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Mental health challenges faced by autistic people

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Mental health challenges impede the well-being of autistic people. This Review outlines contributing neurodevelopmental and physical health conditions, rates and developmental trajectories of mental health challenges experienced by autistic people, as well as unique clinical presentations. A framework is proposed to consider four contributing themes to aid personalized formulation: social-contextual determinants, adverse life experiences, autistic cognitive features, and shared genetic and early environmental predispositions. Current evidence-based and clinical-knowledge-informed intervention guidance and ongoing development of support are highlighted for specific mental health areas. Tailored mental health support for autistic people should be neurodivergence-informed, which is fundamentally humanistic and compatible with the prevailing bio-psycho-social frameworks. The personalized formulation should be holistic, considering physical health and transdiagnostic neurodevelopmental factors, intellectual and communication abilities, and contextual-experiential determinants and their interplay with autistic cognition and biology, alongside resilience. Supporting family well-being is integral. Mutual empathic understanding is fundamental to creating societies in which people across neurotypes are all empowered to thrive.

The mental health of individuals diagnosed with autism ('autistic individuals' hereafter) has a substantial impact on daily functioning and well-being across the lifespan^{1,2}. Understanding mental health challenges experienced by autistic people should consider the contributing neurodevelopmental and physical health factors (Boxes 1 and 2) and be rooted in the appreciation of the neurodiversity paradigm (Box 3), which captures both social and individual origins of disability and suffering^{3,4} but does not reject the biomedical contributors of psychiatric illnesses⁵. The neurodiversity paradigm advocates for social changes inclusive of autistic and other neurodivergent individuals with high and/or complex support needs⁶, such as those

with substantial intellectual, language, speech, motor or learning difficulties, compatible with the focus of contemporary medical care for individuals with developmental disabilities⁷⁸. The harmonization of social and biomedical models of disability, including that pertaining to mental health, is achievable as the neurodiversity paradigm is fundamentally humanistic and compatible with the prevailing bio-psycho-social formulations-two widely accepted stances of contemporary clinical practices^{9,10}. To address mental health suffering in autistic individuals, holistic care must consider the socio-ecological and biological origins and should target support concurrently for neurobiology, psychology and person-environment fit¹¹.

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Co-occurring neurodevelopmental conditions

Neurodevelopmental conditions, including those defined by the DSM-5-TR¹⁰⁹ and ICD-11¹⁰⁸ (that is, intellectual disabilities, ADHD, communication disorders, learning disorders, motor disorders and autism), and the broader ranges of genetic syndromes, environmentally driven conditions (for example, fetal alcohol spectrum disorders) and neurological disorders (for example. epilepsy) often co-occur^{240,241}. For example, the prevalence of intellectual disabilities in the autism population is around 18.6% or 34.8%, depending on how autism is defined²⁴². Meta-analyses show that in autistic people overall, the pooled prevalence is 28% (95% confidence interval, 25-32%) for ADHD¹³ and 10% (6-14%) for epilepsy²⁴³. Longitudinally, autistic children with early-childhood epilepsy have a 72% increase in the likelihood of ADHD diagnoses later in life²⁴⁴. These co-occurrences go beyond diagnostic categories to dimensional traits, necessitating transdiagnostic understandings of neurodivergence²⁴⁵. Because of the early-onset and persistent nature of neurodevelopmental conditions²⁴⁰ including strengths, constraints and differences in information processing and experiences of the world²⁴⁶—these characteristics are 'in the make-up' of an autistic person and contribute to their mental health. Autistic people with and without intellectual disabilities tend to have different patterns of co-occurring diagnoses-the former with more developmental delays and neurological disorders and the latter with more psychiatric diagnoses²⁴⁷. The neurodevelopmental co-occurrences are associated with increased mental health risks. Autistic children who are diagnosed with ADHD are three to four times as likely than those without ADHD to have anxiety, depression or behaviour problems²⁴⁸. As a clinical example, an autistic person can be diagnosed with ADHD and transient tic disorder, additionally having specific executive function and communication difficulties, as well as learning differences and pattern-recognition strengths. A personalized understanding of the mental health impact of the co-occurring categorical and dimensional neurodevelopmental features is essential.

Prevalence of mental health challenges

Current literature offers compelling evidence that psychiatric diagnoses are more prevalent in autistic people than in the general population¹² (Supplementary Table 1). Meta-analyses across 96 studies show that in autistic people overall, the pooled current prevalence estimates are 28% (95% confidence interval, 25-32%) for attention-deficit/hyperactivity disorder (ADHD); 20% (17-23%) for anxiety disorders; 13% (9-17%) for sleep-wake disorders; 12% (10-15%) for disruptive, impulse-control and conduct disorders; 11% (9-13%) for depressive disorders; 9% (7-10%) for obsessive-compulsive disorder (OCD); 5% (3-6%) for bipolar disorders; and 4% (3–5%) for schizophrenia spectrum disorders¹³. Even when considering population-based studies alone, the rates are higher across the board in autistic than in non-autistic people^{13,14}. Following the same trend in the general population, mood and psychotic disorders increase with age¹³⁻¹⁵ (except the infrequent childhood-onset schizophrenia, which has high co-occurrence with autism¹⁶). A Taiwanese national registry study found that the incidence of schizophrenia diagnosis in autistic adolescents and young adults is 10% during ten years of follow-up¹⁷. These trajectories lead to high lifetime prevalence of severe mental illnesses in autistic adults-that is, 9.4% for psychotic disorders, 7.5% for bipolar disorders¹⁸ and 37% for depressive disorders¹⁹. The prevalence of symptoms that are subthreshold to clinical diagnoses can only be higher. Other difficulties are also heightened in autistic people, including feeding and eating problems²⁰⁻²³, trauma and stress-related experiences^{24,25}, substance use²⁶⁻²⁹, catatonia^{30,31}, and suicidal behaviours^{32–35}. Population-level data suggest that by young adulthood, autistic female individuals (assigned at birth) are more likely to have psychiatric diagnoses than male individuals^{36,37}. Despite the notable proportion of autistic people with extensive support needs (for example, having complex medical problems or severe/ profound intellectual disabilities, minimally speaking, or requiring 24/7 support for safety and self-care)¹, the prevalence information on psychiatric illnesses specifically in these subpopulations is limited due to study sample heterogeneity and a lack of validated measurement³⁸. Meta-regression shows that studies including more autistic people with intellectual disabilities report higher rates of co-occurring psychotic disorders¹³. Recent large-scale data also indicate higher rates of disruptive behaviour, anxiety, and mood and psychotic disorders in autistic individuals with intellectual disabilities than in people with intellectual disabilities alone^{39,40}.

