subgroups with high within-group variability and/or large subgroups interpreted as having stable trajectories. Adding to the challenge is that often it is not clear how different studies specified the models used to identify subgroups. In order to better understand the subgroups yielded by any model, especially concerning within-group variability in the parameters (e.g., initial severity level, change over time), it is important to report how the model was specified. Thus, when evaluating the conclusions of different studies regarding the prevalence of severity change, the method for assigning participants into subgroups must also be considered.

While studies have tried to tackle the between-person variability characterizing symptom trajectories in the ways mentioned above, the within-person variability presents a challenge for analysis as well. Studies evaluating symptom severity change across several developmental periods have identified differences in individuals' change patterns across different ages (Georgiades, et al., 2021; Gillespie-Lynch, et al., 2012; Szatmari, et al., 2009; Taylor & Seltzer, 2010; Waizbard-Bartov, et al., 2022), as well as between entire groups evaluated at different developmental periods (Lin, et al., 2022; Seltzer, et al., 2003). Such differences highlight a potential problem when attempting to define an individual's longitudinal symptom trajectory across age (spanning several periods of time) using a single severity change pattern to represent them all in a combined way. Such a trajectory might not be representative of actual severity change. Rather, it could inadvertently mask different severity change patterns occurring across time and development of clinical importance (Seltzer, Shattuck, Abbeduto, & Greenberg, 2004). Evaluating change across specific developmental periods, however, would provide a more precise portrayal of symptom severity change as well as a meaningful context through which change can be understood (Nordin & Gillberg, 1998).

Last, due to the costly and effortful nature of longitudinal data collection, many of the studies reviewed describe repeated reporting and re-analyses of the same samples as additional data waves are collected with time (see Table 1 for an account of specific samples repeatedly used in different studies). In some cases, these follow up analyses yield somewhat different results compared to previous publications (Shattuck, et al., 2007; Taylor & Seltzer, 2010). This issue, typical of longitudinal studies, requires further investigation concerning effects on findings, and specifically on inconsistent findings, in the area of symptom severity change. It is clear, however, that different results reported using the same samples provide additional evidence to the mix of findings when evaluating change patterns across shorter vs longer periods, as well as by using various analytic approaches.

Symptom-domain trajectories

Differences in change patterns between the two autism symptom domains could affect the combined trajectory in several ways. For instance, ADOS CSS scores are biased towards SC symptoms, as items measuring this domain account for roughly two thirds of the items scored in the ADOS severity algorithms (Lord, et al., 2000). This could lead to unequal domain-representation within the combined symptom trajectory. Similar to the fact that different severity change patterns can be averaged-out (increase/decrease) between individuals, this can also occur between the two symptom domains. That is, different (or even opposite) severity change patterns demonstrated by SC symptoms compared to RRB symptoms might average-out within the overall symptom trajectory, masking change occurring in each individual domain. Indeed, SC and RRB symptoms have repeatedly been shown to follow different trajectories across time. SC symptoms, for the most part, show a consistent tendency to decrease in severity (Bal, et al., 2019; Fecteau, et al., 2003; Fountain, et al., 2012; Lord, et al., 2015; McGovern & Sigman, 2005) while RRB trajectories tend to either remain stable (Fountain, et al., 2012; Gillespie-Lynch, et al., 2012; Piven, et al., 1996; Starr, et al., 2003), decrease (Lin, et al., 2022; McGovern & Sigman, 2005; Pellicano, 2012; Shattuck, et al., 2007; Woodman, et al., 2015), or increase in severity for specific individuals, items, or periods (Charman, et al., 2005; Fountain, et al., 2012; Lord, et al., 2015). This potential pitfall can be difficult to identify as most studies evaluate either the combined symptom trajectory or separate domain trajectories, but not both. One way of preventing these issues would be to analyze symptom domains separately, interpreting change patterns for each domain in addition to their combined presentation in the overall symptom trajectory. This could prove highly informative for understanding which of the processes is propelling change (for instance, in response to intervention) and implications of that change (Hus, et al., 2014).

Summary: Methodological impacts on findings in the area of symptom severity change

The variability characterizing autism symptom trajectories renders findings relatively susceptible to, or even biased by, the various research methodologies employed. First, different standardized tools for assessing autism symptoms can contribute to the inconsistent results in this area due to distinct ways of scoring and measuring symptom change, a limited ability to adequately evaluate symptom presentations among adults, and the use of different types of informants (parent-report versus clinician observation), which can lead to conflicting information. Second, various analytic approaches for evaluating change have been used across studies, some of which may inadvertently obscure the between- and within-person differences in change. This can occur by analyzing sample means without considering the variability in change between participants, by dividing individuals into subgroups characterized by high within-group variability that might obscure individual change patterns, and by evaluating change across long durations of time without considering differences across development. In addition, many of the studies reviewed have repeatedly reported on the same cohorts with additional timepoints as these are added to the sample. The impact of repeated analyses of the same data and its effect on findings in the area of symptom severity change requires further investigation. Third, as the two symptom domains show different severity change patterns across time, their composite (overall) symptom trajectory might primarily reflect change in a single symptom domain (usually SC

symptoms), and/or fail to genuinely reflect either of these change patterns. Finally, there is currently no consistent criteria across studies to determine how much change, or proportion of individuals experiencing change, is needed for change to be considered present within a given sample (and clinically meaningful for individuals' everyday life). While interpretation of findings is always subjective to some extent, the use of varied measures and analytic approaches in this area also contributes to inconsistencies in the literature; different aspects of similar results can be highlighted or interpreted in contradicting ways.

Factors associated with symptom severity change

While the high variability characterizing symptom severity change presents a challenge for analysis, the fact that change does not happen uniformly creates an opportunity to evaluate predictors and impacts associated with specific types of change. For example, what factors may account for the different severity change patterns evident between individuals? And why do distinct change patterns seem to characterize specific periods of development? Several factors may impact the main trends identified concerning symptom severity change.

An overall decrease in symptom severity over time appears to be a robust pattern across many studies (Fecteau, et al., 2003; Giserman-Kiss & Carter, 2019; Lord, et al., 2015; McGovern & Sigman, 2005; Szatmari, et al., 2009; Woodman, et al., 2016). Specifically, studies reporting on more recently ascertained cohorts (Clark, et al., 2017; Georgiades, et al., 2021; Waizbard-Bartov, et al., 2022) have also identified higher proportions of individuals that decrease in symptom severity compared to those reporting on older cohorts (Gotham, et al., 2012). This can be understood in several ways. First, an increasing appreciation of the heterogeneity characterizing individuals with autism (Harris, 2019) has contributed to more diversity in samples' symptom presentations, capturing individuals with less severe symptom presentations (Hertz-Picciotto & Delwiche, 2009) as well as more females, and those without cognitive or language impairments (Seltzer, et al., 2003). This change in sample composition could impact findings in the areas of symptom severity change, as it has been shown that decrease in symptom severity, and a faster rate of decrease, are associated with both having lower initial symptom severity during early childhood as well as belonging to a more-recently born cohort (Clark, et al., 2017; Fountain, et al., 2012; Georgiades, et al., 2021; Szatmari, et al., 2015; Woodman, et al., 2016). In addition, an increasingly higher proportion of individuals have access to intensive early intervention, services, and treatments that are specific to autism (Seltzer, et al., 2004; Zwaigenbaum, et al., 2015). Some studies have documented reductions in symptom severity following early interventions aimed at core symptoms, in both short-term (Giserman-Kiss & Carter, 2019) as well as longer-term (Pickles, et al., 2016) outcomes. But this relationship is not consistent across the literature (Gotham, et al., 2012; Waizbard-Bartov, et al., 2020). Future studies would do well to evaluate how differential types and intensity levels of early intervention associate with symptom severity change across the life span. These factors, however, could result in a high and increasing number of individuals experiencing decrements in severity over time, even more so as individuals with milder symptom presentations and higher cognitive, developmental, and language abilities at a young age have been shown to decrease more in autism severity via early interventions (Bentenuto, Bertamini, Perzolli, & Venuti, 2020; Hudry, et al., 2018).

Symptom severity change is also characterized by variability. Differences in other participant-level characteristics might be related to the variability *between*-person–the different severity change patterns demonstrated by individuals. For instance, symptom trajectories have been shown to vary according to sex, with girls more likely to exhibit decreases in symptom severity compared to boys. This sex difference has been found during early childhood (Szatmari, et al., 2015; Waizbard-Bartov, et al., 2020) and middle childhood (Waizbard-Bartov, et al., 2022), and a recent review concluded that autistic females are more likely to have less intense symptoms and to experience reductions in symptom severity during childhood (Lai & Szatmari, 2019).

Higher cognitive/developmental abilities or not having intellectual disability have also repeatedly been associated with decreases in symptom severity during childhood and into adolescence and adulthood, as well as faster rates of decrease (Clark, et al., 2017; Fountain, et al., 2012; Georgiades, et al., 2021; Gotham, et al., 2012; McGovern & Sigman, 2005; Waizbard-Bartov, et al., 2020; Woodman, et al., 2016; Zachor & Ben-Itzchak, 2020). Increases in severity, however, have been linked with both lower (Simonoff, et al., 2019; Waizbard-Bartov, et al., 2020) and higher cognitive ability (Gotham, et al., 2012; Kim, et al., 2016; Venker, et al., 2014), showing a less consistent relationship.

The literature indicates the initial severity level at a young age is not necessarily a good predictor of the future severity change an individual will undergo across life. Symptom severity decrease has been documented for children with either higher (Waizbard-Bartov, et al., 2020) or lower (Szatmari, et al., 2015; Venker, et al., 2014) initial severity levels compared to other children. Increasing severity, on the other hand, has more consistently been shown to occur from initially lower severity levels (Gotham, et al., 2012; Kim, et al., 2016; Venker, et al., 2014; Waizbard-Bartov, et al., 2020). This does not rule out, however, increased severity that occurs from moderate or high initial severity levels, that might be harder to identify due to ceiling effects in measurement.

Family-related and sociodemographic factors have also been associated with differences in symptom severity change, illustrating how environments can affect individual outcomes, often in an unequal way. Decreases in symptom severity (and faster rates of decreases) have been linked with higher parental education levels (Fountain, et al., 2012; Waizbard-Bartov, et al., 2022), not belonging to a family of lower socioeconomic status (Georgiades, et al., 2021), positive comments made by mothers during a structured task (Woodman, et al., 2016), and improvement in mother-child relationship quality (Woodman, et al., 2015). In contrast, belonging to a minority group (not being White and/or having a foreign-born mother) (Fountain, et al., 2012), parents being younger at the time of child's birth (Fountain, et al., 2012; Waizbard-Bartov, et al., 2022), parents with lower educational attainment (Fountain, et al., 2012; Waizbard-Bartov, et al., 2022) and greater neighborhood deprivation (Simonoff, et al., 2019) have been associated with increases in severity (or a lower likelihood for fast decreases in severity). It is possible that caregivers who have abundant resources are more easily able to advocate for their children concerning receiving high quality and intensity of services, and/or to create enriching home and educational environments that promote skill development and support symptom reduction over time (Fountain, et al., 2012), and that children who are exhibiting decreases in symptom severity

may engage more readily with their parents resulting in improvements in relationship quality. However, it is important to note that the literature is not consistent regarding these environmental factors and other studies have not identified such associations with symptom severity change.