Developmental trajectories of mental health challenges

Population-level data show that in autistic people, anxiety disorders often appear first in childhood, while mood and psychotic disorders develop from adolescence¹⁵; the prevalence of psychiatric diagnoses increases during the transition to adulthood³⁷. The typical trajectory of mental health symptoms in autistic people, shown in longitudinal studies and measured by caregiver reports, is characterized by persistence over time⁴¹⁻⁴³, with subgroups showing diverging patterns^{44,45}. In an Australian autistic cohort (many with intellectual disabilities) followed over 18 years, there were small overall reductions in behavioural and emotional challenges over time, but the rates remained high in adulthood; challenges during childhood or adolescence predicted challenges in adulthood⁴⁶. The same pattern of small overall symptom reduction, with a high proportion showing high scores in adulthood (especially on emotional and ADHD symptoms), was observed in a UK autistic cohort followed over 11 years from childhood to early adulthood⁴³. In a Canadian cohort of autistic children, anxious-depressed problems were particularly elevated at preschool age and attention problems at late childhood⁴⁷. A US cohort following autistic people from school age to young adulthood showed increases in anxiety and depressive symptoms, especially in female individuals⁴⁸.

The presence of subgroups is evident, although notably measuredependent. In a US autistic cohort, trajectory-based subgrouping found two subgroups, with one showing low symptoms (that is, attention problems, anxious-depressed symptoms and withdrawn-depressed symptoms) and the other showing elevated symptoms with varied fluctuation over time⁴⁵; importantly, 63% of autistic individuals belonged to one or more subgroups with high-symptom trajectories⁴⁵. Another US autistic cohort showed that in adulthood, internalizing and externalizing symptoms reduced over time, and up to -50% evidenced consistently low symptoms; however, there were subgroups with persistently high-level challenges that remained constant or only mildly declined, and they had the greatest number of psychiatric diagnoses⁴⁴.

Symptom continuity and discontinuity exist. In a UK autistic cohort, adolescent emotional and behavioural disorders were significantly predicted by childhood disorder status, whereas adolescent ADHD diagnosis was not predicted by childhood ADHD diagnosis⁴⁹. All adolescent symptoms were predicted by their childhood counterparts, with an additional heterotypic relation that childhood emotional symptoms predicted adolescent ADHD symptoms, and a sex-moderated homotypic relation that childhood ADHD symptoms predicted adolescent ADHD symptoms nly in female individuals⁵⁰. In a

Co-occurring genetic and physical health conditions

Clinical-level autism presentation is highly prevalent in many genetic syndromes—for example, 61% in Rett's syndrome (female individuals only), 36% in tuberous sclerosis complex, 22% in fragile X syndrome and 11% in 22q11.2 deletion syndrome²⁴⁹. A number of high-impact rare genetic variants¹⁷⁵ and joint effects of many common variants²⁵⁰ are relevant to the emergence of autism¹⁷². Many genetic variants have pleiotropic effects on physical and psychiatric illnesses^{172,173,251}; hence, understanding the genetic background of an autistic person facilitates personalized health care²⁵². For example, an autistic person with 22q11.2 deletion syndrome should be monitored and supported for their social and executive function needs, ADHD, anxiety, and schizophrenia spectrum diagnoses and symptoms^{253,254}; an autistic person with tuberous sclerosis complex should receive early monitoring and medical treatment to reduce seizure risk and improve developmental outcomes²⁵⁵. Autistic people are also more likely than non-autistic people to experience physical ill healthnotably, epilepsy, sleep problems, sensory impairments, atopy, autoimmune disorders, gastrointestinal problems and obesity² that can predispose and precipitate mental health challenges and even premature mortality²⁵⁷. This pattern is more prominent in those assigned female than male at birth^{257,258}, particularly for endocrinological and metabolic problems^{258,259}. Recent surveys also indicate heightened rates of heterogeneous syndromes such as the central sensitivity syndromes (Box 6) in autistic adults²⁶⁰.

Canadian autistic cohort, early childhood irritability positively predicted adolescent depressive symptoms⁵¹.

Later mental health outcomes are probably associated with childhood mental health and cognitive and adaptive skills; however, the relations to autistic traits are equivocal. In a US cohort, greater adaptive skills at nine years old were associated with lower odds of an autistic individual being in the high-symptom trajectory subgroups, whereas higher childhood verbal intelligence quotient was associated with increased odds of belonging to the high-anxiety and high-depressivesymptom trajectory subgroups⁴⁵. In a UK autistic cohort, higher childhood adaptive function and language level predicted a greater decline in conduct and ADHD symptoms over time, whereas higher language level, higher parental education and lower autism characteristics predicted increasing emotional symptoms⁴³. In the same cohort, childhood autistic traits, intelligence quotient and adaptive functioning meaningfully predicted adulthood living situation, employment, education and physical health, but not mental health outcomes⁵². Future longitudinal studies need to assess mental health and relevant cognitive and behavioural constructs in early childhood and harmonize the measures across time points and cohorts to provide a fuller picture⁵³.

Clinical presentations

Psychiatric illnesses in autistic people largely manifest similarly as in neurotypical people. However, neurodivergence, intellectual functioning, communication abilities and preferences can modify an autistic person's mental health experiences and symptoms, intersecting with other biological and social–contextual determinants (Boxes 4 and 5). A thorough review of each condition is beyond the scope of this article; readers can refer to cited reviews^{21,24,25,28,31,33,34,54–62}.

Anxiety

Anxiety symptoms and disorders are the most prevalent mental health challenges experienced by autistic people overall, across the lifespan^{13,25}. Symptoms can fit the traditional categories (that is, separation anxiety, selective mutism, specific phobia, agoraphobia, panic, social anxiety and generalized anxiety) but can also be unconventional manifestations that fall outside of these categories, such as fears of novelty or change, excessive worry about access to focused interests, unusual phobias (for example, specific sounds), or anxiety related to confusion or unpredictability in social situations (rather than a fear of negative social evaluation)²⁵; these unique presentations can be reliably measured⁶³⁻⁶⁶. Furthermore, an autistic person's emotion processing and cognitive style can complicate how one experiences and shows anxiety: alexithymia⁶⁷ and interoception differences⁶⁸ might make it difficult to perceive, delineate and convey anxiety-related feelings, and communication and intellectual differences can modify how anxiety-related feelings are expressed (for example, limited verbal expression, withdrawal or seemingly disruptive behaviours). How the manifestations are perceived and interpreted by others, including clinicians, is complicated by overlapping appearances associated with both autism and anxiety, such as the avoidance of crowd and social encounters, repetitive asking (for reassurance), and increased sensory-seeking and repetitiveness (as coping)²⁵.