Several studies have also found that educational placement differs based on symptom severity change. While specialist school attendance predicts greater relative increase in symptom severity (Simonoff, et al., 2019), individuals that decrease in symptom severity have a higher likelihood of attending inclusive (full or partial) educational settings (Woodman, et al., 2016; Zachor & Ben-Itzchak, 2020). It has also been suggested that the relationship between higher IQ and symptom severity improvement might be exerted through educational placement. Mainstream, inclusive settings associated with higher abilities can expose individuals to new experiences, opportunities for engagement and sophisticated interactions with neurotypical peers who serve as role models (Pellicano, 2012; Simonoff, et al., 2019), and to inclusive practices and environments (Woodman, et al., 2016) that can impact symptom trajectories and outcomes in general (Lord, et al., 2022).

The core symptoms of autism have also been suggested to manifest differently across different periods of development (Nordin & Gillberg, 1998). This likely contributes to the variability *within*-person–differences in severity change in an individual's trajectory across time (Georgiades, et al., 2014). This is part of the concept Georgiades, et al. (2017) termed "chronogeneity: the study of autism heterogeneity in relation to the dimension of time." Varied stages in life are characterized by unique influences, both opportunities as well as challenges, and could thus affect symptom severity in unique ways. Early childhood, usually the time at which children are first diagnosed, is a period characterized by high family involvement and relatively high prevalence of intervention, support, and resources (Lord, et al., 2022; Towle, Vacanti-Shova, Higgins-D'Alessandro, Ausikaitis, & Reynolds, 2018). While severity change is variable during early childhood, most studies indicate symptom severity either decreases (Giserman-Kiss & Carter, 2019) or remains stable (Venker, et al., 2014) across this time, with lower rates of severity increases. Fountain, et al. (2012), for instance, showed substantial decreases in symptoms were most robust before age 6, at which time the rate of severity decrease slowed compared to the rate evident during early childhood. Significant decreases in symptoms, especially in SC symptoms, across early childhood have been suggested to be associated with a parallel development in language ability during this time (Bal, et al., 2019).

During middle childhood, children face a significant transition, entering the school system. Multiple challenges characterize this phase including heightened anxiety, increased social pressure, the need to communicate and form relationships with teachers, adjust to a new schedule, actively engage in the classroom, and various attention and sensory challenges (Bolourian, Stavropoulos, & Blacher, 2019; Nuske, et al., 2019; Sanz-Cervera, Pastor-Cerezuela, Gonzalez-Sala, Tarraga-Minguez, & Fernandez-Andres, 2017; Sparapani, Morgan, Reinhardt, Schatschneider, & Wetherby, 2016). Services and support are usually provided by the school at these ages and are often less accessible compared to early childhood, depending on the child's characteristics (Lord, et al., 2022; Towle, et al., 2018). Several studies have identified a turning point in symptom trajectories at the start

of middle childhood. While symptom severity tends to decrease in these studies across early childhood, during middle childhood it either continues to reduce but at a slower rate (Fountain, et al., 2012; Waizbard-Bartov, et al., 2022), plateaus resulting in symptom stability (Georgiades, et al., 2021), or shifts altogether to increasing severity (Clark, et al., 2017).

As children grow, and especially during the transition to adolescence, they face heightened social intensity and complexity that leads to greater social demand. Such challenges could potentially contribute to the manifestation of new symptoms or exacerbate existing ones (Picci & Suzanne Scherf, 2015; Starr, et al., 2003). Surprisingly, most studies find that many individuals exhibit declines in symptom severity across adolescence and into adulthood (Lin, et al., 2022; McGovern & Sigman, 2005; Pellicano, et al., 2019; Seltzer, et al., 2003; Shattuck, et al., 2007; Szatmari, et al., 2009; Woodman, et al., 2015, 2016), in addition to others that maintain stable severity levels (Pellicano, et al., 2019; Shattuck, et al., 2007; Simonoff, et al., 2019) or increase (Pellicano, et al., 2019). Change, however, is not uniform in rate and seems to slow over time (Szatmari, et al., 2009). Taylor and Seltzer (2010) identified a second turning point in symptom trajectories as individuals face another major transition at the time of exiting the school system. While individual trajectories continued to improve in symptom severity across both adolescence and adulthood, the rate of symptom decrease reduced substantially after leaving school and upon entering young adulthood. Interestingly, the slowing of improvement was most pronounced for those without intellectual disability. In addition to dealing with the change itself, this slowing of improvement might reflect the loss of simulating educational activities and added difficulties brought on by change or reduction in services received (Taylor & Seltzer, 2010). The decrease in services rendered at the entrance to adulthood (Roux, Shattuck, Rast, Rava, & Anderson, 2015), known as the ‘services cliff’, could potentially impact individual outcomes such as symptom severity change patterns (Lord, et al., 2022).