OCD

Challenges in delineating OCD symptoms in autistic individuals result from (1) the seemingly overlapping behaviours seen by others and sometimes overlapping functional impacts between OCD symptoms and autistic restricted, repetitive behaviours (RRB)⁵⁴; (2) the loose use of the terms 'obsession' (to refer to autistic focused interests versus obsessive thoughts of OCD) and 'compulsion' (to refer to autistic sameness behaviours versus compulsive acts of OCD) in daily communication; (3) the ability of an autistic person to detect and communicate the emotional bases and thought sequences of OCD-related behaviours; and (4) whether others can understand the nature of these experiences. Autistic RRB reflect one's natural sensorimotor inclinations and are mostly ego-syntonic, intrinsically soothing and pleasurable for autistic individuals⁶⁹; while OCD compulsions show anxiety-relieving functions as do some autistic RRB and can be temporarily soothing, OCD symptoms are overall distressful and ego-dystonic (unless with poor or absent insight)⁷⁰. OCD obsessions are recurring, intrusive and unwanted, and compulsions are driven by obsessions to prevent dreaded events from happening despite knowing the act will not realistically prevent the feared outcomes. The anxiety-driven OCD compulsions reduce anxiety but reinforce themselves. Some autistic RRB are reflective of an autistic person's anxiety (for example, increased stimming, mannerism or sameness needs), while others are not and typically do not cause distress, although distress can occur when or after RRB are interrupted⁵⁴. When an autistic person has difficulties differentiating and conveying these emotional bases and temporal sequences (due to communication or intellectual abilities, challenges with introspection or alexithymia), or when they communicate via idiosyncratic ways that others are not attuned to, it is difficult to ascertain the nature of these behaviours, and proxy reports are often used for speculation⁵⁵. Phenomenologically, OCD symptoms in autistic compared with non-autistic youth and adults tend to be more severe, especially in hoarding and ordering, with less magical obsessions, and no differences in other dimensions⁵⁵. Like anxiety manifestations, autistic individuals might show ambiguous OCD-like symptoms linked to negative affect but with unclear functions⁶³. Notably, there are certain repetitive-ritualistic behaviours, especially symmetry, ordering and not just right experiences, that can be genuinely difficult to differentiate between OCD compulsions and autistic RRB and might be truly overlapping phenomena.

The neurodiversity paradigm for understanding autistic people's mental health

In the conventional medical literature, autism is defined as a clinical entity by the DSM-5-TR¹⁰⁹ and ICD-11¹⁰⁸ criteria of 'autism spectrum disorder' as one of the 'neurodevelopmental disorders' (for example, http://id.who.int/icd/entity/437815624). Following this nosology, diagnoses co-occurring with autism are traditionally conceptualized as 'comorbidities'²⁶¹ that complicate intervention options for autism, 'comorbid' conditions and their interactions²⁶². In the past three decades, the neurodiversity movement (stemming from the disability rights movement) has challenged the narrow focus of the medical conceptualization of autism that, arguably, overattributes the root of disability to a person's deficits and impairments³. The neurodiversity paradigm upholds the natural diversity in human neurobiology and neurodevelopment, emphasizes individual differences, and rejects the idea that deviance from the norm indicates a flaw to be corrected⁶. Importantly, this approach highlights the socio-ecological origins of disability (including how socio-ecology shapes individual reactions or development that are classified as disorders²⁶³) and calls for social responses of individual well-being⁶. In this conceptualization, mental health challenges are perceived as 'co-occurring' rather than 'comorbid', to be respectful and avoid further stigmatization of autistic people²⁶⁴. Although many mental health challenges have independent origins from that of autism, there are biological, cognitive and social-contextual factors unique to autistic people that can heighten mental health vulnerability (Fig. 1). As a clinician and scientist, I believe that an appropriate understanding of mental health experiences of autistic individuals requires an appreciation of neurodiversity and an acknowledgement of the social and biomedical factors contributing to mental health difficulties and psychiatric illnesses specific to each autistic person. To improve the mental health of autistic people, it is necessary to improve person-environment fit by advocating for environmental adjustments¹¹ and address the double empathy problem¹⁴⁰, although these steps will not be sufficient on their own. Incorporating biological understandings of psychiatric illnesses and corresponding biological and psychotherapeutic interventions is equally fundamental. This stance is compatible with prevailing formulation frameworks used by practitioners such as the bio-psycho-social model¹⁰, as well as common therapeutic stances such as person-centred therapy⁹. An empathic and accurate understanding of autistic people's mental health experiences requires (non-autistic) clinicians' efforts to overcome the double empathy problem during cross-neurotype interactions¹⁴⁰, as well as the appreciation of the commonality of human experiences across neurotypes.

Behaviours that challenge

A notable portion of autistic individuals exhibit severe irritability and impulsive aggression^{56,71}. Furthermore, the prevalence of a very wide range of self-injurious behaviours (for example, hand-hitting, self-scratching, self-biting and hair-pulling) in autistic people overall is estimated as high as 42% (95% confidence interval, 38–47%)⁷². Although these behaviours can be reflective of difficulties in self/

BOX 4

Mental health assessments for autistic people, part A

The general principles of mental health assessments for autistic people are no different from those for anyone else: establishing good rapport, empathic understanding of the person's life experiences across contexts, gathering sufficient collateral information from multiple sources, utilizing measurement-based care when appropriate, carefully considering safety and treating diagnostic/case formulation as an iterative hypothesis-testing process. Meanwhile, clinicians need to appreciate how the autistic person's unique health history (for example, medical conditions and/or other developmental disabilities) and information processing patterns (for example, intellectual and language levels and communication preferences) influence how they perceive, experience and express mental health issues. The 'Autistic SPACE' provides a useful framework for clinical care, emphasizing core autistic needs (sensory needs, predictability, acceptance, communication and empathy) and the importance of physical, processing and emotional space¹⁸⁹. Clinicians should strive to overcome barriers and biases due to differences in neurotype and other socio-demographics in interpreting the autistic person's behaviours and subjective experiences to 'meet people where they are at'-a process fully compatible with the practice of multicultural therapy²⁶⁵. Overcoming the double empathy problem (especially when the clinician is non-autistic) requires mutual efforts, and clinicians are well positioned and trained to adjust their own communication and mentalizing to understand the autistic person's experiences. Autistic individuals find the clinicians' acceptance and understanding to be most critical for successful clinical encounters²⁶⁶. Being familiar with the autistic person's thinking and communication profiles across development helps to capture mental health presentations that are not apparent (for example, attenuated manifestations due to alexithymia or intellectual and/or communication difficulties) and/or are unconventional (for example, autism-specific anxiety symptoms), reduces misinterpretation or mislabelling of behaviours (for example, distress-related behaviour labelled as oppositional or 'disruptive', autistic language features labelled as psychotic, and/or emotion dysregulation labelled as manic), and offers critical reflections on whether certain diagnoses are applicable or helpful (for example, personality disorders)^{267,268}.

emotion regulation and/or consequences of reinforcement, much care should be taken to understand the stress-coping, transactional nature of such behaviours⁷³ and how they signal medical-dental, communication, sameness, sensory and social needs and mismatch⁷¹. Callousunemotional traits (Box 6) are distinct from autistic characteristics⁷⁴ but seem more prevalent in autistic (~22%) than non-autistic youth (~5%) in community-based samples, with similar associations with peerconduct problems and fear-face processing in both populations⁷⁵. Oppositional defiant disorder, when diagnosed in autistic children, shows the same associations as in non-autistic children between the tripartite domains (Box 6) and respective mental health correlates⁷⁶. The concept of pathological/extreme demand avoidance (Box 6) has gained attention to explain and practically support some autistic children and youth, but its nosological boundary and relations to oppositional defiant disorder and anxiety, whether a phenotypic profile of autism or the pathologization of anxiety-driven distress behaviours, remain unresolved and heavily debated⁷⁷⁻⁸⁰.

Mental health assessments for autistic people, part B

Understanding the autistic person's baseline ('normal') and most adapted ('best') mental health experiences, presentations, functioning and well-being status and the contexts of such is fundamental for depicting the person's evolving mental health trajectory. When resources allow and with the autistic person's consent, observing, participating and working with the person in their daily contexts (for example, via home or school visits, or during community or vocational activities) offer ecologically valid information that is complementary to clinic/office-based assessments. Synthesizing discrepancies (if present) among collateral reports and the autistic person's subjective experiences should consider the varying contextual demands, expectations and person–environment fit²⁶⁹. Despite the value of measurement-based care in general²⁷⁰, instrument validity in autistic individuals (especially in those with intellectual disabilities) is often insufficient, and the quantitative responses should be interpreted with caution, especially when autism-specific mental health experiences and manifestations are not captured by general measures. Furthermore, ambiguous, confusing (for example, using metaphoric language) and/or imprecise question wording and response options perceived by the autistic person impede response accuracy. Self-harm and suicide risks and the significant contributing roles of psychiatric illnesses should be evaluated¹⁰⁷, and a tailored safety plan should be created if indicated²⁷¹. For the iterative formulations, the co-occurrence of other neurodevelopmental and physical health conditions and their downstream impacts should be considered. Harmonizing conventional categorical diagnoses with a transdiagnostic lens helps develop practical and feasible support strategies that consider the interplay of biological factors, autistic cognitive features, adverse life experiences and socio-ecology for the unique autistic person (Fig. 1). Tracking mental health in response to context-focused interventions is particularly telling for the iterative formulations.

Depression

Depression is highly prevalent in autistic individuals overall, particularly in adults and female individuals^{13,19}, although with much unknown in those with intellectual disabilities aside from increased prevalence^{57,81}. All criteria-based features apply to autistic people, but there can be unique presentations such as increased irritability, change of focused interests (for example, reduced engagement, increased intensity or shift to negative-dark contents), increased repetitive behaviours and insistence on sameness, change of sensory experiences, decline in adaptive functions, and regressive behaviours^{57,82,83}. Emerging psychometric work has shown that insomnia and restlessness might be central to depression in autistic children, and depressive symptoms are closely clustered with anxiety symptoms but separated from autistic characteristics⁸⁴. Conventional depression measures (for example, the Beck Depression Inventory-II and the Patient Health Questionnaire-9) can be used for autistic youth and adults who can self-report^{85,86}, but new development to improve sensitivity and specificity is needed. Emotional processing, cognitive style, and intellectual and communication abilities can influence how depressive symptoms are perceived and expressed by the autistic person and interpreted by others.

Autistic individuals overall seem more likely to experience subthreshold psychotic symptoms than non-autistic individuals⁸⁷. Schizophrenia spectrum disorder is more frequent in autistic people, especially those with intellectual disabilities, with a similar onset age range compared with non-autistic people^{13,15,18}. Small-scale studies suggest that psychotic presentations in autistic people are more likely to be atypical⁸⁸; in those with intellectual disabilities, core positive symptoms are still key in diagnosing schizophrenia clinically⁸⁹. Diagnostic overshadowing occurs in both directions. Psychotic symptoms can be under-recognized when being misinterpreted as autistic features (for example, disorganization viewed as idiosyncratic thought/speech or behavioural responses to perceptual changes viewed as representing rich fantasy), or autistic characteristics (especially when one is in distress and/or when seen by a clinician who is not familiar with this autistic person) can be misinterpreted as psychotic symptoms (for example, autistic thinking-communication styles viewed as disorganization or positive symptoms, autistic social communication viewed as negative symptoms, or concrete-literal answers to imprecise questions viewed as indicating positive symptoms)^{58,90,91}. In a large clinical cohort of youth who had a clinical-high-risk-for-psychosis profile, comparing autistic youth with non-autistic youth, autistic youth showed more social and social-cognitive difficulties but similar levels of psychotic symptoms, with equivalent conversion-to-psychosis rates (17-18%)⁹². Understanding the autistic person's developmental history, stress-response styles, and the onset pattern and course of possibly psychotic symptoms against their personal baseline is critical.

Bipolar disorders

Clinically, two-way diagnostic overshadowing can occur regarding emotion dysregulation and irritability (especially associated with environment-routine changes) in autism versus pervasive mood fluctuations in bipolar disorders, autistic focused interests versus increased goal-directed behaviours in bipolar disorders, and autistic thinking– communication versus grandiosity and flight of idea in bipolar disorders; developmental history, onset and course (especially the episodic and cyclic patterns of bipolar disorders) are key to differentiation^{59,90,93}. Manic/mixed symptoms in autistic people can manifest primarily by increased irritability and dysphoria, anxiety, stereotypy, aggression, distractibility and hyperactivity^{59,90,94} more so than euphoria⁹³. Abundant psychotic symptoms may increase the risk of a misdiagnosis of schizophrenia⁹³. Autistic compared with non-autistic youth with bipolar disorders seemed more likely to have ADHD, OCD and an earlier onset of mood symptoms^{15,94}.

Sleep problems

Autistic individuals experience various sleep problems including insomnia (for example, difficulties settling and sleep hygiene problems), circadian rhythm sleep-wake disorders (for example, advanced, delayed or irregular phases), increased sleep-onset latency, reduced total sleep time, increased wake after sleep onset, poor sleep efficiency, increased proportion of shallow sleep, parasomnias (for example, sleep walking, sleep terrors and nightmares), sleep enuresis, and obstructive sleep apnoea^{60,95}. These sleep problems substantially influence and are influenced by mental health, daytime functioning and quality of life, particularly externalizing and internalizing symptoms as well as executive functioning^{60,96}.

Feeding and eating problems

Autistic young people frequently experience food selectivity and sensory sensitivity (for example, to food texture) that could fit in an avoidant/restrictive food intake disorder²², ritualistic eating behaviours (for example, specific food presentation), pica, or increased concerns regarding weight, shape or body image (especially in autistic girls and

women)²¹. More autistic traits, diagnosed autism and potentially undiagnosed autism have also been noted in individuals with eating disorders, especially anorexia nervosa^{20,23}. These co-occurrences might imply a shared neurodevelopmental background with sex-modulated and gender-modulated psychopathological trajectories²³ and highlight the health needs of autistic people experiencing feeding and eating problems, including weight (for example, underweight or overweight); nutritional (for example, lack of certain micronutrients), gastrointestinal (for example, constipation) and growth concerns; and daily and social well-being²².