Summary: Individual, environmental and developmental impacts on symptom severity change

Several factors could impact symptom severity change across the life span including broadening the definition of ASD which now incorporates less severe behavioral presentations, as well as the increasing rates of early intervention in the community, both associated with severity decreases. Differences in severity change patterns *between*-individuals could be impacted by differences in other characteristics, as decreases in symptom severity have been associated with being female and having higher IQ and/or not having an intellectual disability. Familial and sociodemographic factors might also impact symptom trajectories including parental education level, familial income, and quality of environment. Educational placement (specialized or inclusive) has also been associated with differing severity change patterns. Symptom severity change is also characterized by *within*-person variability, demonstrating different change patterns within the same person across time/developmental periods. Early childhood is a period in which symptoms tend to either (relatively rapidly) decrease in severity or remain stable for most children. During middle childhood, however, symptom trajectories tend to slow in rate of improvement, plateau, or begin increasing in severity, suggesting that a turning point in symptom trajectories

may exist at around age 6. During adolescence and adulthood, symptom severity has been shown to decrease for many individuals. However, a second potential turning point has been suggested around the time of school exit/entrance to young adulthood, at which point the rate of symptom improvement declines (despite the general trend for decrease to continue). These “turning points” may be impacted by increasing challenges and more limited resources and services as individuals grow older.

Implications and Future Directions

Understanding the ways in which symptom severity progresses over time is a first step. It must be followed by translating this knowledge to impact and support the lives of those in the ASD community. From a research perspective, groups of individuals with different symptom severity trajectories are of interest for genetic and imaging studies (Hus, Pickles, Cook, Risi, & Lord, 2007; Lord, et al., 2015; Szatmari, et al., 2007). Such studies may seek to identify biological mechanisms responsible for changes in severity or resulting from them. For instance, Andrews, et al. (2021) identified an association between trajectories of white matter development and children’s differential symptom severity change patterns across early childhood. Such biology-behavior links, if identified, could be used as biomarkers for expected symptom severity change in an individual over time. Biological features associated with specific severity change patterns at a young age could be used as potential predictors of expected change. Once identified, they can suggest a child’s potential for either symptom severity decrease with time, or, for severity increase and highlight the importance of early intervention to try and prevent this from happening. Biological processes that are found to occur in parallel to specific severity change patterns across time could help in the attempt to uncover biological mechanisms underlying behavioral change.

Although autism symptom severity often changes over time, it remains difficult to predict such change at an individual level. If specific individual traits or environmental factors can be identified that modulate the course of severity change, such factors could be taken into account by professionals as risk and resilience indices of future change and its consequences. For example, being female, having higher IQ (or no intellectual disability), having parents with higher educational attainment, and having a higher-quality environment have all been associated with symptom severity decreases. Experiencing major life transitions and facing social inequities, in comparison, have been associated with worsening change patterns in an individual’s symptom trajectory. While facing such challenges should automatically entitle an individual to more support and resources (regardless of other factors), in reality, that is often not the case. In fact, going through major transitions has been associated with a decline in available resources (Roux, et al., 2015), and recent evidence suggests non-white autistic students receive less special education services compared to white autistic students (Sturm, Williams, & Kasari, 2021). Understanding the full extent of risk these factors pose for an individuals’ outcomes, including their impact on symptom severity change, is relevant for planning support across development. Specifically, they can help create a “road map”, marking potential pitfalls ahead for families, service providers, and case managers supporting an individual across their life. Transition planning, for instance, would do well to consider the potential for different life phases to act as turning points for symptom severity change and plan individualized intervention, adaptations, and

additional supports accordingly to mitigate the risk of symptom increase and maintain or improve functioning (Bolourian, et al., 2019; Georgiades, et al., 2021; Taylor & Seltzer, 2010). In addition, the socio-environmental risk factors described for severity increases stress the importance of providing equal access to resources and intervention for all individuals early on (Fountain, et al., 2012; Zwaigenbaum, et al., 2015).

In addition to implementation of current findings, future research could also expand the assessment of autism symptom severity and change over time through various methodological advances. While the current paper reviews studies utilizing standardized *behavioral* tools alone, novel quantitative, observer-independent measures for assessing autism symptoms and social behavior in general are emerging. Examples include the use of motion tracking to evaluate social symptoms and reciprocity of social interaction (Budman, et al., 2019; Lahnakoski, Forbes, McCall, & Schilbach, 2020), and the use of eye-tracking to analyze visual attention style to social and non-social stimuli as an indicator of autism symptom severity (Frazier, et al., 2018; Wen, et al., 2022). Another advancement made is the broadening diagnostic criteria for ASD, most recently manifested in the new *DSM-5* (American Psychiatric Association, 2013). The majority of samples described in the current review were diagnosed using the *DSM-IV* or *DSM-IV-TR*. Nonetheless, more recently-ascertained samples (Georgiades, et al., 2021; Waizbard-Bartov, et al., 2020) include higher proportions of individuals that change in symptom severity compared to earlier-ascertained samples (Gotham, et al., 2012). Future cohorts which rely exclusively on *DSM-5* diagnostic criteria for study eligibility, may further emphasize the heterogeneity of symptom trajectories and severity change over time. Comparing findings reported from cohorts diagnosed under *DSM-IV* with those diagnosed under *DSM-5* could also be informative regarding the impact of sample diversification on prevalence of symptom severity change. Finally, previous work has shown that specific symptoms change differently across time at an item level. For instance, evaluating change in social-communications symptoms, Bal, et al. (2019) found that the severity of the ADI-R item “Shared enjoyment” tends to decrease over time, while the severity of “Inappropriate Facial Expressions” tends to remain stable. Advances in analysis methods, such as the ongoing development of longitudinal network-model approaches (Borsboom, et al., 2021), could help identify which symptoms are leading processes of change, or stability, over time.