Trauma and stress-related experiences

Autistic individuals are vulnerable to victimization and adverse childhood experiences^{24,97}, with pooled prevalence rates of 47% for bullying, 13% for cyberbullying, 16% for child abuse, 40% for sexual victimization and 84% for any forms of victimization²⁴. Autistic children with intellectual disabilities are particularly vulnerable to maltreatment⁹⁸. Those having more adverse experiences suffer from greater mental health problems (including suicidality) and lower academic functioning⁹⁷. Growing research with autistic adults who can self-report (for example, via online survey) suggests they might experience a broader range of traumatic events beyond conventional kinds⁹⁹, and there are increased rates of post-traumatic stress disorder (PTSD) and PTSD symptoms (particularly related to social stressors and in those with intersecting minoritized race-ethnicity and gender identities) linked to poorer mental health, functional impairment^{100,101} and suicide risks¹⁰². Given the neurotypical-majority social contexts, autistic people might be more vulnerable to developmental trauma¹⁰³ and complex PTSD¹⁰⁴, but more research is needed.

Substance use

Autistic people are perceived to have reduced risks for substance use disorders, although depression, anxiety and ADHD might increase their vulnerability²⁸. Population-based data suggest substance use problems are increasing for autistic people¹⁰⁵. They are associated with increased mortality risks²⁹ and are prevalent especially in those with ADHD, anxiety and impulse-control disorders, with mixed findings in relation to intellectual disabilities^{29,105,106}. Family history of substance use disorder is a consistent risk factor, as well as the autistic person's perceived social difficulties and psychological distress²⁶. Reasons prompting substance use (revealed by self-reporting adults in online surveys) might be different: autistic compared with non-autistic individuals were more likely to use substances for managing behaviour (for example, sensory overload) or mental health concerns²⁷.

Suicide-related behaviours

Autistic individuals have over threefold greater odds than non-autistic individuals of experiencing suicidal ideation, suicide attempt or suicide death³², with the pooled prevalence of suicidal behaviour at 24.3% (95% confidence interval, 18.9–29.6%) in those without intellectual disabilities³⁵. In autistic youth, the meta-analytic prevalence rates are 25.2% (18.2–33.8%) for suicidal ideation, 8.3% (4.3–15.6%) for self-harm or suicide attempts, and 0.2% (0.05–0.52%) for suicide death³⁴. Psychiatric illnesses and interpersonal factors (for example, loneliness, perceived burden and thwarted belonging) might be important proximal suicide risk factors for autistic people^{33,107}.

Catatonia

Catatonia (Box 6) is historically associated with psychosis, typically with an acute onset and a waxing–waning course. It is also associated with autism^{108,109} and can occur on top of the autism–psychosis co-occurrence³⁰. About 10% of autistic individuals have experienced catatonia with an onset age commonly in late adolescence, highly associated with anxiety, OCD symptoms, Tourette syndrome^{31,110}, and other co-occurring neurodevelopmental and paediatric neurodegenerative

Glossary of terminology

Autistic burnout: a state marked by mental-physical exhaustion, interpersonal withdrawal, reduced functioning, executive function difficulties, and increased manifestation of autistic traits and/or reduced capacity to camouflage^{113,114}.

Autistic inertia: difficulties starting and stopping activities, with internal experiences of a tendency to maintain one state, difficulty finding the first step, lack of voluntary control and disconnection between intention and action¹¹⁵.

Behaviour activation: side effects of psychotropic medications including increased activity, impulsivity, insomnia or disinhibition without manic symptoms.

Callous-unemotional traits: a long-standing pattern characterized by low empathy, low guilt or remorse, shallow or deficient affect, and low concern about own actions and performances¹⁰⁹.

Camouflage/camouflaging: strategies neurodivergent people use to model neurotypical behaviours, to minimize the visibility of differences, facilitate social connections and adaptation, and ameliorate fit into society¹⁴³.

Catatonia: a syndrome of primarily psychomotor disturbances, characterized by multiple symptoms of decreased (for example, mutism, negativism or ambitendency), increased (for example, extreme hyperactivity or agitation for no reason with non-purposeful movements) or abnormal (for example, posturing, stereotypy, mannerism, echophenomena, verbigeration, catalepsy or waxy flexibility) psychomotor activities¹⁰⁸.

Central sensitivity syndromes: a syndrome including chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, chronic headache and temporomandibular joint disorder²⁷².

Double empathy problem: a bidirectional breakdown in the mutuality and communication of meaning between autistic and neurotypical individuals, caused by dispositional differences relating to experiences and representations of the social world¹⁴⁰.

Impression management: a human tendency to foster favourable impressions of oneself in others during social interactions to achieve interpersonal or pragmatic goals¹⁴³.

Meltdown: feelings of being entirely overwhelmed by information, senses, and social and emotional stress, extreme emotions, a lack of control and cumulative stress^{61,116}.

Neurotype: a group of individuals whose neurodevelopment and information processing styles are sufficiently similar to be considered a type²⁶⁴.

Pathological/extreme demand avoidance: a behavioural profile characterized by (1) resisting and avoiding the ordinary demands of life, (2) using social strategies as part of avoidance (for example, distracting or giving excuses), (3) appearing sociable but lacking some understanding, (4) experiencing excessive mood swings and impulsivity, (5) appearing comfortable in role play and pretence, and (6) displaying 'obsessive behaviour' that is often focused on other people⁷⁹; the nosology remains unresolved and heavily debated⁷⁷⁻⁸⁰.

Tripartite domains of oppositional defiant disorder: (1) angry and irritable symptoms, (2) argumentative and defiant behaviour, and (3) vindictiveness.

Universal design: stemming from architecture and then education, referring to strategies planned for diversity, designed to be accessible and engaging for as many people as possible.



Fig. 1 | **A** framework to understand mental health challenges faced by autistic **people. a**, Key plausible contributors of mental health challenges in autistic people could be conceptualized into four themes, including shared biological predispositions (green), autism-related cognitive features (yellow), adverse life experiences (grey) and the broader social–contextual determinants (red). **b**, Plausible contributing (although neither sufficient nor necessary) mechanisms for mental health outcomes (blue circles (the most common outcomes) and ellipses (common outcomes)) are denoted by coloured solid arrows reflecting the four themes. The dotted black arrows indicate potential cascading effects on downstream mental health challenges following precedent conditions^{15,127}.

These relations are mostly speculative rather than definitive, as evidence in autistic people is still developing. Other neurodevelopmental conditions (NDCs) and physical health conditions (PHCs) (purple circles) commonly co-occur with autism and are important to consider in understanding autistic people's mental health. Although research has been limited so far, resilience mechanisms that counteract, attenuate or modify the contributing risks and/or that interrupt the cascading effects should be a focus of future research. Such mechanisms could be leveraged as actionable processes for mental health promotion, prevention or intervention tailored to autistic people.

disabilities¹¹¹. Catatonia in autistic individuals is often more gradual and characterized by early signs of increased motor–speech slowness, marked hesitation during movements alongside initiation difficulties, reliance on others' verbal or physical prompts, speech reduction and mutism, mental 'freezing' or being stuck in a loop, 'shutdown' in overwhelming situations, and agitation and self-injurious behaviours uninfluenced by external stimuli; classical catatonic symptoms (for example, waxy flexibility, posturing or stupor) are relatively rare^{31,112}. Catatonia should be assessed for any autistic individual with marked deterioration in movement, speech and function from their personalized baseline^{110–112}, especially on red flags that often got confounded with baseline neurodevelopmental characteristics: worsening of stereotypies, new-onset refusal to eat, new-onset or worsening incontinence, regression in daily living activities, onset or exacerbation of self-injurious behaviours, and purposeless agitation¹¹¹.