The complex development of autism severity change across time suggests symptom trajectories are highly unique, formed in a cascading way through interactions between biological predispositions, individual phenotypes, and inputs from the environment. However, if identified, these unique profiles have great potential for both clinical and research purposes. While high variability in severity change presents a challenge for determining prognosis, it also opens a window for potential gains across time.

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Table 1.

Summary of studies reviewed.

	Study	Sample description	Measures	Analytic approach	Summary of results
1	Starr, et al. (2003)	**Autism and Asperger Syndrome Trajectories Study sample:** 58 children diagnosed with autistic disorder or Asperger syndrome, evaluated at ages 4-6 and again after a 2-year follow-up (ages 6-8).	Parent report: ADI & ADI-R	Mean change in ADI-R subdomain scores (communication, social, and repetitive behaviors) was evaluated for both diagnostic groups.	The autistic disorder group exhibited a larger decrease in communication symptoms while the Asperger group demonstrated a larger increase in social symptoms. RRBs remained stable for both groups across time.
2	Charman, et al. (2005)	**Newcomen Centre, Guy's Hospital London, UK sample:** 26 children evaluated at ages 2, 3, and 7.	Parent report: ADI-R	Mean change in ADI-R subdomain scores (verbal or nonverbal communication, social, and repetitive behaviors) was evaluated for the sample.	Autism symptoms changed across childhood for the three subdomains, but change was highly variable in pattern, rate and across childhood periods. Some children's scores remained stable while others decreased in severity, and to different extents (differences that increased as children grew older). Change also differed between the two periods evaluated (ages 2-3 and 3-7).
3	Lord, et al. (2015)	**Early diagnosis study sample (EDX):** 85 individuals evaluated in early childhood at ages 2, 3, and 5, middle childhood at age 9, and late adolescence at age 19.	Parent report: ADI-R	Three groups were derived based on age 19: ASD-Less Cognitively-Able (VIQ<70), ASD-More Cognitively-Able (VIQ≥70), and Very Positive Outcome (no longer have a clinical diagnosis of ASD). Growth curve analysis for ADI-R subdomains were estimated (social-communication symptoms and two types of repetitive behaviors: repetitive sensorimotor and insistence on sameness) for each group.	All three groups showed decreases in the social-communication domain and in one subtype of RRB (repetitive sensorimotor). Only the ASD-Less Cognitively-Able group increased in one RRB type (Insistence on Sameness). Rate of change differed between the groups. For social-communication symptoms, the ASD-Less Cognitively-Able group decreased in a linear way while both other groups showed quadratic decreases.
4	Fecteau, et al. (2003)	**Hôpital Rivière-des-Prairies, Montréal sample:** 28 verbal children and adolescents between 7-20 years of age.	Parent report: ADI-R; comparing past/ lifetime and current scores	Mean change in ADI-R subdomain scores (communication, social, and repetitive behaviors) & the proportion of participants who either decreased, increased, or remained stable in subdomain items across time.	On average, participants showed significant severity reductions in all subdomains over time. Evaluating severity change patterns individually at the item level, symptoms tended to either decrease in severity or remain stable, with few instances of increasing severity.
5	Piven, et al. (1996)	**University of Iowa Child Psychiatry clinic sample:** 38 individuals with nonverbal IQ≥65, evaluated between 13-28 years of age.	Parent report: ADI-R; comparing past/ lifetime and current scores	Mean change in ADI-R subdomain scores (communication, social, and ritualistic/ repetitive behavior) between past/lifetime and current scores, and the proportion of participants showing decreases in each subdomain across time.	The full sample decreased in both social and communication symptoms and remained stable in ritualistic, repetitive behaviors. Individually, significant decreases in severity were seen in 82% of participants for the social and communication subdomains and for 55% of individuals in ritualistic, repetitive behaviors.
6	Boelte and Poustka (2000)	**Frankfurt University site, International Molecular Genetic Study of Autism Consortium sample (IMGSAC):** 76 individuals aged 15-37 (and an additional 17 characterized with broader autism phenotype).	Parent report: ADI-R; comparing past/ lifetime and current scores	Correlations between ADI-R subdomain scores (communication, social, and restricted, repetitive behaviors) for past/lifetime and current scores for the full combined sample.	On average, there was a moderate tendency for symptom severity to decrease across time, with symptoms being milder at later ages.
7	Seltzer, et al. (2003)	**Adolescents and Adults with Autism Study sample (AAA):** .405 individuals divided into two cohorts: adolescents (*N*=251) evaluated between 10-21 years of	Parent report: ADI-R; comparing past/ lifetime and current scores	Compared current and past/lifetime scores for the ADI-R subdomains (communication, social, and repetitive behaviors) for the adolescent and adult cohorts, and percentage	Average decreases in symptom severity were evident across time, predominantly for social and communication symptoms, for both adolescents and adults. More individuals decreased in items related to social and communication symptoms compared to RRB. Severity

	Study	Sample description	Measures	Analytic approach	Summary of results
		age and adults (*N*=154) evaluated between 21-53 years of age.		of individuals showing symptom decrease at the item level across time.	change patterns varied between the two age cohorts, with adolescents and adults showing different symptom manifestations across time.
8	McGovern and Sigman (2005)	**Marian Sigman's UCLA Longitudinal Autism Project sample:** 48 individuals evaluated at middle childhood (age 12) and late adolescence (age 19).	Parent report: ADI-R; comparing past/ lifetime and current scores at middle childhood and adolescence	Analyzed ADI-R subdomain scores (verbal and nonverbal communication, social, and repetitive behaviors) across 3 time points: past/lifetime, middle childhood and adolescence, using single factor repeated measures GLM in the full sample.	On average, current scores (at both middle childhood and adolescence) showed a decrease in symptom severity for all subdomains compared to early childhood. Social symptoms and RRB also decreased in severity from middle childhood to adolescence.
9	Gillespie-Lynch, et al. (2012)	**Marian Sigman's UCLA Longitudinal Autism Project sample:** Extended the work of McGovern and Sigman (2005) to include an additional time point in adulthood (12, 18 and 26.6 years) for a subgroup of 20 individuals.	Parent report: ADI-R; comparing past/ lifetime and current scores + additional time in adulthood	Compared scores for the ADI-R subdomains (social, nonverbal communication, and repetitive behaviors) for past/lifetime time point and three current scores at middle childhood, adolescence, and adulthood.	No change was evident across adolescence and adulthood for non-verbal communication symptoms and RRBs. Social symptoms decreased in severity across adolescence and increased in severity into adulthood.
10	Shattuck, et al. (2007)	**AAA sample:** Symptom trajectories were evaluated prospectively at 4 time points (every 18 months) across a 4.5-year period for 241 adolescents and adults ranging from 10-52 years of age.	Parent report: ADI-R	Mean sample ADI-R subdomains (social, verbal and nonverbal communication, and repetitive behaviors) were compared between the first and fourth (final) time points & individual change scores were computed for each participant using a standardized mean difference in scores between first and last time points.	On average, most symptom subdomains decreased in severity across the period evaluated (except nonverbal communication symptoms, which remained stable). Symptom severity change was highly variable between individuals; many exhibited stable severity levels (22.9%-54.5% depending on subdomain), a substantial proportion decreased in severity (26.1%-58.5%), and a minority of participants increased in symptom severity (14.5%-25.7%).
11	Taylor and Seltzer (2010)	**AAA sample:** Extended trajectories of Shattuck et al., 2007 to include an additional 5th time point, evaluating autism symptoms across a nearly 10-year period for 242 individuals with a mean age of 16.3 years at study entry.	Parent report: ADI-R	Multilevel growth models were estimated for the full sample using all time points available for each ADI-R subdomains (social, verbal and nonverbal communication, and repetitive behaviors).	All ADI-R subdomains significantly decreased in severity across adolescence and during the transition to adulthood. The rate of decrease varied based on the developmental period being assessed. Specifically, the rate of improvement significantly slowed (reduced by half) after high school exit and during the transition to adulthood.
12	Woodman, et al. (2015)	**AAA sample:** Extended trajectories of Shattuck et al., 2007, evaluating 313 adolescents and adults ranging in age from 10-49 years at Time 1 across 5 time points during an 8.5-year period.	Parent report: ADI-R	Mean sample ADI-R subdomains (social, verbal and nonverbal communication, and repetitive behaviors) were compared between the first and final time points and individual change scores were computed for each participant using a standardized mean difference in scores between first and final time points. Multilevel growth models were also estimated for the full sample using all time points available for each ADI-R subdomain.	On average, all ADI-R domains decreased in severity across the period evaluated, but severity change varied between individuals; 55% (20%-44% depending on specific subdomain) exhibited stable severity levels, 33% (35%-61%) decreased, and 12% (16%-22%) of individuals increased in severity into adolescence and adulthood.
13	Woodman, et al. (2016)	**AAA sample:** Extended trajectories of Shattuck et al., 2007, evaluating 364 adolescents and adults ranging in age from 10-52 years at Time 1 across 2-6 time points during a 10-year period.	Parent report: ADI-R	Change in autism symptoms as well as other outcome variables was examined through hierarchical linear growth modeling. Then, mixture modeling was used to identify latent classes based on all outcome measures combined.	For the entire sample, autism symptoms followed a linear pattern, decreasing in a constant way across the study period. Two latent classes were observed: Class 1 (45%) had a lower initial symptom severity level and a faster rate of severity decrease. Class 2 (55%) had a higher mean

Clin Psychol Rev. Author manuscript; available in PMC 2024 February 01.