Burnout, inertia, meltdown and shutdown

Autistic burnout (that is, intense mental–physical exhaustion, preceded by camouflaging autistic traits, interpersonal interactions, cognitive overload, sensory environments and/or additional stressors or changes^{113,114}), autistic inertia (that is, difficulty stopping, starting and changing tasks¹¹⁵), meltdown (that is, uncontrollable, explosive responses to overwhelming situations^{61,16}) and shutdown (that is, withdrawing from the surroundings, with emotional pain⁶¹) are increasingly recognized by autistic people⁶¹ (Box 6). Studies need to operationalize these experiences, understand their relations to established constructs (for example, depression, anxiety and stress responses), and investigate their short-term and long-term consequences (including possibilities leading to catatonia). Autistic people across ages have voiced that correctly understanding these states, addressing triggers, appreciating their personalized strategies to regain control, carefully using prompts and environmental scaffolding are helpful^{61,115}.

Gender diversity and gender dysphoria

The co-existence of gender diversity and neurodivergence is increasingly recognized, especially the increased autism diagnoses in trans and gender-diverse (TGD) populations¹¹⁷, and increased gender identity diversity in autistic individuals across ages^{118,119}. Clinically, increased rates of gender dysphoria in autistic individuals¹²⁰ and the unique gender-related experiences at this intersection¹²¹ highlight the needs of tailored gender care^{62,122}. TGD youth often experience anxiety, depression, disordered eating and suicidality, which can be understood in a minority stress framework¹²³. Autistic TGD youth experience multiply increased mental health challenges associated not only with stigmatization but also executive function and social difficulties^{124,125}, highlighting the need for personalized mental health support¹²⁶.

Origins of mental health challenges

Alongside unique aetiological pathways for specific illnesses^{25,55,58,127}, there are four overarching themes influencing autistic people's mental health (Fig. 1).

Social-contextual determinants

The inequitable distribution of resources and opportunities results in social gradients that increase an individual's mental health risks and create barriers to care¹²⁸. These social determinants span demographic (for

example, ethnicity and gender), economic (for example, employment, food and housing security), neighbourhood (for example, the built environment), environmental event (for example, natural hazards) and socio-cultural domains (for example, education and discrimination)¹²⁹. Autistic individuals and their families experience intersectional inequities, including disparities related to race-ethnicity¹³⁰⁻¹³² and sexual and gender diversity¹³³ in access to diagnosis, care and resources. For example, transition-age autistic youth in low-income households or who are racial-ethnic minorities are less likely to engage with transition planning, postsecondary education, competitive employment, independent living, social activities and health-care transition services than their racial-ethnic-majority and higher-income autistic peers¹³⁴. Autistic people are particularly vulnerable to negative social determinants. In the USA, households of autistic children, especially those with intellectual disabilities, are more likely to be food insecure than households of children without disabilities¹³⁵. In the UK, less than one third of autistic adults are employed, lower than the average employment rates of all disabled people¹³⁶. Autistic individuals might be over-represented in people experiencing homelessness^{137,138}. Current systems of care often include legacy programmes that exclude some autistic people (for example, using an intelligence quotient cut-off for inclusion), lack integration (for example, across mental health, paediatric and autism services) or have sparse services (for example, in low-resource settings)¹, resulting in fragmented support and substantial access barriers for individuals and their families, especially when an autistic person enters adulthood.

Uniquely, in neurotypical-majority contexts, autistic people's differences are often salient and viewed as impairments; they might receive well-meaning supports that can be potentially partly harmful¹³⁹. Autistic people are also often misunderstood by non-autistic people, as explained by the double empathy problem¹⁴⁰ (Box 6). Autistic people and their families often experience stigma¹⁴¹ and become increasingly isolated from society¹⁴². The pervasive expectation for autistic people to change aggravates their perceived pressure for impression management (Box 6), and for those who are able and willing to, such efforts can come with psychological tolls such as inauthenticity, identity confusion, anxiety and stress/burnout¹¹⁴, theoretically hindering mental health¹⁴³. However, these contextual influences are not unmalleable. Non-autistic people's attitudes towards autistic people are associated with their knowledge of autism and previous contacts with autistic people, highlighting the importance of better public knowledge of autism and high-quality collaborative contacts¹⁴⁴. Reasonable environmental adjustments to enhance person-environment fit improve autistic people's functioning and reduce the overwhelming stress that they endure to accommodate neurotypical environments¹¹.

Adverse life experiences

Adverse life events can serve distal (for example, adverse childhood experiences) and proximal (for example, bully victimization) causal roles for mental health challenges. In autistic children, exposure to family-level stressful life events predicted later internalizing symptoms in those with cognitive flexibility difficulties (but not those without such difficulties), whereas mental health problems did not predict future exposure to family-level stressful life events¹⁴⁵. Bully victimization is causally linked to suicide risk in autistic youth³⁴, especially when they experience multiple types of victimization and particularly teacher harassment146,147. Life experiences also serve mediating roles. Peer problems at ten years old partially mediate the longitudinal association between autistic children's early-childhood irritability and adolescence depressive symptoms⁵¹. In the general population, longitudinal data show that bully victimization substantially mediates the associations between childhood autistic traits and adolescence psychotic-like experiences¹⁴⁸ and depression¹⁴⁹. Negative life experiences partially explain autistic adults' heightened anxiety and depression compared with

non-autistic adults¹⁵⁰. Studies on the causal roles of traumatic events in autistic people's mental health are in their infancy^{25,151}. Considering the well-established detrimental effects of developmental trauma in general¹⁰³ and autistic individuals' vulnerability to traumatic experiences (for example, due to social naivete)¹⁰¹, autistic people are plausibly prone to experiencing the deleterious mental health consequences of traumatic events²⁵. Inadequate medical and mental health care can further aggravate mental health challenges^{152,153}.

Cognitive features

Autistic cognitive features might moderate (when one is exposed to contextual-experiential risks) and mediate mental health outcomes. These features intertwined, have complex developmental relations¹²⁷ and show large variability among autistic individuals¹⁵⁴. In the presence of intellectual disabilities, cognitive limitations might hinder one's coping with stressors, contributing to heightened mental health risks^{39,155}. Intellectual abilities also significantly influence executive function and social cognition¹⁵⁶. In autistic youth, executive function difficulty is the only cognitive feature that shows overarching negative impacts across psychiatric symptoms (especially anxiety) and functional levels^{156,157}. Specifically, reduced cognitive flexibility is strongly associated with increased internalizing (meta-analytic Pearson's r = 0.39) and externalizing symptoms (r = 0.48) in autistic youth¹⁵⁸. Cognitive flexibility also moderates the impact of family-level stressful life events on autistic children's mental health¹⁴⁵. Mid-childhood executive function significantly mediates the associations between early-childhood autistic features and early-adolescence externalizing behaviour, academic functioning and adaptive functioning in autistic youth¹⁵⁹. Executive function difficulty is also an important health-care barrier for autistic adults¹⁶⁰.