	Study	Sample description	Measures	Analytic approach	Summary of results
					initial severity level and decreased at a very slow rate across time.
14	Eaves and Ho (2004)	**Sunny Hill Health Centre for Children sample:** 49 children evaluated at age 2.5 and again at age 5.	Clinician observation: CARS	Mean CARS scores compared across the two time points and individual change in CARS score.	On average, mean symptom levels did not change across early childhood for the full sample. Variability in severity change was evident between children, with 33% showing change in symptom levels (either increase or decrease in severity) across this period.
15	Pellicano (2012)	**University of Western Australia sample:** 37 children with IQs≥80 evaluated across a 3-year period during middle childhood, from an average age of 5.7 to 8.4.	Parent report: SCQ	Mean symptom domain scores (social, communication, and repetitive behaviors) were compared for the entire sample combined across the period studied.	On average, ASD symptomatology improved for all symptom domains across the 3-year period, but magnitude of change differed according to the symptom domain evaluated; improvement was most evident for social interaction symptoms, more than for communication symptoms and RRB.
16	Eaves and Ho (1996)	**Sunny Hill Health Centre for Children sample:** 76 children assessed at an average initial age of 7.6 and again at 11.5 years.	Clinician observation: CARS	Mean sample CARS scores compared across time.	A slight decrease in symptom severity for the full sample was evident during middle childhood.
17	Mesibov, et al. (1989)	**North Carolina's TEACCH program sample:** 89 individuals evaluated from middle childhood (mean age 8.7) into adolescence (mean age 15.9).	Clinician observation: CARS	Mean CARS scores compared across time.	A decrease in symptom severity from middle childhood into adolescence was evident for the full sample.
18	Fountain, et al. (2012)	**California Department of Developmental Services (DDS) records**: Symptom trajectories were evaluated in a large sample of 6,975 children from age 2-14.	Parent report: based on the Client Development Evaluation Report interview, conducted by trained staff at the DDS	Group-based latent trajectory models (for identifying subgroups in the sample) were estimated separately for symptom domains (social, communication, and repetitive behaviors).	Children were characterized by six developmental trajectories for autism symptoms. Most trajectories showed change in severity, but change differed between children and symptom domains. Severity decreases were most evident for SC symptom trajectories while stability was common in RRB trajectories. Symptom trajectories exhibited variable patterns and rates of change; some children showed rapid improvement while others demonstrated slower/less marked improvement over time. Substantial decreases in symptoms were most robust before age 6, at which time the rate of severity decrease reduced compared to the rate evident during early childhood.
19	Szatmari, et al. (2009)	**Autism and Asperger Syndrome Trajectories Study sample:** 64 individuals diagnosed with either Autism or Asperger's syndrome, without intellectual disability, evaluated 2-5 times from age 4-6 to late adolescence (age 17-19).	Parent report: ABC	Individual growth trajectories were estimated using hierarchical linear models and growth curves trajectories for both diagnostic groups (autism and Asperger's syndrome) were compared.	Both diagnostic groups decreased in severity of symptoms across the period evaluated, and at similar rates. The rate of decrease changed across time; improvement slowed or plateaued during later ages.
20	Lin, et al. (2022)	**Children's Mental Health Center of National Taiwan University Hospital Longitudinal Sample:** 106 children (6-11, mean age 9) and 48 adolescents (12-19, mean age 14.5) with FSIQ ≥ 60 evaluated twice across a 7-year period, up to mean ages 16 (children) and 21 (adolescents).	Parent report: SRS	Entire group trajectories for each SRS subdomain (social communication, stereotyped behavior, social awareness, social emotion) were compared from first to second measurement and modeled across time for repeated measurements.	Autistic symptoms were stable for the group of children over time. There was a modest improvement in social communication and decreased stereotyped behaviors in the adolescent group across time.
21	Simonoff, et al. (2019)	**Special Needs and Autism sample (SNAP):** A population-based	Parent report: SRS	Latent growth curve models were estimated for symptom trajectories. Trajectories were	Autism symptom severity remained unchanged for the entire sample over time. But symptom trajectories

Clin Psychol Rev. Author manuscript; available in PMC 2024 February 01.

	Study	Sample description	Measures	Analytic approach	Summary of results
		epidemiological sample of 158 individuals evaluated at ages 10-12, 15-16, and 23 years of age.		also modeled based on school placement: mainstream school (including a special unit in a mainstream school) vs specialist school (a unit or special school for intellectual disabilities, emotional / behavioral problems or autism)	differed based on school placement: individuals attending specialized school increased in severity over time compared to those attending mainstreamed schools, while those attending mainstream schools had lower symptom levels at older ages (23) compared to those attending specialist schools.
22	Kim, et al. (2016)	**Yale Toddler Developmental Disabilities Clinic sample:** Evaluated symptom trajectories (and short -term outcomes) during very early childhood, from age 2 to 3, in a sample of 100 toddlers.	Clinical observation: ADOS CSS	Used hierarchical clustering analysis based on a set of variables assessed at age 2, including ADOS SA and RRB scores as well as additional outcome variables, to identify latent clusters.	Three out of four latent groups in the sample showed stable symptom severity trajectories (based on ADOS CSS) across the one-year period, with only one group (16%) of toddlers showing symptom severity increase.
23	Giserman-Kiss and Carter (2019)	**University-based, Multi-stage Screening Project sample:** 60 children of diverse backgrounds (80% racial/ethnic minorities) evaluated from a mean age of 2.4 to 4.4 years.	Clinical observation: ADOS CSS	Comparing mean ADOS CSS scores across time (and after receiving early intervention).	There was a reduction in ASD symptomology across early childhood for all children combined.
24	Gabbay-Dizdar, et al. (2021)	**National Autism Research Center of Israel sample (NARCI):** 131 children evaluated twice across early childhood; initial assessment at age 1.2-5 and follow up 1-2 years later.	Clinical observation: ADOS CSS	Individual change scores were computed for change in ADOS, SA and RBB CSS. Children were groups based on age at time of diagnosis; younger (<2.5) or older (≥2.5).	Children diagnosed before 2.5 years of age were nearly three times more likely (65%) to exhibit considerable reductions in the severity of social symptoms as compared with children diagnosed at older ages (23%). Reductions in autism severity resulted from decrease in SA symptoms despite increase in RRB.
25	Venker, et al. (2014)	**University of Wisconsin-Madison, Waisman Center, Longitudinal study of early language development sample:** 129 children evaluated 1 to 4 times across early childhood from age 2.5 to age 5.5.	Clinical observation: ADOS CSS	A series of latent-class growth curve models were estimated based on symptom trajectories, identifying 4 latent classes in the sample. Intercept and growth parameters were allowed to vary between, but not within, classes.	Most children (78%) retained stable severity levels, belonging to either persistent-high (36%) or persistent-moderate (42%) trajectory groups. Some variability in severity change was demonstrated, with 8% of children showing “worsening” trajectories and 14% showing “improving” trajectories over time. There was large within-group variability (in individual trajectories) characterizing the groups.
26	Szatmari, et al. (2015)	**Pathways in ASD sample:** 421 children assessed at 3 time points across early childhood, with initial assessment between ages 2-5 and final assessment at age 6.	Clinical observation: ADOS CSS	A semiparametric, group-based approach was used with ADOS CSS to identify different developmental trajectory groups (distinct mixtures of trajectories) within the sample.	Two trajectory groups were identified in the sample. A large proportion (89%) showed stable symptom trajectories across time, while a small group (11%) showed declining symptom severity trajectories.
27	Waizbard-Bartov, et al. (2020)	**Autism Phenome Project sample (APP):** 125 children assessed across early childhood, from age 3 to age 6.	Clinical observation: ADOS CSS	Individual change scores were computed across early childhood, and reliable change in symptom severity was determined using the Reliable Change Index statistic. Children were grouped based on their individual tendency for change across early childhood: decreased, increased or stable severity levels in ADOS CSS.	Approximately half (54%) of children in the sample retained stable severity levels, while nearly half showed symptom severity change over this period. Severity change was highly variable between children, with almost 29% decreasing in severity and almost 17% increasing in severity during early childhood.
28	Clark, et al. (2017)	**Social Attention and Communication Study sample (SACS):** Symptom trajectories were evaluated across 3 time points: at age 2 and again at age 4 during the preschool years, and at 7-9 during early school-age, in a sample of 48 children.	Clinical observation: ADOS CSS	Comparing mean ADOS CSS across time for two outcome groups: A Non-Stable ASD group (children who did not meet the ADOS-2 cut-off score for an autism diagnosis at ages 4 or 7-9), and a Stable ASD group (children who continued to meet the ADOS-2 cut-off score).	Both outcome groups demonstrated change in symptom severity across childhood. The Non-Stable ASD group (27%) decreased in symptom severity consistently across childhood and the Stable ASD group (73%) decreased in severity during the preschool period (age 2-4) with subsequent increases in severity during the early school years (age 4-7/9).