Self/emotion regulation difficulties are associated with meltdown, self-injury, aggression, negative emotions, rumination, psychiatric diagnoses and poorer social outcomes in autistic individuals^{56,73}. Some difficulties are associated with habitual strategies that are typically considered maladaptive (for example, negative rumination, suppression and avoidance) and less use of adaptive strategies (for example, cognitive reappraisal, problem solving and acceptance)⁵⁶. Self/ emotion regulation challenges can stem from autistic sensorimotor and cognitive features during stress coping⁷³. The need for sameness shares early developmental origins with anxiety in autistic children and signposts future anxiety¹⁶¹. Such certainty-seeking can explain an autistic person's experiences of being 'stuck' or 'freezing' in uncertain situations¹⁶². Atypical fear conditioning, modulated by neurobiology¹⁶³, might underlie autistic people's vulnerability to anxiety and traumatic events²⁵. Sensory atypicality (especially hyper-responsivity) correlates with broad-range psychiatric symptoms $^{\rm 164}$ and interacts with certainty-seeking, alexithymia, sleep and ADHD features to potentiate anxiety^{165,166}, increasing vulnerability to depression¹⁵⁶. Rumination might precipitate and maintain depression, especially when focusing on guilty feelings or self-criticism¹⁶⁷.

Some autistic individuals' difficulties with communication, social cognition, social coping and self-advocacy in neurotypical-majority situations put them at great risks of victimization^{24,168}, chronic stress and consequently depression⁵⁷, mediated by quality of social support and feelings of loneliness¹⁶⁹. High social motivation, when juxtaposed with social-communication difficulties, might increase depression risks¹⁷⁰. For autistic people who strive to fit in to the neurotypical majority, the neurotype mismatch and taxing cognitive demands during social interactions potentiate distress¹⁴³ (Box 6). Such chronic distress and trauma vulnerability, alongside acute stressful life events, not only could increase an autistic person's risk for severe mental illnesses such as schizophrenia spectrum disorders (especially in the presence of genetic predispositions)¹⁷¹ but also might prompt self-medication via substances²⁷, which further increases the vulnerability to substance use, mood and psychotic disorders.

Shared genetic and early environmental predispositions

Many rare and common genetic variants exert downstream effects of multiply co-occurring neurodevelopmental and psychiatric conditions, in the context of polygenicity and phenotypic variability¹⁷². The somatic pleiotropy of autism-associated genetic variants increases co-occurring physical health challenges (for example, epilepsy, obesity, and endocrine, feeding and gastrointestinal problems) and downstream mental health impacts¹⁷³. Neurodevelopmental conditions (including autism) and disruptive/impulse-control disorders have strong genetic overlap (family-based genetic correlation, 0.62)¹⁷⁴. Rare variants can contribute to autism and co-occurring neurodevelopmental conditions followed by severe mental illnesses later in life; examples include 22q11.2 deletion, 7q11.23 duplication, 17p11.2 duplication, 3q29 deletion, and other autism-associated protein-truncating or missense variants on the co-occurrences of autism, intellectual disabilities and schizophrenia^{58,172,175}. Common variants show small-to-moderate positive genetic correlations between autism and ADHD as well as major depression, nicotine and cannabis use, schizophrenia, and bipolar disorders^{176–178}. Early environmental factors such as toxic chemical exposure, maternal immune activation and endocrinological alterations have broad neurodevelopmental impacts, leading to the co-occurrence of autism and other neurodevelopmental disabilities^{179,180}, affecting later mental health. Prenatal and postnatal events, especially preterm birth, hypoxia at birth and fetal alcohol exposure, are associated with distinct patterns of co-occurrence of physical, neurodevelopmental and psychiatric conditions in autistic individuals, reflecting the multifinality of these exposures (and/or their genetic underpinnings)¹⁸¹. As an extreme example, extended early institutional deprivation results in the 'quasi-autism' childhood phenotype182, which is longitudinally associated with heightened mental health problems across domains and functional difficulties in adulthood, independent of other deprivation-specific neurodevelopmental problems¹⁸³.

Resilience to mental health challenges

Many autistic individuals demonstrate resilience and do not experience ill mental health¹⁸⁴. In a Canadian autistic cohort, by ten years old, 36% of these individuals had minimal (*T*-score \leq 50) internalizing symptoms, and 49% had minimal externalizing symptoms¹⁸⁵; in a UK cohort, by 13–17 years old, 29% did not meet criteria for any co-occurring DSM-5 disorders⁴⁹. Mechanisms for meaningful outcomes¹⁸⁶ and mental health resilience in some autistic people might be leveraged to enhance other autistic people's well-being¹⁸⁴. Candidates awaiting investigation include ubiquitous individual-level (for example, self-efficacy) or socio-ecological (for example, close friends and effective schools) factors, as well as autistic strengths¹⁸⁷ and autism-related socio-ecology¹⁸⁸.

Support and intervention

A formulation that is developmentally oriented and considers the person's unique autistic background, intellectual and communication abilities, contextual–experiential determinants, and person–environment fit is key to personalized support and advocacy for environmental adjustments^{1,11} and will guide autism-informed mental health care¹⁸⁹ (Boxes 4 and 5). Such a formulation is a space where a neurodivergence-informed paradigm¹⁹⁰ can be harmonized with prevailing clinical stances such as humanistic psychology⁹, the bioecological model¹⁹¹ and the bio-psycho-social formulation¹⁰. To be meaningful and practical in addressing real-life needs, this formulation should be developed collaboratively between the clinician(s), the autistic person and relevant support individuals (for example, families). It should aim at improving quality of life, especially via reinforcing the autistic individual's self-knowledge and self-determination¹⁹².

Attending to how the autistic background, alongside one's intellectual and communication abilities, modifies mental health presentations improves assessment and scaffolds an empathic understanding of the meanings and impacts of these difficulties (Boxes 4 and 5). What are perceived as increased irritability and labelled as 'challenging/ problem behaviours', as well as insomnia, should always flag attention to underlying physical health problems (often alongside communication difficulties), contextual changes and psychosocial stressors (even seemingly minor from a non-autistic person's perspective), and conditioned behaviours shaped by the environment^{71,193}. Addressing social-contextual determinants and implementing environmental adjustments reduce mental health strains in autistic people; examples include preventing bullying to reduce suicide risks³⁴, incorporating family in cognitive behavioural therapy to cope with anxiety¹⁹⁴ and pedagogy that follows universal design (Box 6) to help manage stress in educational settings¹⁹⁵. Although clinical trials on context-focused approaches to improve autistic people's mental health are still sparse, these approaches are conceptually congruent with adapted interventions and practically feasible¹⁹⁶.