	Study	Sample description	Measures	Analytic approach	Summary of results
29	Waizbard-Bartov, et al. (2022)	**APP sample:** Extended trajectories of Waizbard-Bartov, et al. (2020) to evaluate symptom trajectories from early childhood (age 3) up to middle childhood (age 11) in a group of 182 children.	Clinical observation: ADOS CSS	Individual change scores in ADOS CSS were computed across early childhood (age 3-6) and middle childhood (age 6-11) separately, and reliable change in severity was determined using the Reliable Change Index statistic. Children were grouped based on their individual tendency for change across childhood: decreased, increased or stable severity levels.	More than half (51%) of the children changed in symptom severity across time, with 27% decreasing in severity while 24% increased in severity, and 49% remained stable across childhood. Symptom severity change also varied across time; severity decrease was more common during early childhood and severity increase equally common across both periods. But a large increase in SA was evident during middle childhood. At the individual level, most children experienced severity change during only one period and remained stable during the other period.
30	Georgiades, et al. (2021)	**Pathways in ASD sample:** Extended trajectories of Szatmari, et al. (2015) evaluating symptom trajectories across 4 time points, from early childhood (mean age 3.5) up to middle childhood (age 10) for 187 children.	Clinical observation: ADOS CSS	Children were assigned into distinct trajectory groups and (latent clusters) were derived in the sample based on their autism symptoms across time (ADOS CSS as well as SA and RRB scores) and age at assessment.	Two trajectory groups were identified. The first group (73%) showed improvements in symptom severity during early childhood through age 6, at which point the trajectory plateaued across middle childhood. A second group (27%) exhibited reductions in severity during early childhood at a relatively faster pace that the first group and continued to experience decreases in severity during middle childhood as well, but at a slower pace relative to its early childhood improvement.
31	Zachor and Ben-Itzchak (2020)	**Assaf Harofeh Medical Center, Zerifin, Israel sample:** Symptom trajectories were evaluated from toddlerhood (mean age 2.2) up to adolescence (mean age 13.10) for 68 individuals.	Clinical observation: ADOS CSS	Comparing mean ADOS domain scores (SA CSS, RRB CSS) across time and three outcome groups at adolescence: a low-functioning ASD group (IQ<80), a high-functioning ASD group (IQ≥80) and a Best Outcome group (no ASD & IQ≥80).	The group with IQ<80 (63%) increased in symptom severity (specifically SA severity), the group with IQ≥80 (21%) retained stable severity levels (in both domains), and the “Best Outcome” group (16%) decreased in severity (both SA and RRB severity) from toddlerhood to adolescence.
32	Gotham, et al. (2012)	**EDX sample:** 345 individuals were evaluated at 2-8 time points, from early childhood (initial assessment at age 2) up to adolescence (age 15).	Clinical observation: ADOS CSS	Generalized Linear Latent and Mixed Models were estimated and children were assigned to 4 latent trajectory classes based on stability or change in ADOS severity across time.	More than 80% of participants showed stable symptom severity across time, belonging to either a persistent-high (46%) or a persistent-moderate (38%) trajectory group. Small groups either “improved” (decreased in severity; 7%) or “worsened” (increased in severity; 9%) across time.
33	Pellicano et al. (2019)	**University of Western Australia sample:** 27 individuals were evaluated across a 9-year period from middle childhood (mean age 8.5) up to early adulthood (mean age 18).	Clinical observation: ADOS CSS	Comparing mean ADOS CSS scores for the entire sample across time & evaluating individual change in severity using the Reliable Change Index statistic.	For the entire sample combined, mean symptom severity remained stable across the 9-year period evaluated. At the individual level, symptom severity change was common, with more than half of participants experienced significant change over time, either decreasing (29%) or increasing (29%) in severity.

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