Importantly, clinicians should also dedicate efforts to supporting families and loved ones of the autistic person (with consent and as developmentally and socio-culturally appropriate). Across the lifespan, the home is the immediate socio-ecological context that provides an important lever for mental health promotion¹¹. Caregivers (for example, parents) of an autistic child, adolescent or dependent adult are often vulnerable to stigmatization¹⁴¹, parenting stress and mental health challenges, which tend to correlate with the autistic person's mental health¹⁹⁷⁻¹⁹⁹. For autistic individuals in romantic relationships, their partners also navigate ways to support them²⁰⁰. Supporting family/relationship well-being (for example, via mindfulness-based stress reduction, positive psychology, problem-solving or family-systems approaches) is a dynamic and iterative process^{11,201}. It is nevertheless integral to reducing misunderstanding and strains in these relationships, to shape a 'secure base' for an autistic person to grow and thrive.

Current clinical guidance

Mental health interventions for autistic people, pharmacological and non-pharmacological alike, should follow the best available evidence in the general population in the absence of evidence specific to autistic people²⁰², particularly for treating severe mental illnesses such as schizophrenia²⁰³, bipolar disorders²⁰⁴ and major depressive disorder^{205,206}. General preventative factors such as trusted social connections²⁰⁷ and therapeutic factors such as clinician's empathic understanding, access to community, safety, self-care, sense of control, exercise, balanced nutrition and sleep hygiene⁸³ all apply to autistic individuals. Tools designed to support autistic individuals' physical and mental health literacy can facilitate awareness, communication and access to care (Supplementary Table 2). Personalization should consider one's autistic, intellectual and communication characteristics and medical needs. For certain domains, there is emerging autism-specific guidance. Figure 2 summarizes adaptation principles for psychotherapeutic approaches.

For ADHD symptoms, educational-behavioural support and environmental modification should be implemented first²⁰⁸, and if substantial impairments remain, medication treatment should follow meta-analysis-guided recommendations: methylphenidate as the first choice, followed by second-line options among atomoxetine, alpha-2 agonists (guanfacine or clonidine) or amphetamine²⁰⁹. For sleep problems, besides improving sleep hygiene, prolonged-release melatonin alone or combined with cognitive behavioural therapy shows the strongest evidence of benefit^{210,211}. For mood and anxiety symptoms, autism-informed adapted interventions^{196,212} result in moderate reductions of anxiety in children (especially when incorporating family-based approaches) and small reductions of depressive symptoms in adults¹⁹⁴; social skills interventions also result in small reductions of anxiety across ages and moderate reductions of depressive symptoms in children¹⁹⁴. Mindfulness-based intervention might reduce anxiety and depression in autistic adults with mental health diagnoses²⁰². Long-term effects of these interventions are still unclear, and most trials have high risks of bias^{202,213}. Unfortunately, there is a lack of



Fig. 2|**Principles of adapted psychotherapeutic interventions for autistic people.** Key adaptation principles used by current evidence-based, evidenceinformed or developing psychotherapeutic interventions for autistic people are summarized^{196,212,233,238,239}. They are illustrated as general principles (left) and specific adjustment approaches (middle) that can be useful for addressing accessibility barriers associated with the unique cognitive features of autistic individuals (right).

adaptation for those with intellectual disabilities and a lack of inclusion of autistic young people with intellectual disabilities in clinical trials²¹⁴. Although antidepressants are clinically used for anxiety, depression and OCD in autistic individuals, clinical trial findings are inconsistent, and no clear group-level benefits have yet been observed²¹⁵; if clinically indicated for an autistic person, prescribers should follow the principle of 'start low, go slow', and be mindful of behaviour activation adverse effects (Box 6) that might appear in autistic individuals²¹⁶. Mood stabilizers, especially lithium, are recommended based on expert opinions as the first treatment options for manic/mixed episode and maintenance treatment for bipolar disorders in autistic individuals²¹⁷.

For severe irritability and self/emotion regulation difficulties, when other contributors are ruled out and/or when clinically indicated due to acuity and safety concerns, medications should be considered⁷¹. Aripiprazole and risperidone show the most consistent efficacy in reducing irritability and emotion dysregulation; clinical decision-making must consider short-term (for example, sedation and akathisia) and long-term (for example, weight gain and metabolic syndrome) adverse effects^{218,219}. ADHD medications have similar benefits for reducing irritability and emotion dysregulation, although the evidence base for this approach is smaller²¹⁸. Even thinner evidence exists for *N*-acetylcysteine and clonidine, but they are reasonable options on the basis of preferred safety profile (the former) and long-standing clinical-use experiences (the latter)^{L71,216}.

For catatonia, treatment relies on a personalized causal formulation (considering individual vulnerability-sensitivity and socio-ecological factors) to inform prevention of overload, the removal

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of potential medication causes (for example, dopamine antagonists), one-to-one support and prompts to keep the autistic person responsive and active (for example, by levering focused interests)¹¹², and measured use of benzodiazepines (for example, lorazepam; despite established efficacy in neurotypical people, responses are inconsistent and less robust in autistic individuals) and electroconvulsive therapy²²⁰.

There are initial clinical recommendations to tailor gender care to autistic people who need it^{62,121,122}. Autism-informed considerations should be harmonized with the evolving transgender health-care guidelines²²¹.

Ongoing developments

Systems-level efforts to integrate mental health and autism services and ensure smooth transitions across life stages are ongoing²²²⁻²²⁵. Autism-informed measurement-based care is developing²²⁶. Context-focused support for employment²²⁷, education¹⁹⁵, peer environment^{228,229} and family²³⁰ to optimize person–environment fit¹¹ might collaterally reduce mental health difficulties, because these approaches reduce contextual-experiential risks and reinforce resilience¹⁸⁴. There are ongoing efforts in adapting psychotherapeutic models to be neurodiversity-affirming^{231,232} and to better suit autistic people^{196,212,233}, including modifying-integrating cognitive behavioural therapy, mindfulness, mind–body practice, and dialectical behaviour therapy components to address self/emotion regulation difficulties and modified acceptance and commitment therapy to reduce stress in autistic individuals without intellectual disabilities. Whether established brain stimulation interventions (for example, electroconvulsive therapy and transcranial magnetic stimulation for mood disorders, schizophrenia, substance use disorders, PTSD and OCD²³⁴) and new avenues (for example, intravenous racemic ketamine for suicidality²³⁵ or psychedelic therapy with psychological support for depression²³⁶) work similarly in autistic individuals remains to be robustly investigated. Developing socio-culturally safe, trauma-informed, tailored and scalable mental health support for equity-deserving subpopulations is sorely needed, especially for those with extensive support needs¹.

Concluding remarks

Tailored and empathic support for autistic people's mental health requires a neurodivergence-informed, holistic approach that considers their lived experiences, unique socio-ecology, family/relationship well-being, and cognitive, neurodevelopmental and health backgrounds. Just as the evidence in autism intervention science overall is still developing^{11,237}, evidence for and ways to personalize effective mental health interventions remain to be accumulated. Mental health challenges should not be inevitable consequences of being autistic. We need more context-focused, resilience-reinforcing pre-emptive interventions to promote mental health and create societies where people across neurotypes can thrive.

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